

Nutritional status, muscle strength and functional capacity in patients with multiple myeloma

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Abstract

Multiple myeloma is a malignant neoplasm characterized by the clonal proliferation of plasma cells in the bone marrow. The objective of this study was to evaluate possible associations between nutritional status, muscle strength and functional capacity of outpatients with multiple myeloma. This is a cross-sectional study carried out on a non-probabilistic sample of patients with multiple myeloma treated at *Hospital das Clínicas*, in Goiânia. Data were collected between August and December 2015, using interviews and information from medical records. Nutritional status was assessed using the Patient-Generated Subjective Global Assessment; muscular strength measured using Hand Grip Strength and functional capacity, using the *Karnofsky* Performance Scale. The study was approved by the Ethics and Research Committee of that hospital. 52 patients were evaluated, of which 48.1% were malnourished, 30.8% had low muscle strength and 73.1% had impaired functional capacity. Muscle strength and functional capacity were lower in malnourished individuals. It was observed that those who used corticosteroids were 18% less likely to become malnourished (OR=0.18; CI=0.05-0.62; p=0.011), however, it is important to consider the possible causes of bias; on the other hand, patients with low muscle strength or undergoing chemotherapy were approximately four times more likely to be malnourished, respectively (OR=3.46; CI=0.99-12.08; p=0.047) (OR=3.64; CI=1.13-11.69; p=0.027). It was concluded that malnutrition is common in patients with multiple myeloma, indicating the pressing need for appropriate and early nutritional intervention.

Keywords: Nutritional Assessment. Hand Grip Strength. *Karnofsky* Scale. Hematological Neoplasms.

INTRODUCTION

Multiple myeloma (MM) is a malignant neoplasm, characterized by the clonal proliferation of plasma cells in the bone marrow and accounts for approximately 10.0% of hematological malignancies worldwide^{1,2}. MM is slightly more common in men than in women, twice as common in people of African descent than in Caucasians and the average

age at diagnosis is approximately 65 years^{2,3}.

In 2023, 35,730 new cases of MM were diagnosed in the United States, representing 1.8% of all cancers⁴. According to the Brazil Oncology Panel, in the same year, 2,114 cases of MM were diagnosed⁵. In South America, the incidence rate is about 1.7 cases/100,000⁶. Higher incidence and mortality

from MM have been reported in high-income countries. However, other authors observed such conditions in developing countries, thus showing the heterogeneity of this cancer^{7,8}.

When diagnosing MM, anemia, fatigue and bone pain are the most common symptoms. Clinical changes such as osteolytic lesions, kidney damage and hypercalcemia may also be present⁹. Despite advances in treatment, MM remains virtually incurable and patients face a refractory disease, with progressive symptoms and therapy-related problems¹⁰. Both the disease, which leads to increased nutritional demand and metabolic changes, and its treatment can impair adequate food intake and, consequently, lead to compromised nutritional status^{11,12}.

Malnutrition in patients with MM has also been associated with decreased muscle strength, worsened quality of life and prognosis, lower survival, reduced response to specific treatments and greater chemotherapy toxicity^{13,14}. The continuous assessment of nutritional status, in addition to investigating

muscle strength and functional capacity, are relevant aspects. It is essential that the detection, prevention and treatment of malnutrition are carried out as early as possible in these patients^{15,16}.

In view of the increased incidence, prevalence and mortality of MM and its slow and chronic development with significant impairment of patient nutrition, health and quality of life, it is considered essential to understand the relationship between nutritional status, muscle strength, functional capacity and its associated factors. When verifying the scarcity of studies with this specific theme, with a view to controlling these undesirable outcomes in the clinical approach, the need for this type of investigation is justified.

The hypothesis of the present study was that malnourished MM patients have lower muscle strength and greater impairment of functional capacity. Its objective was to evaluate possible associations between nutritional status, muscle strength and functional capacity in outpatients with multiple myeloma.

METHOD

This is an analytical cross-sectional study, carried out at the Multidisciplinary Outpatient Clinic for Chronic Lymphoproliferative Diseases of the *Hospital das Clínicas* of the Federal University of Goiás (HC-UFG/EBSERH), from August to December 2015.

Among the inclusion criteria, the following stand out: patients aged 20 years or over, of both genders, diagnosed with MM, who were undergoing specific multidisciplinary outpatient follow-up during the research period. Those patients who were unable to answer the research questionnaire, or because they did not have companions to assist them, were excluded.

The study population corresponded to the total number of patients seen at the outpatient clinic (n=55). Three patients who were unable to respond to the Patient-Generated Subjective Global Assessment (PG-SGA) were excluded. The non-probabilistic study sample consisted of 52 patients, that is, 94.5% of the availab-

le population, as they were those invited who agreed to be research volunteers.

Data collection was carried out by resident nutritionists from the Multidisciplinary Residency Program in Hematology and Hemotherapy at HC-UFG/EBSERH, at the MM multidisciplinary outpatient clinic. Patients were approached during the care period by the team. A structured questionnaire was applied to obtain identification, socioeconomic and demographic data, and, when necessary, medical records were consulted. The data collected and analyzed were: sex, age, marital status, income, comorbidities, use of corticosteroids, chemotherapy, time since diagnosis, nutritional status, muscle strength and functional capacity.

The PG-SGA, developed by Ottery (1996)¹⁷ and validated by Gonzalez *et al.* (2010)¹⁸, was used to assess nutritional status and detect nutritional risk. The instrument was completed in two stages, the first

being answered by the patient or, when necessary, with the help of the companion, and the second, by the researchers.

A numerical score is generated for each item evaluated, including weight, food intake, symptoms, activity and function, percentage of weight loss, diseases and nutritional needs, metabolic demand and physical examination. The sum of the scores is used to verify the presence of nutritional risk and define specific interventions. Results between zero and one indicate that there is no need for intervention at that moment; between two and three points, the patient and their family member should be approached for food and nutritional education; between four and eight, nutritional intervention is carried out; and equal to or greater than nine, there is a critical need for action by the nutrition team¹⁸.

After completing the PG-SGA data, the patients' nutritional status is classified as: A - well nourished, B - moderate malnutrition or suspected malnutrition and C - severely malnourished¹⁸. To verify the association between the variables of interest in the study, individuals were grouped into two categories: well-nourished (category A) and malnourished (categories B and C).

In addition to PG-SGA, Hand Grip Strength (HGS) was measured to measure the patients' muscle strength. Using a *Takei*[®] portable mechanical dynamometer variation 1-100 kgf and precision of 0.5 kgf, the test was performed on the dominant (DHGS) and non-dominant (NDHGS) upper limb, in a sitting position, with the hips, knees and elbows flexed at 90°, with the forearm in a neutral position. The individual was instructed to apply as much force as possible to the equipment for three seconds. Three measurements were taken on each hand with a one-minute rest interval and the arithmetic mean of the force used in each hand was used as the final measurement¹⁹.

Additionally, the difference in the means of the DHGS and NDHGS measurements was tested using the Student's t test and, as there was no significant difference ($p=0.368$) between the means of the two hands, it was decided to use, in the analysis, the measurement

of the dominant hand. Due to the lack of a cutoff point for classifying HGS values in MM patients, reference values for the healthy Brazilian population were used. Patients who had a HGS lower than the 10th percentile ($HGS < p_{10}$) were classified as "low muscle strength" and those with an HGS greater than or equal to the 10th percentile ($HGS \geq p_{10}$) were classified as "preserved muscle strength"²⁰.

In assessing functional capacity, the *Karnofsky Performance Scale* (KPS) was used, which makes it possible to portray the individual's ability to perform their daily activities. This scale is made up of 11 performance levels, ranging from 0 to 100, divided into intervals of 10, with 100 indicating full health and zero, death²¹.

The KPS was applied by the nursing team and the result was recorded in the medical record, on the same day as the other assessments. In this study, patients who obtained KPS values ≤ 70 were considered to have severely impaired functional capacity, values between 80-90, moderately impaired, and those who obtained $KPS \geq 90$, normal²¹.

The data were entered into a *Microsoft Excel Software* spreadsheet (2007), in double entry and, after checking and consolidation, they were analyzed using the *STATA*[®] statistical package version 12.0. Categorical variables were presented in simple frequency.

To verify the differences between the means of the FAM and KPS variables, according to the PG-SGA categories and scores, the *Kruskall-Wallis* test was performed, and the statistical significance of the differences was verified using the *Bonferroni* test. Data normality was assessed using the *Kolmogorov Smirnov* test. The associations between the independent variables and the outcome (malnutrition) were evaluated using a logistic regression model. In the univariate analysis, the independent variables were tested one by one, so that all variables whose $p < 0.20$ were included in the adjusted (multivariate) model. The variables with $p < 0.10$ remained in the final model and those with $p < 0.05$ and a confidence interval of 95.0% were considered significant.

Individuals were informed about the objectives, risks and benefits of the research and those

who agreed to participate signed the Free and Informed Consent Form (FICF). The study was approved by the Ethics and Research Commit-

tee of the *Hospital das Clínicas* of the Federal University of Goiás, under protocol number 1083367, CAAE 44464015.0.0000.5078.

RESULTS

The demographic, socioeconomic and clinical characteristics of the study population are presented in Table 1. Among the participants, 80.8% had associated comorbidities, the most frequent of which were: Systemic Arterial Hypertension (48.1%), Cardiovascular Disease (15.4%), Kidney Disease (13.5%) and Type 2 Diabetes Mellitus (11.6%) (Table 1). The presence of gastrointestinal symptoms was found in 76.9%, with xerostomia (44.2%), nausea and vomiting (42.3%), anorexia (32.7%) and dysgeusia (25.0%), the most prevalent.

The frequencies of malnourished patients, according to the variables studied, are presented in Table 1. The prevalence of malnutrition was 48.1%, and 11.6% were severely malnourished. The median DHGS was 21.33 Kgf and the KPS was 90. Muscle strength was preserved in 69.2% and functional capacity was compromised in 73.1%, with 17.3% having severely impaired functional capacity, require assistance and are unable to continue their normal activities or perform active work ($KPS \leq 70$) (Table 1). The mean DHGS was 23.77 ± 8.98 kgf and approximately 30.0% of patients were classified

as having low muscle strength ($DHGS < p10$) (Table 1). For NDHGS, the mean was 23.33 ± 9.15 kgf, similar to FAMD.

Regarding the nutritional screening score to define specific nutritional interventions, 84.6% of patients needed nutritional intervention and, in 46.1%, the requirement was critical (Table 2). Table 2 also presents the average muscular strength and functional capacity, which were significantly lower in the categories of severely malnourished and in critical need of nutritional intervention.

In the univariate regression analysis, the variables that entered the model were: marital status, use of corticosteroids, muscle strength (DHGS and NDHGS), functional capacity (KPS) and chemotherapy. Patients who used corticosteroids had 18.0% less chance of malnutrition ($OR=0.18$; $CI=0.05-0.62$; $p=0.011$); on the other hand, those who had impaired muscle strength in their dominant hand or were undergoing chemotherapy had approximately four times more chances of nutritional deficit, respectively ($OR=3.46$; $CI=0.99-12.08$; $p=0.047$) ($OR=3.64$; $IC=1.13-11.69$; $p=0.027$) (Table 3).

Table 1 - Demographic, socioeconomic, clinical and nutritional characterization of patients with multiple myeloma treated at an outpatient clinic in the city of Goiânia-GO, 2015 (n=52).

Variables	Frequency n (%)	Malnutrition n (%)
Sex		
Female	31 (59.6)	15 (48.4)
Male	21 (40.4)	10 (47.6)
Age (years)		
20-59	20 (38.5)	11 (55.0)
≥ 60	32 (61.5)	14 (43.8)
Marital status		
Single	03 (5.8)	1 (33.3)
Married	32 (61.5)	13 (40.6)

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Variables	Frequency n (%)	Malnutrition n (%)
Divorced	05 (9.6)	3 (60.0)
Widowed	12 (23.1)	8 (66.7)
Income (minimum wages*)		
2-4	25 (48.1)	13 (52.0)
<2	27 (51.9)	12 (44.4)
Use of Corticosteroids		
No	33 (63.5)	11 (33.3)
Yes	19 (36.5)	14 (73.7)
Chemotherapy		
No	31 (59.6)	11 (35.5)
Yes	21 (40.4)	14 (66.7)
MM diagnosis time (years)		
< 2	31 (59.6)	16 (51.6)
2-4	11 (21.2)	3 (27.3)
>4	10 (19.2)	6 (60.0)
Systemic arterial hypertension	25 (48.1)	12 (48.0)
Cardiovascular disease	8 (15.4)	2 (25.0)
Kidney disease	7 (13.5)	5 (71.4)
Diabetes	6 (11.5)	2 (33.3)
Dominant Hand Grip Strength (DHGS)		
Preserved muscle strength ($\geq p10$)	36 (69.2)	14 (38.9)
Low muscle strength ($< p10$)	16 (30.8)	11 (68.8)
Functional Capacity (KPS)		
Normal	14 (26.9)	2 (14.3)
Moderately impaired	29 (55.8)	17 (58.6)
Severely impaired	09 (17.3)	6 (66.7)

*The value of the minimum wage in Brazil, in 2015, was R\$788.00 (seven hundred and eighty-eight reais);
KPS: *Karnofsky Performance Scale*.

Table 2 - DHGS and KPS values according to the nutritional status and the score of need for nutritional intervention by the PG-SGA of patients with multiple myeloma, treated at an outpatient clinic in the city of Goiânia-GO, 2015 (n=52).

Variables	n	(%)	DHGS* (kgf)	p	KPS*	p
PG-SGA				0.006		0.001
A	27	51.9	26.83±9.98A		90.0±13.59A	
B	19	36.5	22.23±5.85B		84.7±9.64B	
C	06	11.6	14.93±5.29C		68.3±11.69C	
Nutritional intervention score				0.004		0.001
0-3	08	15.4	32.93±11.38A		98.7±3.53A	
4-8	20	38.5	24.90±7.87B		88.5±14.24B	
≥9	24	46.1	19.78±6.42C		78.7±11.16C	

*Values presented as mean and standard deviation.

PG-SGA: Patient-Generated Subjective Global Assessment; DHGS: Dominant Hand Grip Strength; KPS: *Karnofsky Performance Scale*; Nutritional status classification – A: well nourished; B: moderately malnourished and C: severely malnourished.

Nutritional intervention score: 0-3: no need for nutritional intervention; 4-8: requires nutritional intervention; ≥ 9: critical need for nutritional intervention.

Table 3 - Association test and odds ratio of malnutrition with independent variables in patients with multiple myeloma treated at an outpatient clinic in the city of Goiânia-GO, 2015 (n=52).

Variables	Malnutrition	
	OR (CI-95%)	P
Marital status		
With partner	1.00	
No partner	2.19 (0.71-6.85)	0.25
Use of Corticosteroids		
No	1.00	
Yes	0.18 (0.05-0.62)	0.011
Dominant hand muscle strength		
Preserved	1.00	
Low	3.46 (0.99-12.08)	0.047
Non-dominant hand muscle strength		
Preserved	1.00	
Low	3.76 (0.87-16.29)	0.06
Functional capacity		
Preserved	1.0	
Limited	2.52 (0.56-11.45)	0.22
Chemotherapy		
No	1.00	
Yes	3.64 (1.13-11.69)	0.027

OR: odds ratio; CI: Confidence Interval.

DISCUSSION

The study was conducted with approximately half of the sample with compromised nutritional status, according to the PG-SGA, and with more than $\frac{3}{4}$ of outpatients with MM in need of intervention according to the nutritional risk score. It is noteworthy, therefore, that even in patients receiving assistance, malnutrition was present and could negatively impact the response to antineoplastic treatment and reduce quality of life, in addition to increasing post-surgical complications, due to the risk of infections²².

It was observed that more than two thirds

of patients had symptoms related to the gastrointestinal tract, a condition that generates an inability to consume adequate food and can negatively contribute to nutritional status. In addition to the metabolic stress produced by cancer, which causes physiological changes that interfere with the ingestion, digestion and adequate absorption of food, the presence of xerostomia, nausea, vomiting and dysgeusia, increase the mortality rates of patients with hematological neoplasms²³.

In cancer patients, especially, the identifica-

tion of nutritional status is crucial for adequate and early intervention, avoiding the evolution of malnutrition. The methods chosen for nutritional assessment, on an outpatient basis, depend on the time available for assessment, the level of detail for prescribing the nutritional intervention and the available equipment²⁴.

Currently, there is a wide variety of techniques for determining nutritional status. Among them, PG-SGA is widely used in cancer patients as it is an easy, practical, non-invasive and effective method in clinical practice^{15,25}. In this method, the classification of nutritional status is based on the interpretation of several factors, such as recent changes in body weight, appetite, food intake, presence of gastrointestinal symptoms, change in functional capacity, presence of comorbidities and physical characteristics of the patient^{26,27}.

In a study carried out with patients with hematological malignancies, evaluated by the PG-SGA, the authors observed that 62.73% had moderate malnutrition¹¹. This value is considerably higher than that found in the present study (36.5%), carried out with outpatients with MM, possibly due to the fact that the studied population was hospitalized individuals.

A retrospective study evaluated, using the PG-SGA, 216 Asian patients, adults and elderly people with MM, and found a higher prevalence of malnutrition (71.2%)¹⁵ than the present study. This result was possibly due to the fact that the majority of patients were in intermediate stage of cancer. According to the authors, the ASG-PPP should be an integral part of the clinical assessment, considering that it detects nutritional changes early and identifies the urgent need for team interventions, prior to chemotherapy¹⁵.

Among the important parameters for identifying protein-energy malnutrition are the decrease in muscle mass and strength, and functional capacity. Palmar dynamometry can be a simple, fast and non-invasive way of nutritional assessment, according to the National Consensus on Oncological Nutrition (INCA, 2015)²⁸. In the present study, it was observed that DHGS reduced significantly with the worsening of malnutrition, corroborating another study with a similar

methodology. This was carried out with 76 oncology patients, including hematology, and verified the presence of significantly lower handgrip strength in severely malnourished compared to well-nourished patients¹⁹.

FAM is a functional test widely used to assess muscle strength and functional status in cancer patients. Prospective study, which included 333 European patients with advanced stage cancer, identified a mean FAM value of 31.2 ± 11.9 kgf, 18.0% lower than healthy controls²⁹, findings greater than those obtained in the present study, having in view of the characteristics of the population evaluated. FAM has been associated with increased mortality, reduced overall functional status, and decreased physical performance²⁹.

However, a multicenter, retrospective and observational study with 11,314 patients with different types of cancer, carried out in China, found that FAM was positively correlated with KPS, among other variables, but had a low contribution to the diagnosis and identification of malnutrition³⁰. They concluded that, as FAM is an index that can be affected by a variety of factors, determining cutoff points to identify malnutrition is challenging and, therefore, FAM has limited use as a predictor of nutritional status.

Malnutrition has also been associated with decreased functional capacity, therefore KPS can be a significant predictor of survival and institutionalization time, especially for the elderly. Malnourished patients are more dependent on activities of daily living and cancer, as well as its treatment, can negatively impact physical function, with consequent functional decline and increased dependence to perform these activities³¹. However, it is recognized that KPS is often overestimated and does not reflect the entire functional status, requiring the development of new and reliable tools to assess patients' vulnerability to guide therapeutic decisions³².

In the present study, KPS values were directly associated with the nutritional status assessed by the ASG-PPP and, conversely, with the need for nutritional intervention. Patients with a low KPS value have lower overall survival, which is worrying since we found 17.3%

of individuals with $KPS \leq 70$. These results were lower than those evaluated in elderly people ($n=24$) in a health care service. home care, among which 62.5% had an early indication of palliative care assistance³¹.

A prospective study with a six-year follow-up analyzed the existence of comorbidities, frailty and disability in 801 patients with MM and revealed that approximately 94.0% of these had some functional impairment ($KPS < 90$), of which 56.0 % had severely impaired functional capacity ($KPS \leq 70$)³³. These results were higher than those found in the present study, possibly due to the degree of organ involvement, presence of cytogenetic changes, higher stages of the disease and adverse laboratory values of this sample.

A study that evaluated the quality of life and functional capacity of 29 patients with cancer, 10 gastric and 19 hematological, found that, in both situations, there was a reduction in quality of life, and the KPS values in hematological cancers were significantly smaller when compared to gastric ones. In this group, a negative correlation was also found between KPS and symptoms ($r = -.495$, $p = 0.031$), and KPS and the total sum of the Quality of Life Questionnaire-Core³⁰ by the European Organization for Research and Treatment of Cancer (EORTC QLQ-C30) ($r = -.580$, $p = 0.009$)³⁴. The assessment of functionality, when referring to the ability to perform activities of daily living efficiently and independently, is essential as it identifies risks of functional incapacity, allows us to outline better forms of rehabilitation and gain the patient's co-participation in their treatment³⁵.

Regarding the treatment of MM, several medications are used and therapeutic options have expanded in recent years. The aim of therapy is to control disease progression, with acceptable adverse events, and maintain quality of life for as long as possible. The indication of medications must be individualized and consider age, comorbidities, KPS value and preferences, as well as the duration of response to previous treatments, cytogenetic risk, adverse reactions, among others³⁶.

In treatment, the corticosteroids used can generate adverse effects such as increased

appetite and water retention, and consequently, accumulation of adipose tissue and edema, promoting weight gain³⁷. In the present research, individuals who used such medications obtained lower scores in the initial PG-SGA questions, filled out by the patient, corresponding to weight, food intake, symptoms, and activities and function. Therefore, when relating the use of corticosteroids and their association with nutritional status, patients had lower chances of malnutrition, and, in this case, it is necessary to consider possible analysis biases.

On the other hand, both drug treatment and neoplasia lead to systemic inflammation and changes in the individual's body composition due to increased catabolism and inhibition of protein synthesis. Furthermore, by promoting negative nitrogen balance, it reduces muscle strength, causes malnutrition and compromises quality of life³⁸. A study carried out with 22 individuals undergoing outpatient chemotherapy treatment demonstrated a significant reduction in DHGS and NDHGS in women aged 40 to 59 years ($KS = 1.15$; $p < 0.0001$) and over 60 years ($KS = 1.42$; $p = 0.035$) and in elderly men ($KS = 2.39$; $p < 0.0001$), undergoing chemotherapy treatment³⁹.

Due to its systemic effect, chemotherapy presents several undesirable symptoms such as: pain, nausea, vomiting, diarrhea, change in taste, malabsorption, xerostomia, dysphagia, constipation, among others. Consequently, these symptoms reduce food intake and lead to depletion of nutritional status¹⁴.

As malnutrition is a frequent complication in these cases, it is highlighted that the assessment of nutritional status, muscle strength and functional capacity are important aspects to be considered in the treatment of onco-hematological individuals, as they can directly interfere with the prognosis of the disease. Both the PG-SGA, FAM and KPS are instruments that are easy to apply in clinical practice and guide early nutritional therapy with a view to preventing malnutrition, maintaining or recovering nutritional status. Furthermore, adequate nutritional management controls side effects, improves the immune response, reduces hospital

stay time and promotes quality of life⁴⁰.

As a differential of this study, its originality stands out as it allowed the nutritional status of these patients to be assessed on an outpatient basis, quickly and practically, enabling early

and individualized interventions, when necessary. On the other hand, a limiting factor was the convenience and non-probability sample, which did not allow analyzing the distribution by gender and MM subgroups.

CONCLUSION

Malnutrition was present in almost half of patients with MM, more than two thirds had preserved muscle strength and almost one fifth had severely compromised functional capacity. In relation to DHGS, almost a third of the sample was classified as having low muscle strength. Regarding the nutritional screening score to define specific nutritional interventions, the majority of patients needed nutritional intervention and, in almost half of these, the requirement was critical.

Mean muscle strength and functional capacity were significantly lower in the categories of severely malnourished and in critical need of nutritional intervention. The impairment of nutritional status was greater when DHGS was not preserved or in the presence of chemotherapy treatment, the latter being a situation that must

be carefully evaluated, considering its systemic interface. Furthermore, a condition stands out that requires special attention in interpretation, due to variables that can interfere with outcomes in different ways, such as in cases of corticosteroid use, as they present a lower chance of malnutrition.

The interrelationship and interdependence between nutritional status, muscle strength and functional capacity is reinforced when monitoring outpatients with MM and the necessary care in clinical practice, as surveillance and monitoring must be intensified to improve the quality of life as a whole. This research suggests that longitudinal and nutritional intervention studies should be carried out to recover or prevent the worsening of nutritional status and obtain a more effective response from drug or surgical treatment.

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