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Research article

Physical Rehabilitation in Multiple Myeloma - A Retrospective Analysis and Future Perspectives

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Abstract: Multiple Myeloma is a malignancy characterized by multisystem involvement, including multiple osteolytic lesions, anemia, and renal insufficiency. The debilitating course of this disease highlights the importance of exploring the therapeutic potential of physical rehabilitation in improving patients' quality of life and providing meaningful clinical outcomes. The aim of this study is to investigate the benefits and challenges associated with the implementation of physical rehabilitation programs for patients with multiple myeloma, analyzing the evolution and characteristics of multiple myeloma cases in a medical clinic in Romania. Through this, we seek to contribute to the development of new approaches and protocols in physical rehabilitation, which may improve the therapeutic management and quality of life for patients with this complex condition. A retrospective analysis was conducted on newly diagnosed multiple myeloma patients over a 7-year period (2017-2023) at a clinic in Romania. The collected data included the time of initial diagnosis, patient age, residence (rural or urban), multiple myeloma subtype,treatments initiated, hematological parameters, presence of bone lesions, and comorbidities. We reviewed the existing literature on physical rehabilitation in multiple myeloma and assessed the associated advantages and challenges. Statistical analysis was performed to identify trends and correlations within our cohort**.** Out of a total of 255 patients diagnosed with multiple myeloma at a medical center in Romania, the majority were men from urban areas. It was observed that the average age at diagnosis was lower among patients from urban areas. Additionally, 69.8% of patients presented with bone lesions, while pancytopenias were rarely encountered at the time of diagnosis. Personalization of physical exercises is essential to maximize rehabilitation benefits for patients with multiple myeloma. Complications such as pancytopenias and frequently encountered bone lesions should not discourage the recommendation of rehabilitation. Decisions must be individually tailored and coordinated by a multidisciplinary team to ensure the rehabilitation program's safety and efficacy.

Keywords: physical rehabilitation; multiple myeloma; physical activity, bone lesions

1. Introduction

Multiple Myeloma (MM) is defined by the uncontrolled proliferation of monoclonal plasma cells and excessive protein secretion, leading to bone lesions, bone marrow involvement, and renal impairment [1]. MM primarily affects individuals with a median age of 69 years, and its incidence continues to rise. The American Cancer Society estimates approximately 35,780 new cases in 2024 [2]. Recent therapeutic advancements have significantly improved the quality of care for these patients. A global analysis, including data from 195 countries between 1990 and 2019, highlighted an increase in life expectancy for MM patients, reflecting both the rising incidence of the disease and improvements in treatments that have contributed to reduced mortality [1]. However, MM remains an incurable and profoundly debilitating condition, with a 5-year survival rate of approximately 60% [2]. These patients' quality of life is considerably lower than other neoplasms [3]. Kent EE et al. analyzed 12 types of malignant conditions, identifying multiple myeloma as being most frequently associated with physical and mental health deterioration among elderly survivors [4]. In a recent study that included 22,505 cancer survivors and 244,000 individuals without cancer, MM patients exhibited the most severe functional limitations and ranked second, after lung cancer, in terms of psychological distress and reduced quality of life compared to other cancer types [5]. Quality of life significantly contributes to the prognosis. A study demonstrated an inverse correlation between scores on the health-related quality of life (HRQoL) questionnaire and all-cause mortality across all stages of MM [6]. Challenges for MM patients include varying degrees of anemia, as well as osteolytic lesions, which are present in approximately 80% of patients and lead to pathological fractures and debilitating pain [7]. Bone involvement in MM persists even during periods of remission [8].

The findings above underscore the necessity for ongoing scientific research and enhanced access to effective treatments to address this complex condition adequately.

Rehabilitation has been introduced as an adjunct to standard therapy, yielding favorable outcomes in various neoplasms [9,10]. It encompasses a wide range of complementary methods that address psychological, nutritional, and physical dimensions, aiming to optimize oncologic treatment and improve quality of life from the time of diagnosis [11].

Physical activity has become an integral component of oncologic treatments, aiding in the management of various manifestations associated with neoplasms, such as quality of life, fatigue, depression, muscle strength, and reduced mobility [12–14]. Guidelines issued by the American Society of Clinical Oncology (ASCO), the American College of Sports Medicine (ACSM), the American Cancer Society (ACS), and the National Comprehensive Cancer Network (NCCN) recommend an exercise regimen that includes both aerobic activity (at least 150 minutes of moderate-intensity physical activity per week) and resistance exercises (a minimum of two resistance training sessions per week) [15–18].

Physical rehabilitation in MM is an underdeveloped field. Existing studies are heterogeneous in terms of the types of exercises, duration, methods of assessing effectiveness, and types of patients included. Most studies have included younger patients with stable bone lesions [19–23]. Bone fragility and frequent pancytopenias pose significant challenges in physical rehabilitation programs. The beneficial effects of physical exercises on bone structure are well-known, emphasizing the need for standardized, safe, and effective protocols for patients with MM [24].

2. Materials and Methods

The study was conducted as a retrospective, observational analysis on a population of patients newly diagnosed with MM at the Prof. Dr. Ion Chiricuță Oncology Institute in Cluj-Napoca, Romania, between January 1, 2017, and December 31, 2023, adhering to the STROBE guidelines (Strengthening the Reporting of Observational Studies in Epidemiology) for accurate reporting. The study was

previously approved by the Ethics Committee of the Prof. Dr. Ion Chiricuță Oncology Institute in 2024.

We selected newly diagnosed patients with secretory MM (heavy chains and light chains) during the study period. For each patient, we collected demographic data (gender, age at diagnosis, residence), MM subtype, type of treatment, complete blood count values at diagnosis, presence of bone lesions, and comorbidities.

Inclusion criteria: We included patients over 18 years of age diagnosed with secretory MM. Patient selection was based on a confirmed diagnosis of multiple myeloma, established through clinical and paraclinical analyses, as well as the presence of light or heavy chain secretion in blood or urine, according to international diagnostic criteria. We included patients regardless of existing comorbidities to reflect the clinical diversity and complexity of MM cases. Additionally, we imposed no restrictions related to the type of treatment administered or complete blood count values.

Exclusion criteria: We excluded all patients diagnosed during the selected period with other plasma cell dyscrasias, such as MGUS, smoldering myeloma, solitary plasmacytoma, and systemic amyloidosis, to focus exclusively on active MM cases. Additionally, we excluded patients diagnosed with multiple myeloma prior to the study period (January 1, 2017 – December 31, 2023) to avoid including cases with incomplete or inconsistent medical histories. Furthermore, patients with incomplete data on diagnosis type, treatments administered, or other essential information for our analysis were also excluded.

We thoroughly examined the medical records of the patients included in the study, collecting essential data such as age, gender, residence, MM subtype, complete blood count parameters at diagnosis, presence of bone lesions, initiated treatment, and associated comorbidities. All this information was carefully recorded in our centralized database. Patients whose medical records lacked information deemed less essential to our study were still included, with the missing data marked as "unknown" to maintain the integrity and accuracy of the analysis.

The statistical analysis was conducted using IBM SPSS Statistics v.26.0.0. Data were presented in tables and graphs, including median ages, frequency distributions, and percentages, according to standard practices for reporting quantitative data. Data distribution was assessed using the Kolmogorov-Smirnov and Shapiro-Wilk tests to evaluate normal data distribution. For group comparisons, the chi-square test was applied to categorical data. For data not following a normal distribution, the Mann-Whitney U test was used for two groups, and the Kruskal-Wallis H test for three or more groups, followed post-hoc by the Dunn-Bonferroni test. A p-value <0.05 was considered statistically significant.

3. Results

Of the 255 patients diagnosed with MM included in the study, 131 (51.37%) were men and 124 (48.63%) were women. In 2020, a decrease in the number of newly diagnosed cases was recorded, accounting for 12.2% of the total cases. This trend continued in 2021 with 9.8% and in 2022 with 9.4%. However, in 2023, an increase was observed, with the number of cases reaching 16.9% (Table 1).

Table 1. Distribution of patients diagnosed with multiple myeloma by gender and year of diagnosis

Gender * Year of diagnosis Crosstabulation

			Year of diagnosis							
			2017	2018	2019	2020	2021	2022	2023	Total
Gender	Male	Count	20	32	18	15	12	12	22	131
		% within Gender	15.3%	24.4%	13.7%	11.5%	9.2%	9.2%	16.8%	100.0%
		% within Year of diagnosis	51.3%	61.5%	43.9%	48.4%	48.0%	50.0%	51.2%	51.4%
	Female	Count	19	20	23	16	13	12	21	124
		% within Gender	15.3%	16.1%	18.5%	12.9%	10.5%	9.7%	16.9%	100.0%
		% within Year of diagnosis	48.7%	38.5%	56.1%	51.6%	52.0%	50.0%	48.8%	48.6%
Total		Count	39	52	41	31	25	24	43	255
		% within Gender	15.3%	20.4%	16.1%	12.2%	9.8%	9.4%	16.9%	100.0%
		% within Year of diagnosis	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%	100.0%

The distribution by place of origin showed that 149 patients (58.4%) came from urban areas, while 106 (41.6%) were from rural areas. In urban areas, men constituted a clear majority compared to women (56.4% vs. 43.6%). Conversely, in rural areas, women outnumbered men (55.7% vs. 44.3%) (Table 2).

Table 2. Distribution of patients diagnosed with multiple myeloma by gender and environment

Crosstab

			Environment		
			Urban	Rural	Total
Gender	Male	Count	84	47	131
		% within Gender	64.1%	35.9%	100.0%
		% within Environment	56.4%	44.3%	51.4%
	Female	Count	65	59	124
		% within Gender	52.4%	47.6%	100.0%
		% within Environment	43.6%	55.7%	48.6%
Total		Count	149	106	255
		% within Gender	58.4%	41.6%	100.0%
		% within Environment	100.0%	100.0%	100.0%

The analysis of age at the time of diagnosis revealed that the majority of MM cases were observed in patients aged 70-79 years (n=87), followed by those aged 60-69 age group (n=81). Together, these two age groups accounted for 168 cases (66%), indicating a higher prevalence of MM in older adults, particularly between 60 and 79 years (Figure 1).

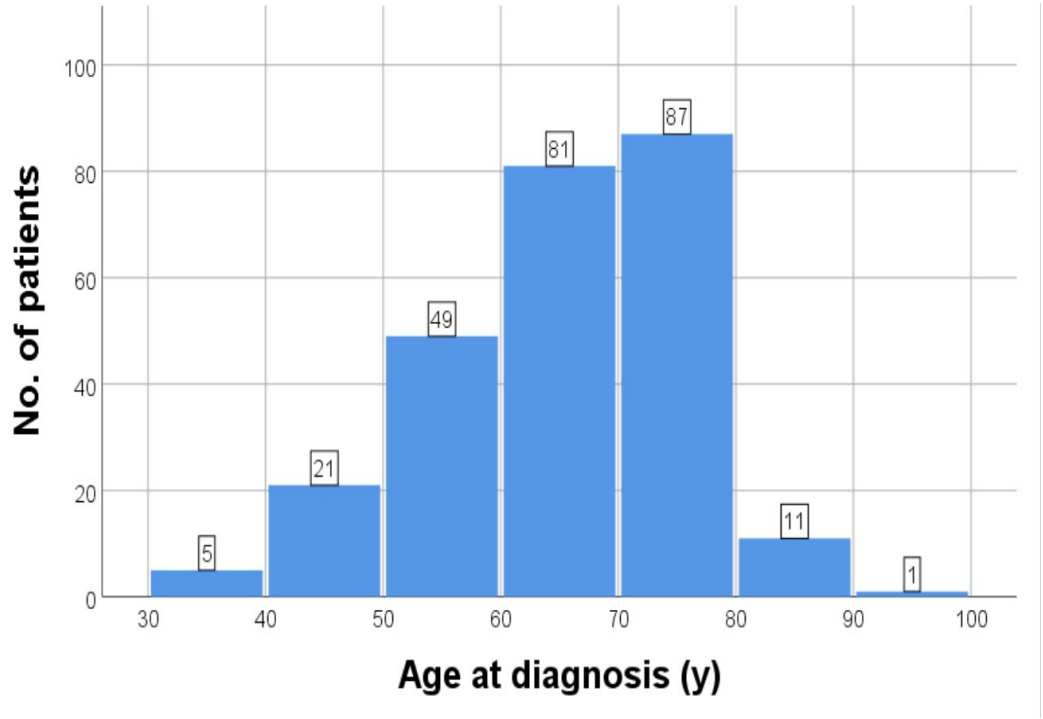

Figure 1. Distribution of patients by age at diagnosis

The average age at diagnosis was similar between men and women (approximately 67 years for men and 66 years for women), with a higher standard deviation among men (11.10) compared to women (10.454), indicating greater variability in the age at diagnosis among men (Table 3).

Tabel 3. Descriptive statistics of age at diagnosis by gender

Descriptives

	Gender			Statistic	Std. Error
Age at diagnosis (y)	Male	Mean		64.79	.970
		95% Confidence Interval for Mean	Lower Bound	62.87	
			Upper Bound	66.70	
		5% Trimmed Mean		65.24	
		Median		67.00	
		Variance		123.200	
		Std. Deviation		11.100	
		Minimum		33	
		Maximum		86	
		Range		53	
		Interquartile Range		15	
		Skewness		-.644	.212
		Kurtosis		.129	.420
	Female	Mean		64.73	.918
		95% Confidence Interval for Mean	Lower Bound	62.92	
			Upper Bound	66.55	
		5% Trimmed Mean		64.86	
		Median		66.00	
		Variance		104.555	
		Std. Deviation		10.225	
		Minimum		37	
		Maximum		91	
		Range		54	
		Interquartile Range		15	
		Skewness		-.275	.217
		Kurtosis		-.250	.431

The analysis of age at diagnosis based on living environment (urban vs. rural) revealed a statistically significant difference between the two groups, as determined by the Mann-Whitney U test (U = 6629.500, Z = -2.185, p = 0.029). Although the median ages at diagnosis were similar between the two environments, the results indicated that the age at diagnosis was significantly lower in the urban environment compared to the rural environment (Table 4 and Figure 2).

Tabel 4. Mann-Whitney U test results for age at diagnosis by living environment

Test Statistics[a]

	Age at diagnosis (y)
Mann-Whitney U	6629.500
Wilcoxon W	17804.500
Z	-2.185
Asymp. Sig. (2-tailed)	.029

a. Grouping Variable: Environment

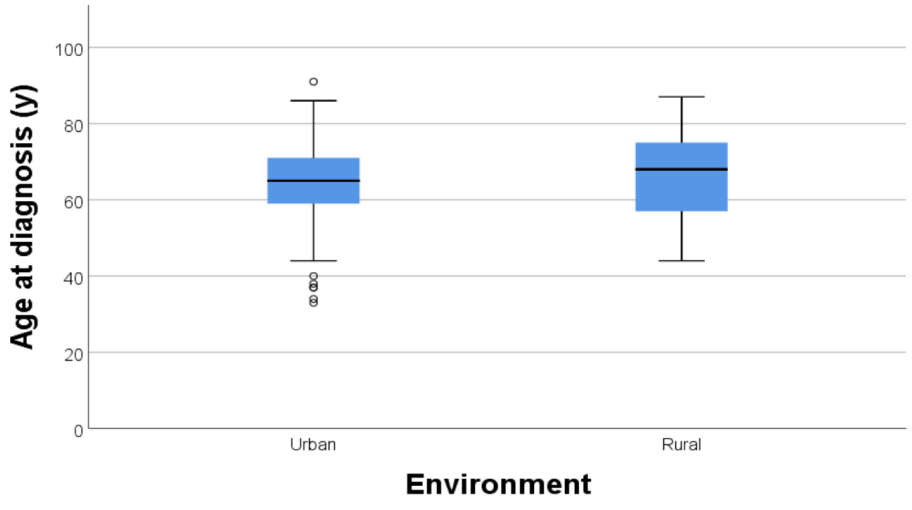

Figure 2. Distribution of age at diagnosis according to living environment (Urban vs. Rural)

Figure 3 shows the distribution of bone lesions among the patients included in the study. Of the total, 69.80% (n = 178) were diagnosed with bone lesions. A smaller percentage, 15.29% (n = 39), had an unknown status regarding bone lesions, while 14.90% (n = 38) did not present any bone lesions. Among patients with bone lesions, 52.2% were men and 47.8% were women. (Figure 3 and Table 5).

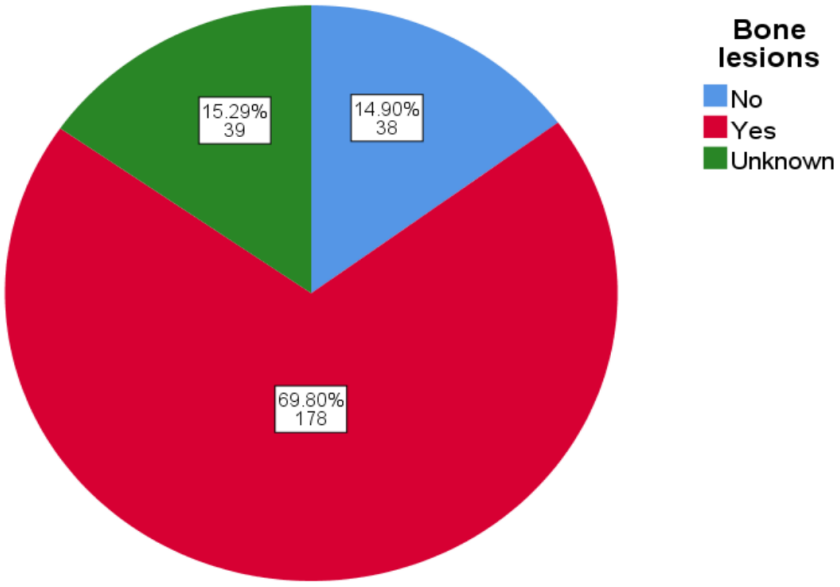

Figure 3. Distribution of bone lesions

Table 5. Distribution of bone lesions by gender

Gender * Bone lesions Crosstabulation

			Bone lesions			
			No	Yes	Unknown	Total
Gender	Male	Count	21	93	17	131
		% within Gender	16.0%	71.0%	13.0%	100.0%
		% within Bone lesions	55.3%	52.2%	43.6%	51.4%
	Female	Count	17	85	22	124
		% within Gender	13.7%	68.5%	17.7%	100.0%
		% within Bone lesions	44.7%	47.8%	56.4%	48.6%
Total		Count	38	178	39	255
		% within Gender	14.9%	69.8%	15.3%	100.0%
		% within Bone lesions	100.0%	100.0%	100.0%	100.0%

In the tables presented below, which describe hemoglobin levels (g/dL) by gender, it is observed that the mean hemoglobin level was statistically significantly higher in men (10.46 g/dL, with a 95% confidence interval ranging from 10.03 to 10.89 g/dL) compared to women (9.72 g/dL, with a 95% confidence interval ranging from 9.36 to 10.07 g/dL). The overall mean hemoglobin level for all patients was 10.10 g/dL. (Table 6, Table 7 and Table 8)

Table 6. Descriptive statistics of hemoglobin levels

Descriptives

			Statistic	Std. Error
Hemoglobin (g/dL)	Mean		10.0993	.14315
	95% Confidence Interval for Mean	Lower Bound	9.8174	
		Upper Bound	10.3812	
	5% Trimmed Mean		10.0244	
	Median		9.7000	
	Variance		5.225	
	Std. Deviation		2.28589	
	Minimum		5.40	
	Maximum		17.10	
	Range		11.70	
	Interquartile Range		3.60	
	Skewness		.481	.153
	Kurtosis		-.531	.304

Table 7. Mann-Whitney U test analysis for comparing hemoglobin levels in patients with and without bone Lesions

Test Statistics[a]

	Hemoglobin (g/dL)
Mann-Whitney U	642.000
Wilcoxon W	873.000
Z	-2.446
Asymp. Sig. (2-tailed)	.014

a. Grouping Variable: Bone lesions

Table 8. Descriptive statistics of hemoglobin levels by gender

Descriptives

	Gender			Statistic	Std. Error
Hemoglobin (g/dL)	Male	Mean		10.4619	.21771
		95% Confidence Interval for Mean	Lower Bound	10.0312	
			Upper Bound	10.8926	
		5% Trimmed Mean		10.3980	
		Median		10.1000	
		Variance		6.209	
		Std. Deviation		2.49183	
		Minimum		6.10	
		Maximum		17.10	
		Range		11.00	
		Interquartile Range		4.40	
		Skewness		.365	.212
		Kurtosis		-.867	.420
	Female	Mean		9.7162	.17825
		95% Confidence Interval for Mean	Lower Bound	9.3634	
			Upper Bound	10.0690	
		5% Trimmed Mean		9.6537	
		Median		9.5000	
		Variance		3.940	
		Std. Deviation		1.98490	
		Minimum		5.40	
		Maximum		14.70	
		Range		9.30	
		Interquartile Range		2.75	
		Skewness		.428	.217
		Kurtosis		-.368	.431

In our study, approximately 10 patients (4%) had hemoglobin levels below 7 g/dL (Figure 4).

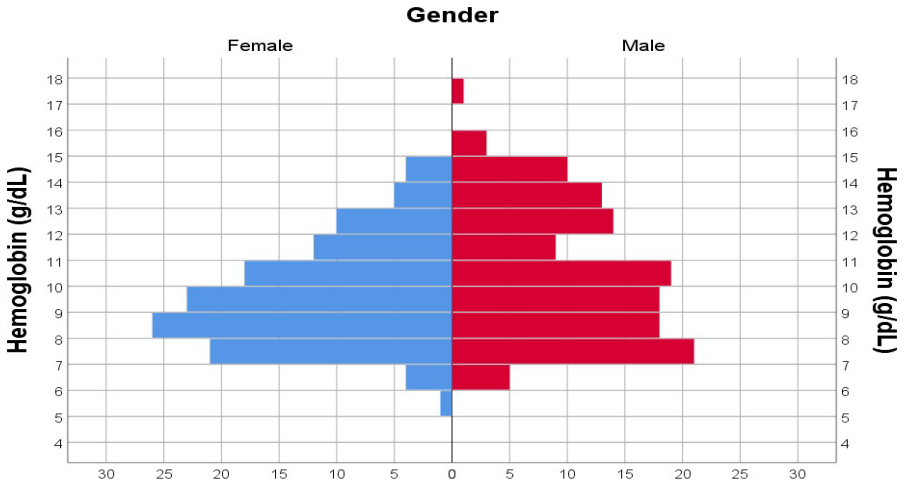

Figure 4. Distribution of hemoglobin levels by gender

The majority of patients, including both men (124) and women (118), had a neutrophil count greater than 1500/µL, indicating that neutropenia was rare in the group (Figure 5).

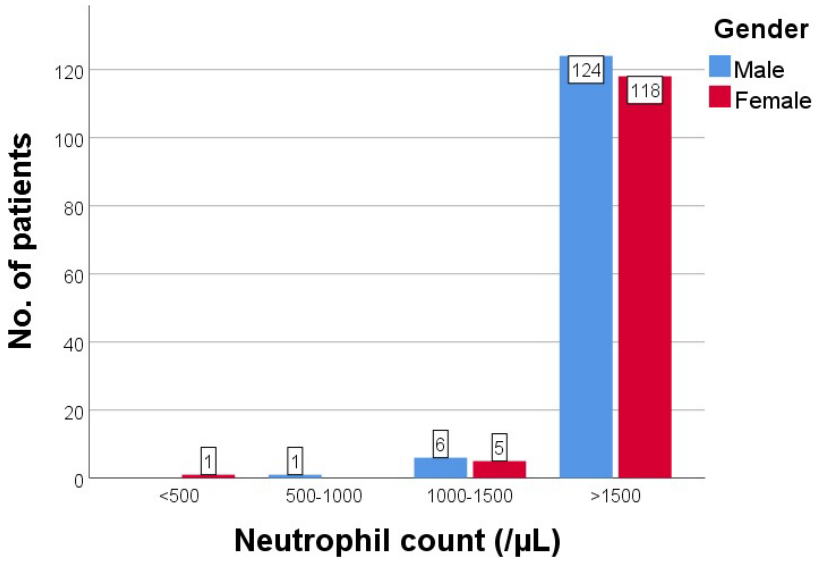

Figure 5. Distribution of neutrophil count by gender

It was observed that the majority of patients, both men and women, had a platelet count above 150,000/µL, with 95 men and 89 women falling into this category. Differences between genders were minimal in the lower platelet count categories, where the number of patients was relatively small in each range. Additionally, the number of patients with very low platelet counts (<20,000/µL) was small (n=4), indicating that severe thrombocytopenia was rare in this cohort (Figure 6).

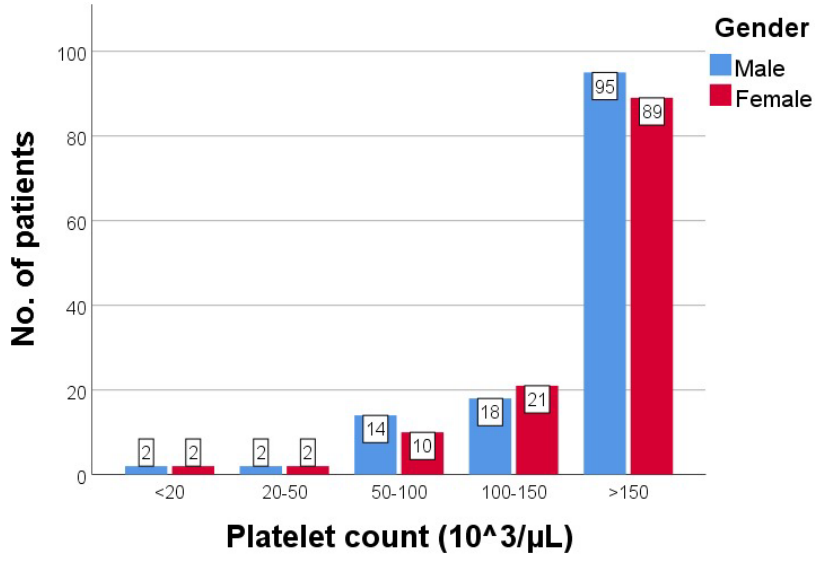

Figure 6. Distribution of platelet count by gender

The majority of MM patients included in this study presented with IgG heavy chains (59.22%) and kappa light chains (43.14%) (Figure 7 and Figure 8).

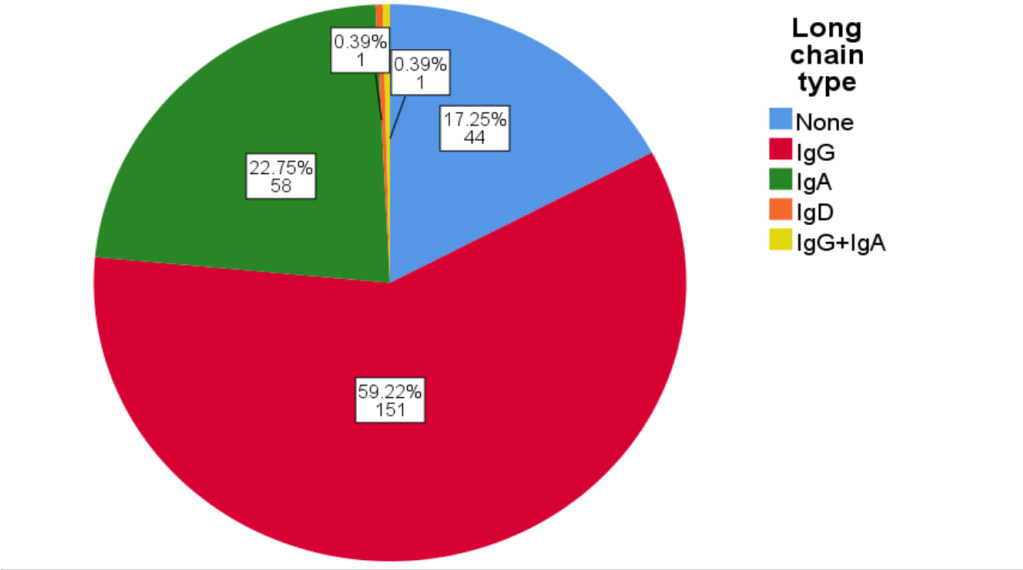

Figure 7. Distribution of immunoglobulin heavy chains

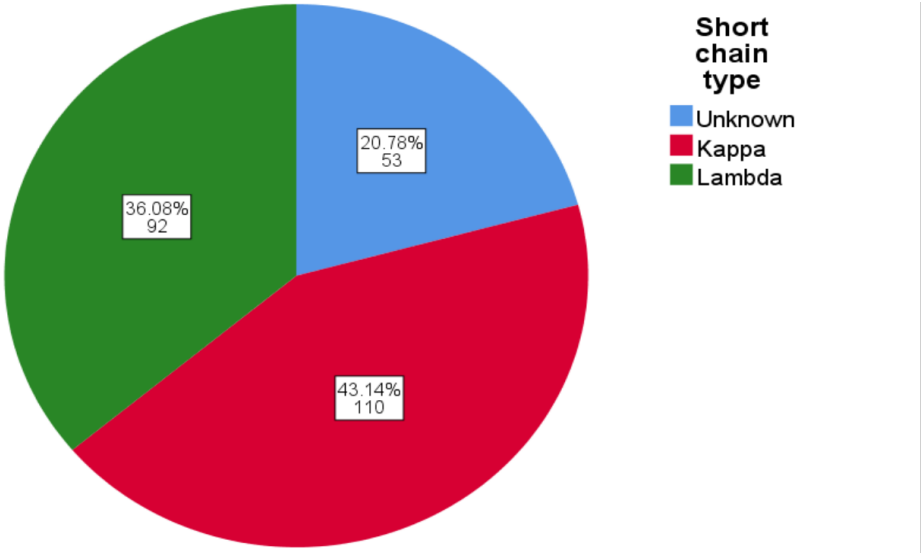

Figure 8. Distribution of immunoglobulin light chains

Approximately 60% of the patients in our cohort had between one and three comorbidities. (Figure 9).

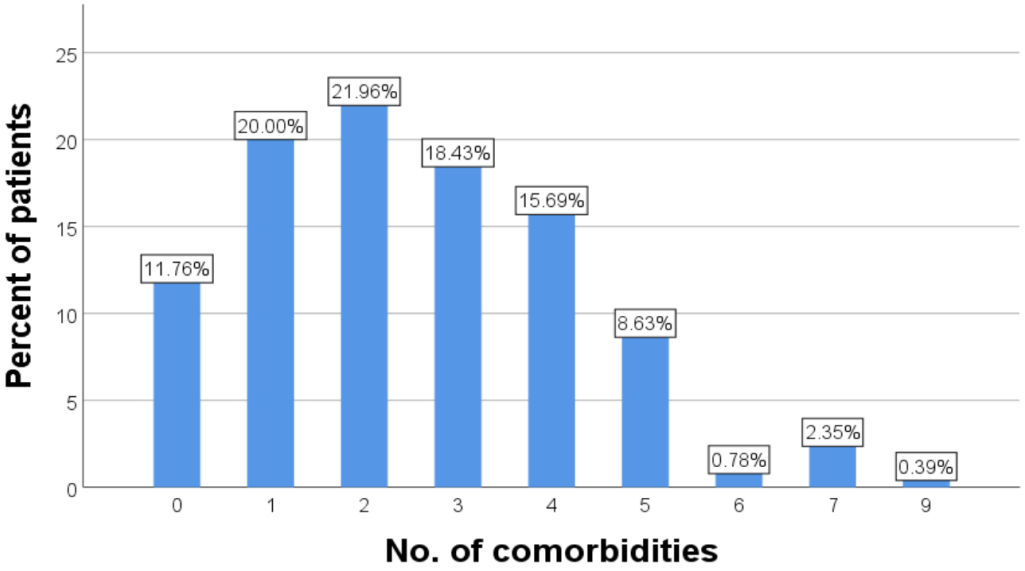

Figure 9. Distribution of the number of comorbidities

Figure 10 presents the types of associated conditions identified among patients. Cardiovascular conditions (62.75%) and gastrointestinal conditions (40.39%) were found to be the most common (Figure 10).

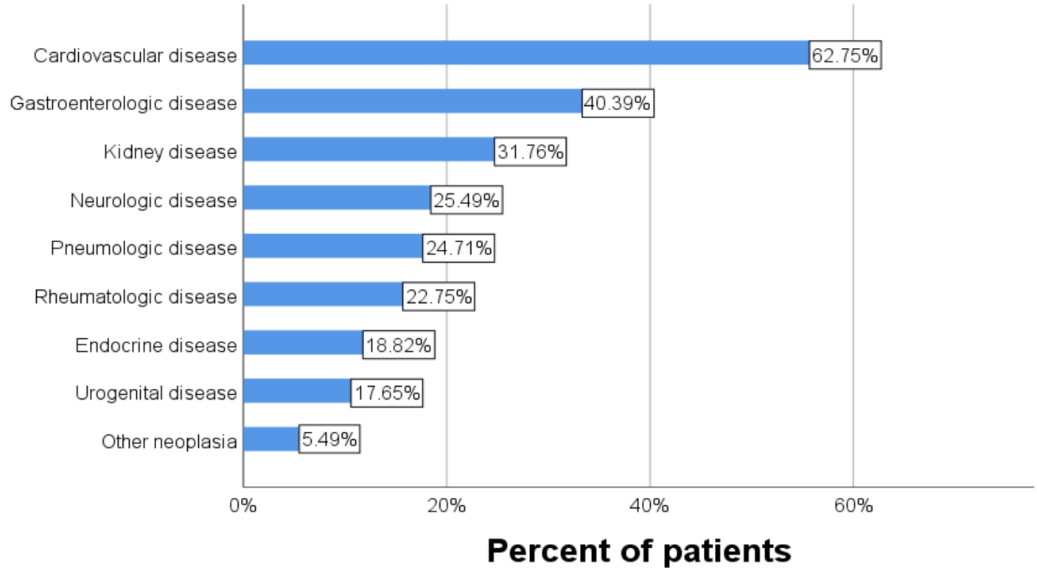

Figure 10. Distribution of comorbidity types

The chart illustrates the percentage of patients who received different treatment regimens for MM. It is observed that the VCD regimen (bortezomib, cyclophosphamide, dexamethasone) was the most frequently used, administered to 36.86% of patients. The next most common treatment regimens were VD (bortezomib, dexamethasone) and DRD (daratumumab, lenalidomide, dexamethasone), used in 15.69% and 12.55% of patients, respectively. Other treatments, such as D-VTD, D-VMP, and VMP, were used in a smaller yet significant percentage of patients. The treatments administered to patients in this study adhered to the therapeutic guidelines for MM valid at the time, ensuring the application of the most effective and up-to-date treatment protocols available (Figure 11).

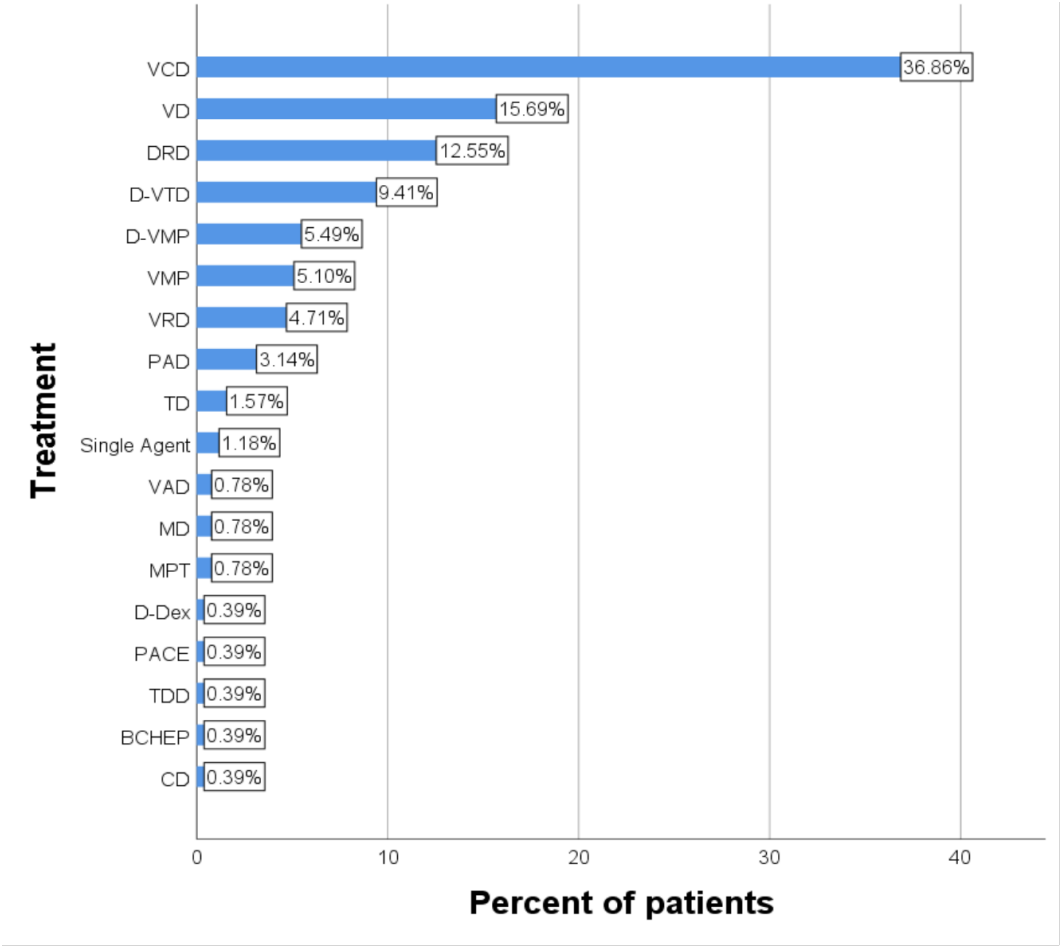

Figure 11. Distribution of treatment types

4. Discussion

International recommendations from organizations such as ASCO, ACSM, ACS, and NCCN, advocate for incorporating physical rehabilitation programs in the therapeutic management plan for cancer survivors [15–18]. The benefits of physical exercise have been demonstrated across various types of solid tumors and have extended to the full spectrum of hematologic neoplasms [10,25,26].

Patients diagnosed with MM experience complex health deteriorations, manifesting through physical, psychological, and emotional dysfunctions. Maintaining a daily routine and engaging in physical activities during treatment

have been associated with fewer side effects, reduced fatigue, and improved quality of life [3]. Decreased functional capacity has been correlated with an increased mortality rate following hematopoietic stem cell transplantation, highlighting the need for early intervention to mitigate physical decline [27,28].

MM is a hematologic malignancy frequently characterized by bone involvement,which often involves unstable lesions and anemia. These factors make physical rehabilitation challenging due to the increased risk of fractures and other complications [29]. These barriers must be carefully assessed and clearly defined to ensure the safe implementation of rehabilitation interventions, allowing MM patients to benefit from the positive effects of physical activity. Pagnotti G.M. et al. demonstrated that repetitive bone loading can promote the normalization of bone formation and resorption processes. Additionally, preclinical studies suggest that these mechanical signals may limit tumor cell proliferation, thereby reducing tumor burden [24].

Our study explored and analyzed the frequency of these challenges at a medical center in Romania. The goal was to identify factors that limit the effective implementation of interventions and to propose solutions to maximize the benefits of physical activity in this population.

Between 2017 and 2023, 255 patients were diagnosed with MM. Our study exclusively included patients with secretory MM, with the IgG subtype being the most frequently observed, consistent with data reported in the literature [30]. A decrease in incidence was observed during the 2020-2022 period, which may be attributed to the onset of the COVID-19 pandemic, a trend observed internationally in multiple types of neoplasms [10,31–33]. Initially perceived as a limiting factor in the provision of physical rehabilitation programs, the implementation of alternative methods through online platforms (applications, websites) has been tested by some researchers, demonstrating their acceptability and feasibility [34–36].

Online exercise programs represent a viable solution for patients facing transportation difficulties. Given that a significant percentage of patients in our study (41.57%) were from rural areas, these programs could have a considerable impact on improving access to necessary treatments. Additionally, our analysis showed that the average age at diagnosis was significantly lower in urban areas compared to rural areas, suggesting that urban residents have easier access to medical services. Transportation concerns have been identified as barriers in several studies [8,37,38]. Other barriers identified in studies include fear of injury and lack of information [24,37]. Therefore, healthcare professionals should address these topics with their patients, limiting self-education from unreliable and non-evidence-based sources.

Our analysis revealed a slight and statistically insignificant gender difference, with a slight male predominance. This result aligns with the literature, which indicates a higher risk of developing MM among men [2]. Dunston et al. found a lower participation rate in physical rehabilitation programs among men [38].

The average age of patients in our study was 67 years for men and 66 years for women, with 66% of patients being over 60 years old. According to data reported by the American Cancer Society, the median age at diagnosis for MM is 69 years, with a range between 65 and 74 years [2]. These observations support the fact that MM is predominantly a condition of middle-aged and older adults.

Given the advanced age and high prevalence of MM among women, osteoporosis is likely to be frequently encountered. The medical records were incomplete and did not include information regarding the presence or severity of osteoporosis in our cohort. Dapunt et al. suggested that assessing osteoporosis should be part of the patient evaluation process before developing an exercise plan, as it can alter fracture risk [39]. QFracture and FRAX® are recommended tools for assessing osteoporosis risk [40].

The presence of bone lesions is not an absolute contraindication for physical activity. However, exercises should be carefully tailored to each patient [41]. It is

essential to avoid high-impact exercises, rotational movements, flexion, and those that generate shearing forces or increased pressure on affected regions [41].

In our cohort, 69.80% had bone lesions. Of these, 52.2% were male and 47.8% were female. Other studies reported higher percentages, up to 80-85% [29,30]. This may be due to more sensitive methods used in the evaluation of lesions. The existing medical information did not allow us to assess the extent of bone involvement. Positron emission tomography-computed tomography (PET-CT) and magnetic resonance imaging (MRI) are considered the most sensitive and specific methods for detecting bone lesions. Although CT has a lower performance compared to the previous methods, it remains an adequate option [42].

Recently, a new system called the Myeloma Spine and Bone Damage Score (MSBDS) has been developed to aid in the evaluation of bone lesions in patients with MM [43]. This system joins other established options for assessing fracture risk, such as the Mirels Score, used for long bones of the upper and lower extremities, and the Spinal Instability Neoplastic Score (SINS), employed for evaluating spinal stability in patients with spinal metastases [44].

Numerous studies propose various types of physical exercises, adapted to different intervals and intensities, with a particular emphasis on personalization. The implementation of these exercises has been evaluated at multiple stages of multiple myeloma (MM) progression, including immediately after diagnosis, during chemotherapy, during hematopoietic stem cell transplantation, during maintenance therapy, and during remission [19–23,45]. The introduction of CAR-T therapy in the treatment of MM underscores the need to investigate the effects of physical rehabilitation in these patients as well [27].

In the absence of standardized protocols, Crevenna R et al. presented an approach model used in Austria, based on a multidisciplinary evaluation of each patient. They proposed the formation of teams composed of specialists from various fields, such as oncology, radiology, radiotherapy, orthopedics, internal medicine, laboratory medicine, sports medicine, nutrition, kinetotherapy, to conduct a detailed patient history, assess comorbidities, and perform comprehensive paraclinical investigations, such as EKG and bone CT. Additionally, they hypothesized, based on their clinical experience, that bone fractures occur more frequently in everyday life when patients pay less attention to how they perform certain movements [40].

The Otago Exercise Program (OEP) is an evidence-based program that combines supervised exercises by a physiotherapist with independently performed exercises at home. The goal of this program is to reduce the risk of falls and improve balance and strength in older adults [46]. Rosko A.E. et al. conducted a feasibility study on a 6-month Otago exercise program. In this study, 30 elderly patients with hematologic malignancies were enrolled, 63% of whom had plasma cell dyscrasias. The evaluation of the results showed that 89% of participants found the program satisfactory and expressed willingness to participate again. Additionally, adherence to the program was higher among patients supervised by a physiotherapist (79%) compared to those who performed the exercises independently at home (66.7%) [37]. These results highlight the importance of professional support to ensure full and effective participation in exercise programs.

A study conducted on 100 MM patients who participated in a precision exercise program (PEP) included both resistance and aerobic exercises. The patients, who were in various phases of treatment, ranged in age from 27 to 83 years, with a median age of 61 years, and the IgG kappa subtype was the most commonly observed. Additionally, 60% of the patients had at least one osteolytic lesion in the spine. The program was conducted at home through a mobile application, following an introductory session provided by a physiotherapist. A primary focus of the precision exercise program (PEP) was the strengthening of core and lower extremity muscles, considering that these areas showed notable weakness, especially following high-dose corticosteroid therapy and hematopoietic stem cell transplantation. The authors

designed a personalized and safe exercise program, even for patients with unstable bone lesions, which led to an improvement in self-efficacy in managing musculoskeletal pain and a reduction in the need for pain control medication. Additionally, patients were advised to engage in moderate aerobic activities for 150 minutes per week and to complete two to three resistance training sessions each week, in accordance with the standards set by the American College of Sports Medicine. The most frequently implemented exercises in the program included coordination activities, such as balance tap, lower body strengthening exercises like squats, sidesteps with a resistance band, and glute bridges. The program also included abdominal muscle strengthening exercises, upper body exercises such as bicep curls and triceps extensions, as well as strengthening of the rhomboid muscles through elastic low rows. Furthermore, the authors suggested that certain aspects should be considered when calculating fracture risk, such as the presence of osteoporosis, diffuse osteolytic infiltration, the existence of vertebral fractures, the stage of the disease and response evaluation, as well as the individual's physical condition [39].

In a study involving 30 patients with MM, 69.2% presented with disseminated bone lesions, and 42.3% had bone fractures without a risk of instability. These patients were included in an outpatient exercise program consisting of resistance and endurance exercises. The resistance exercises were performed on machines targeting major muscle groups, while the endurance exercises were conducted on endurance machines such as ergometric bicycles or cross-walkers. The results showed significant positive improvements in the patients' physical capacity as well as considerable pain relief [47].

Czerwinska-Ledwig O. et al. recommend Nordic walking (NW) as an effective form of physical activity, ommonly used for both elderly individuals and patients with hematologic malignancies. This low-impact exercise involves the use of specially designed poles to engage the upper body muscles, contributing not only to the improvement of overall physical condition but also to increased balance and stability [48].

The Myeloma: Advancing Survival Outcomes Trial (MASCOT) is a randomized controlled clinical trial conducted on 131 MM patients that evaluated the impact of a physical exercise program supervised by physiotherapists on patients who had completed oncologic treatment or were undergoing maintenance therapy. The program included an individually tailored regimen of aerobic and resistance exercises. The aerobic exercises consisted of treadmill walking, ergometer cycling, cross-trainer or stepper workouts, at an intensity ranging from 50% to 75% of the predicted maximum heart rate, with the training duration progressively increased to 30 minutes. The resistance exercises included trunk training as well as upper and lower body workouts using weightlifting equipment, body weight, or resistance bands. The study results indicated significant improvements in lower limb muscle strength and suggested an enhancement in aerobic capacity for participants actively engaged in the program. However, no statistically significant differences were observed between groups regarding fatigue levels [8].

In none of the aforementioned studies were adverse events reported during physical exercises [8,39,47].

Bone involvement in multiple myeloma is the combined result of disease progression and the adverse effects of administered treatments. Although corticosteroids are essential in disease management, they contribute to decreased bone density and muscle strength, thereby increasing the risk of falls and fractures, particularly in elderly patients and during periods of anorexia [6]. Lytic lesions, predominantly located in the axial skeleton, limit physical activity due to fear of further injury or intense bone pain, a common symptom in these patients [39].

The prevalence of pancytopenia poses a significant challenge in designing a physical mobilization plan for patients diagnosed with MM. In our study, a small

percentage of patients (4%) were observed to have hemoglobin levels below 7 g/dL at diagnosis.

In this context, the Canadian Physiotherapy Association has developed specific recommendations. Generally, physical exercise is contraindicated for patients with hemoglobin levels below 7 g/dL due to the increased risk of complications associated with the oxygen transport deficit caused by low hemoglobin levels. However, some studies suggested that physical exercise may be tolerated by patients with hemoglobin levels between 7 and 8 g/dL, although there is an increased risk of cardiovascular and respiratory decompensation [41].

For multiple myeloma patients with thrombocytopenia, the risk of bleeding is considerable. Mobility should be limited to essential activities, such as going to the bathroom, when platelet counts are below 10,000/μL. When platelet counts are between 10,000 and 20,000/μL, light, non-resistance exercises are recommended, such as range-of-motion movements performed while seated or lying down. For platelet counts between 20,000 and 50,000/μL, light resistance exercises using elastic bands are permitted, avoiding activities that involve intense effort or risk of bleeding [41]. In our analysis, 4 patients had platelet counts between 20,000 and 50,000/μL, and 4 patients had counts below 20,000/μL at diagnosis.

Patients with neutropenia should take precautions to reduce the risk of infection, including wearing face masks and maintaining strict hand hygiene before and after exercise. It is recommended that physical therapy and exercises be performed in the patient's room to avoid exposure to infections from common areas or shared equipment [41]. In our study, 1 patient had severe neutropenia below 500/μL.

The need for blood transfusions does not constitute an absolute contraindication for physical exercise, as long as the blood count parameters are above the previously mentioned limits [41].

Another important consideration is the introduction of new criteria for interrupting physical rehabilitation in lymphoma patients, proposed by Moriyama T. et al. These criteria, which included hemoglobin levels between 6.0–7.5 g/dL and platelets between 5,000–20,000/μL, were applied to 153 patients and carefully evaluated by a hematologist, demonstrating their safety [49].

Physical activity has recognized benefits not only in the context of malignant neoplasms but also in other medical conditions [50–53]. Patients diagnosed with MM often present with a complex clinical profile, including multiple comorbidities. Approximately 60% of our cohort had between one and three associated conditions. Cardiovascular involvement was the most frequently encountered, at 62.75%, highlighting the importance of developing appropriate rehabilitation programs to improve quality of life and more effectively manage these types of patients.

To evaluate the effectiveness of rehabilitation programs, various functional tests and standardized questionnaires can be used, including the 6-minute walk test (6MWT), handgrip strength test, International Physical Activity Questionnaire (IPAQ), Falls Efficacy Scale (FES), and quality of life assessment questionnaires such as EORTC QLQ-C30 and its specific module for multiple myeloma patients (QLQ-MY20). The Godin Leisure-Time Exercise Questionnaire (GLTEQ) and the Functional Assessment of Cancer Therapy-General (FACT-G) are also useful [21,28,54,55]. The 6MWT can also serve as a method for identifying patients at increased risk of cancer-related mortality [27].

5. Conclusions

The implementation of physical rehabilitation programs for patients with multiple myeloma presents a challenge for healthcare professionals, primarily due to barriers such as bone lesions and associated pancytopenias. In this context, developing clear guidelines, ensuring adequate logistics, and involving a multidisciplinary team to create a personalized exercise plan can contribute to minimizing the risk of injuries and maximizing the benefits of these programs. Our findings emphasize that, with

careful customization and professional oversight, physical rehabilitation can significantly contribute to the therapeutic management and quality of life for these patients.

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