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Table of Contents:

Vol 12 No. 4, December 2021 - issue cover
(453) The effect of motion games on improving the psychomotor and intellectual performance of children with autism spectrum disorder and intellectual disabilities - MOCANU George-Dănuț, GAVRILA Udreă Maria Balneo and PRM Research Journal. 2021;12(4):289-300 Full Text DOI 10.12680/balneo.2021.453
(454) Complex respiratory and motor rehabilitation program in a patient with post-pulmonary tuberculosis conditions and multiple sequelae after SARS-CoV-2 infection: case report - DAIA Cristina, IONESCU Anca, IONESCU Elena Valentina, ILIESCU Mădălina Gabriela, STANCIU Liliana Elena, CAMBREA Simona Claudia, ILIESCU Dan Marcel, ARGHIR Oana Cristina, GEORGEANU Vlad, VOINEA Felix, BAZ Radu, PAZARA Loredana, ONOSE Gelu Balneo and PRM Research Journal. 2021;12(4):301-305 Full Text DOI 10.12680/balneo.2021.454
(455) The profile of patients with atrial fibrillation scheduled for cardioversion or catheter ablation hospitalized in a Romanian rehabilitation hospital - BLAGA Sorin Nicolae, TODOR Nicolae, ZDRENGHEA Dumitru, ROȘU Radu, CISMARU Gabriel, PUIU Mihai, GUȘETU Gabriel, POP Dana Balneo and PRM Research Journal. 2021;12(4):306-313 Full Text DOI 10.12680/balneo.2021.455
(456) Improving functional and motor capacity through means/resources and methods specific to aquatic activities - CONDURECHE Iustina, CONFEDERAT Luminița, ROTARIU Mariana, TURNEA Marius Balneo and PRM Research Journal. 2021;12(4):314-317 Full Text DOI 10.12680/balneo.2021.456
(457) The importance of association between sexsteroids deficiency, reduction of bone mineral density and falling risk in men with implications in medical rehabilitation - POPA Florina Ligia, BOICEAN Loredana Camelia, ILIESCU Madalina Gabriela, STANCIU Mihaela Balneo and PRM Research Journal. 2021;12(4):318-322 Full Text DOI 10.12680/balneo.2021.457
(458) Effects of low laser level therapy in rehabilitation of patients with COVID19 pneumonia - CIORTEA Viorela Mihaela, ILIESCU Mădălina Iliescu, BLENDEA Eliza, MOTOASCA Irina, BORDA Ileana Monica, CIUBEAN Alina Deniza, UNGUR Rodica Ana, PINTEA Alina Liliana, POPA Florina Ligia, IRSAY Laszlo Balneo and PRM Research Journal. 2021;12(4):323-326 Full Text DOI 10.12680/balneo.2021.458
(459) Cost-effectiveness of home non-invasive ventilation in COPD group GOLD D patients - BERES Enikő, BABES Katalin, BERES Zsolt-Levente, DAINA Lucia Georgeta, DAINA Cristian Marius, CHEREGI Cornel, CIUMARNEAN Lorena, DOGARU Gabriela Balneo and PRM Research Journal. 2021;12(4):327-332 Full Text DOI 10.12680/balneo.2021.459
(460) SIS therapy in the treatment of distal radius epiphyseal fracture (Case report) - JIMBU Diana 1,2, OPREA Doinița 1,2, SARIKAYA Emre1,3, ILIESCU Mădălina Gabriela1,2, IONESCU Elena Valentina1,2, BORDEI Petru1, ENACHE Florin Daniel1,3, IONESCU Constantin1,3, BULBUC Ionuț1,3, OBADĂ Bogdan Balneo and PRM Research Journal. 2021;12(4):333-336 Full Text DOI 10.12680/balneo.2021.460
(461) Age-Related, Sport-Specific Dysfunctions of the Shoulder and Pelvic Girdle in Athletes Table Tennis Players. Observational Study - IORDAN Daniel-Andrei, MOCANU George-Dănuț, MOCANU Mircea-Dan, MUNTEANU Constantin, CONSTANTIN Georgiana Bianca, ONU Ilie, NECHIFOR Alexandru Balneo and PRM Research Journal. 2021;12(4):337-344 Full Text DOI 10.12680/balneo.2021.461
(462) Evaluation of the impact of high-tone therapy on cognitive disorders and quality of life in the complex treatment of patients with comorbid pathology - SHMAKOVA Iryna, PANINA Svitlana, MYKHAYLENKO Volodymyr Balneo and PRM Research Journal. 2021;12(4):345-351 Full Text DOI 10.12680/balneo.2021.462
(463) The importance of body composition assessment in the rehabilitation process - MURGOCI Nicolae Balneo and PRM Research Journal. 2021;12(4):352-364 Full Text DOI 10.12680/balneo.2021.463
(464) Haloaerosoltherapy: Mechanisms of Curative Effect and Place in the Respiratory Rehabilitation - LEMKO Olha, LEMKO Ivan Balneo and PRM Research Journal. 2021;12(4):365-375 Full Text DOI 10.12680/balneo.2021.464
(465) Aphasia after acute ischemic stroke: epidemiology and impact on tertiary care resources - STAN Adina, STRILCIUC Ștefan, GHERGHEL Nicoleta, COZMA Angela, CRISTIAN Alexander, ILUT Silvina, BLESNEAG Alina, VACARAS Vitalie, STANCA Delia, STAN Horatiu MUREȘANU Dașin Balneo and PRM Research Journal. 2021;12(4):376-380 Full Text DOI 10.12680/balneo.2021.465
(466) Essential oils utility implications in symptomatic Burning Mouth Syndrome - PATANO Assunta, DI VENERE Daniela, CECI Sabino, BERATE Pula, CANDREA Sebastian, BABTAN Anida-Maria, AZZOLLINI Daniela, PIRAS Fabio, CURATOLI Luigi, CORRIERO Alberto, VALENTE Francesco, MAGGIORE Maria Elena, MANCINI Antonio, GIOVANNIELLO Delia, NUCCI Ludovica, ELIA Rossella, SIRBU Adina, FEURDEAN Claudia, GALDERISI Andrea, CARDARELLI Filippo Balneo and PRM Research Journal. 2021;12(4):381-385 Full Text DOI 10.12680/balneo.2021.466
(467) Assessment of the importance of physical activity and quality of life for patients diagnosed with osteoporosis during the COVID-19 pandemic - ANTONESCU Oana-Raluca, SILIȘTEANU Andrei Emanuel, RACHERIU Mihaela, MIHALACHE Cosmin Balneo and PRM Research Journal. 2021;12(4):386-391 Full Text DOI 10.12680/balneo.2021.467
(468) Complex aspects of clinical-functional evaluation and ambulatory therapeutic-rehabilitation approach in a young patient with post stroke - spasticity and peroneal nerve palsy - ALBADI Irina, CIOBOTARU Camelia, LUPU Andreea-Alexandra, ONOSE Gelu Balneo and PRM Research Journal. 2021;12(4):392-395 Full Text DOI 10.12680/balneo.2021.468
(469) Elbow rehabilitation using intelligent medical devices - FUIOR Robert, BĂEȘU Andra Cristina, ANDRIȚOI Doru, LUCA Cătălina, CORCIOVĂ Călin Balneo and PRM Research Journal. 2021;12(4):396-399 Full Text DOI 10.12680/balneo.2021.469
(470) Study on cardio-respiratory adaptive mechanisms for performance athletes with physical disabilities - VIZITIU Elena, CONSTANTINESCU Mihai Balneo and PRM Research Journal. 2021;12(4):400-404 Full Text DOI 10.12680/balneo.2021.470
(471) The oral and gut microbiota: beyond a short communication - CECI Sabino, BERATE Pula, CANDREA Sebastian, BABTAN Anida-Maria, AZZOLLINI Daniela, PIRAS Fabio, CURATOLI Luigi, CORRIERO Alberto, PATANO Assunta, VALENTE Francesco, MAGGIORE Maria Elena, MANCINI Antonio, GIOVANNIELLO Delia, NUCCI Ludovica, ELIA Rossella, SIRBU Adina, GALDERISI Andrea, CARDARELLI Filippo Balneo and PRM Research Journal. 2021;12(4):405-411 Full Text DOI 10.12680/balneo.2021.471
(472) The oral and gut microbiota: beyond a short communication - LIUȘNEA Cristian Ștefan Balneo and PRM Research Journal. 2021;12(4):412-417 Full Text DOI 10.12680/balneo.2021.472
(473) Anti-inflammatory effects of exercise training. A systematic review - ONU Ilie, IORDAN Daniel-Andrei, CODREANU Corneliu Mircea, MATEI Daniela, GALACTION Anca-Irina Balneo and PRM Research Journal. 2021;12(4):418-425 Full Text DOI 10.12680/balneo.2021.473
(474) Assessment of the physical and emotional health concerning the students' physical activity during the COVID-19 pandemic - SILIȘTEANU Sinziana-Calina, SILIȘTEANU Andrei Emanuel, ANTONESCU Oana-Raluca, DUICA Lavinia Corina Balneo and PRM Research Journal. 2021;12(4):426-432 Full Text DOI 10.12680/balneo.2021.474
(475) The influence of low back pain on health - related quality of life and the impact of balneal treatment - STANCIU Liliana-Elena, PETCU Lucian Cristian, APOSTOL Șterian, IONESCU Elena-Valentina, OPREA Doinița, OPREA Carmen, ȚUCMEANU Elena-Roxana, ILIESCU Mădălina-Gabriela, POPESCU Marius-Nicolae, OBADĂ Bogdan Balneo and PRM Research Journal. 2021;12(4):433-438 Full Text DOI 10.12680/balneo.2021.475
(476) Occupational therapy interventions in pulmonary rehabilitation - an update in the COVID-19 ERA - CIUBEAN Alina Deniza, CIORTEA Viorela Mihaela, UNGUR Rodica Ana, BORDA Ileana Monica, DOGARU Bombonica Gabriela, POPA Theodor, IRSAY Laszlo Balneo and PRM Research Journal. 2021;12(4):439-444 Full Text DOI 10.12680/balneo.2021.476
(477) Prevalence of Musculo-skeletal Discomfort and Level of Functional Limitations among Physiotherapists in Karachi City - DEEN Nazar, BADSHAH Munair, SHAMIM Muhammad Omar Balneo and PRM Research Journal. 2021;12(4):445-449 Full Text DOI 10.12680/balneo.2021.477

The effect of motion games on improving the psychomotor and intellectual performance of children with autism spectrum disorder and intellectual disabilities

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Abstract

Introduction. Depressive states and anxiety are common symptoms of children with autism spectrum disorder (ASD). The persons with intellectual disabilities show problems related to the development of basic motor skills, having learning problems compared to normal ones, imbalances between the processes of arousal and inhibition, limited motor ability, difficult understanding of language and motor tasks, difficult concentration, mechanical assimilation etc.

Objectives. The study analyzes the effectiveness of structures and motion games, applied in specific activities for children with intellectual disabilities (ID) and autism spectrum disorders (ASD).

Material and Methods. The research involved an experimental group of 5 children with one of these disabilities or their combination (age 10-11 years), included in a training process at the Ion Teodorescu Special Vocational School in Slobozia / Ialomița / Romania and comparing their results with a control group (6 normal children, with an average age of 10 years), between 20.09.2020-10.03.2021. The assessment of the level of psychomotor and intellectual development was made by the Cutout Test, the Cohs Cube Test (light task configurations) and an Attention Flexibility Test (movement to the corners of the room/field depending on the assigned color, counting successful attempts and mistakes).

Results and discussion. The obtained results confirm the working hypothesis, so the use of the structures and games proposed in the program contributes to a significant improvement of the psychomotor and intellectual performances of students with intellectual disabilities and autism spectrum.

Conclusion. Despite all these improvements, they cannot approach or equal the reference values of children without problems, falling into the same age category.

Keywords: *psychomotor skills, adapted physical activities, recovery, children, learning disabilities,*

INTRODUCTION

The persons with intellectual disabilities show problems related to the development of basic motor skills, having learning problems compared to normal ones, imbalances between the processes of arousal and inhibition, limited motor ability, difficult understanding of language and motor tasks, difficult concentration, mechanical assimilation etc. The motivation and the involvement in the effort are limited, being often rejected by those of their age, so limited motor performance. It is necessary to adapt teaching strategies, facilitate access to physical effort, remove social barriers (1). Physical activities must be objectified according to the individual needs of the participants and their disabilities; the volume of information that can be processed is smaller and requires more repetitions (2). Adolescents with health-compromising eating behaviors (HCEBs) as well as those with high BMI values have lower self-

esteem and poorer body image, especially among girls (3).

Depressive states and anxiety are common symptoms of children with autism spectrum disorder (ASD), according to (4). Other authors indicate other symptoms: difficult communication, hyperactivity, destruction of toys, aggression and self-aggression, sleep and eating disorders, poor social interaction, sensory sensitivity etc. (5).

A synthesis of specialized works that address the problem of autism and motor interventions on fundamental movement skills for young people is made by (6,7). For children and young people, physical activity interventions have optimized the balance and fundamental movement skills, but those with disabilities are lagging behind those with normal development. The effectiveness of sensory physical exercise in improving fine and gross motor

skills in children with learning disabilities is reported by (8). In addition to physical exercise, the type of bio-climate (exciting, sedative, tonic) has an effect on therapies applied to the population categories, increasing work capacity and optimizing health (9). The motor skills of children with autism spectrum disorder (ASD) (8-10 years) in Brazil are studied by (10). The more severe the ASD, the greater the deficit in motor skills, and the use of drugs amplifies these manifestations. Positive associations are identified between motor skills and involvement in physical education lessons, respectively with independence in daily activities. The use of physical activities is important for the active lifestyle, the increase of the motor abilities and the quality of life of these groups, ensuring also the widening of the socializing sphere (11,12). The formation of healthy behaviors (related to exercise and nutrition) from an early age are very important in adulthood (13). Anatomical dysfunctions can occur in people with various disabilities, which require recovery processes (14,15).

Movement games stimulates thinking, fights sedentary lifestyle, improves psychomotor skills, increases immunity, is accessible, attractive, spontaneous, being an interesting form of active rest. Organized games are more effective than spontaneous ones, the motor actions performed being a natural tendency of children and a form of communication through body language (16–18).

Physical activities based on attractive exercise games or sports games and other forms of exercise associated with sports, leisure and medical recovery are important factors in optimizing children's health and improving their motor skills (19–21).

The time interval in which semi-structured physical activities are practiced for boys with severe intellectual disabilities (age 9.6 years) counts in the value and the stability of the effects (22). Fundamental movement skills are significantly improved after 1 year (program with 5 workouts / week, 60 min / session), not improved on shorter term / 6 months.

The positive effect of outdoor motion games for improving cognitive functions, increasing the level of social adaptation and psycho-emotional states is highlighted by (23), on a group of 40 students from Ukraine, being a good remedy that can be included in adaptive physical education. The paper of (24) highlights that athletes with intellectual disabilities have increased values of psychological well-being

and higher self-esteem compared to non-athletes. Athletes without obesity / overweight have a better self-esteem and perception of body image.

The positive effect of motion games on children with intellectual disabilities in Ukraine is supported by (25). Increases in psycho-emotional state, cognitive functions are reported, games being an easy remedy, which excludes medication and can be included in adaptive physical education. The influence of dog-assisted therapy on the psychomotor development of children with mild intellectual disabilities is investigated by (26). The study made on 60 children, 10-13 years old, for 10 months confirmed significant improvements for postural imitation tests.

Lack of physical activity and the onset of obesity are factors that can lead to negative functional changes and the manifestation of osteoarthritis, according to (27), and the specificity of certain performance physical activities (table tennis) can cause problems at the lumbar level (28).

Tests and computer games can successfully measure the values of reaction times (simple, cognitive and to visual stimuli), for students who practice different individual sports (boxing, gymnastics, wrestling, karate, etc.). The investigation of (29) signals better values of the simple reaction for the left hand, and for the complex one for the right hand. The more complex the application used, the more efficient the dominant hand. Computer educational games can improve the psychomotor development of children with educable intellectual disabilities, being a useful tool in special education, in terms of design and interaction (30).

The use of virtual reality technology (VR), based on the use of virtual pink dolphins, in the learning process of children with autism is proposed by (31). Improvements in psychomotor skills are found: direction and hand-eye-coordination.

The growing incidence of children with autism and the daily challenges they face are signaled by (32). In addition to difficult social interactions and poor communication, psycho-motor deficiencies are also present. The importance of nonverbal communication and bodily expressiveness in physical activities is emphasized by (33), as a significant variant of information in sports training (gymnastics). Through the first signaling system, useful also for activities with the mentally handicapped, communication can be optimized, feelings and emotions are expressed more easily,

because the language / words are more difficult to understand.

Problems of children with autism are reported by (34), which identifies deficiencies in social interaction, communication, stereotypical behavior, limited involvement in physical effort and low level of fitness. The use of playing games (16 sessions x 60 min) generated a significant improvement in motor skills. The study of (35) performed on young people with autism in Istanbul / Turkey (55 cases, aged 6-26 years), involved in inclusive physical activity (for 3 months, with 2 workouts / week, duration of 45 min) identify favorable effects on social skills.

Material and method

The purpose of the research is the verification of the positive effects of the proposed motion games on the psychomotor skills of students who are affected by ID (intellectual disabilities) and / or ASD (autism spectrum disorder). The study started from the finding that, during physical education classes, but also in other teaching activities, when there is play and movement, students assimilate faster. If we capture their attention and create an atmosphere of acceptance and harmony, the education process will be much easier and more enjoyable.

Working hypothesis: By using and rationally adapting a varied complex of structures and motion games, significant improvements of the psychomotor elements can be obtained at the level of the studied experiment group.

Participants

The investigated subjects are 5 cases (4 boys and a girl, aged 10-11) from the Ion Teodorescu Special Vocational School in Slobozia / Ialomița, with problems related to ASD and ID, which are reflected in behavioral disorders and psychomotor instability, which generates difficulties in adapting to the teaching process. They participated in activities based on different motion games, with various influences on motor behavior and elements of psychomotor skills: attention, coordination, insight, memory, tactile sense, etc. Their results were related to the performance of a control group - normal subjects (6 boys aged 10 years, belonging to Saveni / Ialomița Secondary School). The individual characteristics of the members of the experiment group, related to the level of motor and intellectual development, socialization and the manifested problems are summarized in table 1.

Procedures

The research took place between 20.09.2020-10.03.2021, the physical activities of the subjects in the experiment group focusing on various structures and games with influence on psychomotor skills and intellectual dimension. The rules of academic writing have been followed, according to (36). For reasons related to space, the study can only selectively list some of the variants of games included in the work program:

White, black (memory and reaction time) The game can be played with the players sitting in benches, in the classroom: at the word "WHITE" – they stand up, at the word "BLACK" they sit down

Bouquets (attention) The players move through a running step in a column one or two at a time. At some point, the game leader shouts a number, players must quickly gather in a group of players equal to the number called.

Reverse command – is it ordered to walk slowly, and the group will execute the walk quickly, or the command to raise the right arm is given and everyone raises the left arm.

Rocket (memorizing movements). The teacher performs a series of movements such as: clapping at an accelerated pace, running on the spot, rotating the arms, jumping, squats. The children perform the respective exercises as faithfully as possible.

Relay with circles (orientation, eye-hand coordination, accuracy). In front of each team (2-3 teams) from place to place we stick 3 stakes in the ground. The distance between the stakes will be 7-8 steps. The first player in each team receives 3 circles that he inserts in each stake, from running, and on his return he collects them and hands them to the next player.

Show the alphabet! (insight, memory, tactile sense, hearing) We cutout a number of cards equal to that of the letters of the alphabet. One letter is written on each one and they are shuffled, the called player must order the alphabet of the cards.

Show the sentence (insight, memory) The leader hands them a note containing a sentence. The player must redo the sentence using the cards.

Practice your memory (memory, insight) The leader places 24 different objects on the table and covers the table with a piece of cloth. The players are called, the material is picked up and they are given a minute to memorize as many of the objects on the table as possible. Everyone then writes down on a piece of paper the objects they remember.

What items are missing ? (memory-insight) After placing 30 objects on the table, the leader gives the players 1 minute to memorize them. Then, the players cover their eyes with their palms, while the leader takes an object from the table. The first player to name the object taken by the leader wins it as a trophy.

Reassembly of the illustration (coordination, insight) Cut an image into 10 unequal parts that are mixed and then handed to the players. The time in which the players manage to assemble the image is timed.

Placement of geometric figures (exercise of tactile sense). Cut 10 triangles, squares, circles, rectangles out of cardboard. The geometric figures are placed in the hand of a player whose eyes were previously covered. The player must recognize the geometric figure just by touching it and place it on the correct pile.

Description of tests:

The cutout test it is used to test spatial representations, the perception of their forms and structure, and practical intelligence. Structure of the sample:

A) A support provided with three different configurations (3 cutouts hence the name): square, trapezoid, circle.

B) Square configuration subassemblies (4 figures)

C) Circle configuration subassemblies (5 figures)

D) Trapezoidal configuration subassemblies (5 figures)

The task of the subject is to reconstruct the circle-square-trapezoid configurations, using the subassemblies (B), (C), (D).

The cutout test is applied individually, with imposed times or with free time (until the subject finishes the test). It usually starts with a square and ends with a circle.

Cohs cubes test (37,38) it is used to test the spatial factor of intelligence, nonverbal cognitive skills. The set consists of several variously colored cubes and in different configurations. By combining several cubes, 10 configurations are obtained whose complexity increases from one number to another. The configuration model is given in the task cards. The task of the subject is to build the 10 configurations, using the cubes and reproducing the pattern of the task cards shown. The test of Cohs cubes is applied individually and the time elapsed for the execution of each configuration is recorded, if it is performed within the time limit. Due to the

low intelligence of the subjects, we used the task cards with configurations 0 and 2.

Attention flexibility test: This game takes place in the gym or on the field. Each corner of the room or field will be named a color. Players must also remember when announcing a color by the teacher, to run to that corner. Those who hesitate or make a mistake will be penalized. Methodical hints: to create surprises, other colors besides those assigned to the corners can be called. For small classes, the corners can be called animals or birds. 10 tries are awarded and the number of successes and failures is recorded separately.

The statistical – mathematical analysis: Due to the low number of subjects in both groups, non-parametric (rank-based) procedures for calculating the differences between groups were required for the initial and final tests (Mann-Whitney U test) and the Wilcoxon test (for the data pairs in the experiment group) (39–42). The control group had a single data set, to which the results of the experiment group were reported for both tests. The central tendency indicators (arithmetic mean) were represented graphically to facilitate a better understanding of the dynamics of group performance, being also presented graphs with individual test performance. The statistical calculation was performed using the IBM SPSS software vers. 24.

Results

The data of the average values for the initial and final tests at the level of the experimental group and those of the control group are represented graphically in fig. 1. It is observed that the control group has values higher than the two measurements of the experiment group applied to the whole battery of tests (in the Cohs test and in the Cutout test normal subjects solve the drawn tasks faster / therefore shorter times, and the flexibility test of attention have a higher number of successful attempts, complemented by a lower number of errors)

Table 2 expresses the results of the non-parametric Wilcoxon test (in pairs) at the level of the experiment group. It is observed that all values of Z are related to thresholds $P < 0.05$, so the progress after the implementation of game-based activities is significant, which demonstrates the usefulness of the proposed programs, based on psychomotor

structures and games. Graphs 2 and 3 show the individual values of the 5 subjects in the experiment group for the initial and final tests, respectively, being able to notice the heterogeneity of the results especially at the Cohs test and the relatively close values for the cutout test and attention flexibility.

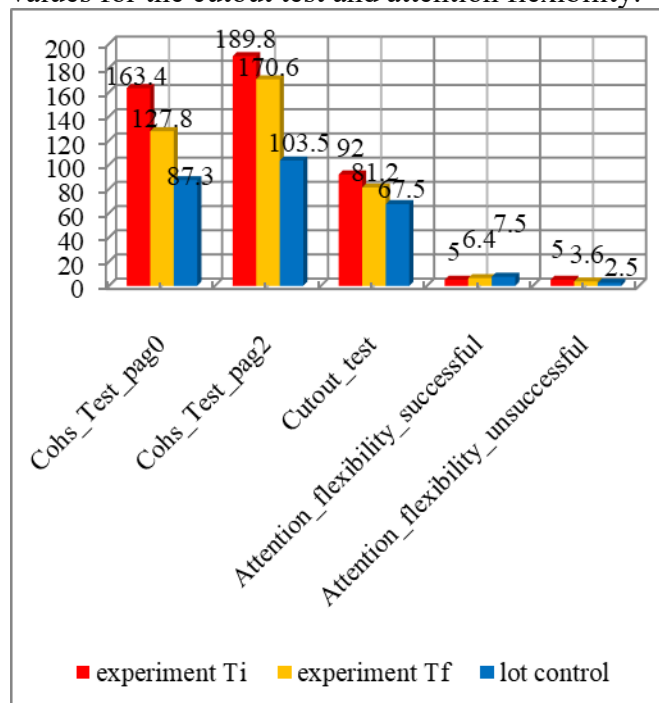


Fig. 1 – Average values in tests for independent groups

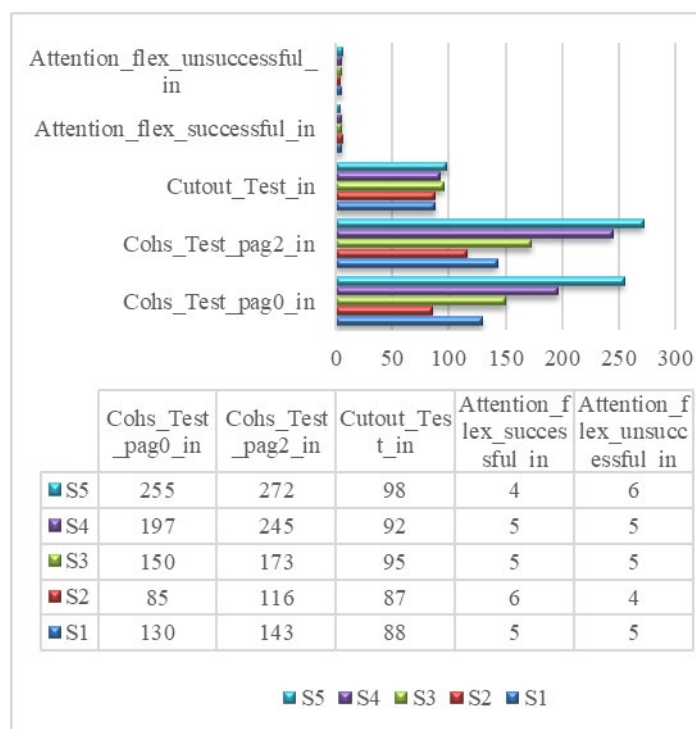


Fig. 2 – Individual values for the experimental group at initial testing

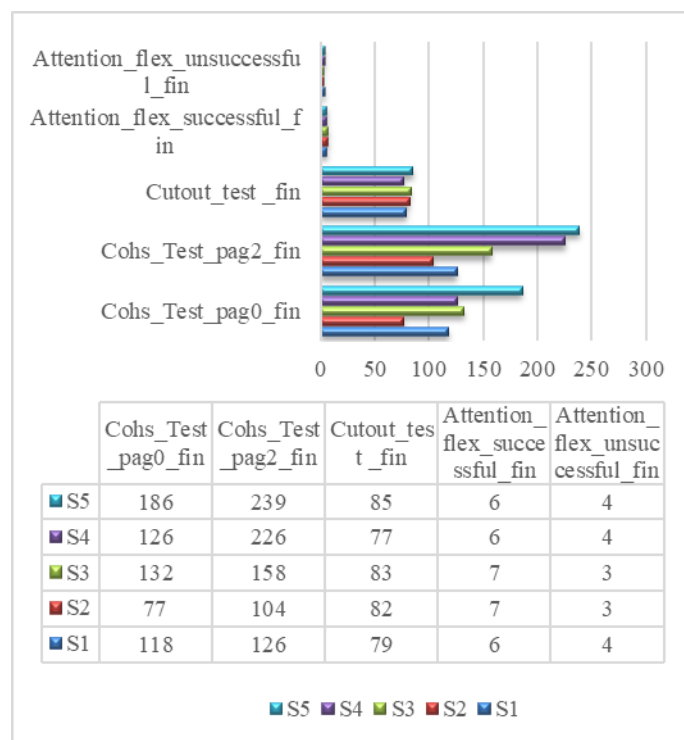


Fig. 3 – Individual values for the experimental group at final testing

Tables 3 and 4 show the results of the nonparametric test Mann-Whitney U (independent samples) at the level of initial and final tests. It is observed at the initial testing that the control group has statistically significantly higher results than the control group, all values of Z correspond to significance thresholds $P < 0.05$, so it is obvious that the reported disabilities have repercussions on the performance of the experimental group. Even if the comparison of the results between the groups for the final test shows that there are samples where the differences are no longer significant / Z values correspond to thresholds $P > 0.05$ (this aspect confirming the progress in the experiment group), the values of the control group remain better at the whole set of tests and even significantly better for the Cohs Test pag2 and the Cutout Test.

Graph 4 shows the dynamics of individual test values for the 6 members of the control group. It is observed that even in the case of subjects without the reported disabilities, there are still obvious variations in test performance.

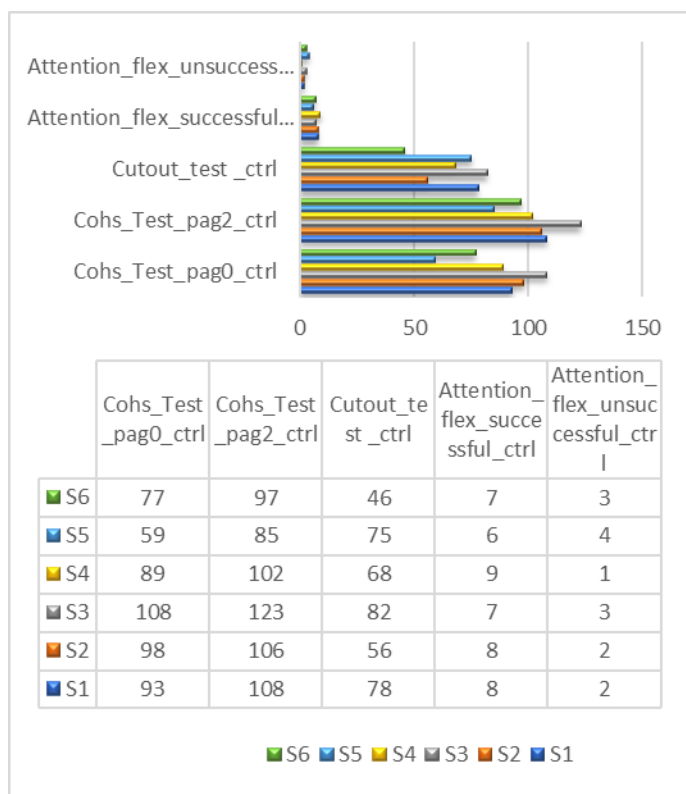


Fig. 4 – Individual values for the control group

DISCUSSION

The specialized literature presents numerous researches that are directly related to our topic. The study of (43) identifies the positive effects of regular sports training proposed by the Integrated Department of Athletes with Disabilities, for children with autism (12 boys involved 13 weeks / 3 weekly sessions / 1 hour / session), through various programs of agility, speed, strength, coordination and balance. Bruininks-Oseretsky tests indicate significant accumulation / progress for the skills tested, so regular training will improve motor skills for those with autism. Activities focused on psychomotor development, games and individual sports are recommended.

Motor skills of locomotion and control of objects, for children with mild intellectual disabilities in the Czech Republic (114 cases with an average age of 10 years) are studied by (44). Even for running, jumping, throwing, poorer results are obtained, with major individual differences. Only some children with intellectual disabilities (ID) have motor results similar to normal ones, but in most cases this aspect is refuted, so the development of motor skills in children with ID is a priority to support their inclusion in school.

The effectiveness of psychomotor intervention programs (PIP) on children with autism (autism spectrum disorder) is studied by (45). The effects of the applied program (10 weeks, 3 times / week, focused on the body scheme, spatial and temporal component) on the studied group (12 children, aged 5.48 years) improved the performance of psychomotor tests, its use being recommended in the school curriculum.

Problems with static balance and motor development in children with intellectual disabilities are reported by (46). The use of psychomotor education programs for children aged 8-12 years (16 weeks, 2 workouts / week, duration of 45 minutes) significantly improved the performance at static balance, thus contributing to an active and healthy lifestyle.

The use of football as a mean of improving motor skills for children with autism (characterized by limited motor and social skills and difficult learning) is analyzed by (47). The use of football structures (24 sessions x 1 hour) has favorable results on psychomotor behavior and forms healthy sports habits. The usefulness of gymnastic exercises on autistic children in Iran (45 cases, 4-12 years) in the autism center in Isfahan (applied 24 weeks, 2 days / week, 45 min / session) is confirmed by the study of (48). Significant improvements are achieved in total motor skills, ball skills, static and dynamic balance, but without clear progress in manual dexterity tests.

The usefulness of the game of hemsball (based on passing a ball in pairs, by throwing it in a circle on the ground) in improving motor skills for children with moderate and mild intellectual disabilities (12-16 years) is reported by (49). The study on 50 subjects aged 12-16 in Turkey who used the hemsball program (12 weeks x 3 days / week x 1 hour / session) generated significant improvements in hand coordination, balance and bilateral coordination, with greater progress being reported in those with moderate intellectual disabilities.

The promotion of technological progress - through the use of LEAP Motion Technology and Psychology - in the detection of hand movements, for the analysis of the level of neuro-development and neurological and cognitive disorders is done by (50). The analyzed sources demonstrate the usefulness of this system for autistic disorders, ADHD, in psychomotor and social rehabilitation, in facilitating learning in different contexts.

The use of a mechatronic training KIT has positive effects on the psychomotor skills for the palm grasp, the rotation of the fist joint and the eye-hand coordination, through a study performed on 6 children with autism (age 4-9 years). Similar results are obtained by using a robot and manipulating it with a joystick, for learning the concept of directions of movement and palmar grasp (51). The use of multisensory virtual games (with manipulation of objects in three dimensions) is proposed by (52) to limit the specific manifestations of ADHD (attention deficit hyperactivity disorder). For the investigated subjects (7-12 years), who found it difficult to maintain voluntary attention for academic and daily activities, there is an increase in the ability to focus and stimulate learning processes.

The use of controlled video games (based on the kinect V2 sensor) is useful in teaching elementary school children (4 cases with intellectual disabilities), with the skill of washing hands, their parents being satisfied with the results of its implementation, according to (53). The use of augmented reality games (AR / augmented reality game) for high school students with intellectual disabilities has improved the skills of subjects related to the use of a banking ATM (automated teller machine), teachers considering it effective in terms of results (54).

The positive effect of motion-based learning games (Kinect) for children with special educational needs is identified by (55). Due to the combination of cognitive and physical tasks, they generate increased academic performance, improved cognitive and motor skills, being recommended to be integrated into the educational process.

The need to expand the notions related to health and physical activities, in order to generate pro-active attitudes related to involvement in physical effort is signaled by (56), and significant differences in parameters related to body composition (BMI, obesity, muscle mass, etc.) between active and semi-active students are highlighted by (57).

A review of the scientific literature on the effectiveness of Serious Games / SGs (based on video games with educational effects) as a way of learning for people with different stages of intellectual disabilities is made by (58). This variant needs to be adapted to individual needs. The effectiveness of Serious Games with psychometric properties is also experimented by (59). They achieve obvious improvements in cognitive abilities,

focusing of visual attention and motivation on a group of 44 students (6-16 years), with ADHD and learning disorders, by implementing a program of 28 sessions x 28 weeks x 10 minutes, based on 10 games for multiple intelligences. The importance of Serious Games, based on software technologies, for children with autism is also supported by (60), through their educational efficiency, as communication therapy, improvement of social behavior and as psychomotor treatment. The positive effects of Serious Games on students with deficient attention, memory and poor motor control, with mental or developmental disabilities, compared to standard methods are highlighted by (61). The efficiency of Serious Games on people with intellectual disabilities and those with autism spectrum (characterized by problems of social, emotional and communication behavior, even if some autistic people have high intellectual availability and others have cognitive disabilities) is also reported by (62,63). Technological advances (software and computer games) are solutions to improve these problems, depending on the deficiencies found: literacy, daily activities, language, psychomotor skills, etc., teachers and specialists in special education confirm their value and usefulness.

CONCLUSIONS

The obtained results confirm the working hypothesis, so the use of the structures and games proposed in the program contributes to a significant improvement of the psychomotor and intellectual performances of students with intellectual disabilities and autism spectrum. Despite all these improvements, they cannot match the benchmarks of children without problems in the same age group. A limitation of the study is the small number of subjects included in the study, which does not allow the generalization of the results. Another limitation is the non-use of Serious Games variants, often used and analyzed in some mentioned studies, this aspect being a future research direction, in order to see their efficiency in comparison with the classic training and recovery variants.

Declaration of conflict of interests

There is no conflict of interest for any of the authors regarding this paper.

Informed consent

The investigated subjects and legal guardians were informed about the purpose and methodology of the study presented, expressing their agreement to the

processing and publication of the results of the current study, in compliance with the rules on personal data protection.

Author contribution

The authors of this article have equal contribution and equal rights over it.

Table 1 – Analysis of the individual defining particularities for the experiment group

Subject /gender	Ages	Diagnostic	Psychic, motor and behavioral characteristics
M.E. /M	11	Autism spectrum disorder and mental retardation	The learning process is severely affected due to mental retardation and autism spectrum disorder. Motor coordination is good, and the body scheme was mastered. The dominant laterality is right. Fine and coarse motor skills are affected. Space-temporal orientation is difficult to achieve. Operates with simple notions and understands cause-effect relationships only in terms of simple life situations. The thinking is slow, in the operational-concrete stage. The memory is long lasting, but it stores mechanically. The language is medium developed, and the oral expression is grammatically incorrect. The student has attention disorders, but with help he remains stable in the task and completes it. He participates in activities unequally, fluctuating, but if he is kept in the task with motivations or rewards he manages to complete all the work tasks. As a social relationship is a sociable type, but with low resistance to frustration.
C.M. /F	11	Epilepsy and mental retardation	The student comes to school uncared for. She has a tendency to steal and is mean to her classmates. She lies a lot at school, but also at home. She has a poor thinking, with training tendencies, he can hardly distinguish the essential. She generally learns with some interest, trying to outperform her colleagues. She can keep her concentration and attention but only if she is closely guided. Psychomotor development: motor coordination is good. The body scheme is mastered. Right dominant laterality. Fine and coarse motor skills are affected. She has moments when she loses her balance. The space-temporal orientation is achieved at a low level.
A.A. /M	10	Highly functional autistic, but with emotional disorders.	He is a disciplined student, enjoying the sympathy of his colleagues. The learning process is done at a very good level for the requirements of the special school. Psychomotor development: motor coordination is good. The body scheme is mastered. Right dominant laterality. Fine and coarse motor skills are slightly affected. The space-temporal orientation is good. Thinking is specific to the stage of concrete operations. Understands complex notions and cause-effect relationships. The memory is long lasting. It is capable of abstraction and generalization. Vocabulary is well developed. Shows will and interest in school activities. In relationships with colleagues and teachers he is an example student.
B.S. /M	10	Autism spectrum disorder and severe developmental delay	The learning process is severely affected due to mental retardation in development. Motor coordination is severely impaired. The body scheme is mastered. Dominant left laterality. Fine and coarse motor skills are affected. The space-temporal orientation is achieved with an imbalance. Thinking is specific to the pre-operational stage, understands simple notions. The memory is short-lived, it forgets very quickly. Vocabulary is low. He has attention disorders, his concentration is low, he gets tired quickly. Load stability is fluctuating and volume is low. It is difficult to train in tasks, but if he receives a reward he participates. The student is shy, not very communicative. He has moments when he can't control himself and he becomes aggressive for those around him due to seemingly minor reasons.
C.C. /M	11	Slightly delayed development	Motor coordination is good. The body scheme is mastered. Right dominant laterality. Fine and coarse motor skills are within good limits. The space-temporal orientation is almost normal. He understands complex notions and can handle himself at home for a few hours. The memory is long lasting. The vocabulary is rich and is expressed clearly and correctly. It does not show attention disorders, it can concentrate quite well, it is stable. He is active in lessons, showing an intrinsic motivation. He is sociable and behaves appropriately.

Table 2 / Wilcoxon^a nonparametric test results (pairs) / experimental group (N=5)

Test	Mean	Std. Deviation	Std. Error Mean	Mean Difference	Z	Sig. (2-tailed)
Cohs_Test_pag0_initial	163.4000	65.1175	29.1214	35.6000	-2.023 ^b	0.043
Cohs_Test_pag0_fin	127.8000	39.0025	17.4424			
Cohs_Test_pag2_initial	189.8000	66.5635	29.7681	19.2000	-2.023 ^b	0.043
Cohs_Test_pag2_fin	170.6000	59.8565	26.7686			
Cutout_Test_initial	92.0000	4.6368	2.0736	10.8000	-2.023 ^b	0.043
Cutout_Test_final	81.2000	3.1937	1.4282			
Attention_flexibility_successful_initial	5.0000	0.7071	0.3162	-1.4000	-2.070 ^c	0.038
Attention_flexibility_successful_final	6.4000	0.5477	0.2449			
Attention_flexibility_unsuccessful_initial	5.0000	0.7071	0.3162	1.4000	-2.070 ^b	0.038
Attention_flexibility_unsuccessful_final	3.6000	0.5477	0.2449			

a. Wilcoxon Signed Ranks Test; b. Based on positive ranks.; c. Based on negative ranks.

Table 3 / Mann-Whitney U nonparametric test results (independent samples) / *initial testing* / control group (N=6), experimental group (N=5).

Test	Lot	Mean	Std. Deviation	Std. Error Mean	Mean Difference	Z	Sig. (2-tailed)
Cohs_Test_pag0	control	87.3333	17.2356	7.0364	-76.0666	-2.008	0.045
	experiment	163.4000	65.1175	29.121			
Cohs_Test_pag2	control	103.5000	12.5976	5.1429	-86.3000	-2.556	0.011
	experiment	189.8000	66.5635	29.7681			
Cutout_test	control	67.5000	13.9391	5.6906	-24.5000	-2.739	0.006
	experiment	92.0000	4.6368	2.0736			
Attention_flexibility_successful	control	7.5000	1.0488	0.4281	2.5000	-2.690	0.007
	experiment	5.0000	0.7071	0.3162			
Attention_flexibility_unsuccessful	control	2.5000	1.0488	0.4281	-2.5000	-2.690	0.007
	experiment	5.0000	0.7071	0.3162			

Table 4 / Mann-Whitney U nonparametric test results (independent samples) / *final testing* / control group (N=6), experimental group (N=5).

Test	Lot	Mean	Std. Deviation	Std. Error Mean	Mean Difference	Z	Sig. (2-tailed)
Cohs_Test_pag0	control	87.3333	17.2356	7.0364	-40.4666	-1.921	0.055
	experiment	127.8000	39.0025	17.4424			
Cohs_Test_pag2	control	103.5000	12.5976	5.1429	-67.1000	-2.191	0.028
	experiment	170.6000	59.8565	26.7686			
Cutout_test	control	67.5000	13.9391	5.6906	-13.7000	-2.104	0.035
	experiment	81.2000	3.1937	1.4282			
Attention_flexibility_successful	control	7.5000	1.0488	0.4281	1.1000	-1.824	0.068
	experiment	6.4000	0.5477	0.2449			
Attention_flexibility_unsuccessful	control	2.5000	1.0488	0.4281	-1.1000	-1.824	0.068
	experiment	3.6000	0.5477	0.2449			

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WEB OF SCIENCE

Complex respiratory and motor rehabilitation program in a patient with post-pulmonary tuberculosis conditions and multiple sequelae after SARS-CoV-2 infection: case report

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Abstract

Introduction: A great variety of medical issues can occur after the COVID-19 infection including fatigue, muscle weakness, locomotor disability, self-care dysfunction, polyneuropathy, persistent dyspnea on exertion and a hypercoagulable state.

Materials and methods: This paper presents the case of a nonsmoker 49-year-old male with right lung lower lobe lobectomy for post tuberculosis bronchiectasis and diabetes mellitus, who developed multiple serious physicals, neurological, hematological and respiratory consequences, related to critical COVID-19 infection and prolonged hospitalization,

Results: A favorable evolution of the patient's respiratory sequels and motor impairment on both lower limbs was noticed after a complex individualized rehabilitation program started in the post COVID-19 Rehabilitation Department of Balneal and Rehabilitation Sanatorium, Techirghiol, Romania, consisting in better functional parameters and exercise tolerance, significant improvement in daily activities, remission of exertional dyspnea, social and family reintegration.

Conclusions: multidisciplinary approach and complex individualized programs of rehabilitation is required after a critical form of COVID in a patients known with tuberculosis, and other complex pathologies, in order to restore physical function and mobility and optimize respiratory parameters.

Keywords: COVID-19, Rehabilitation, Tuberculosis,

INTRODUCTION

A new strain of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) was identified causing a very contagious infection, firstly described in Chinese patients, involving mostly human respiratory system¹. Covid 19 is a challenging and polymorph pathology, ranges from asymptomatic to a severe respiratory form, implying extensive pneumonia and even death². The list of the suggestive symptoms of COVID-19 includes fever, cough, breathing difficulty, chills, myalgia, headaches, sore throats, loss of taste (ageusia) and/or odor (anosmia), headache, conjunctivitis, and gastrointestinal problems^{3,4}. In a community-based study, involving self-reported symptoms to predict potential SARS-CoV-2 infection, via mobile application, the most prevalent symptoms were fever, persistent cough, fatigue, shortness of breath, diarrhea, delirium, missed meals, abdominal pain, chest pain and hoarse voice⁵. COVID-19 may also lead to long-term respiratory and cardiovascular consequences, physical and psychological dysfunctions, requiring early

multidisciplinary rehabilitation^{6,7}. The risk of death in Romanian hospitalized COVID-19 patients is greater⁸ than in tuberculosis⁹ or HIV patients¹⁰. Considering this data, our aim is to highlight the benefits of a complex rehabilitation program in a patient with post-pulmonary conditions and multiple sequelae after COVID-19.

Case report

History data

We report the case of a professional driver, nonsmoker male, aged 49 years old, with a suggestive medical history of recent COVID-19 infection known with diabetes mellitus, right lung lower lobe lobectomy for post tuberculosis bronchiectasis, in 1997. The patient was diagnosed and treated in Belgium, from December 2020 to February 2021, for a critical type of SARS-CoV-2 infection. The disease debuted with myalgia, fever, and fatigue while the patient was driving in Belgium. The COVID-19 infection was confirmed by positive RT-PCR testing and hospitalization was decided due to the

presence of additional temporal-spatial disorientation. Despite the administration of antivirals, dexamethasone, invasive ventilation, and extracorporeal membrane oxygenation were required, after 10 days of hospitalization in the intensive care unit of Jan Palfijn Gent University Hospital, for an acute respiratory distress syndrome (ARDS). Extubation was considered after another two weeks of intensive medical care and the patient was then transferred to the Pulmonology Department for ventilator associated pneumonia caused by *Pseudomonas Aeruginosa* and *Klebsiella pneumoniae*, which treated and cured with a selected efficient combination of antibiotics (piperacillin – tazobactam, meropenem and ciprofloxacin). Following this long hospitalization period, a slow progressive favorable evolution was noticed, but it was grafted with multiple complications, consisting in difficulties in speech, swallowing and dysphagia, after prolonged oro-tracheal intubation, requiring special speech therapy exercises and feeding by nasogastric tube. Type 2 diabetes mellitus was revealed by persistent hyperglycemia and elevated values of glycated hemoglobin (8.6) requiring therapy by rapid acting insulin in combination with methformin. At discharge, after two months, the treatment recommended were: pregabalin 150 mg twice a day, metformin 850 mg three times daily, and 0.4 mg of tamsulosin and 60 mg of gliclazide once a day.

Patient's evaluation

In February of 2021, the patient was admitted to the Balneal and Rehabilitation Sanatorium of Techirghiol (BRST), Romania. At admission, he complained of mechanical pain in the right knee, hands and fists, hypoesthesia and paresthesia of the distal region on both lower limbs, muscle weakness with marked muscle atrophy and motor impairment on both lower limbs, bilateral motor dysfunction on the dorsiflexion of the foot (mostly on the left side), persistent exertional dyspnea, marked physical asthenia, fatigue and general deconditioning due to the prolonged hospitalization. Clinical examination revealed: motor deficit in both legs, mostly on the left leg ; left muscular force were dorsiflexion 2+, inversion 3+, plantar flexion 4+; right muscular force: dorsiflexion 3+, inversion 4, plantar flexion 5, dorsal hypoesthesia of the left leg. The pain in the right knee was associated with slight antero-posterior instability, generalized muscle hypotrophy in the lower limbs.

The 6-minute walking test (6MWT) was performed, covering a distance of 290 meters, and revealed exertional dyspnea and mild desaturation (**Table 1**). Performance of daily activities was evaluated on a scale with 10 points, from 0 to 10, 0 meaning “no problems” and 10 meaning “cannot be performed”. The ability of climbing stairs 5, running 7 and lifting weights 6.

TABLE 1. 6 minutes walking Test at admission in Balneal and Rehabilitation Sanatorium of Techirghiol

Before walking	After walking for 290 meters
TA = 120/80 mmHg	TA = 140/90 mmHg
AV = 96 rpm	AV = 106 rpm
SpO2 = 99%	SpO2 = 94%
WITHOUT dyspnea	Dyspnea
TOTAL DISTANCE COVERED = 290 meters	

Paraclinical blood exam emphasized increased d-dimers up to 5380 ng/ml 24 times higher compared to normal value, and anticoagulation with apixabam pills of 2.5 mg twice a day was initiated after cardiologist evaluation. Pelvis radiography showed femoral impingement by elevation of the bilateral cervical-cephalic lateral contour, especially on the left side.

Electromyographic investigation: mixed symmetrical, predominantly motor polyneuropathy with mostly distal involvement.

Ultrasound examination of the left common peroneal nerve revealed peripheral nerve imaging of injury, with clear configuration and detachment without extensive pressure.

Chest computed tomography revealed: subpleural area of fibrosis and traction bronchiectasis in the left lower lung lobe, right lower lung lobe lobectomy and mediastinum shift to the right hemithorax.

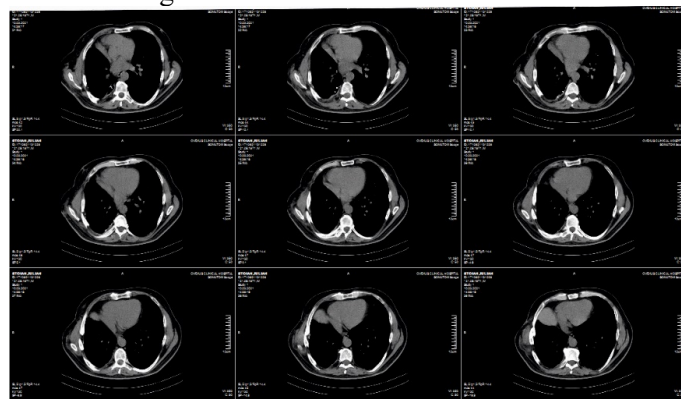


Figure 1 Chest computed tomography

The rehabilitation program

During hospitalization in the balneal rehabilitation department, several therapeutic procedures were recommended.

Hydro-kinesitherapy in the therapeutic pool with hypertonic saline mineral water at 36°C for 20 minutes to assist gait and joint mobility.

Bilateral electrostimulation of the legs to assist and recover the lost movement of the lower legs.

Nano-pulsed electromagnetic field and deep bilateral posterior thoracic oscillation, to stimulate the diaphragm muscle.

Galvanic bath, bilateral knee ultrasound, cervical-dorsal lumbar drainage, lower limb lymphatic drainage and trophic massage in order to improve lower limbs circulation and regain muscle trophicity and improve mobility.

Also, the patient benefited from a generalized toning kinesitherapy, kinetic respiratory exercises and treadmill exercises.

Clinical and functional results

After nearly three weeks of rehabilitation, the patient has improved the general condition

At discharge he did not have muscle or joint pain, no fatigue or physical asthenia. The remission of exertional dyspnea was noted.

The motor deficits diminished motor for both legs as follow: left muscular force dorsiflexion 3+, inversion 4+, plantar flexion 5, right muscular force: dorsiflexion 4, inversion 4, plantar flexion 5.

Muscles trophicity was improved. There was a significant clinical improvement of the 6 MWT without dyspnea or desaturation (**Table 2**), increased performance of daily activities, with the ability of climbing stairs 3, running 5 and lifting weights 4.

TABLE 2. 6 minutes walking Test at discharge from Balneal and Rehabilitation Sanatorium of Techirghiol

Before walking	After walking for 410 meters
TA = 120/80 mm Hg	TA = 145/90 mm Hg
AV = 85 rpm	AV = 113 rpm
SpO2 = 97%	SpO2 = 96%
WITHOUT dyspnea	WITHOUT dyspnea
TOTAL DISTANCE COVERED = 410 meters	

Discussion

In our reported case, we emphasized a complex rehabilitation program consisting in procedures for recovering the bilateral motor deficit of the both lower limbs. The patient had diabetic polyneuropathy but also post-COVID-19 physical deficits, including muscle weakness, induced by prolonged immobilization, neurological impairment, and/or nutritional disorders. Also, the direct infection of the nervous and muscular system, neuroinflammation, post-viral autoimmune response, hypercoagulability, metabolic or hypoxic lesions are assumed as main mechanisms for motor deficits after COVID 19^{11,12}.

Considering the dysfunctional aspects of the post-acute COVID-19 syndrome, mentioned in our reported case, i.e. skeletal muscles and peripheral nerve pathology, the efficacy of rehabilitation was obvious. Complex physical procedures electrostimulation of affected muscles, galvanic bath for reeducation of sensitivity, lymphatic drainage in both lower limbs, toning massage, hydro-kinesitherapy for toning and joint stabilization are the guarantor of successful recovery of the lower limbs and the contributor for a better insertion into pre-existing

socio-professional and family activities^{13,14}. Personalized plans of rehabilitation must be designed according to the age, sex, lifestyle, hobbies, occupation and physical condition of the COVID-19 patients because they might have different degrees of dysfunction¹⁴⁻¹⁶.

Since SARS-CoV-2 may be prevalent for a long period of time and their sequels as well¹⁷, routine clinical medical practice has to be adjusted for a greater awareness of early rehabilitation benefits. Initiating rehabilitation in the early stage after the COVID-19 disease¹⁸ is required in order to prevent negative neurological effects and to improve the functional parameters especially respiratory ones and to improve patients 'quality of life'¹⁹. As a result of the procedures consisting in stimulation of diaphragm muscle and chest drainage, by deep vibrations, the patient gained autonomy, the walking distance improved considerably by more than 120 meters, and the daily activities were return close to normal. We consider early rehabilitation intervention made immediately after the discharge from intensive care, critical for reducing the burden of the post COVID-19 syndrome, especially in this case with previously altered lung function, caused by TB, with lung fibrosis and respiratory muscle atrophy²⁰. The sequels from TB and COVID conditions worse lung capacity²¹ and decrease the tolerance for effort. Respiratory rehabilitation plays an important role in the recovery of body integrity from a pulmonary point of view²⁰. There are no sufficient data about the complexity and variability of the lung damage caused by coupled COVID-19 infection and pulmonary TB, and there is limited scientific knowledge and/or evidence about respiratory rehabilitation in patients with both TB and COVID-19²². Owing to lung fibrosis and bronchiectasis, as sequelae of previous pulmonary TB, ventilator associated pneumonia or COVID-19 infection itself, it is difficult to establish their etiology, but further programs of RR are needed and are essential to improve breathing, quality of life and for decreasing the emotional distress²³. In addition, lung function can be increased through alleviating the neuromuscular weakness by early rehabilitation²⁴.

Recurrent elevation of D-dimers, at more than 60 days after the onset of the COVID-19 infection, could have been a risk factor for death, caused by a lung infarction²⁵. Therefore, the risk of thrombosis should be considered, especially in patients with severe/critical forms and prolonged hospitalization.

Long COVID-19 syndrome is difficult to manage in patients with previous long-term conditions caused by TB disease¹⁷. Various sequelae of COVID-19 infection need to be promptly identified because of their life-threatening potential²⁶. Further studies are needed to investigate the persistent or recurrent hypercoagulable state, as well as to assess the risk of residual TB lung lesions in patients with immunosuppression caused by

diabetes and COVID-19. In conclusion, after a critical form of COVID-19, patients can experience a variety of negative consequences requiring multidisciplinary approach and complex individualized programs of rehabilitation in order to restore physical function and mobility, improving daily activities and tolerance to the effort

Author contributions

All the listed authors contributed equally to this paper.

CD, AI, EVI, MGI, LES, SCC, DMI, OCA, VG, FV, MNP, RB, LP: conceptualization, study design, methodology preparation, evaluation of the patient, collecting the data about the patient, analyze the data, writing and editing.

All authors read and approved the final version of the article.

Ethics approval and consent to participate

This study was conducted in accordance with the declaration of Helsinki and with approval from the Ethics Committee of Balneal and Rehabilitation Sanatorium of Techirghiol from Romania, No 132/ 22.02.2021 Written informed consent was obtained from the patient.

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Conflict of interest

The authors declare no conflict of interest.

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The profile of patients with atrial fibrillation scheduled for cardioversion or catheter ablation hospitalized in a Romanian rehabilitation hospital

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Abstract

Objectives - Structural cardiac, mainly atrial remodeling in non-valvular atrial fibrillation (NVAF) creates conditions for thromboembolic complications, despite the optimization of oral anticoagulant treatment over the past years. This study aims to provide a comparative analysis of patients with NVAF, with and without atrial thrombotic masses, in an integrated approach using clinical, electrocardiographic, anatomohemodynamic cardiac findings assessed by echocardiography, as well as an evaluation of the inflammatory status based on the usual screening blood markers. **Methods** – The study was based on the anonymous analysis of the medical records of 50 patients with NVAF monitored in a center of cardiology in Cluj-Napoca between March 2019 – February 2020, who received optimal oral anticoagulant treatment, all undergoing transesophageal ultrasound prior to cardioversion or ablation therapy. The statistical data processing methods were based on the “chi square” test and overall model fit logistic regression. **Results** – Atrial thrombotic complications were found in 7 (14%) patients with NVAF. These had, compared to patients without thrombotic masses, a mean CHA2DS2-VASc scale of 3 versus 2.76 ($p=0.05$), more frequently other atrial tachyarrhythmias ($p<0.01$), a more expressed inflammatory reaction ($p=0.02$), as well as a reduction of LVEF ($p<0.01$) and the peak left atrial appendage emptying velocity ($p<0.01$). **Conclusions** – In addition to a high CHA2DS2-VASc score, left anatomohemodynamic cardiac alteration, atrial arrhythmic complexity and background inflammatory status create conditions for high thromboembolic risk in patients with NVAF.

Keywords: non-valvular atrial fibrillation, cardiac thrombosis, left ventricular ejection fraction, inflammatory status, peak left atrial appendage velocity,

INTRODUCTION Atrial fibrillation (AF) represents the most usual sustained cardiac arrhythmia in adults, being at the same time the most frequent arrhythmic cause of hospitalization (1). In the presence of AF, the risk of thromboembolic complications – in the first place ischemic stroke – as well as the development of heart failure increases (biunivocal relationship).

Non-valvular atrial fibrillation (NVAF) evolves with a 5-fold increase in the risk of ischemic stroke. At present, NVAF benefits from the oral anticoagulant therapeutic contribution of both antivitamins K (AVK) and direct oral anticoagulants – non-vitamin K oral anticoagulants (NOAC), the therapy being monitored in relation to the CHA2DS2-VASc thromboembolic risk scale and the HAS-BLED hemorrhagic risk scale, according to current guidelines (2,3).

While the detrimental effects of NVAF on hemodynamics are well known and some factors that underlie the development of arrhythmia are also known (age, hypertension, diabetes mellitus, high body mass index, cardiomyopathy), no simple and reliable markers are available which allow accurately predicting the risk of arrhythmia as well as intracardiac (intraatrial) thrombosis.

Analyzed separately, inflammatory markers, natriuretic peptides and adiponectin – although recognized as risk markers – are not specific enough to be used in a simple predictive manner (4).

Atrial fibrosis – a revealing element of atrial myopathy in patients with NVAF – develops in the context of the activation of coagulation proteins (it is currently accepted that AF entails a state of hypercoagulability) and of a concomitant increase in collagen synthesis (5). In close relationship with structural remodeling in NVAF is ionic remodeling, which has a strong arrhythmogenic effect (6,7,8).

Atrial remodeling in patients with NVAF has been the object of many echocardiographic studies over the past 3 decades, some of which relatively recent (9,10).

An extensive comparative analysis of patients with NVAF, related to the presence or absence of extensive cardiac (atrial) thrombosis, conducted by using clinical, electrocardiographic, anatomohemodynamic cardiac (left) findings assessed by echocardiography, as well as by evaluating the behavior of usual blood screening markers of the inflammatory status, was the object of the current research.

Material and methods

The studied cases were included in a retrospective observational study, performed by the anonymous analysis of the medical record documentation in the period March 2019 – February 2020 in the Clinic of Cardiology of the Clinical Rehabilitation Hospital in Cluj-Napoca, in a group of 50 patients with NVAF. All patients were on treatment with oral anticoagulants, NOAC or AVK and underwent transesophageal ultrasound prior to cardioversion (CV), sinus rhythm (SR) or ablation therapy (AB). The relationship between oral anticoagulant treatment and NVAF was flexible, in accordance with the current guidelines (11,12).

The general design of the research was focused on two distinct subgroups of patients with NVAF, with and without current cardiac (atrial) thrombosis or spontaneous (echocardiographic) contrast. The study inclusion criteria were based on the (documented) current or past presence of NVAF.

The exclusion criteria referred in the first place to patients diagnosed with valvular AF (mechanical prostheses, moderate or severe hemodynamic mitral stenosis).

In the second place, patients with NVAF who had one of the following conditions over the last six months were not included in the analysis:

- acute myocardial infarction
- acute infections (with or without acute cardiac involvement)
- surgical interventions (mainly for neoplasms), associated or not with radiotherapy and/or chemotherapy

To evaluate the risk of initiation and development of the prothrombotic intracavitary cardiac status, we used in the research three categories of study methods by which we analyzed four categories of parameters: clinical, electrocardiographic, echocardiographic and biohumoral blood parameters.

This clinical population study aimed to evaluate the demographic data (mainly patients' age and sex), history of stroke, as well as peripheral ischemic embolic events and NYHA classification. Based on the data collected from each patient, we calculated the scores of CHA2DS2-VASc thromboembolic risk and HAS-BLED hemorrhagic risk. The means of these two scores were analyzed comparatively in the two subgroups of patients with NVAF. In the clinical study, we also monitored the possible individual presence of a gastrointestinal and/or hepatic disease with a risk of hemorrhagic events, as well as of other medication, possibly interfering with the oral anticoagulant treatment. The patients were enrolled individually taking into consideration the type of NVAF, clinically defined as a first episode, paroxysmal (with or without recurrences), persistent (with or without recurrences), persistent in the long term, and permanent, according to current guidelines. In the clinical study, we

also analyzed the conventional electrocardiographic examination of all patients (single or repeated), as well as Holter electrocardiographic monitoring (performed in some patients), in order to evidence other potential, clinically suggested atrial tachyarrhythmias, alongside or in association with NVAF.

The analyzed blood (laboratory) examinations referred on the one hand to the functional biochemical hepatorenal status and on the other hand, to the possible presence of a background inflammatory status of the patients, supported by the usual screening examinations – ESR, CRP, fibrinogen, uric acid – those with pathological values (between 1-4) being retained, without aiming to extend this objective by using much more sensitive biomarkers.

The echocardiographic examination of patients with NVAF was aimed in the first place at quantifying the anatomohemodynamic cardiac (mainly left) status with focus on the left atrial cavity size, on the main morphofunctional parameters of the left atrial appendage (LAA), as well as the left ventricular ejection fraction LVEF. In the second place, we monitored the possible presence of thrombotic cavity masses and/or the spontaneous contrast (SC) image, in the given arrhythmic context. We used the data obtained from transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE). We assessed the values of the left atrial (LA) telesystolic diameter (mm), LAA emptying velocity (m/sec) – LAA Vmax –, LAA opening (cm) – LAAO –, LVEF values (%), all this alongside the topography of the thrombotic intracavitary masses or the SC image.

Statistical analysis

For statistical processing, based on the data of the investigated patients – data initially collected in EXCEL format –, the second storage file (“database”) processed in Stat view format was created. To compare the parametric variables, the Student t test was used, with the significance level set at $p \leq 0.05$. The measurement of the “association”, among categorical variables was performed with the “chi square” test (χ^2), the significance of the association being similar to that for p values < 0.05 .

The correlation of two parametric variables such as LVEF, of the values of the studied parameters in LA and LAA, of thromboembolic and hemorrhagic risk scales as well as inflammation biomarkers (IFBM) was expressed by means of Pearson's correlation coefficient or r. The correlation was considered significant at $p < 0.05$. The correlation of non-parametric values (e.g. the clinical type of NVAF versus NYHA class) was expressed using Spearman's correlation coefficient, with the same significance value of $p < 0.05$. In the categories of parametric as well as non-parametric variables, to express the influence of a variable considered “independent” (predictive factors) on other variables considered

“dependent” (outcome variables), the simple and multiple linear regression model was used, the correlation, regression coefficients and the intercept being interpreted in the spirit of statistical requirements, according to the accepted level of significance (13). The numerical categorical parameters with statistical significance underlying multivariate analysis were expressed distinctly, but also synthetically (multivariate score) using ROC curves. Statistical analysis was based on the IBM SPSS software, version 22.

Results

Of the 50 patients with NVAf, 7 (14%) patients had, in a cumulated manner, an echocardiographic image of cardiac thrombosis (CT) – 6 patients, and spontaneous contrast (SC) – one patient. The thrombotic cavitary masses were distributed as follows: LAA – 3 patients, right atrium (RA) – 2 patients, LA – 1 patient. The SC image was also found in LA.

The comparative evaluation of clinical, electrocardiographic, echocardiographic, biohumoral blood parameters of inflammation and statistical analysis, using the Student t test, in patients with NVAf with and without CT/SC are shown in Table 1.

The mean age of patients with NVAf and thrombotic cardiac complications was 65.28 ± 7.8 years, compared to those without these complications (62.06 ± 9.5 years), a statistically insignificant difference ($p=0.31$).

Intracardiac thrombotic /SC masses were found in 5 male patients and 2 female patients with NVAf, with a similar percentage distribution of men in the group with CT/SC (71.42%) and without CT/SC (62.76%).

The functional cardiac behavior expressed by NYHA classes in patients with NVAf with and without CT/SC is also of interest. If in the first situation, 85.72% of the patients were assigned to NYHA classes II and III (distributed in equal proportions in these classes) and the rest of 14.28% belonged to NYHA class I, in the second situation NYHA class I included 58.13% of patients, the rest being distributed in NYHA classes II and III.

Patients with NVAf and CT/SC have a history of cumulated thromboembolic cerebral or peripheral events 6 times more frequently than those without current CT/SC, the difference being statistically significant for AVK ($p=0.02$).

In 4/5 of patients with NVAf – both in the group with and without CT/SC – the clinical types of AF, found in similar proportions, were represented by paroxysmal-recurrent and persistent AF.

Of all patients with NVAf, 11 (22%) patients had associated intermittent atrial flutter (AFL) and/or focal atrial tachycardia (FAT).

An important difference of the subgroups of patients with NVAf, in relation to the presence/absence of CT/SC, is the association of other atrial tachyarrhythmias (AFL,

FAT) in a much higher percentage in the first situation (85.71%) compared to the second (11.62%) ($p<0.01$).

The cardiogenic substrate of NVAf was dominated by ischemic heart disease (IHD) in over $\frac{3}{4}$ of the cases, in both groups of patients (with and without CT/SC).

High values of the usual inflammation biomarkers (IFBM) evaluated in all patients with NVAf and CT/SC were also found in a high percentage in patients without CT/SC, the difference being however statistically significant ($p=0.02$).

Oral anticoagulation in patients with CT/SC was dominated by the use of AVK. This was performed in 71.42% of the patients compared to patients with NOAC (28.56%), while in patients without CT/SC, the percentages of AVK (51.16%) and NOAC (48.84%) were relatively similar.

The CHA2DS2-VASc thromboembolic risk score in both groups of patients with NVAf ranged between 1-5, having a slightly higher mean value in the subgroup of patients with CT/SC – 3 – compared to patients without CT/SC – 2.76, reaching the level of statistical significance ($p=0.05$).

The HAS-BLED hemorrhagic risk score had a slightly higher mean value in the case of patients with NVAf and CT/SC, compared to those without thrombotic complications (1.85 versus 1.72).

The analysis of echocardiographic anatomohemodynamic and functional parameters of the left heart provided interesting results regarding patients with and without CT/SC. The mean values of the LA telesystolic diameter, slightly increased compared to the upper limit of normal, were similar in the two subgroups (42.42 versus 43 mm). However, the considerable decrease of the mean LAA Vmax value (0.31 m/sec) in patients with CT/SC, compared to the mean value of 0.59 m/sec found in patients without CT/SC, highly statistically significant ($p<0.01$), is of interest. In the same line falls the decrease in the mean LAAO values in patients with CT/SC compared to those without CT/SC, without reaching the threshold of statistical significance.

Extremely relevant among echocardiographic parameters is the mean LVEF value, considerably decreased in patients with NVAf and CT/SC (42%), compared to the mean value of patients without CT/SC (51.93%) ($p<0.01$).

The study of the correlations between two parametric values that reached the threshold of statistical significance, using Pearson's correlation coefficient or r , expressed a variation in the same direction (direct correlation) when analyzing the behavior of LAA Vmax (m/s) versus LVEF (%) (Figure 1).

We found a significant indirect correlation between IFBM and LVEF (Figure 2), LAA Vmax (m/s) respectively (Figure 3).

In univariate analysis, the impact on thrombogenesis/thromboembolism – as an endpoint – of LAA Vmax, LVEF and IFBM is found by testing the sensitivity and specificity of ROC curves, illustrated in Figure 4.

The multivariate analysis of prothrombotic/thromboembolic risk – according to the mathematical model of logistic regression adapted to the studied cases – allowed including maximum 5 variables of the group of those with certain statistical significance. The representation of the 4 categories of studied parameters (clinical, electrocardiographic, echocardiographic, blood IFBM) was taken into consideration. For clinical parameters, we chose to include the history of thromboembolic events (stroke), over the CHAD2DS2-VASc scale (due to the strength of statistical significance, more obvious in the first situation). Thus, the logistic regression mode included the personal history of thromboembolic events, LAA Vmax and LVEF, arrhythmic complexity (instability) defined by the presence of other atrial arrhythmias, in addition to atrial fibrillation and usual inflammation IFBM. The LAA Vmax – atrial arrhythmic complexity (instability) pair was detached, reaching each a final p value = 0.04. The details of mathematical-computer processing are illustrated in Table 2.

The complete unfolding of the mathematical logistic regression model, in a synthetic form, of prothrombotic/thromboembolic risk in the studied cases with NVAF is also found in the multivariate risk score, illustrated in Figure 5.

Last, but not least, hemorrhagic complications, absent in patients with NVAF and CT/SC, were found in 13.95% of patients without CT/SC, being represented by ecchymoses, epistaxis, gingivorragia, macroscopic hematuria.

Discussions

The thrombogenic/thromboembolic context in the analyzed NVAF cases was assessed using four categories of parameters. These were clinical, electrocardiographic, echocardiographic and biohumoral blood parameters. For clinical parameters, we analyzed the CHA2DS2-VASc thromboembolic risk scale, as well as the presence of personal thromboembolic history. Electrocardiographically, by conventional monitoring we evaluated atrial arrhythmic complexity (instability), retaining the presence of other atrial tachyarrhythmias alongside atrial fibrillation, at various succession moments. Echocardiographically, we assessed the behavior of some anatomohemodynamic parameters (of the left heart), focusing on LA, LAA Vmax, LAAO, LVEF, alongside the presence of intracardiac thrombotic masses and/or SC appearance. For the usual blood screening biomarkers of inflammatory status, we

analyzed the behavior of ESR, CRP, fibrinogen and uric acid.

NVAF is an important condition of thromboembolic risk with a cardiac starting point. The presence of thrombosis located in LA increases the risk of stroke 2.5-3 times (14). This requires permanent anticoagulation of patients with NVAF. About one fifth of the causes of ischemic stroke are based on the cardioembolic mechanism (15). AF is known to be the most frequent cause of cardioembolic ischemic stroke (16). Research over the past decade has highlighted the fact that excessive extrasystolic supraventricular ectopic activity is correlated with a high risk of AF and stroke (17). At the same time, it was emphasized that LA can be a source of thromboembolic ischemic stroke secondary to atrial myopathy, even in the absence of AF (18, 19, 20). Currently, the idea is accepted that if after ischemic stroke the presence of frequent atrial extrasystoles is found, this is associated with atrial remodeling and dysfunction, revealing elements of early left atrial remodeling (21). Furthermore, the increase in LA volumes – an aspect observed in our cases as well – and the alteration of LA function are associated with a decrease in the LAA emptying velocity, which we also found in our cases, predominantly in NVAF cases that developed thrombosis located in LA, LAA respectively.

The identification of the intermittent presence, in the context of NVAF, in our study, in a proportion higher than 85% of other atrial tachyarrhythmias (AFL, FAT, independent or associated) is an argument for the presence of atrial remodeling in the group of patients who developed CT and central or peripheral cardioembolic events.

Atrial remodeling in patients with NVAF approached by echocardiography is considered not only through the morphological component – focused on LA size – but also through the functional component. The integrated approach of these 2 components underlay the definition of the concept of atrial remodeling (22). This is a dynamic process, in which atrial fibrosis, contractile status alteration, inflammation, fat infiltration, ischemia and ion channel dysfunction with the generation of electrical instability, the main actor being the calcium ion, play a role (23). The behavior of the right atrium (RA) in patients with NVAF was also monitored, which opened the way to the concept of biatrial remodeling in patients with NVAF (24).

In patients with NVAF, high LA values associated with the arrhythmic context and stasis represent a triad of prothrombotic intracavitary risk.

TEE, complementing the findings of TTE, provided in TM and two-dimensional modes, has a major contribution to the anatomohemodynamic evaluation of LA and LAA, offering significant diagnostic elements, both regarding prothrombotic cavitory risk in patients

with NVAF and the diagnosis of developed intracavitary thrombotic masses. TEE allows an accurate evaluation of the LA surface (25). In LAA, using TEE, biphasic pulsed Doppler flow is recorded (positive flow meaning emptying and negative flow being recorded during filling). An emptying velocity value <0.25 m/s shows the presence of a LA with thromboembolic arterial risk. The normal velocity of LAA flow is >0.4 m/s. Values lower than $0.20\text{--}0.25$ m/s are considered to have the significance of major cardioembolic risk. In our cases with NVAF who developed CT, the mean LAA emptying velocity value was 0.31 m/s, lower than in patients with NVAF without thrombotic masses of LA or LAA, where the mean value of this parameter by TEE was 0.59 m/s. The opening of LAA was also evaluated by TEE; the mean value in patients with NVAF and CT was 0.97 cm, compared to 1.52 cm in patients with NVAF without CT. The presence of SC and sludge in LA and LAA is also evidenced using TEE. The decrease of LVEF $<50\%$ correlated with the mentioned LA and LAA abnormalities significantly increases cardioembolic risk in patients with NVAF. TEE also allows assessing the behavior of thrombotic masses formed in LA or LAA.

TTE examination was also focused on the evaluation of LVEF. For each patient, the mean value of three LVEF determinations, in the arrhythmic context of NVAF was retained. The assessment of the contractile status of the left ventricle, starting from its importance in the determinism of left ventricular systolic performance in patients with NVAF, adds to the value of the LA cavity size an additional pathogenic significance in the determinism of cardioembolic risk in patients with NVAF.

In relation to the thrombogenic process, in patients with NVAF, assessing their background inflammatory status is also of interest, as it is known that prothrombotic status and thrombogenesis are closely related to IF and endothelial dysfunction. In our cases, we analyzed the presence of IFBM evaluated as part of the routine screening (ESR, CRP, fibrinogen, uric acid). The numerical presence, isolated or associated in various combinations, of their pathological values was 100% in patients who developed thrombotic masses and 88.37% in those without thrombotic masses. In addition to this general context, in patients with NVAF and intraatrial/or LAA thrombosis, the presence of altered anatomohemodynamic parameters such as the reduction of LVEF, LAA Vmax, atrial dilation increases thrombogenic and cardioembolic risk (26,27).

The predictors of stroke in NVAF in our cases are represented by LA dilation, the presence of the SC image in LA, the presence of thrombosis in LAA (half of the cases with thrombi are located here), and the decrease in LAA Vmax to a value of 0.31 m/s and in LVEF, along

with an increase in atrial electrical instability through the increase of arrhythmic complexity at atrial level.

Relevance and limitations of the study

The approach through a multimarker analysis of thromboembolic risk in NVAF, by evaluating some clinical parameters (clinical type of AF, NYHA class, presence of thromboembolic history, evaluation of thromboembolic and hemorrhagic risks, by specific risk scales), echocardiographic anatomohemodynamic cardiac parameters – mainly of the left heart – in addition to the diagnostic impact of intracardiac thrombotic masses, electrocardiographic parameters of complex atrial arrhythmic instability, as well as taking into consideration a possible contributive thrombogenic quota of patients' background inflammatory status in a retrospective evaluation over one year represents an integrated approach, in a personal concept, of the research. Certainly, this intention leaves the way open for future research, especially by integrating the contribution of a more extensive study on inflammation, its interrelation with hemodynamic and oxidative stress in patients with NVAF, resulting in the diagnostic optimization of the thrombogenesis process, as well as the efficiency of oral anticoagulant therapy.

The limitations of the study are represented in the first place by a relatively reduced number of cases, given the study inclusion criteria for patients with NVAF (exclusion of patients with valvular F) in the year preceding the COVID-19 pandemic.

A second limitation of the study is using, with the aim of unifying the collected data – within the anatomohemodynamic cardiac parameters evaluated by echocardiography – the telesystolic diameter of LA, less reliable than its area or especially its volume. We used LA diameter because this was found in all echocardiographic results, the other two atrial parameters being mentioned sporadically and separately.

Conclusions

The mean CHA₂DS₂-VASc value, statistically significantly higher in patients with NVAF and intracardiac thrombotic masses compared to that of patients with NVAF without intracardiac thrombotic masses, confirms the value of element revealing thromboembolic risk of this scale. In the given context, the alteration of left cardiac anatomohemodynamic status, associated with atrial arrhythmic complexity, occurring on an inflammatory background, forms a triad of increased thromboembolic risk in patients with NVAF.

Abbreviations

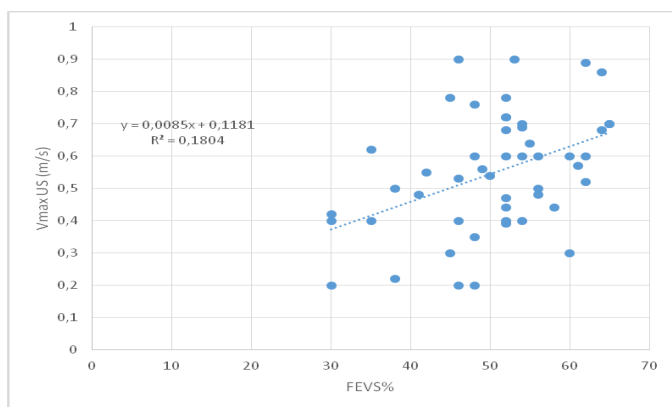
AB = ablation, RA = right atrium, LA = left atrium, AVK = antivitamins K, IFBM = inflammatory biomarkers, CF = control of frequency, IHD = ischemic heart disease, SC = spontaneous contrast, CV = cardioversion, LAAO = left atrial appendage opening, TEE = transesophageal echocardiography, TTE = transthoracic echocardiography, AF = atrial fibrillation, NVAF = non-valvular atrial fibrillation, LVEF = left ventricular ejection fraction, AFL = atrial flutter, IF = inflammation, NOAC = non-vitamin K oral anticoagulant,

RF = radiofrequency, SR = sinus rhythm, CT = cardiac thrombosis, emptying velocity
LAA = left atrial appendage, LAA Vmax = left atrial appendage

Table 1. Structure and main characteristics of the subgroups of patients with NVAf, with and without cardiac thrombosis or spontaneous contrast (echocardiographic)

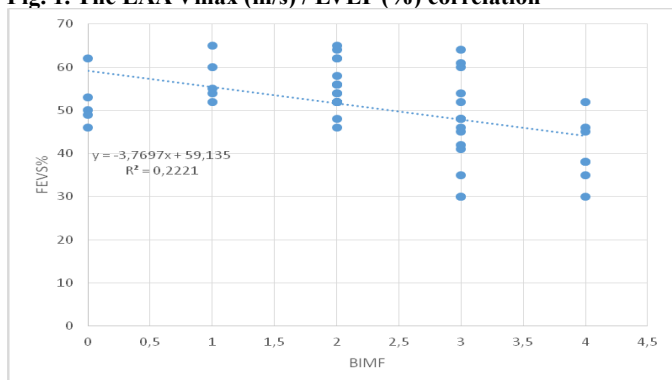
Total number of patients with NVAf (n=50)	NVAf with CT/SC (n=7)	NVAf without CT/SC (n=43)	P
Age (years)	65.28±7.8	62.06±9.5	0.31
Men (n%)	5/7(71.42%)	27/43(62.76%)	0.99
NYHA class			
I	1/7(14.28%)	25/43(58.13%)	0.08
II	3/7(42.86%)	14/43(32.55%)	0.92
III	3/7(42.86%)	4/43(9.32%)	0.07
Thromboembolic history			
Stroke	4/7(57.14%)	5/43(11.62%)	0.02
SE	1/7(14.28%)	0/43	0.48
NVAf - type			
Paroxysmal	1/7(14.28%)	3/43(6.97%)	0.48
Paroxysmal-recurrent	3/7(42.86%)	18/43(41.86%)	0.72
Persistent	3/7(42.86%)	17/43(39.53%)	0.80
Persistent-recurrent	0/7	3/43(6.97%)	0.45
Permanent	0/7	2/43(4.65%)	0.50
AF+other atrial arrhythmias	6/7(85.71%)	5/43(11.62%)	<0.01
NVAf substrate			
IHD	5/7(71.42%)	35/43(81.39%)	0.92
HC	1/7(14.28%)	3/43(6.97%)	0.93
TCM	1/7(14.28%)	2/43(4.65%)	0.89
IDCM	0/7	1/43(2.32%)	0.60
ASD	0/7	1/43(2.32%)	0.60
VSD	0/7	1/43(2.32%)	0.60
Oral anticoagulation			
NOAC	2/7(28.56%)	21/43(48.84%)	0.56
AVK	5/7(71.42%)	22/43(51.16%)	0.56
Blood IFBM	7/7(100%)	38/43(88.37%)	0.02
CHA₂DS₂-VASc score			
1	0/7	9/43(20.93%)	0.68
2	3/7(42.86%)	10/43(23.22%)	0.53
3	2/7(28.56%)	11/43(25.58%)	0.77
4	1/7(14.28%)	8/43(18.60%)	0.80
5	1/7(14.28%)	5/43(11.62%)	0.67
Mean of the CHA ₂ DS ₂ -VASc scale	3	2.76	0.05
HAS-BLED score			
1	1/7(14.28%)	18/43(41.86%)	0.33
2	6/7(85.71%)	18/43(41.86%)	0.08
3	0/7	7/43(16.28%)	0.90
Mean of the HAS-BLED score	1.85	1.72	0.69
Echocardiographic parameters			
LA (mm)	42.42	43	0.76
LAA Vmax (m/s)	0.31	0.59	<0.01
LAAO (cm)	0.97	1.52	0.21
LVEF (%)	42	51.93	<0.01
Treatment			
CV	0/7	19/43(44.18%)	0.12
AB	0/7	20/43(46.51%)	0.10
CF	7/7(100%)	4/43(9.31%)	<0.01
Hemorrhagic complications	0/7	6/43(13.95%)	0.097

Data represent the mean ± SD, number and percentage of patients (%). NVAf, non-valvular atrial fibrillation; IHD, ischemic heart disease; HC, hypertensive cardiomyopathy; TCM, tachyarrhythmic cardiomyopathy; IDCM, ischemic dilated cardiomyopathy; ASD, atrial septal defect; VSD, ventricular septal defect; IFBM, inflammation biomarkers; CV, cardioversion; AB, ablation; CF, control of frequency; LA, left atrium; LAA, left atrial appendage; LVEF (%), LV ejection fraction; LAA Vmax, LAA emptying velocity; LAAO, LAA opening; SC, spontaneous contrast; CHA₂DS₂-VASc, thromboembolic risk score; HAS-BLED hemorrhagic risk score; ES, systemic embolism; CT, cardiac thrombosis; SC, spontaneous contrast; NOAC, non-vitamin K antagonist oral anticoagulants; AVK, antivitamins K; p>0.05, statistically insignificant (NS).



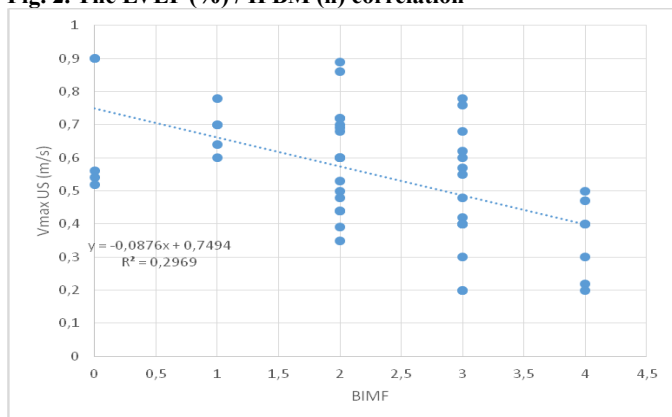
$r=0.424744$ $p=0.02$

Fig. 1. The LAA Vmax (m/s) / LVEF (%) correlation



$r= -0.471248$ $p=0.01$

Fig. 2. The LVEF (%) / IFBM (n) correlation



$r= -0.54486$ $p<0.01$

Fig. 3. The LAA Vmax (m/s) / IFBM (n) correlation

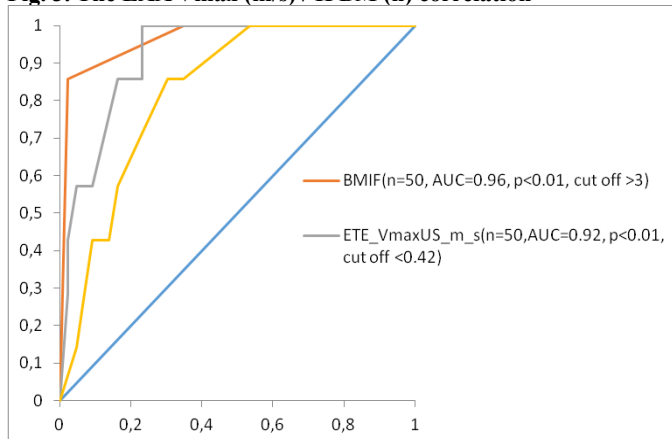


Fig. 4. ROC curves of IFBM, LAA Vmax and LVEF in relation to thrombogenic/thromboembolic risk in patients with NVAf

Table 2. Multivariate analysis, by logistic regression, of prothrombotic/thromboembolic risk in the studied patients with NVAf

Logistic regression

Overall Model Fit	
Null model -2 Log Likelihood	40.496
Full model -2 Log Likelihood	10.208
Chi-squared	30.288
DF	2
Significance level	$P < 0.0001$
Cox & Snell R^2	0.4543
Nagelkerke R^2	0.8185

Coefficients and Standard Errors				
Variable	Coefficient	Std. Error	Wald	P
TEE_LAA Vmax m s	-25.49805	12.85457	3.9346	0.0473
Other atrial arrhythmias n	6.42251	3.13857	4.1874	0.0407
Constant	5.6994			
Variables not included in the model				
IFBM				
TTE_LVEF%				
APP2_n				

Odds Ratios and 95% Confidence Intervals		
Variable	Odds ratio	95% CI
TEE_LAA Vmax_m_s	8.44E-12	9.64521E-023 to 0.7385
Other atrial arrhythmias_n	615.5475	1.3112 to 288976.6688

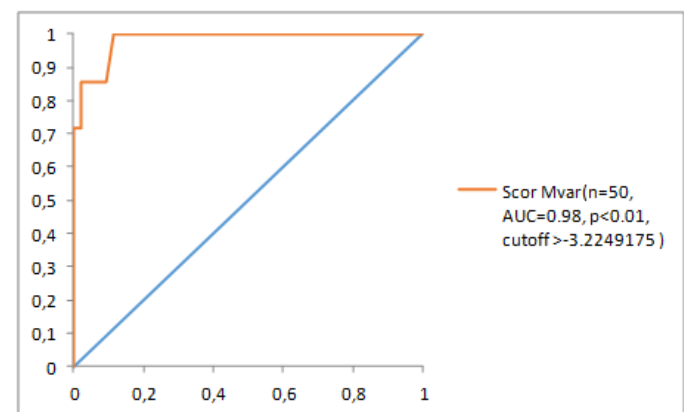


Fig. 5. Multivariate prothrombotic/thromboembolic risk score of the studied patients with NVAf

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Improving functional and motor capacity through means/resources and methods specific to aquatic activities

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Abstract

Introduction. Exercise programs in the aquatic environment have as their main objective the improvement and maintenance of physical capacity/ capability, these being in continuous development and diversification. Water exercise amplifies the effects of general physical exercise, by allowing a more precise control over the movement of each body segment and of the body as a whole. The aquatic environment offers a number of beneficial effects compared to ones offered by the terrestrial environment. The benefits obtained through the aquatic activities are fundamental and are reflected throughout the entire body including both motor, functional and aesthetic level.

Material and method. The objective of this study is represented by the identification of new forms of physical exercise that will increase the motor's capacity. In order to achieve this goal, several methodological requirements were met, such as: successive engagement of the joints and muscle groups in effort (starting with the neck's muscles, shoulders, arms, torso and legs, simultaneously with scapular-humeral joints, spine and coxo-femoral joints and legs), the gradually usage of exercises, starting with the most basic and then increasing the complexity of the exercises, the usage of the accessible exercises in the beginning of the training, executed with high amplitude and reduced speed, focusing on the correctness of the execution, the selection and the adequate/ appropriately usage of the initial positions according to the subject's particularities and the shape/form of the exercise, the optimal control of the effort, achieved through a number of iterations, optimal execution time and breaks, the sets of general physical exercises will consist of sets of 8-12 exercises/reps, the principle of symmetry in the execution of the exercises has to be respected, the continuity of practicing a set of exercises for 6 to 8 consecutive lessons, the recommended work method is fragmented-imitative, efficiently combining the explication with the demonstration, the number of repetitions and the movement's correction.

Results and discussions. Analyzing results obtained after the evaluation, we have noticed significant growth in the functional and motor capacities.

Conclusions. The systematization of water activities on objective criteria effectively contributes to their knowledge, while allowing them to be included in the spectrum of recreational, sporting, relaxing or therapeutic activities.

Keywords: *aquatic activities, physical exercise, evaluations,*

INTRODUCTION

The aquatic environment offers a number of opportunities compared to the terrestrial one [1]. The benefits obtained from performing aquatic activities are fundamental and are reflected on the whole body both motor, functional and aesthetic [8,11].

Effort capacity is defined as the ability of an organism to produce as much mechanical work as possible and to maintain it for as long as possible. In other words, the more effort a person can sustain in terms of intensity and duration, the better his capacity for effort is [15]. The improvement of this parameter can be achieved through training, this being in fact, along with the series of technical-tactical skills, the final goal of the training process on which sports performance depends directly [6,7].

The aims of the study is improve somatic parameters, functional and motor capacity by implementing exercise

programs performed in water by people aged between 40 and 55 years [2,5]. In establishing the hypothesis we started from the assumption that performing water activities by people aged between 40 and 55, will improve their motor and functional capacity, compared to activities in the terrestrial environment (physiotherapy room) [9].

General objectives:

- improving somatic parameters;
- improving functional capacity;
- achieving an optimal psycho-physical balance;
- awareness of the advantages and characteristics of performing activities in the aquatic environment;
- diversification of exercise programs [10].

The stages of this research focused on the following aspects:

- establishing study groups;

- periodizing the research and establishing the conditions for conducting the study;
- establishing specific training objectives;
- selecting and elaborating the means of action specific to aquatic activities;
- elaboration of aquagym programs on difficulty levels;
- establishing evaluation tools and rules [13].

Matherial and Methods

The study was conducted over a period of 3 months, and consisted of 3 sessions per week, with a duration of 50 minutes.

The research included a number of 45 subjects, organized in three groups: two experimental groups and a control group. The experimental groups were formed each of 15 subjects aged between 40-45 years, as follows [12]:

- the first experiment group (E1), consisting of subjects, who performed a specific program of aquagym exercises;
- the second experiment group (E2), consisting of patients who practiced a specific program of aquagym exercises using various devices such as dumbbells or steppers;

The control group (C) consisted of patients aged between 40 and 55 years who performed ground exercise program. The research included two tests, a initial test and a final test, arranged as follows:

- initial testing;
- implementation of the proposed programs of aquatic activities and those in the gym;
- final testing [14].

Aquagym operational programs were differentiated on three levels: beginner, intermediate and advanced, depending on the degree of difficulty, intensity and complexity of the drive systems [4]. Measurements and tests applied in research: abdominl muscle strenght, strenght of the back muscle, trunk mobility, unipodal balance test [3].

Results and Discussion

Abdominal muscle strenght. Following the research approach, by calculating the difference of the arithmetic mean between the two tests, the control group registered a progress of only 1.39 executions, a value lower than those performed by the experimental groups. The results are presented in Fig.1.

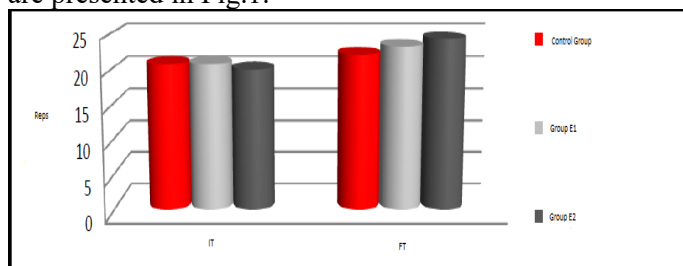


Fig.1. Graphical representation of aritmetic means regarding abdominal muscle strenght

In the experimental groups, the differences were thus the E1-Aquagym group registered a value of the average difference of 2.53 executions and the E2-Aquagym group of 4.44 executions. Referring to the qualifying-value correspondence grid, to the abdominal test, women, it is observed that at the initial testing all the groups involved in the experimental research, are at the weak level. After carrying out the programs within the proposed activities, the control group and the experimental group E1-Aquagym, remain at the same level of appreciation, registering a slight improvement of the results but below 23 executions, while the experimental group E2-Aquagym obtained more significant progress, climbing the appreciation grid to a below-average level, with an average value of 24.43 executions.

By applying the t-Student test and calculating the p correlation index, it highlights the following compared to the control group: the average performance obtained in the initial test differs significantly from the average performance obtained in the final test in the E1-Aquagym experimental sample and strongly significant in the E2 experimental group-Aquagym, which supports the acceptance of the research hypothesis.

Strenght of the back muscle. Following the statistical-mathematical analysis of the individual values, all the samples of the research at the strength test of the back muscles registered obvious progress between the two tests, but the progress of the experimental groups was superior to the control one.

The E1 – Aquagym experiment group obtained at the initial testing an arithmetic average of 28.87 executions, and at the final testing 32.03 executions, with average progress of 3.18 executions (Fig.2.). The E2-Aquagym experiment group recorded arithmetic mean the difference between tests of 4.64 executions, resulting from the value of the average of the initial test of 27.98 executions and that of the arithmetic mean of the final test of 32.43 executions.

The arithmetic mean at the initial testing of the control group was 28.94 executions, and at the final testing of 30.47 executions, the difference of the averages being 1.63, lower progress obtained compared to the two experimental groups (Fig.2.).

The analysis performed with the t-Student test for the paired samples highlights between the control group and the E1-Aquagym experiment group, a statistically insignificant difference $p < 0.062$ being greater than 0.05, which requires the acceptance of the null hypothesis.

In the case of the comparative analysis between the control group compared to the E2-Aquagym experiment group, the t-Student test shows a statistically significant difference, $p < 0.005$, being much smaller than 0.06, which determines the acceptance of the alternative hypothesis.

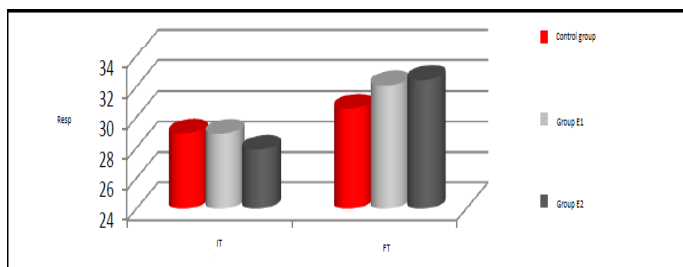


Fig.2. Graphical representation of arithmetic means regarding the strength of the back muscles

Trunk mobility. The E1 experiment group, which performed the specific activity of aquagym, obtained at the initial test a value of the arithmetic mean of 2.44 cm, and at the final test 5.06 cm, with a difference of the averages of 2.57 cm (Fig.3.).

The E2 experiment group obtained an average value of 2.32 cm at the initial test and at the final test 6.02 cm, the progress being 3.67 cm, the highest compared to other research samples (Fig.3.).

The control group obtained at the initial testing an average value of 2.54 cm, and at the final testing of 3.99 cm, with average progress of 1.47 cm, lower than the progress of the experimental groups (Fig.3.).

The progress of the E1 group compared to the control group was 1.14 cm, between the E2 group and the control group of 2.27 cm, and between the E1 and E2 groups of 1.12 cm.

The results of applying the t-Student test, for paired data, are not significant, $p > 0.05$. These effects are explainable because mobility develops relatively hard compared to the age of the participants. The null hypothesis is accepted.

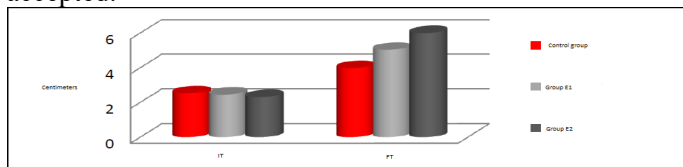


Fig.3. Graphic representation of trunk mobility

Unipodal balance test. Following the statistical analysis, all samples show increases in the time of maintaining the unipodal balance position, for both legs, at the final test compared to the initial one, highlighted by the graphical representation in figures no. 4, 5. The control group recorded a difference in the arithmetic mean between the tests, in the unipodal balance test on the left leg of 11.52 sec., And on the right leg of 12.62 sec (Fig.4.).

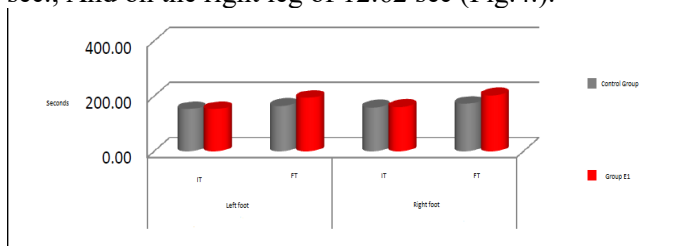


Fig.4. Graphical representation of the unipodal balance E1

The E1-Aquagym experimental group recorded a progression of arithmetic means between tests on the left leg of 40.84 sec. and 41.86 sec on the right leg (Fig.4.). The greatest progress in this test was registered by the experimental group E2-Aquagym, as follows: on the left leg the difference of the averages between the two tests was 67.73 sec., And on the right leg 68.51 sec (Fig.5.).

Following the analysis of the individual results obtained at the initial and final testing, regardless of the sample, it is observed that the values obtained are higher for the right leg. By statistical analysis, all the values of the significance threshold at the initial test differ significantly from the average performance obtained at the final test in the case of the experimental sample E1-Aquagym and strongly significant in the experimental group E2-Aquagym, compared to the control group.

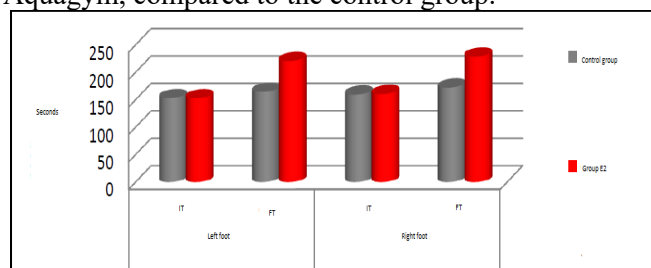


Fig.5. Graphical representation of the unipodal balance E2

ANTHROPOMETRIC PARAMETERS

Body weight. The differences between the arithmetic means in the research, highlight the following weight loss according to table no. 40, as follows: the control group of 0.985 kg, the experimental group E1- Aquagym of 0.964 kg, and the experimental group E2 that performed the programs specific to the aquatic activity Aqua gym of 1.340 kg (Fig.6.).

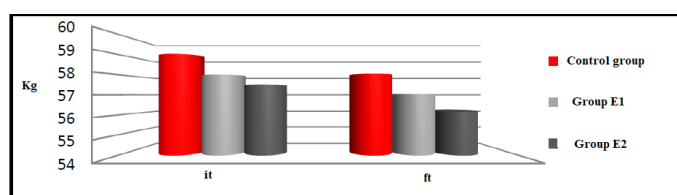


Fig.6. Graphical representation of arithmetic means of body weight

The results of applying the t-Student test, for paired data, are not significant, $p > 0.05$, in the case of the experimental group E1-Aquagym. The null hypothesis is accepted. For the E2-Aquagym experimental group compared to the control group, the statistical analysis calculated with the t-student test, indicates a significant threshold, $p < 0.018$, thus accepting the research hypothesis.

Body mass index. The E1-Aquagym experiment group obtained at the initial test a value of the arithmetic mean of 21.26, and at the final test 20.91, resulting in a difference of 0.35, falling on the assessment grid at the normal level both in the test initial as well as the final

one. The E2-Aquagym experiment group obtained arithmetic mean value of 20.76 in the initial test and 20.26 in the final test, the difference being 0.5, also falling within the normal level of the index. lean body mass (Fig.7.).

The control group obtained an average value of 21.03 at the initial test, and 20.66 at the final test, with a difference of 0.37, within the normal weight. There was an average BMI difference of 0.14 between the experimental groups, and between the E1 and the control group of -0.2, and between the E2 and the control group of 0.16.

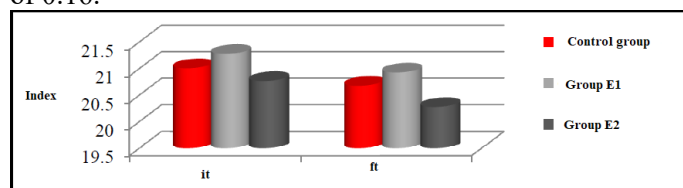


Fig.7. Graphical representation of the arithmetic means of the body mass index

The application of the t-Student test, to the control group and the E1-Aquagym experiment group, shows a statistically insignificant difference, which means that the null hypothesis is accepted. Following the application of the statistical analysis of the t-Student test between the control group and the experiment group E2- Aquagym, there is a statistically significant difference, $p < 0.012$ lower than $p < 0.05$, which determines the acceptance of the alternative hypothesis.

Conclusions

The systematization of water activities on objective criteria effectively contributes to their knowledge, while allowing them to be included in the spectrum of recreational, sporting, relaxing or therapeutic activities. Introduction of a new activity, with a specific, innovative methodology called aqua gym, is part of the modern development and research trends of the activities domestically and internationally. Studying the development of motor skills through aquatic recreational activities, it is a modern trend, which in general can contribute to improvement human performance.

Author contributions.

All the authors had the same contribution.

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The importance of association between sexsteroids deficiency, reduction of bone mineral density and falling risk in men with implications in medical rehabilitation

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Abstract

Introduction. Endocrino-metabolic rehabilitation represent one of the most complex sector in clinical medicine, regarding functional rehabilitation. Sex hormones deficiency plays an important role in the etiology of osteoporosis in men. At the same time, with age, the trophic role of androgens on muscle decreases and determines an increased frequency of falls. The objective of our study is to determine the association between sexsteroids deficiency, reduction of bone mineral density (BMD) and falling risk in men.

Methods. Our retrospective cross-sectional study included 146 men aged between 65–85 years with low BMD (study group) and 121 men with normal BMD (control group). The measurement of Total testosterone (Tt), free testosterone (Tf) and estradiol (E₂) serum levels was performed using the immunoassay or the immunoenzymatic methods. Femoral neck and lumbar spine BMD was determined using Dual-energy X-ray absorptiometry (DEXA). The risk of falls was assessed by Tandem Standing, Up & Go, Chair – Rising and walking speed tests.

Results. We found a significantly association between Tf and E₂ deficiency and low BMD (p=0.007). Also, in men with reduced BMD (study group) we observed significant lower levels of Tf (p<0.001) and E₂ (p=0.003) compared to control group. E₂ deficiency was associated significantly with low BMD and increased fall risk (p=0.001). At the same time the results highlighted significant lower levels of Tf in patients with BMD reduction and increased risk of falls (p=0.002). Tt deficiency was not associated with BMD reduction (p=0.088) or increased risk of falling (p=0.277).

Conclusions. This research revealed a significant association between male sexsteroids deficiency, low BMD and increase of falling risk, with implications in rehabilitation program. The risk of ostoporosis and for falling in man can be estimated by determining serum Tf and E₂ levels.

Keywords: *sexsteroids deficiency; bone mineral density; falling risk,*

INTRODUCTION

Osteoporosis and sarcopenia are common in elderly men causing frequent falls and disability. The role of sexsteroids deficiency on bone metabolism and physical activity in men is inconclusive. There are studies that highlight the association between sex hormone deficiency, bone mineral density (BMD) reduction and increased fall risk (1,2). The role of androgens versus estrogens in bone turnover regulation is not fully known in men. There are proofs to support the importance of androgens and estrogens in regulating bone turnover in men. Estradiol (E₂), derived from the conversion of testosterone under the influence of aromatase at target cells level (skin, fat, skeleton), helps to preserve bone health in men (3,4). Several data shows a connection between decreased serum testosterone levels with age and decreased muscle mass and strength. By reducing trophic role of androgens on muscle results limitation of physical activities and increased frequency of falls (5,6). The

influence of sex steroids on BMD and on falling risk has been less studied in Romanian males. Therefore our research targets to analyse the association between sexsteroids deficiency, reduction of BMD and falling risk in men.

Methods

We present a retrospective cross-sectional research for a four years period, which included 146 men (study group) diagnosed with osteoporosis or osteopenia by World Health Organisation (WHO) criteria for osteoporosis (7). According to the WHO the osteoporosis is defined if T score ≤ -2.5 SD and osteopenia with -2,5 SD < T score < -1 SD. The T score was assessed by dual-energy X-ray absorptiometry (DEXA). Also we included in statistical analyses a control group with 121 men with normal bone mineral density (T score ≥ -1SD). All this patients were evaluated after having given theirs informed consent. The age of men in the study population at baseline was

between 65 and 85 years. For both groups the exclusion criteria were inability to walk without assistance, any type of neoplasia, psychiatric diseases that can influence patients compliance and cognitive ability, dizziness, thyroid diseases, central nervous system medication, alcohol and tobacco use. The evaluation of the subjects involved performing anamnesis, physical examination, body mass and height. Body mass index (BMI) was calculated according to the formula body mass (kg) / height (m²) in subjects undressed and without shoes. For all patients BMD was evaluated at the lumbar spine and hip with a DEXA machine LUNAR DPX-NT densitometer (Medtel, Australia).

Blood samples were collected between 7.00 and 9.00 a.m. after an overnight bed-rest; last meal was on the proceeding day at 6 p.m. The centrifuged serum was stored at -20° C until examination. The hormonal evaluation - total testosterone (Tt), free testosterone (Tf) - were performed by electrochemoluminescence immunoassay (ECLIA). Estradiol (E2) serum concentration was determined by the immunoenzymatic method (ELISA - Enzyme-linked Immunosorbent Assay). For all this we used a COBAS 6000 analyzer (Roche Diagnostics, USA). Normal values of sex steroids are: Tt between 2,25 and 8,00 ng/ml, Tf between 5.472-41.76ng/L, E2 between 28.0-156 pmol/L. We considered sexsteroid deficiency the situation with Tt below 2.25 ng/ml, Tf below 5.472 ng/L and E2 below 28 pmol/L.

We evaluated the risk of falls in men from both groups using four tests considered as good independent predictors for falls. According to National Institute for health and Clinical Excellence (NICE) guidelines older people are considered vulnerable to risk of falling (8,9). We applied the gait and balance assessment by using following tests:

- a) „**Tandem Standing**” test evaluates the balance. The patient is asked to stand with the ankles closed for 10 seconds, than in half tandem 10 seconds to. After that the patient stands in tandem 10 seconds. Inability to stand in this position last at least 10 seconds indicates a high risk of falling.
- b) „**Up & Go**” test assesses the time that a person gets up from a chair, walk three meters, turn around, walk back to the chair, and sit down. During the test, the person is expected to wear their regular footwear and use any mobility aids that they would normally require. Values greater than 12 seconds represent a risk factor for falls.
- c) „**Chair – Rising global test**”. Tested person must rise 5 times from a chair with standard height of 45 cm without using arms. If the test is carried out more than 10 seconds or cannot be performed at all, the risk of falling is high.
- d) During the test for **normal walking speed assessment**, the patient is asked to walk normally. It

is determined the time necessary to walk a distance of 4 meters. Navigate to a distance less than 1m/s indicate an increased risk of functional decline and it is correlated with falls.

Time in seconds was measured for each test and each patient. It was considered an increased risk of falls in patients presenting recorded values above the normal range (8,9).

The Ethics Committee of the Academic Emergency Hospital of Sibiu accepted the study and encouraged the publication of results.

SPSS, version 18.0 (IBM-SPSS 18.0, Armonk, New York, USA) was used for statistical analysis. For statistical significance the value of p was set at p < 0.05. A t test (Student's t test) for continuous variables and chi-square tests for categorical variables were used to identify the association between the study variable. We also used Mann-Whitney test for comparing 2 groups. In tables 2 * 2 with ordinal / nominal data we used the Chi-square test.

Results

Our research data highlights that the mean age of patients enrolled in the study was 72.87 ± 5.09 years. We have not noticed statistically significant differentiation between study and control group regarding the age (study group 73.48 ± 5.160; control group 72.12±4.929; p=0.102) and BMI (study group 25.69±3.64; control group 25.79±2.68; p=0.800) of the patients (Table I).

The results revealed a significant lower mean value for BMD in study group (Lumbar BMD 0.91±0.068 g/m²; Hip BMD 0.80±0.07 g/m²) versus control group (Lumbar BMD 1.14±0.02 g/m²; Hip BMD 0.98±0.02 g/m²) for both places investigated namely the spine (p<0.001, r=0.85) and hip (p<0,001, r=0.82).

We found no statistically significant differences between groups (study group 3.98±1.41ng/ml and control group 4.34±1.35 ng/ml) regarding mean level of Tt (p=0.061). Regarding Tf levels, the results showed that they are significantly lower in study group (6.56±2.76 ng/L) versus control group (7.65±2.44 ng/L) (p<0.001, r=0.25). At the same time mean we observed significant lower levels of E2 in study group (38.35±16.60 pmol/L) comparing to control group (45.70±10.76 pmol/L) (p=0.003, r=0.18). The results presented prove that low BMD was significantly associated with low levels of Tf and E2. Low BMD and Tt were not associated.

The sexsteroids deficiency was considered if at least one sexsteroid was found below normal level. The results revealed this deficiency in 45.21% of patients with low BMD (66 patients from study group) and only in 24.8% of cases from control group (30 patients) (p=0.001).

The division of patients with lower Tt (study group: 22 patients, 15.1%; control group: 10 patients, 8.3%) or normal Tt (study group: 124 patients, 84.9%; control group: 111 patients, 91.7%) is not significantly different

among groups ($p=0.088$). Regarding Tf, lower Tf levels are more frequently (1.95 times) in study group (82 patients, 56.2%) comparing with control group (48 patients, 39.7%) ($\chi^2(1)=7.2$, $p=0.007$). Referring to E2, lower than normal levels are more frequently (6.88 times) in study group (52 patients, 35.6%) than in control group (9 patients, 7.4%) ($\chi^2(1)=7.2$, $p=0.007$). Presented results shows that low BMD was significantly associated with low TF and E2 levels.

The risk of falling assessed by 4 tests revealed significant differentiation between the two groups ($p<0.001$). Men with reduced BMD showed a higher risk of falls in comparison with the control group. The analyze of risk of falls in men included in both groups of this research revealed an increased risk of falling in 74.6% of patients (109 cases) from study group and in 59.5% of men (72 subjects) from the control group ($p=0.001$). For study group a 2.5 times increased risk of falling was observed, compared to control group, ($\chi^2(1)=11.05$, $p=0.001$) (Table I).

Parameter		Study group		Control group		p
Absolute frequency		146		121		
Increased fall risk	Yes	109	74.6%	72	59.5%	0.001*
	No	37	25.3%	49	40.5%	

* $p<0.05$ Statistically significant

Table I Falling risk in patients included in the research

Lower than normal categories of tandem standing test are more frequently (2.5 times) in the study group comparing with control group ($\chi^2(1)=11.05$, $p=0.001$). Higher than normal categories of Up & Go test and Chair rising test are more frequently (2.5 times) in the study group comparing to control group ($\chi^2(1)=11.05$, $p=0.001$). The frequency of categories of lower than normal walking speed were higher for study group compared to control group ($\chi^2(1)=181$, $p<0.001$) (Table II).

Test		Study group		Control group		p
Absolute frequency		146		121		
Tandem standing	Normal	37	25.3%	49	40.5%	0.001*
	Low	109	74.6%	72	59.5%	
Up & Go	Normal	37	21.0%	49	40.0%	0.001*
	High	109	79.0%	72	60.0%	
Chair rising	Normal	37	21.0%	49	40.0%	0.001*
	High	109	79.0%	72	60.0%	
Walk speed	Normal	38	26.1%	121	100%	<0.001*
	Low	108	73.9%	0	0%	

* $p<0.05$ Statistically significant

Table II The average time calculated for the tests performed for the two groups of patients

The average time calculated for each test performed was different for the two groups of patients ($p=0.001$) (Table III). Tandem standing is statistically significant lower in study group comparing with control group ($p<0.001$, $r=0.30$), size effect being considered medium. Up & Go is statistically significant higher in study group comparing with control group, ($p<0.001$, $r=0.30$), size effect being considered medium. Chair rising is statistically significant higher in study group in comparison with control group, ($p<0.001$, $r=0.30$), size

effect being considered medium. Walking speed is statistically significant lower in study group than in control group, ($p<0.001$, $r=0.58$), size effect being considered large.

Test	Study group	Control group	p
TANDEM STANDING (seconds)	9.19±2.37	10.48±2.26	<0.001*
UP AND GO (seconds)	14.68±2.54	13.13±1.87	<0.001*
CHAIR RISING (seconds)	12.89±2.49	11.36±1.86	<0.001*
WALK SPEED (seconds)	3.74±0.35	4.17±0.37	<0.001*

Values are expressed as mean ± SD;

* $p<0.05$ Statistically significant

Table III Mean value of gait and balance assessment tests in patients included in the research

Regarding the presence of sexsteroids deficiency a statistically significant difference has been found ($p=0.001$) in men with increased risk of falling compared with those without risk in both study group.

For the subgroup of patients with increased risk of falling, no statistically significant differentiation were revealed between study group and control group in terms of mean value of Tt ($p=0.465$) and E2 ($p=0.373$). Tf levels were statistically significant lower in study group versus control group, ($p=0.002$, $r=0.23$), size effect being small to medium (Table IV). It follows the association between lower Tf levels, reduced BMD and increased risk of falling.

Sex steroid	Group	Number of patients	Mean value	Standard Deviation	Standard Error Mean	p
Total Testoster one (ng/ml)	Study	109	3.68	1.33	.12756	0.465
	Control	72	3.68	1.16	.13758	
Free testoster one (ng/L)	Study	109	5.89	2.42	.23200	0.002*
	Control	72	6.50	2.02	.23806	
Estradiol (pmol/L)	Study	109	38.02	16.41	1.5723	0.373
	Control	72	41.93	11.80	1.3910	

* $p<0.05$ Statistically significant

Table IV The average values calculated for the sex steroids in patients with increased risk of falling from study and control groups

For the subgroup of patients with increased risk of falling, no differentiation were found for the division of patients in categories of Tt ($p=0.277$) and Tf ($p=0.665$) between control and study group. Instead lower categories of E2 levels were more frequently (3.9 times) in study group than in control group ($\chi^2(1)=12.06$, $p=0.001$). For the patients with increased risk of falling from study group, the risk of having a lower than normal value of E2 is 1,54, and the 95% confidence interval is between 1.250 and 1.906 (Table V). E2 deficiency was associated significantly more frequent with low BMD and increased fall risk.

Sex steroid		Study group		Control		p value
Total testosterone categories	Low	22	20.2%	10	13.9%	
	Normal	87	79.8%	62	86.1%	0.277
Free testosterone categories	Low	76	69.7%	48	66.7%	0.665
	Normal	33	30.3%	24	33.3%	
Estradiol categories	Low	39	35.8%	9	12.5%	0.001*
	Normal	70	64.2%	63	87.5%	

* p<0.05 Statistically significant

Table V Distribution of sex steroids categories in patients with increased fall risk

Discussion

Sexsteroids have a recognized influence on bone in men. Both estradiol and testosterone are indispensable for keeping bone health status in men (10,11). Current researches reveals that E2 is the main sexsteroid needed to maintain bone homeostasis in men (12). In older men, the reduction in BMD is largely due to estrogen deficiency (70–85%), while androgens play a secondary role. It has been shown that in elderly men E2 is inversely associated with BMD and can predict fractures better than testosterone(13,14).

Like the results of other studies (15-17), we found a statistically significant association between sex hormones deficiency, especially with decreased serum levels of Tf and E2 and the reduction of bone density ($p=0.001$). Similar to the results of other studies our research did not find an association between low BMD and Tt (18-20).

The relationship between sexsteroids deficiency and falling risk was poorly studied and is unclear. It is known that with age appears a gradual decline in testosterone production and BMD (21). Muscle tissue contains androgen receptors and testosterone may influence the risk for falls through effects on strength and neuromuscular coordination. A previous study revealed the association between lower testosterone levels and increased fall risk in older men. Estradiol levels did not significantly affect the risk of falling (1). Also Auyeung et al. demonstrated that only estradiol is positively bound to muscle strength and physical performance in men (22). In this context we can mention that the administration of modern testosterone supplements may favorably influence the circulating level of testosterone, which may improve BMD and the risk of falling (23).

Androgen deficiency represents a risk factor for falls due to reduced anabolic role of androgens on muscles (1). The decrease of androgens causes muscle mass reduction and fat mass increasing (24-26).

In our study sexsteroids deficiency was significantly more common in men with risk of falls compared to those without risk of falls ($p=0.001$). In addition the increased risk of falling was significantly associated with low serum levels of sex hormones ($p=0.001$) in patients with low BMD.

Our results related to Tf corresponding to those in the literature. Orwoll et al. demonstrated a higher falling risk

in men with low levels of bioavailable testosterone (1). Their observational study included 2587 community-based men aged 65 to 99 years. Sexsteroids levels and physical performance were measured. Estradiol levels did not significantly affect the risk of falling (1).

References related to the correlation between the risk of falling and estradiol levels are poorly represented in the literature. A cross-sectional study that included 1489 community-dwelling older men revealed that total and free testosterone levels were connected to muscle mass, muscle strength and physical activity. The authors found that total E2 level was associated with reduced muscle strength (22).

Vandenput and colleagues (6) described in their study the association between low Tt and Tf, but not E2 or SHBG = sex hormone binding globuline, and increased falling risk in elderly men. Insted our study revealed that increased falling risk was significantly more common in men with reduced BMD and sexsteroids deficiency, especially Tf and E2 deficiency.

The analysis of the role of these factors in the development of osteoporosis and fall risk in men was restricted by the lack of free estradiol and SHBG determination. Further researches in this direction would be helpful.

Rehabilitation programs for this patients increase the strenghtness of osteoarticular system, and can contribute in quality of life (27-29).

Conclusions

Our research has shown the association of sexsteroids deficiency with reduction of bone mass and increased risk of falls in men. Of sexsteroids only the decrease Tf and E2 levels was associated with an increase of risk for osteoporosis and for falling in males. Measurement of sexsteroids in men may have predictive value in detecting the risk of osteoporosis and falling.

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Patient Consent

All the patients gave the informed consent for the study.

Authors' contributions

The authors contributed equally to the acquisition, analysis and interpretation of the data and to the redaction of the manuscript. The final manuscript was read and agreed by authors.

Conflicts of interest

The authors declare that they have no conflict of interest.

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Effects of low laser level therapy in rehabilitation of patients with COVID19 pneumonia

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Abstract

Introduction. An unprecedented public health crisis has been triggered worldwide by SARS-CoV-2's high contagiousity and it's mortality rates of 1-5%. Although the majority of COVID-19 cases have a good outcome, there is a small percentage that develop severe pneumonia and cytokine storm and may be in the need of mechanical ventilation.

Methods. Identifying the exact drivers of the excessive inflammation and the biomarkers that can predict a hyperinflammatory response to SARS-CoV-2 would be extremely helpful in finding efficient anti-inflammatory interventions that may stop the progression to acute respiratory distress syndrome (ARDS).

Results. In the search for such interventions we have identified the promising effect of low level LASER therapy (LLLT) on lung inflammation from COVID-19 pneumonia. Due to its well known anti-inflammatory effect and modulatory activity on immune cells, laser therapy may be able to decrease lung and systemic inflammation without affecting lung function in acute lung lesions, relieve respiratory symptoms, normalize respiratory function and stimulate the healing process of lung tissue. The recovery time may also be significantly shortened and all blood, immunological and radiological parameters may improve.

Conclusions. This findings need further confirmation from clinical trials but we are hopeful for their contribution on the global battle against COVID-19 pandemic.

Keywords: SARS-CoV-2, pneumonia, low LASER level therapy, anti-inflammatory effect, cytokine storm,

INTRODUCTION

SARS-CoV-2 (Severe Acute Respiratory Syndrome Coronavirus 2) belongs to the betacoronaviruses group, line 2, Sarbecovirus subgenus. Coronaviruses are enveloped viruses, of the single-stranded RNA type with positive polarity (+ssRNA), with large dimensions, of about 125 nm (1). SARS-CoV-2 causes a respiratory infection called COVID-19 (Coronavirus infectious disease-2019), with an average incubation period of about 5 days (with limits between 2 to 14 days). The disease is characterized by predominantly respiratory symptoms (fever, cough, difficulty in breathing) of moderate intensity in 80% of cases, but may have severe manifestations (bilateral interstitial pneumonia - the most common complication in coronavirus infection), with progression to respiratory failure, Acute respiratory distress (ARDS) as the leading cause of death (1).

Current data suggest that 80% of cases are asymptomatic or mild; 15% of cases are severe (the disease requires oxygen administration) and 5% are critical, requiring mechanical ventilation and interventions that support

vital functions (2). Patients who have survived this condition may develop - as a complication, a syndrome characterized by physical, mental and cognitive disorders. The "intensive care syndrome" may also develop which, in addition to methods of recovery of the respiratory system, may require complex musculoskeletal rehabilitation (2).

LASER therapy is a non-invasive, atraumatic, aseptic physiotherapy procedure with many applications in the field of medical rehabilitation, from pain therapy to the direct action it has on tissue and biological process stimulation, being an alternative to avoid the renal and hepatic side effects of analgesic and anti-inflammatory medication (3,4). The effects of LASER therapy are photochemical in nature, by absorbing LASER light at the level of photoreceptors, which triggers biological changes at the cellular level and increased intercellular activity, depending on the wavelength. Among the benefits of this therapy we mention: the analgesic, anti-inflammatory, anti-edematous effects, the improvement

of blood and lymphatic circulation, muscle relaxation, acceleration of nerve and bone tissue regeneration, stimulation of immunity, decrease of the healing time of wounds and scars (5).

In SARS-CoV-2 viral pneumonia, low level LASER therapy (LLLT) reduces inflammation without affecting lung function in acute lung lesions, relieves symptoms and stimulates the healing process of lung tissue (6). Other forms of physical therapy, such as low intensity pulsed ultrasound technique, with intensity typically less than 100 mW/cm², with antiinflammatory (7) and antioxidant effects (8) is also proposed now as treatment modality for discrete pulmonary lesions in patients with COVID-19 (9).

Discussion

The physiopathology and mechanism of action of LASER in acute lung inflammation

At the alveolar level, the virus infects type II pneumocytes having an initial stage of viral replication and a second stage of proinflammatory programmed cell death. Some molecular patterns are then released, and recognized by neighbouring epithelial cells, by endothelial cells and by alveolar macrophages. They trigger the inflammatory response by generating proinflammatory chemokines and cytokines such as IL-1 β , IL-6, IL-7, IL-8, IL-10, TNF α , which further attract inflammatory cells such as monocytes, macrophages and lymphocytic T cells. Severe COVID-19 have been associated with elevated inflammatory markers and increased cytokine levels. These markers are prognostic for the requirement of mechanical ventilation, the development of ARDS, and death in COVID-19 (10).

In the case of a dysfunctional response, immune cells continue to accumulate, producing excessive cytokines, which causes an excessive inflammatory response, the so-called cytokine storm. At the pulmonary level, this inflammatory process results in the thickening of the alveolar interstitium with the accumulation of fibrin and the formation of hyaline membranes, with the increase of capillary permeability and the activation of coagulation. All this leads to pulmonary oedema, with massive alveolar destruction, fibrosis, respiratory failure and acute respiratory distress syndrome (11).

The main actions of interleukin 6 (IL-6) on lymphoid and non-lymphoid cells are mechanisms that modulate the body's immune and inflammatory responses. Although many of these functions overlap with those of type 1 interleukin (IL-1), such as the synthesis of acute phase reactants and fever, IL-6 also has anti-inflammatory effects. Similarly IL-1, the most important source of IL-6 is represented by macrophages, being synthesized by T and B lymphocytes, by fibroblasts and by endothelial cells, by keratinocytes, synoviocytes, chondrocytes and epithelial cells. Thus IL-6 is produced in response to bacterial and viral infections, to inflammation or trauma,

quickly reaching detectable plasma levels, unlike many other cytokines(12).

In addition to proinflammatory actions, IL-6 also mediate a number of anti-inflammatory effects, while IL-1 and TNF induce each other's synthesis, as well as that of IL-6, IL-6 completes this inflammatory cascade because it inhibits IL-1 and TNF syntheses (12). IL-8 contributes to the pathophysiology of ARDS, neutrophil chemotaxis and survival in lungs and TNF- α is responsible for the adhesion and activation of neutrophils, the procoagulant effect and oedema. It can also stimulate the release of IL-6 (11,13). Monocyte chemotactic protein (MCP-1) is a chemokine with a crucial role in monocyte recruitment. Its level increases in lung inflammation. Monocyte migration may be reduced after therapy due to decrease in MCP-1 (14).

On the other hand, the role of IL-10 is not clear yet. Some authors have reported it as a predictor of poor prognosis, while others know it as a regulatory cytokine that is released during the cytokine storm. Its role is to limit the immune response to pathogens and to restrict host cell damage. Several studies have stated that an imbalance between TNF α and IL-10 levels increases host cell damage and the risk of complications (15).

Another theory in the physiopathology of COVID-19 pneumonia is the role of decreasing the number of CD4 + and CD8 + T cells and lymphocyte imbalance. T cells play an important role in the immune response against viral pathogens. CD4 + helper T cells guide B cells, and cytotoxic T cells and CD8 + cytotoxic cells eliminate viral pathogens by releasing molecules such as perforin, granzyme, and IFN γ (16).

In acute lung inflammation, LLLT can increase TNF α levels and improve the balance of inflammatory processes. It significantly reduces IL-8 levels, can alleviate ARDS and reduces mortality (16).

Photomodulatory therapy also contributes to healing by promoting apoptosis of inflammatory cells while suppressing apoptotic pathways in lung tissue. In a model of acute lung injury, low-intensity laser therapy reduced DNA fragmentation and apoptotic way activity by increasing B-lymphoma-2 (Bcl-2) cells, the key regulator of the intrinsic or mitochondrial way for apoptosis in alveolar epithelial cells, while promoting DNA fragmentation in inflammatory cells (17).

In pulmonary idiopathic fibrosis, the laser inhibits pro-inflammatory cytokines and increases the expression of proliferating cellular nuclear antigen, it attenuates airway remodelling by balancing proinflammatory and anti-inflammatory cytokines in lung tissue, and inhibiting fibroblast secretion of pro-fibrotic cytokines. It offers synergy in combination with medical treatment. It has a synergistic anti-inflammatory action on alveolar macrophages associated with N-acetyl cysteine, effective against cough and lung diseases (18).

Photomodulatory therapy is proving to be able to enlarge CD + and CD8 + cells and improve the balance between them. While this therapy has been widely used to improve healing, potential negative results have also been observed. Laser therapy could induce fibroblastic migration which, in turn, causes the deposition of collagen in the lung tissues and thus the appearance of pulmonary fibrosis (19).

On the other hand there are studies claiming that photobiomodulatory therapy can have an anti-fibrotic effect by lowering TGF β in both fibroblast cells and lung tissue (20).

Therapeutic technique and LLLT dosing

The Multiwave locked system (MLS) LASER therapy used in these studies uses a mobile scanner with 2 laser diodes, emitted in pulsed mode at 905 nm and 808 nm, respectively, the two wavelengths of t LASER working simultaneously and being synchronized. The scanner is positioned above the lung area at about 20 cm, each lung being scanned from the top to the base (21). The LASER field was focused on the median edge of the scapula, opening the lung fields, thus reducing the thickness of the chest wall to theoretically improve laser penetration into lung tissue (21).

The therapeutic dose used according to calculations performed by Dr. Soheila Mokmeli, co-author of the main study conducted with Dr. Scott Sigman-main investigator and lead author of the first use of LASER therapy in the treatment of a patient with COVID-19 induced pneumonia, was just over 0.01 J/cm² of LASER energy in the lungs. This dose was able to penetrate the chest wall into the lung tissue creating an anti-inflammatory effect that theoretically blocked the effects of the cytokine storm seen in COVID pneumonia (21,22).

Therapeutic protocol for various forms of SARS-CoV2 virus infection

We present below the main parameters of LLLT depending on the severity of COVID-19 infection (Tabel I for mild form of COVID-19, Tabel II for moderate and severe forms of COVID-19).

Laser type	Average power	Dosage	Area	Time required	Sessions
Infrared laser (780-900 nm) or Red light laser (630-660 nm)	50-100 mW	4-6 J/cm ²	10 cm ²	1-2 minutes/c m ²	3-8 sessions once/day

Table I. Therapeutic protocol: COVID-19 mild form

Laser type	Average power	Dosage	Area	Time required	Sessions
Infrared laser (780-900 nm) or Red light laser (630-660 nm)	50-100 mW	6-10 J/cm ²	10 cm ²	2-3 minutes/c m ²	3-10 sessions once/day

Table II. Therapeutic protocol: COVID-19 moderate – severe forms (23)

Clinical trials have shown that the laser used in COVID-19 pneumonia has reduced respiratory symptoms by normalizing respiratory function; the recovery time has been significantly shortened and all blood, immunological and radiological parameters have improved (24).

We mention the post-treatment results for the patients in the first randomized pilot study that involved patients with confirmed COVID-19, conducted in August 2020 by Dr. Sigman:

1. SaO₂ increased from 93-94% to 97-100%
2. The O₂ requirement decreased from 2-4 L/min to 1L/min
3. The RALE radiographic score improved from 8 to 5
4. Pneumonia severity index improved from class V (142) to class II (67)
5. Pulmonary indices, Brescia-COVID and SMART-COP, both decreased from 4 to 0
6. PCR normalized; from 15.1 mg/dL to 1.23 mg/dL
7. Ferritin decreased from 359 ng/mL to 175 ng/mL
8. Clinical recovery was a total of 3 weeks, while the mean time is usually 6 to 8 weeks.

The results confirm the anti-inflammatory effects described above as evidenced by the reduction in the levels of pro-inflammatory dosed markers, IL-6 and ferritin.

Another strength of the therapy is that the method of scanning of this LASER does not present any risk of contamination, because LASER does not come into direct contact with the patient.

Conclusion

Low LASER level therapy (LLL) can be added to conventional treatment in patients with COVID-19, at different stages of the disease, due to its anti-inflammatory effect and its ability to reduce the recovery time of patients.

Scientific evidence shows that LLLT attenuates cytokines and inflammatory chemokines in the cytokine storm at several levels. In addition, LLLT promotes apoptosis of inflammatory cells and protects alveolar cells from damage. These findings suggest that LASER therapy is a feasible way to treat ARDS.

Conflict of Interest

The authors declare that they have no conflict of interest.

Author contribution

All authors with equal contribution.

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Cost-effectiveness of home non-invasive ventilation in COPD group GOLD D patients

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Abstract

Introduction. Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality, estimated to be the third most common cause of death by 2020. The natural evolution of the disease is characterized by frequent exacerbations, severe exacerbations evolving with respiratory acidosis. Introducing home non-invasive ventilation (NIV) in the management of COPD group GOLD (Global Initiative for Chronic Obstructive Lung Disease) D patients generates supplementary costs, but the decreasing of the number of severe exacerbations will decrease the costs of drug treatment and hospitalization. This balance can be verified through a careful study of cost-effectiveness through modern methods of assessing the costs and years of life gained in relation to quality of life.

Material and method. This prospective study took place in the Emergency Department of the Bihor County Clinical Emergency Hospital, Oradea, between 01 October 2017 – 31 October 2018, with a follow-up period of 2 years. We included 36 Group risk D COPD patients, presented with severe exacerbation that required NIV; the patients were divided into two study groups according to the treatment scheme after discharge (standard medication according to GOLD guidelines and long-term oxygen therapy - LTOT vs. LTOT + NIV). We follow-up at 2 years with the study group, and analyze the following: number of exacerbations (moderate and severe), number of hospitalizations, mortality rate in two years, average costs for the treatment of exacerbations and for stable COPD periods, quality adjusted life year (QALY).

Results and discussions. From 36 enrolled, 10 patients benefited from home NIV. The number of exacerbations was significantly lower in the NIV group compared with the LTOT group (1.72 ± 0.79 vs 3.54 ± 1.18). The incremental cost-effectiveness ratio (ICER) showed a net gain of 31% from gross product (GDP) per capita ($5,641.71 \pm 1,737.0$ -euro vs $9,272.3 \pm 3,681.9$ euro) per quality adjusted life year (QALY) for each patient.

Conclusions. Introduction home-NIV demonstrated clinical improvement and higher cost-effectiveness over LTOT alone in Class Risk D, COPD patients after discharge following a severe exacerbation.

Keywords: chronic obstructive pulmonary disease, non-invasive ventilation, cost-effectiveness, quality adjusted life year,

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) remains one of the leading global causes of mortality and morbidity (1,2,3,4), estimated to be the third most common cause of death by 2020 (3,5). The natural evolution of the disease is characterized by frequent exacerbations (2,4), decreased quality of life, especially in COPD risk class C and D, and increased economic costs (3,4).

Severe COPD exacerbations are associated with respiratory acidosis and hypercapnia, usually determined hospital admission and need for ventilatory support (7,8,9,21). Although non-invasive ventilation (NIV) proved his efficiency in COPD patients with acute respiratory failure, persistent hypercapnia after discharge is associated with increased mortality rate and early readmission (3). Before 2013 the readmission rate was 20% (4), and in some countries (USA and UK for

example) hospitals are penalized for readmissions under 28 days. These factors contributed to the increased interest in development of new therapies to prevent relapse in these patients (5,6). The hospital, through the management system created (rules, principles, decision-making procedures) has the primary objective of providing quality, efficient and high-performance medical services (7,8).

One of these relatively new treatment options is home-NIV added to the long-term oxygen therapy (LTOT), in COPD Group D patients with chronic hypercapnia (12,16). Clinical efficiency of home-NIV raised controversies between researchers because some of the clinical studies didn't show any improvement in hypercapnia level or on mortality. However, the question remains if in these studies NIV wasn't or not applied in an optimized manner, selection of patients was correct or

not (13). Recently, European Respiratory Society Task Force (ERSTF) reviewed and published in 2019 evidence-based recommendations for the clinical application of LTH-NIV in chronic hypercapnic COPD patients (14).

Introducing home- NIV in the treatment scheme of COPD patients generates supplementary charges, but clinical improvement with reducing number of exacerbations leads to decreased hospitalization costs and pharmaceutical treatment expenditures (17,18). This balance can be verified only through a careful study of cost-effectiveness with modern methods including cost assessment and gained quality adjusted life years (QALY) (19,20). These studies are specific for every country, health systems varying in characteristics and individual costs (22,23). The aim of our study was to evaluate the clinical and economic impact of NIV supplementation to LTOT compared to standard therapy with LTOT in COPD group D patients with severe hospitalized exacerbation.

2. Material and method

2.1. Study selection

This prospective, observational study took place in the Emergency Department of the Bihor County Clinical Emergency Hospital, Oradea, between 01 October 2017 – 31 October 2018, with a follow-up period of 2 years. The inclusion criteria were: patients with a documented diagnosis of COPD, Class risk D, aged ≥ 40 years, hypercapnia > 55 mmHg and respiratory acidosis which required NIV. The exclusion criteria were: pregnancy, any oncologic diagnosis in the last 5 years, younger than 40 years, unable to sign informed consent. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee of County Clinical Emergency Hospital, Oradea.

2.2. Objectives

The main objectives of the study were: the number of exacerbations (moderate and severe), readmission rate and general mortality rate in the observation period (24 months). Secondary objectives were economic data, QALY, ratio between costs/QALY. The difference in costs / QALY ratio was compared to the gross domestic product (GDP) per capita to demonstrate the economic importance of the gain or loss through this intervention in the treatment scheme of Class risk D COPD patients.

2.3. Data collection

Data were collected from the patient's medical record obtained after evaluation in the Emergency Department, and a number was allocated after study inclusion. The following data were collected: age, gender, location of residency (urban or rural), cigarette-smoking history, arterial blood gas parameters (P_{CO_2} (mmHg), pH, P_{O_2} (mmHg)), number of moderate and severe exacerbations (defined by the GOLD 2017), mortality rate. The study population was divided by the treatment

scheme in two samples (LTOT or LTOT+NIV). This division was undertaken in order to facilitate a comparison of the clinical factors as well as the economic factors.

Patient follow-up was realized by phone combined with verification of electronic registers of all hospitals in Bihor County with respiratory ward. The compliance with the NIV was checked up with the company who lease the NIV device (from the digital register of each device).

The follow-up criteria were the following:
treatment scheme: LTOT or LTOT+NIV;
daily usage of LTOT and NIV (h/day);
number of recurrences in follow-up period (moderate and severe);
number of hospital admission for exacerbation;
all-cause mortality.

According to the collected data non-compliant patients (oxygen usage under 18 h/day and NIV usage under 6 h/day) and those who changed the treatment regimen during the follow-up period (LTOT to LTOT+NIV or inversely) were excluded.

2.4. Economic study

The best economic indicator for a medical intervention is the incremental cost-effectiveness ratio (ICER) or cost / effect difference.

In our case the effect was represented by the Quality Adjusted Life Years (QALY), and the costs were calculated adding the next amounts (standard prices according to the National Health Assurance's expenses list):

costs of baseline treatment (bronchodilators and respiratory anti-inflammatory drugs) – approximately 63 euro / month;

costs of treatment for moderate exacerbation (without admission): medical consult 6 euro + medication (antibiotics, oral anti-inflammatory and mucolytic drugs) approximately 31 euro = 37 euro / exacerbation;

costs of treatment for severe exacerbation (with admission): amount charged per case = standard amount per case x severity index = 323 euro x 2.6337 = 850 euro / exacerbation (27);

expenses of LTOT: 40 euro / month;

expenses of domiciliary NIV: 120 euro / month.

Approximation of QALY was made based on utility values taken from BLISS study average life quality scores (26):

stable COPD patient's utility score: 0.6014,

during moderate recurrence: 0.5112 (1 month),

In case of severe exacerbation, the first month is noted with 0.2556 and 0.4511 for the next 2 months.

2.5. Statistical analysis

The data were collected in 2016 Microsoft Excel software (version 18.2006.1031.0, Microsoft, Redmond, Washington, DC, USA), and transferred to SPSS

software (IBM SPSS Statistics 25.0.0.0, Armonk, New York, NY, USA) for the statistical analysis. The quantitative variables were expressed by their average \pm standard deviation (SD), respectively median and interquartile range in case of skewed distribution; and number of observations with percentage in case of categorical variables. The type of distribution for continuous variables was determined using the Kolmogorov-Smirnov test. Statistical significance was set at $p < 0.05$. The comparison of the study groups was realized with Student t-test, respectively Mann-Whitney (in case of skewed distribution) and chi-square test with Yates' correction for categorical variables.

ICER was calculated using the usual formula: $C1 - C0 / E1 - E0$. C1 = total cost of care for patients from LTOT+NIV group. C0 = total cost of care for patients from LTOT group; E1 = QALY for LTOT+NIV group. E0 = QALY for LTOT group.

3. Results

The study included 53 patients with COPD Class risk D presented with respiratory acidosis required NIV. 5 patients were excluded due to non-compliance to the treatment (3 non-compliance to NIV and 2 non-compliance to LTOT) and 2 due to transition between groups (both from LTOT group to LTOT+NIV group). From the remaining 46 patients only 36 could be contacted by phone to confirm the number of recurrences in the follow-up period. 10 patients benefited from domiciliary NIV. The baseline characteristics of the 2 study groups are presented in Table 1.

Table 1. Baseline characteristics of the study groups

Demographic characteristics	LTOT + NIV group (n=10)	LTOT group (n=26)	Statistical significance (p)
Gender (Male/Female)	4/6	13/13	0.8684
Age (years) – average \pm SD	68.5 \pm 9.5	69.8 \pm 10.7	0.7364
Provenience (Urban/Rural)	3/7	11/15	0.7666
Follow-up period (months) – average \pm SD	17.2 \pm 3.1	17.1 \pm 3.5	0.9231
LTOT = long time oxygen therapy; NIV = non-invasive ventilation; SD = standard deviation			

3.1. Clinical results

The evolution of clinical criteria for the 2 groups is presented in the next table (Table no. 2).

Table 2. Evolution of clinical criteria for the study groups

Clinical characteristics	LTOT + NIV group (n=10)	LTOT group (n=26)	Statistical significance (p)
Number of moderate exacerbations – average \pm SD	1.34 \pm 0.62	1.23 \pm 0.68	0.6761
Number of severe exacerbations – average \pm SD	0.39 \pm 0.60	2.3 \pm 0.94	<0.0001
Total number of exacerbations – average \pm SD	1.72 \pm 0.79	3.54 \pm 1.18	0.0001
General mortality rate – percentage (%)	10.00%	11.54%	0.6452
LTOT = long time oxygen therapy; NIV = non-invasive ventilation; SD = standard deviation			

We can easily observe the higher number of moderate exacerbations in the LTOT+NIV group, but this is counterbalanced by the increased number of severe exacerbations in the other group, resulting in significantly better evolution for patients with NIV.

A total of 4 deaths were registered, 1 from the LTOT + NIV group and 3 from the LTOT group which didn't indicate a statistically significant difference (10% vs 11.54% ($p = 0.6452$)).

3.2. Economic results

The total costs of the care in the follow-up period were divided into 2 categories:

- costs of the baseline care: price of the chronic medication + rent of the medical device (LTOT) / devices (LTOT + NIV);

- costs of the recurrences: costs of the care for moderate exacerbations x number of moderate recurrences adding the charges for hospital admission x number of severe exacerbations for each patient.

The average values for the above amounts for the 2 study groups are shown in the following table (Table 3).

Table 3. Average costs of care in the follow-up period for the 2 study groups

Costs of medical care	LTOT + NIV group (n=10)	LTOT group (n=26)	Statistical significance (p)
Baseline care (euro) – average \pm SD	3,833.2 \pm 687.3	1,751.7 \pm 359.9	<0.0001
Recurrences (euro) – average \pm SD	499.4 \pm 596.8	2,976.8 \pm 1,438.2	<0.0001
Total (euro) – average \pm SD	4,332.6 \pm 812.5	4,728.45 \pm 1,736.0	0.4961
LTOT = long time oxygen therapy; NIV = non-invasive ventilation; SD = standard deviation			

The baseline costs were significantly greater for patients who benefit from domiciliary NIV, but the expenses with recurrences were meaningful lower, such that the total costs were approximately equal for the 2 groups (slightly greater for LTOT group).

QALY calculation was made adding the utility values for each month depending on the number of recurrences in the follow-up period for each patient. The average QALY and the corresponding ICER values are shown in the next table (Table 4).

Table 4. Cost-efficiency analysis for the study groups

Cost-efficiency analysis	LTOT + NIV group (n=10)	LTOT group (n=26)	Statistical significance (p)
QALY – average \pm SD	0.8012 \pm 0.17	0.5295 \pm 0.11	<0.0001
ICER – average \pm SD	5,641.71 \pm 1,737.0	9,272.3 \pm 3,681.9	0.0054
LTOT = long time oxygen therapy; NIV = non-invasive ventilation; SD = standard deviation; QALY = Quality Adjusted Life Years; ICER = Incremental Cost-Effectiveness Ratio			

The above data demonstrates the superiority of the LTOT + NIV treatment scheme over the LTOT in 4th GOLD stage COPD patients with a net gain of 3,630.6 EURO per QALY. Both quality adjusted life years and cost-efficiency ratio are more advantageous for patients with domiciliary NIV.

A better visual representation of the differences is shown in the next plot graph with each case (Figure 1):

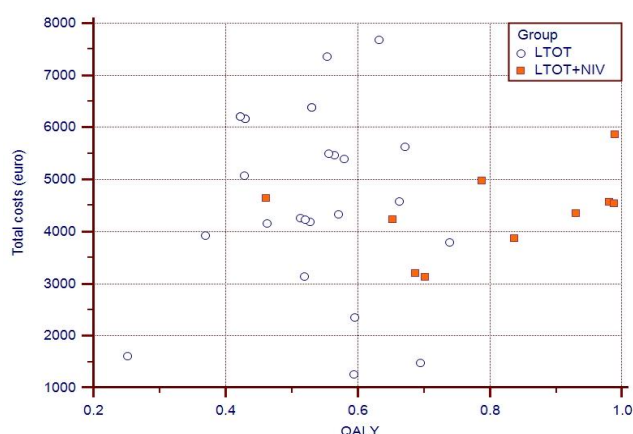


Fig. 1. Cost-efficiency plot graph for the study groups

4. Discussion

The current study demonstrates the superiority of the treatment scheme containing home-NIV for patients with Class risk D COPD after a severe, life-threatening exacerbation. The data shown presents significant differences to the RESCUE trial (29). That multicentre, randomized trial didn't show dissimilarity regarding the period to the next admission or mortality in the first 12 months after the introduction of NIV. Differences can be explained by inclusion criteria used (without clear diagnosis of Class Risk D COPD patients, only hypercapnia over 45 mmHg at discharge), which can lead to inclusion of less severe cases (with reversible hypercapnia) and better prognosis.

Discussions related to the changes in life quality due to introduction of home- NIV are intense, starting from Australian trial of Non-invasive Ventilation in Chronic Airflow Limitation (30). Our study did not assess directly, with individual questionnaires, the quality of life in the groups, but uses estimated values from literature taking into account the months spent with the treatment of exacerbation. These variations would be lost in case of direct measurement which cannot be made every month. Thus, our results related to the evolution of life quality and implicit QALY, are relative, not evaluating directly the life quality changes determined by NIV itself.

The patient selection process indicates a low rate of enrolment (only 54.5% of initially identified patients were enrolled because of high loss rate in follow-up) which denotes the gravity of disease and also assures that we have selected a representative cohort who benefit most from domiciliary NIV.

Patients with COPD in this stage of the disease with chronic respiratory failure (with hypoxemia and hypercapnia) have reserved prognosis and limited pharmacological therapeutic options (the use of LAMA/LABA treatment consistent with the GOLD

treatment recommendations, in patients with a high symptom load or LAMA/LABA/CSI, in exacerbating patients) (32).

. Our improvement indicator in this study was the readmission rate for a severe exacerbation, without significant difference in general mortality rate. Even so, avoiding readmission has a beneficial effect on preserving pulmonary function and on health related quality of life.

Cost-efficiency assessment of home-NIV in different stages of COPD has been a debated topic in recent years, showing great differences between stable patients and those after a life-threatening recurrence. Analysing these articles, we can conclude that there is no considerable clinical or economic benefit for stable patients (17). However, patients recently discharged after a severe exacerbation represented a separate cohort to which most authors indicate a clinical improvement, without a correct assessment of health-related quality of life they concluded a higher cost-efficiency of NIV + LTOT vs LTOT alone (12,15). The possibility of infection or the carrying of resistant multidrug strains is not negligible, which leads to high costs or poor prognosis for these patients (33).

Reporting the cost-efficiency index to the GDP per capita is a current practice in health management. In our case the net gain of ICER represents 31% from GDP per capita for every patient who was treated with domiciliary NIV over LTOT alone (GDP per capita for Romania in 2019 = 12482.9 USD (31)). This is a considerable amount, and if the clinical evolution is also positive, this intervention worth considering in the selected group of patients. This approach may also be seen as a palliative measure in these advanced COPD patients, often with comorbidities (as sleep apnea) where the prognosis and complex unmet needs are difficult to recognized and fulfilled (34,35,36).

4.1. Study limitations

Some of the study characteristics can determine statistical bias or limitations to draw significant clinical or economic conclusions:

The reduced number of cases may not be representative for the whole cohort; increasing the study period or an eventual extension of study centres would increase the power of clinical and economic significance.

The costs of care in case of moderate and severe recurrences were approximated due to the great variability in duration of treatment, in-hospital days and other related expenses not covered by the insurance.

Assigning the utility values through approximation from previous studies can distort the real values resulted from assessment with individual questionnaires (EQ-5D-5L (28)), but also has the advantage to have distinct values for different stages of the disease over one single assessment in the case of individual questionnaires.

5. Conclusions

Introduction of home-NIV for patients with COPD Class risk D, is an expensive treatment option with multiple positive effects, but also some negative consequences (for example over life quality in general). Clinical and economic results should be interpreted taking into account the strong points and the limitations of the study.

The total number of recurrences showed a better result for the patients treated with home- NIV, especially on account of severe exacerbations with approximately the same general mortality. The baseline costs were significantly higher for the NIV group, but were compensated by the reduced charges for recurrence's treatment. The costs related to QALY showed even higher differences, reaching a net gain of approximately 31% of GDP per capita.

Author contribution

Conceptualization, E-B, K-B, L-G-D and Z-L-B.; methodology, K-B, L-G-D, C-M-D; software , L-G-D,C-M-D.; validation, E-B, K-B, Z-L-B and L-D; formal analysis, L-G-D, C-M-D.; investigation, E-B, K-B, Z-L-B; resources, Z-L-B,E-B.; data curation, L-G-D, E-B, K-B.; writing—original draft preparation, E-B, Z-L-B.; writing—review and editing, Z-L-B, L-D.; visualization, L-D, K-B; supervision, E-B, Z-L-B, L-D, D-G; project administration, L-D, L-G-D, C-M-D.; funding acquisition, none. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflict of interest.

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SIS therapy in the treatment of distal radius epiphyseal fracture (Case report)

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Abstract

Introduction. Fractures of the distal radius epiphysis are the most common fractures of the upper limb, present both in the general population active following major trauma and in the elderly population in minimal trauma due to osteoporosis. Among the adjuvant therapies for orthopedic treatment of distal radius epiphyseal fracture we can list Super Inductive System (SIS), a therapy based on the interaction between the electric field and the human body with the improvement of the healing process by acting on the pathophysiological stages of bone callus.

Material and method. A clinical case study was performed on a 28-year-old patient, hospitalized and treated in the neurosurgery department of the Constanta County and Emergency Hospital for a polytrauma by road accident (passenger) with amyelotic cervical vertebral trauma, thoracic trauma and trauma to the right upper limb, subsequently performing 12 SIS therapy sessions at the Balneal and Rehabilitation Sanatorium of Techirghiol. CT examination of the cervical spine reveals fractures of C4 vertebra (the blade and pedicle) and C5 vertebra (vertebral body, lamina and pedicle). Right forearm radiography reveals fracture of the right radial styloid. After conservative treatment of the cervical injury and orthopedic treatment of the upper limb injury, the clinical evolution is favorable, allowing the patient to be discharged and allowed to do 12 sessions of SIS therapy, 3 times a week, within 4 weeks. The subsequent clinical and paraclinical evolution was favorable for the outpatient orthopedic ambulatory reevaluation performed at 5 weeks.

Results and discussions. Due to the type of fracture of the radial distal epiphysis (linear fracture without displacement), absence of comorbidities and young age, led to the indication of orthopedic treatment with immobilization in the antebrachio-palmarcast, which allowed subsequent physiotherapy.

Keywords: *radial fracture, callus, polytrauma, cervical spine, lamina, Super Inductive System,*

INTRODUCTION

The radius is a long, paired bone located on the side of the forearm, on the side of the ulna and on the thumb. It has a body and two epiphyses. The distal or inferior epiphysis is much larger (1-3). The fracture of the distal extremity of the radius is one of the most common fractures of the upper limb. Among the most important causes of fracture can be listed the important traumas, if we talk about the general active population or the minimal traumas due to osteoporosis if we talk about the elderly population (4). According to the Frykman classification, there are eight types of fractures, the first two being extraarticular and the rest intraarticular (5). Clinical examination of the patient with fracture of the distal radius epiphysis reveals: localized edema, bruising, deformity at the fracture site and sensitivity to palpation (4,5).

Among the treatment methods of the distal radius epiphyseal fracture we can list the orthopedic treatment, whose effectiveness can be improved by the Super Inductive System (SIS) (6). SIS therapy is based on the

interaction of high intensity electric field and human body that produce the following changes: intensification of blood circulation in the affected area, facilitating the formation of fibrocartilaginous callus, initiating the process of progressive cartilage mineralization and promoting bone remodeling (6-10).

The objective of this case presentation is to demonstrate the effectiveness of physiotherapy treatment with Super Inductive System in the fracture of the distal radius epiphysis, with a new evidence of effectiveness of rehabilitation treatments on musculo-skeletal pathologies (11,12).

Material and method. We present the case of a 28-year-old patient, without significant personal pathological history, who is hospitalized in the neurosurgery department of the Constanta County Emergency Hospital for a polytrauma due to a road accident (passenger) with amielic cervical trauma, thoracic trauma and right upper limb trauma. Clinically at hospitalization the patient is conscious, cooperative,

Material and method. We present the case of a 28-year-old patient, without significant personal pathological history, who is hospitalized in the neurosurgery department of the Constanta County Emergency Hospital for a polytrauma due to a road accident (passenger) with amielic cervical trauma, thoracic trauma and right upper limb trauma. Clinically at hospitalization the patient is conscious, cooperative, Glasgow Scale GCS = 15, with no signs of meningeal irritation, no cranial nerve deficiencies, no motor deficits (upper right limb difficult to examine in the context of functional impotence and edema due to fracture of the distal radius), without sensitivity disorders, ROT present symmetrically bilateral, RCP in flexion, bilateral with neck pain and pain in the right upper limb (distal extremity). Examination of the native craniocerebral computed tomograph does not reveal post-traumatic intracranial lesions. The cervical spine CT scan shows fracture lines without displacement of the lamina and the right pedicle at the level of the C4 vertebra (fig. 1, 2) and the vertebral body, the lamina and the right pedicle of the C5 vertebra (fig. 1, 2). without changes in the axis of the cervical spine. Radiography of the right anterbrate shows a fracture without displacement of the right radial styloid. The patient is hemodynamically and cardio-respiratory stable on presentation, with BP = 130/70 mmHg, AV = 70 bpm and SpO2 = 100%

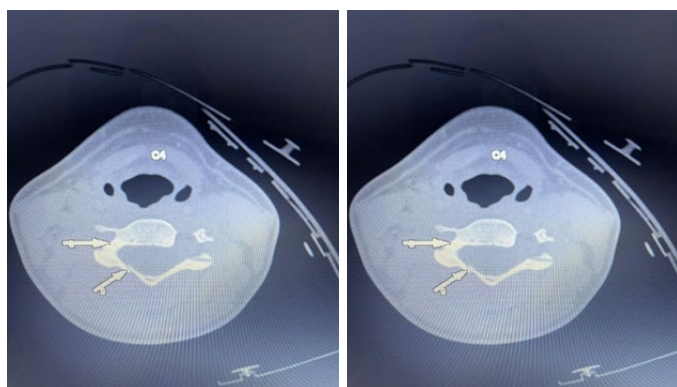


Fig 1. Tomographic image of the cervical spine, centered on the C5 vertebra and the C4 vertebra

Immobilization in Philadelphia collar and orthopedic treatment with immobilization in the right antebrachio-palmar cast is performed with radiographic control before (fig. 3.A, 3.B) and after reduction (fig. 4.A, 4.B).

The favorable clinical evolution after a week of rest and antialgic, anti-inflammatory and anticoagulant

treatment allows the patient to be discharged and to start the therapy with Super Inductive System at the Balneal and Rehabilitation Sanatorium of Techirghiol. There are 12 SIS therapy sessions divided into 3 sessions per week, within 4 weeks, using the A-1014 program. After the last SIS session, a right forearm control radiograph is performed, which shows a very good paraclinical evolution with the total callus of the fracture line of the distal epiphysis of the radius (fig. 5.A, 5.B).

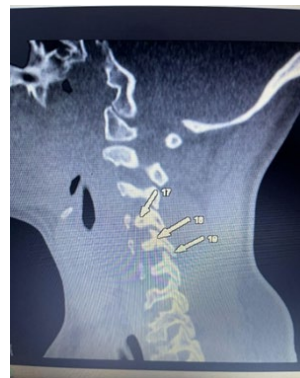


Fig 2. Tomographic image of the cervical spine, highlighting the fracture lines of the C4 and C5 vertebrae .



Fig 3-X-ray of the left forearm, before the orthopedic reduction of the fracture of the distal epiphysis of the radius, the lateral incidence (A) and antero-posterior (B).

Results and discussions. The causes of fractures of the distal radius epiphysis are represented by severe traumas, including in the context of polytraumas in the active population or by minimal traumas in the elderly population in the context of osteoporotic pathology (4). Distal radius epiphyseal fractures represent approximately 12% of total upper limb fractures, being the most common types of fractures in this segment (5).

The treatment of fractures of the distal radius epiphysis can be surgical or orthopedic, considering the type of fracture (linear or comminutive, with or without displacement), the associated injuries (in the context of polytraumas) and the patient's comorbidities (5,9). Adjuvant physiotherapy treatment is performed after treating acute lesions and clinical and biological stabilization of the patient, but preferably as early as posttraumatic, to increase the effectiveness of treatment (4,6). Physiotherapy in radius fractures may consist of therapy with SIS (Super Inductive System – fig. 6), which is a treatment divided into 3 weekly sessions, up to a total of 15 sessions. The center of the applicator is positioned above the affected area at a minimum tissue distance. The recommended intensity during the operation is above the sensitivity threshold, up to the motor threshold. (10). The evolution is followed clinically and imagistically, performing a forearm radiograph at the end of the physiotherapy sessions. The presence of the cast is not a contraindication to the use of SIS therapy, its effectiveness not being affected (10).



Fig 4- Left forearm radiograph, after orthopedic reduction of the distal radius epiphysis fracture, lateral incidence (A) and antero-posterior incidence (B).



Fig 5- X-ray of the left forearm, at 5 weeks , lateral incidence (A) and antero-posterior incidence (B).

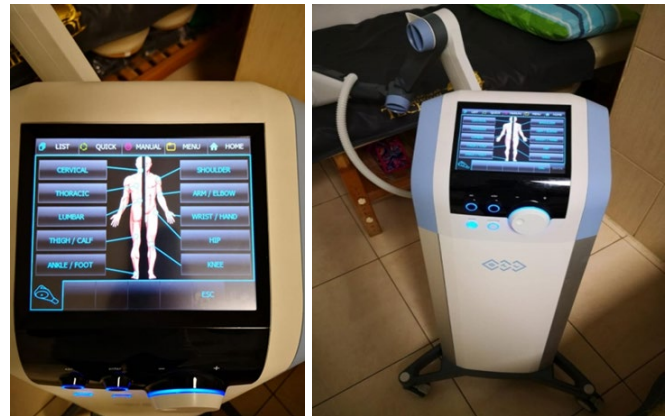


Fig 6- Super Inductive System (personal archive)

Conclusions

The mechanism of fracture of the distal epiphysis of the radius was by the hyperextension of the hand on the forearm, by supporting it on the car board, at the moment of impact. The type of fracture of the radial epiphysis (linear fracture without displacement), the absence of comorbidities, the young age and the indication of orthopedic treatment with immobilization in the antebrachio-palmar cast, made possible the subsequent physiotherapy. A favorable factor in the patient's evolution was the absence of post-traumatic mielic lesions, secondary to C4 and C5 fractures, with the absence of neurological deficits at hospitalization (Frankel "E" score), which allowed shortening the hospitalization period and early recovery by SIS therapy. The young age and the patient's compliance at the treatment (avoiding traumas, maintaining the prone position of the forearm and maintaining the integrity and functionality of the cast) led to a good imaging evolution with complete callus to the control radiograph at 5 weeks. The clinical evolution was favorably influenced by the symptomatic treatment, by the therapy with Super Inductive System and by the methods of reducing the edema (prone position and ice applications), by remitting the pain symptoms produced by the post-traumatic edema. Electrotherapy using new innovative methods such high intensity electromagnetic field, and other methods (13-16) can contribute in future development of the rehabilitation programs for many pathologies.

Author contributions regarding this study:

All authors (JD, OD, SE, IMG, IEV, BP, EFD, IC, BI, OB) had equal contribution.

Ethics approval and consent to participate:

The approval of the local ethics committee (Ethics Committee for Scientific Research of the St. Andrew Emergency County Clinical Hospital of Constanta), (approval no 348/25.05.2021) was obtained prior to write the study. Informed consent from the patient was obtained.

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The authors declared no conflicting interest.

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Age-Related, Sport-Specific Dysfunctions of the Shoulder and Pelvic Girdle in Athletes Table Tennis Players. Observational Study

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Abstract

Background: Postural skills are fundamental in motor activities, so far no evidence of a direct relationship has been found, it is therefore recommended to consider the following directions, the higher the level of sports competition, the better the body posture; or better athletes also have a better body posture. Around the age of 11-14 years, it is a period of aggressive development, if the rapid growth of the bone system is not associated and symmetrical with the development of soft tissues serious postural deficiencies may develop in table tennis players.

Methods: We used the web camera – photographic method (38) related to the Sensor Medica software that allows the acquisition of images in order to detect postural deficiencies and we considered it necessary to have a clear image of the level of technical-tactical training of female juniors III using 5 tests specific to topspin attack in order to assess the influence of body posture on such tests. Eighteen female juniors III (the mean \pm SD age, height and weight were 11.1 ± 0.2 years, 147.7 ± 2.6 cm, 39.0 ± 2.0 kg). Descriptive statistical analysis was performed on the procedures for establishing the normality of data distribution, Levene's Test for Equality of Variances, the t test for independent samples. The confidence interval was set at 95% ($p < 0.05$).

Results and Conclusions: Since Sig. (2-tailed) or $p < \alpha = 0.001$ and taking into account that the confidence interval limits for the difference between the sample mean and the reference value (95% CI for the mean difference) do not contain the zero value, it is accepted that there are statistically significant differences between the shoulder inclination for the female athletes in the sample studied and the reference value. We identified that at the level of alignment between anatomical landmarks, the percentage of deficiency of the entire lot of female juniors III in the case of shoulders is 100% and at the level of PSIS is 66%, which validates several studies that stated that in this period of aggressive growth correlated with repetitive unilateral executions specific to the topspin attack lead to postural deficiencies. In terms of the influence of body posture on the quality level, we identified that Group 1 – (without PSIS imbalance) has a higher average overall efficiency of the 5 tests (11.33) compared to Group 2 (8.58), even if from a statistical point of view these differences are not significant.

Keywords: *Body posture, Asimmetry, Topspin attack, Table tennis, Sensor Medica,*

1. Introduction

Given that sports training begins during the period of aggressive growth and development of the body, the impact on the athlete is very strong, which is why it is necessary to study the relationship between body posture and sports performance (1).

Body posture is maintained by a low effort of the musculoskeletal system, without any discomfort (2, 3), also postural control involves the body's ability to maintain a state of balance in the orthostatic position – static posture and during movement – dynamic posture (4). Postural stability depends on a complex relationship between several systems such as the visual, vestibular, and peripheral somato-sensory (leg) to maintain the

center of gravity of the body (5).

Functional disorders of body posture in school-age children are reported by (6, 7, 8) identifying the most common abnormalities of the musculoskeletal system (9) leading to its overload.

Around the age of 11-14 years, it is a period of aggressive development, if the rapid growth of the bone system is not associated and symmetrical with the development of soft tissues serious postural deficiencies may develop (10, 11). Another study by (12) states that in the tennis subject, the asymmetry of the muscular system starts at an early age, which creates problems in the spine.

The highest chances of changing body posture are mostly found in girls compared to boys, because this growth period is also influenced by the hormone called estrogen, which interacts with growth hormones and other specific factors, these potential etiological factors creating postural changes (13).

The most common deviations from a correct body posture are in the pelvis and shoulders, which are asymmetrical (14, 15). Following the same authors to state that if frontal scoliosis is present in athletes, this deficiency can cause a series of symptoms that are manifested in stress and fatigue in the tissues of the spine, negatively affecting sports performance in various ways.

A synthesis of specialized scientific articles addressing the evaluation and influence of postural control on performance athletes is made by the authors (16, 17, 18, 19, 20).

Table tennis is one of the most popular sports games, technical-tactical skills are very well recognized as the most important performance elements (21). The repetitive unilateral execution at high speed is performed every time the topspin attack is performed, which produces vicious body positions, implicitly the appearance of possible long-term pain in the spine, an aspect that may emphasize the fact that a correct posture indicates that athletes can support a higher intensity training without pain (22, 23). Positive results in competitions were obtained by high-level athletes due to good body posture and motor activities that reflected the level of athletic skills (24,25). For control and postural efficiency they require long-term specific training (26) to rebalance the bone and muscle-joint asymmetries. The most offensive shot in table tennis is topspin forehand, this procedure is extremely important for an aggressive player requiring correct biomechanics (27). For an efficient execution, an adjusted body position is required, a specific type of footwork, which modifies the kinematic chain of the body segments leading to a great variety and variability of movement (28, 29).

2. Materials and methods

The aim of this preliminary research was to detect postural deficiencies in junior female athletes (10-12 years) and to know the relationship/influence of body posture on the qualitative level of topspin attack.

This preliminary study started from the finding that following the implementation of an opinion survey on the influence of body posture on the topspin attack addressed to female juniors III coaches within the Romanian Table Tennis Federation in 2020 (February-March), it turned out that postural deficiency negatively influences the biomechanics of topspin execution, and that pain occurs predominantly in the lumbar region due to the repetitive execution of the topspin attack (30).

H1: It is assumed that through postural assessment we

will be able to identify and highlight the postural deficiencies encountered in this age category.

H2: The lot of subjects without deficiencies obtains significantly improved results in the tests for evaluating the qualitative level of the topspin attack, by comparison with the results of the lot with postural deficiencies.

2.1. Participants

The inclusion criteria were age between 10-12 years, girls and volunteers were found to participate in this scientific endeavor. Eighteen female juniors III (the mean \pm SD age, height and weight were 11.1 ± 0.2 years, 147.7 ± 2.6 cm, 39.0 ± 2.0 kg). All players were right-handed, this being determined by the hand in which they held the racket (31).

The lot was divided into 2 groups. Group 1. consisted of 6 female athletes (mean seniority in performance sports is 4.1 ± 0.1 years) with a mean value of 0° inclination in PSIS (posterior superior iliac spine). Group 2. – 12 female athletes (mean seniority in performance sports is 4 ± 0.3 years) with a mean value of 3.33° inclination at the same level.

These were in the first 50 positions of the National Ranking and are part of 7 sports clubs from A.C.S.O.V Pantelimon, C.S.M. Buzău, C.S.S. Sfântul Gheorghe, L.P.S. Slatina, A.C.S. Activ Galați, F.C. Argeș and C.N.A.V. Râmnicu Sărat.

In the locations of the sports clubs where they carried out their trainings, the qualitative evaluation of the topspin attack was also performed.

Following the evaluation with modified Adams forward bending test – MAFBT (32) no subject involved had axial rotation of the vertebral plates in the spine.

The tested subjects and their legal guardians were informed in advance about the purpose and tasks of the research in which they participated voluntarily, expressing their agreement on our scientific approach. We have complied with international conventions aimed at personal data processing and ensuring anonymity (Helsinki Declaration).

2.2. The Organization of the Research

The subjects were evaluated during the period 18.08.2020 – 31.08.2020 (the female juniors were in the preparatory period and had 3-5 workouts per week and a duration of 2 h/session), we used the web camera – photographic method (38) related to the Sensor Medica software that allows the acquisition of images in order to detect postural deficiencies in frontal plane (rear view) and we focused on the alignment of the shoulder and pelvis (PSIS).

The data processing software called FreeStep by Sensor Medica, which is endorsed by the French Association of Posturology (33), the instructions for use are detailed in (34).



Figure 1 – The FreeStep software webcam

The Postural Assessment was performed near sports clubs and more precisely in cities with specific equipment in Bucharest, Galați, Brașov and Pitești.

The participants had the same distance from the webcam, which is mounted on a leveled tripod stand (figure 1), the clothing was scarce for better visibility of the anatomical landmarks and the hair in a bun so that the protrusion of the C7 vertebra could be seen. They were asked to adopt a normal, orthostatic position, with the arms close to the body, relaxed, looking forward, the head in a natural position and with the legs in extension parallel to each other.

2.3. Tests related to topspin attack:

The tests were performed on an official table tennis court – called Donic (figure 2), Tibhar and Butterfly rackets (I.T.T.F. approved) and a set of 50 balls, with the size of 40.25 mm (I.T.T.F. approved);



Figure 2 – Completion of the execution of the topspin forehand attack

Before each evaluation session of each subject, a warm-up was performed with the game partner, which consisted of 5 minutes of executions with topspin forehand and backhand.

The technical-tactical tests specific to the topspin forehand and backhand attack were chosen because they were previously described and used by (35, 36, 37, 42). We considered it necessary to have a clear picture of the level of technical-tactical training of female juniors III using 5 tests specific to the topspin attack with the help of the game partner (coach):

1. Topspin with diagonal forehand performed from blockage;

* made of 5 series, counting in a series each success of the examined subject (the ball passed over the net, landing in the opponent's court, diagonally).

2. Topspin with diagonal backhand performed from blockage;

* made of 5 series, counting in a series each success of the examined subject (the ball passed over the net, landing in the opponent's court, diagonally).

3. Diagonal Butterfly performed from blockage;

* made of 5 series, counting in a series each success of the examined subject (the ball passed over the net, landing in the opponent's court, diagonally).

4. Line Butterfly performed from blockage;

* made of 5 series, counting in a series each success of the examined subject (the ball passed over the net, landing in the opponent's court, in line)

5. Multiball (topspin with forehand + topspin with backhand performed diagonally from no-spin ball, followed by the same technical procedures achieved from backspin ball)

* made of 10 series of 4 balls each. They were counted in a series as successful, only when the female athlete hit all 4 balls effectively (they passed over the net, landing in the opponent's court).

2.4. The statistical – mathematical analysis

It was performed using the IBM SPSS version 24 Software and procedures for determining the normality of data distribution, Levene's Test for Equality of Variances, t test for independent samples. The confidence interval was set at 95% ($p < 0.05$), according to (39, 40, 41).

3. Results

This preliminary study shows that the photography method with the help of the Sensor Medica software is reliable in detecting postural deficiencies.

Figure 3 shows the subject with scoliotic attitude, a model of body posture related to Group 1. The cause is in the thoracic region, which means that the dorsal convexity is on the left side, the inclination of the shoulder is 7° (table 1) to the right, the mean value being 2.5° inclination.

They are without pelvic imbalance, in the PSIS (posterior superior iliac spine) the angular value in the case of the subject is 0° and the mean angular value of the entire lot is also 0°.

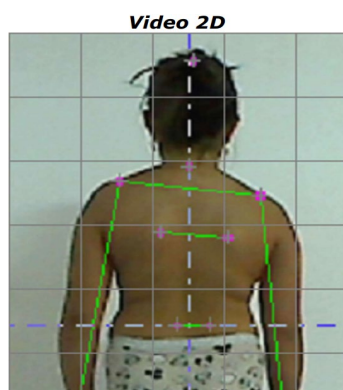


Figure 3 – Picture of one of the subjects of Group 1 in frontal plane (rear view)

Table 1 – The results of the postural measurements in frontal plane related to figure no. 3

Measurements	
<i>Results</i>	<i>Angle °</i>
Shoulder tilt	7° LF^
Ground distance left shoulder mm	1206
Ground distance right shoulder mm	1235
Scapulae tilt	5° LF^
Sips tilt	0°

In figure 4 we present a body posture model related to Group 2, with scoliotic attitude, 3° imbalance of the PSIS (pelvis), the convexity at the lumbar level is on the right side, the mean value being 3.3°. The subject has a shoulder inclination of 2° (table 2) to the left, and the mean angular value of the entire lot is 2°.



Figure 4 – Picture of one of the subjects of Group 2 in frontal plane (rear view)

Table 2 – The results of the postural measurements in frontal plane related to figure no. 4

Measurements	
<i>Results</i>	<i>Angle °</i>
Shoulder tilt	2° RG^
Ground distance left shoulder mm	1013
Ground distance right shoulder mm	1006
Scapulae tilt	2° RG^
Sips tilt	3° LF^

Table 3. - Results of the analysis of Mean, Std. Deviation and Std. Error Mean for the entire lot for postural assessment

Variables	N	Mean	Std. Deviation	Std. Error Mean
Shoulder inclination – angle (°)	18	2.28	1.526	0.360
PSIS inclination – angle (°)	18	2.33	2.029	0.478

*PSIS – posterior superior iliac spine.

Table 3 presents the data of the angular mean values of the entire lot of 18 subjects regarding the postural evaluation in frontal plane, the shoulder inclination is 2.2° and the PSIS inclination is 2.3°.

Table 4. - Results of the analysis of degrees of freedom, Sig.(2-tailed), Mean difference and 95% CI for the entire lot for postural assessment

Variables	Test Value = 0					
	t	df	Sig. (2-tailed)	Mean Difference	95% Confidence Interval of the Difference	
					Lower	Upper
Shoulder inclination – angle (°)	6.331	17	0.000	2.278	1.52	3.04
PSIS inclination – angle (°)	4.879	17	0.000	2.333	1.32	3.34

Table 4 presents the results of degrees of freedom, Sig. (2-tailed), Mean difference and 95% CI of the entire lot for shoulder inclination: the mean value of the sample studied for shoulder inclination is 2.278°. The value of the t test = 6.331. The 95% confidence interval for the difference between the sample mean and the reference value is (1.52°, 3.04°). Since Sig. (2-tailed) or $p < \alpha = 0.001$ and taking into account that the confidence interval limits for the difference between the sample mean and the reference value (95% CI for the mean difference) do not contain the zero value it is accepted that there are statistically significant differences between the shoulder inclination for the female athletes in the sample studied and the reference value.

The percentage of female athletes for whom the shoulder inclination deviates from the reference value is 100%.

For the PSIS inclination, the mean value of the sample is 2.333. The calculated t test value = 4.879. The 95% confidence interval for the difference between the sample mean and the reference value is (1.32°, 3.34°). Since Sig. (2-tailed) or $p < \alpha = 0.001$ and since the confidence interval limits for the difference between the sample mean and the reference value do not contain the zero value, it turns out that there are statistically significant differences between the PSIS inclination for the female

athlete in the studied sample and the reference value. The percentage of female athletes for whom the PSIS value deviates from the reference value is 66.66%.

Table 5. – The results of the 2 groups regarding the influence of body posture on the qualitative level of the topspin attack

Variables	Groups	N	Mean Rank	Sum of Ranks
Topspin with diagonal forehand performed from blockage	Group 1. (without PSIS imbalance)	6	11.67	70.00
	Group 2. (with PSIS imbalance)	12	8.42	101.00
	Total	18		
Topspin with diagonal backhand performed from blockage	Group 1. (without PSIS imbalance)	6	8.08	48.50
	Group 2. (with PSIS imbalance)	12	10.21	122.50
	Total	18		
Diagonal Butterfly performed from blockage	Group 1. (without PSIS imbalance)	6	10.58	63.50
	Group 2. (with PSIS imbalance)	12	8.96	107.50
	Total	18		
Line Butterfly performed from blockage	Group 1. (without PSIS imbalance)	6	12.17	73.00
	Group 2. (with PSIS imbalance)	12	8.17	98.00
	Total	18		
Multiball (topspin with forehand + topspin with backhand performed diagonally from no-spin ball, 56 followed by the same technical procedures achieved from backspin ball)	Group 1. (without PSIS imbalance)	6	8.42	50.50
	Group 2. (with PSIS imbalance)	12	10.04	120.50
	Total	18		
Total	Group 1. (without PSIS imbalance)	6	11.33	68.00
	Group 2. (with PSIS imbalance)	12	8.58	103.00
	Total	18		

Table 5 identifies the mean value of the 2 groups regarding the influence of body posture on the quality level, listing part of them:

Test 1 – Topspin with diagonal forehand performed from blockage in the case of Group 1 (without PSIS imbalance) the mean value of successes is **11.67** and of Group 2 (with PSIS imbalance) is **8.42**.

Test 3 – Diagonal Butterfly performed from blockage in the case of Group 1 (without PSIS imbalance) the mean value of successes is **10.58** and of Group 2 (with PSIS imbalance) is **8.96**.

Test 4 – Line Butterfly performed from blockage in the case of Group 1 (without PSIS imbalance) the mean value of successes is **12.17** and of Group 2 (with PSIS imbalance) is **8.17**.

From the total of the 5 tests it resulted that Group 1 (without PSIS imbalance) has a better quality level, of **11.33** points vs. Group 2 (with PSIS imbalance) which has a mean value of **8.58**.

Table 6 presenting Levene's Test confirms the equality of the variances of the two groups for topspin with diagonal backhand performed from blockage ($F = 0.355$ and $p = 0.559 > \alpha = 0.05$), diagonal Butterfly performed from blockage ($F = 0.533$ and $p = 0.476 > \alpha = 0.05$), line Butterfly performed from blockage ($F = 1.362$ and $p = 0.260 > \alpha = 0.05$), multiball ($F = 2.197$ and $p = 0.158 > \alpha = 0.05$), total ($F = 0.239$ and $p = 0.632 > \alpha = 0.05$). Consequently, the result of the t test is read on the first line of the previous table (assumed equal variances) in these cases. The variances of the two groups are not equal for topspin with diagonal forehand performed from blockage ($F = 9.654$ and $p = 0.007 < \alpha = 0.05$).

The t test for two independent samples shows that the difference between the means of the two groups (with and without imbalances) is not statistically significant at

the significance threshold $p < 0.05$ for any test: $t = 1.427$, $p = 0.208$ for topspin with diagonal forehand performed from blockage, $t = -0.985$, $p = 0.339$ for topspin with diagonal backhand performed from blockage, $t = 0.258$, $p = 0.800$ for diagonal Butterfly performed from blockage, $t = 1.941$, $p = 0.07$ for line Butterfly performed from blockage, $t = -0.662$, $p = 0.518$ for multiball, $t = 0.833$, $p = 0.417$ for the total. This conclusion is also supported by the fact that the 95% confidence interval of the difference between the means does not contain the zero value for any test.

The difference between the means of the two groups is 4.01667 for topspin with diagonal forehand performed from blockage, -1.88333 for topspin with diagonal backhand performed from blockage, 0.38333 for diagonal Butterfly performed from blockage, 1.83333 for line Butterfly performed from blockage, -0.583 for multiball, 4.29167 for the total.

Table 6. - Significance of differences between mean values in topspin-related tests (group 1 n=6 and group 2 n=12)

Variables	Groups	Mean	Mean Difference	Std. Deviation	Std. Error Mean	Levene's Test for Equality of Variances		t	Sig. (2-tailed)
						F	Sig.		
Topspin with diagonal forehand performed from blockage	Group 1. (without PSIS imbalance)	9.1000	4.01667	6.74774	2.75475	9.654	0.007		
	Group 2. (with PSIS imbalance)	5.0833		1.99537	0.57601			1.427	0.208
Topspin with diagonal backhand performed from blockage	Group 1. (without PSIS imbalance)	5.8000	-1.88333	3.56651	1.45602	0.355	0.559	-0.985	0.339
	Group 2. (with PSIS imbalance)	7.6833		3.93350	1.13550				
Diagonal Butterfly performed from blockage	Group 1. (without PSIS imbalance)	5.6333	0.38333	2.30969	0.94293	0.533	0.476	0.258	0.800
	Group 2. (with PSIS imbalance)	5.2500		3.22392	0.93066				
Line Butterfly performed from blockage	Group 1. (without PSIS imbalance)	5.4667	1.83333	2.35514	0.96148	1.362	0.260	1.941	0.070
	Group 2. (with PSIS imbalance)	3.6333		1.63336	0.47151				
Multiball (topspin with forehand + topspin with backhand performed diagonally from no-spin ball, 56 followed by the same technical procedures achieved from backspin ball)	Group 1. (without PSIS imbalance)	1.83	-0.583	1.472	0.601	2.197	0.158	-0.662	0.518
	Group 2. (with PSIS imbalance)	2.42		1.881	0.543				
Total	Group 1. (without PSIS imbalance)	27.8333	4.29167	10.32001	4.21313	0.239	0.632	0.833	0.417
	Group 2. (with PSIS imbalance)	23.5417		10.29991	2.97333				

4. Discussion In the specialized literature, we do not find much scientific research in our direction of interest that highlight the reality in the table tennis subject in this age category.

Thus, body asymmetry is possible to result from the practice of table tennis, however, according to knowledge (42), the effect of table tennis on body asymmetries has not yet been assessed and further attention is required.

In another study (43) the coaches of junior high-performance table tennis female athletes state that more than 50% say that the topspin attack is directly responsible for the pain in the lumbar region. Being also confirmed by the fact that the unilateral executions specific to table tennis resulted in slight asymmetries in the shoulders and pelvis causing musculoskeletal imbalances/deficiencies, aspects reported by (44).

The authors (45) assume that a negative influence of a

vicious position in bipedalism on body health is expressed especially in primary school age. However, even if postural skills are fundamental in motor activities, so far no evidence of a direct relationship has been found, and it is recommended that the following directions be considered, the higher the level of sports competition, the better the body posture; or better athletes also have a better body posture (1) in children and adolescent athletes.

Hypertrophy in the hitting upper limb is evident and is due to systematic involvement in specific training since the age of 5-6 in tennis (47), a subject related to table tennis, in which unilateral motor executions are performed, which is why muscle imbalances are inevitable materializing in postural deficiencies that, if not treated in time, will consolidate and pain will appear at the level of the entire musculoskeletal system.

In order to regain postural control, relatively short periods are needed by introducing specific motor programs, thus favoring and accelerating the body's ability to recover and adapt, which is stated by (48).

The percentage of female juniors III assessed, for which the PSIS deviates from the reference value is 66.66%, thus detecting imbalances in the pelvis, therefore, the authors consider it appropriate (49) to pay special attention to children and adolescents, because a correct body posture in adulthood is based on those stages of growth.

In the profile materials found, for a correct posture all the angular values between the anatomical landmarks must be equal to 0° otherwise, the postural problems must be marked (50).

A study (46) on 83 top table tennis, tennis and badminton Slovenian players, it has been found that the most vulnerable regions are at the ankle joint and the spine, which is why they have stated that improvement programs need to be included because they are essential for the well-being of the body and for optimal health (51, 52).

5. CONCLUSIONS We believe that this scientific research should be of real interest and useful to researchers in the field, performance coaches/analysts and especially physiotherapists, in order to give importance to the assessment and early detection of postural deficiencies in order to implement an individualized program to compensate for the imbalances encountered in the muscle-joint system and with possible beneficial implications on the topspin attack.

We found that at the level of alignment between anatomical landmarks, the percentage of deficiency of the entire lot of female juniors III in the case of shoulders is 100% and at the level of PSIS is 66%, which validates several studies that have stated that in this period of aggressive growth correlated with repetitive unilateral executions specific to topspin attack lead to postural

deficiencies (hypothesis no. 1 is confirmed).

From the point of view of the influence of body posture on the quality level, we found that Group 1 - (without PSIS imbalance) has a higher average total efficiency of the 5 tests (11.33) compared to Group 2 (8.58), even if from a statistical point of view these differences are not significant (hypothesis no. 2 is not confirmed).

The highest score and efficiency was at test no. 4 called *Line Butterfly performed from blockage* (in which the game partner sent the ball diagonally and the subject sent it in line from forehand and backhand) in the case of Group 1.

Limitations The results recorded cannot be universal, due to the limited number of subjects investigated, due to the fact that it is an individual sport and a limited age category. Another limitation of the study is that the analysis of postural imbalances in the sagittal plane implicitly on those of the knees were not analyzed.

Declaration of conflict of interests There is no conflict of interest for any of the authors regarding this paper.

Informed consent

The investigated subjects and their legal guardians were informed about the purpose and methodology of this study, expressing their agreement to the processing and publication of the results of this scientific approach, in compliance with the rules on personal data protection.

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Evaluation of the impact of high-tone therapy on cognitive disorders and quality of life in the complex treatment of patients with comorbid pathology

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Abstract

Introduction. Comorbidity is an independent risk factor for mortality and significantly influences the prognosis and quality of life.

Purpose: to evaluate the impact of high-tone HiTOP 4 touch therapy on cognitive disorders and quality of life in the complex treatment of patients with comorbid pathology.

Methods: complex treatment of 2 groups of patients with inclusion in the basic treatment regimen of high-tone therapy was carried out - a total of 80 patients (men - 34, women - 46) aged 41 to 79 years old, group I - patients with hypertension and chronic cerebral ischemia (CCI) - 38 patients and group II - patients with hypertension, CCI and concomitant diabetes mellitus (DM) type 2 - 42 patients. The average age in group I was 61.5, in group II - 65.5. Group I received lisinopril and amlodipine in one tablet, group II received metformin in addition to the above therapy. Both groups received a course of 10 sessions of high-tone therapy using the device HiTOP 4 touch (Germany) according to the general method: 2 electrodes on the feet, 2 on the forearms and one on the neck-collar area. All the patients were assessed for their cognitive condition, degree of anxiety and depression, and estimated for quality of life before and after a course of high-tone therapy. In order to do this, we used valid assessment tests, such as the Montreal Cognitive Assessment Scale (MoCA), the Hospital Anxiety and Depression Scale (HADS), and the SF-36 Quality of Life Questionnaire. **Results:** the course of high-tone therapy for patients with hypertension and CCI led to improved quality of life, on all indicators of the SF-36 scale, except for pain intensity, increased cognitive functions by 3.52 points on the MoCA scale, reduced anxiety by 2.06 points and depression by 1.92 points on the HADS scale. The course of high-tone therapy for patients with CCI, hypertension and type 2 DM resulted in a significant improvement of 5 out of 8 quality of life indicators on the SF-36 scale, cognitive functions by 2.27 points on the MoCA scale and reduced anxiety by 4.3 points, and depression by 0.53 points on the HADS scale.

Conclusion: the inclusion of high-tone therapy in the complex treatment of patients with comorbid pathology improves cognitive functions, reduces anxiety and depression, improves quality of life.

Keywords: *comorbid pathology, high-tone therapy, cognitive functions, anxiety, depression, quality of life,*

INTRODUCTION

Comorbidity is an independent risk factor for mortality and significantly influences the prognosis of disease and life. The number of comorbid diseases increases with age: 10% - under the age of 19 and 80% - persons aged 80 and older [1].

According to a British study (2000-2014), the most common comorbidities in age- and sex-standardized models were hypertension (28.9%), depression (23.0%), arthritis (20.9%), and asthma (17.7%) and anxiety (15.0%). In the presence of comorbid pathology, the severity of its course increases and the prognosis worsens; difficult primary diagnosis of the disease; treatment of several diseases requires taking into account the interaction of drugs; a significant increase in medical resources is needed; risks of side effects increases; patients' adherence to treatment decreases; the need for additional research grows [2].

The prevalence of dementia reaches 40 million people worldwide and is expected to double every 20 years to

more than 110 million in 2050. Vascular dementia is the second most common disease after Alzheimer's disease, which is estimated to account for about 20% of cases [3, 4, 5]. Type 2 DM doubles the risk of dementia and Alzheimer's disease. It has been suggested that Alzheimer's disease may be a consequence of a particular form of cerebral insulin resistance and impaired glucose regulation [6, 7].

Patients with vascular dementia have a lower rate of decline in cognitive function in comparison with patients with Alzheimer's disease. The progression of vascular cognitive impairment can be slowed or stopped by using optimal approaches to therapy that emphasizes the need to consider new methods of physiotherapy, which include high-tone therapy [8].

Complex treatment corresponds to the WHO's direction "Rehabilitation 2030": in-depth integration of rehabilitation services into the health care system and strengthening of cross-sectoral linkages to meet the needs

of population and the inclusion of rehabilitation services into the range of public health services. Currently, 2.4 billion people in the world have health problems that need rehabilitation [9].

High-tone therapy is a new step in the field of electrotherapy. Its main mechanism of action is a direct effect on cell metabolism, in order to transfer as much energy as possible through high frequencies in the range between 4096 and 32768 Hertz. Capacity frequencies up to 5000 mW enter directly into the body. The main direction of the action of high-tone therapy is to increase the number of mitochondria, which play an important role in comorbid diseases [10].

In order to date, the mitochondrial bioenergetic etiology of many diseases has been proven. The bioenergetic paradigm of metabolic and degenerative diseases, cancer and aging was proposed by Dr. Douglas Wallace and he was later awarded the Paul Jansen Prize by Johnson & Johnson in the field of biomedical research in 2017. This bioenergetic paradigm is presented in Figure 1 [11].

The brain needs a lot of energy, especially in conditions of insufficient blood supply in the process of chronic cerebral ischemia. It is necessary to maintain the resting potential, to restore the concentration of ions after synaptic transmission (from 40 to 60% of ATP energy), to support synthetic and catabolic processes. The brain has neither glucose nor ATP reserves, so the brain is critically dependent on the every second supply of glucose, oxygen and ATP production, which occurs mainly in mitochondria [12].

Purpose: to evaluate the impact of high-tone HiTOP 4 touch therapy on cognitive disorders and quality of life in the complex treatment of patients with comorbid pathology.

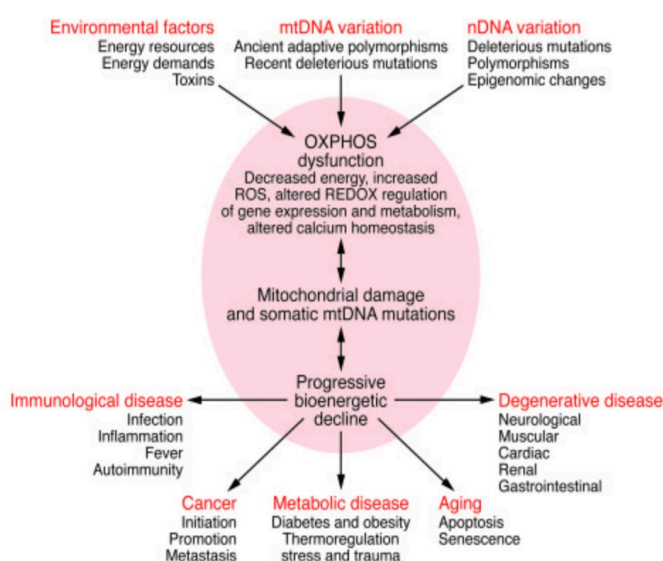


Fig.1 Bioenergetic paradigm for metabolic and degenerative diseases, cancer, and aging.

Materials and methods. Complex treatment of 2 groups of patients with inclusion in the basic treatment regimen of high-tone therapy - a total of 80 patients (men - 34, women - 46) aged 41 to 79, group I - patients with hypertension and CCI - 38 patients and II group - patients with hypertension, CCI and concomitant type 2 DM - 42 patients. The average age in group I was 61.5, in group II - 65.5. The diagnosis of hypertension was established based on the criteria of the recommendations of the European Society of Cardiology and the European Society of Hypertension (ESC/ ESH 2018) [13], the diagnosis of type 2 DM was established according to the criteria of the American Diabetes Association (ADA 2018) [14]. The diagnosis of CCI, which corresponds to the term cerebral small vessel disease, was confirmed on the basis of the criteria of the recommendations of the European Stroke Organization (ESO 2018) [15]. Group I received lisinopril and amlodipine in one tablet, group II received metformin in addition to the above therapy. Both groups received a course of 10 sessions of high-tone therapy using the device HiTOP 4 touch (Germany) according to the general method: 2 electrodes are placed on the feet, 2 - on the forearms and one - on the neck-collar area.

All the patients were assessed for the level of their cognitive condition, degree of anxiety and depression, and estimated for quality of life before and after a course of high-tone therapy. In order to do this, we used valid assessment tests, such as the Montreal Cognitive Assessment Scale (MoCA), the Hospital Anxiety and Depression Scale (HADS), and the SF-36 Quality of Life Questionnaire.

Among the screening scales for revealing cognitive disorders, the most common are the Montreal Cognitive Assessment Scale (MoCA) and the Mini Mental State Examination (MMSE). The MoCA scale is considered to be more sensitive to vascular cognitive impairments than the MMSE scale [16].

The sensitivity of the MoCA scale to mild cognitive impairments is 90%, and to Alzheimer's disease is 100%. MoCA is an "ideal" screening test for moderate cognitive impairments. The sensitivity of the MMSE scale to mild cognitive impairments is 18%, and to Alzheimer's disease is 78%. MMSE is more suitable for detecting dementia, with a low sensitivity to mild cognitive deficit [17].

Assessment of the quality of life of patients with DM and comorbidities is a necessary tool in the practice of physicians, which is confirmed by the global interest in this issue - over the past 5 years, 1950000 articles have been published [18].

SF-36 consists of 8 scales, where a higher index proves a higher quality of life:

1) Physical Functioning (PF), which reflects the degree to which physical condition limits the performance of

physical activity. Low indexes on this scale indicate that the patient's physical activity is significantly limited by his health.

2) Role-functioning due to physical condition (Role-Physical Functioning - RP) - the impact of physical condition on daily role-playing activities. Low indexes on this scale indicate that daily activities are significantly limited by the patient's physical condition.

3) The intensity of pain (Bodily Pain - BP) and its impact on the ability to engage in daily activities, which also includes work at home and outside the home. Low indexes on this scale indicate that pain significantly limits the patient's activity.

4) General Health (GH) - patient's assessment of his current health and treatment prospects. The lower the index on this scale, the lower the health index.

5) Vital activity (Vitality - VT) means feeling full of strength and energy or, conversely, exhausted. Low indexes indicate fatigue and decreased vital activity of the patient.

6) Social Functioning (SF) is defined by the degree to which a physical or emotional condition limits social activity or communication. Low indexes confirm a significant restriction of social contacts, a decrease in the level of communication due to the deterioration of physical and emotional state.

7) Role-functioning due to emotional state (Role-Emotional - RE) involves assessing the degree to which the emotional state interferes with work or other daily activities (including large expenditures of time, reducing the amount of work, decreasing its quality). Low indexes on this scale are interpreted as a limitation in the performance of daily work due to deteriorating emotional state.

8) Mental Health (MH) characterizes mood, the presence of depression, anxiety, a general indicator of positive emotions. Low rates indicate the presence of depressive, anxious feelings, mental distress.

The calculation of all values for the assessment of quality of life was performed in accordance with the instructions for processing data obtained using the SF-36 questionnaire and computer programs, according to special algorithms [19, 20].

Statistical analysis of the obtained data was performed using the packages STATISTICA 7.0 and Microsoft EXCEL 2003 with the integration of AtteStat 12.5, SISA Internet calculator (Simple Interactive Statistical Analysis). The average sample values of quantitative characteristics are given in the form of $M \pm m$, where M is the sample average, m is the mean error. Shares (percentages) are presented with 95% confidence intervals. In all the procedures of statistical analysis when testing null hypotheses, the critical level of significance p was assumed to be equal to 0.05.

Results and discussion. The results of MoCA testing before and after the rehabilitation course in group I (hypertension, CCI) are presented in Figure 2.

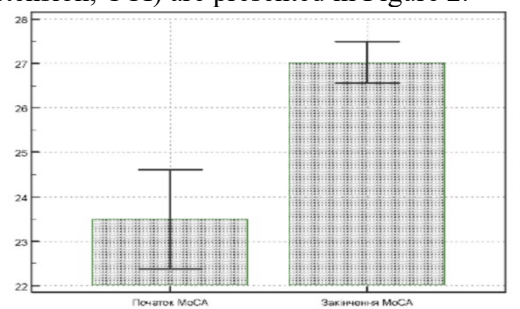


Fig. 2. Results of the MoCA test before and after undergoing high-tone therapy in group I.

After the course of high-tone therapy, the results of the MoCA test increased by 3.52 points: from 23.5 to 27.02 points ($p < 0.001$).

Data from testing of cognitive disorders in patients of group II are presented in Figure 3.

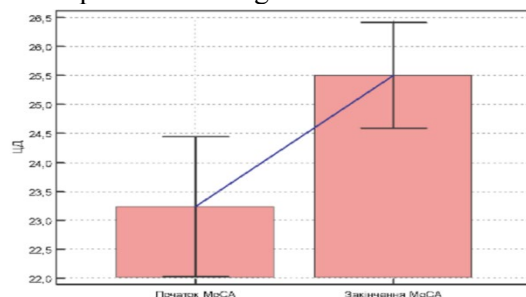


Fig. 3. Results of the MoCA test before and after undergoing high-tone therapy in group II.

The initial indicators of MoCA testing in group II were 23.23 points, and after the course with the use of high-tone therapy - 25.5 points. Improvement of cognitive functions by 2.27 points ($p < 0.05$). High-tone therapy for patients of group II is less effective that fact can be explained by more complex metabolic brain damage in concomitant type 2 diabetes, namely impaired insulin signaling, neuroinflammatory and oxidative stress, as well as defects in mitochondrial metabolism and regulation of coactivator 1 α receptor, sirtuin proliferator and peroxisome proliferator of SIRT-PGC-1 α receptor and tau protein signaling. Cognitive disorders can occur in the earliest stages of diabetes and is further exacerbated by metabolic syndrome. It should be noted that the strengthening of glycemic control in type 2 diabetes is not associated with improved cognitive function [21].

Cognitive deficits in CCI are manifested not only by slowing of mental activity, impaired attention, decreased speech activity and memory impairment, but also by affective and personality changes (depression, apathy, abulia, anxiety, irritability, emotional lability,

deceleration) that in case of progressing can lead to the development of vascular dementia. Determining the level of anxiety and depression in this group of patients is extremely important, as in the presence of increased anxiety increases the likelihood of fatal myocardial infarction by 2.3 times, and the risk of sudden death increases by 4.5 times [22, 23]. According to a study by the Helmholtz Center in Munich (n = 3428 men, 45-74 years, 10 years of follow-up), it was determined that the effects of depression on the cardiovascular system have the same effect as obesity and high cholesterol. Therefore, it has been recommended to standardize diagnostic tests to check for depression in patients with heart disease, as it plays a vital role in the impact on their health [24].

The level of anxiety and depression using the Hospital Anxiety and Depression Scale (HADS) before and after a course of high-tone therapy in group I is presented in Figure 4.

In group I (hypertension, CCI) the level of anxiety at the beginning was 8.63 points, which corresponds to subclinically expressed anxiety, and after undergoing a course of high-tone therapy - 6.57 points, i.e. the level of anxiety decreased by 2.06 points ($p < 0.01$).

Before treatment, the level of depression was at the upper limit of normal - 6.86 points, and then decreased to normal - 4.94 points (- 1.92 points), ($p < 0.05$).

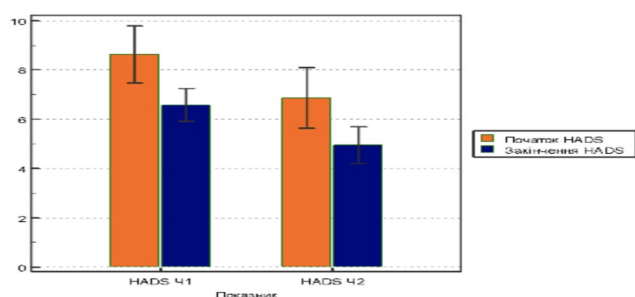


Fig. 4. The level of anxiety and depression on the HADS scale before and after the course of high-tone therapy in group I.

In determining the level of anxiety and depression in group II the results were obtained and presented in Figure 5.

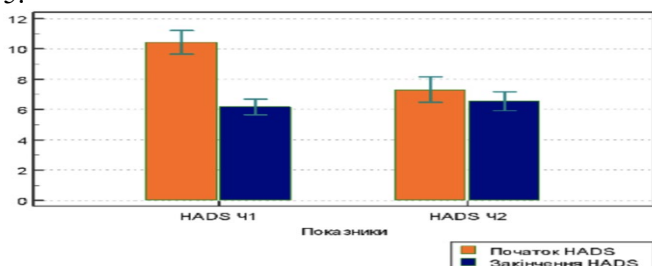


Fig.5. Level of anxiety and depression on the HADS scale before and after the course of high-tone therapy in group II

In group II, the initial level of anxiety was 1.77 points higher than in group I, and amounted to 10.4 points, which corresponds to clinically pronounced anxiety. After undergoing a course of high-tone therapy it was 6.1 points, i.e. returned to normal, the difference was 4.3 points ($p < 0.01$).

The level of depression at the beginning of therapy was 7.03 points, which corresponds to subclinically expressed depression, and after undergoing a course of high-tone therapy, it decreased by 0.53 points to normal (6.5 points) ($p < 0.05$).

A comparative analysis of the initial data of groups I and II for each criterion for assessing the quality of life of SF-36 was carried out. It is presented in table 1 and figure 6.

Table 1 - Comparison of the original data of groups I and II on the scale SF-36

Quality of life indicators	I group (hypertension, CCI) $\pm m$	II group (DM, hypertension, CCI) $\pm m$	p
PF	76,84 \pm 2,85	57,38 \pm 4,1	<0,001
RP	50 \pm 4,78	55,57 \pm 4,51	>0,05
BP	58,89 \pm 4,31	43,19 \pm 3,79	<0,05
GH	62,23 \pm 2,37	49,38 \pm 3,43	<0,01
VT	47,5 \pm 3,17	41,9 \pm 3,87	>0,05
SF	62,18 \pm 3,9	60,83 \pm 3,85	>0,05
RE	44,57 \pm 5,64	41,33 \pm 6,55	>0,05
MH	52,52 \pm 3,14	40,14 \pm 1,84	<0,01

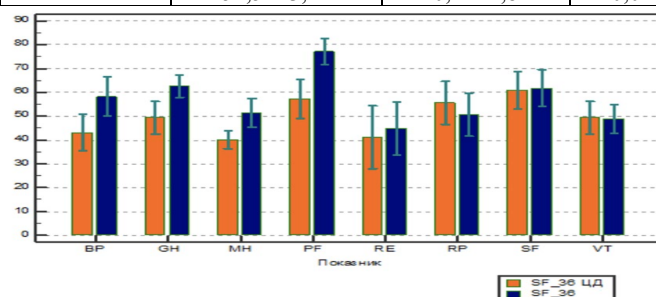


Fig. 6. Comparison of the original data on the SF-36 scale between groups I and II.

Note: BP - pain intensity, GH - general health, MH - mental health, PF - physical functioning, RE - role functioning due to emotional state, RP - role functioning due to physical condition, SF - social functioning, VT - vital activity.

According to the results of comparison of the initial data in group I (hypertension, CCI), the following indicators were higher: PF - physical functioning ($p < 0.001$), BP - pain intensity ($p < 0.05$), GH - general health ($p < 0.01$), MH - mental health ($p < 0.01$), which indicates a better initial general health of this group of patients than in patients with concomitant type 2 DM. Only one indicator was lower in group I compared to group II - RP - role functioning due to physical condition, but this indicator did not reach the level of statistical significance.

It should be noted that according to the literature sources, patients with type 2 DM have a low quality of life, which is often associated with depression, and also they have complications in the form of diabetic polyneuropathy, which also leads to a lower pain intensity and general condition indicators [18, 25].

The results of the assessment of quality of life before and after undergoing a course of high-tone HiTOP 4 touch therapy in group I (hypertension, CCI) are presented in Figure 7.

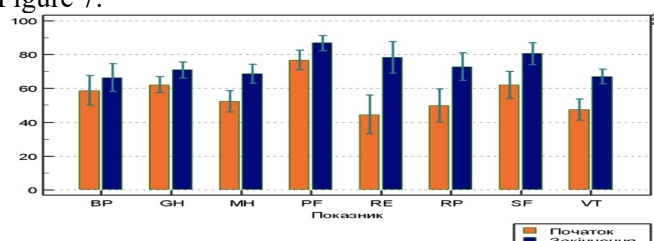


Fig. 7. Indicators of the SF-36 scale in group I before and after undergoing high-tone therapy

In the pathogenesis of CCI in hypertension there is arteriosclerosis (lipohyalinosis) of small penetrating arteries and arterioles (hypertensive arteriopathy) [22]. The use of supra-tone frequency currents improves microcirculation, including in the brain, which can help restore the patient's psycho-neurological status and improve his quality of life. Thus, in group I, such indicators of the SF-36 scale as MH - mental health ($p < 0.001$), RE - role functioning due to emotional state ($p < 0.001$), VT - vital activity ($p < 0.001$) greatly increased and reached the maximum statistical significance.

The use of high-tone therapy in group I led to an increase in quality of life in other indicators: GH - general health ($p < 0.05$); PF - physical functioning ($p < 0.05$); RP - role functioning due to physical condition ($p < 0.01$), SF - social functioning ($p < 0.01$).

Only the indicator of BP - pain intensity did not reach the level of statistical significance ($p > 0.05$). It should be noted that the intensity of pain in group I may have been due to concomitant pathology of the musculoskeletal system, which according to the literature occurs in 52% of patients with hypertension [26].

Figure 8 shows the dynamics of quality of life on the SF-36 scale before and after undergoing a course of high-tone therapy in group II.

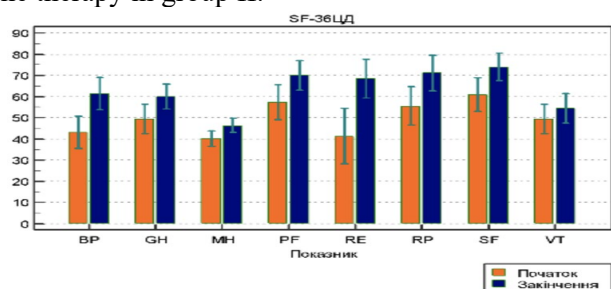


Fig. 8. Indicators of the SF-36 scale in group II before and after undergoing high-tone therapy

During the analysis of indicators after undergoing a course of high-tone therapy in group II, the following indicators of quality of life improved: BP - pain intensity ($p < 0.01$), MH - mental health ($p < 0.05$), RE - role functioning due to emotional state ($p < 0.01$), RP - role functioning due to physical condition ($p < 0.05$), SF - social functioning ($p < 0.05$).

The indicator of pain intensity in group II of patients was mainly due to diabetic polyneuropathy as a complication of DM (according to ambulatory cards 80% of patients with type 2 diabetes). It indicated statistically significant regression after the rehabilitation course.

Thus, 5 out of the 8 indicators of quality of life on the SF-36 scale have undergone a statistically significant improvement, which proves the high efficiency of this rehabilitation method in comorbid pathology and substantiates its use. Up to this date, studies have shown little or moderate benefit in improving the quality of life of patients with DM [18].

Thus, the use of supra-tone frequency currents in patients with comorbid pathology (hypertension, CCI, type 2 DM) significantly improves cognitive function, reduces anxiety and depression, improves quality of life.

To understand the mechanism of action of supra-tone frequency currents on the pathogenesis of CCI, we must remember that we primarily influence the mitochondria. As mentioned above, the main mechanism of action of high-tone therapy is to increase energy balance due to influence on mitochondria. To date, mitochondrial function in lymphocytes has been shown to be a potential biomarker of neurodegeneration progression, as peripheral mitochondrial function is associated with moderate cognitive disorders due to impaired mitochondrial ATP production, oxidative stress, and increased proton outflow. Thus, high-tone therapy is pathogenetically substantiated in the cerebral small vessel disease [27].

High anxiety is often combined with several pathologies of the nervous system. Existing treatments (e.g., cognitive-behavioral therapy and anxiolytic drugs) help to achieve remission in only 50% of adults, while more than a third of patients with anxiety disorders are resistant to treatment. Due to the limited effectiveness of existing (psychological and pharmacological) treatments, there is a need to develop new methods of treatment based on a deeper understanding of the molecular mechanisms underlying the pathogenesis of anxiety [28, 29, 30].

Recent studies show that impaired neuroplasticity and stability may underlie the pathophysiology of anxiety disorders. It has been suggested that the release of mitochondrial calcium (Ca^{2+}) plays a key role in modulating the tone of synaptic plasticity in various neuroanatomical areas, including those involved in the pathophysiology of anxiety. Mitochondria also play a role in calcium homeostasis. Calcium (Ca^{2+}) is the main

secondary messenger that helps regulate both neurotransmission and short-term and long-term plasticity of neurons in the brain [31]. The fine spatial and temporal organization of intracellular calcium signals is important for the functioning of the central nervous system (CNS). Signals are transmitted throughout the CNS due to local changes in the concentration of Ca^{2+} . Thus, Ca^{2+} signals that are required for synaptic transmission and, therefore, for the transmission of information throughout the CNS are transmitted to the mitochondria, where it is assumed that Ca^{2+} modulates mitochondrial metabolism with activation of the tricarboxylic acid cycle, ATP synthase and aspartate carrier, followed by ATP increase [32, 33].

A study of the relative role of mitochondrial buffering and the endoplasmic reticulum Ca^{2+} showed that dendritic mitochondria rapidly accumulate Ca^{2+} , while the endoplasmic reticulum shows a more delayed increase in Ca^{2+} during high-frequency stimulation. Thus, it is possible that the regulation of mitochondrial function plays an important role in regulating the synaptic power of neurons that mediate complex behavior [34].

Identification of key pathophysiological components is vital for the development of new approaches to therapy, such as the use of high-tone therapy, which directly influences the mechanism of metabolic dysfunction of the brain and has a confirmed result according to MoCA testing.

There is another extremely important mechanism in the effect of high-tone HiTOP 4 touch therapy on mitochondria in the pathogenesis of many neurodegenerative diseases. N-acetylaspartate (NAA) is synthesized in the mitochondria of neurons from aspartate and acetyl-coenzyme by aspartate-N-acetyltransferase (ANAT), and is a precursor of an important neurotransmitter and one of the most common dipeptides contained in the human brain. That is, influencing the mitochondria, we enhance the synthesis of NAA in the neurons of the brain. After synthesis of neurons in the mitochondria, NAA enters glia cells - oligodendrocytes and astrocytes. It is established that NAA is one of the main regulators of osmotic processes in the brain and is considered as a signaling molecule in the system of neuron-glia interaction, also involved in the synthesis of brain lipids, can serve as a source of aspartate, acyl groups in myelin synthesis. From neurons to oligodendrocytes, it enters as a key metabolite for myelin synthesis. Therefore, by influencing the mitochondria, we trigger neurorepair processes that are important in many diseases of the brain, including CCI [35].

Thus, the use of high-tone therapy in patients with comorbid pathology (hypertension, CCI, type 2DM) improves cognitive impairments, reduces anxiety and depression, improves quality of life, which is probably

due to the influence of supra-tone frequency currents on the molecular mechanisms of cells, and it is on the mitochondria.

Conclusions

1. Patients with hypertension and CCI indicators on the scale of quality of life SF-36 had significantly better indicators of physical functioning ($p < 0.001$), pain intensity ($p < 0.05$), general health ($p < 0.01$), mental health ($p < 0.01$) in comparison with patients with concomitant DM. The level of anxiety was significantly higher in the group patients with type 2 DM than in the other group of patients with hypertension ($p < 0.05$).
2. The course of high-tone therapy given to patients with hypertension and CCI led to an improved quality of life, on all indicators of the SF-36 scale, except for pain intensity ($p > 0.05$), increased cognitive function by 3.52 points on the MoCA scale (0.001), reduction of anxiety by 2.06 points ($p < 0.01$) and depression by 1.92 points ($p < 0.05$) on the HADS scale.
3. Carrying out a course of high-tone therapy in patients with CCI, hypertension and type 2 DM led to a significant improvement of 5 out of 8 indicators of quality of life on the SF-36 scale, cognitive functions by 2.27 points ($p < 0.05$) on the MoCA scale, reduction of anxiety by 4.3 points ($p < 0.01$) and depression by 0.53 points ($p < 0.05$) on the HADS scale.

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The importance of body composition assessment in the rehabilitation process

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Abstract

Introduction. This personal study provides several aspects of the importance of body composition assessment in rehabilitation process in order to manage fat mass (FM), fat-free mass imbalances (FFM), pre-sarcopenia status, sarcopenia and risks association and to improve global functionality. Health outcomes and risk estimations regarding fat mass and skeletal muscle mass (SMM) plays a major role and should be integrated into the rehabilitation process routine in order to avoid functional impairment and physical disability by applying specific kinetic programs. **Material and method.** A number of 14 subjects classified as outpatients who have received physical therapy at home- kinesiotherapy for post-fracture / dislocation status of the lower limbs in accordance with the medical recommendations and legislation in force. At the end of the rehabilitation phase, the body composition was measured using bio impedance in order to adjust the next step of the active rehabilitation. The measurements were obtained with a completely bioelectrical impedance analyzer (BIA). Single frequency BIA (SF-BIA) was used. For each subject major body compartments determined as FFM (including bone mineral tissue, total body water-TBW and visceral protein), SMM and FM were measured as a tissue-system by means of linear empirical equations stored in the system memory together with personal physical data. IBM SPSS software version 25 was used for statistical analysis. **Results and discussions.** Four age groups determined as follows: 21.43% for 18-39 years, 50-69 years, >70 years each and 35.71% for 40-49 years, based on the rate of muscle loss, because its integrity is essential for rehabilitation program. From the 14 subjects there are 57.14 % men and 42.86% women, from urban environment 78.57% and rural 21.43%. Mean Age is 48.79 years \pm 18.792 Std. Deviation. Fat mass from BIA recorded 21.43% cases low and normal each, and high/very high 57.14% of total cases. Consequently, of BMI (body mass index) association, 57.14% are at normal weight, 35.71% overweight and with obesity and 7.14% underweight. One Sample Chi-Square test applied to BMI Type Associate with FM reveals the statistical significance, $< .05(.014)$. Fat-free mass index (FFMI), fat mass index (FMI), skeletal mass index (SMI) were computed by adjusted with height square. FMI somatotype components results are 64.3% adipose cases, 21.4% intermediate and 14.3% lean. One Sample Chi-Square test applied to FMI Types reveals the statistical significance $< .05(.046)$. Regression equation of standard BMI and FMI with scatter plots for 77.8% of cases was computed in the present study. FFMI somatotype components recorded 57.1% intermediate cases, 21.4% slender and solid each. Regression equation of standard BMI and FFMI with scatter plots for 57.4% of cases was computed. Three patients exceeded 15 seconds at the chair stand test so probable sarcopenia was identified. From BIA were extracted the value for the skeletal mass and SMI was calculated by height adjusted: 13 (92.86%) cases have normal values and one (7.14%) case have optimal value. Regression equation of standard BMI and SMI with scatter plots for 66.4% of cases was computed. Pearson correlation (CI =99%) denotes strong statistical relationship between BMI and FMI ($r=0.882$), FFMI ($r=0.815$), Age ($r=0.659$), Water ($r=-0.693$). FMI also correlates strongly with Age ($r= 0.707$), Water ($r=-0.925$) and Proteins values ($r=-0.819$). FFMI also correlates strongly with SMI ($r=0.984$). Water correlates with Protein ($r=0.848$, CI = 99%). Beta regression analysis strongly correlates SMI prediction with FFMI ($\beta=0.731$), Water ($\beta=0.138$) and Protein ($\beta=-0.370$) for $p<0.05$. Anova significance of .000 (CI=99%) with applicability of 99.8% of the cases ($R^2 =0.998$) proved that constant predictors: Water (%), FFMI, Proteins (%), FMI, BMI interact to influence SMM variability. 64.25% of subjects recorded an insufficient water level and 71.43% of subjects recorded an insufficient proteins level. Body composition evaluation should be integrated into routine clinical practice for the initial assessment and sequential follow-up and the strongest point of BIA is the possibility to replace invasive laboratory analysis with a quick, noninvasive test that can be carried out in a medical office. Body composition evaluation should be performed at the different stages of the disease, during the course of treatments and the rehabilitation phase. **Conclusions.** For each patient specific kinetic program will be developed. FMI increase (64.3% adipose cases) denotes the risk of metabolic syndrome and insulin resistance. Consequently, resistive and concentric exercises will be applied. For FFMI loss (57.1% intermediate cases, 21.4% slender) and SMI increasing (92.86% cases have normal values but not optimal ones, 21.43% pre-sarcopenia detected by positive chair test) resistance, eccentric/concentric exercises should be applied. All kinetic programs will be preceded by warm-up and followed by stretching taking into account cardiac reserve for each patient. Maximal/sub-maximal force exercises will be used age-related. Additional water (64.25% of subjects recorded an insufficient water level) and proteins levels (71.43% of subjects recorded an insufficient proteins level) must be balanced by nutritional support in accordance with rehabilitation consult and current physician approval in the interdisciplinary team. BIA may be an important supporting tool for health professionals in order to customize the rehabilitation programs for each patient.

Keywords: *body composition, rehabilitation, bioelectrical impedance, fat-free mass index, fat mass index, skeletal muscle index,*

1. Introduction This personal current study proposes that the body composition evaluation should be integrated into the rehabilitation process routine in order to reduce the clinical and functional consequences of diseases in the setting of a cost effective medico-economic approach.

1.1 Body composition models and measurement methods. Body composition comprises five level components defined as atomic, molecular, cellular, tissue system and whole body being described as a two, three or four compartment model, which can be used combined for a better understanding. A two-compartment model example is body weight (BW) = fat mass (FM) + fat-free body mass (FFM); a three-compartment model in which BW = fat + water (TBW- total body water) + residual (glycogen+ minerals + protein) and BW = fat (FM)+ bone mineral + lean soft tissue (FFM equivalent); and a four compartment model in which BW = fat (FM)+ water (TBW)+ minerals + residual (glycogen + protein).(1, 2) Measurement technologies currently available for body composition levels are specified in Table 1.

Table 1 Body composition components and measurement method (1, 3, 4)

Level	Items	Recent methods	Other
Atomic	Hydrogen, Carbon, Oxygen (95%)	Neutron activation analysis	Whole-body 40 potassium counting
Molecular	Lipid + Water+ Proteins+ Glycogen + Minerals	Bio impedance analysis Dual energy X-ray absorptiometry Multicompartment models	
Cellular	Cells + Extracellular Fluid and Solids		Tracer dilution
Tissue system	Adipose Tissue+ Skeletal Muscle+ Skeleton+ Visceral Organs and Residual	Computerized axial tomography Magnetic resonance imaging	Ultrasound 24-h urinary creatinine and 3-methyl histidine excretion
Whole body			Anthropometry

1.2. Health outcomes and risk estimation regarding FM/FFM and SMM

The most common way to evaluate body composition is at molecular level according to Fat-free mass (FFM) referred as lean body mass and fat mass (FM). FFM can be divided into various items: bone mineral, extracellular water (ECW), intracellular water (ICW) and visceral protein. Total body water (TBW) represents the sum of ECW and ICW, in a normal hydration state = 73.2% (5, 6, 7, 14). These estimations are important health outcomes in relation to the management of sarcopenia (low muscle mass and functional impairment, physical disability, gait speed and mortality) and in the process of identifying the risk of excess fat. (1, 2). Sarcopenia defined as an age-related loss of skeletal muscle mass

(SMM), muscle strength (dynapenia), and physical function integrity are important facts in the etiology of disability. (8, 9, 10, 11).

Direct (cadaver dissection) and indirect methods were developed to estimate FM and FFM, bone minerals and skeletal muscle mass (SSM) – Table 2.

Table 2 Indices and predictive techniques after (12, 13, 14, 15)

Simple measurements or indices (3)	Features	Method type
Skinfold thickness measurements	Assessment of subcutaneous fat depots; can be converted into standard deviation score (SDS) format for longitudinal evaluations	Indirect
Body mass index (BMI, calculated as weight/height ²)	Index of relative weight, often expressed as SDS to take into account gender and sex. BMI is predictive of clinical outcomes such as type 2 diabetes, metabolic syndrome	Indirect
Waist circumference (WC)	Predictive of adverse outcomes such as lipid profile or insulin resistance	Indirect
Predictive techniques	Features	Method type
Bioelectric impedance analysis (BIA)	Measures impedance of the body to a small electric current. Conventional BIA analysis measures properties of the FFM only, indicating whether changes in lean mass are in the same direction as body weight, but should not be used to estimate change in fat mass.	Double Indirect
Dual energy x ray absorptiometry (DXA)	(DXA) measures bone mineral mass, which is calculated from the differential absorption of x rays of two different energies. Values of FM and FFM are calculated for whole body using instrument specific algorithms. Ionising radiation dose equivalents of contemporary instrumentation are below background levels.	Indirect
Densitometry	FM and FFM, requires measurement of total body density (body mass/body volume). Body volume was measured by hydro-densitometry or plethysmography. Densitometry monitors changes over time in overweight or obese individuals, and its accuracy is less likely to be confounded by longitudinal changes in fitness than DXA	Indirect
Isotope dilution (hydrometry)	Deuterium dilution can be used to measure TBW, allowing estimation of FFM. A dose of water labelled with deuterium is given and, following equilibration, enrichment of the body water pool measured using samples of either saliva, urine, or blood. Samples are generally analysed by isotope ratio mass spectrometry	Indirect
Magnetic resonance imaging	MRI is an imaging technique that estimates the volume rather than the mass of adipose tissue. By analysing the absorption and emission of energy in the radio frequency range of the electromagnetic spectrum, the technique produces images based on spatial variations in the phase and frequency of the energy absorbed and emitted.	Double Indirect
Other techniques	Total body electrical conductivity (TOBEC) a whole body potassium scanning (TBK)	Indirect
Multi-component models	Gold standard for in vivo measurement. The three-component model divides body weight into fat, water, and remaining fat-free dry tissue, and requires measurements of body weight, body water by hydrometry, and body volume by densitometry. The four component model divides fat-free dry tissue into protein and mineral, and requires the same data plus measurement of bone mineral by DXA	Indirect or double indirect

Application of the combination of these methods may reduce the misdiagnosis FFM variability. Multicomponent models are considered accurate to act as reference or criterion methods for the molecular approach to measuring body composition (fat and fat-free masses).

Material and method

Material 14 subjects classified as outpatients who have received physical therapy-kinesiotherapy at home for post-fracture / dislocation status of the lower limbs in accordance with the medical recommendations and legislation in force. (Period March-October 2021).

Method At the end of the rehabilitation phase, the body composition was measured using bio impedance in order to adjust the next step of the active rehabilitation.

The measurements of bioelectric impedance were obtained with a whole bioelectrical impedance analyzer (Amazfit Smart Scale - Body Composition Analyzer, Declaration of Conformity with directives 2014/53/EU and 2014/65/EU) from the own endowment of the practice cabinet. It was used a single frequency BIA (SF-BIA) of 50 kHz for body impedance components resistive and reactive ones. The method is based on the conduction of a painless low-intensity, imperceptible electrical current (500 to 800 μ A) at a fixed (\approx 50 kHz). Measurement of body composition using bioelectric impedance is based on prediction equations. For each subject major body compartments determined as FFM (including bone mineral tissue, total body water and visceral protein), SMM and FM were measured as a tissue-system. TBW, SMM and FFM using SF-BIA were automatically estimated by means of linear empirical equations stored in the system memory together with personal physical data (age, weight, height).

Exclusion criteria: pregnant women, people wearing a pacemaker, subjects with skin lesions and altered fluid balance

Inclusion criteria: before the test: no alcohol for at least 8 h, no food and no drinking water for at least 4 h;

Procedure: the subjects were positioned vertically with arms and feet spread apart and shoes and socks removed and the conducting surfaces enter in contact with one of the body extremities, foot-foot in this case. The vertical model is easy to apply due to the fact that requires the subject to stand up barefoot on the electrodes platform (foot-foot touch). The system is a portable scale of facile use.

Results interpretation referred to Body Composition Zepp Analyser used, revised European consensus on definition and diagnosis of sarcopenia (16), fat-free mass index cut-off (FFMI = FFM/height²) and fat mass index cutoffs (FMI = FM/height²) (16, 17,18), BMI cutoffs and its association with percent body Fat (%) (18, 19). Age groups were established based on the rate of muscle loss (16, 20). IBM SPSS software version 25 was used for statistical analysis.

Results

Demographic variables.

There are four age groups as follows: 21.43% for 18-39 years, 50-69 years, >70 years each and 35.71% for 40-49 years based on the rate of muscle loss, because its integrity is essential for rehabilitation program, according to Fig. 1 - Age Groups based on the rate of muscle loss. Reason for age group distribution was the variability of muscle mass with aging.

Variation of muscle mass and strength decreases with aging so up to 40 years are maximal levels and between 40 and 50 years

and over, loss of leg muscle mass is 1–2% per year and loss of strength levels 1.5–5% per year. As a result, 25 % of people under the age of 70 years and 40 % of those over the age of 80 years are sarcopenic. (16, 20, 21, 22, 23, 24)

From the 14 subjects there are 57.14 % men and 42.86% women, from urban environment 78.57% and rural 21.43%, according to Fig. 2 - Gender Distribution Pyramid, Fig. 3 - Environment Distribution.

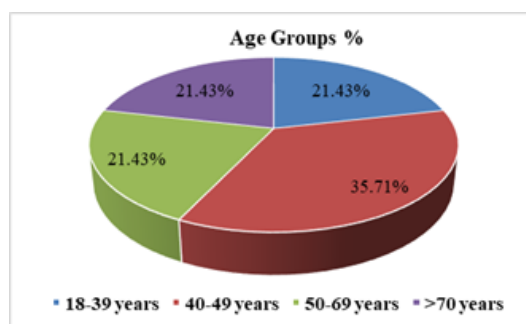


Fig. 1 Age Groups based on the rate of muscle loss

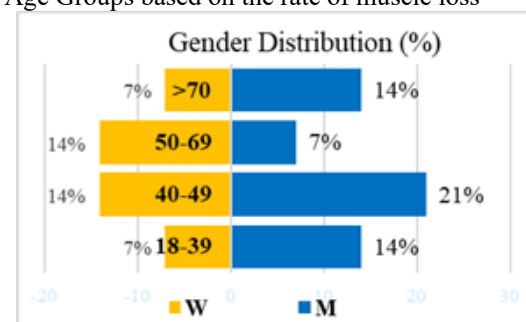


Fig. 2 Gender Distribution Pyramid

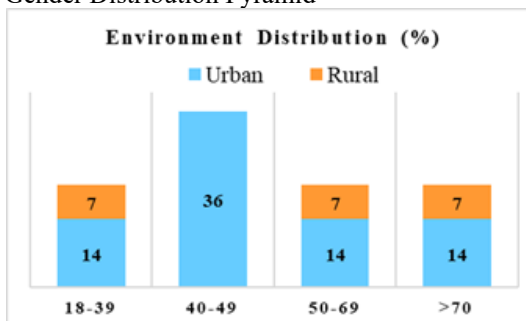


Fig. 3 Environment Distribution

Mean Age is 48.79 years \pm 18.792 Std. Deviation, Weight 74.41 kg \pm 17.99 Std. Deviation, Height (m) 1.70 m \pm 0.081 Std. Deviation as specified in Table 3 - Mean, median, standard deviation on the studied sample. Frequency of Age Groups, Weight and Height including percentiles presented in Fig.4, Fig. 5 and Fig. 6.

Table 3 Mean median, standard deviation on the studied sample

Statistics		Age	Weight (Kg)	Height (m)
N	Valid	14	14	14
	Missing	0	0	0
Mean		48.79	74.4107	1.7057
Median		44.50	73.1250	1.7000
Std. Deviation		18.762	17.99798	.08055
Minimum		18	48.50	1.58
Maximum		78	104.10	1.84
Percentiles	25	39.75	57.6125	1.6300
	50	44.50	73.1250	1.7000
	75	67.75	89.0125	1.7675

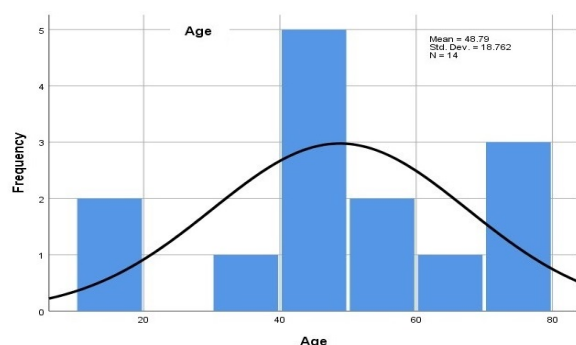


Fig. 4 Frequency of Age Groups including percentiles

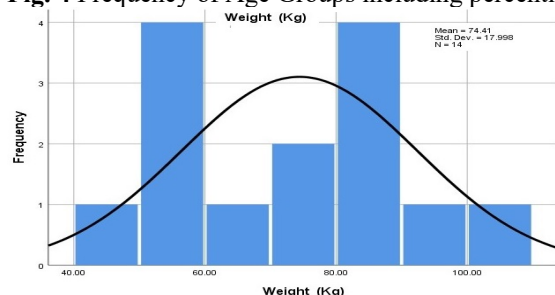


Fig. 5 Frequency of Weight including percentiles

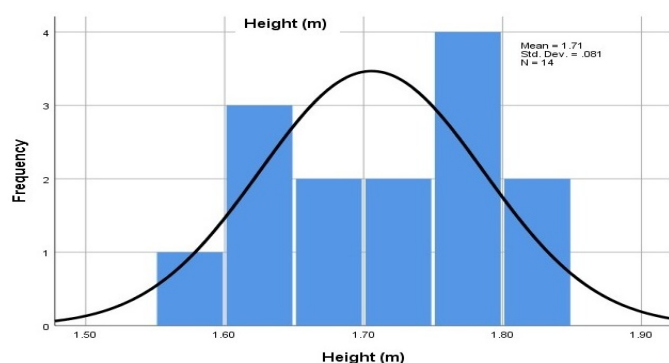


Fig. 6 Frequency of Height including percentiles

Health outputs

Standard BMI interpretation denotes 7.14% of cases underweight, 50% of normal weight and 42.86% overweight and obese. Fat mass from BIA recorded 21.43% cases low and normal each, and high/very high 57.14% of total cases. Association with Corporal Fat (%) from BIA was proceed according to Weight Classification (18, 19)

Table 4 Weight Classification

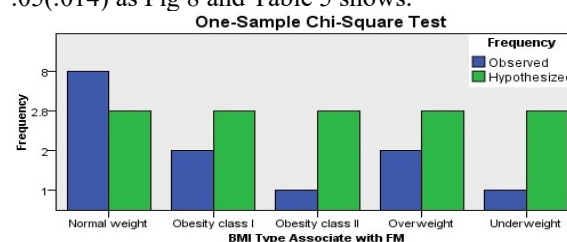
BMI kg/m2	Weight Classification (18,19)	Males FM(*)	Female FM(*)
18.5-24.9	Normal weight	<=26.0	<=34.0
18.5-24.9	Overweight	>26	>34
25.0-29.9	Normal weight	<=31.0	<=39.5
25.0-29.9	Overweight	>31	>39.5
30.0-34.9	Obesity class I	>=35	>=43
>=35	Obesity class II	>=39	>=50

As a result, 57.14% are at normal weight, 35.71% overweight and with obesity and 7.14% underweight as Table 5 shows.

Table 5 BMI Type Associate with FM

BMI Type Associate with FM					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Normal weight	8	57.1	57.1	57.1
	Obesity class I	2	14.3	14.3	71.4
	Obesity class II	1	7.1	7.1	78.6
	Overweight	2	14.3	14.3	92.9
	Underweight	1	7.1	7.1	100.0
	Total	14	100.0	100.0	

One Sample Chi-Square test applied to BMI Type Associate with FM reveals the statistical significance by rejecting the null hypothesis of equal distribution. The significance level is < .05(.014) as Fig 8 and Table 5 shows.



Total N	14
Test Statistic	12.429
Degrees of Freedom	4
Asymptotic Sig. (2-sided test)	.014

1. There are 5 cells (100%) with expected values less than 5. The minimum expected value is 2.800.

Fig. 8 Chi-Square test BMI Type/FM

Table 5 Hypothesis Test Summary BMI Type/FM

Hypothesis Test Summary				
	Null Hypothesis	Test	Sig.	Decision
1	The categories of BMI Type Associate with FM occur with equal probabilities.	One-Sample Chi-Square Test	0.014	Reject the null hypothesis.
Asymptotic significances are displayed. The significance level is .05.				

Fat mass (FM) was deducted from corporal fat percentage adjusted by weight. The results body composition is based on the same principle as BMI calculation, towards the systematic normalization for body height of (FMI) (kg)/height² (m) = FM index. FMI types lean, intermediate and adipose used to evaluate general relationships between the body composition indices and somatotype components.

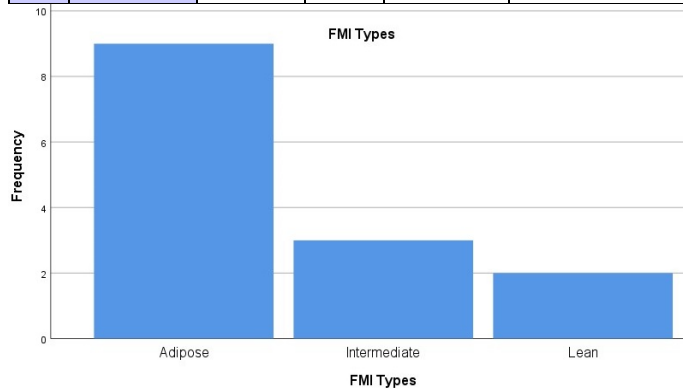
Table 6 FMI Types somatotype components

FMI Types (17)	Lean	Intermediate	Adipose
Males	<1.7	1.7-4.4	>4.4
Females	<3.4	3.4-6.4	>6.4

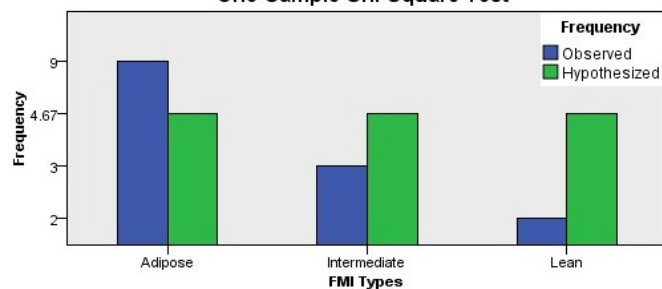
Applying to FMI Types somatotype components to the present sample results 64.3% adipose cases, 21.4% intermediate and 14.3% lean as Table 7 and Fig 9 of frequency. Age group distribution of 64.3% adipose cases comprises: 1 subject of 18-39 years, 4 cases of 40-49 years, 2 cases of 50-69 years and 2 cases of >70 years.

Table 7 FMI Types

FMI Types					
		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Adipose	9	64.3	64.3	64.3
	Intermediate	3	21.4	21.4	85.7
	Lean	2	14.3	14.3	100.0
	Total	14	100.0	100.0	

**Fig. 9** Frequency of FMI Types

One Sample Chi-Square test applied to FMI Types reveals the statistical significance by rejecting the null hypothesis of equal distribution. The significance level is $< .05(.046)$ as Fig 10 and Table 8 shows.

One-Sample Chi-Square Test

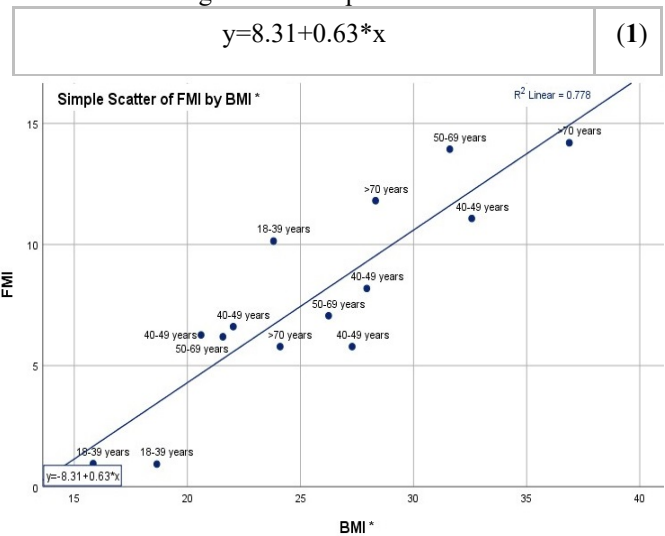
Total N	14
Test Statistic	6.143
Degrees of Freedom	2
Asymptotic Sig. (2-sided test)	.046

1. There are 3 cells (100%) with expected values less than 5. The minimum expected value is 4.667.

Fig. 10 Chi-Square test for FMI Type**Table 8** Hypothesis Test Summary for FMI Type

Hypothesis Test Summary				
	Null Hypothesis	Test	Sig.	Decision
1	The categories of FMI Types occur with equal probabilities.	One-Sample Chi-Square Test	0.046	Reject the null hypothesis.
Asymptotic significances are displayed. The significance level is .05.				

Regression equation (1) was computed in the present study by taking into consideration standard BMI (x) and FMI (y) with scatter plots for 77.8% of cases, strong relation between the two variables as Fig 11 shows – personal contribution

**Fig. 11** Scatter plots/ regression equation of standard BMI (x) and FMI (y)

Fat-free mass (FFM) was determined by summing the amounts adjusted by weight of various components: bone mineral (%); water seen as total body water (%) and visceral protein (%). A fat-free mass index (FFMI = FFM/ height²) may also eliminate the influence of stature in comparing FFM by FFM index calculation.

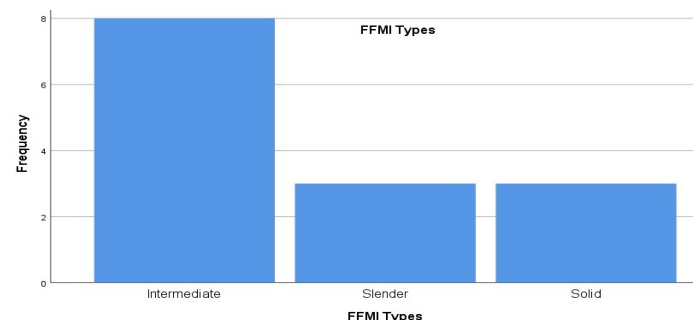
Table 9 FFMI Types somatotype components

FFMI Types (17)	Slender	Intermediate	Solid
Males	<16.5	16.5–19.9	>19.9
Females	<14.4	14.4–17.1	>17.1

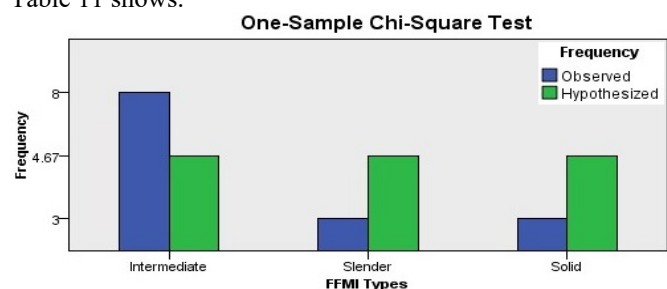
Applying to FFMI Types somatotype components to the present sample results 57.1% intermediate cases, 21.4% slender and solid each as shown in Table 10 and Fig 12 of frequency. Age group distribution of 21.4% slender and solid each cases comprises: 2 subjects of 18-39 years, 1 case of 40-49 years for slender and 2 cases of 40-49 years and 1 case of >70 years for solid.

Table 10 FFMI Types

FFMI Types				
		Frequency	Percent	Valid Percent
Valid	Intermediate	8	57.1	57.1
	Slender	3	21.4	21.4
	Solid	3	21.4	21.4
	Total	14	100.0	100.0

**Fig. 12** Frequency of FFMI Types

One Sample Chi-Square test applied to FFMI Types reveals no statistical significance by retaining the null hypothesis of equal distribution. The significance level is $> .05(.168)$ as Fig 13 and Table 11 shows.



Total N	14
Test Statistic	3.571
Degrees of Freedom	2
Asymptotic Sig. (2-sided test)	.168

1. There are 3 cells (100%) with expected values less than 5. The minimum expected value is 4.667.

Fig. 13 Chi-Square test for FFMI Type

Table 10 Hypothesis Test Summary for FFMI Type

Hypothesis Test Summary				
	Null Hypothesis	Test	Sig.	Decision
1	The categories of FFMI Types occur with equal probabilities.	One-Sample Chi-Square Test	0.168	Retain the null hypothesis.
Asymptotic significances are displayed. The significance level is .05.				

Regression equation (2) was computed in the present study by taking into consideration standard BMI (x) and FFMI (y) with scatter plots for 57.4% of cases, strong relation between the two variables as Fig 14 shows – personal contribution.

$$y = 7.26 + 0.37 * x \quad (2)$$

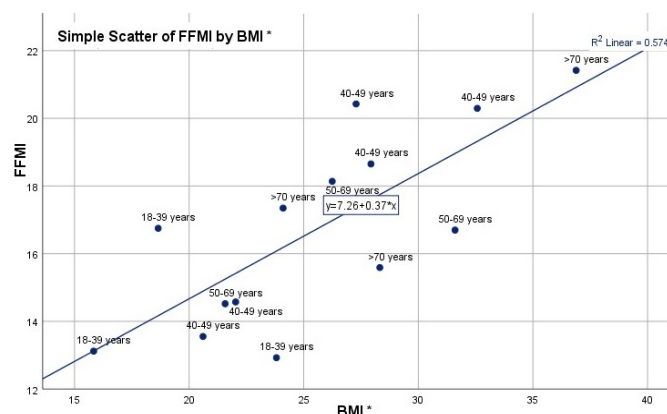


Fig. 14 Scatter plots/ regression equation of standard BMI (x) and FFMI (y)

European consensus on definition and diagnosis of sarcopenia specified the factors that cause sarcopenia. Factors usually interact. Categorised as primary age-associated muscle loss and secondary based on physical inactivity determined by

inflammatory conditions, sedentary behaviour, limited mobility or bed rest, under-nutrition or malabsorption over-nutrition or obesity. (16) All 14 subjects have a sedentary behaviour and physical inactivity due to the specific condition post-fracture / dislocation status of the lower limbs so at the end of rehabilitation. SMM and strength were evaluated according to EWGSOP2 practical algorithm. The chair stand test (also called chair rise test) was used for strength of leg muscles. The chair stand test measures the time needed for a patient to rise five times from a seated position without using arms. Since the chair stand test requires both strength and endurance, this test is a qualified but convenient measure of strength. It is used to identify low muscle strength. If time exceed 15 seconds for five rises, the test is positive. Three patients exceeded 15 seconds at the chair stand test so probable sarcopenia was identified: 2 woman and one man, one woman underweight, lean (FMI Type), slender (FFMI Type), age group 18-39 years, one woman adipose (FMI Type), intermediate (FFMI Type) and one man normal weight, intermediate (FM/FFM Type), both group age > 70 years. From BIA were extracted the value for the skeletal mass and SMI was calculated by height adjusted: 13 (92.86%) cases have normal values and one (7.14%) case have optimal value. EWGSOP2 sarcopenia cut-off points for low muscle quantity was used < 7.0 kg/m² for men and < 5.5 kg/m² for women. (16, 25).

Regression equation (3) was computed in the present study by taking into consideration standard BMI (x) and SMI (y) with scatter plots for 66.4% of cases, strong relation between the two variables as Fig 15 shows – personal contribution.

$$y = 3.15 + 0.24 * x \quad (3)$$

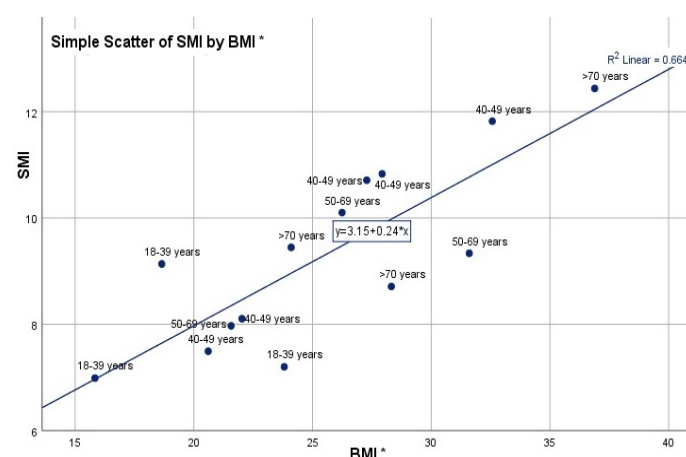


Fig. 15 Scatter plots/ regression equation of standard BMI (x) and SMI (y)

Pearson correlation were computed for BMI, FMI, FFMI, Age, Water (%), Protein (%) according to Table 11 and Fig 16. Strong statistical relationship were found between BMI and FMI ($r = 0.882$, CI = 99%), FFMI ($r = 0.815$, CI = 99%), Age ($r = 0.659$, CI = 99%), Water ($r = -0.693$, CI = 99%). FMI also correlates strongly with Age ($r = 0.707$, CI = 99%), Water ($r = -0.925$, CI = 99%) and Protein values ($r = -0.819$, CI = 99%). FFMI also correlates strongly with SMI ($r = 0.984$, CI = 99%). Water correlates with Protein ($r = 0.848$, CI = 99%). Negative values descending trend of one independent variable influenced by the ascending trend of the dependent variable.

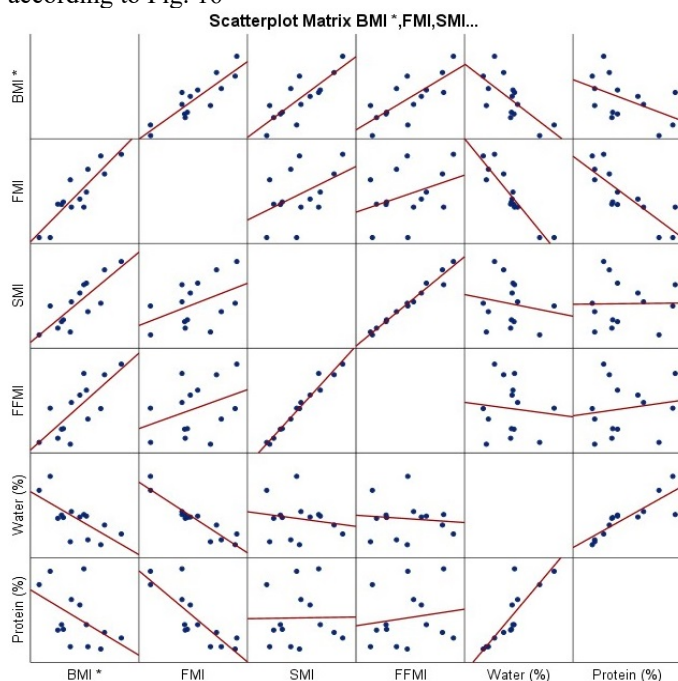
Table 11 Pearson Correlation

Pearson Correlations (r)								
		BMI *	FMI	FFMI	SMI	Age	Water (%)	Protein (%)
BMI *	r	1	.882**	.758**	.815**	.659*	-.693**	-0.494
	p		0.000	0.002	0.000	0.010	0.006	0.073
FMI	r	.882*	1	0.363	0.454	.707*	-.925**	-.819**
	p	0.000		0.202	0.103	0.005	0.000	0.000
FFMI	r	.758*	0.363	1	.984**	0.340	-0.098	0.153
	p	0.002	0.202		0.000	0.234	0.738	0.601
SMI	r	.815*	0.454	.984**	1	0.369	-0.170	0.014
	p	0.000	0.103	0.000		0.194	0.560	0.963
Age	r	.659*	.707**	0.340	0.369	1	-.670**	-0.516
	p	0.010	0.005	0.234	0.194		0.009	0.059
Water (%)	r	-	-	-	-	-	1	.847**
	p	0.006	0.000	0.738	0.560	0.009		0.000
Protein (%)	r	-	-	0.153	0.014	-	.847**	1
	p	0.494	.819**	0.601	0.963	0.059	0.000	

** . Correlation is significant at the 0.01 level (2-tailed).

* . Correlation is significant at the 0.05 level (2-tailed).

Matrix correlation representation with regression equation based on points cloud dispersion based on group age are according to Fig. 16

**Fig. 16** Matrix correlation representation

Beta regression analyse was applied to index predictors for skeletal mass variation in order to identify interdependency of action. SMI was considered depended variable and constant predictors established were Water, FFMI, Protein, FMI and BMI. Anova significance of .000 (CI=99%) with applicability

of 99.8% of the cases ($R^2 = 0.998$) proved that constant predictors: Water (%), FFMI, Protein (%), FMI, BMI interact to influence SMM variability according to Table 12 R Square, Table 13 ANOVA and Table 14 Variables Entered/Removed

Table 12 R Square

Model Summary				
Model	R	R Square	Adjusted R Square	Std. Error of the Estimate
1	.999 ^a	0.998	0.996	0.10240

a. Predictors: (Constant), Water (%), FFMI, Protein (%), FMI, BMI*

Table 13 ANOVA

ANOVA ^a						
Model		Sum of Squares	df	Mean Square	F	Sig.
1	Regression	37.690	5	7.538	718.894	.000 ^b
	Residual	0.084	8	0.010		
	Total	37.774	13			
a. Dependent Variable: SMI						
b. Predictors: (Constant), Water (%), FFMI, Protein (%), FMI, BMI *						

Table 14 Variables Entered/Removed^a

Variables Entered/Removed ^a			
Model	Variables Entered	Variables Removed	Method
1	Water (%), FFMI, Protein (%), FMI, BMI * ^b		Enter

a. Dependent Variable: SMI

b. All requested variables entered.

Beta regression analyse strongly correlates SMI prediction with FFMI ($\beta=0.731$), Water ($\beta=0.138$) and Protein ($\beta=-0.370$) for $p<0.05$. Pearson correlation denotes the action of each variable independent but beta regression analyse emphasizes interdependency between different predictors.

According to Zepp analyser 64.25% of subjects recorded an insufficient water level, age group distribution being as follows one case at 18-39 years, 3 cases at 40-49 years, 2 cases at 50-69 years and 3 cases over 70 years.

According to Zepp analyser 71.43% of subjects recorded an insufficient proteins level, age group distribution being as follows one case at 18-39 years, 4 cases at 40-49 years, 3 cases at 50-69 years and 2 cases over 70 years.

Discussions

Bioelectrical impedance analysis (BIA) is widely used as a quick, non-invasive and low-cost technique to estimate human body composition. The human body can be divided into different compartments. Body composition evaluation allows measurement of the major body compartments: FFM (including bone mineral tissue), FM, and total body water. Fat-free mass (FFM) or lean body mass includes all body parts that are not fat mass (FM). (26)

Fat mass determination is important for the onset and progression of obesity. Adipose tissue is a key factor in modulating lipid and glucose homeostasis. Given the role of fat and lean tissue in lipid metabolism and insulin resistance, assessing the body's tissue composition is an important part of the management of the diabetic patient. (27)

Changes in body compartments are detected with the techniques of body composition evaluation. The relation between FFM loss and mortality has been extensively shown with BIA, which is the most used method in clinical situation as nursing home residence, chronic heart failure, chronic obstructive pulmonary disease, dialysis, cancer, liver transplantation, amyotrophic lateral sclerosis, Alzheimer's disease. (28-41)

BIA measures the phase angle and a low phase angle is related to survival in geriatrics, oncology, HIV infection/AIDS, amyotrophic lateral sclerosis, peritoneal dialysis, and cirrhosis. The phase angle is associated with reduced survival. The relation of phase angle with prognosis and disease severity reinforces the interest in using BIA for the clinical management of patients with chronic diseases at high risk of undernutrition and FFM loss. FFM loss or a low phase angle is related to mortality in patients with chronic diseases, cancer (including obesity cancer patients), and elderly patients in long-stay facilities. A low FFM and an increased FM are associated with an increased period in adult hospitalized patients. The relation between FFM loss and clinical outcome is shown in patients with sarcopenic obesity. (28, 42-46). The increased prevalence of obesity together with chronic illnesses associated with fat-free mass (FFM) loss leads to an increased prevalence of sarcopenic obesity. FFM loss is related to increasing mortality, and impaired quality of life. The magnitude of the changes in this group of healthy men with few medical problems suggests that stronger exercise recommendations are needed to prevent sarcopenia and the early onset of disability. (47)

Consensus paper on sarcopenia by EWGSOP2 focuses on low muscle strength, detection of low muscle quantity and quality to confirm the sarcopenia diagnosis, updates the clinical algorithm that can be used for sarcopenia and provides clear cut-off points for measurements of variables that identify and characterise sarcopenia. Sarcopenia increases risk of falls and fractures, impairs ability to perform activities of daily living, mobility disorders and contributes to lowered quality of life. Sarcopenia is a progressive and generalised skeletal muscle disorder that is associated with increased adverse outcomes including fractures, falls, physical disability and mortality. Sarcopenia is probable when low muscle strength is detected. A sarcopenia diagnosis is confirmed by the presence of low muscle quantity or quality. When low muscle strength, low muscle quantity/quality and low physical performance are all detected, sarcopenia is considered severe. (16, 48-58)

Bioelectrical impedance analysis (BIA) has been explored for estimation of total or skeletal mass. BIA equipment does not measure muscle mass directly, but instead derives an estimate of muscle mass based on whole-body electrical conductivity. BIA equipment is

affordable, widely available and portable, especially single-frequency instruments. Since estimates of muscle mass differ when different instrument brands and reference populations are used, cross-validated Sergi equation for standardisation are needed. (59, 60).

Body composition evaluation should be integrated into routine clinical practice for the initial assessment and sequential follow-up. (28). The strongest point of BIA is the possibility to replace invasive laboratory analysis with a quick, noninvasive test that can be carried out in a medical office. Body composition evaluation should be performed at the different stages of the disease, during the course of treatments and the rehabilitation phase.

Conclusion

There are four age groups as follows: 21.43% for 18-39 years, 50-69 years, >70 years each and 35.71% for 40-49 years based on the rate of muscle loss, because its integrity is essential for rehabilitation program. From the 14 subjects there are 57.14 % men and 42.86% women, from urban environment 78.57% and rural 21.43%. Mean Age is 48.79 years \pm 18.792 Std. Deviation, Weight 74.41 kg \pm 17.99 Std. Deviation, Height (m) 1.70 m \pm 0.081 Std. Deviation. Standard BMI interpretation denotes 7.14% of cases underweight, 50% of normal weight and 42.86% overweight and obese. Fat mass from BIA recorded 21.43% cases low and normal each, and high/very high 57.14% of total cases. Consequently, of BMI association, 57.14% are at normal weight, 35.71% overweight and with obesity and 7.14% underweight. One Sample Chi-Square test applied to BMI Type Associate with FM reveals the statistical significance, the significance level is $< .05(.014)$. Applying to FMI Types somatotype components to the present sample results 64.3% adipose cases, 21.4% intermediate and 14.3% lean. Age group distribution of 64.3% adipose cases comprises: 1 subject of 18-39 years, 4 cases of 40-49 years, 2 cases of 50-69 years and 2 cases of >70 years. One Sample Chi-Square test applied to FMI Types reveals the statistical significance, the significance level is $< .05(.046)$. Regression equation (1) was computed in the present study by taking into consideration standard BMI (x) and FMI (y) with scatter plots for 77.8% of cases, strong relation between the two variables.

$$y=8.31+0.63*x$$

(1)

Applying to FFMI Types somatotype components to the present sample results 57.1% intermediate cases, 21.4% slender and solid each. Age group distribution of 21.4% slender and solid each cases comprises: 2 subjects of 18-39 years, 1 case of 40-49 years for slender and 2 cases of 40-49 years and 1 case of >70 years for solid. Regression equation (2) was computed in the present study by taking

into consideration standard BMI (x) and FFMI (y) with scatter plots for 57.4% of cases, strong relation between the two variables.

$y=7.26+0.37*x$	(2)
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All 14 subjects have a sedentary behaviour and physical inactivity due to the specific condition; SMM and strength were evaluated according to EWGSOP2 practical algorithm. Three patients exceeded 15 seconds at the chair stand test so probable sarcopenia was identified: 2 woman and one man, one woman underweight, lean (FMI Type), slender (FFMI Type), age group 18-39 years, one woman adipose (FMI Type), intermediate (FFMI Type) and one man normal weight, intermediate (FM/FFM Type), both group age > 70 years. From BIA were extracted the value for the skeletal mass and SMI was calculated by height adjusted: 13 (92.86%) cases have normal values and one (7.14%) case have optimal value.

Regression equation (3) was computed in the present study by taking into consideration standard BMI (x) and SMI (y) with scatter plots for 66.4% of cases, strong relation between the two variables.

$y=3.15+0.24*x$	(3)
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Pearson correlation were computed for BMI, FMI, FFMI, Age, Water (%), Protein (%). Strong statistical relationship were found between BMI and FMI ($r=0.882$, $CI=99\%$), FFMI ($r=0.815$, $CI=99\%$), Age ($r=0.659$, $CI=99\%$), Water ($r=-0.693$, $CI=99\%$). FMI also correlates strongly with Age ($r=0.707$, $CI=99\%$), Water ($r=-0.925$, $CI=99\%$) and Protein values ($r=-0.819$, $CI=99\%$). FFMI also correlates strongly with SMI ($r=0.984$, $CI=99\%$). Water correlates with Protein ($r=0.848$, $CI=99\%$). (Fig 17-23)

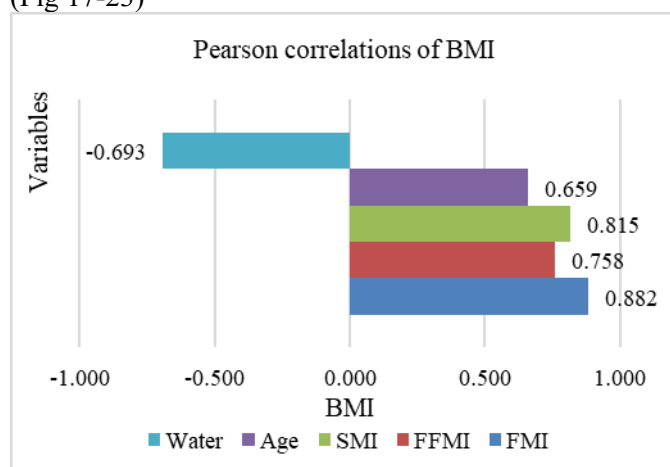


Fig. 17 Pearson Correlation of BMI

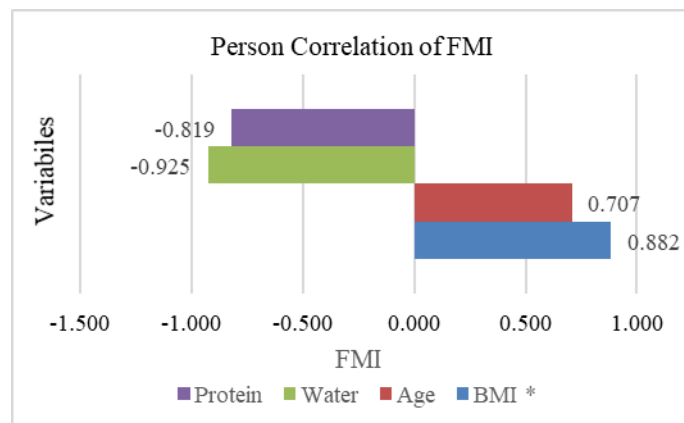


Fig. 18 Pearson Correlation of FMI

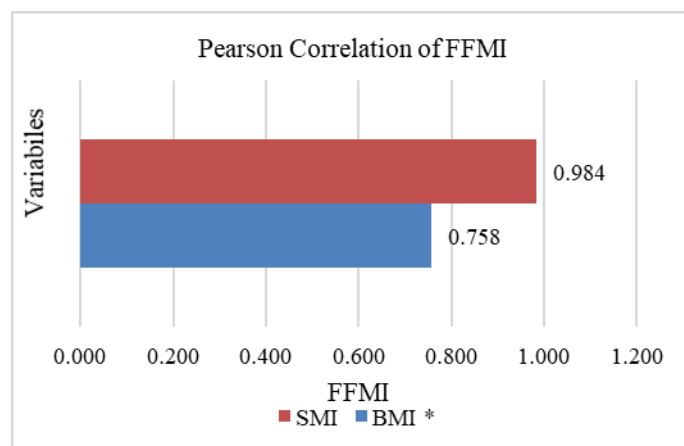


Fig. 19 Pearson Correlation of FFMI

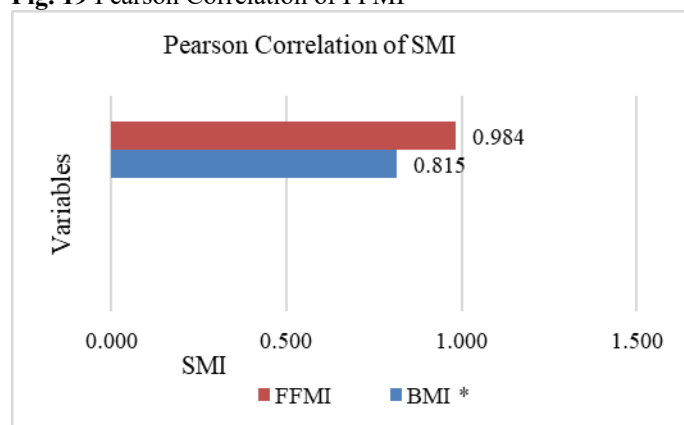


Fig. 20 Pearson Correlation of SMI

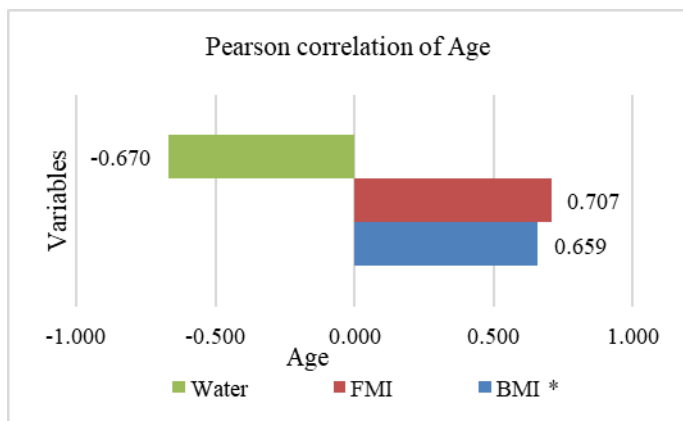


Fig. 21 Pearson Correlation of Age

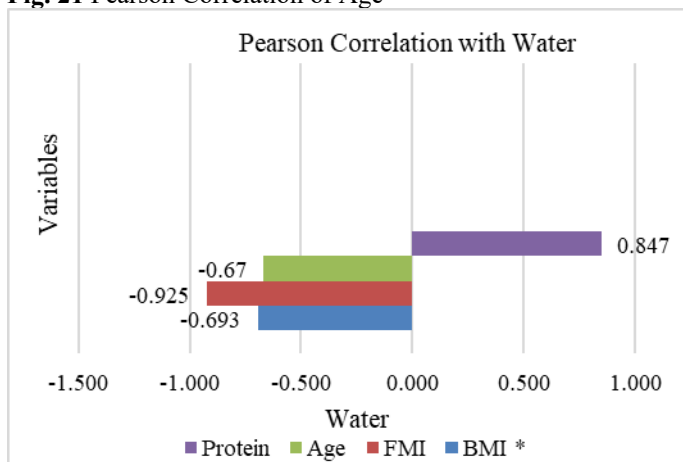


Fig. 22 Pearson Correlation of Water

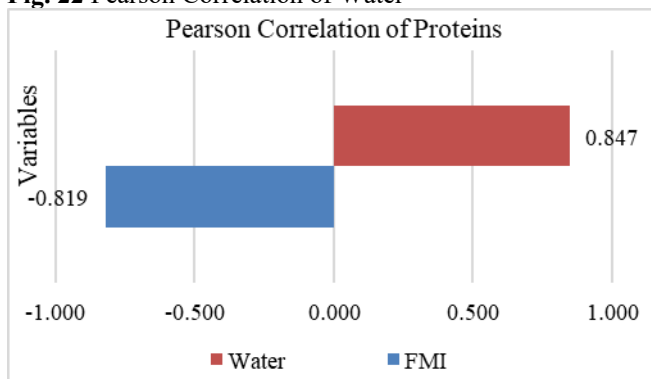


Fig. 23 Pearson Correlation of Proteins

Beta regression analyse strongly correlates SMI prediction with FFMI ($\beta=0.731$), Water ($\beta=0.138$) and Protein ($\beta=-0.370$) for $p<0.05$. Pearson correlation denotes the action of each variable independent but beta regression analyse emphasizes interdependency between different predictors. Anova significance of .000 (CI=99%) with applicability of 99.8% of the cases ($R^2=0.998$) proved that constant predictors: Water (%), FFMI, Protein (%), FMI, BMI interact to influence SMM variability.

According to Zepp analyser, 64.25% of subjects recorded an insufficient water level. For this issue age group distribution is as follows: one case at 18-39 years, 3 cases at 40-49 years, 2 cases at 50-69 years and 3 cases over 70 years. The amount of 71.43% of subjects recorded an insufficient proteins level. For this issue age group distribution is as follows: one case at 18-39 years, 4 cases at 40-49 years, 3 cases at 50-69 years and 2 cases over 70 years.

Conclusions regarding all 14 subjects can be summarized in ascending order as in Fig 24.

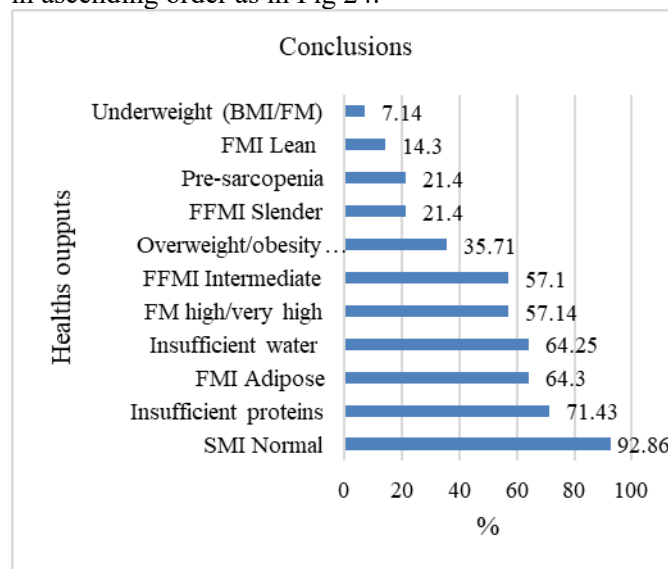


Fig 24 Conclusions regarding all 14 subjects

Finally conclusion: for each patient specific kinetic program should be developed. Rehabilitation programs is essential, but it is very important that the programs to be customized for each patient.

FMI increase (64.3% adipose cases) denotes the risk of metabolic syndrome and insulin resistance. Consequently, resistive and concentric exercises will be applied preceded by warm-up and followed by stretching. For FFMI loss (57.1% intermediate cases, 21.4% slender) and SMI increasing (92.86% cases have normal values but not optimal ones, 21.43% pre-sarcopenia detected by positive chair test) resistance, eccentric/concentric exercises should be applied taking into account cardiac reserve for each patient, preceded by warm-up and followed by stretching. Maximal/sub-maximal force exercises will be used age-related. Additional water (64.25% of subjects recorded an insufficient water level) and proteins levels (71.43% of subjects recorded an insufficient proteins level) must be balanced by nutritional support in accordance with rehabilitation consult and current physician approval in the interdisciplinary team as Fig. 24 - Flow diagram of specific intervention shows. Advantages of this approach are effort capacity increasing, cardiovascular factors

improvement (decrease in lipid fractions, normalizing glycemic status and blood pressure normalizing, weight loss and reducing the depression risk), preventing, delaying, treating, even reversing sarcopenia by effective interventions and reducing associated risks.

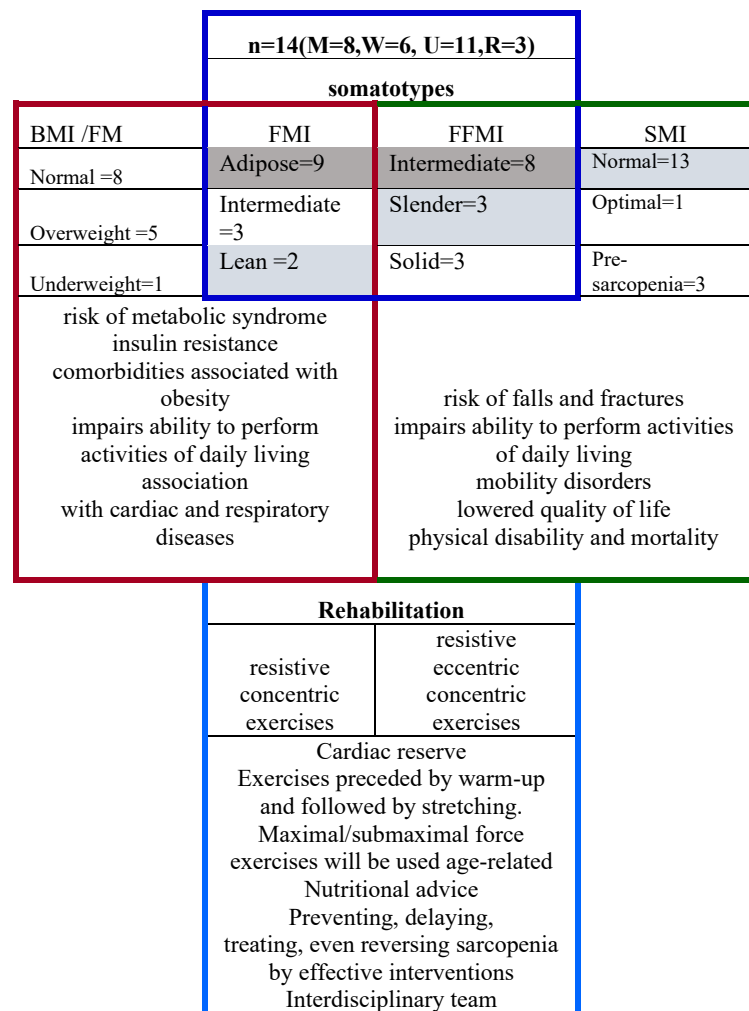


Fig. 25 Flow diagram of specific intervention (M=men, W=women, U=urban, R=rural)

Limits of the present study are the number of patients, SF BIA and for more accuracy multi-frequency BIA can be used and the combination of other methods may reduce the misdiagnosis FFM variability.

Because of its simplicity, low cost, quickness of use at bedside, and good reproducibility, BIA appears to be the technique of for the systematic and repeated evaluation of FFM/SMM/FM, identifying masked obesity. With additional calculation as FMI, FFMI, SMI allows assessing and monitoring individuals suffering from consequences and comorbidities associated with obesity. Optimal care for people with pre-sarcopenia /sarcopenia is essential because the condition has high personal, social and economic burdens when untreated. BIA may be an important supporting tool for health professionals.

Declaration of conflict of interests

There is no conflict of interest for the author regarding this paper.

Informed consent

The investigated subjects were informed about the purpose and methodology of the study presented here, expressing their agreement to the processing and publication of the results, in compliance with the rules on personal data protection.

The present study was performed in accordance with the ethical standards. All patients included in the present study gave their informed consent.

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Haloaerosoltherapy: Mechanisms of Curative Effect and Place in the Respiratory Rehabilitation

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Abstract

Introduction. Management of patients with chronic pathology requires development of long-term programs with organic combinations of medicamental and non-medicamental influences. Haloaerosoltherapy is a group inhalation of rock salt aerosol with concentration of more than 2-3mg/m³ and certain dispersion (with presence of large-, medium- and small-grained aerosol) aboveground.

Material and method. On the basis of literature data review and results of own researches a comprehensive description of haloaerosoltherapy, its mechanisms, available technologies, indications and effectiveness at pulmonary pathology was given.

Results and discussion. Basis of haloaerosol curative influence is hyperosmolar stimulus that improves drainage function of bronchi and provides sanitizing effect, which causes further changes at local and systemic levels. This justifies haloaerosoltherapy usage as method of rehabilitation treatment. Comparison of haloaerosoltherapy and other methods of halotherapy (use of halite), in particular, "salt rooms (caves)" was made. It has been proven that "salt rooms" can be used only as spa procedure.

Conclusions. Application of term "halotherapy" to all methods that use halite or underground treatment is incorrect. This determines necessity for stop using this term. It is necessary to differentiate clearly applied methods of treatment using terms that reflect the essence of therapeutic effect. Haloaerosoltherapy should be considered a method of respiratory rehabilitation with a proven mechanism of action and effectiveness. Haloaerosol is obtained using specific devices - halogenegenerators. The effectiveness of haloaerosoltherapy immediately after the course of treatment and in remote period is testified.

Keywords: *Respiratory rehabilitation, halotherapy, haloaerosoltherapy, speleotherapy,*

INTRODUCTION

Management of patients with chronic pathology requires treatment not only in the acute period, but also needs development of treatment programs beyond the period of exacerbation, aimed at the stabilization of pathological process, prevention of the exacerbations' recurrence and progression of the disease. Long-term management programs for patients with chronic diseases should be based on a rational combination of basic medicamental treatment and various non-medicamental influences that organically complement each other. In particular, in the rehabilitation of pulmonary patients, methods that help the patient get rid of bad habits (smoking), give psychological support are used, training programs for patients are developed, physical training, respiratory physiotherapy are recommended etc.

Speleotherapy and halotherapy are among the methods already used as means of respiratory rehabilitation. However, in most cases, the medical community does not have a clear understanding of the peculiarities of these methods' influence and their possibilities. In our previous works, we have already tried to differentiate the varieties of these techniques and indicate their place in the system of pulmonary rehabilitation. In particular, article published in the journal "Asthma and Allergy" [1] is devoted to speleotherapy, highlights the

mechanisms of its influence on the human organism, clearly emphasizes that speleotherapy is the usage for therapeutic purposes karst caves and mine workings (most often salt). Therefore, a mandatory component of such treatment is the stay of patients for some time in underground conditions, and any treatment or prevention technologies carried out above-ground have no speleotherapeutic effect and cannot be called speleotherapy.

In our next publication [2] the questions of development of "artificial analogues of speleotherapy" were considered. These analogies describe methods of influence, which try to imitate some factors of underground conditions, various techniques that relate to halotherapy (halite - mineral of sodium chloride). The term "halotherapy" was proposed by Pavel Gorbenko in 1985 to describe methods of above-ground use of halite in form of dry aerosols [3]. Based on the analysis of literature data, it was proved that most rational is usage of dry aerosols of rock salt (haloaerosols) with certain characteristics of concentration and dispersion. Two terms were proposed to use: haloaerosoltherapy - the therapeutic use of aerosol media of rock salt as a group inhalation, and haloinhalation therapy - individual inhalations of dry haloaerosols or wet inhalations of sodium chloride solutions. Numerous studies also prove that

the usage of "salt rooms (caves)", in which the walls are covered with salt, but without halogenerators (devices that create aerosol media of rock salt) have no therapeutic effect in pathology of bronchopulmonary system and upper respiratory tract and can be used only as a spa treatment [4-7].

The aim of the study - on the basis of literature data review and results of own researches to give a comprehensive description of haloaerosoltherapy, mechanisms of its influence on the human organism, available technologies of procedures, indications for use and effectiveness at pulmonary pathology.

Scientific basis of the method. Scientific investigations concerning development of treatment methods that could to some extent imitate therapeutic effects of salt mines proved that today the *only such factor* is creation of dry aerosols of rock salt. By haloaerosoltherapy (HAT) we mean the usage of dry aerosol media of rock salt with certain parameters of concentration (not less than 2-3mg/m³) and appropriate dispersion in the form of group inhalations, which are created using special devices - halogenerators.

From the very beginning, physicochemical investigations and study of certain parameters of dry haloaerosol were of great importance in the development of HAT method and especially in substantiation of haloaerosol usage. These investigations were originated from the study of speleotherapy mechanisms. It was proved that the peculiarities of crystal structure of the dispersed phase of haloaerosol provide certain active properties and increase effectiveness of its influence [8], and certain physical parameters (surface energy, negative charge, concentration) play a leading role in providing antibacterial and hypoallergenic environment [4,9]. It was shown that the efficiency of air purification depends on the concentration of haloaerosol and increases in proportion to its level [9]. The importance of nano-structure of the dispersed phase of haloaerosol is also pointed out by other researchers [10].

In addition, based on detailed studies of the physical and chemical properties of different types of rock salt, it has been proved that not every salt can be used equally successfully to create aerosol media, and the origin (source) of the salt should be considered as the most important factor [5,10,11]. Polish scientists have proved that the higher is the content of insoluble components in salt, the less suitable it is for creation of aerosol media. Among the studied varieties of rock salt in Poland (Wieliczka, Bochnia and Kłodowa deposits), the best, in their opinion, is salt from Kłodowa deposit, which contains 95% NaCl and has a high iodine content (6,7mg/kg) that increases its value [11]. In addition, researchers stated that Dead Sea salt obtained by evaporating of seawater is not suitable for creating dry aerosol media.

At the same time, it should be noted that rock salt of the Solotvyno deposit (Transcarpathian region of Ukraine) contains 98% NaCl and different microelements (magnesium, potassium, calcium) [1,8], which may play certain role in metabolic processes, although these questions have not been studied in detail.

There is also the question of possibility of "salt load" during haloaerosoltherapy procedures. Polish researchers have calculated that during the procedure with dry haloaerosol concentration of 10-15mg/m³, which is most often used, the patient receives on average only about 13mg of sodium chloride, which cannot adversely affect patient's organism [11,12]. However, it should be

noted that as the concentration of haloaerosol increases, the dose of sodium chloride entering the patient's organism may be elevated. This requires a balanced approach, taking into account peculiarities of pathological process and presence of comorbid pathology.

Technology of haloaerosol procedures. The key point in the creation of aerosol media is functioning of halogenerator and possibility for dynamic control over parameters of generated therapeutic haloaerosol. The first halogenerator was developed by scientists in Uzhhorod (Ukraine) in 1982 [13]. However, it was not possible to create the desired haloaerosol concentration and dispersion. Today, a new type of halogenerators has been developed, in which mechanical grinding of salt is combined with simultaneous separation of obtained particles, which makes it possible to generate haloaerosols with different dispersion and achieve their high concentrations [14-15]. In particular, according to different investigations, the concentration of haloaerosol depending on the characteristics of the halogenerator can range from 3-4mg/m³ to 90mg/m³ [4,11,16]. The most commonly used concentrations of haloaerosol are up to 15mg/m³, which can be used for both therapeutic and prophylactic purposes [9,17-19]. The use of haloaerosol media at higher concentrations is possible only for therapeutic purposes, according to careful analysis of comorbidities and development of appropriate procedure technologies [7,15,20-22].

A special laser-optical system was also developed that can work in aggressive rock salt environment and measure the concentration of aerosol and its dispersion. This allows to control the process of creating aerosol environment, changes of its parameters during the treatment process and to create aerosol environments with specified parameters [15,23,24].

Besides the concentration of haloaerosol, other parameters are of significant importance in the assessment of treatment environment, in particular questions of room ventilation and bacterial contamination. Unfortunately, these requirements are not clearly regulated. Regarding the size (volume) of the room where procedures are performed, in most cases standard of 3-6m³ of air volume per patient is used. A comfortable air temperature (20-23°C) at humidity of 40-60% are recommended. However, the last two parameters of conditions above-ground significantly depend on weather factors [3,25-27].

The initial overall bacterial contamination of air in treatment rooms for haloaerosoltherapy (with permanent use of halogenerator) does not exceed 100 microbial bodies per 1m³, and after the procedure the microorganisms concentration doubles [25,28]. In "Halotherapy salon" (Romania), where halogenerator does not work during all procedures, the background concentration of bacteria in the air is 197-300 per 1m³ [29], and in "sylvinitic speleoclimatic chamber" (Russia), in which none halogenerator is used, this value reaches 800 microbial bodies per 1m³ [30]. This fact once again emphasizes the role of appropriate concentrations of haloaerosol in purification of air from bacterial contamination.

Thus, the main active factor of HAT is a haloaerosol of certain concentration (not less than 2-3 mg/m³) with certain sizes of dispersed phase [7,11,17]. Aerosol particles with a size of 2-8µm, which influence all parts of bronchial tree, are of leading importance. Their relative content should be 70-80%. The

larger aerosol particles settle in upper respiratory tract, causing appropriate clinical effects and can be used in some ENT pathology. The dispersed phase of aerosol less than $1\mu\text{m}$ does not remain in the airways, and therefore does not provide hyperosmolar stimulation, which is the basis of the mechanism of haloaerosol influence and, therefore, can not have therapeutic effect [5,7,11,31]. It is also necessary to control sanitary and hygienic indicators, first of all bacterial air pollution. All other characteristics are additional and do not play a significant role in the treatment process.

During the course of HAT, two periods are distinguished: adaptation period and main treatment period. The necessity for adaptation period at the beginning of treatment is conditioned by irritating effect of haloaerosol on the respiratory tract mucosa. It includes 3-4 procedures with gradual increase in its duration: for adults – 15-30-45-60 minutes; for children 10-20-30 minutes. The main treatment period includes daily HAT seances with maximum duration of 60 minutes for adults and 30 minutes for children [18-20,27]. That is, duration of one procedure is determined by patient's age, peculiarities of disease, its severity, presence of comorbid pathology and possible influence of HAT on it, as well as some other modifying factors. In particular, for patients with COPD two daily seances of HAT for 30 minutes each, with an interval of 3-4 hours are used. This is due to fact that first 30 min of the procedure is the period of maximal concentration of haloaerosol, which increase the intensity of haloaerosol influence, on one hand, and on the other – 3-4 hours interval helps to avoid severe balneological reactions [31].

Mechanisms of therapeutic effect. The basis of haloaerosol influence is a hyperosmolar stimulus, which is realized primarily in improving the rheological properties of sputum and stimulating the ciliated epithelium, which leads to increased mucociliary clearance and bronchial drainage function (Fig.1) [10,22,32].

Distinct manifestation of this clinical effect is realized beginning with the 3-4th procedure in both adults and children with bronchopulmonary pathology and is described by almost all researchers who analyze condition of patients during HAT [4,9,18,21,28,33-35]. Increased sputum discharge is accompanied by some usual natural deterioration of bronchial patency, which is manifested clinically in cough increasing, may be associated by increase in wheezing and confirmed by changes in spirometric pulmonary function test (PFT) [34-37]. In particular, S.F.Goncharuk et al (2006) [36] according to the results of dynamic control of external breathing function indices during the course of HAT revealed that in children with bronchial asthma after the first five procedures there is a tendency for reducing the integrated rate of bronchial patency (forced expiratory volume by the first second - FEV_1) and significant decrease in the patency of small bronchi. Procedures were performed daily, except weekends at haloaerosol concentration of $12\text{-}14\text{mg}/\text{m}^3$. Subsequently, by the 10th procedure, all indices increased. Authors also noted that some indices increased significantly only up to the 15th procedure, and largest value of vital capacity was registered for the 20th procedure. This study on one hand clearly confirms effect of HAT on bronchial drainage and presence of balneoreactions during treatment, and on the other - substantiates the duration of treatment and breaks down all

"commercial" approaches to prescribing short courses of HAT (less than 10 procedures even for children).

These data were also confirmed by results of examination of children with recurrent bronchitis aged 5-10 years and category of frequently ill children (more than 4 episodes of acute respiratory diseases (ARD) during a year) [21,37]. In these children from the second to the tenth HAT procedure manifestations of rhinitis and increased wet cough were observed, but without signs of ARD. This was regarded as a reaction of mucosa of ENT organs and respiratory tract to the dry haloaerosol. It should be emphasized that significant increase of morning and evening peak flow data was registered only from the 10th day of treatment.

Similar regularities were observed in dynamic (weekly) registration of spirometric PFT indices in adult patients with bronchial asthma [27]. It was found that indices of spirometric PFT reach a maximum in the third week of treatment (15th-16th procedure of HAT) and then increased less markedly. That is, minimal number of procedures per course of treatment for adults and children with asthma should be at least 15-16, and for the category of "frequently ill children" - 13 seances, accounting additional prescription of certain other physiotherapeutic procedures [20].

Balneological reactions that occur during HAT, which is performed according to the technology of procedures, are usually mild or moderate. They may be accompanied by short-term (within 2-3 days) increase in the frequency of rescue medications (inhaler) use by patients with moderate or severe bronchial asthma or COPD, but as a rule do not require another additional prescriptions. During bronchial tree clearing, clinical manifestations become less intensive, which is confirmed by appropriate functional studies [21,34-37].

It is also considered that haloaerosol causes/intensifies elimination of biologically active substances, which helps to reduce or stop bronchospasm and, consequently, improves bronchial drainage, reduces bronchial obstruction and is accompanied by decrease of histamine level in blood [9,10,38,39].

Moreover, haloaerosol provides bactericidal effect, which has been proven by experimental and clinical investigations [10,25,40]. In particular, it was demonstrated in experiment that dry highly dispersed aerosol has inhibitory effect on the growth and viability of microorganisms, changes their biological properties [41]. At the same time, there was elevation of electrophysiological functional activity of epithelial cells and increase of their colonization resistance, which indicates improvement of protective properties of respiratory tract cells.

In addition, in frequently ill children of two age groups (7-10 years and 11-15 years) the morphofunctional status of oropharyngeal mucosa with determination of cell composition, character of biocenosis and colonization activity of pathogenic and opportunistic microflora were studied [42,43]. In treatment of children HAT was used with haloaerosol concentration of $3\text{-}4\text{mg}/\text{m}^3$, 10 procedures per course of treatment (procedures were performed daily for two weeks except weekends). Improvement of the studied parameters were detected. According to researchers, these changes indicate significant bacteriostatic and sanogenetic effect of haloaerosol, although duration of treatment course (10 procedures) accounting the

dynamics of spirometric PFT indices should be considered insufficient. Sanitizing effect in combination with increased bronchi drainage function leads to decrease of inflammatory process activity in bronchi and is accompanied by improvement of mucosal immunity and reduced bronchial hyperactivity.

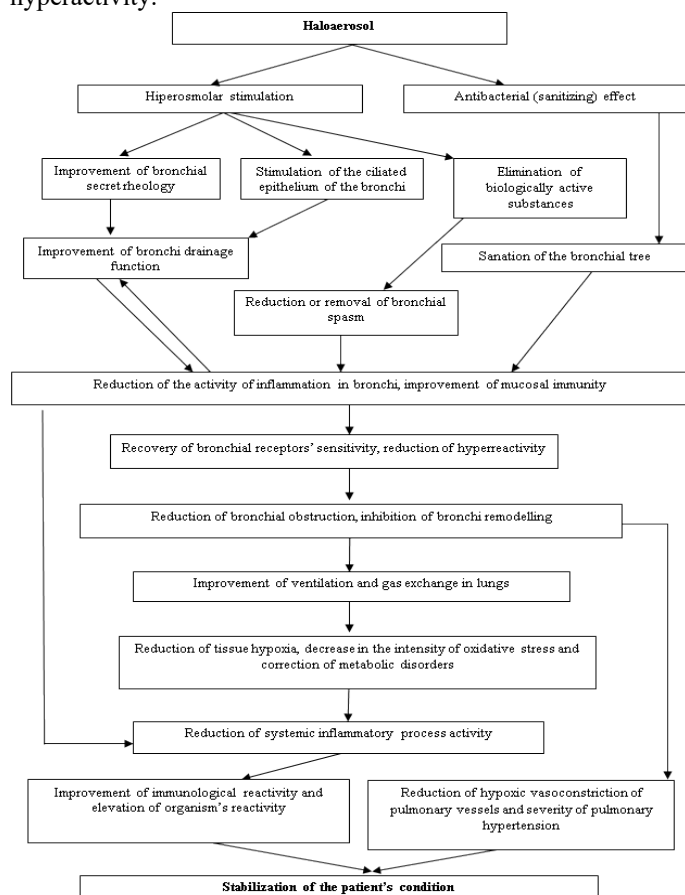


Fig. 1. Mechanisms of curative influence of haloaerosoltherapy. The activity of inflammatory process in bronchial tree has been precisely studied in patients with COPD of different severity and under the influence of different treatment regimens. Cellular composition of sputum was studied, as well as content of lipid peroxidation (LPO) products and stable metabolites of nitric oxide (NO), interleukin-8 (IL-8) in exhaled air condensate and serum [44-47]. It was testified that positive changes of these indices at the local level are more intensive than at systemic one. This confirms significant local effect of HAT with controlled concentration and dispersion of haloaerosol and its therapeutic effect at COPD patients in general. Expressiveness of these changes during HAT procedures with increased intensity of aerosol influence is more significant [19,44,46].

The decrease of local inflammatory process activity in bronchi under the influence of HAT was also proved on the basis of NO levels study in exhaled air (FeNO) in children with bronchial asthma [6]. Moreover, authors compared effectiveness of treatment with the usage of halogenerator and in the "salt room" without usage of such device and noted positive dynamics only when using halogenerator.

Improvement of mucosal immunity indices under the influence of HAT was analyzed in details at frequently ill children. Normalization of secretory immunoglobulin A (sIgA) levels in

saliva at these children were revealed [42,43]. In patients with COPD, dynamics of these changes is less expressed and depends on the disease's severity [19].

Reducing of bronchial hyperactivity in patients with bronchial asthma is of particular interest and has been noted by a number of researchers [6,33,48,49]. They are unanimous in testifying that reduction of bronchial hyperactivity in patients with bronchial asthma under the influence of HAT occurs. Some of them [6,33] associate this effect with decrease of inflammatory activity in bronchial tree, and others [49] do not find such relationship, but in the latter case, course of treatment was only 10 procedures.

Experimental studies have also been conducted on mice, which prove presence of link between decrease in bronchial hyperactivity and decrease in proinflammatory cytokine levels and inflammatory activity in bronchi under the influence of inhalation of brine from Wieliczka (Poland) [50].

Recovery of sensitivity to basic bronchodilators (β_2 -agonists and cholinolytics) is very important in the management of patients with bronchial asthma and COPD. In this aspect reduction of frequency of rescue medications usage is actual, which is often combined with decrease in the dose of basic drugs, and these changes take place on the background of improved spirometric PFT indices and clinical course of disease [22,27,51]. In particular, at patients with persistent bronchial asthma analysis of changes in the frequency of rescue medications (β_2 -agostists) usage and changes in PFD data under the influence of HAT depending on disease's severity and treatment regime was conducted. It was shown that under the influence of all treatment regimes frequency of rescue medications daily use is reduced in 1,4-2,7-4,3 times. It is most expressed while using treatment complexes with increased haloaerosol intensity, when indices of spirometric PFD significantly increased by 10-15% [22]. It was also noted that among patients who, according to functional tests with bronchodilators before treatment, were insensitive to neither β_2 -agostist nor cholinolytic (iprotropium bromide), in 60-67% of cases, sensitivity to at least one of them recovered. These changes depended on HAT regime and significantly increased effectiveness of basic treatment. After the course of HAT only 30-40% of patients remain resistant to bronchodilators, which determines the necessity to find other mechanisms of bronchial obstruction.

Due to decrease in the activity of local inflammatory process in bronchi, which is accompanied by recovery of receptor apparatus sensitivity, decrease in bronchial obstruction was observed. These factors in complex contribute to inhibition of bronchial remodeling processes and are, above all, actual for COPD patients. Decrease in bronchial obstruction is manifested by elevation of ventilation indices and is noted by all researchers while using HAT, ie when using aerosol media of rock salt, created by halogenerator with observance of requirements for concentration ($>2\text{-}3\text{mg/m}^3$) and appropriate dispersion [52]. The expressiveness of spirometric PFT data growth depends on a number of factors: nosology and disease's severity, sensitivity to certain bronchodilators, age of patient and others. These factors determine individual regimes of HAT, as well as possibility and feasibility of its combination with other medicamental and non-medicamental influences [18,19,27,51].

For example, in patients with persistent mild and moderate bronchial asthma, most effective is usage of two consecutive (without a break) 30-minute procedures of HAT, which increases the intensity of haloaerosol influence and allows to reduce the course of treatment to 15-16 procedures [27]. In severe asthma, it is more expedient to use standard method of treatment - daily 45-60 minutes procedures of HAT, 18-20 for treatment course. At the same time, in patients with COPD, in order to prevent severe balneal reactions, it is recommended to take a break (3-5 hours) between two 30-minute procedures. To intensify the immunorehabilitation effect in COPD patients, treatment complexes with additional prescription of medicines with immunomodulatory and antiviral activity have been developed [19,53,54].

In children with bronchial asthma, recurrent bronchitis or category of "frequently ill children", treatment complexes using singlet oxygen therapy, vibroacoustic therapy, laser therapy, interference therapy, etc. are proposed. However, in all cases it is necessary to follow scientifically substantiated approaches to the differentiated prescription of treatment complex, accounting the disease's peculiarities and existing modifying factors [20,39].

It should be emphasized that for patients with bronchial asthma and COPD, the course of HAT does not automatically cancel basic therapy. During HAT, basic medicament treatment and dosage of some medicines may be changed, but this question is decided individually. According to some researchers, HAT plays the role of additional (complementary) therapy [48,55], which improves the effectiveness of complex treatment and patients quality of life.

Increase in spirometric PFT data is naturally accompanied by improvement of gas exchange in lungs and decrease of tissue hypoxia. This can be evidenced by previous results, which were obtained in rehabilitation treatment of convalescents after COVID-19. Under the influence of HAT, saturation increased from $95,7 \pm 0,39\%$ to $97,8 \pm 0,36\%$ ($p < 0,001$) and distance that patients passed in 6-minute test increased from $462,4 \pm 6,15\text{m}$ to $494,2 \pm 6,35\text{m}$ ($p < 0,001$). These changes were simultaneously accompanied by significant decrease in dyspnea severity before and after test, which was determined by Borg scale and pulse frequency. This fact confirms improvement of gas exchange in lungs under the influence of HAT, recovery/improvement of functional state of patients and opens prospects for a new direction in HAT usage - rehabilitation after COVID-19.

All above aspects of the mechanism of haloaerosoltherapy influence lead to a decrease in the intensity of oxidative stress and correction of metabolic disorders, which is especially relevant for patients with COPD [46,56-58]. M.Gabor et al. (2018) [46] studied the intensity of lipid peroxidation (LPO) in blood, saliva and condensate of exhaled air in COPD patients, as well as main enzymes of antioxidant defense (AOD) in red blood cells under the influence of different regimes of HAT. It was showed that by the end of treatment course the intensity of LPO decreased. In the condensate of exhaled air this dynamics was more pronounced, and was accompanied by certain recovery of AOD activity. Expressiveness of these changes depended on the applied HAT regime [45,46]. Decrease in the intensity of oxidative stress was also observed in convalescents after community-acquired pneumonia and in children with recurrent bronchitis and frequently ill children [59-61].

Decrease of inflammatory process activity in bronchi contributes to the reduction of systemic inflammation activity, which is characteristic for COPD patients. Studies have shown that course of HAT in COPD patients leads to predominant lowering of pro-inflammatory cytokines production, which leads to certain correction of balance between pro- and anti-inflammatory cytokines [47].

Lowering the proinflammatory cytokines levels with certain recovery of cytokine balance under the influence of HAT were also observed in convalescents after community-acquired pneumonia and in the group of frequently ill children, as well as in children with recurrent bronchitis [62-65]. It was also noted that in patients with persistent bronchial asthma, recovery of cytokine balance is accompanied by reduction of eosinophils number and decrease in total IgE level [66]. This makes it possible to consider inhibition of inflammatory activity, both local and general, as very important component of the mechanism of haloaerosoltherapeutic influence.

It is sanitizing effect of HAT and reducing the activity of local and systemic inflammatory processes that indirectly determine improvement of immunological reactivity and increase the resistance of organism. Improvement of nonspecific resistance of organism is noted by many researchers at different diseases in adults and children (chronic bronchitis, bronchial asthma, COPD, recurrent bronchitis and the recovery period of frequently ill children, etc.). Increase of phagocytic activity of neutrophils and monocytes [47,67-70], improvement of mucosal immunity indices are indicated [19,42,43,71]. Elevation of phagocytes microbicidity is noted, which is associated with decrease in endotoxemia at patients with bronchial asthma and COPD [57].

Detailed studies of cellular immunity in different contingents of patients were also performed: bronchial asthma, chronic bronchitis and COPD, convalescents after community-acquired pneumonia, children with bronchial asthma, recurrent bronchitis and frequently ill children [10,19,39,67,69,71]. In all cases, there were positive changes in studied indices (increase in T-lymphocytes number in cases of their low level, improvement/rebalancing of ratio between helpers and suppressors, elevation of natural killers number, etc.). Expressiveness of this dynamics depended on peculiarities of changes in certain nosology, disease's severity and other modifying factors. It is noted that dynamics of cellular immunity denotes the direction of immune response towards normalization with recovery of appropriate relationships between cellular subpopulations.

Study of apoptosis processes of lymphocytes and neutrophils, which were conducted in COPD patients, is of particular significance. Under the influence of HAT, there was a decrease in readiness to lymphocytes' apoptosis, which is the basis for recovery of their amount and subpopulation composition [72]. At the same time, there was decrease in expression of activation markers on neutrophils, which was associated with an elevation of intensity of their apoptosis [47]. This contributes to the inhibition of neutrophilic inflammation in bronchial tree and, from the standpoint of pathogenesis, substantiates usage of HAT in rehabilitation treatment of COPD patients.

Improvement of non-specific protection indices in combination with correction of cellular immunity make it possible to talk

about immunorehabilitation effect of HAT, which results in stabilization of patients status and improving the clinical course of disease and patients quality of life in general at chronic pathology, or health improving in cases of recovery after acute or recurrent disease.

Long-term results of HAT use in patients with bronchopulmonary pathology. The effectiveness of HAT as method of pulmonary rehabilitation is evidenced by evaluation of long-term treatment results. In particular, 360 patients with moderate bronchial asthma were assessed for quality of life before and immediately after course of HAT using the EQ-5D-5L questionnaire. Before treatment, respondents rated the quality of life on average by $54,7 \pm 4,1$ points, and after it – $62,7 \pm 2,3$ points ($p < 0,05$), which indicates significant improvement in this index [73]. In addition, efficacy of treatment during a year after HAT was studied using questionnaire and results were compared with the status of patients during a year before treatment. It was found that after HAT the disease's course significantly improved. This was manifested by reduction of asthmatic attacks frequency more than in 2 times, frequency of outpatient treatment – in 2 times, and inpatient - by 45%, which resulted in a significant decrease of incapacity days number (42%) [74].

Similar regularities were observed in COPD patients [75]. Duration of remission in these patients amounted from $6,3 \pm 0,15$ to $10,2 \pm 0,68$ months, depending on the disease's severity and used treatment regime. Best results were obtained when treatment with increased haloaerosol intensity (two 30-minute procedures per day) was used. Weinreich et al (2014) also noted improving the quality of life under the influence of HAT in COPD patients [52].

According to various authors, especially indicative are results of HAT usage in children, at which effectiveness of treatment immediately after HAT is more than 95% [20,39,76]. Immediate results of treatment were confirmed by observation data in the remote period for one year after course of rehabilitation treatment [77]. Thus, in frequently ill children, frequency of ARD during a year after HAT decreased from $4,6 \pm 0,24$ to $3,4 \pm 0,27$ episodes per year ($p < 0,01$), and duration of one episode of disease decreased from $9,67 \pm 0,9$ days to $6,9 \pm 0,5$ days ($p < 0,02$). The number of days during which the child did not attend school decreased from $26,8 \pm 1,5$ to $19,0 \pm 1,5$ days ($p < 0,01$). Similar regularities are observed in children with bronchial asthma or recurrent bronchitis, which allowed to recommend HAT as method of rehabilitation and secondary prevention in children.

The usage of HAT in upper respiratory tract pathology. In addition to the pathology of broncho-pulmonary system, HAT is widely used in upper respiratory tract diseases of both allergic and infectious-inflammatory origin [33,78-81]. These studies are close to clinical investigations that were conducted in group of frequently ill children. In allergic rhinosinusitis, in addition to positive dynamics of clinical symptoms and rhinoscopic picture, there was lowering of histamine level in blood and reduction of eosinophils number in peripheral blood taken from nasal sinuses [78,79].

In patients with subobstructive adenotonsillar hypertrophy after 10 seances of HAT there was a decrease in severity of adenoids and/or hypertrophy of tonsils. This process was accompanied by hearing improvement at almost half of patients [80]. Besides

this, it was found that HAT helps to improve morpho-functional status and protective properties of oropharyngeal mucosa [42,43], as well as promotes recovery of mucociliary transport speed [81].

Differences between HAT and "salt rooms (caves)". Once again, we want to emphasize differences between HAT, as method of treatment with existing curative factor and proven mechanism of therapeutic effect and all varieties of "salt rooms", "caves", "live air rooms", etc., where only "medical design" is present in form of walls decoration, lighting, musical accompaniment, etc. Comparative characteristics of these methods are given in table 1.

Table 1 Comparative characteristics of the curative factors of speleotherapy (ST), haloaerosoltherapy (HAT) and «salt rooms» (SR)

Main characteristics	ST	HAT (<15 mg/m ³)	HAT (>15 mg/m ³)	«Salt room»
Concentration of the haloaerosol	4-24 mg/m ³	4-12 mg/m ³	16 mg/m ³ and more	<2 mg/m ³ , in the majority of cases <1 mg/m ³
Large-grained haloaerosol	+	++	+++	-
Medium-grained haloaerosol	+	+++	+++	-
Small-grained haloaerosol	+++	+++	+++	+ (<1µm)
Low microbial content in the air	+++	+	++	-
Hypoallergic medium	+++	+	+	-
Isolation from the environment	+++	-	-	-
Possibility for modeling the aerosol parameters	-	+++	+++	-
Fields of use:				
Health improvement	±	++	±	+
Treatment	+++	+++	+++	-
Secondary prophylactics	+++	+++	+++	-
Duration of the treatment procedure: - for adults - for children	5-12 hours 3-5 hours	30-60 min 15-30 min	30-60 min 15-30 min	not regulated (1-10 hours 1-10 hours)
Duration of the course of treatment	18-25 procedures	18-22 procedures	16-20 procedures (for adults) 13-18 (for children)	not regulated (from 5 to 20 procedures)

As can be seen from the table in "salt rooms" main acting factor - haloaerosol in adequate concentration and dispersion – is not present. So these techniques can only be used as spa procedure.

However, in general, questions of unified approaches to haloaerosoltherapy procedures, parameters of created haloaerosol environment, number of procedures for course of treatment and regime of their prescription are still not approved. This may be ground for discrediting this method. As

long as there is no clear understanding in medical community of what haloaerosoltherapy exactly is, which criteria of haloaerosol environment and treatment process in general must be complied, precise control of relevant specialists over all business proposals such as "salt rooms" will be ensured - the clear distinction between method of treatment, spa procedure, or simply profanation, will not be achieved. Necessity for differentiation of various types of halotherapy is pointed out by other researchers [12,82]. In this regard, it should be emphasized that usage of the term "halotherapy" today should be considered as incorrect. When using term "halotherapy" there is no clear differentiation of the nature of used influence, and this is the basis for discreditation of HAT as method of treatment.

Analysis of incorrect usage of HAT and doubtful (negative) assessments of its effectiveness. One of the reasons for skepticism about HAT is its incorrect use in some cases, when, based on the mechanism of therapeutic effect, there are no grounds for its prescription. In particular, there are cases when in advertising publications concerning usage of halotherapy in form of "salt rooms" (without specifying presence of haloaerosol) for patients with arterial hypertension and cardiovascular disease are indicated. This is completely not justified by mechanism of therapeutic effect of haloaerosols. Moreover, presence of arterial hypertension and coronary heart disease with severe clinical manifestations is one of contraindications for HAT.

Along with that, in the publication of Matsegora NA et al [83] effectiveness of HAT in patients with mild and moderate persistent bronchial asthma with concomitant coronary heart disease of I and II functional classes has been evaluated. It was found that complex treatment that included basic therapy of asthma (salmeterol with fluticasone propionate) and HAT contributed to improvement not only of spiographic parameters, but also into positive dynamics of Holter ECG monitoring data in form of significant decrease in mean daily heart rate and frequency of supraventricular extrasystoles. Authors explain this fact by reducing use of short-acting β_2 -agonists and by positive influence on autonomic nervous system. However, in any case, presence of concomitant cardiovascular pathology requires balanced personalized approach to HAT usage. By the way, authors of the above-mentioned work used terms speleotherapy and halotherapy and only detailed analysis of this publication revealed that they used HAT.

An example of incorrect assessment of halotherapy efficiency in COPD patients is the review by R.Rashleigh et al [84]. Authors selected 151 publications for initial analysis, but later narrowed this analysis to 4 publications on formal approach. In particular, authors did not consider works that were not published in English. As a result, they compared data on effects of haloaerosoltherapy (group inhalation of haloaerosol with certain concentration above-ground), which was used in patients beyond exacerbation, halo-inhalation therapy, which was carried out using individual inhaler during exacerbation and two publications on speleotherapy in karst caves with no presence of halite. However, these are different methods that cannot be compared. In addition, one of papers on karst cave treatment was published in 1986, when the term COPD was not yet used at all and contained data on patients

with chronic bronchitis and bronchial asthma. From these facts, we can conclude that authors do not understand difference between these methods, and their conclusion, although positive, regarding the use, as they affirm, of "halotherapy" cannot be considered correct.

The publication by Agnihotri NT et al. [85] is also incorrect, because authors, without analyzing available scientific researches, believe that halotherapy (without concretisation of what exactly method is used) refers to methods that have profound psychological influence on patients while objective physical benefit of method is absent. Therefore, clear differentiation of halotherapy methods is needed using appropriate terms that clearly indicate the main factor, which is used.

Doubtful publications on double-blind placebo-controlled studies also do not contribute to the approval of HAT as method of rehabilitation treatment [48,76]. Such researches must include placebo, in this case in form of aerosol, which by external signs completely corresponds to tested therapeutic factor, but does not contain it. Patients perceive haloaerosol in therapeutic concentrations (more than $2-3\text{mg}/\text{m}^3$) visually and organoleptically (salty taste). In addition, according to Polish researchers, list of substances that can be used to create such aerosols is limited. Even evaporated Dead Sea salt is not suitable for creation of such haloaerosols [11]. The question is, what was used as placebo? None of the above publications contains such data, and without this information, adequacy of these researches is questionable.

Conclusions

1. Usage of the term "halotherapy" for all methods that use halite (mineral of sodium chloride) or treatment in mine workings or karst caves is incorrect. This determines necessity for stop using this term. It is necessary to differentiate clearly applied methods of treatment using terms that reflect the essence of therapeutic effect.

2. Haloaerosoltherapy should be considered as method of respiratory rehabilitation with proven mechanism of action and effectiveness, as clearly is defined the main active factor - rock salt aerosol, which has certain concentration ($>2-3\text{mg}/\text{m}^3$) and dispersion with presence of small-, medium- and large-grained phase. Haloaerosol is obtained using specific devices - halogenerators. Haloaerosol parameters are controlled in dynamics of procedures and can vary within certain limits while used for different nosologies.

3. Basis of the mechanism of haloaerosol influence at its appropriate concentration and dispersion is hyperosmolar stimulus that provides enhanced drainage function and sanitizing effect, which causes further changes at local and systemic levels.

4. Main requirements to the technology of haloaerosoltherapy procedures, their duration and number are defined, certain medical complexes of its use with other non-medicamental and medicamental means are developed. Effectiveness of haloaerosoltherapy after course of treatment and in remote period has been proven.

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Aphasia after acute ischemic stroke: epidemiology and impact on tertiary care resources

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Abstract

Introduction. This study aimed to reveal the disease burden of aphasia after acute ischemic stroke (AIS) at the national level and investigate the impact of aphasia on tertiary care resources and patient outcomes. We aimed to investigate the length of stay (LOS) and discharge modified Rankin Scale (mRS) score in aphasic, acute ischemic stroke (AIS) patients in order to estimate aphasia-related disease burden at a national level.

Material and method. The local database from the Cluj-Napoca Emergency County Hospital (CNECH), the second largest stroke center in Romania was used to export demographics, baseline clinical and laboratory data, inpatient length of stay (LOS), NIH Stroke Scale (NIHSS), and discharge modified Rankin Scale (mRS) score data for all AIS patients admitted during March 2019.

Results and discussions. Of 92 patients included in the study, 30 (32.6 %) had aphasia on admission. In a marginally significant unadjusted hierarchical multiple regression model, individuals with aphasia had a LOS of 1.86 days longer than stroke survivors without aphasia. In an adjusted version of the model, the NIHSS score at baseline was a significant predictor for LOS. In addition, the presence of aphasia was associated with a 1.49 increase in the mean mRS score. Aphasia was a marginally significant predictor for increased LOS. Presence of aphasia was more likely to produce a poor functional outcome.

Conclusions. Considering an estimated impact of approximately EUR 3 million on direct medical expenditure annually, future policymaking efforts should improve prevention of stroke and improved access to post-stroke aphasia care in Romania.

Keywords: *aphasia; acute ischemic stroke; length of stay; disability, outcome,*

INTRODUCTION

In the context of ever-growing pressure on health system resources related to population aging, increase in morbidity and mortality due to non-communicable diseases, as well as the impact of the COVID-19 pandemic, culprits such as stroke, which have significant contributions to the global burden of disease have come into the spotlight of health economists seeking to find ways to increase value for money.

Data from 32 European countries showed that in 2017 the cost of stroke reached €60 billion, with direct medical costs accounting for almost half of this staggering figure. Health expenditure for stroke varies greatly between western and eastern European countries (1). Romania has one of the lowest proportions of Gross Domestic Product allocated to healthcare, historically at around half of the European Union average. As evidenced by the most recent cost of illness studies, access to proper stroke care infrastructure, staff, and supplies are limited accordingly (4).

Aphasia, or difficulty in producing or comprehending spoken or written language, is one of the most

debilitating manifestations of AIS, affecting 21%-38% of all cases (2). Patients with post-stroke aphasia are shown to have increased mortality, long-term disability, and more complications than stroke survivors without aphasia (3). Despite anecdotal reports that access to care such as speech therapy for aphasia is notoriously low in Romania, few studies have reported insight on the epidemiology of aphasia at the national level and its impact on hospital resources. Moreover, data regarding the current cost and precise cost structure related to stroke are scarce (4). We hypothesize that inappropriate access to care for post-stroke aphasia may lead to substantial direct and indirect costs regardless of economic perspective.

In this article, we scanned our hospital's electronic records for relevant information in the context of aphasic AIS patients. Then, based on identified variables, we analyzed the length of stay (LOS) and discharged modified Rankin Scale (mRS) score for these patients to estimate aphasia-related disease burden at a national level.

2. Materials and Methods

2.1. Study population

A retrospective analysis of data regarding all patients with AIS admitted in the first 24 hours after onset to a primary acute stroke center from CNECH during March 2019 was performed. Data extracted from our local registry included demographic variables, baseline clinical and laboratory variables, LOS, NIHSS, discharge mRS scores, and discharge location. Only patients with index symptomatic AIS in the middle cerebral artery (MCA) territory and a pre-stroke mRS score of 0 or 1 were included. NIHSS and mRS were performed by trained neurologists during standard clinical care.

2.2. Exposure and outcome definitions

The NIHSS was performed for each patient on admission (5). Aphasia was defined as having a score of 1 or greater on admission NIHSS question 9. Aphasia type was classified according to Boston Classification System by speech-language pathologists using standardized tests. (6). Outcomes of interest included LOS and mRS scores at discharge. Poor functional outcome was defined as a mRS score of 3 or above at discharge (7).

2.3. Statistical analysis

Frequencies means and standard deviations were used for the descriptive analysis. Two hierarchical multiple regression analyses were conducted with LOS and mRS scores as dependent variables. In the first step, an unadjusted model was tested, with aphasia as a single predictor. Age and NIHSS scores were added as predictors in the second step to adjust for their effects. Assumptions of the multiple regression analysis were also tested to ensure the reliability of the analysis. Analyses were run in SPSS (IBM, Armonk, NY, USA).

3. Results

3.1. Assumptions' check

Collinearity analysis showed no multicollinearity in the data, as proved by Variance Inflation Factor (VIF) scores below ten and tolerance scores above 0.2. VIF values were as follows: unadjusted models: VIF= 1, tolerance = 1; adjusted models: VIF scores of 1.34, 1.07, 1.39; tolerance scores of 0.74, 0.93, 0.71. Analysis of Durbin-Watson statistic for the model with LOS was 2.23, for the model with mRS score was 2.22, therefore showing that the values of the residuals are independent. The standardized residuals versus standardized predicted values plot indicated no signs of funneling, suggesting that the homoscedasticity assumption is met. The P-P plot suggests that the assumption of normality of the residuals was met—inspection of the Cook's distance values no compelling cases (all values lower than 1).

3.2. Main analysis

The descriptive statistics of all variables are shown in Tables 1 and 2. Separate values are provided for patients with and without aphasia. Hierarchical regression

analysis in the model with LOS as dependent variable indicated in the unadjusted model that aphasia was a marginally significant predictor ($F(1, 90) = 3.79$, $p = 0.055$), accounting for 0.040 % of the variance in LOS.

Table 1. Baseline demographic information for patients with and without aphasia.

	Aphasia (N= 30)	No aphasia (N= 62)
Variable	Frequency (percent)	Frequency (percent)
Female sex	20 (66.7)	30 (48.4)
Thrombolysis	7 (23.3)	7 (11.3)
Medical history		
Atrial fibrillation	15 (50)	11 (17.7)
Symptomatic Carotid stenosis	1 (3.3)	6 (9.7)
Smoking	5 (16.7)	12 (19.4)
Dyslipidemia	24 (80)	52 (83.9)
Hypertension	24 (80)	52 (83.9)
Aphasia type		
Broca	9 (30)	
Mixed transcortical	12 (40)	
Global	7 (23.3)	
Anomic	2 (6.7)	
Discharge deposition		
Home	20 (66.7)	57 (91.9)
Another department/center	4 (13.3)	2 (3.2)
Deceased	4 (13.3)	1 (1.6)
Senior care centre	2 (6.7)	2 (3.2)

Table 2. Demographic and outcome information for patients with and without aphasia

	Aphasia (N= 30)	No aphasia (N= 62)
Variable	Mean (Standard Deviation) Minimum - Maximum	Mean (Standard Deviation) Minimum - Maximum
Age (years)	74.86 (11.51) 41 - 97	70.83 (10.82) 40 - 88
LOS (days)	9.76 (5.51) 0 - 25	7.90 (3.58) 0 - 19
NIHSS score	13.70 (8.74) 1 - 30	5.80 (4.94) 1 - 25
Discharge mRS score	3.26 (2.03) 0 - 6	1.77 (1.62) 0 - 6

As shown by regression coefficients in Table 3- unadjusted model, having aphasia marginally increased the mean LOS by 1.86 days. Adjusting for the effects of age and NIHSS score resulted in an overall significant model ($F(3, 88) = 4.53$, $p = 0.005$) and explained an

additional 0.134% of the variance in LOS. Examination of individual predictors indicated NIHSS score to be the only significant predictor in the model. Effects of aphasia and age were not significant. As shown by regression coefficients in Table 3 - adjusted model, the predicted LOS for a patient without aphasia, of mean age and mean NIHSS score was 11.30 days. A one-unit increase in the NIHSS score predicted a 0.20 day increase of this mean LOS.

Hierarchical regression analysis in the model with mRS score as dependent variable indicated in the unadjusted model that aphasia was a significant predictor ($F(1, 90) = 14.43$, $p < .001$), accounting for 0.138 % of the variance in mRS scores. As shown by regression coefficients in Table 4 - unadjusted model, having aphasia increased the mean mRS score by 1.49 points compared to the mean scores of 1.77 for patients without aphasia. Adjusting for the effects of age and NIHSS score resulted in an overall significant model ($F(3, 88) = 41.68$, $p < 0.001$) and explained an additional 0.587% of the variance in mRS scores. Examination of individual predictors indicated significant effects for age and NIHSS score. As shown by regression coefficients in Table 4 - adjusted model, the predicted mRS score for a patient without aphasia, of mean age and mean NIHSS score was -1.26. A one unit increase in the NIHSS score predicted a 0.18 point increase of this means mRS score.

Table 3 Regression coefficients for the length of stay (LOS) model

Unadjusted model					
	B	SE	β	t	P
Constant	7.90	0.547		14.46	<.001
Aphasia	1.86	0.957	0.201	1.94	.055
Adjusted model					
	B	SE	β	t	P
Constant	11.301	2.847		3.97	<.001
Aphasia	0.537	1.065	0.058	0.50	.615
Age	-0.064	0.040	-0.165	-1.60	.113
NIHSS	0.201	0.069	0.340	2.90	.005

Table 4. Regression coefficients for modified Rankin Scale (mRS) model

Unadjusted model					
	B	SE	β	t	p
Constant	1.774	0.224		7.91	<.001
Aphasia	1.492	0.393	0.372	3.80	<.001
Adjusted model					
	B	SE	β	t	p
Constant	-1.260	0.851		-1.48	.143
Aphasia	-0.066	0.319	-0.017	-0.208	.836
Age	0.028	0.012	0.164	2.31	.023
NIHSS	0.183	0.021	0.716	8.85	<.001

4. Discussion

This study evaluated all available information on post-AIS aphasic patients in the Romanian patient pathway. Our main results show that aphasia is associated with prolonged LOS during acute stroke admission and a higher mRS score at discharge. These findings are in accordance with recent studies highlighting the underrecognized effect of communication impairment on stroke patients' outcomes (2,3). However, as opposed to our study, extensive international literature indicates aphasia is a significant predictor for prolonged LOS even after adjusting for NIHSS score and other variables, such as inpatient complications. We assert that contrasts between these observations could be explained either by our sample not being representative of the Romanian population (which could be the case given the limited timeframe for data collection) or by essential differences in care standards between countries. Neurorehabilitation procedures are generally not initiated in Romania's initial post-AIS inpatient admission. Therefore the decision to discharge patients might not incorporate their recovery potential (17). An alternative explanation would be that the sample size for various independent variables is too low to be used in the regressive model.

Over the last few years, studies have shown that aphasic patients have more disability at discharge (defined as a mRS score of 3-6) than non-aphasics (8). These findings remain even after accounting for NIHSS scores and inpatient complications. In contrast, patients with hemiparesis are not at higher odds of having a discharge mRS of 3-6 after adjusting for the same parameters (2). Furthermore, aphasia at baseline was also associated with a poorer mRS at three months in a retrospective analysis on 8904 stroke patients (9). These data align with our results that show that aphasia increases the mean mRS score at discharge by 1.49 points.

In the present study, aphasic and non-aphasic patients had a mean LOS of 9.76 and 7.9 days, respectively, lower than the previously reported mean for other countries (11) but similar to that obtained in another Romanian regional study (4). We found that the presence of aphasia marginally prolongs LOS by 1.86 days, as compared to non-aphasic patients. However, when controlling for age and NIHSS score, the effect of aphasia alone was no longer significant. This observation does not necessarily imply that aphasia no longer has an impact, as the NIHSS score includes a measure of aphasia, which we could not separate from the total score due to limitations in data collection. In a retrospective analysis on 1847 stroke patients, after adjusting for NIHSS score and inpatient complications, a 1.22 day increase in LOS was reported in aphasics (2). In addition, in a retrospectively examined cohort of 3200 stroke patients, the LOS was 8.6 days in aphasic patients compared to 7.2 days in non-aphasic ones (3).

Several possible explanations account for a longer LOS in these patients. One is that a failure to communicate and understand commands can impair physical therapy, thus prolonging motor recovery (10,12). Moreover, aphasics have been shown to develop more complications (such as sepsis, pneumonia, neurological worsening, and myocardial infarction) than non-aphasics (2). This finding could result from difficulty expressing complaints and symptoms worsening or properly following instructions (2). Another pertinent explanation is that these patients sometimes have problems finding a suitable rehabilitation placement either because they do not necessarily have associated motor deficits or cannot perform occupational therapies (3,10).

Considering that acute LOS is responsible for more than 65% of the total inpatient costs, prediction of this outcome variable is essential for the precise planning of the health care system resources. The LOS-associated costs account for acute hospital beds, intensive use of neuroimaging, medication, and paramedical resources (13). Unfortunately, data regarding the costs of stroke care in Romania are limited. However, a recent analysis showed that the average cost per stroke inpatient care episode summed up to EUR 995 in 2017, while the mean LOS was 9.9 days (14). Thus, we estimated that the average cost for a one-day hospital stay for stroke was about EUR 100 in our country in 2017. Assuming a 30% aphasia rate among 55,000 new ischemic stroke cases annually (15) and considering a 1.86 day LOS prolongation, we concluded that aphasia adds EUR 3 million annually to the care of these patients in Romania. Compared to a recent study that estimated that aphasia adds a cost of about EUR 1.77 billion annually in the US (2), the financial burden seems to be minimal in our country. In truth, with an annual expenditure of only EUR 7.15 per capita and a total allocation of EUR 140 million in 2017 for stroke, Romania was at the bottom among European countries and far away from the American expenditure for stroke (14). Consequently, aphasia's financial burden is considerable and represents a challenge for the limited local healthcare system budget.

We acknowledge several limitations to this study, including a small patient sample and a larger group of non-aphasics as compared to aphasics. This could account for aphasia not being a predictor for longer LOS in the adjusted model instead of similar research (2). Second, only the total NIHSS score was available for analysis, so we could not evaluate which individual NIHSS sub-components apart from aphasia correlate with LOS. Moreover, as the scope of the study was limited and focused on aphasia, no regression models were run with additional comorbidities as predictors of LOS. In addition, previous studies have found that aphasic patients have more inpatient complications than non-

aphasics and that a significant part of the relationship between aphasia and LOS is explained by these complications (2). However, due to lack of homogeneity in data reporting, we could not adjust for inpatient complications when assessing LOS. As a consequence, the overall impact of aphasia could be overestimated in the present research. Aphasia outcome at 3 months is related with to the initial severity of language disorder, infarct's size and location and with to a range of patient-related indices like educational level (16). However, such variables were not analysed in our study, since the main objective was to assess short-term outcomes in these patients. The strengths of the present study lie in the novelty of the data, being the first in Romania to address the financial burden of stroke-related aphasia. Future research could focus on how different types of aphasia impact acute stroke outcomes. In addition, upcoming studies could investigate whether those outcomes are influenced by receiving aphasia therapy during hospitalization.

5. Conclusions

Overall, our study showed that aphasia in stroke patients is associated with increased disability at discharge and prolonged LOS, which significantly add to the burden of the health care system in Romania. These findings suggest that better management of communication disorders during acute stroke hospitalization is needed. Likewise, the results of this study can be used as a baseline for measuring cost-effectiveness of new or improved stroke care strategies. Access to information regarding stroke care is scanty and limited to medical records and focused registries with low sample sizes. Romania must make important strives to improve the quality of healthcare information systems to allow appropriate appraisal of standards of care for stroke patients.

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Essential oils utility implications in symptomatic Burning Mouth Syndrome

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Abstract

Introduction. Burning mouth syndrome (BMS) is a clinical condition characterized by the presence of chronic pain in absence of clinically visible lesions of the oral mucosa. The etiology is uncertain and the therapeutic strategies still controversial. The objective of this prospective study is to analyze the efficacy of essential oils-based mouthwashes in the therapy of BMS.

Material and method. This study included 16 patients affected by BMS who were treated with essential oils-based mouthwashes and glucose solution on alternated days for 30 days. Symptomatology was evaluated after 15, 30 and 90 days.

Results and discussions. At the end of the treatment, most of the patients (67%) referred an improvement of symptoms up to complete remission in 90 days.

Conclusions. Based on this study, essential oils-based mouthwashes could represent a valid aid in the treatment of BMS. Further studies are necessary in order to identify effective and standardized therapeutic protocols.

Keywords: *Burning Mouth Syndrome; oral rinse; essential oils; therapeutic strategies,*

INTRODUCTION

Burning mouth syndrome (BMS) is a clinical condition characterized by burning symptoms and chronic pain, affecting the oral mucosa, not referable to objective alterations of the physiological muco-membranous architecture of tissues of the oral cavity (1, 2). It is a difficult pathology for both the operator and the patient due to absence of a clear etiological definition and well-defined and effective therapeutic plans (3).

The most controversial aspect of BMS is represented by the presence of a single symptom (stomatopyrosis) which can potentially manifest itself as many clinical conditions such as nutritional deficiencies, hormonal imbalances, diabetes (4). These aspects lead to the differentiation of BMS in two types:

- Primary, characterized by the absence of associated clinical conditions
- Secondary, characterized by the presence of

associated clinical conditions

The prevalence of BMS in the general population is between 2.5 and 5% (5). In most cases, BMS affects females (F:M ratio = 7:1) in the menopausal and postmenopausal age (between 55 and 75 years), while it is very rare in young people and never observed in children.

In order to make the clinical classification more understandable, in 1989, Lamey and Lewis suggested a classification, in which three clinical forms of BMS were present, based upon variation of symptoms during the day (6):

1. Absence of burning sensation at awakening, onset of symptoms during the morning and exacerbation in the evening (often associated with nutritional deficiencies);
2. Continuous symptoms throughout the day (associated with anxiety);

3. Intermittent symptoms with days of remission and days of exacerbation (associated with allergic states).

Burning sometimes referred to as a sense of scalding or tingling, is always present. Although it can be located in any area of the oral cavity, it always arises bilaterally and affects in most cases the tip of the tongue and the anterior 2/3, the hard palate and the lower lip while rarely, the floor of the mouth and the oropharynx (7).

The burning symptom has a moderate intensity but sometimes can be quite severe. The values reported by the Visual Analogic Scale are between 5 and 8. The course is chronic; it lasts at least 4-6 months up to 12 years. It is often accompanied by a sensation of xerostomia (50-60% of cases) and by hypogeusia and dysgeusia, referring to a persistent perception of bitter or metallic taste (30% of cases).

Regarding the etiological hypotheses, local and systemic factors can be distinguished. Among the local etiological factors there are:

- Vices (bruxism, grinding, biting of the lips and / or cheeks);
- Dental treatments;
- Infectious agents (*Candida Albicans*, *Enterobacter*, *Klebsiella*);
- Allergic reactions to particular substances (Mercury, Nickel Sulphate, Methyl-Methacrylate Monomers)
- Salivary changes:
 - quantitative: decrease in salivary flow;
 - qualitative: alteration of salivary concentrations

of proteins (mucins) and salts (potassium and sulphates)

- Peripheral neuropathies (8).

On the other hand, systemic factors include:

- Menopause;
- Vitamin (Vitamin B and folic acid) and mineral (Iron and Zinc) nutritional deficiencies;
- Diabetes;
- Psychological disorders: anxiety, depression, hypochondria, cancer-phobia, alexithymia, neurosis and psychoasthenia).

The frustrating aspect of this clinical condition is the difficulty in identifying the agent triggering the symptoms and consequently identifying an appropriate therapeutic protocol. However, it seems that certain molecules play an interesting role in the symptomatic treatment of BMS.

Typically, prescribed therapy consists of (9):

- Clonazepam: this benzodiazepine not only has an anxiolytic effect but also acts at the level of sensory receptors producing a moderate analgesic effect;
- Salivary substitutes;
- Vitamin supplements (with zinc);
- Benzydamine HCL 3% solution: it is a mild anesthetic (it is assumed that the patient with BMS has a peripheral neuropathy due to epithelial atrophy making the nerve endings more superficial with consequent amplification

of symptoms even for mild stimuli);

- Topical antihistaminics;
- Antidepressants;
- Capsaicin: acts on substance C (an important molecule in neurotransmission). Although not extensively evaluated, capsaicin seems to be able to block the burning receptors with a homeopathic mechanism;
- Alpha-lipoic acid: an essential oil that acts as a mitochondrial coenzyme and that takes part in various phases of the Krebs cycle with a double effect

Antioxidant effect, meaning the capacity of the enzymatic or not enzymatic system of limiting the harmful effect of reactive chemical species (RCS). These molecules have in common a marked tendency to react. They are physiologically produced; however, an imbalance between production and elimination determines a condition of oxidative stress, which can occur in physiological conditions, for example in case of inflammation, or pathological conditions, if it persists over time. In this case, it can be correlated with numerous pathophysiological and pathological states such as senescence, diabetes mellitus type II, atherosclerosis, Alzheimer disease), cancer, COPD, hepatopathies and more (10-12).

It was shown that *in vitro*, alpha lipoic acid presents 4 antioxidants activities: the ability to cross-link metals, to eliminate reactive oxygen, to regenerate endogenous antioxidants and to repair oxidative damage (13).

The neuroprotective effect is given to the ability to cross the blood brain barrier and increase the energy availability, hence its use in multiple sclerosis and BMS, since considered by some authors a peripheral neuropathy with an unknown etiology (14). On the basis of these considerations, a prospective study was carried out to assess whether and to what extent the treatment with essential oils-based (menthol, eucalyptol, thymol) mouthwash was able to reduce the symptoms of patients suffering from BMS.

Material and Method

Sixteen patients with symptoms compatible with BMS were recruited. Patients underwent an odontostomatological examination, blood routines (complete blood count, glycemia, iron, transferrin, vitamin B12, folate), intraoral tongue brushing for the evaluation of any mycosis. Based on their symptoms, only patients who did not present other possible causes were included in the study.

The inclusion criteria were: males and females (>45years old), with BMS symptoms, no ongoing drug treatment (antiretroviral, antihistamine, anticholinergic, narcotic, anti-inflammatory drugs), no other treatments for BMS. Those who refused to continue the treatment for 90 days were excluded.

The present prospective clinical study was based in

University of “Aldo Moro”, Bari (Italy), in full accordance with ethical principles, including the World Medical Association Declaration of Helsinki and the additional requirements of Italian law. Furthermore, the University of Bari, Italy, classified the study to be exempt from ethical review as it carries only negligible risk and involves the use of existing data that contains only non-identifiable data about human beings. Informed consent was obtained from the subjects involved in the study. Written informed consent has been obtained from the patient to publish this paper.

The essential BMS was diagnosed in 12 of these subjects, and in 4 individuals with no characteristic symptoms. They were aged between 44 and 78 years. Using a single-blind control method, for 3 months every other day patients were asked to use:

- Essential oils-based mouthwash (3 oral rinses lasting 60 sec / day);
- Sweetened saline solution (same dosage and method of administration).

Symptoms were assessed by compiling a visual-analog scale (V.A.S.) (Fig. 1) after 15 days, 30 days and 90 days.

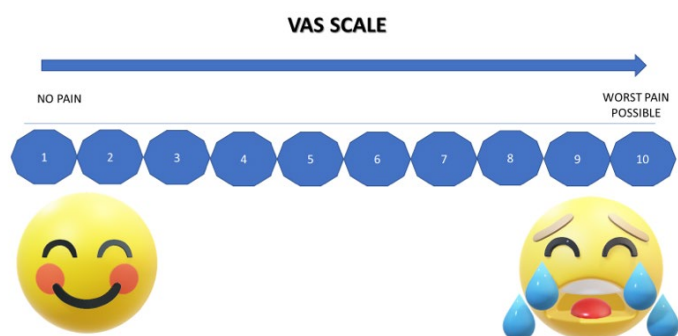


Fig. 1. VAS scale in symptomatic pain assessment.

Results

This study was performed on 16 patients with BMS with the mean age (Fig. 3) of 61.3 years ranged from 44 to 78 years, including 9 women (56%) and 7 men (44%) (Fig. 2).

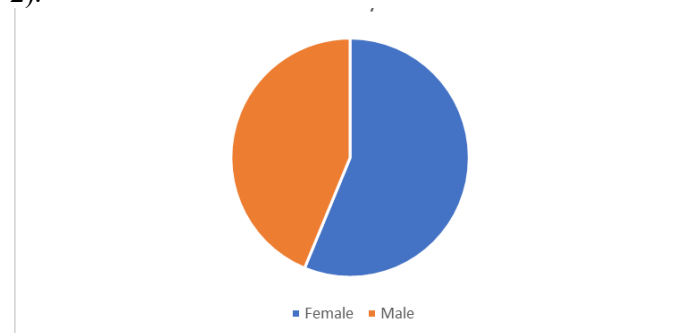


Fig. 2. Gender repartition of the included subjects.

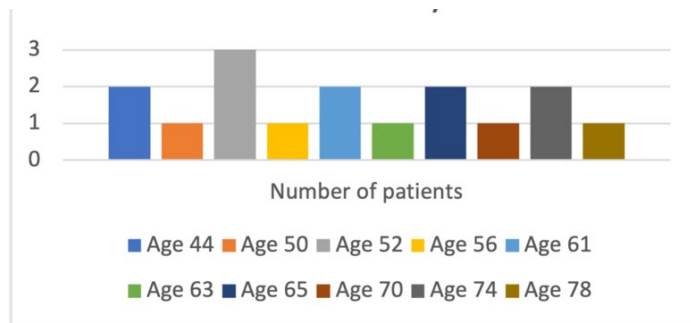


Fig. 3. Age range of the included subjects

- 67% of patients (Fig. 4) reported a reduction of symptoms after administration of essential oils-based mouthwash (3 oral rinses lasting 60 sec / day) followed by a remission of pain with relief of the patient;
- 13% of subjects reported no difference in symptomatology;
- 5% of patients reported an increased level of pain when taking both the control solution and the essential oils-based mouthwash.

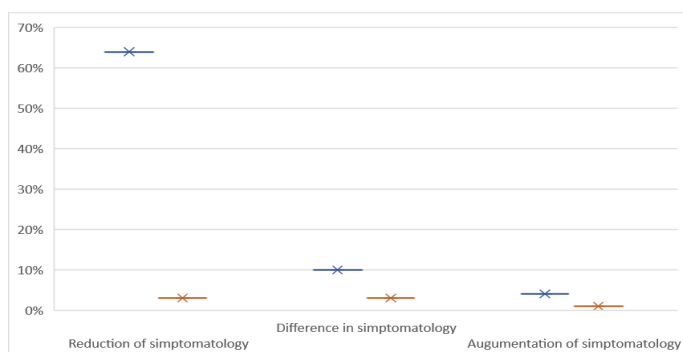


Fig. 4. Symptomatology assessment after treatment.

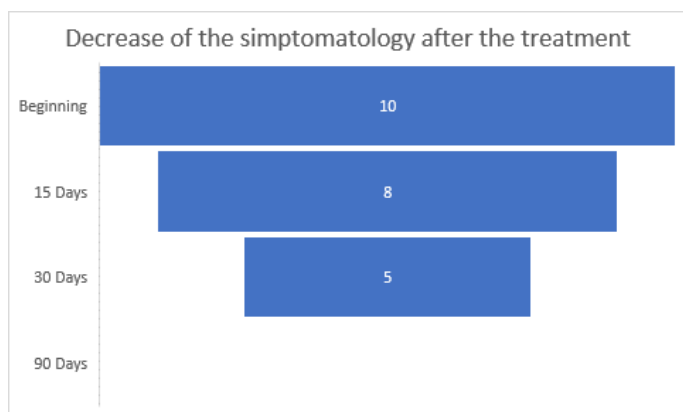


Fig. 5. VAS scale during BMS treatment.

Regarding the trend analysis of the symptoms, a reduction in VAS was reported by patients (Fig. 5), on average, from a value of 10 before treatment to a value of 8 after 2 weeks, until a VAS value of 5 after 30 days of treatment. Patients underwent a 90-days follow-up in which the total absence of symptoms was reported.

Discussion

The BMS still represents a particularly frustrating pathology for both the patient and the clinician today. The real problem is to define the etiological factors that play the key role in the pathogenesis and therefore to establish an effective therapeutic protocol (15).

It is believed that in the evaluation of the patient with BMS it is essential to investigate the psycho-social status, establishing a relationship *ad personam* that can be corroborated through optimal counseling between the patient and the clinician. The histological picture of BMS it is completely devoid of pathognomonic signs; sometimes the presence of sporadic hyphae of *Candida Albicans* can be found (16). The diagnosis of this syndrome is mainly based on an accurate medical history concerning the psycho-social status of the patient, the reported symptoms and the total absence of stomatognathic clinical signs. In any case, it is important to reassure the patient of the absolute benignity of her clinical condition. The therapeutic approaches used so far seem to alleviate the symptoms but they are often based on personal empirical experiences and not always reproducible on a large scale (17).

The results of the present study show that essential oils-based mouthwashes are useful in reducing the symptoms of patients with BMS. This benefit may be linked to the anti-inflammatory, antioxidant, immune-stimulating and antimicrobial properties of essential oils (18-20).

Furthermore, the pharmacological activity of essential oils on the central nervous system is well known and therefore, they are already used as complementary therapy in subjects suffering from symptoms such as pain, convulsions and cognitive impairment by oral intake, inhalation or aromatherapy (21-24). This action on the central nervous system could be useful in BMS, for which a neuropathic origin has been hypothesized, characterized by dysfunctional cranial nerves (25). In addition, the anxiolytic, antidepressant and sedative effect of essential oils plays an important role in patients with BMS (26, 27). Actually, subjects affected by this clinical condition tend to be more apprehensive, depressed and introverted.

Limitations of the study include low sample size and the pattern that does not grant a high level of evidence (such as the evaluation of non-specific placebo effect). Finally, the essential oils-based mouthwash effects have only been tested on the short term (90 days).

Conclusion

Based on the research conducted, it is possible to reach the conclusion that the action of essential oils seems to produce positive effects on symptoms control. The pilot study is preliminary and needs further evaluation. However, the first results show a partial improvement of symptoms in patients treated with essential oils-based mouthwash.

Conflicts of interest

The authors declare no conflicts of interest.

Author contributions.

Patano Assunta and Di Venere Daniela contributed equally as first co-author of this paper. Sirbu Adina and Cardarelli Fillippo contributed equally as last co-author of this paper.

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Assessment of the importance of physical activity and quality of life for patients diagnosed with osteoporosis during the COVID-19 pandemic

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Abstract

Introduction. Osteoporosis is one of the most important ten diseases worldwide, still causing extreme suffering to patients and huge costs to the health system. The rapid increase of the population's aging was involved in many aspects of human health, and, among these ones, osteoporosis was one of the main public health issues.

The aim of the study was to assess the importance of physical activity and the quality of life in patients diagnosed with osteoporosis during the COVID-19 pandemic.

Material and methods. The study is longitudinal, it was conducted in an outpatient setting for a period of 1 year and it included 20 patients diagnosed with osteoporosis. The demographic variables (age, living environment, body mass index) were assessed, and as parameters: pain (VAS scale), fracture risk (FRAX score), quality of life (Qualeffo-41 questionnaire), bone mineral density at the spine and at the femur (DEXA). The patients received pharmacological treatment such as bisphosphonates and underwent physiotherapy for pains: low frequency currents (TENS), ultrasound and physical therapy.

Results and discussions. In all the studied cases, it was considered that the pain decreased following the use of the medicinal and physiotherapeutic treatment. This is an expected result given that other studies have shown this. Postmenopausal women in Romania with osteoporosis have a lower HRQoL than healthy controls, measured with the SF-36 instrument and the total QUALEFFO-41 score.

Conclusions. The obtained data point out the correlation between bone mineral density, fracture risks and exercises in patients diagnosed with osteoporosis. The FRAX score is useful to identify patients who need the combination of drug therapy and exercises to prevent vertebral and non-vertebral fractures in the next 10 years.

Keywords: *osteoporosis, physical activity, quality of life, COVID-19,*

INTRODUCTION

Osteoporosis is one of the most important ten diseases worldwide, still causing extreme suffering to patients and huge costs to the health system [1]. The rapid increase of the population's aging was involved in many aspects of human health, and, among these ones, osteoporosis was one of the main public health issues [2]. Osteoporosis is a disease of the skeleton characterized by low bone mass or by diminished bone mineral density, by damage to the bones' micro-architecture and by increased fracture risks [3]. In this disease, the bones become so fragile that a simple fall or even common movements, such as bending or coughing, can cause a fracture [4]. In general, the incidence of osteoporosis is higher in women than in

men, with a male / female ratio of 1: 4 [5]. Different risk factors for the development of osteoporosis can be classified into unchangeable (female gender, old age, dementia, personal history of fracture, family background of fracture in a first degree relative) and potentially changeable risk factors: smoking [6], early menopause, low calcium intake, vitamin D deficiency and sedentary lifestyle [2].

The normal development of the bones depends on the percentage of calcium (having in view that 99% of the total calcium is found in the skeleton) [7] and magnesium (60% is found in the bones) [8], and it is necessary to know the intervals of normal reference for these ions.

Several diseases are associated with an increased risk of generalized osteoporosis in adults: hypogonadal conditions, endocrine disorders, nutritional and gastrointestinal disorders, hematological disorders, selected inherited disorders, certain drugs, immobilization and pregnancy [5]. The assessment of the bone density is usually made on women over the age of 50, it is quick and painless, and it can predict whether or not there will be bone issues. In addition, the doctor can prescribe an appropriate treatment based on the test results or can recommend a change of lifestyle.

There are several methods to measure the bone density: osteosonography, Dual-X-Ray-Absorptiometry, osteodensitometry, QCT - quantitative tomography of the spine, pQCT - peripheral computed tomography or HRpQCT - high resolution peripheral computed tomography [9].

In Romania, only the first two methods are used to determine the bone density. In the National Program of Endocrine Diseases, in patients with osteoporosis, only the results of the DEXA diagnosis obtained after scanning the spine from L1 to L4 are used to validate the application of the program [10].

DEXA scanning is a widely accepted radiological instrument that can detect osteoporotic bone changes earlier and with greater accuracy than simple X-rays of the bone system. The DEXA radiological system is a device that uses two X-ray beams, each with a different energy level to determine their attenuation, namely by reducing the intensity of the X-ray beam as it passes through the patient's body. The use of two different X-ray energies enables the radiological installation to record different attenuation profiles. Attenuation is largely determined by the density and thickness of the tissue. For the low energy beam, the attenuation is higher in the bone than in the soft tissue. In the case of the high energy beam, the bone attenuation is similar to the one of the soft tissue. By using two different energies, two equations are created, the solution of which is the two unknown: the density of the bone and the one of the surrounding soft tissue [11]. Measuring bone density means estimating the total amount of the bone substance present in a given volume. The method called dual energy X-ray absorption (DEXA) actually measures the density of an area (g / cm^2). Some indicators are used in measuring density by this method such as [1]:

The T-score: it is obtained when the bone mineral density is compared with the normal value (considered at the age of 30).

The Z-score: it is obtained by relating to normal values for the same age and sex

In the current practice, the T-score is the most used indicator [12]. If its value is less than -2.5, the diagnosis is osteoporosis. Osteopenia is characterized by a T-score value between -2.5 and -1.0 [13].

The WHO classification, according to the Z-score, is used in perimenopausal and postmenopausal women, but not in healthy premenopausal women, because the relationship between BMD and fracture risk is not well established in this category. The Z-score is used for clinical diagnosis in premenopausal women if they have fragility fractures or if low bone mineral density (determined by DXA) is associated with risk fracture factors. These risk fracture factors are: age, smoking, low body mass index (BMI), low calcium intake, vitamin D deficiency, sedentary lifestyle, early estrogen decrease, dementia, alcoholism, low visual acuity, history of falls, low bone mineral density. In order to improve health and to avoid complications caused by osteoporosis, medicine must find effective and accepted solutions to increase bone and muscle anabolism [14]. After a certain age, a lifestyle should be established to help improving the health and it should include the increase of the physical activity, quitting smoking, reducing alcohol consumption, reducing the risk of falling and providing an adequate diet, calcium and vitamin D [15,16].

Thus, physical exercise has been recommended by the WHO as physical therapy for the prevention and treatment of non-drug osteoporosis [16,17]. Exercises can prevent osteoporosis in the elderly as a preventive strategy without medication.

The interaction of mechanical loading, of hormones (estrogen, testosterone) or of cytokines, but also signaling pathways induced by effort, increase the bone remodeling and reduce the bone resorption [18]. The disorder of bone angiogenesis is associated with many bone diseases, including osteoporosis, whereas exercise improves bone angiogenesis by regulating key angiogenic mediators [2]. Throughout life, the bones are reshaped, which means that they are continuously resorbed by osteoclasts and replaced with new bones produced by osteoblasts. This process enables keeping mechanical strength and repairs. The lack of balance in the remodeling activity where the resorption exceeds the formation can lead to physiopathological changes noted in osteoporosis [18].

Progress has been made in bone molecular biology and a protease called cathepsin K (CatK) has been identified, secreted by osteoclasts in the process of the bone resorption, resulting in the bone matrix degradation and the decomposition of the mineral components of the bone tissue. The parathyroid hormone also intervenes in the bone formation, by indirectly increasing the proliferation of osteoblasts and by regulating calcium homeostasis [19].

In the case of fractures, action is taken to control pain, for the early mobilization, to limit disability, to restore functions and to prevent further fractures.

There are several treatment options that include conventional analgesia, osteoporosis pain relievers, minimally invasive procedures, electrotherapy

modalities, external support devices and exercises [20]. In the case of physical exercises done by patients with osteoporosis, without the control of a specialist, it was found that there is insufficient cooperation between physiotherapists and specialists involved in the treatment, not being able to provide a constant follow-up of their frequency and correctness [21,22]. Ultrasound therapy is a commonly used way to treat pain syndrome in osteoporosis. However, its effects on osteoporosis are unclear, but therapeutic ultrasound will help reduce bone-related pains, it will improve exercise capacity, and it will reduce the risk of osteoporosis [23].

The aim of the study was to assess the importance of physical activity and the quality of life in patients diagnosed with osteoporosis during the COVID-19 pandemic.

Material and methods

The study is longitudinal, it was conducted in an outpatient setting for a period of 1 year and it included 20 patients diagnosed with osteoporosis.

Inclusion criteria:

- Patients with a definite diagnosis of osteoporosis
- Age > 50 years
- Postmenopausal women
- Patients without decompensated chronic conditions

Exclusion criteria

- Patients < 50 years of age
- Non-cooperating patients
- Patients who did not want to participate in the study
- Patients with severe conditions contraindicating physiokinetotherapy (heart failure, atrial fibrillation, myocardial infarction, stage II-III hypertension)

The assessment of the patients was done at the beginning of the physiotherapy treatment period, at the end and after 1 year. The demographic variables (age, living environment, body mass index) were assessed, and as parameters: pain (VAS scale), fracture risk (FRAX score), quality of life (Qualeffo-41 questionnaire), bone mineral density at the spine and at the femur (DEXA). The VAS scale is a method by which the patient assesses pain (0-absence of pain, 10-unbearable pain). The FRAX score enables the calculation of the probability that a patient may suffer a major osteoporotic fracture in the next 10 years. The Qualeffo-41 questionnaire assesses the quality of life in people with osteoporosis, it consists of 41 questions, marked from 0-4, grouped into 5 areas: pain (5 questions), physical function (17 questions), social function (7 questions), general perception of general health (3 questions) and mental function (9 questions).

DEXA is an absorption method with dual energy X-ray that determines the T- score and the Z - score. The patients received pharmacological treatment such as bisphosphonates and underwent physiotherapy for pains:

low frequency currents (TENS), ultrasound and physical therapy. TENS was applied for analgesic purposes, muscle relaxation and to improve the peripheral circulation, with the following parameters: the frequency of 50-100Hz, the intensity of 10-40 mA and a duration of 10 minutes. The ultrasounds were applied for analgesic, decontracting purposes, with the following parameters: pulsed shape, the frequency of 1 MHz, the power of 0.5W / cm² with a duration of 5 minutes.

Physical therapy was made daily for 10 days and then 3 times/ week and it included active-passive mobilizations performed with low to medium intensity, in order to promote bone strengthening (dancing, walking), exercises for toning muscles (by using elastic bands) so as to increase flexibility, to keep the correct posture, balance exercises that improve coordination and prevent falls.

The pursued objectives were:

- Pain relief
- Keeping / increasing joint mobility, muscle tone
- Prevention of fracture risk
- Re-education of breathing
- Correction of vicious attitudes and posture

Statistical analysis

The obtained data at the initial, final and control assessment times were statistically processed by using Microsoft Excel 10.

The median, standard deviation were calculated whereas the t-student test was applied to confirm the working hypothesis. The chosen level of statistical significance was 5% and in this context p should be less than 0.05 (p < 0.05)

Results

Table no. 1. Demographic traits of the study group

Traits/ age group (years)		50-54	55-59	60-64	65-69	70-74	>75
Number		2	4	4	5	4	1
Environment	Urban	1	3	2	2	2	0
	Rural	1	1	2	3	2	1
Status							
Single		1	1		1	1	
Married			2	2	2		
Divorced		1		1			
Widow			1	1	2	2	1

The patients participating in the study had an average age of 64 (64 ± 6.71), and they were in equal numbers from urban and rural areas, whereas the average height was 167 cm (167.5±3.35). There is a decrease in the average weight of patients by 1,145 between moments M1 and M2, by 1.4% between moments M2 and M3 and by 2.52% between moments M1 and M3. The Body Mass Index registered a decrease of 0.22% between moments M1 and M2, of 1.23% between moments M2 and M3 and of 2.43% between moments M1 and M3.

As for the pain, it was assessed by using the VAS scale and it decreased by 28.57% between moments M1 and

M2, by 40% between moments M2 and M3 and by 57.74% between moments M1 and M3.

Table no. 2. Evolution of the parameters: weight, body mass index and pain

Parameters / Moments	M1 (M±STD DEV)	M2 (M±STD DEV)	M3 (M±STD DEV)
Body weight (Kg)	79.5±9.4	78.6±9.26	77.5±9.09
Body Mass Index (BMI)	27.99±2.96	27.65±2.96	27.31±2.91
VAS scale	7±0.71	5±0.49	3±0.79

For the T-score that assesses the mineral bone density the following data were obtained:

- For the spine, the T score at the moment M1 had values between -2.5 ÷ -2.9 in 13 patients (65%), values between -3 ÷ -3.4 in 4 patients (20%), between -3.5 ÷ -3.9 in a patient (5%) and over -4.5 in one patient (5%). At the end of M3, the T - score had values < -2.5 in 3 patients (15%), values between -2.5 ÷ -2.9 in 10 people (50%), between -3 ÷ -3.4 in 4 people (20%), values between -3.5 ÷ -3.9 for one person (5%), between -4 ÷ -4.5 for 2 people (10%) and over -4.5 for one person (5%).
- For the hip, at the initial moment M1, the T score had values < -2.5 in 16 patients (80%), and for 2 patients (10%) values between -2.5 ÷ -2.9 and > -3. At the end of M3, the T score had values < -2.5 in 17 patients (85%), between -2.5 ÷ 2.9 in 2 patients (10%) and > -3 in one patient (5%).

The values of the t-student test were statistically significant of 0.0007 for the spine between M1 and M3, and of 0.0036 at the hip.

Table no. 3. The average T-score at the level of the spine and of the hip

Parameters / Moments	M1 (M±STD DEV)	M3(M±STD DEV)
T -score in the spine	-2.85±0.63	-2.6±0.61
T-score in the hip	-1.6±0.99	-1.2±0.92

In order to assess the fracture risk, the FRAX score was calculated, which enabled showing the major risk of osteoporotic fracture for the first 10 years and the risk of initial fracture at the initial time M1 and at the control time M3.

Table no. 4. FRAX score: Fracture risk

Parameters / Moments	M1(M±STD DEV)	M3 (M±STD DEV)
Major risk of osteoporotic fracture for the first 10 years	7.25±2.31	7.2±2.47
Initial fracture risk	1±0.86	1±0.89

The quality of life of patients with osteoporosis was assessed by the questionnaire Qualeffo-41 and it recorded an increase of 44.16% between moments M1 and M2, of 41.7% between moments M2 and M3, and of 67.49% between moments M1 and M3.

Table no. 5. The assessment of the quality of life for patients in the group

Parameters / Moments	M1(M±ST DEV)	M2(M±ST DEV)	M3(M±ST DEV)
Quality of life	141.5±13.3	79±11.03	46±3.07

The values of the T-student test were statistically significant for the spine between M1 and M3 de 0.0007, whereas in the hip it was 0.0036.

Discussions

In all the studied cases, it was considered that the pain decreased following the use of the medicinal and physiotherapeutic treatment. This is an expected result given that other studies have shown this. For example, in Miyakoshi's study [24], the subscale scores of 36 items of the health survey in the short form (SF-36) for physical role, body pain, general health, and emotional role were all significantly lower in the osteoporosis group than in the volunteer group ($p < 0.05$ each).

Postmenopausal women in Romania with osteoporosis have a lower HRQoL than healthy controls, measured with the SF-36 instrument and the total QUALEFFO-41 score [25]. There are also studies which show that osteoporosis may or may not cause any symptoms. About 60% of women with compression fractures do not realize they have had a fracture. Advanced cases suffer from deformities and changes in the mechanics of the spine and only in these cases is the pain noted [26]. It has been found that exercises and the application of recovery programs are effective in preventing falls or bone loss, having in view that over 90% of the hip fractures are due to falls [27, 28].

Following the comparative analysis between the results obtained for the T-score, in the final moment compared to the initial one, we can say that the pharmacological and physiotherapeutic treatment enabled the decrease of the T-score values in the spine, it decreased the number of patients diagnosed with osteoporosis but in 3 patients the diagnosis changed from osteoporosis to osteopenia. By studying the action mechanisms of the osteoporotic medication, it was noted that the maximum effect of treatment is obtained when their administration is combined with the physiotherapeutic treatment [29,30].

Another DXA test is recommended to patients undergoing treatment for osteoporosis, in which stagnation or improvement in the bone mineral density shows a favorable response to the treatment. Another DXA test is done when the results may influence clinical

management: one year after the commencement of the medication therapy, six months after the commencement of the corticosteroid therapy, or less frequently when testing does not bring new information [31]. In order to measure changes in the mineral bone density by using DXA, it is recommended to use the same device. Changes determined on different DXAs can only be quantified if a calibration is made between the two devices [32].

Conclusions

The obtained data point out the correlation between bone mineral density, fracture risks and exercises in patients diagnosed with osteoporosis. The FRAX score is useful to identify patients who need the combination of drug therapy and exercises to prevent vertebral and non-vertebral fractures in the next 10 years. Osteoporosis is considered a public health problem that affects the quality of life of patients with this diagnosis and also therapeutic, social and economic costs.

Declaration of conflict of interests

There is no conflict of interest for any of the authors regarding this paper.

Accordance to ethics standards

The study complies with the rules of ethics and deontology according to the legislation in force.

Author contribution

The authors of this article have equal contribution and equal rights over it.

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Complex aspects of clinical-functional evaluation and ambulatory therapeutic-rehabilitation approach in a young patient with post stroke - spasticity and peroneal nerve palsy

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Abstract

Introduction. Spasticity, a common post-stroke complication associated with signs and symptoms of upper motor neuron syndrome (1), occurs with a 35% prevalence one year after brain injury (2) and can be severely disabling in young patients (3), regarding locomotor dysfunction and also regarding the quality of life. Stroke incidence in young patients increased in the last decades, being correlated with the increasing substance abuse and sedentariness, excessive alcohol consumption, and smoking (4). Peroneal nerve palsy is the most common cause of neuropathy of the lower limb and, in most cases, is caused due to nerve lesion in the fibula head area (5).

Material and method. We present the complex case of a young male patient, former alcohol and narcotics user, who suffered an ischemic stroke in the right middle cerebral artery territory along with a posttraumatic paresis of the right peroneal nerve. The patient presents motor deficit – right spastic hemiplegia, right foot drop, locomotion and self-care disorders.

Results and discussions. The patient followed medical treatment (antiepileptic, neurotrophic factors, vitamins, antiplatelet) and rehabilitation treatment adapted to the current clinical-functional status (thermotherapy, lasertherapy, magnetotherapy and individual kinesiotherapy), with slow favorable evolution of the improvement of locomotion and quality of life disorders.

Conclusions. Therapeutic-rehabilitation management of the spastic patient with disability due to brain injury and peripheral traumatic neuropathy represents a challenge because it doesn't exist a miraculous treatment (yet) to cure completely these nervous injuries.

Keywords: *post stroke spasticity, peroneal nerve palsy, rehabilitation,*

INTRODUCTION

”Stroke is a medical condition characterised as rapidly developing clinical signs of a focal or global injury of cerebral function usually lasting more than 24 h or leading to death, with no apparent cause than vascular origin” (6). From the etiological point of view, stroke can be ischaemic stroke – 80-85% (tromboembolic source: atrial fibrillation, myocardial infarction, valvulopathies, congenital cardiac defects, disturbances of the fluid-coagulant balance, atherosclerosis) or hemorrhagic stroke - 10-15% (haematomas caused by craniocerebral trauma, broken arteriovenous malformation, hypertensive encephalopathy, thrombocytopenias, hemophilia) (7). Stroke is a major public health problem - in Romania and worldwide and more than 60.000 strokes occurs each year in Romania. Stroke is the second common cause of death after coronary heart disease; unfortunately,

Romania has one of the highest stroke mortality rate in Europe (8).

Spasticity, a common post-stroke complication, associated with signs and symptoms of upper motor neuron syndrome (9), occurs with a 35% prevalence one year after brain injury (10), and can be severely disabling in young patients (11), regarding locomotor dysfunction and also regarding quality of life.

Stroke incidence in young patients increased in the last decades, being correlated with the increasing substances abuse together with sedentariness, excessive alcohol consumption and smoking (12).

Peroneal nerve palsy is the most common cause of neuropathy of the lower limb and in most cases is caused due to nerve lesion in the fibula head area (13).

Material and method

Having the patient's consent, the paper presents the case of a patient aged 39, retired on medical case, from the urban area who was admitted to the Rehabilitation, Physical Medicine and Balneology Ambulatory of the Teaching Emergency County Hospital "Sf. Apostol Andrei" Constanta, during the period 05.01.2021-18.01.2021 for: left spastic hemiplegia, right foot drop, functional impotence for walking and self-care, consecutive. From the personal physiological and pathological antecedents, we remember: an ischemic stroke in the right middle cerebral artery territory (2018), a chronic hepatitis C virus and a right tibia and fibula fracture operated (2015). Our patient was known with risk factors: former alcohol, narcotics user, former smoker and he had an unhealthy lifestyle. The present suffering began suddenly (April 2018) with rapidly progressive motor deficit on the left side, with the preservation of the state of consciousness, but with sleepy state, in addition of the left facial asymmetry. He was admitted to the Clinic of Neurology / Teaching Emergency County Hospital "Sf. Apostol Andrei" Constanta, where he was diagnosed with right ischemic stroke (thrombotic mechanism), with left hemiplegia and left facial palsy and followed anticoagulant, antihypertensive, hypolipemic, hydroelectrolytic rebalancing with favorable evolution. The patient continued at home the pharmacological treatment initiated in the hospital and required permanent assistance from his mother for the daily self-care activities. In evolution, he presented a state of progressive physical deconditioning, with the installation of vicious positions (see below) on the limbs. His chronic treatment was with: antiepileptic, neurotrophic factors, vitamins and antiplatelet.

General clinical examination at presentation:

- Conscious, afebrile, influenced general state
- Normal weight (BMI = 24 kg / m²)
- Normal coloured skin and mucosa, bilateral foot onychomycosis
- BP = 140 / 80 mmHg, AV = 72 b/ min rhythmically
- Pulmonary stethacoustics - no significant changes
- Peripheral arteries pulse present

Neuro-myo-arthro-kinetic exam:

- facial asymmetry through the left central face paresis
- complete motor deficiency - plegia type at upper left limb and paresis type at lower left limb, with pyramidal hypertonia
- left shoulder sub-luxated, internally rotated, elbow in semi flexion, hand in pronation, fingers in palm flexion
- lower left limb posture in external rotation,

deformed foot in equine var, fingers in hammer

- upper left limb motor control: no motor control at any level
- lower left limb motor control: moderate motor control at the proximal and intermediate level, absent at the distal level
- hyperkinetic deep tendon reflexes in upper and lower left limbs, Hoffman reflex and palmomental reflex present, exhaustible clonus patellar, Babinski (+), Rossolino reflex present, on the left side
- no sensitivity disorders
- right leg muscle hypotrophy
- post surgery scar on the right leg
- right foot drop
- spine - accentuation of physiological curves, left dorsal-lumbar scoliosis, pain on palpation of the lumbar segment, limited active mobilization.



Fig. 1. The right calf - keloid scar

Functional evaluation

He realizes independently the mobilization in bed, the transfer from dorsal decubitus to lateral decubitus and from lateral decubitus in the sitting position shortened - maintained without support. He was able to perform and maintain orthostatism with support in a Canadian cane but with gait disorders. The patient had psycho-emotional and cognitive status disorders: psycho-motor agitation. The patient was assessed functionally at admission and discharge using the following scales:

- Modified Ashworth = 3 (admission), 3 (discharge)
- Penn = 1 (admission), 1 (discharge)
- Visual Analogue Scale (VAS) = 0 (admission), 0 (discharge)
- Activity Daily Living (ADL) = 5/ 6 (admission), 5/ 6 (discharge)
- Functional Independence Measure (FIM) = 101/ 126 (admission), 105/ 126 (discharge)
- Quality of Life (QOL) = 85/ 112 (admission), 91/ 112 (discharge)
- Barthel index – 80/ 100 (admission), 80/ 100 (discharge).

Paraclinical investigations

- Blood Tests showed hepatic cytolysis syndrome (ALT=124 U/L, AST=52 U/L, GGT=457 U/L) and hypercholesterolemia (LDL=197 mg/dL)
- electrocardiogram was within normal limits
- Brain CT: infra and supratentorial pericerebral fluid spaces with dimensions within the age limits. The absence of evocative images for acute ischemia, intra/ extracerebral blood accumulations or tumor masses. Symmetrical ventricular system with normal dimensions. Normally positioned median structures.
- Brain IRM: isolated and confluent lesions located capsulo-nuclear and periventricular on the right side associated with right unilateral cortical edema, rather in an infectious-inflammatory context than an ischemic vascular one (clinical-biological corroboration and imaging monitoring). The suspicion of encephalitis is excluded by the repetition of brain MRI which suggests a cerebral infarction in the right middle cerebral artery territory with hemorrhagic transformations, and also by repeated lumbar punctures. HIV or syphilis, as well as other infectious agents, are excluded by laboratory tests.

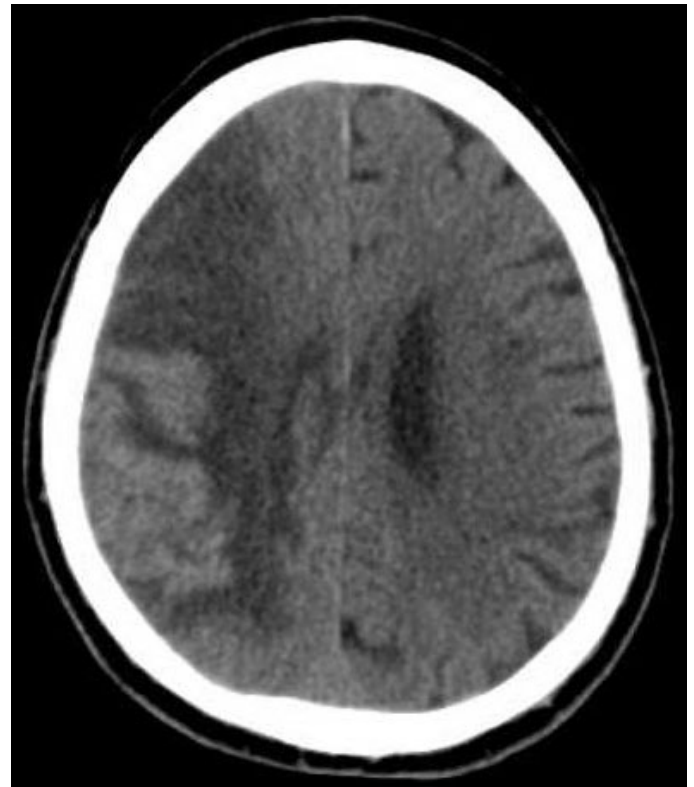


Fig. 2. MRI aspect recorded in April 2018

- Right leg x-ray: synostosis (bone bridge) at the level of the 1/3 proximal on a 5 cm area between tibia and right fibula. Old fractures strengthened at the diaphysis of the right tibia and fibula.

Positive diagnosis of our patient is: Spastic left hemiplegia, predominantly facio-brachial, secondary to an ischemic stroke in the right MCA territory (April 2018). Hypercholesterolaemia. Right peroneal nerve palsy. Chronic hepatitis C virus. Medium dysfunction of mobility, self-care and social interaction.

Differential diagnosis is made:

For HEMIPLEGIA with: lower motor neuron syndrome (diabetic polyneuropathy, polyradiculoneuritis, brachial plex lesions) and upper motor neuron syndrome (Spinal Cord Injury, Brain Trauma, Multiple Sclerosis, Brain Tumors, Nervous System Infections).

For STROKE with: cerebral hemorrhage (subdural, subarachnoid).

For PERONEAL NERVE PALSY with: HIV-Associated Multiple Mononeuropathies, Toxic Neuropathy, Vasculitic Neuropathy, Radiculopathy, Diabetic Polyneuropathy, Charcot Marie Tooth disease, Myopathy, Post-polio syndrome.

The clinically-functional evolution of the patient

The patient performed: lasertherapy and local thermotherapy (paraffin applications) with miorelaxation effect, low frequency current electrotherapy (TENS) at left shoulder and left wrist for analgesic effect, magnetotherapy for sedative effect, kinesiotherapy (postures, passive mobilisation, passive-active mobilisation, bed-side joint stretching and stabilisation exercises, scripotherapy, exercises on the stall bars, exercises on the bicycle, exercises on the foot pedals, walking between parallel bars, stepper exercises, walking with one-sided support).

The evolution of the patient was slowly favorable by improving the level of collaboration, improvement of the motor control at the lower limb, the patient in the end being able to stand, constantly without the need of the assistance of another person, can walk with Canadian cane support and supervision from another person, improvement of locomotion, improvement of quality-of-life disorders.

Possible complications are complications of motor deficiency (decubitus lesions, urinary tract infections, intestinal transit disorders, fractures due to locomotor disorders), complications of treatment (digestive, cerebral hemorrhagic risk, etc.) or complications of the associated diseases (Chronic hepatitis C virus)

Prognosis:

Ad vitam: is favorable in the short term but reserved in the long term if he does not respect the treatment and the interdiction to consume alcohol/ narcotics.

Ad Functionem: favorable under conditions of compliance and continuation of the neuromuscular recovery program.

Ad laborem: medical retiree, requires permanent companion.

Conclusions

The specificity of the case consists in the association of an upper motor neuron syndrome with a lower motor neuron syndrome in a young patient former alcohol and narcotics user. Therapeutic-rehabilitation management of the spastic patient with disability due to brain injury and peripheral traumatic neuropathy represents a challenge because it doesn't exist a miraculous treatment (yet) to cure completely these nervous injuries.

Conflict of interest

There is no conflict of interest for any of the authors regarding this article.

Informed consent

In this article was included an informed consent that was obtained from the patient.

Author contributions

All authors has equal contributions in this publication.

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Elbow rehabilitation using intelligent medical devices

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Abstract

The purpose of this paper is to demonstrate that the process of elbow joint rehabilitation can be monitored and improved using intelligent medical devices. During the study, an orthosis-type medical device was developed that monitors the mobility of the elbow joint in case of pathology. This device is useful in monitoring flexion movements (forward and backward), as well as internal and external rotation. For this purpose, a set of sensors were used that will capture the necessary and specific information, and the extracted data will be transmitted to a microcontroller for processing. The orthosis is one that can be customized according to the patient's pathology because it will analyse the data collected and interpret the values according to the calibration performed on the patient. The orthosis can be used both in the evaluation of joint dysfunctions at the elbow and in a rehabilitation program to avoid vicious positions. The positioning of the orthosis will be done together with the specialist doctor or in the presence of a physiotherapist, following the detailed clinical examination, so that the calibration of the sensors can be performed correctly. The device can emit warning sequences that will depend on the movements that the patient will perform, movements that can be sudden or accidental.

Keywords: *elbow joint, orthosis, physiokinetotherapist, rehabilitation, health improvement,*

INTRODUCTION

Three bones participate in the composition of the elbow joint, which join in the middle part of the arm. The distal portion of the arm bone - the humerus meets the proximal ends of the arm bones that articulate with it: the radius on the outside, and on the inside, the ulna (Fig.1) [1].

Several ligament structures contribute to joint stabilization on both the inner and outer sides of the elbow [2]. The elbow is the second most common segment dislocated after the shoulder and this dislocation is most common in children but is not excluded in adults and there are cases / causes such as: falling on an outstretched hand, accidents car, improper removal or twisting, sudden shooting, sports injuries. Tendonitis is common in adults. Other common causes of elbow pain are bursitis, arthritis, elbow infections, fracture and dislocation of the elbow [2].

Because the patient needs to recover from trauma to the upper limb, he should be made aware that surgery is only half of the therapeutic path he must take to return to the desired state of normalcy. If the doctor's instructions are not followed and the execution is done randomly, the patient risks damaging the degree of mobility of the elbow and even have a negative impact on surgery [3].

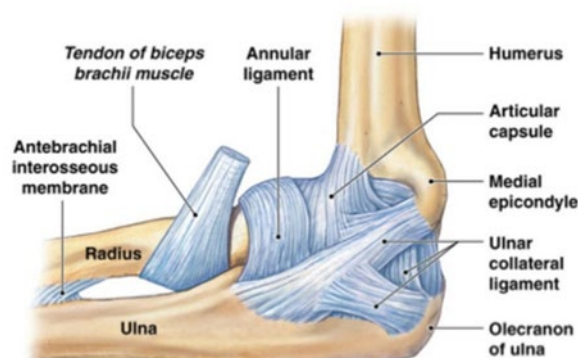


Fig. 1 Elbow joint structure

Current smart orthoses are based on a set of sensors that can monitor the position of the upper limb affected by an accident, regardless of its nature, and have the role of helping in good pre and postoperative recovery [4].

2. MATERIAL AND METHOD

The basic idea of this work is to create an intelligent device that could be used in monitoring and rehabilitating the elbow joint. The designed and realized system consists of an Atmega328 microcontroller located on the Arduino Nano development platform connected to a

series of input and output elements according to figure. 2.

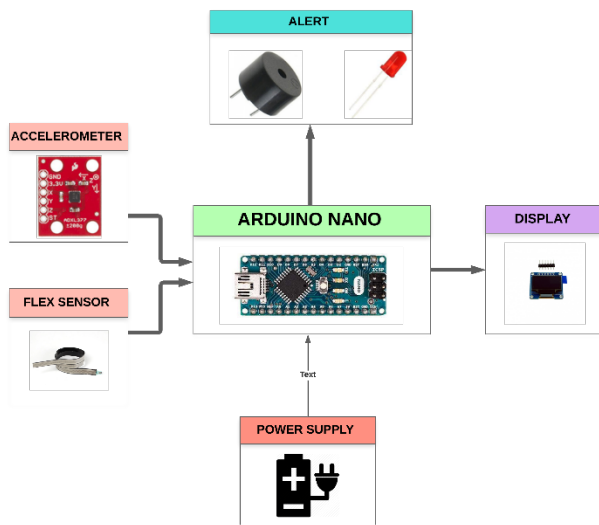


Fig. 2 Block diagram of the device

The main components of the orthosis are represented by bending sensor, accelerometer, display, and on the warning side we opted for a buzzer and an LED, all managed through the microcontroller platform, mentioned above [5].

The main sensor is of the flex type which changes its resistance in proportion to the degree of bending. The sensor can be bent at about 90 degrees in both directions, and the value read on an analog port varies between 0 and 1023, corresponding to the degree of bending [6]. A 10 K Ω resistor is mounted on the GND pin of the sensor coupled in the resistor divider configuration together with the sensor. (Fig.3).

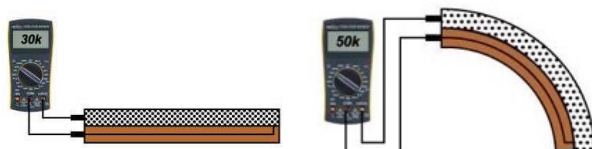


Fig. 3 Principle of operation of the bending sensor

Accelerometer is used can detect hand movements, relative to the 3 axes. The mobility of the 3 axes is determined according to the position it will take at the time of calibration, allowing the measurement of inclination changes of less than 1 degree. It works at a supply voltage between 2.8 and 3.3V (Fig.4).

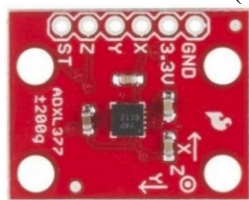


Fig. 4 Accelerometer ADXL 377

For the warning, the patient opted for both visual and acoustic elements. A passive piezoelectric buzzer was used, so that when the patient has a recorded deficient hand position, he corrects it through the alert [7]. Visual signals were generated by the attached LEDs, one red to warn of the incorrect position and another blue to highlight the correct position.

3. RESULTS AND DISCUSSIONS

Rehabilitation following elbow injury or elbow surgery follows a sequential and progressive multiphased approach. The phases of the rehabilitation program should overlap to ensure proper progression. The ultimate goal of elbow rehabilitation is to return the patient to his or her previous functional level as quickly and safely as possible [8].

The first phase of elbow rehabilitation is the immediate motion phase. The goals of this phase are to minimize the effects of immobilization, reestablish nonpainful range of motion (ROM), decrease pain and inflammation, and retard muscular atrophy.

Following the attachment of the device to the orthosis and the tests performed, a series of values were obtained that correspond to the degree of mobility (physiological) depending on the movements that the subject frequently performs: extension, hyperextension, flexion, pronation, supination [9]. The calibration of the device was performed after recording the values returned by the bending sensor by a correlation between the minimum value and the maximum value achieved following a flexion and a complete extension completed by pressing the push-button.

Depending on the calibration of the bending sensor, a normal position of the orthosis and two required situations were established. Thus, the orthosis, whether fixed or dynamic (mobile), is very common in people who have suffered a fracture, surgery or in the case of diseases that require complete immobilization, and the injured limb must be properly fixed, more precisely, there is no flexion / extension angle [10].

The early phases of rehabilitation also focus on voluntary activation of muscle and retarding muscular atrophy. Subpainful and submaximal isometrics are performed initially for the elbow flexor and extensor, as well as the wrist flexor, extensor, pronator, and supinator muscle groups [11].

The positioning of the orthosis will be done together with the specialist doctor or in the presence of a physiokinethotherapist, following the detailed clinical examination, so that the calibration of the bending sensor and the accelerometer can be performed correctly.

Following the attachment to the orthosis of the method performed and the tests performed, a series of values were obtained that correspond to the degree of mobility (physiological) but also a set of 2 applicability of the orthosis depending on the required needs.

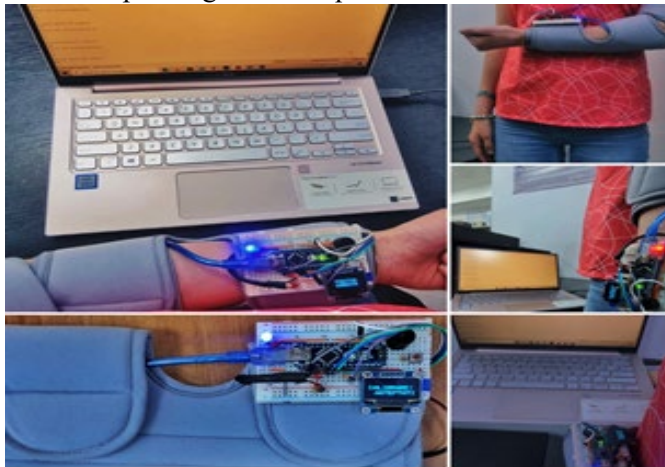


Fig. 6 Testing Application 1

Application 1 - If the person requires a permanent immobilization, the elbow joint will form an angle of 180° together with the arm and forearm, and the value obtained and displayed on the serial is less than 640. The warning is made if this value is outdated, followed by related messages. (Fig.6)

Application 2 - When the subject in question performs an arm movement of less than 90° , the equivalent value returned by the microcontroller sensor will be greater than 720 and will display "Correct Position" on the screen, thus facilitating a more efficient recovery.

Otherwise, the message "Incorrect position" will appear after the calibration value, followed by an audible and visual warning by means of a red LED and a buzzer that emits a warning signal. (Fig.7)



Fig. 7 Testing Application 2

Accelerometer values	Application 1									
	Correct position					Incorrect position				
	X=22	X=15	X=18	X=22	X=25	X=22	X=24	X=23	X=22	X=27
	Y=17 0 Z=10 0 X=10 Y=15 0 Z=10 0	Y=16 5 Z=10 0 X=15 Y=15 3 Z=10 0	Y=15 5 Z=10 0 X=23 Y=14 9 Z=10 0	Y=14 9 Z=10 0 X=20 Y=14 5 Z=10 0	Y=17 0 Z=10 0 X=26 Y=17 0 Z=10 0	0 Y=17 Z=14 2 X=28 9 Y=40 Z=24 0	0 Y=15 Z=25 7 X=23 0 Y=30 Z=17 7	0 Y=22 Z=17 8 X=22 5 Y=32 Z=16 8	4 Y=18 Z=15 6 X=22 1 Y=19 Z=14 9	0 Y=25 Z=18 9 X=30 9 Y=17 Z=25 9
Flex sensor values	430	563	599	585	525	676	689	759	679	789
	487	536	423	467	588	726	625	715	856	812

Table 1. Values sensors application 1

Accelerometer values	Application 2									
	Correct position					Incorrect position				
	X=36	X=22	X=20	X=22	X=19	X=12	X=22	X=15	X=19	X=17
	4 Y=37 Z=35 0 X=19 3 Y=45 Z=36 5	0 Y=42 Z=32 0 X=22 4 Y=39 Z=34 9	0 Y=39 Z=37 1 X=19 5 Y=37 Z=36 9	5 Y=49 Z=35 0 X=22 5 Y=42 Z=32 0	5 Y=45 Z=36 5 X=19 5 Y=45 Z=36 7	7 Y=17 Z=0 0 X=15 Y=16 Z=0 0	8 Y=18 Z=0 0 X=16 Y=17 Z=0 0	8 Y=18 Z=0 0 X=15 Y=16 Z=0 0	8 Y=18 Z=0 0 X=17 Y=17 Z=0 0	0 Y=17 Z=0 0 X=17 Y=17 Z=0 0
Flex sensor values	674	694	705	539	588	787	895	834	815	845
	694	562	652	698	625	914	865	862	756	832

Table 2. Values sensors application 2

4.CONCLUSIONS

The preliminary results of the device meet the required requirements so that by using the orthosis and permanent monitoring can improve the degree of mobility of the patient depending on the movements he wants to perform with minimal discomfort. It is a discreet, portable device that can be used at the patient's home, office or walk. The device is light and does not limit daily activities.

In the future we will try to improve the elements used (a more precise bending sensor, a correlation between two accelerometers to highlight the degree of mobility, one at the elbow joint and the second at the wrist) to monitor even the slightest imbalance in this region through pronation and supination. The aim is to miniaturize the assembly by making a wiring harness containing all the components in an ergonomic housing and mounting a vibration motor for warning.

In order to be able to highlight the degree of mobility and precision of the orthosis, a few 4 subjects were introduced who had in the past certain difficulties of mobility of the upper limb. These difficulties are due to injuries during physical activities or during daily activities. Together with a physiotherapist, depending on the degree of impairment and the two applicability of the orthosis, the patient's recovery program and the functioning of the orthosis were established.

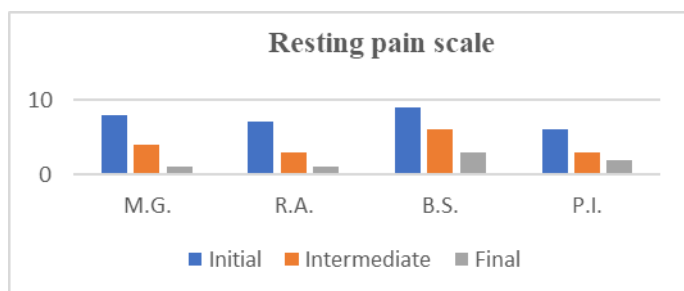


Fig. 8 Resting pain scale

Following the application of the proposed physiotherapy program combined with the use of smart orthosis, we found that many of the initial objectives were successfully met in a much shorter time. To highlight the evolution of patients, initial, intermediate and final evaluations were performed using one of the most common evaluation scales - the visual analog scale or the pain scale.

As we can see from Fig 8 and Fig 9, after the initial evaluation at exercise the patients presented a pain with values between 8 and 10 (10 being the maximum pain) and at the end of the recovery program, the pain decreased, reaching values between 2 and 4.

Now, regarding the pain at rest, at the initial evaluation the patients presented a pain between 6 and 9, and at the final evaluation the values came to be between 1 and 3. We can thus observe a significant decrease in pain, both in effort and at rest, this being the first goal of our recovery.

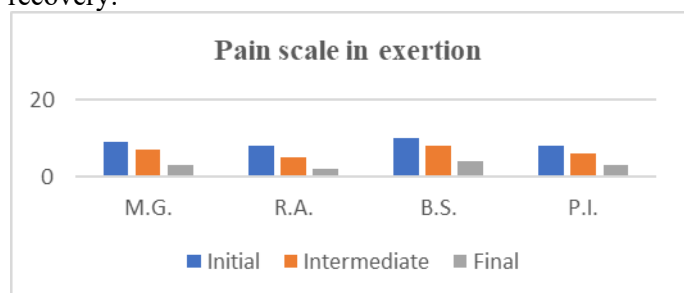


Fig. 9 Pain scale in exertion

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Study on cardio-respiratory adaptive mechanisms for performance athletes with physical disabilities

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Abstract

Introduction. Recently, the emphasis has been on the problems faced by performance athletes with physical deficiencies of the spine. **The aim** of the paper is to train coaches in awareness of physical problems, especially of the spine in swimming athletes aged 10-12 years and the development of kinetic programs on land in order to correct them.

Material and method. Research on the effectiveness of kinetic programs as means of correction are very numerous and, in this regard, we aim to select the most effective exercises to correct deficiencies acquired by swimmers and change the functional parameters of the cardio-respiratory system during their training. In order to highlight the need for kinetic correction programs, the coach must work in collaboration with the sports doctor and the physiotherapist in order to prevent possible deviations from normal somatic-functional values.

Results and discussions. Regarding the estimation of the adaptive possibilities of the cardio-respiratory capacity, hence the need to apply a complex of tests to assess the effort capacity of athletes.

Conclusions. In this sense, we will submit to the study the performance group from the University Sports Club from Suceava, and the recovery programs will take place within the Swimming and Kinesiology Complex, Suceava.

Keywords: *adaptive mechanisms, performance swimmers, functional physical deficiencies, kinetic means,*

INTRODUCTION

This paper aims to address the issue of mechanisms for adapting cardio-respiratory functions to performance athletes who may have vicious postures or even functional physical deficiencies. For swimmers in the prepubertal period from a somatic-functional point of view, compared to the effectiveness of training programs that depend on the knowledge of the coach, requires a correlation between children's abilities and proposed objectives.

In this sense, when designing a training program must be based on an assessment of the somatic-functional abilities that the athlete has.

The problem is to detect in time the possible deviations from the morph-functional status, and then through an estimate based on the results obtained at the initial evaluation we will be able to coordinate the training program in order to obtain the desired performance.

In the literature, body posture is a function of the human body based on the synergistic and coordinated action of the elements of the musculoskeletal system and the central and peripheral nervous system to maintain, body stability, balance and constant relationships between body segments, between body and environment [1].

It is known that about 99% of total calcium is found in the skeleton and 1% in extravascular fluid and plasma. Low calcium intake can be the cause of rickets in

children, which will later cause changes in the physical development of adolescents and adults. That is why it is considered important to know the normal reference intervals for calcium, depending on age, sex, physical activity [2].

In addition to calcium, magnesium is also important in muscle contraction, insulin metabolism, heart excitability and in influencing vasomotor tone.

Magnesium is an important nutrient for the body, as it is the fourth mineral with a role in preventing and treating some pathologies. Approximately 30-40% of the total quantity of magnesium in the human body is found in muscles and soft tissues, 1% in the skeleton, a small quantity in the plasma and approximately 60% in the bones. Along with calcium, sodium and potassium ions, magnesium ions regulate the mechanism of blood clotting and neuromuscular excitability. On the other hand, magnesium is involved in energy metabolism, in the synthesis of protein, of the deoxyribonucleic acid and of the ribonucleic acid, in the glucose homeostasis and in the mineral metabolism.

The decrease in the amount of magnesium in the blood can cause the disruption of the activities of some enzymes and the development of certain metabolisms. The consequences are irritability, nervousness, lack of concentration, changes in the heart rate and and in the

normal activity of the heart, and also the possibility of high blood pressure. The poor nutrition and the lack of an adequate intake of calcium and magnesium influenced the capacity for muscle contraction, strength and the ability for muscle coordination [3].

One of the essential trace elements is iron that is found in the human body in a quantity of 3-4 g. Most of this amount is found in hemoglobin whose role is to transport oxygen and carbon dioxide between the lungs and tissues, but also to regulate blood pH.

For biological systems that use iron in metabolic processes, the balance between the two oxidation states is very important. (Fe^{2+} and Fe^{3+}) [4]. In the onset of postural deficits, there occur, in addition to heredity, the environmental factors, the endocrine activity and the hormone secretion, the biomechanical factors or the metabolic ones [5].

Regarding the performance swimmer, at the prepubertal age there are various causes (overload of the osteo-myo-arthro-kinetic apparatus through various mechanisms) that can determine in time, the installation of postural deficiencies of the spine, with implications on cardio-respiratory function.

At the same time, the causes that can be incriminated can be of an endocrine-metabolic nature, by the fact that the organism can have a vulnerable genetic baggage prone to the installation of these deficits.

If the aquatic environment normally influences the human body by the following aspects:

- The horizontal position of the body, which ensures the relaxation of the muscles and frees the spine from body weight;
- Water pressure on the chest determines the development of cardio-respiratory function muscles, morph-functional adaptive processes, thermoregulation of lung capacities, joint mobility, psycho-motor adaptive processes, improvement of motor and psycho-motor schemes stored in memory, especially during raising and developing children [6].

It is known from the literature that the frequency of breathing is related to the swimming technique and can have values between 30-40 resp. / min.

In this sense, we can specify that swimming influences the increase of the thoracic perimeter, of the vital capacity, of the respiratory flow and of the maximum oxygen consumption, but most of the times the means used improperly during the trainings can lead to the installation. Certain physical deficiencies of the spine [7]. For sports people, physical effort is supported by nutrient intake. Carbohydrates are considered a fuel for exercises that take place with intensity ranging from medium to high. Reducing the amount of carbohydrates below 40% can lead to decreased glycogen stores and the occurrence of fatigue or exhaustion. We must not forget fats, considered a source of energy and the consumption of

which depends on the type of exercise and its intensity.

It is important to consider protein intake that is useful for strength and endurance, especially if the glycogen reserve has decreased. The need for proteins depends on the type of physical activity, its intensity and the body mass index. Water is another important nutrient in physical activity. If 1% of the body weight is lost, the consequence may be a decrease in the effort capacity [8].

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In this sense, we aimed to follow athletes who tend to have postural deficits and their influence on the performance of cardio-respiratory capacity during sports training.

2 The hypothesis of this study: it is assumed that by applying a work program developed based on evaluations of effort capacity, its effectiveness can be managed in order to achieve sports performance.

3 The aim of our study is to conduct on-ground exercise programs on the status of female athletes, members of the research group, focusing on meeting the objectives of the programs, especially aimed at improving cardio-respiratory capacity by correcting physical deficiencies at the time of evaluation.

Material and method

The research was carried out on a number of 15 swimming athletes aged between 10 and 12 years (3 athletes diagnosed with thoracic-lumbar C scoliosis, 3 athletes with kyphosis, 2 athletes with kyphotic attitude and 7 athletes with a normal spine) for a period of six months. The research took place at the Swimming and Kinesiology Complex in Suceava between: January 1, 2021 - June 30, 2021 (Table 1):

- Stage I consisted in identifying the subjects to be studied and performing the initial evaluation of the functional parameters;
- The second stage consisted in the application of the actual program elaborated based on the performed evaluations;
- Stage III consisted of the final evaluation, analysis and interpretation of the data obtained in order to draw conclusions regarding the study.

Results and discussion

Table 2 Heart rate

Statistical indicators	Normal Heart Rate			Effort Heart Rate			Heart Rate after 5 minutes		
	IT	TF	D	IT	TF	D	IT	TF	D
X	69.40	68.07	1.33	135.60	128.93	6.67	73.13	68.60	4.53
σ	3.30	2.93	1.25	6.41	2.64	4.08	3.70	3.03	2.28
CV%	4.76	4.31	93.54	4.72	2.05	61.16	5.06	4.42	50.22

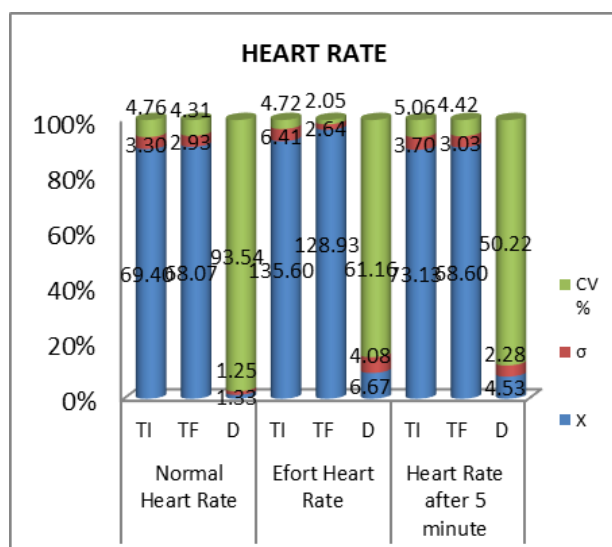


Figure 1 Heart Rate

Table 1 Presentation of the work program

Work program-model		
General objectives	Educating the complex neuromuscular and psychic reflex of correct postural attitude of athletes.	
	Toning the specific muscles to maintain the correct postural attitude of the athletes.	
	Ensuring the formation of self-control in static and dynamic activities.	
	Awareness of a correct postural attitude at all times in all static and dynamic activities of athletes.	
Normal postural attitude	Objective	Specific development of the back muscles, thoracic muscles, diaphragm muscles, abdominal and sacro-lumbar muscles, arm, thigh and leg muscles.
	Content - prevention	Static and dynamic exercises to maintain / increase proprioceptive abilities and correct body posture.
Kyphotic attitude -	Objective	Development of the back muscles by toning in shortening conditions. Development of trunk muscles by toning in shortening conditions. Development of the muscles of the anterior part of the thorax by toning in conditions of elongation.
	Content	Exercises for training and educating the correct postural attitude of the body in orthostatic position, lying down, with objects (sticks, elastic bands, balls, weights)
Total kyphosis	Objective	Toning the back muscles in conditions of shortening through exercises performed concentrically and inside the contraction segment. Toning of the anterior muscles of the thorax and abdomen through exercises performed eccentrically and outside the contraction segment. Correction of secondary deficiencies.
	Content	Static exercises in supine position, orthostatism and hanging Dynamic exercises with objects and devices
Thoracic - lumbar "C" scoliosis (left)	Objective	Differentiated toning of the posterior muscles Toning in conditions of shortening the muscle groups from the convexity by concentric movements and inside the contraction segment. Toning in conditions of elongation of muscle groups from the concavity of the curve and outside the contraction segment. Straightening the pelvis and balancing the scapular girdle Creating a reflex of correct postural attitude.
	Content	Static exercises: From fundamental positions and their derivatives with asymmetric structure Exercises by asymmetrical arrangement of the limbs, torso and lower limbs Dynamic exercises: Upper limb exercises Trunk exercises Lower limb exercises Breathing exercises Applied exercises Postural reeducation exercises.

A difference of 1.33 b / min can be seen from table no. 1 in the normal heart rate test.(Table 2) In the heart rate effort test a difference of 6.67 b / min was obtained and in the heart rate test after 5 min the average difference between the initial and final testing is 4.53 b / min.(Figure 1)

The change in the heart rate is a component of the cardiovascular system's ability to adjust cardiac output according to the demands of the physical effort.

An increased heart rate will determine the increase in the amount of oxygen in the myocardium [9].

Table no. 3 Respiratory rate

Statistical indicators	Respiratory rate at rest			Respiratory rate in effort			Respiratory rate after 5 min post effort		
	IT	TF	D	IT	TF	D	IT	TF	D
X	21.07	20.47	0.60	33.27	29.27	4.00	22.33	20.87	1.47
σ	1.34	1.20	0.61	4.33	3.04	1.71	1.30	1.15	1.09
CV%	6.36	5.88	101.84	13.01	10.40	42.82	5.82	5.50	74.13

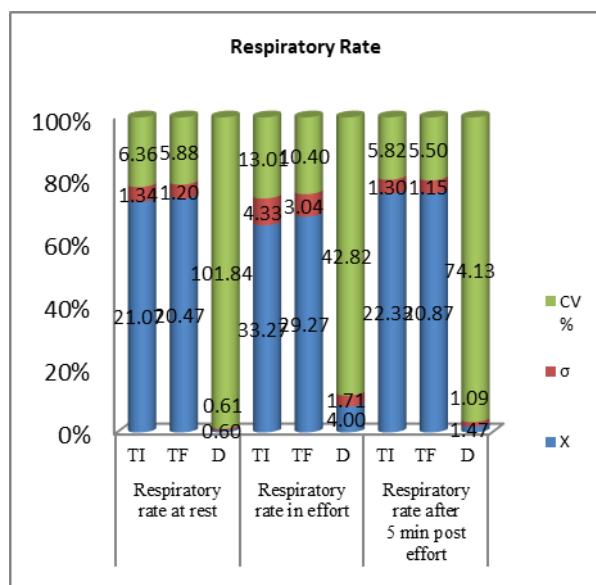


Figure 2 Respiratory Rate

In the table (Table 3) above we can specify that in the respiratory rate of rest test the difference of the average central tendency is 0.60 resp. / min.

In the respiratory rate of effort test the average difference is 4 resp. / min, and in the respiratory rate test after 5 min post effort the average difference between the initial and final testing is 1.47 resp. / min. (Figure 2).

The reference intervals for the respiratory and heart rate are in accordance with the existing derived diagrams that depend on the age [10].

The increase in the heart rate variability is considered a marker of parasympathetic activity and relaxation [11].

Table no.4 Swimming-specific tests

Statistical indicators	Prone floating			Mushroom float			Front sliding with crawl legs		
	IT	TF	D	IT	TF	D	IT	TF	D
X	18.27	23.53	5.27	18.67	21.20	2.53	11.53	15.40	3.87
σ	2.26	2.94	1.44	4.22	4.12	1.15	0.88	1.36	1.26
CV%	12.40	12.50	27.27	22.62	19.43	45.28	7.67	8.81	32.53

Regarding the specific swimming tests, an average difference of 5.27 sec is observed in the prone floating test, in the mushroom float test the average difference is 2.53 sec. (Table 3) And in the front sliding with crawl legs test, a difference of 3.87 m is observed. (Figure 3) Not all statistical indicators have been calculated in this study, due to the small group of subjects. In the performance group under study, we found different cases of postural attitudes and deficits of the spine. The study will be extended over a longer period of time and we will continue the research in order to obtain conclusive results.

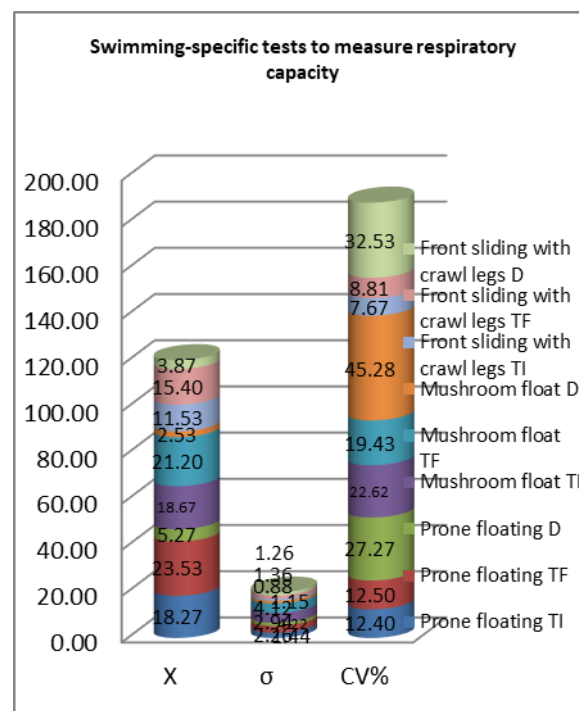


Figure 3 Swimming-specific tests

Conclusions

- Recent studies show that the prepubertal period is a stage of growth and development that requires special attention from parents and coaches;
- The study showed that even in performance sports vicious postural attitudes and even the installation of physical deficiencies of the spine can be acquired;
- The difference in group mean results is significant in all tests proposed in the study;
- Swimming athletes obtained positive results in terms of performance, due to the ability to adapt to cardio-respiratory processes achieved due to the program;
- In the specific test of swimming "front sliding with crawl legs" the group average shows a difference of 3.87 m, which confirms that, the kinetic means on land help to increase sports performance.

Author contribution

All the authors had the same contribution

Accordance to ethics standards

The study complies with the rules of ethics and deontology according to the legislation in force

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The oral and gut microbiota: beyond a short communication

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Abstract

Introduction. The current treatment and prevention of oral disorders, dental caries, periodontal and gum diseases, follow a very non-specific control of plaque as the main causative factor. The main therapeutically approach is carried out on the sole perspective to keep the levels of oral bacteria in an acceptable range compatible with one-way vision of oral-mouth health, as something completely separated from a systemic microbial homeostasis (dysbiosis) concomitant present in the gut. A sealed compartmental view which sees separate and incommunicable responses to a specific condition without considering the presence of interacting confounding factors can negatively influence the diagnosis a diseases and of course its progression. A general non-specific antimicrobial with more general antiplaque therapy based mainly on oral care products together with surgery interventions represent at the moment the only mechanical responses in treating oral diseases.

Material and method. The present paper is a narrative review concening interactions between oral and gut microbiota, with a focus on the interdisciplinary approach in antimicrobial treatment. Pubmed, Cochrane Library database were used for searching engines. Key words used were as follows: “inflammatory bowel syndrome (IBS)”, “ulcerative colitis”, “oral dysbiosis”, “gut dysbiosis”, “probiotics”, “periodontitis”.

Results and discussions. Literature research showed that there are few issues to be discussed the ever increasing resistance to antibiotics, the high consumption of industrial food and sugars and their negatively effect on gut and oral microbiota. There is a need to highlight and develop a novel philosophical approach in the treatments for oral diseases that will necessarily involve non-conventional antimicrobial solutions. Such approaches should preferably reduce the consumption of both intestinal and oral microbiota, that are intimately connected and host approximately well over 1000 different species of bacteria at 10⁸–10⁹ bacteria per mL of mucous and saliva. Preventive approaches based upon the restoration of the microbial ecological balance, rather than elimination of the disease associated species, have been proposed.

Conclusions. Having both oral-gut microbiota screened is an essential moment that influence the healthy immune modulatory and regenerative capacity of the body and, the new proposed formula integrates a wider screen on the patients where oral condition is strictly evaluated together with gut screen; therefore any proposed treatment will be inevitably sustained by the use of prebiotics and probiotics to promote health-associated bacterial growth.

Keywords: *inflammatory bowel syndrome (IBS), ulcerative colitis, oral dysbiosis, gut dysbiosis, probiotics, periodontitis,*

INTRODUCTION

A new direction in oral health treatment the immune-metabolic approaches

Despite of all negative aspects regarding isolation and socio-physical restrictions, pandemic difficult period was a good opportunity for studying disease physiopathology, immunologic aspects, human organism's interactions, focusing on finding prevention strategies (1-5). The fact that there is a strict connection between gut microbiota, oral microbiota and metabolic functions the healthy state of human metabolism has become a prerogative in medical practice. Principles such as 'mind and body medicine' are more and more adopted, considering that there is strong literatur evidence that a large number of diseases are psychosomatic (6).

In first instance, the body metabolism depends on a symbiotic relation of the whole types of bacteria, archaea, viruses, fungi, and host eukaryotic cells that colonize human gastrointestinal tract (GI) and that is known under the name of gut microbiota (7, 8). Moreover, upper part of GI tract communicates to respiratory system, contributing to bacterial variety and pathogenesis (9). The presence of these variegate forms of microorganism is vital for the life and evolution of human species, the main activity is to obtain from food essential nutrients compound for the production of great variety of bio-molecules, amino acids, hormones, vitamins and short-chain fatty acids (SCFAs). In addition supervise and control as perfect metabolic engines the whole system homeostasis from gut up to the brain through the regulation of connected other activities within cells, tissues and organs such as glycolysis, acid/Krebs cycle regulation and oxidative phosphorylation (10). Recent studies have been elucidating how gut microbiota eventually affect the oral microbiota. The mechanism start with the quality of ingested food that in turns affect microbiota that exert a direct or indirect stimulatory effect on immune cells, in particular, T cells, B cells, Dendritic (DCs) and macrophages (11-16).

Oral and gut dysbiosis are indicators of poor systemic health conditions such as the metabolic syndrome and other systemic chronic degenerative diseases (17). The gut and oral cave have a strict and very unique relation with the metabolic syndrome that eventually conduct led to the insurgence of chronic degenerative metabolic condition such as type-2 diabetes, hypercholesterolemia, kidney decay, liver steatosis, cardiovascular break-down and neurodegenerative diseases (18, 19). Both gut and oral pathogens have the ability of migrate and locate well away from their original location due to chronic inflamed "leaky mucosa" they can pass through and via local oral and mesenteric blood circulation can enter into the systemic circulation (19, 20) (Fig. 1).

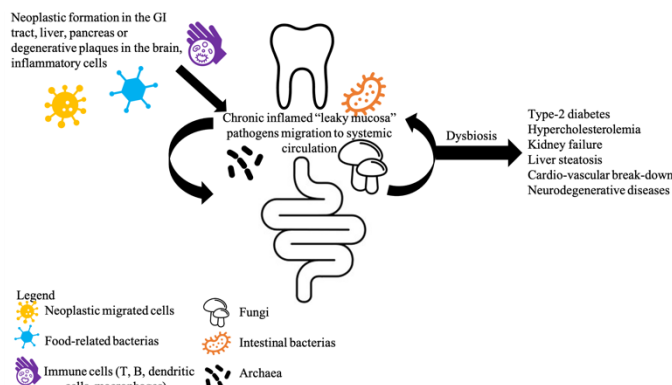


Fig. 1. Negative influence of oral cavity-gut dysbiosis on metabolic and inflammatory diseases onset and progression.

Macrophages are seen to migrate in chronic condition, the experimental outcomes showed their presence from oral location towards lungs (contributing to the respiratory impairment inflammatory profile), heart or even to brain scattering detrimental inflammatory responses that led to chronic tissue inflammation, infection and death (21, 22). Macrophage mobility is the result of their specific trait and high heterogeneity both in normal and in pathological conditions, and they can also lead to impaired metabolic profile (23). The macrophages are able to execute two main immune functions under local and systemic condition, they polarize into M1 the proinflammatory phenotype triggered by signal from LPS and Th1 proinflammatory cytokines and interleukins such as TNF- α , IFN- γ and IL-1 β , IL-2, IL-4, IL-6 and IL-17 whereas immune-modulatory M2 phenotype triggered by Th2 cytokines IL-4, IL-5 and IL-13 as well as anti-inflammatory cytokines and interleukins like IL-10 and TGF β , glucocorticoid and steroid hormones such as DHEA and estrogen (24-26).

The negative chronic activity scattered by an over expression of M1 phenotype is basically explained by the fact that dysbiosis is characterized by the presence of pathogens that use glucose as main source of energy subverting the activity of intracellular chemical mediators including the ATP together with an uncontrolled growth of reactive oxygen species (ROS) (24-26). However, this scenario suggests that once oral pathogens have crossed the mucosa barrier the body is already facing a systemic outbreak. The evidences are confirmed by the high presence of inflammatory and infection patterns caused by either pathogenic attack or high presence of inflammatory mediators which eventually results in a disease (27). Recently, last epidemiological studies showed that upper respiratory airways are sensitized by the presence of certain viruses, making tissue susceptible to infection (28, 29). Furthermore, many are the lines of evidence that have strongly confirmed the cross-talk

existent between oral and gut dysbiosis and the consequent insurgence of neoplastic formation in the GI tract, liver, pancreas or degenerative plaques in the brain (30). The histo-pathology outcomes provided the unconfutable proof oral/gut pathogens in the affected organ and surrounding tissues (27-30) (Fig. 2).

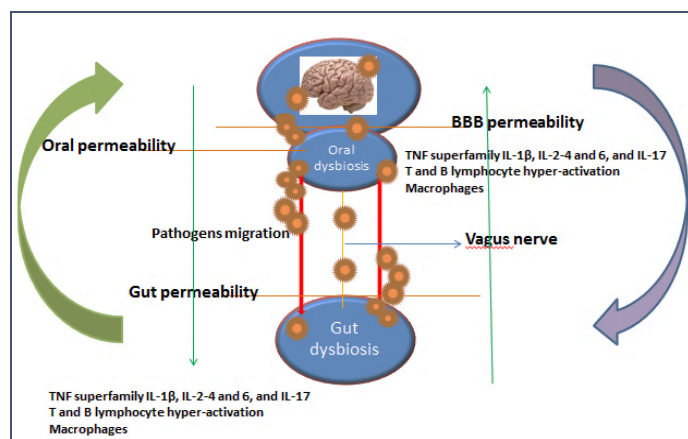


Fig. 2. The strict connection between CNS and Gut-Oral microbiota. This connection has physical connection through the afferent and efferent pathways of *Vagus* nerve CNS and Gut. Under microbiota dysbiosis CNS, Gut and Oral barrier become “leaky” or highly permeable allowing both pathogens and immune agents cross through scattering inflammations, infections and thus degenerations. Event that explains degenerative patterns and including IBS, ulcerative colitis, depression, Parkinson’s disease, Alzheimer’s disease and Multiple sclerosis.

As for the interactions with other humans’ body organs and biofluids, dysbiosis is aggravated by the presence of illicit substances (such as nicotine, cannabinoids) and dysregulation of parasympathetic and sympathetic nervous systems (31-34).

Material and Method

The present paper is a narrative review concening interactions between oral and gut microbiota, with a focus on the interdisciplinary approach in antimicrobial treatment. Pubmed, Cochrane Library database were used for searching engines. Key words used were as follows: “inflammatory bowel syndrome (IBS)”, “ulcerative colitis”, “oral dysbiosis”, “gut dysbiosis”, “probiotics”, “periodontitis”. Literature research resulted in 62 number of papers concerning the main subject.

Results

Regarding clinical manifestation from oral dysbiosis pathogens, here are always shared patterns found in these types of scenario, clinical and non-clinical symptoms usually start in patients mostly in their 40’ and 50’s with metabolic unspecific complaints, fatigue, food intolerance, fatigue, skin problems, oral mouth condition, aching joint and cognitive impairments. Dysbiosis also manifest in all cervicofacial structures, leading to

acute/chronical soft tissue inflammatory diseases (temporo-mandibular joint dysfunction, oral mucosa frailty, decreased turnover potential), impaired bone regeneration (which also affects subsequent treatment) and more important dental tissue microbial contamination (35-39). Also, modulated immune response could influence the microbial differentiation capacity and bactericidal effect (40, 41).

It must be highlight that the ageing process *per se* is contradistinguished by a progressive regression of beneficial commensal microbes that let over-growth the pathogenic commensal level thereby generating dysbiosis. A second common trait of these conditions is the presence of a chronic inflammatory state which negatively affects the regenerative mechanism impairing the apoptosis mechanism of normal somatic senescent cells, thereby enabling tumor and degenerative patterns development (27-30). Although no conclusive evidence have explicitly demonstrated the hypothesis between metabolic syndrome patients and brain degenerative patterns is driven by oral dysbiosis as cause of blood-brain barrier (BBB) dysfunction, the direct involvement of activated macrophages that crossed the BBB initiating local inflammatory responses has been under investigation and has given interesting clinical results. The idea is that collapsed BBB may follow a similar pattern found in impaired gut and oral mucosa barriers. The chronic inflammatory systemic condition of metabolic syndrome patients facilitates metabolic endotoxemia by increasing the permeability and therefore the uncontrolled passage of bacteria, immune cells such as macrophages and gut-oral derived endotoxins such LPS that in turns stimulate the activity of local microglia (42-49).

Discussion

Do probiotics will serve as therapeutic useful tools or they may just remain a myth? Despite existing controversial position on the topic, many lines of evidence and clinical studies have confirmed the validity of probiotics in the management of many condition either in gut dysbiosis such as IBS or oral dysbiosis such as periodontitis, there is a large increasing scientific support in using probiotic as therapeutic. Interventional studies have shown that the association of probiotics improves metabolisms’ biochemical parameters, increase the level of benefic bacterias (lactobacilli and bifidobacterias), the level of immunoglobulines implicated in membrane defence (such as IgA) and Il-10 (with an anti-inflammatory effect) (48-50).

On the other side, oral cavity health is an important key factor not only for dental tissue development and function, prosthetic durability and mechanical properties, but also in bacterial spreading and multiplication (51-54). All the intervention performed on oral cavity’s tissues, having thr purpose of improving oral status –

from dental hygiene training, mechanical plaque removal, use of additional antibacterial substances, up to etiological dental and periodontal initial therapy have as a first result the reduction of microbial load, but also the disruption of multiplication and needed nutrients and of course the degree of tissue oxygenation, an important factor in bacterial endurance (55-57). One of the most effective technology is laser therapy, which through its intensity, improves cellular adhesion (fibronectin, mesenchymal stem cells, collagen fibers), neovascularisation, infected wound healing and microbial count (58, 59). Red and near-infrared (NIR) lights improve tissue healing by downregulation of proinflammatory cytokines and increased angiogenesis (60). All the up-described mechanism reflect on gastrointestinal tract, through direct flow due to pharynx and esophagus, and by means of vascular and lymphatic system. Previous studies have already proved there is a clear interconnection between oral and general pathology. More advance molecular diagnostic methodology has allowed investigating the systemic interferences and connections of the oral dysbiosis in human disease (61, 62). One of the presents' impediment is the lack of interdisciplinary examination in GI chronic diseases, and the exiguous in consensus regarding treatment protocols targeting the same class of bacterias but with different location. Another hindrance is that usually medical practitioners interact with the patients in the acute phases of oral cavity and gut pathologies, and the focus is on eradicating the acute symptoms and control the disease. Moreover, the fact that microbes and toxins outreach several barriers and produce distance-related lesion is not taken into consideration. Majority of the treatment don't benefit of an initial microbiological examination, neither an inflammatory profile. This type of approach could enhance a treatment strategy based on early diagnosis and multiorgan-target, which will ultimately result in a controlled and improved oral and general health status.

Conclusion

The interaction of metabolic disturbances in oral microorganisms will surely help to understand the aggressive mechanism that from oral dysbiotic environment invade other organs or system. Studies in oral complex microbiota certainly will open up the possibility of better diagnosing and therefore treating chronic inflammatory degenerative diseases interconnected with oral pathogens.

Conflicts of interest

The authors declare no conflicts of interest.

Author contributions.

Berate Pula and Candrea Sebastian contributed equally as first co-author of this paper. Sirbu Adina and Cardarelli Fillippo contributed equally as last co-author of this paper.

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The oral and gut microbiota: beyond a short communication

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Abstract

Introduction. Currently, the crises triggered by the pandemic, in the fields of health, freedom of movement, economic, with impact in the social and cultural spheres, bring back today the practical applicability of the concepts of fitness and wellness.

Material and method. In our study we will refer to the effects of the pandemic on health (everyone's well-being), to see how they accentuated the negative effects of the risks that specialists linked to sedentary lifestyle; increased stress; static anti-physiological positions for prolonged periods of time, which result in cardiovascular disease, metabolic syndrome and even cancer, to which is added an irrational diet. We will also refer to the relationship between the quality of life of people and the need to find the most effective ways to combat the negative effects of risk factors, by overcoming the obstacles posed by the financial situation and cultural patterns both in terms of lifestyle, as well as the eating behavior of people from different backgrounds.

Results and discussions. We are of the opinion that specialists must go in their approaches, from the cultural understanding of man, to find ways to individualize the means of intervention so as to achieve the proposed objectives. The framework could be, for children and adolescents - the reorganization of school physical education, and for young people and adults - leisure activities, in which the emphasis could be falls on the concepts of Fitness and Wellness, with a beneficial effect on quality of life and personal satisfaction.

Conclusion In this context, we believe that it is necessary to reconsider the need to make the population aware of the formation of a healthy lifestyle. The means could be physical fitness, wellness, rational nutrition and recovery according to the effort made, their benefits can have a major impact on health and prolong life expectancy.

Keywords: *Fitness, Wellness, Health, Physical education, cultural perspectives,*

INTRODUCTION

Currently, much is discussed about personal well-being, either as a physical condition (or fitness) or as wellness, but in the conditions of the coronavirus pandemic it has been experienced that this type of good cannot be approached by man - social being, than in direct relation and interdependence with the public good. After World War II, scientific discoveries and the progress of medicine had created the possibility of controlling infectious diseases. (1), so that most specialists focused on the non-communicable diseases, determined by the lifestyle of modern societies, that they will be responsible for 70% of deaths worldwide by 2020, according to the WHO (2) estimate. A sedentary lifestyle has developed what specialists call *Sedentary Death Syndrome* (SeDS), which involves a clinical framework of disorders in the body, determined by several factors, which increase mortality (3). It was also determined the need to address - the problem of health as a whole - body, mind and soul (4).

In fact, prior to this period to which we refer, in this study, specialists addressed the issue of quality of life defined, in general, as well-being, both related to the human person and society, manifested by: increasing fitness physical, emotional stability, spiritual maturity,

financial and social security, etc. (5). Both Fitness and Wellness are linked by their meanings, to the concept of health, each of which involves choices for a healthy lifestyle.

Following the evolution of what WHO specialists defined as the Covid pandemic, we find a very high rate of diseases with severe forms, which led in very large proportions - up to 90% to death in some areas, with a prevalence of comorbidities: obesity, diabetes (6) and cardiovascular diseases (7), in increasing the negative effects of those who developed acute respiratory syndrome - SARS-CoV - 2. (8).

In this context, a number of authors resume the discussion on the prevention of diseases that threaten the life of contemporary man, due to the way of life, the specifics of the professions, which have been shown to often involve activities qualified to be sedentary (office work e.g.), as well as the habit of preferring convenience over physical exertion - and we are talking about the modernization of means of travel for example. Prevention, maintenance and / or recovery of optimal health can be achieved in rich Western countries by choosing methods to obtain and maintain fitness / fitness, through an adequate diet, relaxation / meditation,

intellectual activities / learning carried out in friendly environments both in nature / outdoors (outdoor) and in social, which is also related to the concept of leisure that we talked about on other occasions (9).

Material and method.

During the development of our study, we tried to better understand the meanings of the concepts of fitness, wellness and lifestyle, in a broader context, which included other concepts including health. Insisting on the problem of health, we can not only talk about disease prevention but also about the recovery of health, in conditions of diseases and maintaining optimal health. In principle, more and more specialists turn to the holistic perspective, understanding that in fact the physical and spiritual complexity of the human being, makes necessary complex, interdisciplinary approaches. In order to correctly understand these approaches, we believe it is necessary to understand the meanings of the concepts we operate with, and this was the objective of this study.

Concepts and paradigms are sometimes marked by visions such as holistic, relational (10) and positive about the world, ideologies in the social environment, as well as philosophical currents, so we can talk about the existentialist perspective (11) and multidisciplinary (12; 13). If in the beginning health was defined as actually the absence of the disease, now specialists talk about the clear difference between health and disease, showing that someone can be clinically healthy but not well (14), which leads to in fact, an older idea, which belonged to Jerry Lafferty (15), had spoken of a five-element model of the concept of wellness: physical, social, mental, emotional, spiritual, and shared by other specialists (16; 17). Jerrold S. Greenberg (14) adds the idea of mental health to intellectual wellness. To these dimensions will be added, in time, the occupational one, to which (18)

The father of the modern wellness movement is considered to be Halbert Louis Dunn (19, 20, 21), who defined wellness as a balance between individual physical health and the external environment, taking to another level the ideas of Donald B. Ardell (22, 23), which spoke of the health determined by the harmony between body, mind and soul.

Later, Royda Crosse, Donald R. Nicholas, David C. Gobble and Beth Frank (24) will establish the current model of wellness, including as variables: culture (education, training na) age and sex, thus proposing a new dimension - wellness vocational. The latter will be added to the other five dimensions of the concept of wellness: physical, spiritual, emotional, social and intellectual, the concept of personal wellness. These ideas were not really new either, for let us not forget that Bill Hettler (25) spoke a few decades earlier of the six

dimensions of wellness: physical, emotional, spiritual, intellectual, social and occupational.

As a result, the concept of health can be understood from a multidimensional perspective, being a dynamic state, in a continuous evolution, which can be controlled by man, so as to avoid diseases (26), the ideal being the healthy and proactive adult, able, through knowledge and understanding of benefits, to choose a healthy lifestyle (27). Most authors will associate wellness with quality of life, in which the emphasis is on the factors that condition the lifestyle, being added a new dimension - environmental: environmental wellness (28). From this perspective, specialists find a close and interdependent relationship of the concept of wellness with the determinants of quality of life in a positive sense: physical activity determined by physical condition and physical fitness (29).

In postmodern society, health risks are increasing, the alarm has been sounded for two decades by the World Health Organization, which includes: irrational, often deficient diet, iron deficiencies, contaminated water, inadequate health measures. personal hygiene, and polluted air. All this is found in underdeveloped areas, marked by poverty and all its effects and have led to what experts call the epidemic of Noncommunicable Diseases, given that it causes about 71% of deaths worldwide (30). But at the same time, in societies that promote the consumer economy, the risks that lead to disease are also food, this time irrational (31), in excessive amounts or with excess fat, salt and sugar, sedentary lifestyle, stress and alcohol, tobacco or drug use. The reduction of risks that cause lifestyle diseases associated with workplace stress, such as cardiovascular disease, metabolic syndrome, diabetes, cancer, has concerned a large number of authors, including Briand Luke Seaward (32, 1) and Christiane Jennen and Gerard Uhlenbuck, (33). The first author insists on the negative influence of stress in determining these diseases (34). In the same vein, specialists are increasingly focusing on a means of prevention, treatment and maintenance of health, available to all - a healthy lifestyle.

It is seen as an alternative for the prevention of noncommunicable diseases from the perspective of a relatively new branch - Lifestyle Medicine, introduced in a university environment at Loma Linda, California in 2004 and then at Harvard, in 2007, here appearing the Institute of Style Medicine of life. However, the global Lifestyle Medicine movement will begin with the establishment of a medical-scientific community, through the American College of Lifestyle Medicine, ALMA - the Australian Lifestyle Medicine Community and the European Society of Lifestyle Medicine (35). Moreover, the latest WHO data indicate that one in ten people suffer from a mental illness during their lifetime (36, 37), and the pandemic has worsened.

The idea was born and consolidated that lifestyle is fundamental in obtaining and maintaining an optimal state of health, this including a balanced diet, physical activity (physical condition / fitness) and an adequate recovery. It is integrated in the practice of modern medicine, as a complementary element to therapy, having the effect of reducing the action of risk factors on chronic diseases (35). There are many arguments and we will only mention here that a series of studies have shown that lifestyle can be, for example, the only comprehensive, non-pharmaceutical, effective treatment by reducing body weight, able to control metabolic problems of people suffering from DM2 (Diabetes), ie hyperglycemia, insulin resistance, dyslipoproteinemia and hypertension (38). Speaking of modified lifestyle, specialists refer to therapeutic education, nutrition, exercise and healthy habits (39).

Results and discussions

We find that there have been changes, over time, in health paradigms, specialists redefining this concept from an interrelational perspective (10) or holistic wellness (40). Until now, health was related to the body in which physiological systems were approached in isolation (41). Concern for body image has given rise to several movements and currents, which promote exercise as an important means that can influence both health and quality of life.

Also, regarding the concept of fitness, we notice semantic evolutions, as new models appear and are promoted, some even talking about the fitness style - related to lifestyle and methods to keep the body in excellent physical condition.

We also talked about the concept of fitness on other occasions, when we tried to determine its semantics (42), starting from the perspectives of authors such as: Carl Casperson, Kenneth Powell and Gregory M. Christenson (43), Charles Corbin and Ruth Lindsey (44), Claude Bouchard (45), to H. David Clarke and H. Harrison Clarke (46), who talk about a full and balanced life and Nastas H. Douglas, and Alan C. Lacy (47), which recall the two areas of physical fitness - the one that is correlated with health and the one that is related to abilities / skills (skill).

Physical fitness has been understood as a means of preventing illness, preserving and increasing professional capacity, optimizing the body's motor skills, well-being of the person, recreation / relaxation, self-realization, socialization, etc. The multiple meanings make it difficult to determine the exact ends, depending on different situations, health, value systems (good, beauty) and other criteria.

Scientifically, the Toronto Model was created (45), which is based on the idea that the basis for health are the components of physical fitness (Health Related Fitness),

physical activity being considered a *conditio sine qua non*. (48)

As for the concept of lifestyle, it is defined by the authors as a daily way of life, which helps man to improve the body's energy reserves and stay healthy, begins to undergo changes, involving evolutions towards new behavioral habits and as well as various preferences for what can be generally defined as appropriate physical activity.

Understanding the importance of lifestyle, some experts have tried to find the best ways to raise awareness of the benefits of a healthy lifestyle, as well as the most effective tools to determine health and wellness (28). These authors, starting from the request made to the University of Arizona by Canyon Ranch - a private commercial organization (49), for a program designed and implemented for its customers, speak of the theoretical model promoted by it - Total Personal Concept (TPC) , which made some people remember holistic medicine (50).

Ralph F. Renger and colleagues (28), starting from the complexity of the human being, argued that it should be viewed from every possible perspective (intellectual, emotional, social, spiritual and physical). At the same time, they defined wellness as the optimal state of well-being that an individual is able to achieve, given a set of circumstances. For them it is important first of all to know how to develop skills and abilities in specific areas of wellness, then the desire to improve their quality of life, and the recommendations were for people to take care of their physical appearance, to use in constructively the mind, to channel their energy positively, to express their emotions, to be creative in their realities with others, to be attentive to spiritual needs and to interact with their environment. (28)

The ideas are not really new, but the authors manage to synthesize the beliefs of the time in the field of Melvin J. Witmer and Thomas J. Sweeney (12) and will inspire the authors of the later period, including John W. Travis and Regina Sara Ryan (51), David J. Ansbaugh, Michael H. Hamrick, and Frank D. Rosato (52), Dianne Hales (53), Gordon Miller, and Leslie T. Foster (54). It is interesting to believe the holistic perspective of Dianne Hales (53), who speaking of wellness, defines it as the sum of the absence of negative elements (illness and disease) and the presence of positive elements (physical health and happiness).

An important role in these approaches undoubtedly belongs to physical activity, which has beneficial effects on physical condition and implicitly on the ability to perform this type of activity. (55), As for the optimal level of physical condition, it is reached when man can safely and efficiently perform daily tasks, as well as those that occur along the way, without reaching an energy deficit for the activities of leisure, recreational (56; 57)

Conclusion

Given all this, we believe that specialists (theorists in physical education and sports, doctors, sociologists, etc.) must go in their efforts, from the understanding of man from a cultural point of view (values, moral norms that are on the basis of conceptions, individual or group mentality), in order to find ways to individualize the means of intervention, so as to achieve the proposed objectives. The framework could be, for children and adolescents - the reorganization of the school physical education activity, with a greater number of hours for physical activity and an adapted program, and for young people and adults - leisure activities, in which the emphasis could be falls on the concepts of Fitness and Wellness, with a beneficial effect on quality of life and personal satisfaction.

In this context, we believe that it is necessary to reconsider the need to make the population aware of the formation of a healthy lifestyle, which involves giving up habits and choices that are risk factors and adopting protective factors, not only at the individual level but also at the social level. The means could be physical fitness, wellness, rational nutrition and recovery according to the effort, their benefits can have a major impact on health and prolong life expectancy. We believe that the conditions are favorable, as more and more young people and adults have become aware of the importance of exercising, restoring and adopting a balanced diet, in order to ensure and maintain optimal health and adequate muscle tone.

In addition, education can promote a healthy lifestyle, and such approaches have already emerged, and the imposition of the concepts of wellness and wellbeing, along with fitness and nutrition, when we talk about lifestyle are evidence of changes that occur in the paradigms of health, which is recognized as a value in modern society. And in time, probably, a healthy lifestyle will be able to offer a greater capacity to the human body to defend itself in the perspective of new, unwanted, but possible epidemiological challenges.

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Anti-inflammatory effects of exercise training. A systematic review

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Abstract

Introduction: The diseases number with a known inflammatory etiology is constantly increasing. Cardiovascular and neurodegenerative diseases, osteoporosis, cancer, asthma, atherosclerosis, type 2 diabetes and obesity are associated with chronic low-grade inflammation. There is evidence that individuals who engage in intense physical activity or who exercise regularly, shows changes in biomarkers associated with chronic inflammation. Physical exercise is useful in preventing many diseases, due to improved cardiorespiratory, metabolic, musculoskeletal function. All these improve the immunity and antioxidant capacity, thus reducing the incidence of acute and chronic inflammatory diseases.

Materials and Methods: In this study were included 90 bibliographic sources, of which the title contains the following keywords: exercise - 23, inflammation - 27, anti-inflammatory - 6, IL-6 - 13, IL-10 - 4, myokine - 3, IL-15 - 3, irisin - 6, obesity - 11, chronic inflammation - 7. This study discussed aspects of exercise, pro- and anti-inflammatory cytokines, immunological mechanisms, the dual role of IL-6 cytokine, and the anti-inflammatory effects of physical exercise.

Results: Physical exercise is an efficient clinical tool, that limits chronic inflammation activating the immune system that will increase the level of anti-inflammatory IL-6 myokine. There is a direct relationship between the volume and intensity of exercise and the amount of IL-6 myokine in the blood stream.

Conclusions: These studies contribute significantly to the understanding of the mechanisms of the anti-inflammatory effect of exercise. More studies on chronic low-grade inflammatory diseases are needed to understand their pathophysiology, and that will inspire the specialists improve long-term treatment strategies.

Keywords: *physical exercise, chronic low-grade inflammation, anti-inflammatory, IL-6, myokine,*

INTRODUCTION

An active lifestyle with regular physical activity and / or constant training exercise is an effective strategy for the prevention and treatment of many chronic diseases without medication. Current scientific evidence has established positive correlations between a active physically lifestyle and health benefits (1). According to the Physical Activity Guidelines for Americans, the benefits of physical activity are: reduce the risk of all-cause and mortality specific disease, improved physical function and improved quality of life for individuals with various chronic medical conditions; reduce risk of cancer; reduced gestational diabetes risk for pregnant women; reduce the risk of fall-related injuries for older adults (2). According to the guide, patients with chronic diseases should practice exercise with moderate-intensity at least 150 minutes a week, or at least 75 minutes a week of exercise with vigorous-intensity to improve health (2). Physical exercise can be used as a primary non-

pharmacological clinical tool, for the prevention of many afektions, due to improvements in cardiorespiratory, metabolic, musculoskeletal function, and for the management of chronic pain (2-5). A constant training with moderate-intensity exercise improves the immunity and antioxidant capacity, reduces oxidative stress and increases energy efficiency, thus reducing the incidence of acute and chronic inflammatory diseases (6-8).

Inflammation is a complex biological response of the immune system that prevents, limits, protects and repairs the damage caused by invasion of the pathogens agents, irritating factors, diseased cells or endogenous biomolecules (8). Acute inflammation is a beneficial transitory response for the body, while a persistent inflammatory response is associated with pathology (8,9). Cardiovascular and neuro-degenerative diseases, osteoporosis, postmenopausal breast cancer, colon cancer, asthma, atherosclerosis, dementia, depression,

type 2 diabetes and obesity have the chronic inflammation response, from pathophysiological common point of view. This chronic inflammation diseases, are part from "the diseasome of physical inactivity", even if they are apparently unrelated. It is interesting that the disease of physical inactivity represents very different diseases, but they share pathogenetic mechanisms, and it seems that type 2 diabetes plays a central role (8-14).

METHOD

Systematic Search Strategy. To realize this systematic review, we searched for relevant open access articles in the fields of: medicine, biochemistry, exercise physiology, and physical education and sports. We use 6 international databases: Elsevier, ISI Web of Knowledge, PEDro, NCBI / PubMed, NCBI / PMC and Cochrane.

Considering the niche area of this systematic review, we cite 46 articles from the years 2021-2010, and 44 between 2010-1982. Keywords combinations searched in the context were: exercise, anti-inflammatory effect, cytokines, myokines, inflammation, anti-inflammatory, CRP, IL-6, IL-15, TNF- α , IL-10, myokine, irisin, obesity, type 2 diabetes and chronic inflammation. Eligible articles were analyzed in detail regarding exercise and its anti-inflammatory role.

Inclusion and Exclusion Criteria. The articles included in this systematic review are following the methodology presented above, with the all keyword combinations present in the title. Cross-sectional studies, non-randomized controlled trials, randomized controlled trials, and reviews were included. As exclusion criteria, the articles studied in the next phase do not meet the relevance criteria.

RESULTS

This study included 90 bibliographic sources, which were obtained after applying PEDro selection filters and removing duplicates from a total of 134. These 90 bibliographic sources passed the relevance criteria in the areas listed above and the keywords. This study discussed aspects of exercise, pro- and anti-inflammatory cytokines, immunological mechanisms, the dual role of IL-6 cytokine, and the anti-inflammatory effects of physical exercise.

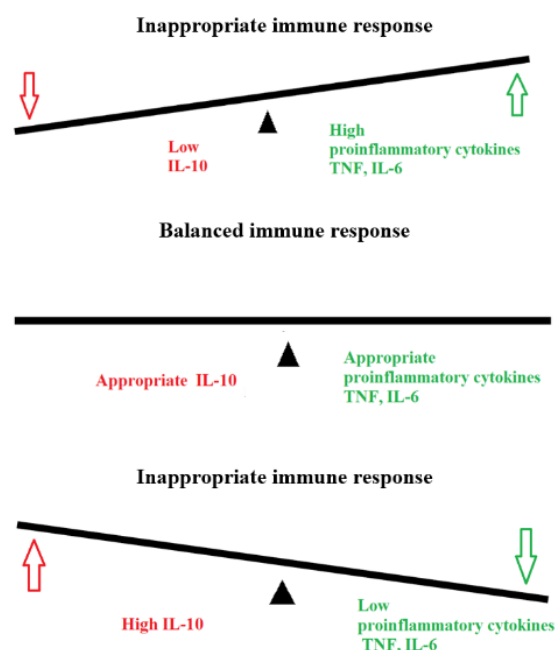
Proinflammatory and anti-inflammatory cytokines

Physical exercise done regularly, guides the immune system to generate anti-inflammatory responses, which is there as a key factor in improving health condition, and controlling the persistent inflammation in chronic diseases (6,15). Activation of the immune system results in the release of cytokines, which are small proteins secreted and released by cells that have a specific effect on interactions and communications between cells. There are both proinflammatory and anti-inflammatory cytokines. Proinflammatory cytokines are: IL-1, IL-6, IL-8, IL-12, TNF- α , IFN- γ , VEGF and IL-1 β . Anti-inflammatory cytokines are : IL-2, IL-4, IL-10, IL-11 and

IL-13 (11-15).

Musculoskeletal, cardiovascular, diabetes and several other chronic diseases are associated with chronic inflammatory processes. Chronic diseases that have an low-grade inflammatory component, are specific to the elderly and sedentary individuals. It is proven that biomarkers of low-grade systemic inflammation in physically active or physically trained individuals are reduced, this being associated with the anti-inflammatory effects of the physical exercises (16-23).

Figure 1. IL-10 on the immune balance. When IL-10 production is low, inflammation increases, leading to tissue destruction (above). If IL-10 production is too high, the infection cannot be stopped and may result a chronic infection (below). If IL-10 is maintained in a state of equilibrium (adequate amount of IL-10) between immunopathology and chronic infection and thus both scenarios can be avoided (middle).



Circulating C-reactive protein (CRP) is an excellent biomarker of chronic and acute inflammation. CRP is an acute-phase protein which is synthesized by hepatocytes during inflammatory or infectious processes in response to pro-inflammatory cytokines. The increased concentration of CRP in serum levels, is correlated with increased body mass index (BMI), metabolic syndrome / diabetes, chronic infection, on smokers and individuals with below-normal high-density lipoprotein cholesterol (24-30).

Pro-inflammatory cytokines are used as biomarkers of chronic and acute inflammation. The proinflammatory cytokines TNF- α (Tumor Necrosis Factor-alpha) and IL-6 (interleukin-6) stimulate the liver release of CRP, and elevated serum or plasma levels are associated with low disease resistance, muscle loss, decline in physical function, and early death (31-35).

The anti-inflammatory cytokine IL-10, is the most studied and used in clinical practice, due to its clinical potential for applications. Due to this potential for clinical applications, extensive research on IL-10 has been conducted in both animal and human models to a better understanding of his activity. The dominant function of IL-10 is as an immunosuppressive cytokine, and can have an immunostimulatory effect on certain cell types. Immunologically, IL-10 levels are important in the management of inflammatory processes and destruction of pathogens. When a high level of inflammation is induced, the quantitative level of IL-10 increases to limit the immune response to avoid damaging the host. When IL-10 production is insufficient, the level of proinflammatory cytokines increases leading to damage to the host (Figure 1) (36).

The pro- and anti-inflammatory properties of the IL-6 cytokine

IL-6 is a cytokine with pro- and anti-inflammatory properties and its involved in inflammation and infection responses, and also in the regulation of metabolic and regenerative processes. IL-6 realizes the maintenance of bone homeostasis, and many neural functions. IL-6 is secreted by T cells and macrophages that promote immune system activation and inflammation, and is generally considered a proinflammatory cytokine. However, IL-6 has anti-inflammatory and immunosuppressive effects, when its derived from skeletal muscle, and that will decrease the proinflammatory response of the immune system (43-45). Pro- and anti-inflammatory differential effect of IL-6 has been shown to be induced by physical exercise intensity (figure 2). Muscle production of anti-inflammatory IL-6 is controlled by Ca^{+2} and glycogen stimuly activated by the muscle contraction. After the end of the physical exercise, IL-6 will reach the plasma peak, and will return to basal levels after a few hours, the values depending on the intensity and duration of the effort (45-47).

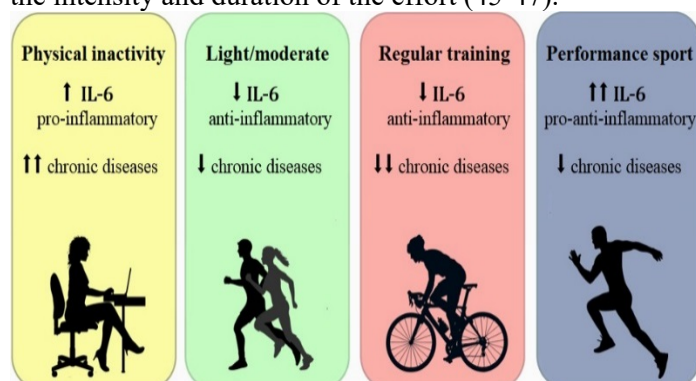


Figure. 2 The effects of physical inactivity and different intensities of exercise on the inflammatory response of IL-6 and on the outcome of health (chronic diseases).

The increase in IL-6 levels is closely related to muscle mass and muscle groups involved in contractile activity.

The higher number of muscle groups are involved in contraction, the higher IL-6 plasma value. Another factor that increases the value of IL-6 post-exercise, is the increase in exercise intensity. Exercises with light-moderate intensity and intermittent exercise protocols of shorter duration, will generate modest increases values in IL-6 (48,49). In performance athletes who have an extended duration of exercises, more than 2.5 hours (marathon runners), the blood and muscle levels of IL-6 will increase up to 100 times, being accompanied by increased levels of anti-inflammatory inhibitors and cytokines (IL-1 α and IL-10) (50-52).

Anti-inflammatory effects of physical exercise

Anti-inflammatory cytokines, especially IL-10 and IL-6, belong to a group of regulatory mediators that govern the response of the proinflammatory cytokine TNF- α , IL-1 β , IFN- γ , and others. Exercising with moderate intensity and regularity, ensures optimal control of the immune system, that will be able to decrease the chances of developing chronic diseases and to improve the defense against infections (figure 2) (3,53).

Another pathway that shows how exercise exerts its anti-inflammatory effect include: the release of IL-6 into the general circulation from contracting muscle fibres, that will subsequent increases IL-10 and IL-1 receptor antagonist in circulating levels. Physical exercise done regularly, increased the numbers of IL-10-secreting regulatory T cells circulating levels, which will lead to reduction of the pro-inflammatory monocytes. Another mechanisms is to limit the infiltration into adipose tissue of macrophages and/or monocytes (54-56).

Further anti-inflammatory effect of regular exercise is given by the interaction between the contracted muscle and the mediated cells, which receive signals transmitted by myokines (IL-8 and IL-15). Myokines are produced during muscle contractions and IL-1 receptor antagonists and sTNF-R are released, molecules that will generate anti-inflammatory effects (57).

General mechanisms by which exercise generates anti-inflammatory environment

Increased levels of circulating cortisol and adrenaline induced by the physical exercise. Secretion of the hormones cortisol and adrenaline is increased during physical exercise, through activation of the sympathetic nervous system (SNS) and the hypothalamic – pituitary – adrenal (HPA) axis. Cortisol is a steroid hormone secreted from the adrenal cortex in response to stress, and that has potent anti-inflammatory and catabolic effects. Adrenaline is a catecholamine secreted from the adrenal medulla in response to stress, that has effects on the cardiovascular system and metabolism. And it also has some immunosuppressive effects, that decrease the pro-inflammatory cytokines. Adrenaline its a fast-acting fighting hormone produced by the adrenal glands at direct signals from the brain under a stressful stimulus.

Cortisol is not released instantly like adrenaline, but rather lasts a few minutes because the amygdala is gradually activated. The levels of the two hormones increase during the physical exercise, and once released, adrenaline activates the sequential releases of corticotropin-releasing hormone, adrenocorticotrophic hormone, and cortisol. The increase in circulating cytokine concentrations is given by these hormonal responses, and the increase in plasma cortisol and adrenaline levels are related to the duration and intensity of exercises. Increased plasma cortisol levels appears to be mediated by exercise-induced IL-6, and after a vigorous long term physical exercise the cortisol show an immunosuppressive action (58-62).

Effects of exercise on visceral adiposity. Visceral adipose tissue or white adipose tissue (WAT) is the „fuel storage” organ, and a key component of metabolic homeostatic mechanisms. WAT has a major role in lipid and glucose metabolism, being involved in a wide range of other biological processes. Hormones and adipokines and other biologically active agents are released from fat cells, and influence many physiological and pathological processes (63). Increased WAT deposition is a risk factor for the development of many chronic inflammatory conditions, including type 2 diabetes and obesity, cardiovascular diseases and chronic pain (14,23,64). WAT produces adipokines, including TNF- α , IL-6, IL-18, and leptin, and excessive WAT causes a reduction in plasma anti-inflammatory mediators, that leading to the development of systemic inflammatory conditions (13). Immune infiltration of macrophages and T cells in WAT, generates and maintains the inflammatory state and its correlates with a sedentary behavior and obesity (65-68). Exercising regularly decreases the activation of the immune system in WAT, and prevents the risk of type 2 diabetes and obesity. The volume of exercise is directly proportional to the anti-inflammatory effect. The higher the training volume and exceeding 45 min / workout, the greater the loss of WAT (69-71).

Increased levels of anti-inflammatory myokines (IL-6, IL-15 and Irisin) from skeletal muscles. Skeletal muscle contraction produces myokines, such as IL-6, IL-15 and irisin. Myokines exert either autocrine, paracrine or endocrine effects, mediating communication between muscles and other organs, including adipose tissue, bones, brain, liver, intestines, pancreas, muscle and skin. Myokines exert their effects on lipid and glucose metabolism, bone formation, etc.

Myokine IL-6 is plays multifunctional roles in the regulation of the immune system, nervous system, and glucose homeostasis. Myokine IL-6 mediates the anti-inflammatory effects associated with exercise both acutely with each workout and as a consequence of training adaptation, including reduced WAT. Blocking IL-6 signaling has been shown to compromise exercise-

induced WAT reduction in obese individuals. Myokines can be considered useful biomarkers for monitoring the type and amount of exercise that is needed to prescribe exercise for individuals with diabetes, neurodegenerative disease, or cancer (67-74).

IL-15 play a significant role in lipid metabolism, preventing obesity. IL-15 is an anabolic factor present in the muscle, and high expression of IL-15 prevents increasing of visceral fat, and its related to reduced WAT mass. IL-15 has been shown to be increased in trained human muscle (75-78).

Irisin is a myokine that induces thermogenic actions in adipose tissue in humans, being released into the circulation through physical exercise training. Irisin, expressed in a PGC-1 α -dependent manner to produce FNDC5. Irisin is expressed in muscle and released into the bloodstream, through the control of the peroxisome proliferator-activated receptor- γ coactivator 1 α (PGC-1 α). Irisin has been involved in the downregulation of insulin resistance pathway, which is controlled by physical exercise. Irisin levels from circulation are lower in older than in younger subjects. Moderate / vigorous aerobic exercise like running and swimming, upregulates the expression of irisin at mRNA, protein, and plasma levels (79-87).

Toll-like (TRLs) receptors and immune regulation. TLRs receptors have a crucial role in the detection of microbial infection. Systemic inflammation is controlled by signaling TLRs. TLRs are highly conserved transmembrane proteins that helps on detection and recognition of microbial pathogens, that triggers the endogenous danger signals of tissue damage, such as heat shock proteins. Chronic exercise has been shown to decrease the cell surface expression of TLRs on immune cells, and inactivity correlates with the activation of TLRs, which are linked in the development of chronic diseases (88-90).

Summary and Future Directions

In this review, we present a number of key points of the physical exercise effects that represent an effective strategy for the prevention and treatment of many chronic inflammatory diseases without medication. The main benefits of physical exercise are: reducing the risks of diseases with high mortality, improving physical function and improving the quality of life; reduces the risk of cancer. In order to be effective in controlling chronic inflammation, a minimum of 150 minutes per week, moderate-intensity exercise is required, or at least 75 minutes per week of vigorous-intensity exercise.

Physical exercise is an efficient clinical tool, that limits chronic inflammation using complex mechanisms to activate the immune system that increase the level of anti-inflammatory cytokines, and limit pro-inflammatory cytokines from blood plasma and serum. TNF- α and IL-6 pro-inflammatory cytokines are used as biomarkers of

chronic and acute inflammation and stimulate the liver release of CRP. Elevated serum or plasma levels are associated with low disease resistance, decline in physical function, and early death. IL-10 is an immunosuppressive cytokine, with an important role in the management of inflammatory processes and destruction of pathogens.

The key player in this review is myokine IL-6. It is a cytokine with pro and anti-inflammatory properties that is involved in responses to inflammation and infection, as well as in the regulation of metabolic and regenerative processes. IL-6 is secreted by T cells and macrophages that promote activation and inflammation of the immune system and is generally considered a proinflammatory cytokine. However, IL-6 has anti-inflammatory and immunosuppressive effects when derived from skeletal muscle, and this will decrease the proinflammatory response of the immune system. The higher volume and intensity of the exercise, the higher the IL-6 levels are.

Identifying the mechanisms underlying the anti-inflammatory effects of exercise use is important, because they can serve as directions for future studies to improve pharmaceutical and physiotherapeutic treatments. Also a better understanding of the mechanisms that are responsible for the control and reduction of chronic inflammation will inspire specialists improve long-term treatment strategies. However, for new research directions it requires a comprehensive understanding of the relation between chronic low-grade inflammation and physical exercise.

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Author contribution

All authors have consistently contributed to this article

Declaration of conflict of interests

There is no conflict of interest for any of the authors regarding this paper

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Assessment of the physical and emotional health concerning the students' physical activity during the COVID-19 pandemic

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Abstract

Introduction. SARS CoV-2 caused the third global pandemic and by applying quarantine / isolation / lockdown, the movement was restricted, the physical contact between people was reduced, the physical activity was low, but the activities using electronic devices at home were frequent.

The aim of the study was to assess the physical and emotional health in relation to the physical activities done during quarantine/ isolation during the pandemic.

Material and method. The study was cross-sectional and consisted of completing an online questionnaire. It was conducted in a period of 6 months and it included 334 students. In order to point out the symptoms caused by quarantine / isolation/ lockdown, we considered it useful for students to participate by completing an online questionnaire about physical activities, physical health and emotional state, related to the implications of participating in online courses.

Results. The questions in this questionnaire were grouped on the following aspects: physical activity, physical health, emotional state, all in the context of the pandemic period, including the period in which the academic activity was online. Thus, in the first year, there is a positive correlation between physical condition, physical activity, emotional signs and cognitive ones. In the second year, the positive correlation is present between the physical and the affective signs, whereas the negative correlation is between the affective signs, the cognitive ones and the physical activity. In the third year, the positive correlation is obvious between the affective signs, the cognitive ones and the physical activity, whereas the negative one between the physical and cognitive signs, as well as between the physical activity and the cognitive and physical signs.

Discussions. There is a link between emotional and cognitive symptoms and physical health. Fear, anxiety, behavioral disorders, and limited physical activity among students during this period can be a public health issue.

Conclusions. The COVID-19 pandemic affected the physical and mental state, with a greater resonance for youth, especially pupils and students. Many of them had emotional, behavioral, physical and cognitive symptoms. These symptoms are found to a greater extent in students in the final years, due to the social impact, social and professional integration.

Keywords: *physical health, mental state, students,*

INTRODUCTION

SARS CoV-2 caused the third global pandemic, and the WHO named it Coronavirus 2019 (COVID-19) (1). By applying quarantine / isolation / lockdown, the movement was restricted, the physical contact between people was reduced, the physical activity was low, but the activities using electronic devices at home were frequent (2). Young people, particularly, found it very difficult to manage this isolation. Even before the pandemic, some adolescents preferred to spend their free time in static, sedentary activities to the detriment of physical activity (3).

This is the reason why there were frequent back pains, which is why the need for early intervention is identified . Physiological factors, age and sex (4) amplified during this period by social, demographic and psychosocial

factors are decisive in triggering back pain (5), especially since there are major physiological and biomechanical changes in adolescents (6,7). The body posture is important and sustained by the coordinated action of the elements of the musculoskeletal system, of the central and peripheral nervous system, and also by the percentage of calcium (8) and magnesium (9), given that the skeleton contains about 99% of total calcium whereas magnesium occurs in muscle contraction. This is why it is important to know the normal reference intervals for these ions, in relation to age, sex and the type of physical activity done.

Adolescents and young adults have predominant dorsal and lumbar pains in comparison to adults whose cervical pain is more common (10,11).

For young people, physical exercise, especially in the open air, influences muscle contraction, static and dynamic balance, by maintaining basic motor skills. During the pandemic, they could not be maintained.

The good results obtained in the professional activity of young people depend on the level of physical training but also on the health and motor skills, acquired by physical exercises (12).

Blanco (13) assessed the physical activity of students before the pandemic and during quarantine / isolation and found a decrease in the physical activity and an increase in the sedentary period according to several factors: sex, age, body mass index, alcohol consumption, tobacco, diet, anxiety/ depression.

An episode of a depressive nature in this age group can cause disorders in the context of anxiety, by influencing the lives of the affected persons (14).

Zhang's (15) study in 2020 assessed the impact of physical and social isolation on the level of physical activity and on the emotional moods of young people. The results showed an average of about 23 minutes of physical activity per day, with higher values in boys. As for emotional states, it was found that females better managed and tolerated inactivity periods and the ones caused by isolation.

Kang's study (16) also assessed issues related to the physical and mental condition of adolescents during the pandemic. The results indicated only 12 minutes of physical activity and over 350 minutes of sedentary lifestyle. In this study the results pointed out the lower emotional impact on girls. The study concluded that adolescents had a sedentary lifestyle during the pandemic.

Chen's study (17) aimed at investigating the prevalence of physical activity and the assessment of sedentary behaviour in young people of 10-18 years old and at the same time to evaluate the connection of the two parameters with age and sex. Also based on the questionnaire, physical activity and sedentary behaviour were assessed.

Olaimat's study (18) conducted during the pandemic period debated the importance of the elements of respiratory gymnastics for preventive and curative purposes in order to improve students' lifestyles.

In Romania, on 16th March 2020, the lockdown caused by the COVID-19 pandemic was imposed, and influenced first the elderly (19) and later the youth (20).

Adolescents and young people, by practicing physical activity regularly, have tried to reduce stress, to tone the body muscles, especially the respiratory ones, in order to cope more easily with this pandemic.

The development of the academic activity in the online environment represented for students the decrease of the physical activity by affecting the motor and sensitive behaviour. Thus, there were changes in emotional states,

the anxious states were more intense, coordination, control and ability decreased.

The occurrence of these elements also involved information from the media, which intensified the uncertainty on the data about the virus.

In the university, especially for the students from the Department of Physical Education, the reduction of the physical activity also meant the diminution of the ability specific to the sport they practised.

At the Faculty of Physical Education and Sports there are also students with different disabilities, represented mainly by vertebral static disorders (kyphosis, scoliosis, back pain and low back pain).

The pain symptoms in this case were accentuated, in the context of online academic activities, during which the students spent approximately 10-12 hours/day on the computer, laptop or phone, in a sitting position.

This position accentuated the pain, maintained the deficient position, secondarily influencing the circulatory system, by accentuating the stasis at the level of the lower limbs, but also on the respiratory system, by influencing the position of the thorax.

Daily physical exercises lead to an increased quality of life with lower blood pressure, increased exercise ability and improved mental state (21). Moreover, the diet was influenced during this pandemic by the consumption of foods that would require energy consumption to prevent the accumulation of calories.

In the normal development of young people, especially students, it is very important that the diet be controlled and correlated with regular physical activities, thus keeping the adequate health conditions (22).

This shows once again the prophylactic role offered by regular exercises, a diet adapted to the type of effort made. We are thus talking about primary prophylaxis in order to avoid the onset of certain diseases, but also about secondary prophylaxis for students who already have a pathology and want to avoid complications.

In 2020, Flandios (23) published a study on the relationship between pandemic isolation, stress and eating disorders of more than 50,000 French students.

The young people should be aware of the importance to have good health and the value of physical activity, which has leads to changes in the quality of life and lifestyle (24). In the context created by the pandemic, it was necessary to find solutions to practise physical exercise at home, regardless of the age group (25).

In addition, under the stress conditions caused by the COVID-19 pandemic, exercise may be a prophylactic component to reduce stress that is known to influence cognitive symptoms (26,27)).

The benefits of physical activities are very important and can influence the evolution to well-being and health: increased joint mobility, increased muscle elasticity involved in exercise, increased muscle strength and

endurance, increased ability and coordination, improved static balance and dynamic one, the improvement of the emotional state.

The aim of the study was to assess the physical and emotional health in relation to the physical activities done during quarantine/ isolation during the pandemic and the proposal made by specialists for physical exercises to help students eliminate back pain and stress.

Material and method

The study was cross-sectional and consisted of completing an online questionnaire.

It was conducted in a period of 6 months and it included students from the Faculty of Physical Education and Sports from "Stefan cel Mare" University Suceava.

Suceava County was the most affected at the beginning of the pandemic, quarantine was first imposed at the national level and later at the regional one.

In order to point out the symptoms caused by quarantine / isolation/ lockdown, we considered it useful for students to participate by completing an online questionnaire about physical activities, physical health and emotional state, related to the implications of participating in online courses.

There were discussions with students and their consent was requested, by taking into account the fact that the collected data is for research purposes only and will not be used elsewhere, by keeping the anonymity of those who fill in the questionnaire and by ensuring the confidentiality of the data.

The questionnaire was filled in by 334 students from the 1st-3rd years of the above faculty. Among the students who filled the questionnaire, 162 (48.51%) were male and 172 (51.49%) were female.

According to the study years, we interviewed 115 (34.43%) students from the first year, 111 (33.24%) from the second year and 108 (32.33%) from the third year. (Table 1)

Table 1. Socio-demographic characteristics of the study group

Gender	1st year		2nd year		3rd year	
F	61	(86.67%)	59	(93.11%)	52	(85.19%)
M	54	(13.33%)	52	(6.89%)	56	(14.81%)

Age	M	F	M	F	M	F
18-20 years	20	22	14	18	-	-
21-24 years	16	21	17	17	27	24
25-29 years	12	10	13	14	18	19
30-34 years	3	5	5	6	6	5
> 35 years	3	3	3	4	5	4

Residence environment	M	F	M	F	M	F
Urban	35	31	28	33	30	26
Rural	19	30	24	26	26	26

Statistical analysis

The median and standard deviation were calculated. The Chi-Square test was applied to compare the percentages of risk that were perceived by the students participating in the study.

Correlations were also calculated with the variables sex, age and residence place.

The data were analyzed by using the SPSS program. Values for $p < 0.05$ were considered statistically significant for a 95% confidence interval.

Results

The questions in this questionnaire (Table 2) were grouped on the following aspects: physical activity (physical exercise- duration, frequency, physical activity at home or elsewhere), physical health (fatigue, headache, exhaustion, appetite disorders, myalgias, sleep disorders), emotional state (cognitive disorders- attention disorders, concentration disorders, affective disorders- fear, anxiety, panic, irritability), all in the context of the pandemic period, including the period in which the academic activity was online.

Table 2. Questionnaire on the physical, cognitive and emotional symptoms caused by the COVID-19 pandemic Pearson's correlation coefficient r was also calculated as it estimates the connection degree between the variables.

In the first year the direct correlation was obtained:

- weak between cognitive symptoms and emotional symptoms = 0.202
- very weak between
 - ✓ physical health and emotional symptoms = 0.148
 - ✓ physical activity and emotional symptoms = 0.156
 - ✓ cognitive symptoms and physical health = 0.173
 - ✓ physical activity and cognitive symptoms = 0.148
 - ✓ physical health and physical activity = 0.039

In the second year it was obtained:

- the direct correlation:
 - ✓ very poor between physical health and emotional symptoms = 0.053
- the inverse correlation, the two variables varying in the opposite direction
 - ✓ weakness between physical activity and physical health = 0.293
 - ✓ very weak between
 - ✚ emotional symptoms and cognitive symptoms = 0.127
 - ✚ emotional symptoms and physical activity = 0.041
 - ✚ cognitive symptoms and physical health = 0.033
 - ✚ cognitive symptoms and physical activity = 0.199

In the third year, a direct correlation and an inverse one were pointed out:

- the direct correlation
 - ✓ weak between emotional symptoms and physical activity = 0.215
 - ✓ very weak between emotional symptoms and cognitive symptoms = 0.019
- the inverse correlation
 - ✓ weak between
 - ✚ cognitive symptoms and physical health = -0.222
 - ✓ very weak between
 - ✚ physical activity and physical health = -0.073
 - ✚ physical activity and cognitive symptoms = -0.029

Table 2. Questionnaire on the physical, cognitive and emotional symptoms caused by the COVID-19 pandemic

QUESTION	Answer	1st year (%)		2nd year (%)		3rd year (%)	
		M	F	M	F	M	F
1. What symptoms did you feel during the pandemic, in the period when the academic activity was online?	Fatigue	7 (12.96%)	11 (18.03%)	9 (17.31%)	12(20.34%)	13 (23.21%)	11 (21.15%)
	Malaise	10 (18.52%)	16 (26.23%)	8 (15.38%)	14(23.73%)	13 (23.21%)	10 (19.28%)
	Decreased appetite	8 (14.81%)	10 (16.39%)	9 (17.31%)	10(16.95%)	9 (16.07%)	10 (19.28%)
	Muscle aches	17 (31.48%)	14 (22.95%)	16 (30.77%)	15(25.42%)	12 (21.43%)	12 (23.08%)
	Disorders	12 (22.23%)	10 (16.39%)	10 (19.23%)	8 (13.56%)	10 (17.86%)	9 (17.31%)
2. Can you specify what were your reactions in the pandemic, when the academic activities were suspended?	Fear	10 (18.52%)	14 (22.95%)	8 (15.38%)	15(25.42%)	12 (21.43%)	12 (23.08%)
	Panic attack	8 (14.81%)	8 (13.11%)	10 (19.23%)	10(16.95%)	7 (12.51%)	7 (13.46%)
	Restlessness	11 (20.37%)	15 (24.59%)	10 (19.23%)	10(16.95%)	12 (21.43%)	10 (19.28%)
	Uncertainty	15 (27.78%)	12 (19.67%)	14 (26.92%)	14(23.73%)	13 (23.21%)	11 (21.15%)
	Impaired sleep	10 (18.52%)	12 (19.67%)	10 (19.23%)	10(16.95%)	12 (21.43%)	12 (23.08%)
3. Can you specify which of the food groups you consumed most often during the lockdown/ quarantine / alert period?	Fats	18 (33.34%)	19 (31.15%)	20 (38.46%)	20(33.89%)	18 (32.14%)	16 (30.77%)
	Proteins	20 (37.04%)	22 (36.07%)	15 (28.85%)	20(33.89%)	21 (37.51%)	24 (46.15%)
	Carbohydrates	16 (26.63%)	20 (32.79%)	17 (32.69%)	19(32.21%)	23 (41.07%)	12 (23.08%)
4. During the quarantine / isolation period, was your physical activity influenced?	Yes, totally	27 (50%)	29 (47.54%)	23 (44.23%)	27(45.76%)	24 (42.86%)	20 (38.46%)
	Moderately	12 (22.23%)	13 (21.31%)	10 (19.23%)	12(20.34%)	17 (30.36%)	22 (42.31%)
	Not really	10 (18.52%)	7 (11.47%)	11 (21.15%)	10(16.95%)	12 (21.43%)	8 (15.38%)
	Not	5 (9.26%)	2 (3.28%)	8 (15.38%)	10(16.95%)	3 (5.36%)	2 (3.85%)
5. Can you specify if the period of emergency / lockdown determined the occurrence or accentuation of some cognitive disorders (attention disorder, memory disorders, concentration disorders, excessive care)?	Care disorder	10 (18.52%)	21 (34.33%)	11 (24.14%)	20(33.89%)	15 (26.79%)	17 (32.69%)
	Concentration disorder	12 (22.23%)	20 (32.79%)	14 (26.92%)	17(28.81%)	14 (25%)	12 (23.08%)
	Memory disorder	10 (18.52%)	11 (18.03%)	10 (19.23%)	9 (15.25%)	12 (21.43%)	10 (19.28%)
	Excessive care	8 (14.81%)	6 (9.84%)	12 (23.08%)	10(16.95%)	12 (21.43%)	9 (17.31%)
	I do not know	4 (7.41%)	3 (4.92%)	3 (5.77%)	3 (5.08%)	3 (5.36%)	4 (7.69%)
6. Can you specify what other symptoms you felt during the quarantine /isolation period during online education?	Pain in the cervical spine	11 (20.37%)	14 (22.95%)	10 (19.23%)	11(18.64%)	11 (19.69%)	9 (17.31%)
	Pain in the spine	19 (35.18%)	20 (32.79%)	12 (23.08%)	21(35.59%)	17 (30.36%)	19 (36.54%)
	Pain in the lumbar spine	12 (22.23%)	13 (21.31%)	12 (23.08%)	16(27.12%)	13 (23.31%)	17 (32.69%)
	Lower limb pain	5 (9.26%)	8 (13.11%)	14 (26.92%)	8 (13.56%)	9 (16.07%)	6 (11.54%)
	Visual acuity disorders	7 (12.96%)	6 (9.84%)	4 (7.69%)	3 (5.08%)	6 (10.71%)	2 (3.85%)

Table 3. Average and standard deviation in the 1st, 2nd and 3rd study years regarding aspects of physical health, physical activity, emotional and cognitive symptoms

Aspects regarding	1st year (Median \pm STD)	2nd year(Median \pm STD)	3rd year(Median \pm STD)
Physical activity	3.64 \pm 0.79	3.59 \pm 0.85	3.85 \pm 0.79
Physical health	9.34 \pm 2.52	9.29 \pm 2.536	9.08 \pm 2.37
Emotional symptoms	6.63 \pm 1.84	6.61 \pm 2.34	6.52 \pm 2.09
Cognitive symptoms	6.67 \pm 2.07	6.64 \pm 2.01	6.85 \pm 2.23

Thus, in the first year, there is a positive correlation between physical condition, physical activity, emotional signs and cognitive ones. In the second year, the positive correlation is present between the physical and the affective signs, whereas the negative correlation is between the affective signs, the cognitive ones and the physical activity. In the third year, the positive correlation is obvious between the affective signs, the cognitive ones and the physical activity, whereas the negative one between the physical and cognitive signs, as well as between the physical activity and the cognitive and physical signs.

Discussions

There is a link between emotional and cognitive symptoms and physical health. Especially in the context of the COVID-19 pandemic, the period characterized by restrictions and fear of addressability to a doctor. Often the symptoms presented by a person can be aggravated by the anxiety caused by a possible condition and the impact of certain information transmitted by the media. Fear, anxiety, behavioral disorders, and limited physical activity among students during this period can be a public health issue. Some students try to hide these symptoms from the people close to them, even if they need specialized help (28,29). Cognitive and emotional

disorders can influence activities at school and at university (30). Depression can develop in over 50% of people who have experienced an anxiety episode (31).

Some studies (32) show on the one hand that students may have certain symptoms, which fall into emotional and cognitive disorders, in comparison to people in the same age group but who do not attend university, and on the other hand students may have a high level of stress in comparison to other people of the same age (33). This can be determined by taking exams, assessments, affecting the quality of life and sleep (34).

Students who exercise reduce the effects of stress, improve sleep quality and emotional state, in comparison to students who do not do any physical activity (28,35).

There are studies (34) that report the increase of stress-related diseases in students, accompanied in some cases by mental disorders. The greater the stress, the less the ability to learn, to pay attention, there a diminished academic performance (36).

Even if it is a cross-sectional study, the questions in this questionnaire try to point out the most important symptoms with an impact on the mental, emotional, behavioral development, and last but not least the physical development among students. Longitudinal studies are needed to show the consequences of the COVID-19 pandemic on the youth, including students, but also among other population groups.

After analyzing the online questionnaires, the nutritional behaviour, the development of physical activities and the emotional state of the students from the Faculty of Physical Education and Sports, exercises were designed according to their age, abilities, sex, presence of disabilities and functional capacity. Thus, the students received online instructions about some exercises.

Warm-up exercises

Starting from the orthostatic position

a. For the trunk and upper limbs

- The torso in slight extension to enable inhaling and then in slight flexion to enable exhaling
- Trunk inclinations - to enable asymmetrical breathing, especially useful for students with scoliosis - convex inhaling and concave exhaling are favored
- Active movements of the upper limbs for breathing exercises
- Maintaining positions involves static and dynamic contractions of the back muscles, shoulders and shoulder blades
- The abduction movements of the upper limbs enables inspiration, the adduction movements enable the expiration

b. For lower limbs

- Walking on the spot, easy running
- Slight jumps on the spot with the lower limbs close and then apart and abductions of the upper limbs
- Kneeling, squatting

The exercise itself

1. Dorsal decubitus position

- Knee flexion and in turn bringing them to the chest on inspiration and return on expiration
- Vertical shear of the lower limbs at 90°, then at 60°
- Alternate lifting of a lower limb with the knee extended as high as possible
- Horizontal bicycle
- Bending the knee and touching it with the opposite upper limb
- Applying resistance to the abdomen (a book can be used) to increase respiratory capacity

2. Ventral decubitus

- Head extension with support on the lower limbs
- Trunk extension by grasping the ankles with the hands

3. Lateral decubitus

- Raise the free lower limb to 30°, 45°, 60°
- Flexion of the lower limb and touching the floor with the knee

4. Position seated

- Anterior flexion of the torso, knees apart and touching the ground under the chair with your fingertips

5. Knee position

- Knee support, abdominal isometric contraction for 5-6 seconds and relaxation for 10-12 seconds

Each exercise must be repeated 10 times, in 2 sets and accompanied by breathing. At the end of the exercise, the upper and lower limbs will be shaken to relax.

It was explained to the students that it is very important to focus on breathing to regulate emotional state and to reduce anxiety (37). These exercises were recommended daily, and for special situations, 2-3 times a week.

Conclusions

The COVID-19 pandemic affected the physical and mental state, with a greater resonance for youth, especially pupils and students. Many of them had emotional, behavioral, physical and cognitive symptoms. These symptoms are found to a greater extent in students in the final years, due to the social impact, social and professional integration.

In the first year the symptoms from the cognitive and emotional sphere were correlated, but in the second and third year their correlation appears with the physical health condition and the development of physical activities.

Conflict of Interest:

The authors declared no conflicting interest.

Informed consent

The investigated subjects were informed about the purpose of the study, agreeing to the processing of the results of the completed questionnaires, in compliance with the rules on the protection of personal data.

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The influence of low back pain on health – related quality of life and the impact of balneal treatment

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Abstract

Introduction. Low back pain has a direct and proportional impact on function and a general one on the quality of life. The present study aims to evaluate the functional impact of low back pain using specific self-assessment tools as indexes of appreciation and epidemiological correlations of potential risk factors involved. The conceptual model of our research is based on the importance of correlating symptoms with clinical assessment, using scales of pain, disability, quality of life, and determination of epidemiological correlations of these areas and the determined factors of the pathology.

Material and method. The study group is made up of 106 cases with clinical diagnostic of low back pain, admitted from 28 September 2020 to 28 March 2021, at Balneal and Rehabilitation Sanatorium of Techirghiol. After performing anamnesis, general clinical examination, specific neuro-musculo-skeletal examination, the patients filled the surveys highlighting the impact of their low back pain on functionality and disability deriving from it. The survey included the Oswestry Disability Index, the Functional Independence Measure (FIM) instrument and the Visual analog scale (VAS) score evaluated at the moment of hospitalization and at discharge. Statistical analysis of data was carried out and correlations between variables resulting from study were highlighted. The study was conducted according to the norms of deontology and medical ethics. The authors declare no conflict of interest.

Results and discussions. Lumbar pathology is common in patients who are hospitalized for a complex balneary-physical-kinetic treatment at Balneal and Rehabilitation Sanatorium of Techirghiol. About 80% of patients who have addressed to our unit in which the study was conducted, have presented low back pain. The majority of patients were females, representing 57,55% of the total number. Regarding the patients' age, 58,5% of them were in the 50-70 years interval. The study reveals a major positive impact of our treatment on spinal symptomatology, an effect pointed out by the relevant statistical differences between the admittance and discharge VAS scores ($p < 0.001$). Reporting the investigated disability with the Oswestry questionnaire of painful lumbar syndrome, and functional evaluation scale (FIM) demonstrates the impact of this pathology on the patient's social life, once again emphasizing the special attention to be paid to axial pathology, both as curative treatment and the importance of prophylactic treatment. Statistical analysis of identified risk factors, reveals the importance of prophylaxis and patient's education in this area. A strong and important statistical correlation was found between the Oswestry total score and the walking and standing items, and a moderate, but strong correlation with the other items. Regarding the sex life item, the correlation is existent, but at a modest level.

Conclusions. The study reveals the importance of correlation of the data obtained from anamnesis, the general clinical examination and the specific examination neuromioarthrokinetic with assessment tools that determine the level of functional independence, the functional impact on social life in high-frequency pathologies treated in medical facilities that provide healthcare in the field of medical recovery. It is necessary to quantify the therapeutic results obtained, in order to assess the level of improvement in quality of life.

Keywords: low back pain, balneal, functional indicators, quality of life,

INTRODUCTION

Low back pain is a very common symptom. It occurs in high-income, middle-income, and low-income countries and all age groups from children to the elderly population. Globally, years lived with disability caused by low back pain increased by 54% between 1990 and 2015, mainly because of population increase and ageing, with the biggest increase seen in low-income and middle-income countries (1-3). Low back pain is now the leading

cause of disability worldwide.

Low back pain has a direct and proportional impact on function and a general one on the quality of life. The present study aims to evaluate the functional impact of low back pain using specific self-assessment tools as indexes of appreciation and epidemiological correlations of potential risk factors involved. The conceptual model of our research is based on the importance of correlating

symptoms with clinical assessment, using scales of pain, disability, quality of life, and determination of epidemiological correlations of these areas and the determined factors of the pathology (4).

The Orthopedic Section of the American Physical Therapy Association (APTA) has an ongoing effort to create evidence-based practice guidelines for orthopedic physical therapy management of patients with musculoskeletal impairments described in the World Health Organization's International Classification of Functioning, Disability, and Health (ICF).

Material and method

The study group is made up of 106 cases with clinical diagnostic of low back pain, admitted from 28 September 2020 to 28 March 2021, at Balneal and Rehabilitation Sanatorium of Techirghiol. After performing anamnesis, general clinical examination, specific neuro-musculoskeletal examination, the patients filled the surveys highlighting the impact of their low back pain on functionality and disability deriving from it. The survey included the Oswestry Disability Index, the Functional Independence Measure (FIM) instrument and the Visual analog scale (VAS) score evaluated at the moment of hospitalization and at discharge. Statistical analysis of data was carried out and correlations between variables resulting from study were highlighted.

The Oswestry Disability Index (ODI) has been developed to assess pain-related disability in people with acute, subacute, or chronic low back pain. Since it was first published in 1980, several different versions have been developed. The ODI covers 1 item on pain and 9 items on activities of daily living (personal care, lifting, walking, sitting, standing, sleeping, sex life, social life, and traveling), making a total of 10 items. The ODI has adequate content validity, as it covers activities of daily living that are commonly experienced by patients with back pain. However, it lacks generic activities such as work, leisure, recreation, or sporting activities. The ODI has high internal consistency, with Cronbach's alpha between 0.71 and 0.87. It correlates with other measures of disability, such as the Roland-Morris Disability Questionnaire (RDQ) and shows moderate correlation with pain scales and the Short Form. Administration of the ODI questionnaire over the phone has excellent test-retest reliability when compared to face-to-face administration. Telephone administration is a convenient and reliable option for obtaining follow-up outcomes data. Telephonic administration of the ODI is scientifically valid and should be an accepted method of data collection for state-level and national-level outcomes projects (5-7).

The Functional Independence Measure (FIM) score is just one of many tools that clinicians can use to determine independence or amount of assistance needed in a rehabilitation setting as well as after discharge. The

FIM was also developed to offer a uniform system of measurement for disability based on the International Classification of Impairment, Disabilities and Handicaps for use in the medical system in the United States (McDowell & Newell, 1996). The FIM assesses six areas of function (Self-care, Sphincter control, Transfers, Locomotion, Communication and Social cognition), which fall under two Domains (Motor and Cognitive). It has been tested for use in patients with stroke, traumatic brain injury, spinal cord injury, multiple sclerosis, and elderly individuals undergoing inpatient rehabilitation and has been used with children as young as 7 years old. The FIM consists of 18 items assessing 6 areas of function. The items fall into two domains: Motor (13 items) and Cognitive (5 items). The motor items are based on the items of the Barthel Index. These domains are referred to as the Motor-FIM and the Cognitive-FIM (8).

The patients admitted underwent specific rehabilitation treatment which included a wide range of therapies. All patients received balneotherapy with the use of the local natural sources – the mineral water of the lake Techirghiol and also peloid therapy using the sapropelic mud extracted from the bottom of the lake. Electrotherapy varied from low, medium and high frequency electrical currents. The patients also underwent kinetotherapy and kinesiotherapy with the assistance of specialized physiotherapists

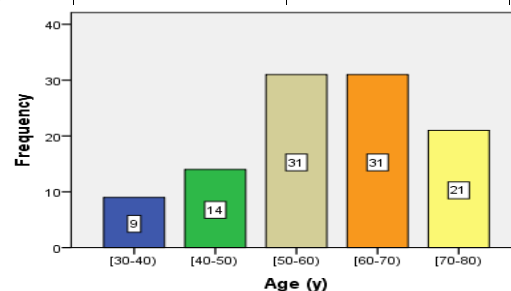
Results

Lumbar pathology is common in patients who are hospitalized for a complex balneal-physical-kinetic treatment at Balneal and Rehabilitation Sanatorium Techirghiol

The majority of patients were females, representing 57,55% of the total number. Regarding the patients' age, 58,5% of them were in the 50-70 years interval.

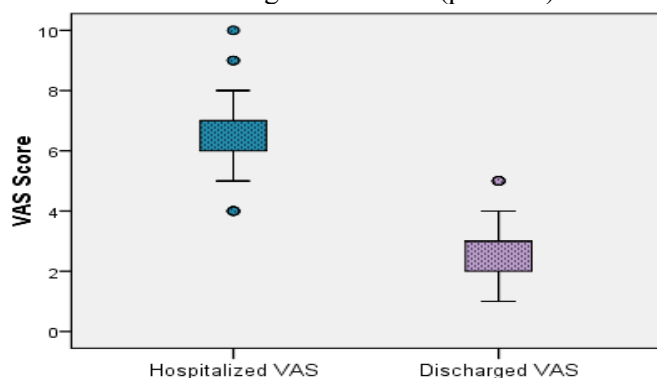
Table 1 – Total Score Oswestry Questionnaire - Spearman's rho

Spearman's rho	Correlation Coefficient	Sig. (2-tailed)	N
Pain intensity	.513	.000	106
Personal care	.576	.000	106
Lifting weights	.623	.000	106
Walking	.715	.000	106
Clinostatism	.685	.000	106
Orthostatism	.768	.000	106
Sleep	.562	.000	106
Sexual life	.313	.001	106
Social life	.670	.000	106



Graph 1 – Age interval distribution

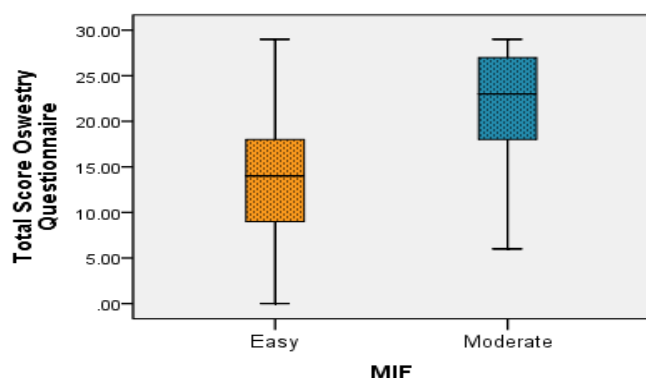
Regarding the urban/rural distribution- 74,53% of the patients were from urban areas, perhaps also due to the easier accessibility to medical services, in general. The study reveals a major positive impact of our treatment on spinal symptomatology, an effect pointed out by the relevant statistical differences between the admittance and discharge VAS scores($p < 0.001$).



Graph 2 - Box-Plot representation of the distribution of VAS scores at admission and VAS at discharge

There are significant differences between median VAS scores at admission and discharge ($p < 0.001$, Wilcoxon signed-rank test). Admission VAS scores were higher than discharge VAS scores.

Reporting the investigated disability with the Oswestry questionnaire of painful lumbar syndrome, and functional evaluation scale (FIM) demonstrates the impact of this pathology on the patient's social life, once again emphasizing the special attention to be paid to axial pathology, both as curative treatment and the importance of prophylactic treatment. Statistical analysis of identified risk factors reveals the importance of prophylaxis and patient's education in this area.



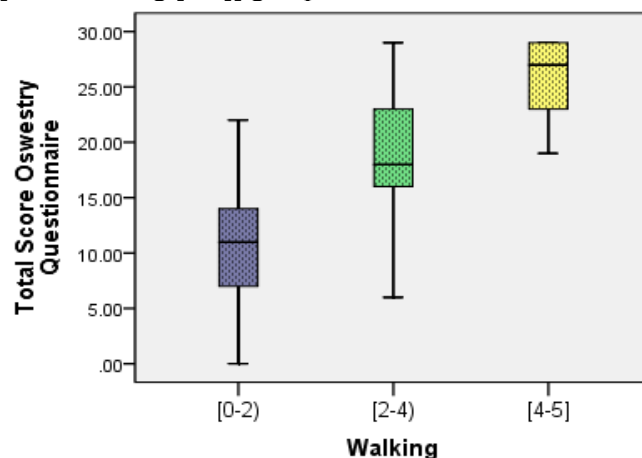
Graph 3 - Box-Plot representation of the distribution of MIF and Oswestry Total Score Questionnaire

A strong and important statistical correlation was found between the Oswestry total score and the walking and standing items, and a moderate, but strong correlation with the other items. Regarding the sex life item, the correlation is existent, but at a modest level.

There are significant differences between the median values of the Oswestry scores corresponding to the three

groups Walking [0-2]/[2-4]/[4-5]] ($p = 0 < 0.05$, Independent Samples Median test).

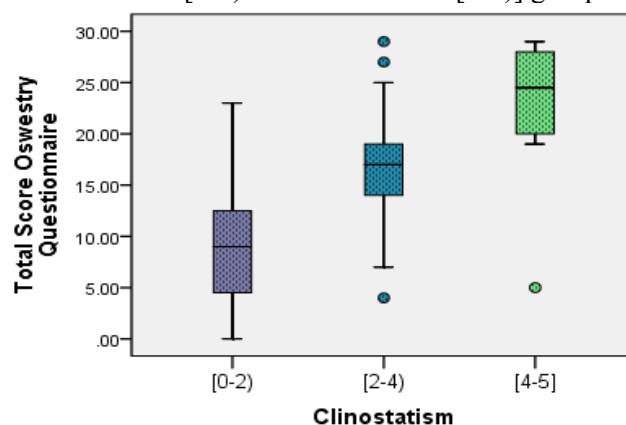
The distribution of scores Oswestry differed in the Walking [0-2]/[2-4]/[4-5]] groups, scores Oswestry were higher in the Walking [4-5] group than in the Walking [0-2] and Walking [2-4]] groups



Graph 4 - Box-Plot Representation of Oswestry Questionnaire Total Score Distribution and movement

There are significant differences between the median values of the Oswestry scores corresponding to the three groups Clinostatism [0-2]/[2-4]/[4-5]] ($p = 0 < 0.05$, Independent Samples Median test).

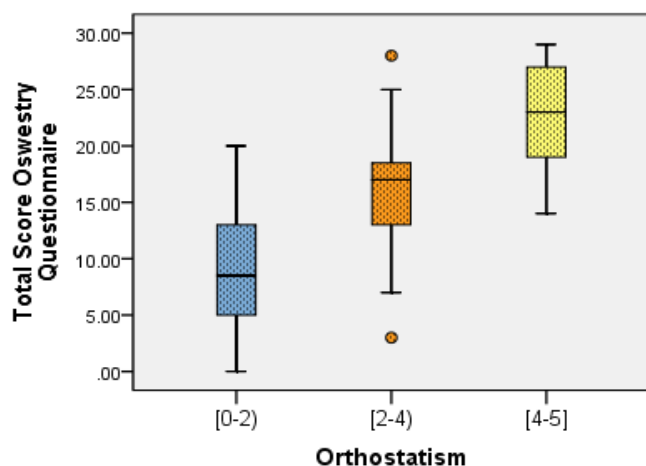
The distribution of scores Oswestry is different in the three Clinostatism groups [0-2]/[2-4]/[4-5]], the Oswestry scores were higher in the Clinostatism [4-5] group than in the Clinostatism [0-2] and Clinostatism [2-4]] groups.



Graph 5 - Box-Plot Representation of Oswestry Questionnaire Total Score Distribution and Clinostatism

There are significant differences between the median values of the Oswestry scores corresponding to the three groups Orthostatism [0-2]/[2-4]/[4-5]] ($p = 0 < 0.05$, Independent Samples Median test).

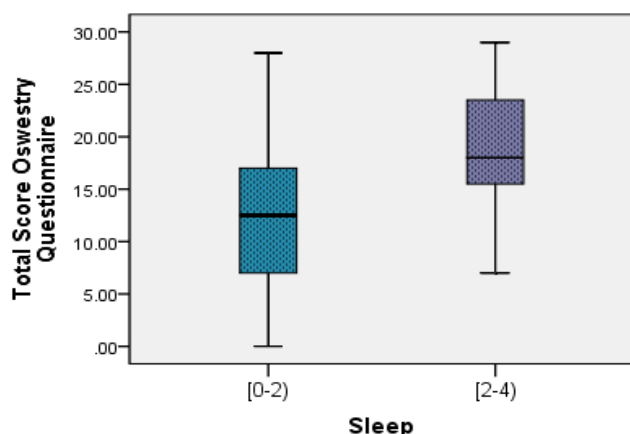
The distribution of scores Oswestry is different in the three Orthostatism groups [0-2]/[2-4]/[4-5]], the Oswestry scores were higher in the Orthostatism [4-5] group than in the Orthostatism[0-2] and Orthostatism [2-4]] groups.



Graph 6 - Box-Plot Representation of Oswestry Questionnaire Total Score Distribution and Standing

There are significant differences between median Oswestry values, corresponding to the two groups Sleep [0-2)/[2-4) ($p = 0 < 0,05$, Independent Samples Median test).

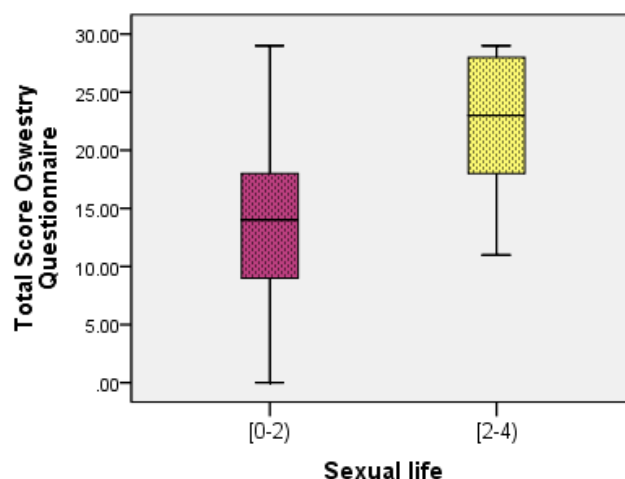
The distribution of scores Oswestry differed in the two Sleep [0-2)/[2-4)] groups, scores Oswestry were higher in the Sleep [2-4)] group, with values ranging from 15-20, than in the Sleep [0-2)] group, with values ranging from 6-17



Graph 7 - Box-Plot Representation of Oswestry Questionnaire Total Score Distribution and Sleep

There are significant differences between median Oswestry values, corresponding to the two groups Sexual Life [0-2)/[2-4) ($p = 0 < 0,05$, Independent Samples Median test).

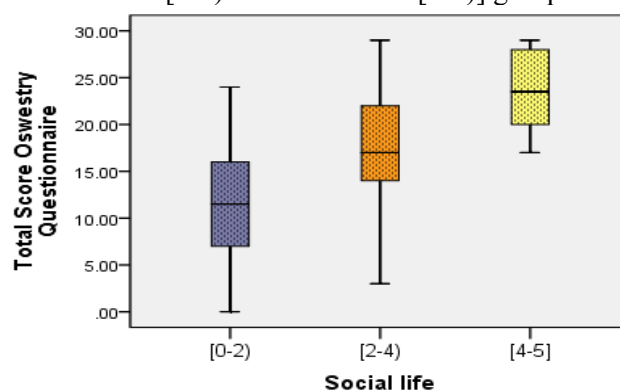
The distribution of scores Oswestry is different in the two Sexual Life groups [0-2)/[2-4)], scores Oswestry were higher in the Sexual Life [2-4) group, with values ranging from 18-28, than in the Sexual Life [0-2) group, with values ranging from 9-18.



Graph 8 - Box-Plot Representation of Oswestry Questionnaire Total Score Distribution and Sexual Life

There are significant differences between the median values of the Oswestry scores corresponding to the three groups Social Life [0-2)/[2-4)/[4-5)] ($p = 0 < 0,05$, Independent Samples Median test).

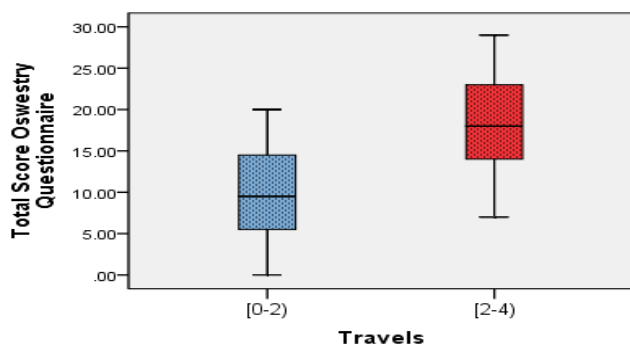
The distribution of scores Oswestry is different in the three Social Life groups [0-2)/[2-4)/[4-5)], the Oswestry scores were higher in the Social Life[4-5) group than in the Social Life [0-2) and Social Life [2-4)] groups.



Graph 9 - Box-Plot Representation of Oswestry Questionnaire Total Score Distribution and Social Life

There are significant differences between median Oswestry values, corresponding to the two groups Travels [0-2)/[2-4) ($p = 0 < 0,05$, Independent Samples Median test).

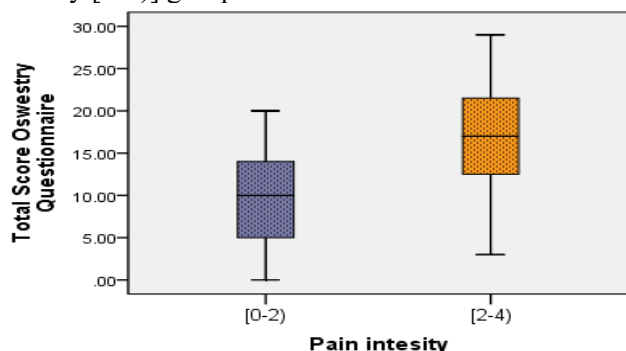
The distribution of scores Oswestry differed in the two Travels [0-2)/[2-4)] groups, scores Oswestry were higher in the Travels [2-4)] group, with values ranging from 15-23, than in the Travels [0-2)] group, with values ranging from 5-15.



Graph 10 - Box-Plot representation of the distribution of the Oswestry Questionnaire Total Score and Travels

There are significant differences between median Oswestry values, corresponding to the two groups Pain intensity [0-2]/[2-4] ($p = 0,001 < 0,05$, Independent Samples Median test).

The distribution of Oswestry scores differed in the two Pain intensity [0-2]/[2-4] groups ($p < 0,001$, Independent Samples Mann-Whitney U test), Oswestry scores were higher in the Pain intensity [2-4] group than in the Pain intensity [0-2] group



Graph 11 - Box-Plot representation of the distribution of Oswestry Total Score Questionnaire and pain intensity

Discussions

The results show a clear predominance of low back pain in female patients as opposed to males, which needs to be addressed if it has true gender preponderance or is given by a population disbalance in favor of more females than males (4,9-12). As we can see, the age distribution is mostly in late adulthood and early elderhood, but nevertheless the balance is towards more advanced age, clearly suggesting a degenerative problem (13). Almost three quarters of the patients come from urban setting, which is due most likely to the access to medical services, as opposed to rural population who, by the nature of rural lifestyle, should have a distribution in accordance with rural/urban general distribution.

During the hospitalization period, with the help of the specific rehabilitation therapies, we observed a clear reduction of the algic syndrome, a thing that was reported by all patients by the means of the common VAS pain score. As the pain subsided, the general mobility has

improved, with a direct influence over the overall functionality (14), as shown by the functional evaluation scale, indicating that the balneotherapy and the usage of physical therapy might be useful as a prophylactic treatment, not only as curative treatment (15,16).

After analyzing the distribution of the total Oswestry score and comparing it with each individual item, we observe that low back pain affects proportionally each aspect of the patient life. Similar distributions of the patients in 3 groups were found for the walking, standing, lying down and social life, and in 2 groups for sleeping, sexual life, travelling, and pain intensity. We know that a cause of insomnia is chronic pain, and we observed an improvement of the quality in sleep as we managed to decrease the pain felt in LBP syndrome (17,18), and it should be monitored on a longer period of time to verify if it is a consistent improvement. We should take into consideration the specific socio-economical factors of the Romanian nationality patients when analyzing some aspects of the everyday life such as sexual life (19) which has shown a clear improvement, but still with a notable dissatisfaction (from social viewpoint, as there is certain stigma about this essential aspect of life) and travelling (from the economical perspective, is quite prohibitive), which also showed a statistically relevant improvement(20). The clearest affliction is observed at patients in standing position, where they felt it has the greatest impact of the overall quality of life in comparison with all the other aspects of life (21). We can also see that the patients had a more direct approach when it comes the pain intensity with either considering the pain to be a big problem or a small nuisance that they could live with it, aspects shown in many other clinical studies from this field (22-26).

Conclusions

The study reveals the importance of correlation of the data obtained clinical exam with self-assessment tools, that determine the level of functional independence and the functional impact on social life. It is necessary to quantify the therapeutic results obtained, in order to assess the level of improvement in quality of life.

Low back pain (LBP) is the second leading cause of disability in the world. The level of disability in patients with LBP is an important outcome measure for clinical practice and research (27,28). The Oswestry Disability Index (ODI) is one of the most commonly used scales that assess the disability related to LBP.

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Occupational therapy interventions in pulmonary rehabilitation – an update in the COVID-19 ERA

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Abstract

Background. As symptoms of COVID-19 infection are varying in severity and type, the long-term disability is yet to be established due to a short time-window since the pandemic started. Most survivors will have persistent pulmonary symptoms even after the infection, which raises the awareness of the importance of pulmonary rehabilitation in these patients, as they are mostly young, with severely diminished quality of life as they are unable to perform their basic activities of daily living as before. Occupational therapy is a form of rehabilitation treatment aimed at maximizing functionality and independence in performing activities of daily living, improvement of the patient's autonomy and prevention of further functional decline.

Objective. The purpose of the current work is to review the most important occupational therapy interventions applicable during a pulmonary rehabilitation program for chronic pulmonary pathologies, that can also be applied in COVID-19 survivors with persistent respiratory symptoms.

Discussion. The main objectives of occupational therapy in pulmonary rehabilitation are training using breathing techniques at rest and during task performance, upper limbs training to increase exercise tolerance, programming and simplifying daily activities, informing patients of the importance of asking for help, planning the day/week, organizing the environment, educating the patient. All these objectives can be achieved in a simple way and at low-cost.

Conclusions. Occupational therapy intervention during comprehensive pulmonary rehabilitation must be promoted to specifically evaluate and solve problems related to respiratory disability. Occupational tasks should be related to symptoms occurring during specific activities. Standardized protocols and definition of outcomes during occupational therapy intervention are lacking.

Keywords: occupational therapy, pulmonary rehabilitation, COVID-19, activities of daily living, quality of life.

1. INTRODUCTION

On March 11 2020, coronavirus disease 2019 (COVID-19) was declared a global pandemic by the World Health Organization (WHO). COVID-19 is caused by the coronavirus SARS-CoV-2 and can present with a wide spectrum of clinical symptoms. The long-term issues experienced by survivors of COVID-19 after discharge are yet to be established, but previous coronavirus outbreaks of severe acute respiratory syndrome (SARS) in 2002 and Middle East respiratory syndrome (MERS) in 2012 could be helpful in predicting postdischarge symptoms, as it was found that one-quarter of survivors of SARS and MERS had reduced lung function and exercise capacity at 6 months postdischarge (1).

In the COVID-19 era, the importance of pulmonary rehabilitation (PR) has arisen. Until 2020, most rehabilitation guidelines dealt with chronic pulmonary conditions. Among the variety of pulmonary conditions, the most disabling are the chronic pathologies, like chronic obstructive pulmonary disease (COPD) and

idiopathic pulmonary fibrosis (IPF) (2). COPD is a multi-factorial progressive chronic lung disease that causes airflow obstruction, that results in persistent and progressive breathlessness, productive coughing, fatigue and recurrent chest infection (3). COPD is sometimes associated with extrapulmonary disorders such as muscle wasting, osteopenia, cardiovascular disease and depression (4). IPF is a chronic progressive disorder with a poor prognosis (5). The hallmark symptom is progressive dyspnea, frequently accompanied by a nonproductive cough, that causes exercise limitation. The presence of dyspnea and exercise limitation lead to difficulties in performing activities of daily living (ADLs) or instrumental activities of daily living (IADLs) and contribute to impairments in the patients' quality of life (QoL) (6).

As symptoms of COVID-19 infection are varying in severity and type, the long-term disability is yet to be established due to a short time-window since the pandemic started. Some studies have concluded that most

survivors will have persistent pulmonary symptoms even after the infection, which raises the awareness of the importance of PR in these patients as they are mostly young, with severely diminished QoL as they are unable to perform their basic ADLs or IADLs as before. A recent report on postdischarge symptoms and rehabilitation needs in survivors of COVID-19 infection in the United Kingdom reported extremely high levels of fatigue, breathlessness, persistent symptoms relating to communication, voice, swallow, and laryngeal sensitivity, problems in mobility, self-care or usual activities. More importantly, the duration of symptom persistence appears to be greater than that seen in community-acquired bacterial pneumonia (7). Additionally, a study conducted on an Italian population of 143 individuals at 7 weeks after hospital discharge found that most subjects still experience fatigue, breathlessness and joint pain (8).

PR is an important component in the management of chronic pulmonary pathologies, as it is proven to significantly relieve dyspnea and fatigue, improve emotional function and enhance the sense of control that individuals have over their condition, being overall beneficial in improving QoL and exercise capacity (9). Thus, the goals of PR are to stabilize or reverse the disease process, alleviate symptoms, restore functional capacities as much as possible, reduce disability, and enhance QoL. A multidisciplinary rehabilitation team working with the patient can design an individualized treatment program to meet this end (10).

Occupational therapy (OT) is a form of rehabilitation treatment aimed at maximizing functionality and independence in performing activities of daily living (ADLs), instrumental ADLs (IADLs), improvement of the patient's autonomy and prevention of further functional decline. When OT is part of PR, the outcome for patients with chronic respiratory impairment is improved (11). Occupational therapists are rehabilitation professionals who work to help individuals engage in ADLs and other meaningful "occupations" that affect their health, well-being, and participation in life roles (12,13).

OT goals in PR are patient centered and patient driven and includes ADL evaluation and training to increase functional endurance, instruction and training in appropriate breathing techniques, evaluation and strengthening of the upper extremity, instruction for work simplification and energy conservation, evaluation of the need for adaptive equipment, assistance in adapting leisure activities, education in stress management and relaxation techniques (12-14).

Pulmonary patients usually report a certain degree of fatigue while performing most ADLs. During simple tasks, like "combing hair" or "tying shoes", chronic pulmonary patients tend to develop a breathing pattern:

rapid, irregular shallow breathing during the activity and rapidly and deeply afterwards. This is due to the rapid and ineffective shallow breathing during the bending and arm muscle activity, resulting in compensatory hyperventilation (15).

Additionally, other relatively simple tasks, like sweeping, changing a light bulb, lifting a pot or erasing a blackboard result in 50%-60% oxygen consumption of the maximal oxygen uptake and increases the minute ventilation, which can explain the sensation of dyspnea and physical discomfort in pulmonary patients. When tasks become more intense, walking while carrying weights or climbing stairs, the dyspnea increases (16).

2 Objective

Considering that most pulmonary patients experience certain symptoms while performing ADLs or IADLs, the overall QoL is severely diminished. At the present time, the long-term effects of COVID-19 can only be speculated, but most survivors deal with persistent respiratory symptoms, like fatigue and dyspnea, which can be also managed by a comprehensive PR program that should include OT. As these symptoms are similar to those in patients dealing with COPD or IPF, there are no limits into using the techniques we have in order to increase QoL in these patients post-infection. The lack of knowledge about OT roles and benefits may be hampering its inclusion in PR programs and preventing people with respiratory diseases from getting the best evidence-based care.

Thus, the purpose of the current work is to review the most important OT interventions applicable during a PR program for chronic pulmonary pathologies like COPD or IFD, that can also be applied in COVID-19 survivors with persistent respiratory symptoms.

3 Discussion

The main objectives of OT in PR are training diaphragmatic breathing at rest and during task performance, upper limbs training to increase exercise tolerance, programming and simplifying daily activities, informing patients of the importance of asking for help, planning the day/week, organizing the environment, educating the patient. All these objectives can be achieved in a simple way and at low-cost (17).

3.1 ADL evaluation and training using breathing techniques

Patients with chronic pulmonary conditions are often limited in their ability to perform their ADLs mostly due to the presence of dyspnea, which is the most obvious sign that an individual is having difficulty breathing. In its most severe form, the patient is short of breath at rest and is not able to utter a short phrase without gasping for air. Often, patients with COPD hold their breath, breathe shallowly and fast, or elevate their shoulders as they breathe. Associated with dyspnea, the patient can experience extreme fatigue, cough, confusion, impaired

judgement (18).

The therapist should observe and note the patient's breathing pattern during the ADL evaluation and should identify the precipitating factors (e.g., "Mr. F. becomes short of breath when washing his face while seated in front of the sink"). Also, the oxygen saturation (O2Sat) with activity should also be measured by pulse oximetry, and if it falls below 90% as the patient performs basic ADLs, the use of oxygen with certain activities should be considered. If the patient does not have home oxygen, the physician should be informed in order to prescribe oxygen supplementation at home. Also, as part of the functional assessment, measurements of heart rate and blood pressure should also be taken (19). Pausing an activity should occur if SpO2 drops below target or Borg scale dyspnea score > 3 with consideration of breathing technique like pursed lip breathing with resumption of exercise intervention once SpO2 reaches target (20,21).

Breathlessness can be reduced in patients with COPD by teaching them to adopt dyspnea control postures. For example, when sitting, the patient should slightly bend forward at the waist while supporting the upper body by placing the forearms on the table or on his/hers thighs. When standing, leaning forward and propping the body on a counter or shopping cart may help with the issue (22,23).

It is important that OT specialists teach the patient breathing techniques to use during the performance of ADLs. Pursed-lip breathing prevents tightness in the airway by providing resistance to expiration. This technique is performed by a nasal inspiration followed by expiratory blowing against pursed lips to decrease airway collapse, reduce respiratory rate and dynamic hyperinflation during exercise training with the aim of an overall increase endurance (23). It increases the use of the diaphragm and decreases accessory muscle recruitment (24). Instructions for pursed-lip breathing are the following: (a) purse your lips as if you are going to whistle; (b) slowly exhale through pursed lips—you should feel some resistance; (c) inhale deeply through your nose; and (d) it should take you twice as long to exhale as it does to inhale. After learning pursed lip breathing, the patient should use these breathing techniques while performing tasks that previously caused them to be breathless (23,24).

Also, timing the breath during an activity could also be helpful. For example, the patient should breathe out while pushing the vacuum cleaner and breathe in while pulling the vacuum cleaner. Moreover, exhaling when lifting an object puts less pressure not only on the lungs but also on the cardiovascular system as it prevents the Valsalva maneuver (25).

Another technique that stimulates the use of the diaphragm to improve chest volume is diaphragmatic breathing. The technique can be taught with the patient

positioned in a comfortable position, like sitting, semi-fowlers position (sitting at a 45° angle), side-lying, or sitting with trunk flexion. The OT specialist should position the pelvis (posterior pelvic tilt), neck (extension), eyes (upward) and upper and lower extremities (external rotation and flexion). Moreover, providing external stimulus can facilitate the technique. For example, placing one hand of the patient on the abdomen near the umbilicus and the other on the sternal manubrium and instruct him to observe the increasing of the abdomen and decreasing of the chest while the therapist should loudly inhale and exhale alongside the patient. The patient is asked to "breathe into your hand" while inhaling through the nose and exhaling orally with pursed lips (26). An easier method is by placing a small paperback novel on the abdomen just below the thorax. The person lies supine and is instructed to inhale slowly and make the book rise. Exhalation through pursed lips should cause the book to fall.

IADLs include activities that support daily life and enable an individual to successfully live life to its fullest and interact with his/her environment and community. Examples of IADLs include home management, shopping, meal preparation, driving and community mobility, pet care, financial management, medication management, care of others, leisure tasks, employment, education, rest/ sleep, and social participation. The OT may provide recommendations to modify tasks or alter the environment to reduce extraneous effort and decrease activity demand. Energy conservation techniques are commonly embedded into IADL re-training. Examples of recommendations include making larger meals to freeze, letting dishes air dry, grouping task items together to minimize unnecessary searches, sliding rather than carrying items, shopping with someone who can carry grocery bags, or using grocery home delivery services (27).

As individuals with COPD or IFD experience dyspnea mostly during the performance of an activity, another intervention should be made into managing dyspnea-related anxiety. This can be achieved by monitoring and adjusting their breathing in a controlled therapeutic environment and implementing dyspnea control postures, paced activity, and breathing techniques while ensuring safe performance of the activity (28).

Active cycle of breathing techniques can be used to ventilate obstructed lung areas. Autogenic drainage can be used to mobilize and centralize secretions with short breaths to collect secretions in the peripheral airways, followed by normal breaths to collect secretions into the intermediate airways, and deep breaths and huff cough to expel secretions (29,30). A huff cough is performed with an open glottis as it creates an increase in the linear velocity of the expiratory airflow and propels secretions. By initiating a forced expiration at a low lung volume the

equal pressure point is moved to the periphery and small airways, while a forced expiration from a high lung volume will move the equal pressure point centrally towards the large central airway (31).

Additionally, posturing the patient plays an important role in respiratory function, and it is effective, simple, and easy to accomplish. Positioning should be used over other techniques like postural drainage given the pathophysiology of COVID-19 and the observed V/Q mismatch (32-34). Patients should be encouraged to adopt, whenever possible, a sitting and standing position to maximize lung function, increase lung compliance and elastic recoil, shift mediastinal structures and provide mechanical advantage in forced expiration (35).

PR or breathing exercises should be stopped if chest pain, palpitations, and dizziness occur, or if SpO₂ does not recover and the patient is unable to maintain Borg scale dyspnea score below 4, with rest and oxygen supplementation (36).

3.2 Upper Extremity Function

Pulmonary patients are often treated with steroids, have systemic inflammation, are older and hypoxic, and therefore often have muscle weakness. Patients with COPD commonly use the accessory muscles of the shoulder girdle to help them breathe, making it difficult for them to use these muscles while conducting an unsupported upper extremity activity (37). Many patients with COPD report disabling dyspnea for daily activities involving the upper extremities like lifting objects or grooming at work levels much lower than for lower extremity exercises (38,39).

The main objective in training the upper extremity is to increase exercise tolerance. Patients should be taught strategies to program their activities with distinct levels of demand. They should always start with light and slow activities, such as personal hygiene from a sitting position, with support of the upper extremity while brushing teeth, combing hair, shaving, applying make-up, and continue with those that can't be performed with the upper extremity supported, like showering or armpit shaving (40).

Upper extremity strengthening has been found to improve the quality of life by increasing the capacity to work and reducing the oxygen requirement of upper extremity activity. Use of free weights, Theraband®, an arm ergometer, and other upper body strengthening techniques are all helpful in increasing upper body strength. Additional improvement in functional status is seen when leg training is added (41,42).

3.3 Work Simplification and Energy Conservation

Fatigue, shortness of breath, and limited endurance are common factors that may limit performance and participation. OT strategies should be aimed at modifying tasks and making recommendations regarding the use of

assisted devices and/or adaptive equipment to reduce effort associated with the performance of daily routines. Work and/or ADL performance capacity are significantly reduced in patients with COPD or IPF, and they should benefit from instruction in work simplification and energy conservation. Energy conservation techniques are tools that aim at reducing the energy expenditure during the performance of ADLs, decreasing the sensation of dyspnea and increasing the functionality (43).

These interventions should include simple strategies such as eliminating unnecessary steps, sitting versus standing if possible, setting up task equipment in advance to minimize effort and using lightweight tools or utensils. Additionally, patients are encouraged to pace themselves through activities and take rest breaks prior to experiencing fatigue (44).

Bathing is a particularly strenuous activity as the hot humid air makes breathing difficult, which is why it is recommended to use a ventilation fan or leave the door open while bathing to keep the humidity level down. Also, the use of a chair in the shower and a thick terry robe after showering instead of toweling off are two suggestions that are helpful in reducing energy expenditure.

Also, unsupported UE activity is very fatiguing, and the patients should be taught to support their arms during certain UE activities such as hair combing or shaving. Also, as mentioned above, scheduling of activities that require more energy expenditure for the time following the use of a bronchodilator will also allow patients to accomplish more.

As the pulmonary disease progresses, some adaptive equipment can be useful. Because bending over to tie shoes or put on pants may cause significant shortness of breath, elastic shoe laces, a long-handled shoehorn, or a reacher to assist with putting on slacks may be helpful.

Simplifying task performance by adapting the environment should also be included in the OT interventions: elevation of the toilet seat, hand rails in the bathroom or bedroom, long-handled shoe horns, walkers with seats and bags etc (45).

3.4 Stress and Anxiety Management

Stress and anxiety are common by-products of respiratory disorders. Due to the fact that COVID-19 has caused a public emergency, patients with COVID-19 may demonstrate different degrees of psychological disorders, such as anger, fear, anxiety, depression, insomnia, and loneliness (46). Providing education to help individuals manage their shortness of breath is an important step in lessening anxiety and promoting participation in the treatment program. Interventions include strategies to help clients prioritize activities and create a balanced lifestyle, increase awareness of body and mind interaction to manage breathing, increase confidence to manage stressors and perform daily activities with more

confidence, and provide education on a variety of relaxation methods. These could include progressive muscle relaxation techniques, pursed-lip breathing technique, and diaphragmatic breathing (47).

Additionally, teaching patients methods to cope with extreme shortness of breath can lessen their fear. Leaning forward and resting their arms on the table releases the diaphragm and makes breathing easier. Using pursed lip and/or active expiration helps to slow the pace of breathing so that the patient is not breathing shallowly and rapidly.

Also, a stress management technique such as visualization may help patients calm themselves by mentally transporting them out of the stressful situation. It is important that the patient practice these options prior to actually needing them. Having a well-practiced plan of action for the panic associated with breathlessness will give patients confidence in their ability to control the situation (48).

4 Conclusions

The three major components of the medical system are prevention, treatment and rehabilitation, all being equally important. OT intervention during comprehensive PR must be promoted to specifically evaluate and solve problems related to respiratory disability. Occupational tasks should be related to symptoms occurring during specific activities. Standardized protocols of OT during PR and definition of outcomes during OT intervention are lacking.

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6. Author contribution

All authors have consistently contributed to this article.

7. Declaration of interests

This article does not contain any studies with human or animal subjects. This study did not require written consent from patients. The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Prevalence of Musculo-skeletal Discomfort and Level of Functional Limitations among Physiotherapists in Karachi City

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Abstract

Introduction:

Musculoskeletal discomfort is one of the most prevalent muscular pain condition hindering normal activities reported by physical therapists and health care professionals generally engaged in handling and mobilizing patients. The study was conducted to find the prevalence of musculoskeletal discomfort and level of functional limitations in physiotherapists.

Method:

This research was questionnaire based cross sectional study conducted in Karachi city from January to April 2019. Data collection was completed from registered physical therapists employed in different institutions. Two questionnaires were filled by the physiotherapists. Questionnaire 01, including thirteen questions on functional activities of daily life which are potentially related to functional areas of Neck Disability Index (NDI). Questionnaire 02 was based on 1987 version of Nordic musculoskeletal questionnaire.

Results:

Participation of 80 physical therapists in the study. 75% was directly involved with patient handling and 25% were teachers. A total of 35% therapists reported 7 days symptoms prevalence with a higher prevalence in cervical (77.1%), lower back (68.6%) and upper back (51.4%). Similarly 65% workers showed previous 12 month symptoms with higher prevalence in neck (72.3%). Gender prevalence of 7 days and 12 months was high in female therapist.

Conclusion:

It has been concluded that 12 month prevalence of musculoskeletal discomfort was 65%, whereas 7 days was 35% and level of functional limitation from activities was insignificant.

Keywords: *Epidemiology; musculoskeletal discomfort; Severity; Physical therapy,*

INTRODUCTION

National Institute for Occupational Safety and Health (NIOSH, 1997) in the USA describes musculoskeletal disorders as a condition which distresses any region of the body's musculoskeletal system encompassing skeleton, neurovascular bundles, tendons, ligaments, cartilage and discs as penalties from repetitive activities and job demands. ¹. The grounds of Musculoskeletal disorders in the workstation remain various and poorly understood. ² Musculo-skeletal symptoms with no fundamental pathology are both diagnostic and management dilemma for medical professions. Idiopathic musculoskeletal ache is probably to happen in 4.2% to 15.5%. ³ Pain is the peak complains, its worldwide common origin is muscular disorder and is classified according to locality of pain. First is an upper limb complaint comprising any trauma or illness situated from lower cervical spine, shoulder up to fingers secondly is lower limb pain syndromes from hips to toes and the

recorded one is low backache ⁴. These disorders impact body's muscular system, bones and joints, tendons and ligaments, nervous system and grow over time, triggered either by the work itself and workstation. Health complications range from discomfort, minor pains and uneasiness to more thoughtful medical situations demanding time off work and even medical management. ⁵ The working circumstances of male and female have been declared in certain studies which revealed high prevalence in female and they were less skilled with low pay and poorer controller of job stresses and advanced level of demands comparatively to male. ^{6,7} The life time prevalence of work related musculoskeletal disorders (WRMDs) among physical therapists is 68% in the United Kingdom 55% and 91% in Australia, and 85% in Turkey. ⁸ Another study showed the prevalence upto 64% and 93% ⁹. Even though prevalence rates of musculoskeletal disorders differ broadly depending on

the body areas considered and the appliances applied for the assessment of signs and symptoms. Prevalence rates of more than 30% have been reported in several European epidemiological researches.¹⁰ One wide-ranging study of WRMDs in physical therapists scrutinized their prevalence in nine different body areas. The peak twelve-monthly prevalence of WRMDs in physical therapists was in the low back (45%), wrists and hands (29.62%), upper back (28.73%) and neck (24.74%). Females were more suffering as compared to male from spinal and upper limb symptoms.¹¹ Younger had the peak prevalence.¹² Musculoskeletal disorders caused more serviceable restrictions in well-being states associated with disability and financial prudence in all regions of earth.¹³ Investigation uncovered the fact that job-linked musculoskeletal syndromes have a substantial influence on physical therapists with 1–6 physical therapists reported taking sick time, altering practice routines, shifting work surroundings or sendoff the occupation owing to WMSDs.¹⁴ Developing risk features for WMSDs is expected to drawn from care events like lifting, patients mobility with exercises, application of high level of force and adopting hazardous postures has been consistently connected with WRMDs and kinesiological analysis has confirmed very high associated musculoskeletal loads.¹⁵ Physical therapists consistently involved in manual therapy such as mobilization and manipulation and prone them to causative elements which linked to job ailments of both acute and chronic musculoskeletal illness.¹⁶

The current study was designed in the same context to evaluate the burden of musculoskeletal discomfort and to initiate appropriate preventative plan.

METHODOLOGY:

This study was Cross-sectional research accomplished in City of Karachi, Pakistan from January to April 2019. Post research approval was obtained from the institutional Ethical Review Board, Islam Medical and Dental College, Sialkot. All registered physiotherapist working in public or private institutions, clinics, hospitals, self-employed and academic background in various specialties were conversant. The self-made questionnaire (01) was composed of socio-demographic, functional activities limitations questions closely related to neck pain and disability index (NDI) outcome measure while one question was about smoking habits and medication each. The questionnaire 02 implemented was standard version (1987) of Nordic Musculoskeletal Questionnaire, having questions related to different body areas including neck, shoulder, elbows, wrists, upper back, mid back, lower back, upper legs, knees, lower legs, and ankle joints with the descriptions of severity and frequency of symptoms, related work activities and the nature of discomfort and mode treatment taken to release pain. The questionnaires were filled by 100

registered physiotherapists to authorize and confirm their position and status with respect to the study measures. The Inclusion criterion was age range of 20-50 years, both sexes and registered practicing physiotherapists. Exclusion criteria included non-registered and non-working physiotherapists, musculoskeletal and metabolic injuries and pregnant females. The participants were informed about the purpose and content of this research and written consent was taken. Total 100 proformas were distributed and 90 participants responds and return the forms. Out of 90 participants 10 were excluded due exclusion criteria and 80 were analyzed.

RESULTS

80 participants were interviewed (51% were males and 49% females). 58% were in the age group of 20-30 and 31% were in 30-40 years. Majority (75%) clinical therapists or hospital and 25% were in academic setting. Duration of their working was assessed and it was found that 47% participated were working as physiotherapist for the last 1-3 years followed by 24% were working for the last 4-6 years. Majority (73%) were working for a minimum of 8 hours whereas remaining was for 12 hours or more. The prevalence of 7 days' symptoms of job-related musculoskeletal disorders was found in 35 %, whereas 12 months prevalence was found in 65%. In case of musculoskeletal discomfort, 36% participants were suffering with it for the last 7 days and 32% for 10-12 months (Table 1 Section A).

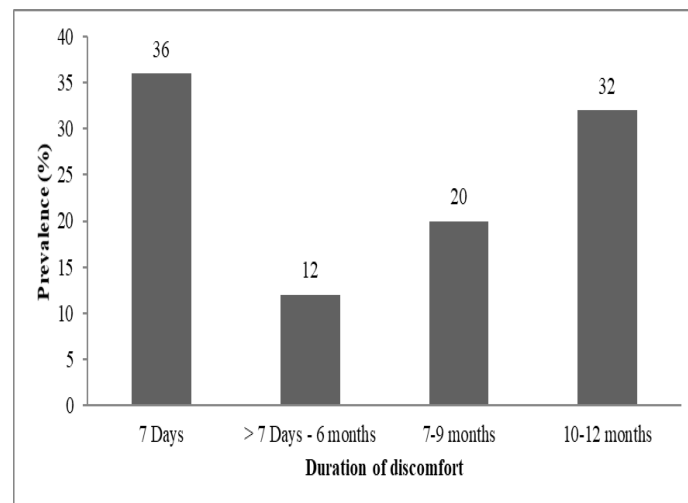


Figure 1. Distribution of duration of musculoskeletal discomfort

The prevalence of 7 days' symptoms of work-related musculoskeletal disorders was found in 35 % which revealed that majority of the physiotherapists were suffering with neck pain (77.1%), lower back (68.6%) and upper back (51.4%). The major remaining conditions were lower leg, mid back, knees, shoulder etc. Similar conditions were found in 12 months' prevalence, which was in 65% participants (Table 2).

Table 1. Detailed characteristics of participants in the current study

Demographic and job / Section A		N	%
Age (years)	20-30	58	58.0
	30-40	31	31.0
	40-50	11	11.0
Gender	Male	51	51.0
	Female	49	49.0
Designation	Academic	25	25.0
	Clinical/Hospital/Home	75	75.0
Educational level	Graduation	43	43.0
	Master	53	53.0
	PhD	4	4.0
Working experience (Years)	1 – 5	53	53.0
	6 -10	34	34.0
	> 10	13	13.0
Practicing duration as Physiotherapist (Years)	1-3	47	47.0
	4-6	24	24.0
	7- 9	18	18.0
	> 9	11	11.0
Working hours per day (hours)	8	73	73.0
	12	21	21.0
	>12	6	6.0
7-days symptoms prevalence	No	65	65.0
	Yes	35	35.0
12-Months symptoms prevalence	No	35	35.0
	Yes	65	65.0
Suffering from musculoskeletal discomfort	7 Days	35	35.0
	> 7 Days - 6 months	12	12.0
	7-9 months	20	20.0
	10-12 months	32	32.0
Musculoskeletal discomfort / Section B			
Position which aggravates yours musculoskeletal discomfort most	Standing	31	31.0
	Sitting	37	37.0
	Bending	20	20.0
	Walking	6	6.0
	Lying	3	3.0
	Bending of knee	2	2.0
	Static work	1	1.0
Position which relieves your musculoskeletal discomfort most	Standing	10	10.0
	Sitting	13	13.0
	Bending	7	7.0
	Walking	10	10.0
	Lying	49	49.0
	Relax	11	11.0
Problems / Section C			
Does your musculoskeletal discomfort made you absent from work?	Yes	10	10.0
	No	74	74.0
	Often	16	16.0
Does your musculoskeletal discomfort restrict you from Lifting?	Yes	21	21.0
	No	60	60.0
	Often	19	19.0
Does your musculoskeletal discomfort make disturbance in your sleeping?	Yes	16	16.0
	No	65	65.0
	Often	19	19.0
Does your musculoskeletal discomfort creating problem in managing personal care?	Yes	11	11.0
	No	77	77.0
	Often	12	12.0
Does your musculoskeletal discomfort made you restricted from driving?	Yes	17	17.0
	No	67	67.0
	Often	16	16.0
Does your musculoskeletal discomfort restrict you from recreational activities?	Yes	12	12.0
	No	68	68.0
	Often	20	20.0
Describe your activity level	Sedentary	5	5.0
	Active	68	68.0
	Very Active	27	27.0
Which of the following describes your posture most of the time?	Sitting	28	28.0
	Standing	57	57.0
	Walking	15	15.0
What type of medication have you used	Nil	60	60.0
	Analgesic	40	40.0

Table 2. Comparison of 7 days and 12 month symptoms prevalence along with 7-days and 12 months gender prevalence of musculoskeletal discomfort of body parts.

Body Parts	Prevalence											
	7-days symptoms Prevalence		12-Months symptoms Prevalence		7 days gender prevalence				12 month gender prevalence			
					Male		Female		Male		Female	
	N	%	N	%	N	%	N	%	N	%	N	%
Neck	27	77.1	47	72.3	10	76.9	17	77.3	27	71.1	20	74.1
Shoulder	15	42.9	29	44.6	3	23.1	12	54.5	16	42.1	13	48.1
Elbows	12	34.3	20	30.8	3	23.1	9	40.9	8	21.1	12	44.4
Wrists	12	34.3	18	27.7	3	23.1	9	40.9	9	23.7	9	33.3
Hands	13	37.1	17	26.2	3	23.1	10	45.5	8	21.1	9	33.3
Upper Back	18	51.4	32	49.2	6	46.2	12	54.5	20	52.6	12	44.4
Mid Back	15	42.9	23	35.4	4	30.8	11	50.0	15	39.5	8	29.6
Lower Back	24	68.6	38	58.5	6	46.2	18	81.8	20	52.6	18	66.7
Upper Legs	11	31.4	12	18.5	2	15.4	9	40.9	5	13.2	7	25.9
Lower Legs	16	45.7	22	33.8	6	46.2	10	45.5	12	31.6	10	37.0
Knees	15	42.9	21	32.3	2	15.4	13	59.1	7	18.4	14	51.9
Ankles	11	31.4	17	26.2	2	15.4	9	40.9	10	26.3	7	25.9

The same prevalence of 7 days' symptoms was assessed gender wise. It was found that the major symptom like neck pain was same in both male (76.9%) and female (77.3%).

The prevalence of 12 months' symptoms through gender difference revealed that neck related musculoskeletal disorder was the highest in both the groups. (Table 2).

The data was further analyzed for the frequency of musculoskeletal discomfort time period of the development of these symptoms in four time periods i.e., every day, 1-2 times per day, per month and per year as shown in Table 3.

Table 3. Frequency and Severity of 12-Months Prevalence of musculoskeletal discomfort symptoms by body parts.

Body Parts	Frequency								Severity							
	1-2 times/year		12- times/month		1-2 times/week		Everyday		Mild		Moderate pain with no reduction in activity		Sever pain with reduction in activity		Unbearable pain off work	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%	N	%
Neck	16	34	19	40.4	8	17	4	8.5	22	46.8	18	38.3	6	12.8	1	2.1
Shoulder	14	48.3	8	27.6	4	13.8	3	10.3	16	55.2	10	34.5	1	3.4	2	6.9
Elbows	14	70	5	25	1	5	-	-	18	90	2	10	-	-	-	-
Wrists	15	83.3	3	16.7	-	-	-	-	16	88.9	2	11.1	-	-	-	-
Hands	11	64.7	4	23.5	1	5.9	1	5.9	11	64.7	6	35.3	-	-	-	-
Upper Back	11	34.4	15	46.9	5	15.6	1	3.1	15	46.9	10	31.2	6	18.8	1	3.1
Mid Back	9	39.1	9	39.1	3	13	2	8.7	15	65.2	5	21.7	3	13	-	-
Lower Back	9	23.7	13	34.2	9	23.7	7	18.4	15	39.5	12	31.6	8	21.1	3	7.9
Upper Legs	11	91.7	1	8.3	-	-	-	-	9	75	3	25	-	-	-	-
Lower Legs	10	45.5	9	40.9	1	4.5	2	9.1	11	50	9	40.9	1	4.5	1	4.5
Knees	7	33.3	7	33.3	1	4.8	6	28.6	10	47.6	9	42.9	1	4.8	1	4.8
Ankles	11	64.7	4	23.5	2	11.8	-	-	12	70.6	4	23.5	1	5.9	-	-

DISCUSSION

The physical therapists working for hours are prone to develop musculoskeletal discomforts. To our knowledge interaction of muscular discomfort and activity limitation has not been addressed before. This study established the prevalence of musculoskeletal discomfort as a result of work correlated musculoskeletal complaints in physical therapists during the past 12 months was 65 % and 7 days prevalence was 35 % which is greater in comparison to previously reported statistics in different regions of the biosphere.¹⁷ The higher 12-month prevalence (occurrence) observed in this study can be illuminated by the circumstances under which physical therapists doing practice in Karachi City, particularly in public sector health center's organizations. For the reason that rehab units are short-staffed, such that a high quantifiable clinical workload is inescapable. Although the City government has tried attempts to ensure that all elementary hospital equipment is ergonomically suitable, other factors, such as increased patient-to-therapist ratios, low counted physical therapist staff, patient interaction time and therapists working in all specialties, might influence the higher incidence of WRMDs. Additionally, physical therapists were engaged with more than one patient simultaneously in some specialty areas, frequent home visits program and riding motor bikes import the high professional work-load makes them more vulnerable to musculoskeletal discomfort and injuries.¹⁸ The overall prevalence of musculoskeletal discomfort in all body regions was high in females. Neck pain (77.3%) was most prominently noted in females while 76.9 % in males. Accordingly, back pain was noted most prevalent in females and then in males. Our research findings were supported from international studies which suggest high musculoskeletal disorders in female due to physical weakness as compared to males, which showed 76% prevalence.¹⁹

In this study posture was one of the variable which aggravates musculoskeletal discomfort that sitting positions accounts 37 % of the discomfort followed by standing posture (31 %) which probably shows static muscle work for a long period and aggravates muscular discomfort. The releasing position for all the muscular discomfort was lying position which probably showed no muscular activity. Our findings are consistent with the international study which concludes that physiotherapists working in pediatrics and musculoskeletal departments showed 67.7% musculoskeletal disorders due to static muscle work positions either sitting or standing.²⁰

In this study, the 7 day prevalence showed that neck pain accounts 77%, lower back pain 68.6% and upper back 51.4% and above calculations were found in 65% of our total sample size though intercontinental studies states that posterior lower spinal region was the utmost noted location for emerging job-related musculoskeletal

disorders among physical therapists (51.7%), persuaded by the cervical (46.5%) and the dorsal spine region (44.8%). The variations in these calculations may be due to the working environment, life style, ethnic values, socioeconomic status and daily working hours.²¹

In our study 60% of the physiotherapists were not restricted from lifting, 77% having no noticeable problems in self-care and also work off ratio was not significant because 74% were on duty despite of their musculoskeletal discomfort and 60% were not using any medications or physician help which showed consistency with the international study which concluded that physiotherapists took treatment from expert physiotherapists of different specialty, do not seek extra medical help and showed little limitation in their daily life.²²

Conclusions

There were 3 significant outcomes in our study:

- 1) 12-month occurrence of WMSDs among physical therapists in the City of Karachi was common; with the Neck pain affected most followed by lower back pain.
- 2) WMSDs were not associated to the member's demographics features.
- 3) Work responsibilities were not suffered by musculoskeletal ailments.

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