

Research article

# The COVID-19 pandemic has revealed an increase in cancer diagnoses and a decrease in prehabilitation programs among patients in Transylvania

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**Abstract: Introduction:** The COVID-19 pandemic has brought significant disruptions to the landscape of oncological medicine, resulting in postponed cancer diagnoses and treatments, poor implementation of prehabilitation programmes, and an overall altered general care. **Purpose:** This paper aims to evaluate the impact of the COVID-19 pandemic on the profile of patients admitted to a clinical Hospital from Transylvania, and to evaluate its detrimental effect on the implementation of prehabilitation/rehabilitation programs for patients diagnosed with cancer. **Material and methods:** The study compared two groups of patients, the ones admitted to the hospital in the year before the pandemic (2019) and the others admitted in 2020. We recorded the number of new cancer diagnoses, the performed interventions of prehabilitation/rehabilitation and we compared the results. **Results:** The diagnosis of cancer was statistically significantly more frequent in the pandemic year 2020 compared to the same timeframe in 2019. Additionally, fewer interventions of physical prehabilitation or rehabilitation were applied during the pandemic period. **Conclusions:** The COVID-19 pandemic had a detrimental effect on the cancer patient's benefit from prehabilitation/rehabilitation interventions

**Keywords:** rehabilitation programs, cancer, COVID-19 pandemic, physical prehabilitation, personalized physical prehabilitation.

## 1. Introduction

Coronavirus disease 2019 (COVID-19) is acknowledged nowadays as one of the pandemics with the most detrimental effects on the health systems worldwide, with important implications not only for respiratory medicine professionals, but also for professionals involved in cancer care [1]. The COVID-19 pandemic has drastically transformed cancer care, with disruptions that affected every aspect of cancer care. These alterations ranged from delayed cancer diagnoses and treatment to the suspension of clinical trials, and have also reduced the patient's access to prehabilitation, rehabilitation, and psychosocial support [2, 3].

In Romania, the first case of COVID-19 was reported in Gorj County, on the 26<sup>th</sup> of February 2020. As of the conclusion of February, Romania had verified a cumulative of three COVID-19 cases, all of which were individuals who had recently returned from Italy [4]. Furthermore, in Romania, the state of emergency was implemented from March 24<sup>th</sup> until May 15<sup>th</sup>, 2020, followed by the implementation of the state of alert from May 16<sup>th</sup>, 2020, until April 9<sup>th</sup>, 2022. Among the measures imposed were the suspension of outpatient medical care for non-urgent cases without the potential for aggravation, as well as the admission of non-medical emergency patients in non-COVID-19 healthcare facilities [5].

Globally, within the field of oncological pathology, the volume of screenings experienced a substantial decline amid the pandemic; nevertheless, their precision reached its zenith in the initial stages of the crisis. This occurrence is attributed to the prioritization of patients displaying distinct signs and symptoms of neoplastic pathology [6]. Despite this, there was a notable decrease in overall new cancer diagnoses throughout the pandemic, resulting in markedly unfavorable outcomes for undiagnosed patients [7]. Recently, Decker et al. demonstrated that, during the initial phase of the COVID-19 pandemic, there was a 23% decline in cancer diagnoses across all prevalent cancer sites. While there was a subsequent recovery as the pandemic evolved, a complete restoration has not been achieved up to the present [8].

Regarding treatment, a retrospective analysis encompassing 25 million patients across Europe during the period from March to July 2020 revealed a 51% reduction in surgical procedures, a 43% decrease in chemotherapy sessions, a 44% downturn in immunotherapy treatments, and a 40% decline in radiotherapy courses [9].

Another reason for the presentation of oncology patients in the healthcare system during the quarantine was concurrent infection with SARS-Cov-2. Despite presenting symptoms comparable to those of the general population (fever, dry cough, fatigue) [10], mortality and morbidity were higher in this group of patients [11].

The physical prehabilitation and rehabilitation programs for patients with cancer have long been recognized as a critical component of their holistic care, aiming to improve their quality of life, functional abilities, and overall well-being. However, the emergence of the COVID-19 pandemic introduced unprecedented challenges to these programs, significantly impacting the already vulnerable population of cancer patients [12]. Amid the COVID-19 outbreak, new guidelines have been introduced to offer alternative cancer treatment options [13]. The practical use of prehabilitation in real-world settings varies, and its adoption has faced difficulties amidst the challenges posed by the COVID-19 pandemic. Nevertheless, there are no established guidelines for cancer prehabilitation during the COVID-19 pandemic, as this field is relatively novel [12, 13].

Our study primarily aimed to compare the total number of hospital admissions, the diagnoses, and the types of malignancies at admission and/or discharge in a tertiary non-COVID University Hospital located in Transylvania, Romania, during a non-pandemic year (2019) versus the year 2020 amidst the COVID-19 pandemic. Additionally, we sought to highlight the challenges associated with providing necessary prehabilitation and rehabilitation measures to these patients. This article also endeavors to discuss and underscore the significance of prehabilitation for individuals with oncological conditions, not only for improving prognosis but also for enhancing the overall quality of life across physical, social, psychological, and vocational dimensions.

## 2. Results

During the specified period of 2019, out of a total of 7,704 admissions, 1,232 were hospitalizations for a form of neoplasia. The most common afflictions were head and neck cancers (236 cases) at 19.2%, in the colon and rectum (232 cases) at 18.9%, and in the uterus and its annexes (108 cases) at 8.8%. During the specified period of 2020, out of a total of 1,776 admissions, 347 were hospitalizations for a form of neoplasia. The most common afflictions were in the colon and rectum (69 cases) at 19.9%, in the head and neck (60 cases)

at 17.3%, and in the lungs and pleura (33 cases) at 9.5%. These sites of cancer development represented more than 50% of all recorded cancer sites, as illustrated in the following table (Table I).

Table I. Common sites of cancer development in the studied populations

	2019	2020
<b>Head and neck cancers</b>	236 (19.2%)	60 (17.3%)
<b>Colon/rectum cancer</b>	232 (18.9%)	69 (19.9%)
<b>Uterus/annexes cancers</b>	108 (8.8%)	27 (7.7%)
<b>Lungs and pleura</b>	77 (6.2%)	33 (9.5%)
<b>Other sites</b>	579 (46.9%)	158 (45.5%)
<b>Total</b>	<b>1232 (100%)</b>	<b>347 (100%)</b>

The cancer diagnosis frequency showed a statistically significant difference between the two groups ( $p < 0.001$ ). Additionally, statistically significant differences were noted between the two periods in terms of neoplasia localization for esophageal cancer ( $p = 0.002$ ), liver cancer ( $p = 0.002$ ), lung/pleural cancer ( $p = 0.04$ ), kidney cancer ( $p = 0.03$ ), skin ( $p = 0.03$ ), and other types of cancer ( $p = 0.02$ ).

We did not observe a statistically significant difference between the two studied periods in terms of the number of neoplastic deaths: 19 out of 1,230 in 2019 and 7 out of 347 in 2020 ( $p = 0.5432$ ). Also, we did not find a statistically significant difference between the two studied periods regarding neoplastic-related deaths recorded in individuals over 65 years old: 614 deaths in 2019 and 165 deaths in 2020 ( $p = 0.4298$ ).

The differences between the two timeframes regarding the number of cancer diagnoses is summarized in the following figure (Figure 1).

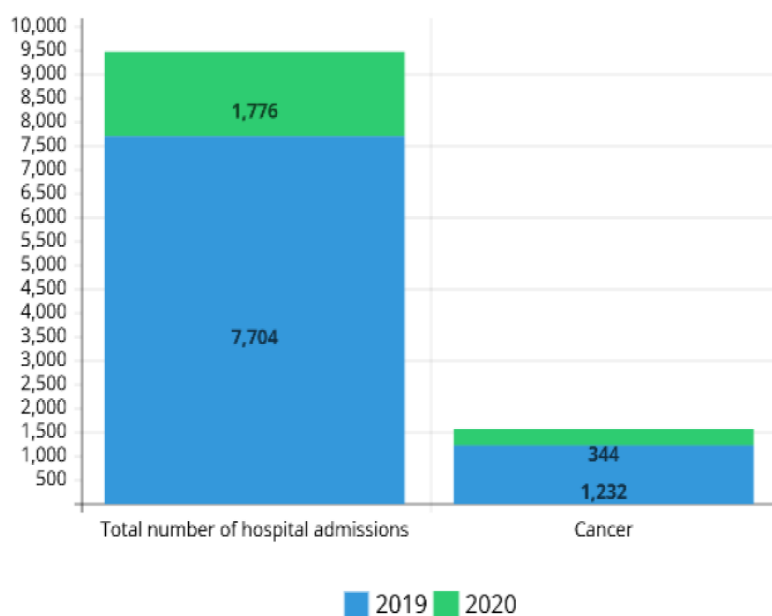
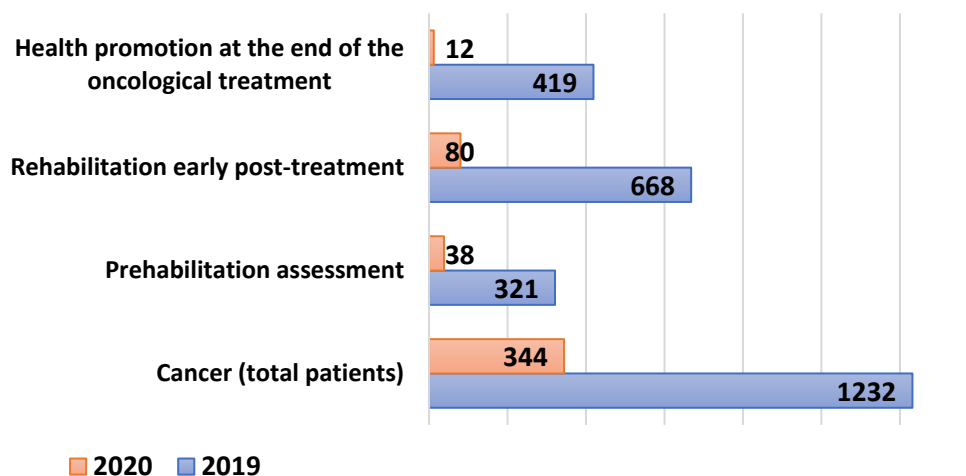


Figure 1. Differences between COVID-19 and non-COVID-19 timeframes regarding the total number of hospital admissions and the established diagnosis of cancer

Documented practices of prehabilitation, early rehabilitation and late rehabilitation (health promotion after the finishing of the treatment) were recorded. We found that these important interventions were clearly underperformed in both evaluated timeframes (with the reserve that maybe some interventions were applied, but not mentioned written in the patient documents). Prehabilitation and health promotion after the treatment initiation were the most deficient, as seen in the following figure (Figure 2).



**Figure 2.** Documented services of pre-/rehabilitation offered to cancer patients diagnosed and treated in the COVID-19 and non-COVID-19 timeframes

### 3. Discussion

Although we observed a statistically significant difference in the number of hospitalizations between the two examined periods, this was predictable given that access to medical services was restricted strictly to emergency cases.

Despite the fact that the number of diagnosed neoplasms was higher during the pandemic period, we cannot assert that the number of neoplastic cases increased "per se" because hospitalizations were limited during this period. The profile of hospitalized patients changed with the restrictions imposed by the evolution of the pandemic in Romania in 2020. The isolation of patients in individual rooms led to an evident limitation in the total number of admissions, with many cases being medically and surgically urgent, involving complex pathologies. However, we did not observe statistically significant differences in terms of the number of neoplastic deaths, neither in general nor in patients over the age of 65, as in other reports [2], allowing us to empirically conclude that the number of cancer survivors has remained constant or improved. Still, there are studies that reported higher percentages of deaths due to COVID-19 in cancer patients [14].

The most common locations of neoplasia diagnosed during the pandemic, in order of frequency, were in the colon/rectum, the head and neck, and in the lungs. These findings partially overlap with the conclusions of other reports [15]. This could be explained by nutritional peculiarities, specific environmental factors of this region, as well as the way the pandemic was managed at the national level, which created an additional stressful climate and sensitized the population to a more rigorous observation of symptoms [2, 3, 15]. Furthermore, these patients were not provided with any additional recommendations beyond the existing therapeutic protocols, despite numerous recent studies highlighting the importance of prehabilitation in this type of pathology [11, 16].

The noticeable shift in the most frequent cancer site, transitioning from head and neck cancers to colonic/rectal cancer before and during the pandemic, can be largely attributed to the hospital's designation for treating infectious digestive disorders. This resulted in a reduction in the number of admissions to the Ear, Nose, and Throat (ENT) section of the hospital. Within other hospitals with designated ENT centers, the count of head and neck cancers was elevated in the pandemic year of 2020. Additionally, the patients exhibited more advanced and neglected neoplastic diseases [17].

As the number of cancer survivors increases, the need to understand the issues they face following treatment, how these issues are resolved, and how we can support them in managing these challenges becomes increasingly important [18]. It has been observed that

people face special challenges when concluding primary cancer treatment, with many of them feeling vulnerable and disoriented during this transition from patient to survivor [18, 19].

Surgery is a cornerstone of oncologic treatment, and recovery methods have improved the safety and outcomes for patients. However, postoperative complications prolong the duration and frequency of hospitalizations, impact the quality of life of patients, affect functional reserves, and in the long term, can have implications for mortality [20].

The preoperative period can provide an opportunity to enhance physiological reserves in anticipation of neoadjuvant therapies and surgical intervention, aiming to improve their outcomes and expedite healing [20, 21]. Prehabilitation is, in fact, an ongoing cancer care process that involves physical and psychological assessments, establishes a baseline functional level, identifies deficiencies, and provides interventions that promote physical and mental health to reduce the incidence and/or severity of potential future deficiencies [20, 22]. This interventional process is based on three components: 1. physical management, 2. nutritional care, and 3. psychological management [23]. In fact, the prehabilitation process is not "one-size-fits-all" but involves personalized assessments and interventions [20].

A differentiation must be made between structured and planned programs aimed at improving cardiovascular or general muscular status and, in this case, targeted physical exercises that focus on training or retraining specific muscles to facilitate disease-specific outcomes, such as improving swallowing in head and neck cancer survivors [24], urinary continence in prostate cancer patients [25], and reducing pain and disability in the arm, shoulder, and upper quadrant in breast cancer patients, for example. All of these interventions fall within the process of neoplastic rehabilitation [26].

Prehabilitation (with all its components: physical, psychological, nutritional) should be part of an integrated continuum of care [20]. A single approach may not succeed in changing outcomes, but when combined with other interventions, it can have a significant effect. This effect is often referred to as the "sum of small gains," where multiple interventions, while each may have a small benefit on its own, can have a synergistic effect when combined [27]. Although prehabilitation is different from other preoperative preparations, there is some overlap, and it is important for prehabilitation to be part of a continuum of care, where preoperative changes are supported throughout the perioperative period, much like in enhanced recovery programs [20].

Among the most common neoplastic locations identified in our study were those in the colon/rectum, in the head and neck cancers, and in the lung/pleura. This could be due, on the one hand, to the early symptoms in these types of cancer, and on the other hand, more likely to the respiratory or digestive symptoms of various viral variants of SARS-CoV-2.

In the following, we will provide a brief presentation of the data that provide strong arguments in favor of prehabilitation for the more common forms of neoplasia identified in our study.

In the case of head and neck cancer, there is limited data in the specialized literature [28]. Furthermore, the wide variability in study designs in this niche makes it difficult to establish conclusive results. We did not find data involving physical exercise for this pathology, except in terms of nutritional prehabilitation: the issue of early oral feeding was raised [29, 30], without a consensus being reached on this matter.

In the case of resectable and advanced gastroesophageal adenocarcinoma, perioperative chemotherapy represents the gold standard of therapy, as demonstrated in two randomized studies [31, 32]: survival was significantly improved compared to using surgery as monotherapy. However, 70% of patients were unable to receive the complete therapeutic regimen, which involves 2-4 cycles of chemotherapy before and 2-4 cycles after surgery. The major reason for the partial or complete impossibility of postoperative chemotherapy was the presence of postoperative complications, severe weakness, and compromised nutritional and physical status. The benefits of prehabilitation in this type

of cancer would be particularly significant because surgery is associated with high morbidity/mortality, and also because the physical and nutritional levels of these patients are precarious, with many experiencing cachexia [33].

The PREHAB study [33], which aimed to evaluate the effectiveness of prehabilitation compared to conventional therapy in patients with gastroesophageal adenocarcinoma undergoing perioperative chemotherapy, demonstrated that prehabilitation improved postoperative morbidity, length of hospital stays, and the nutritional and physical status of these patients. Future studies will need to specify whether prehabilitation can increase the percentage of patients who can benefit from complete oncologic therapy, thereby increasing the number of survivors.

Thoracotomy or minimally invasive video-assisted thoracoscopic surgery is currently the most effective curative treatment for non-small cell lung cancer in stages I, II, and IIIA [34]. Advances in early preoperative staging, modern surgical techniques, and more efficient adjuvant treatments have led to an increase in the number of survivors [35, 36]. Lung cancer surgery is associated with morbidity, functional limitations, and a decreased quality of life. Rehabilitation, in this case, can be a key component in improving outcomes and the quality of life of these patients [37, 38]. Furthermore, rehabilitation for survivors could be associated with health benefits, further extending survival and quality of life [39]. Sommer MS et al. [35] aimed to establish the effect of postoperative physical exercises on the quality of life after pulmonary resection for non-small cell lung cancer and determine whether different times of initiating physical exercise have an influence on the exercise capacity of these patients. Through a meta-analysis, they showed that physical exercise improved exercise capacity and the physical component of HR-QoL but did not register any beneficial effect on the mental component of HR-QoL. Another study demonstrated the beneficial effect of physical prehabilitation in improving aerobic capacity, physical fitness, and quality of life [40]. The early initiation of physical exercises within 2 weeks after pulmonary resection did not provide any additional benefit to exercise capacity, with the note that these findings should be interpreted with caution due to the heterogeneity of exercise programs, methodological limitations, subjective factors, small sample sizes, and a limited number of included studies [35]. Certainly, future studies, likely including multimodal rehabilitation programs, will need to specify when after surgery physical exercises should be initiated to achieve the best results and to prevent/minimize postoperative complications.

Cavalheri and Grager [41] aimed to summarize the role of physical exercise in the context of lung cancer, including individuals with bone metastases, and investigate the potential effect of physical training in slowing tumor growth [41]. Bone metastases are present in approximately 20-30% of lung cancer patients at the time of diagnosis, and another 35-40% of patients develop bone metastases during the course of the disease [42]. In the past two decades, studies on physical exercise in cancer patients excluded individuals with bone metastases due to the potential risk of fractures, spinal cord compression, or exacerbation of bone pain. Given the emerging evidence (in neoplastic populations other than lung cancer) that physical exercise is safe, well-tolerated, and helps maintain self-reported physical function, especially in men with bone metastases and prostate cancer without significant bone pain [43], they recommend physical training for individuals with bone metastases under the supervision of a specialized oncology physiotherapist.

There is promising evidence from preclinical studies [44, 45] that have shown that physical exercise can inhibit tumor growth: associations with intratumorally immune cell infiltration or inclusion of natural killer (NK) cells have been observed. Although these preclinical studies indicate that exercise could induce intra-tumoral adaptations, with increased immune cell infiltration and upregulation of pro-apoptotic proteins, further research on human models is needed to examine whether the effects of physical training on lung cancer progression are similar to those observed in mice.

In the case of colorectal cancer, the initial introduction of prehabilitation programs using intense physical exercises showed poor compliance and modest changes in

postoperative functional capacity [20, 46]. Nevertheless, the implementation of structured multimodal prehabilitation protocols, encompassing aerobic and resistance exercises, protein supplementation, and relaxation strategies, has demonstrated a favorable influence on preoperative physiological reserves, maintaining functional capacity levels post-surgery. More than 80% of patients adhering to the multimodal prehabilitation program restored their initial functional walking capacity values within 8 weeks. In contrast, only 40% of patients without prehabilitation returned to their initial values [47].

Recently, a consensus among a group of experts in colorectal surgery has highlighted the potential benefits of preoperative exercise interventions for patients undergoing tumor resection, with ongoing studies set to determine the impact of supervised exercises on survival [48, 49].

While early evidence that prehabilitation can support better outcomes in populations undergoing colorectal cancer surgeries is encouraging, it remains to be seen whether preoperative interventions will also reduce the number and severity of complications [20, 50, 51].

Regardless of the cancer type, prehabilitation programs must continually evolve and consistently improve for the benefit of oncological patients. A recently published study has demonstrated that a combination of telemedicine and prehabilitation ("teleprehabilitation") was found to be beneficial to patients and resulted in high satisfaction levels [52]. This could become one of the future backbones of the modern prehabilitation programs.

The limitations of this research encompass the small sample size and its retrospective design. Additionally, due to design constraints, it was not feasible to delineate the number of hospitalizations during the pandemic attributed to SARS-CoV-2 infection versus those related to clinical manifestations of a neoplastic condition. Caution is warranted in interpreting the results as the hospital's designation during the pandemic prioritized digestive infections, potentially inflating the incidence of colorectal cancers. Furthermore, a lack of consistency was noted in the reports evaluating the applied methods of prehabilitation and rehabilitation in the study populations. Lastly, the findings cannot be broadly generalized due to the unique characteristics of the study populations.

As a "take-at-home" message concerning prehabilitation or rehabilitation in cancer patients during the COVID-19 pandemic, it is crucial to emphasize that physical pre-/rehabilitation programs in the cancer care continuum are unequivocally essential. These programs encompass a broad spectrum of interventions, including exercise, physical therapy, occupational therapy, and psychological support. Their primary objective is to address the physical and psychological consequences of cancer and its treatment, such as pain, fatigue, muscle weakness, and emotional distress.

When delving into the psychological toll and resilience, it is important to acknowledge that the detrimental impact of the pandemic on cancer rehabilitation extends beyond the physical aspects. The fear of contracting the virus, combined with isolation and disruptions to daily routines, has heightened emotional distress. However, it's crucial to highlight the resilience and resourcefulness demonstrated by both patients and healthcare teams, who have found innovative ways to continue rehabilitation.

It is currently suggested that the experiences and lessons learned during this challenging pandemic may pave the way for innovations in remote rehabilitation and a more patient-centered approach to care. Moving forward, research efforts should focus on designing robust studies to identify the actual challenges in cancer prehabilitation. Pinpointing the issues associated with prehabilitation in cancer will pave the way for further studies to assess the most effective methods of enhancing the quality of these interventions, which are crucial for oncological patients.

#### **4. Materials and Methods**

The study was carried out at CF Clinical Hospital in Cluj-Napoca, Romania. It involved a comparison between patients admitted during the COVID-19 pandemic

period, spanning from March 1, 2020, to December 31, 2020, and another group of patients from the corresponding period in the preceding year (March 1, 2019, to December 31, 2019). The study followed a retrospective descriptive design and adhered to the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines for reporting observational studies, ensuring robust and comprehensive reporting.

For each of these time frames, we systematically recorded the overall number of hospital admissions within the Internal Medicine, Surgery, and ENT Departments. This documentation encompassed primary diagnoses of cancer upon admission and discharge, as well as active cancer diagnoses at discharge for individuals with pre-existing cancer diagnoses.

We gathered all available information from the hospital database, without applying any preliminary exclusion criteria, to provide the most accurate representation of the hospital's actual situation during those times. Each patient diagnosed with cancer was counted once, based on their initial entry with the respective ICD-10 diagnosis.

The following inclusion criteria were used: adult patients (aged >18 years), admitted to the Clinical Hospital CF Cluj-Napoca in the Sections Internal Medicine, Surgery, and ENT, as follows:

- a) Patients with a previous oncological diagnosis who presented to the outpatient clinic for continuation of treatment;
- b) Patients with a previous oncological diagnosis who presented to the outpatient clinic for medical emergencies;
- c) Newly diagnosed patients with any form of neoplasia.

The following exclusion criteria were applied: pediatric patients (aged <18 years); patients with a previous oncological diagnosis who have been biologically and radiologically documented to be in remission and patients who have not been diagnosed with a form of neoplasia during hospitalization or previously.

All patients admitted to the hospital during the 2019-2020 period were examined. They were categorized into two groups. The first group consisted of patients meeting the inclusion criteria and hospitalized within the one-year period preceding the declaration of the state of emergency (March to December 2019). The second group included subjects hospitalized during the state of emergency (March to December 2020).

For each subject included in the study, we recorded their type of neoplasia. Subsequently, we compared the frequency of different forms of neoplasia between two periods: the pre-pandemic phase and the period during the state of emergency for the COVID-19 pandemic. Additionally, we documented the practices of prehabilitation, early rehabilitation, and late rehabilitation (health promotion after the completion of treatment). In cases where there were no explicitly described interventions in the patient records, they were categorized as "not performed", even if they might have had benefited by some minor interventions.

Statistical analysis was performed using the MedCalc® Statistical Software version 22.006 (MedCalc Software Ltd, Ostend, Belgium; <https://www.medcalc.org>; 2023). Data was expressed as frequency and percentage, as it is the standard for reporting quantitative data. Comparison between groups were performed using the chi-square test, as it provides an objective method of investigating the probabilities of individuals being in specific categories/groups, hence why it is used for qualitative data. A p-value <0.05 was considered statistically significant.

## 5. Conclusions

More newly diagnosed cancer cases were in the cohort of patients admitted to a University Clinical Hospital from Transylvania during the pandemic year 2020, compared to the same timeframe in 2019. The patients had insufficient programs of prehabilitation/rehabilitation applied during both studied periods of time. There is a clear need to implement tailored programs of pre- or rehabilitation to promote a better quality of life for cancer-suffering patients.



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