QUALITY OF LIFE AND ASSOCIATED FACTORS IN ELDERLY PEOPLE WITH MULTIPLE MYELOMA TREATED IN THE UNIFIED HEALTH SYSTEM (SUS)

QUALIDADE DE VIDA E FATORES ASSOCIADOS EM IDOSOS COM MIELOMA MÚLTIPLO TRATADOS NO SISTEMA ÚNICO DE SAÚDE (SUS)

CALIDAD DE VIDA Y FACTORES ASOCIADOS EN PERSONAS MAYORES CON MIELOMA MÚLTIPLE ATENDIDAS EN EL SISTEMA ÚNICO DE SALUD (SUS)

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ABSTRACT

Multiple Myeloma (MM) is a plasma cell cancer that mainly affects the elderly population, with an average age of 70 years. It represents around 2% of cancers and ranks second among hematological neoplasms. Despite the improvement in survival of individuals with MM, it is still an incurable pathology marked by relapses and remissions. Impacts of the disease on the Health-Related Quality of Life (HRQoL) of these elderly people are observed. In patients living with cancer, the factors that negatively affect HRQoL, when minimized, lead to better clinical outcomes. The present study aimed to evaluate HRQOL and associated factors in elderly people with MM in first line of treatment or relapses, treated at the Hospital das Clínicas of the Federal University of Pernambuco (HC-UFPE). This is a cross-sectional, quantitative study where participants were characterized from a sociodemographic and clinical point of view and comparisons were made with HRQoL scores. HRQoL was assessed using the following questionnaires: Quality of Life Questionnaire of European Organization Research for Treatment of Cancer (EORTC-QLQ C-30) and Quality of Life Questionnaire of Multiple Myeloma-20 (EORTC QLQ-MY20). Of the 27 patients included, the majority are between 60 and 69 years old, are black, married, have low education, IgG Kappa subtype, less than 5 years of illness, submitted to only one line of treatment, with no history of Bone Marrow Transplant (BMT), present multimorbidity and polypharmacy, good performance status index and advanced staging. Low education, widowed/divorced, multimorbidity and

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worse Performance Status demonstrated significant deterioration in HRQoL. Contemplating and controlling the multifactorial aspects of elderly people with MM are strategies to improve HRQoL.

Keywords: Aged. Multiple Myeloma. Quality of Life.

RESUMO

O mieloma múltiplo (MM) é um câncer de células plasmáticas que acomete principalmente a população idosa, com idade média de 70 anos. Ele representa cerca de 2% dos cânceres e ocupa a segunda posição, dentre as neoplasias hematológicas. Apesar da melhora da sobrevida dos indivíduos com MM, esta patologia ainda é considerada como incurável, marcada por recaídas e remissões, com impacto sobre a qualidade de vida relacionada à saúde (QVRS) das pessoas acometidas por ela. Em pacientes convivendo com o câncer, os fatores, que interferem negativamente na QVRS, quando minimizados, acarretam melhores desfechos clínicos. O presente estudo objetivou avaliar a QVRS e os fatores associados em idosos com MM em 1ª linha de tratamento ou recaídos, tratados no Hospital das Clínicas da Universidade Federal de Pernambuco (HC-UFPE). Trata-se de um estudo transversal, quantitativo, no qual os participantes foram caracterizados do ponto de vista sociodemográfico e clínico e foram obtidas comparações com os escores de QVRS. A QVRS foi avaliada a partir dos questionários: Quality of Life Questionnaire of European Organization Research for Treatment of Cancer (EORTC-QLQ C-30) e Quality of Life Questionnaire of Multiple Myeloma-20 (EORTC QLQ-MY20). Dos 27 pacientes incluídos, a maioria se encontra entre 60 e 69 anos, são pretos e/ou pardos, casados, possuem baixa escolaridade, subtipo IgG Kappa, com menos de 5 anos de doença, submetidos apenas a uma linha de tratamento, sem passado de transplante de medula óssea (TMO), apresentam multimorbidade e polifarmácia, bom índice de desempenho e estadiamento avançado. Baixa escolaridade, viúvos e/ou divorciados, multimorbidade e pior "Performance Status" demonstraram deterioração significante na QVRS. Contemplar e controlar os aspectos multifatoriais dos idosos com MM são estratégias para melhorar QVRS.

Palavras-chave: Idoso. Mieloma Múltiplo. Qualidade de Vida.

RESUMEN

El mieloma múltiple (MM) es un cáncer de células plasmáticas que afecta principalmente a la población de edad avanzada, con una edad media de 70 años. Representa aproximadamente el 2% de los cánceres y ocupa el segundo lugar entre las neoplasias hematológicas. A pesar de la mejora en las tasas de supervivencia de las personas con MM, esta enfermedad aún se considera incurable, caracterizada por recaídas y remisiones, lo que afecta a la calidad de vida relacionada con la salud (CVRS). En pacientes con cáncer, los factores que afectan negativamente la CVRS, al minimizarse, conducen a mejores resultados clínicos. Este estudio tuvo como objetivo evaluar la CVRS y los factores asociados en personas de edad avanzada con MM en tratamiento de primera línea o con recaídas, tratadas en el Hospital de Clínicas de la Universidad Federal de Pernambuco (HC-UFPE). Se trata de un estudio transversal, cuantitativo, en el que se caracterizó a los participantes desde un punto de vista sociodemográfico y clínico y se realizaron comparaciones con las puntuaciones de CVRS. La CVRS se evaluó mediante el cuestionario de la Organización Europea para la Investigación del Cáncer (EORTC-QLQ C-30) y el Cuestionario de Calidad de Vida del Mieloma Múltiple-20 (EORTC QLQ-MY20). De los 27 pacientes incluidos, la mayoría tenía entre 60 y 69 años, era de raza negra o mestiza, estaba casada, tenía bajo nivel educativo, presentaba subtipo IgG Kappa, tenía menos de 5 años de enfermedad, recibía solo una línea de tratamiento, no tenía antecedentes de trasplante de médula ósea (TMO), presentaba multimorbilidad y polifarmacia, presentaba buen estado general y se encontraba en estadio avanzado. El bajo nivel educativo, la viudez o el divorcio, la multimorbilidad y un estado general más bajo demostraron un deterioro significativo de la CVRS. Abordar y controlar los aspectos multifactoriales de los pacientes mayores con mieloma múltiple son estrategias para mejorar la CVRS.

Palabras clave: Adulto Mayor. Mieloma Múltiple. Calidad de Vida.

1 INTRODUCTION

Multiple myeloma (MM) is considered a hematological cancer that mainly affects the elderly population. Among all cancers, MM represents about 2% and occupies the second position among hematological neoplasms, representing 10% to 15% of them, surpassed only by non-Hodgkin's lymphoma (Guedes; Becker; Teixeira, 2023).

Multiple myeloma is a neoplasm of plasma cells in the bone marrow. These cells produce and secrete monoclonal immunoglobulins (Ig) or fragments of them – monoclonal protein, which promote high morbidity, mainly caused by: bone destruction and pathological fractures, impairment of normal bone marrow with consequent anemia, renal dysfunction, susceptibility to infections and potential loss of functionality (Nielsen *et al.*, 2020). The advancement of therapeutic options to combat the disease has generated a significant increase in the survival of patients affected by it, however, MM remains a cancer with no cure (Cowan *et al.*, 2018).

According to the World Health Organization (WHO), in 2020, MM was responsible for 176,404 new cases and 117,077 deaths (Brasil, 2022). The pathology mainly affects individuals over 65 years of age, male, with a mean age of 70 years and an incidence ranging from 4.5 to 6 per 100,000 per year. In Brazil, the total number of cases diagnosed in 2022 was 4,568, where 2/3 were 60 years of age or older, with an estimated incidence of 9 cases per 100,000 elderly people per year (Brasil, 2023).

The elderly population is the most affected by MM, which, in addition to living with all the complexities related to aging, is faced with cancer, starting to live with a pathology that demands numerous health interventions. From this perspective, the impacts of the disease on the health-related quality of life (HRQoL) of these elderly people are observed.

HRQoL refers to the individual's perception of their living condition influenced by the disease or its treatment. Therefore, promoting better HRQoL to patients is one of the main goals of treatment for multiple myeloma (Ludwig *et al.*, 2019).

For a reliable assessment of the impact of medical interventions or the presence of diseases such as cancer on HRQoL, important measurement instruments have been used that have been developed and properly evaluated. The scientific literature has several instruments for assessing quality of life (QoL). For cancer patients, the European Organization for Research and Treatment of Cancer (EORTC) has a number of instruments. An example is the *Quality of Life Questionnaire of the European Organization Research for Treatment of Cancer* (EORTC QLQ-C30*),* a generic instrument that assesses HRQoL in patients living with cancer (Sully *et al.*, 2019). In order to complement this broader assessment, the EORTC has developed specific modules for the different types of cancer, such as the QLQ-MY20 (*Quality of Life Questionnaire of Multiple Myeloma-20)* for assessing HRQoL in people with MM (Nielsen *et al.*, 2020).

In view of the adversities experienced by patients with multiple myeloma, the present project aims to evaluate the impacts of this disease and its treatment on the HRQoL of elderly patients with MM.

2 METHODOLOGY

2.1 TYPE OF STUDY

This is a cross-sectional study that included elderly people diagnosed with MM, in the first line of treatment or relapse and/or refractory to subsequent lines of therapy.

2.2 PLACE AND PERIOD OF THE STUDY

The study participants were selected during the months of May to September 2023, from the Department of Hematology of HC-UFPE, considered a reference in the treatment of MM. The HC-UFPE is located in Recife, Pernambuco, is a public university hospital, certified by the Ministries of Education and Health, offers assistance services to the community and helps to train and qualify professionals, also acting as a field of scientific production.

2.3 ELIGIBLE POPULATION

Considering that the disease is a rare condition, despite its increase in terms of incidence, due to population aging, the calculations of the National Cancer Institute (INCA) do not allow the identification of a precise prevalence rate. Thus, searching the universe of users with MM declared in follow-up by the Hospital Cancer Registry of HC-UFPE, in the last ten years, a total of 98 registered patients were identified. Of these, 32 were alive and being followed up in the hospital, who were summoned for the research. Five patients did not respond to the questionnaires: two due to exclusion criteria - diagnosis of dementia and no indication for treatment; one refused; another was not in clinical condition, as he was in serious condition in the intensive care unit; and one, was not contacted, despite some attempts. In all, 27 patients completed the research.

2.4 INCLUSION AND EXCLUSION CRITERIA

Individuals of both sexes, aged 60 years or older, diagnosed with MM, followed up at the Hematology Service of HC-UFPE.

The exclusion criteria were: asymptomatic multiple myeloma, i.e., no indication for treatment; and diagnosis of dementia described in the medical records.

2.5 DATA COLLECTION

2.5.1 Dependent variable: HRQoL in elderly patients with MM

To assess HRQoL, the participants answered the EORTC questionnaires QLQ-C30 and QLQ-MY20, validated for Brazilian patients in Portuguese and available free of charge for research purposes. Permission to use the tool was approved by the responsible group, upon request.

The QLQ C-30 instrument (version 3.0) has 16 domains, distributed in 30 questions, which form 4 scales: Global Health Status and Quality of Life Scale (one domain; two items); Functional Scale (five domains; fifteen items); Symptom Scale (nine domains; twelve items), and Financial Hardship Scale (one domain; one item). In the questionnaire, questions 1 to 28 present the answers on a four-point *Likert* scale, so that the answers vary from no (score value = 1) to very much (score value = 4). Questions 29 and 30 are presented on a seven-point *Likert* scale , in which one corresponds to very bad and seven to excellent.

The QLQ-MY20, also developed by the EORTC, was applied together with the QLQ-C30, as it is a specific scale for people with MM. This instrument has 20 items, divided into two domains with two assessment scales in each of them. The first domain is the symptom scales, in which symptoms of the disease are evaluated (items 31 to 36) and the side effects of treatment (items 37 to 46). The second domain is functional scales, which assesses body image (single item 47) and future perspectives (items 48 to 50). In this module, the options also follow the four-point *Likert* scale, so that the answers range from no (score value = 1) to very much (score value = 4).

2.5.2 Independent variables

a) Sociodemographic data (gender, age, race, education and marital status).
b) Multimorbidity defined by the simultaneous presence of two or more chronic diseases (Harrison *et al.*, 2014).
c) Polypharmacy defined by the continuous and simultaneous use of five or more medications other than those related to the treatment of MM (Guthrie *et al.*, 2015).
d) *Functional status* of the patient recorded in the medical record using the *Performance Status* scale developed by Oken *et al.* (1982) with the Eastern Cooperative Oncology Group (PS-ECOG). This instrument is widely used to assess how oncological disease affects daily living skills.
e) Time of diagnosis of MM.
f) MM staging, according to Durie-Salmon and ISS.
g) Number of treatment lines for MM.

h) Past autologous HSCT/BMT.

2.6 DATA ANALYSIS

For data analysis, a database was built in the Microsoft Excel spreadsheet, which was exported to the SPSS software, version 18, where the analysis was performed. To characterize the sociodemographic and clinical profile of the patients evaluated, the percentage frequencies were calculated and the respective frequency distributions were constructed. In the comparison of the percentages of the categories of the variables evaluated, the chi-square test was applied to compare the proportion.

To calculate the HRQoL score, the EORTC group provides, along with the instruments, manuals to guide the achievement of the scores, in order to ensure standardization and reliable results. To perform the calculations, the score obtained is used, according to the coded answer options from one to four. First, the average score for each scale was estimated, which was considered the raw score (*Raw Score – RS).* The second step was to use a linear transformation to standardize the raw score in a range of 0 to 100 points. The *SR* is calculated with the items of each scale of the evaluation. Using the QLQ-MY20 symptom scale as an example, the SR is the mean of the scores of items 31 to 36. Considering the following formula: RS = (Item 1 + Item 2 + ... +Item n)/n. With linear transformation, the score (*Score* = S) is obtained. For the calculation, the SR and the variation of the answer options of the items are used.

It is important to consider that there is a correction in the formula for obtaining the scores for each evaluation scale. This is due to the fact that the interpretation of higher scores on the scales may represent high ("better") levels of functionality or high ("worse") levels of symptoms. In this sense, it is understood that the interpretation of the scores varies according to the evaluation scale, but the obtaining of the scores is standardized for the same interval.

The variation used in the linear transformation was obtained by subtracting the largest answer option of each item by the lowest answer option value in the same item. As the version used has options of four answers (1. no; 2. little; 3. moderately; 4. very), the value of the variation was 3, except for the items of global health status/QoL of the QLQ-C30, in which the answer options ranged from 1 to 7. In the scales that exist related to previous questions, such as 36 and 42, the score was calculated according to the items answered.

In the evaluation of the QLQ-C30 and QLQ-MY20 QoL score, the normality of the score was investigated using *the Kolmogorov-Smirnov* test and, once normality was indicated, descriptive statistics were obtained from the means and standard deviation. The comparison of the QoL score between the personal and clinical profile of the patients evaluated was performed using the Student's t-test and the ANOVA tests, depending on the number of categories of the explanatory variable evaluated. All conclusions were drawn considering a significance level of less than 5%.

2.7 ETHICAL ASPECTS

The present research complied with the ethical precepts of Resolution 466/12 of the National Health Council. The study was approved by the Human Research Ethics Committee of the HC-UFPE and approved under CAAE: 67986723.0.0000.8807.

Written consent was obtained prior to data collection, duly signed by each participant. The respondents were selected from the hematology outpatient clinics of the HC-UFPE, based on previously established criteria. After explaining the research procedures, objectives, benefits and potential risks to the participants, reading the Informed Consent Form (ICF), approved by the Ethics Committee, and signing it, the researcher made the Quality of Life Questionnaires available to each participant: EORTC QLQ-C30 and QLQ-MY20, so that they could be completed with the application mediated by the researcher. The researcher was asked for permission to access information contained in her medical record, according to a pre-established form. In addition to answering a complementary questionnaire with sociodemographic data, in order to update possible older information contained in medical records, such as current marital status and education.

The confidentiality and privacy of the volunteers will be preserved, whose data will be studied and disclosed only in events or scientific publications anonymously, and initials or any other indications that may identify them will not be used.

The data collected in the research from questionnaires and medical records will be stored, for a minimum period of 5 years, in personal computer files, under the responsibility of the main researcher – Maria Carolina Mendonça Corrêa Lima, at the address: Rua Hoel Sette, nº 139, apt. 404, CEP 52050-090, Jaqueira, Recife, Pernambuco.

3 RESULTS

A total of 27 elderly people were included in the study, 14 females (51.9%) and 13 males (48.1%). Regarding the age group, 15 were between 60 and 69 years old (55.6%); 9, from 70 to 79 years old (33.3%); and 3, in the 80 and over age group (11.1%). The majority is black (74.1%). Regarding education, only 2 had completed higher education (7.4%) and most of them had incomplete primary education (55.6%). More than half are married (55.6%); 4 are single (14.8%); 4 divorced (14.8%); and 4, widowers (14.8%). Although a slightly higher frequency was found in females (51.9), the proportion comparison test was not significant for the gender factor (p-value = 0.847), indicating that the number of patients of both sexes is similar. For the other sociodemographic variables, the proportion comparison test was significant (Table 1).

Table 1

Distribution of the sociodemographic profile of older adults with MM treated at HC-UFPE, 2023

Rated Factor	n	%	p-value
Gender			
Female	14	51,9	0.847[1]
Male	13	48,1	
Age (years)			
60 to 69	15	55,6	
70 to 79	9	33,3	0.018[1]
80 and over	3	11,1	
What is your skin color?			
White	7	25,9	0.012[1]
Black/brown	20	74,1	
Schooling			
No schooling	4	14,8	
Incomplete elementary school	15	55,6	
Complete Elementary School	3	11,1	<0.001[1]
High School	3	11,1	
Higher/Graduate	2	7,4	
Marital status			
Single	4	14,8	
Married	15	55,6	0.004[1]
Divorced	4	14,8	
Widower	4	14,8	

Legend: [1]p-value of the chi-square test for proportion comparison.

Source: prepared by the authors (2024).

Table 2 shows the distribution of the clinical profile of the elderly investigated, where it is verified that most were diagnosed with MM IgG Kappa (51.9%), followed by MM Kappa (14.8%) and MM IgG (11.1%). Duration of illness of less than 5 years prevails (74.1%);

patients submitted to only one line of treatment (51.9%); without having gone past BMT (74.1%); with multimorbidities (81.5%), in polypharmacy (59.3%); with 0 to 2 points in the PS-ECOG classification (70.4%) and Dürie & Salmon III Staging (81.5%). It is also verified that there was a tendency towards not being eligible for BMT (66.7%), since there was a lack of sufficient data in medical records on BMT eligibility, which was present in 21 of them.

As well as for the calculation of ISS staging, found in only 16 of the medical records, with a tendency towards a higher prevalence of ISS staging III. Although a higher prevalence of patients with the profile described was found, the proportion comparison test was not significant for the following factors: number of treatment lines (p-value = 0.062) and polypharmacy (p-value = 0.336), indicating that the number of patients in each category of these factors is similar.

Table 2

Distribution of the clinical profile of older adults with MM treated at HC-UFPE, 2023

Rated Factor	n	%	p-value
Diagnosis			
MM IgA	1	3,7	
MM IgA Kappa	1	3,7	
MM IgA Lambda	1	3,7	
MM IgG	3	11,1	
MM IgG Kappa	14	51,9	<0.001
MM IgG Lambda	2	7,4	
MM Kappa	4	14,8	
MM Lambda	1	3,7	
Duration of illness			
Less than 5 years	20	74,1	0.012[1]
5 years and older	7	25,9	
Number of treatment lines			
One line	14	51,9	
Two to 3 rows	9	33,3	0.062[1]
4 or more lines	4	14,8	
BMT Past			
No	20	74,1	0.012[1]
Yes	7	25,9	
Eligible for BMT†			
No	14	66,7	0.127[1]
Yes	7	33,3	
Multimorbidity			
Yes	22	81,5	0.001[1]
No	5	18,5	
Polypharmacy			
Yes	16	59,3	0.336[1]
No	11	40,7	
PS-ECOG			
0 to 2	19	70,4	0.034[1]

3 to 4	8	29,6	
Dürie & Staging			
Salmon	5	18,5	0.001[1]
Ia, Ib, IIa, IIb	22	81,5	
IIIa, IIIb			
ISS*			
I and II III	7	43,7	0.617[1]
	9	56,3	

Legend: [1]p-value of the Chi-square test for proportion comparison. †The number of observations is lower due to the lack of description in the medical records. *The number of observations does not coincide with the sample size, as data are missing for the calculation.

Source: prepared by the authors (2024).

Tables 3 and 4 show the frequency distribution of the items evaluated in the EORTC QLQ-C30 (*Quality of Life Questionnaire of Cancer* 30, version 3.0).

For the "global health"/QoL domain of the QLQ-C30 instrument, the mean percentage score was 68.2%. It was verified that the items in which the patients reported being moderately and very frequent, which denote worse HRQoL, were: item 1 - has some difficulty when making great efforts, for example, when carrying a heavy shopping bag or a suitcase (66.6%); item 2 - has some difficulty when taking a long walk (51.9%); and item 28 - their physical condition or medical treatment has brought financial difficulties (51.8%). It should be noted that the first two items are part of the functional scale related to physical performance.

In addition, the items most frequently mentioned by the patients, which denote better HRQoL, were: item 8 - had shortness of breath (77.8%); item 15 - has vomited (92.6%); and item 17 - has had diarrhea (85.2%). All make up the scale of symptoms.

Table 3

Frequency distribution of the items evaluated in the EORTC QLQ-C30 Version 3.0 of the elderly with MM treated at HC-UFPE, 2023

Rated Item	Item Frequency			
	No	Little	Moderate	Very much

1. Do you have any difficulties when you make great efforts, for example when carrying a heavy shopping bag or a suitcase?	6(22,3%)	3(11,1%)	9(33,3%)	9(33,3%)
2. Do you have any difficulties when you go for a long walk?	8(29,6%)	5(18,5%)	2(7,4%)	12(44,5%)
3. Do you have any difficulties when you take a short walk outside the house?	15(55,6%)	4(14,8%)	5(18,5%)	3(11,1%)
4. Do you have to stay in a bed or chair during the day?	13(48,2%)	1(3,7%)	5(18,5%)	8(29,6%)
5. Do you need help feeding, dressing, washing, or using the bathroom?	18(66,7%)	3(11,1%)	2(7,4%)	4(14,8%)
During the last week:				
6. Has it been difficult to work or carry out your daily activities?	10(37,1%)	6(22,2%)	4(14,8%)	7(25,9%)
7. Has it been difficult to practice your *hobby* or participate in leisure activities?	8(29,6%)	6(22,2%)	3(11,1%)	10 (37,1%)
8. Did you have shortness of breath?	21(77,8%)	2(7,4%)	4(14,8%)	0(0,0%)
9. Have you been in pain?	11(40,8%)	4(14,8%)	9(33,3%)	3(11,1%)
10. Did you need to rest?	11(40,8%)	3(11,1%)	6(22,2%)	7(25,9%)
11. Have you been having trouble sleeping?	15(55,6%)	4(14,8%)	3(11,1%)	5(18,5%)
12. Have you been feeling weak?	13(48,2%)	2(7,4%)	5(18,5%)	7(25,9%)
13. Have you been having a lack of appetite?	16(59,3%)	4(14,8%)	3(11,1%)	4(14,8%)
14. Have you been feeling nauseous?	18(66,7%)	5(18,5%)	3(11,1%)	1(3,7%)
15. Have you been vomiting?	25(92,6%)	1(3,7%)	0(0,0%)	1(3,7%)
16. Have you been constipated?	15(55,6%)	5(18,5%)	5(18,5%)	2(7,4%)

17. Have you been having diarrhea?	23(85,2%)	2(7,4%)	0(0,0%)	2(7,4%)
18. Have you been tired?	17(63,0%)	2(7,4%)	6(22,2%)	2(7,4%)
19. Has the pain interfered with your daily activities?	13(48,2%)	6(22,2%)	4(14,8%)	4(14,8%)
20. Have you had difficulty concentrating on things such as reading the newspaper or watching television?	19(70,4%)	3(11,1%)	3(11,1%)	2(7,4%)
21. Did you feel nervous?	12(44,5%)	7(25,9%)	4(14,8%)	4(14,8%)
22. Have you been worried?	10(37,1%)	7(25,9%)	7(25,9%)	3(11,1%)
23. Did you feel irritated easily?	15(55,6%)	6(22,2%)	3(11,1%)	3(11,1%)
24. Did you feel depressed?	18(66,7%)	4(14,8%)	2(7,4%)	3(11,1%)
25. Have you had trouble remembering things?	16(59,3%)	5(18,5%)	5(18,5%)	1(3,7%)
26. Has your physical condition or medical treatment interfered with your family life?	14(51,9%)	3(11,1%)	5(18,5%)	5(18,5%)
27. Has your physical condition or medical treatment interfered with your social activities?	11(40,8%)	5(18,5%)	5(18,5%)	6(22,2%)
28. Has your physical condition or medical treatment brought financial hardship?	8(29,7%)	5(18,5%)	7(25,9%)	7(25,9%)

Source: prepared by the authors (2024).

Table 4

Frequency distribution of items 29 and 30, evaluated in the EORTC QLQ-C30 Version 3.0 of the elderly with MM treated at HC-UFPE, 2023

Rated Item	Score assigned to the item						
	1	2	3	4	5	6	7

29. Like You would classify the your overall health during the last week?	3 (11,1%)	0 (0,0%)	2 (7,4%)	5 (18,5%)	6 (22,2%)	2 (7,4%)	9 (33,4%)
30. How You Would you rate your overall quality of life over the past week?	2 (7,4%)	0 (0,0%)	2 (7,4%)	4 (14,8%)	6 (22,2%)	4 (14,8%)	9 (33,4%)

Source: prepared by the authors (2024).

Table 5 illustrates the frequency distribution of the items evaluated in the EORTC QLQ-MY20. It is verified that the items in which the patients reported being moderately and very frequent, which denote worse HRQoL, were two items of the symptom scale: having bone pain (48%) and having back pain (48%); and an item related to future prospects: having been concerned about their health in the future (66.6%).

In addition, the items most frequently mentioned by the patients, which denote better HRQoL, were: having chest pain (77.8%) and having acidity or heartburn (70.4%).

Table 5

Frequency distribution of the items evaluated in the EORTC QLQ-MY20 of the elderly with MM treated at HC-UFPE, 2023

Rated Item	Item Frequency			
	No	Little	Moderate	Very much
31. Did you have pain in your bones?	12(44,5%)	2(7,4%)	7(25,9%)	6(22,2%)
32. Did you have back pain?	7(25,9%)	7(25,9%)	8(29,7%)	5(18,5%)
33. Did you have pain in your hips?	16(59,3%)	1(3,7%)	6(22,2%)	4(14,8%)
34. Did you have pain in your arm or shoulder?	16(59,3%)	2(7,4%)	4(14,8%)	5(18,5%)
35. Did you have chest pain?	21(77,8%)	3(11,1%)	2(7,4%)	1(3,7%)

36. If so, did the pain increase with activity?	21(77,8%)	4(14,8%)	1(3,7%)	1(3,7%)
37. Did you feel drowsy?	18(66,7%)	5(18,5%)	3(11,1%)	1(3,7%)
38. Do you feel thirsty?	12(44,5%)	4(14,8%)	7(25,9%)	4(14,8%)
39. Did you feel sick?	19(70,4%)	3(11,1%)	5(18,5%)	0(0,0%)
40. Did you have dry mouth?	15(55,6%)	7(25,9%)	4(14,8%)	1(3,7%)
41. Have you had hair loss?	16(59,3%)	5(18,5%)	5(18,5%)	1(3,7%)
42. If so, have you been annoyed by hair loss?	26(96,3%)	1(3,7%)	0(0,0%)	0(0,0%)
43. Had numbness (tingling) in the hands or feet?	11(40,8%)	5(18,5%)	5(18,5%)	6(22,2%)
44. Have you felt restless or agitated?	15(55,6%)	2(7,4%)	6(22,2%)	4 (14,8%)
45. Did you have acidity or heartburn?	19(70,4%)	1(3,7%)	7(25,9%)	0(0,0%)
46. Did you have burning or irritation in your eyes?	16(59,3%)	7(25,9%)	2(7,4%)	2(7,4%)
47. Did you feel physically less attractive about the outcome of your illness or treatment?	13(48,2%)	5(18,5%)	7(25,9%)	2(7,4%)
48. Have you been thinking about your illness?	9(33,4%)	6(22,2%)	5(18,5%)	7(25,9%)
49. Have you been worried about death?	15(55,6%)	2(7,4%)	5(18,5%)	5(18,5%)
50. Have you been worried about your health in the future?	4(14,8%)	5(18,6%)	9(33,3%)	9(33,3%)

Source: prepared by the authors (2024).

Regarding the mean and standard deviation of the QLQC30 and QLQ-MY20 instrument score, according to the domain evaluated, it was found that there was a higher mean percentage QoL score in the "side effects" domain of the QLQ-MY20 instrument

(77.2%), followed by the "disease symptoms" domain (71.0%) and "body image" (69.1%). The domain with the lowest mean QoL percentage was "future perspectives" (53.1%). For the "global health"/QoL domain of the QLQ-C30 instrument, the mean percentage score was 68.2%. Even though there were occasional differences in the QoL score between the domains evaluated, the distribution comparison test was not significant (p-value = 0.064), indicating that there is no relevant difference in the mean QoL score of the patients in the domains evaluated.

Table 6 shows the mean and standard deviation of the QLQ-C30 and QLQ-MY20 scores, according to the sociodemographic profile. It is verified that for the "global health"/QoL domain of the QLQ-C30 score, none of the factors of the sociodemographic profile was significant to change the level of QoL.

For the QLQ-MY20 instrument, in the "symptoms of the disease" domain, the only significant variable was schooling (p-value = 0.027), with complete elementary school and higher education/graduate education presenting the highest mean QoL score. In the group of patients with no schooling, QoL in this domain was lower.

For the "treatment side effects" and "body image" domains, none of the sociodemographic profile factors were significant in significantly altering the patients' QoL level. For the "future perspectives" domain, there was statistical significance of the marital status factor (p-value = 0.034), with the lowest mean QoL score for widowed patients (25.0%), followed by divorced (38.9%) and married (55.6%). Single was the marital status with the highest percentage QoL score (86.1%).

Table 6

Mean and standard deviation of the QLQ-C30 and QLQ-MY20 scores, according to the sociodemographic profile of the elderly with MM treated at HC-UFPE, 2023

Sociodemographic factor assessed	Global health QLQ-C30	QLQ-MY20 Rated Domain			
		Symptoms of the disease	Side effects of treatment	Body image	Future prospects
Sex					
Male	70.2±30.3	73.8±30.4	82.6±16.7	73.8±29.8	57.1±28.9
Female	66.0±30.9	67.9±22.0	71.3±16.2	84.1±39.6	48.7±38.4
p-value	0.723^1	0.574^1	0.086^1	0.476^1	0.523^1
Age (years)					
60 to 69	67.8±31.9	68.9±31.6	78.0±16.3	66.7±35.6	51.1±35.6
70 to 79	76.9±18.1	79.0±15.4	76.7±21.7	77.8±28.9	55.6±28.3
80 and more	44.4±45.9	57.4±22.5	74.4±6.9	55.6±50.9	55.6±48.4
p-value	0.279^2	0.438^2	0.947^2	0.593^2	0.947^2

What is your skin color?					
White	85.7±12.5	70.6±25.2	79.5±12.5	76.2±31.7	63.5±37.2
Black/brown	62.1±32.2	71.1±27.4	76.3±18.7	66.7±35.9	49.4±32.1
p-value	0.072[1]	0.968[1]	0.680[1]	0.540[1]	0.348[1]
Schooling					
No schooling	62.5±22.0	38.9±19.2	66.7±13.6	33.3±27.2	44.4±45.4
Incomplete elementary school	72.8±34.4	75.9±26.2	78.2±17.5	73.3±33.8	57.8±30.6
Complete Elementary School	80.6±26.8	90.7±8.5	78.9±21.7	77.8±38.5	40.7±42.1
High School	44.4±25.5	57.4±11.6	76.7±23.3	66.7±33.3	37.0±32.1
Higher/Graduate	62.5±5.9	88.9±7.9	88.3±7.1	100.0±0.0	77.8±31.4
p-value	0.598[2]	0.027[2]	0.687[2]	0.171[2]	0.630[2]
Marital status					
Single	62.5±33.7	72.2±29.0	87.5±8.8	83.3±19.2	86.1±21.0
Married	65±27.5	71.1±29.0	78.7±17.3	73.3±31.4	55.6±25.5
Divorced	62.5±27.6	63.9±30.6	69.2±21.3	58.3±50.0	38.9±44.9
Widower	52.1±41.0	76.4±14.6	69.2±17.3	50.0±43.0	25.0±36.7
p-value	0.530[2]	0.935[2]	0.362[2]	0.494[2]	0.045[2]

Legend: [1]p-value of the Student's T-test for independent samples.[2]p-value of the ANOVA test. Note: Mean±Standard deviation.

Source: prepared by the authors (2024).

Table 7 presents the mean and standard deviation of the QLQ-C30 and QLQMY20 scores according to the clinical profile of the patients evaluated. It is verified that for the global health score of the QLQ-C30, none of the factors of the clinical profile was significant to change the QoL.

For the QLQ-MY20 instrument, in the "disease symptoms" domain, the significant variables were: multimorbidity (p-value = 0.043), with the group of patients with less than two comorbidities having the highest mean QoL percentage score (92.2%); and the variable PS-ECOG (p-value = 0.005), with the group of patients with 0 to 2 points having the highest mean percentage score of QoL (79.8%).

In the "side effects of treatment" and "symptoms of the disease" domains, the PS-ECOG variable was significant in altering the QoL score (p-value = 0.001), with the group of patients with 0 to 2 points having the highest mean percentage QoL score (83.7%).

For the "body image" and "future perspectives" domains, no statistical significance was found for any of the variables of the clinical profile to significantly alter the QoL score.

Table 7

Mean and standard deviation of the QLQ-C30 and QLQ-MY20 scores, according to the clinical profile of older adults with MM treated at HC-UFPE, 2023

Clinical factor assessed	Global health QLQ-C30	Assessed domain nn QLQ-MY20			
		Symptoms of the disease	Side effects of treatment	Body image	Future prospects
MM IgA Diagnostics					
	16,7	66,7	100,0	66,7	55,6
MM IgA Kappa	0,0	0,0	73,3	33,3	44,4
MM IgA Lambda	50,0	61,1	76,7	100,0	55,6
MM IgG	63.9±55.5	64.8±33.5	85.6±12.6	55.6±50.9	55.6±48.4
MM IgG Kappa	73.8±18.7	79.4±21.9	77.9±16.9	76.2±30.5	54.8±31.0
MM IgG Lambda	100.0±0.0	75.0±11.8	85.0±7.1	83.3±23.6	88.9±15.7
MM Kappa	64.6±25.8	58.3±23.4	54.2±3.2	41.7±41.9	19.4±31.9
MM Lambda	91,7	100,0	100,0	100,0	88,9
p-value	0.071[2]	0.101[2]	0.069[2]	0.510[2]	0.386[2]
Duration of illness Less					
than 5 years	67.9±28.4	70.3±25.6	74.5±17.4	71.7±31.1	54.4±33.4
5 years and older	69.0±36.9	73.0±30.5	84.8±14.9	61.9±44.8	49.2±35.6
p-value	0.934[1]	0.818[1]	0.178[1]	0.530[1]	0.728[1]
Number of treatment lines					
One line	72.6±29.7	67.9±27.4	70.5±16.3	71.4±31.6	57.9±36.0
Two to 3 rows	64.8±26.6	67.9±26.8	83.3±18.2	66.7±37.3	44.4±27.2
4 or more lines	60.4±43.8	88.9±18.7	86.7±8.2	66.7±47.1	55.6±41.6
p-value	0.726[2]	0.352[2]	0.101[2]	0.942[2]	0.649[2]
Transplant past					
Yes	75.0±23.1	73.0±34.0	80.0±18.6	71.4±40.5	52.4±35.6
No	65.8±32.3	70.3±24.1	76.2±17.0	68.3±33.3	53.3±33.5
p-value	0.498[1]	0.818[1]	0.620[1]	0.843[1]	0.950[1]
Eligible for TMO Yes					
	63.1±34.0	66.7±35.1	75.7±16.3	52.4±32.5	50.8±40.0
No	66.1±30.4	69.0±21.7	75.2±18.6	73.8±32.5	57.1±33.4
p-value	0.841[1]	0.849[1]	0.955[1]	0.171[1]	0.705[1]

Multimorbidity (two or more)					
Yes	67.4±32.2	66.2±26.7	75.9±17.4	68.2±34.9	51.5±32.6
No	71.7±20.1	92.2±8.4	82.7±16.6	73.3±36.5	60.0±39.8
p-value	0.782¹	0.043¹	0.437¹	0.770¹	0.618¹
Polypharmacy (5 or more)					
Yes	67.2±29.9	68.1±28.5	75.6±17.6	79.2±26.9	56.9±28.7
No	69.7±31.7	75.2±23.5	79.4±17.1	54.5±40.2	47.5±40.1
p-value	0.836¹	0.496¹	0.585¹	0.067¹	0.480¹
PS-ECOG					
0 to 2	71.1±29.3	79.8±23.9	83.7±14.9	75.4±29.0	59.1±29.6
3 to 4	61.5±32.7	50.0±19.9	61.7±11.4	54.2±43.4	38.9±39.4
p-value	0.460¹	0.005¹	0.001¹	0.147¹	0.155¹
Staging					
Dürie & Salmon Ia, Ib, IIa, IIb	70.0±16.2	76.7±14.9	88.0±9.6	73.3±27.9	73.3±18.6
IIIa and IIIb	67.8±29.5	69.7±28.4	74.7±17.6	68.2±36.3	48.5±34.6
p-value	0.886¹	0.603¹	0.119¹	0.770¹	0.136¹
ISS					
I and II	67.9±35.5	64.3±33.2	75.2±18.6	71.4±35.6	±33.2
III	73.1±20.7	84.0±15.3	83.3±9.6	85.2±29.4	±28.4
p-value	0.714¹	0.135¹	0.277¹	0.411¹	0.928¹

Note: Mean±Standard deviation.

Legend: ¹p-value of the Student's t-test for independent samples. ²p-value of the ANOVA test.

Source: prepared by the authors (2024).

4 DISCUSSION

Because it is a rare neoplasm, 2% of cancers (CDC, 2022) and the specific age group being studied – MM in the elderly, the reduced casuistry investigated in the present study is justified. A similar trend was also observed in other studies, such as the study by Mian *et al.* (2020), when trying to understand the changes that occurred in the geriatric domains and in the QoL parameters in elderly people undergoing treatment for MM, even if carried out in more than one center, had a total of 36 participants.

In this study, there was a slight predominance of females, with no statistical significance. This demographic profile is in line with that described in the literature, in which MM is more prevalent in males (Brazil; INCA, 2018). However, a German study that specifically evaluated older adults with MM also demonstrated a slight predominance of females (Alobaidi *et al.*, 2020).

The age and marital status prevalent among the elderly investigated (55.6% were between 60 and 69 years old and 55.6% were married) are in agreement with the results of other research groups (Jensen *et al.*, 2022; Lakshmi *et al.*, 2022; Suzuki *et al.*, 2022). 74.1% self-declared themselves as black or brown. And 70.4% had incomplete primary education or no schooling, differing from the profile found by Nabulsi *et al.* (2020), in its large retrospective cohort, from 14 oncology centers that included 521 elderly people with MM, of which 69.1% had high school or higher education. This fact is probably related to our less privileged socioeconomic profile, since the study was entirely conducted in a public hospital in northeastern Brazil.

Regarding the clinical variables of the participants, the most frequent type of MM was IgG (70.4%), which is in accordance with the profile described in the national and international literature and similar to that found by Suzuki *et al.* (2022), in its multicenter prospective cohort.

The scarcity of real-life data related to HRQoL in patients with MM motivated a German group, which conducted a large multicenter observational study, demonstrating the following clinical profile: 86% had a PS-ECOG of 0 to 2; 44% were in ISS stage III; only 35% had undergone autologous BMT; most were in the first line of chemotherapy, as well as having less than 5 years of disease (Engelhardt *et al.*, 2021). These clinical data corroborate our findings and are in agreement with Jensen *et al.* (2022) regarding the higher prevalence of multimorbidity and polypharmacy.

Age was a key factor associated with HRQoL in a study conducted by Dimopoulos *et al.* (2014), while in our study, although not statistically significant, the increase in age, represented by the subgroups of 70 to 79 years and 80 years and more, seemed to have influenced worse HRQoL scores assessed by the "global health"/QoL of the CLQ-C30 and in three domains of the QLQ-MY20 ("disease symptoms", "side effects of treatment" and "body image"). However, it is interesting to note that this pattern was not repeated with the "future perspectives" in which the older age group obtained higher HRQoL scores. These findings may suggest inherently higher expectations in younger populations.

Jensen *et al.* (2022), in an American cohort, did not show a statistically significant association between the variables: sex, race, education, and marital status with HRQoL. In the present study, no significant differences were observed by sex or race, despite a trend towards higher QoL scores in men, especially in the domain that evaluates treatment side effects.

Regarding education, this was the only sociodemographic variable that was significantly associated with the "symptoms of the disease" domain (p-value = 0.027), where individuals without education had the worst QoL scores. The items evaluated in this domain are mainly related to pain, a common symptom in patients with MM. These data suggest that analgesic management may have been inadequate on the part of the patient, providing us with important information regarding the need for greater multidisciplinary support, in order to minimize suffering during the trajectory of these individuals.

Our results showed an association between marital status and the "future perspectives" domain, in which widowed and divorced individuals obtained a lower QoL score (p-value = 0.034). Ramsenthaler *et al.* (2019) showed that loneliness and depression were associated with the deterioration of HRQoL in terms of functional problems in patients with MM. It would be a plausible justification for the marked difference observed in our participants. This aspect should be considered in future studies for the implementation of multidisciplinary programs aimed at the early diagnosis and management of depression and/or anxiety in this group of patients.

The association observed in the disease symptoms domain and the presence of multimorbidity (p-value = 0.043) was also demonstrated by van der Poel *et al.* (2015) when comparing deterioration of HRQoL in the elderly and young people with MM, denoting that the symptoms of MM can be intensified or even shared in the presence of other diseases. Thus, global health care is of paramount importance to promote better HRQoL in older adults with MM.

Several previous studies have demonstrated a relationship between performance status as an independent factor associated with HRQoL, in which scores greater than 2, assessed by the PS-ECOG, were associated with low HRQoL scores (Despiégel *et al.*, 2019; Engelhardt *et al.*, 2021; Jensen *et al.*, 2022; Ramsenthaler *et al.*, 2019). This study reinforced the conclusions of these authors, since the group of patients with PS-ECOG scores from 0 to 2 points had the highest mean percentage QoL score in the following domains: "side effects of treatment" (p value = 0.005) and "symptoms of the disease" (p value = 0.001). This knowledge corroborates the importance of considering even more "physiological age", rather than chronological age in therapeutic decisions.

Our research identified patterns consistent with other observational studies, in which patients who received lines of subsequent treatments had worse HRQoL. Ludwig *et al.* (2022), in a real-life German study, pointed out that in relation to "global health"/QoL, the mean HRQoL score was 49.5. However, when assessing the average in patients undergoing first-line therapy, the score rose to 61.7. A survey in the USA with almost 200 patients, also showed a trend of decreasing global health status scores of the EORTC QLQ-C30 with a greater number of lines of treatment, although the relationship was not statistically significant (Hu *et al*., 2016). The mean score found for this domain in our study was 68.2 and, likewise, it found a decreasing score as the number of lines of therapy increased, decreasing from 72.6 in patients undergoing one line of treatment to 60.4 in those with four or more lines.

Despite the trend, we did not find a statistically significant difference. These data suggest that early and effective treatment of MM offers the best opportunity to improve or maintain HRQoL, but the considerable deficits in HRQoL experienced in later stages of the disease (which may be due to disease progression, accumulated toxicity, or increasing age) also deserve recognition in future treatment decisions (Despiégel *et al.*, 2019).

Contrary to our expectations, BMT history or BMT eligibility did not influence HRQoL scores, and in none of the HRQoL scales did the differences approach the threshold for a statistically significant result. This result surprised us, since eligible patients or those who underwent BMT tend to be younger, have fewer comorbidities, and have better PS, when compared to those who are ineligible. It is possible that emotional issues, particularly the impact of diagnosis, may counterbalance the better overall health status that this BMT-eligible population would have (Robinson Jr *et al*., 2016). Prospective studies are needed to better elucidate the relationship between transplant eligibility and HRQoL in elderly patients with MM.

Analyzing the global health status scores of the EORTC QLQ-C30 and the 4 domains of the QLQ-MY20 ("disease symptoms", "side effects", "body image", and "future perspectives"), the largest difference was between the EORTC QLQ-C30 global health status score and the future perspectives of the QLQ-MY20. Information such as this can be useful in studies of HRQoL in MM, helping to establish the factors that have the greatest influence on the overall health status score.

The patients with MM included in the questionnaire had satisfactory HRQoL with a high score in the "global health status" domain – 68.2. Previous studies have shown that a 6-point difference in the mean EORTC QLQ-C30 "global health"/QoL score, when compared with the adult population, would be estimated to be clinically significant in HRQoL for MM patients. The normal mean "global health"/QoL score in the adult population was 71.2 (Robinson Jr *et al*., 2016), a value that was not higher than 6 points in relation to the mean score of the individuals in our study.

Fatigue and pain are core symptoms, and in this study we demonstrate that these symptoms are closely related to impairment of physical functioning, which again is related to substantial skeletal involvement. These findings support a proactive strategy of MM patients to prevent skeletal injuries and fractures. Thus, the reduction of pain and fatigue and the improvement of physical functioning should be the target of future rehabilitation and palliative intervention studies.

Our findings also favor strategies that identify groups at higher risk for depression and anxiety; care processes that aim beyond the control of MM contemplating the related multifactorial aspects, with special consideration for the individual performance status and the need to control and treat comorbidities, in addition to individualizing therapeutic modalities; and, finally, the trend towards worse QoL scores, which individuals in later lines of therapy demonstrated, suggests the need for early use of effective treatment measures in order to delay the progression of the disease, achieve remission and preserve HRQoL for as long as possible.

To analyze the deterioration of HRQoL, a larger study with a longer follow-up is needed. In addition, a prospective design of this study will provide important information about changes in HRQoL and disease-specific symptoms over time and allow us to better determine causal associations. Further research on the longitudinal impact of MM and its treatment on HRQoL is warranted to improve the understanding of how different factors influence HRQoL across all lines of care and allow for personalized patient optimization/management. Further analysis is needed to determine the best way to preserve QoL in specific subgroups of patients with MM.

Our study contributed to broadening the understanding of HRQoL in elderly patients with MM treated in the SUS. Although we have a small sample, in addition to the fact that the study took place in a single center, which makes generalizations difficult, our results seem to be in agreement with other research groups. We also had as limitations the fact that there was some missing information in the medical records, such as ISS staging and eligibility for BMT. However, some of the strengths of our study were the use of a specific instrument, validated for Brazil, to measure HRQoL in patients with MM, given the scarcity of Brazilian studies that used such a questionnaire, in addition to the use of primary data.

5 CONCLUSION

This observational study demonstrated that most of the elderly patients with MM followed up at the HC-UFPE are between 60 and 69 years old, declared themselves black or brown, have a low level of education and are married. Despite the slight predominance of women, there was no statistical significance in relation to gender.

Regarding the clinical profile of these individuals, the most common MM subtype was IgG Kappa, with less than five years of disease, submitted to only one line of treatment, no history of BMT, with multimorbidity and polypharmacy, with a good performance index and advanced Dürie & Salmon – III staging.

The items that had the most negative impact on HRQoL were related to physical performance, bone pain, and concern about the future. While the least mentioned focused on the scales of symptoms and side effects related to gastrointestinal complaints such as vomiting, diarrhea and heartburn.

The participants of the research presented satisfactory HRQoL, with a good score in the domain of "global health status"/QoL – 68.2. According to the domains evaluated using the QLQ-MY20 questionnaire, specific for MM, a better mean percentage QoL score was found in the "side effects" domain. On the other hand, "future perspectives" showed the lowest mean QoL percentage.

In the bivariate analysis of HRQoL scores based on the QLQ-C30 and QLQ-MY20 questionnaires, according to the sociodemographic profile, it was found that for the "global health" domain, none of the sociodemographic factors evaluated was significant to change the level of QoL. While the "disease symptoms" domain of the QLQ-MY20 was negatively related to low level of education, as well as worse indices in the "future perspectives" domain among widowed and divorced marital statuses. Of the clinical variables investigated, multimorbidity and worse *performance status* were the only ones capable of demonstrating significant deterioration in HRQoL.

A prospective design to analyze HRQoL in elderly patients with MM would be justified to better determine the causal associations with the sociodemographic and clinical profile variables, in addition to providing information on changes in HRQoL over time. The evaluation of the longitudinal impact of the burden of disease and the lines of treatment will allow us to have a personalized management in therapeutic decisions with the objective of preserving the HRQoL of these individuals in the best way.

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