Quality of Life Assessment with EORTC QLQ in Patients with Multiple Myeloma: Multicenter Study

Multipl Miyelom Tanılı Hastalarda EORTC QLQ ile Yaşam Kalitesi Değerlendirmesi: Çok Merkezli Çalışma

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ABSTRACT

Objective: Both the length of the treatment period and the diversity of the agents used in the treatment significantly affect the quality of life (QoL) of the patients with multiple myeloma (MM). With the aid of the EORTC Quality of Life Questionnaire Consisting of 30 Questions "EORTC QLQ-C30" and the Quality of Life Questionnaire Multiple Myeloma Module "QLQ-MY20", we aimed to obtain data on quality of life in MM patients in a representative sample of the general population of our country.

Methods: One hundred sixty eight patients from 6 different centers followed between 2018-2020 were included in the study. The QLQ-C30, and the QLQ-MY20 questionnaires specific for MM patients were used and the results were reported statistically.

Results: Seventy eight (46%) of the patients were female, while 90 (54%) were male. The median age was 64 (22-84). When the findings were analysed, it was found that there was a greater effect on the symptom scale compared to the functional scale.

Conclusion: The importance of the treatment-related side effect management, together with the adequate administration of appropriate symptomatic treatment in holistic treatment management were emphasized as effective factors in terms of the QoL of patients with MM.

Keywords: Multiple myeloma, quality of life, chemotherapy

ÖZ

Amaç: Hem tedavi süresinin uzunluğu, hem de tedavide kullanılan ajanların çeşitliliği multipl miyelomlu (MM) hastaların yaşam kalitesini (YK) önemli ölçüde etkiler. Otuz sorudan oluşan EORTC Yaşam Kalitesi Anketi "EORTC QLQ-C30" ve Yaşam Kalitesi Anketi-Multipl Miyelom Modülü "QLQ-MY20" yardımıyla MM hastalarında yaşam kalitesine ilişkin verileri elde etmeyi amaçladık.

Yöntem: 2018-2020 yılları arasında takip edilen, 6 farklı merkezden 168 hasta çalışmaya dahil edildi. MM hastalarına özel QLQ-C30 ve QLQ-MY20 anketleri kullanılmış ve sonuçlar istatistiksel olarak rapor edilmiştir.

Bulgular: Hastaların 78'i (%46) kadın, 90'ı (%54) erkekti. Ortanca yaş 64 (22-84) idi. Bulgular incelendiğinde semptom ölçeğinde fonksiyonel ölçeğe göre daha fazla etkinin olduğu görüldü.

Sonuç: Bütüncül tedavi yönetiminde, uygun tedavinin yeterli uygulanması ile birlikte tedaviye bağlı yan etki yönetiminin önemi, MM'li hastaların yaşam kalitesi açısından etkili faktörler olarak vurgulanmıştır.
Anahtar Kelimeler: Multipl miyelom, yaşam kalitesi, kemoterapi

INTRODUCTION

Hematological malignancies are among the most common cancers worldwide.[1] Multiple myeloma (MM) is the second most common hematological malignancy, and its treatment procedure have improved considerably over the years.[2,3] It is important to investigate the long-term toxicities of the treatments and quality of life (QoL) measurements of the patients since there is still no cure opportunity.[4] Although patients may enter a period of stability during which they only need minimal or maintenance therapy, they generally face a progressive disease.[5] Additionally, it is known that patients MM suffer from more symptoms than other hematological cancers.[3] These include bone pain and fractures due to bone destruction; constipation, nausea, confusion due to hypercalcemia, recurrent infections due to immunodeficiency and weakness due to anemia. The rate of anxiety and depression in patients with hematological malignancies during the treatment was found to be 35%.[6] Treatment-related toxicities increase with the progression of the treatment step and may require the termination of treatment.[7] Today, the concept of QoL in patients diagnosed with MM has become important due to the prolonged chemotherapy process with the addition of new treatment agents.

The European Organisation for Research and Treatment of Cancer (EORTC) developed an integrated, modular approach to evaluate the QoL of cancer patients. A basic "EORTC Quality of Life Questionnaire Consisting of 30 Questions" is used for this (EORTC QLQ-C30). Additionally, "the Quality of Life Questionnaire Multiple Myeloma Module" (QLQ-MY20) is a special questionnaire designed for patients with MM patients.[8] Both of these questionnaires were presented to the patients in Turkish for our study.

This study aimed to obtain data on the QoL in MM patients in a representative sample of the general population of Turkey through the EORTC QLQ-C30 and QLQ-MY20 questionnaires. The interpretation of these data will assist clinicians in planning interventions for symptoms at early stages of the disease. Therefore, we evaluate the effect of the disease and its primary systemic treatment on health-related QoL in patients with MM.

METHODS

A total of 168 patients from 6 different centers diagnosed with MM between 2018 and 2020 were included in our study after obtaining their written informed consent. The questionnaires were answered cross-sectionally with the support of a physician by the patient or by the patient's relatives in case the patient had difficulty answering the questionnaire. The QLQ-C30 and the QLQ-MY20 questionnaires specific to MM patients were used. Version 3.0 of the EORTC QLQ-C30 has 30 questions and contains three sections: functional scales, symptom scales, and global health status/QoL. The functional scales are physical, role, emotional, cognitive and social functioning. The symptom scales are fatigue, dyspnea, insomnia, appetite loss, nausea and vomiting, constipation, diarrhea, weakness, pain and financial difficulties.[9] The reliability and validity of the Turkish version of the EORTC QLQ-C30 has been proven.[10] EORTC QLQ-MY 20 includes 4 sections and 20 questions, including MM-related disease symptoms, side effects of treatment, body image, and future perspective.[9] The Turkish version of the QLQ-MY20 questionnaire is reliable and valid for assessing QoL in patients with MM and can be used in clinical trials in the Turkish population.[11]

Statistical Analysis

A response scale of "not at all," "a little," "quite a bit," or "very much" was used to evaluate the items of both the EORTC QLQ-C30 and the EORTC QLQ-MY20. All scores were linearly converted to a 0-100 scale. High scores for functional scales and QoL in the EORTC QLQ-C30 indicate better function and better overall QoL, while high scores for symptom scales indicate more symptoms. In the EORTC QLQ-MY20, on the other hand, higher scores for symptom scales consisting of "MM-related disease symptoms" and "side effects of treatment" again indicate more symptoms, while higher scores for "body image" and "future perspective" indicate better functioning. Chi-square test was used to compare categorical data and unpaired t-test was used to compare continuous data. Pearson correlation test was used for correlation analysis. Mann-Whitney U test was used for comparisons between two groups of quantitative variables that did not show normal distribution. Cronbach's alpha coefficient was used to determine the internal consistency of the scales. Pearson correlation test was used for correlation analysis. It includes the mean, median, floor and ceiling values of the QLQ-C30 parameters in this study.

RESULTS

Out the 168 patients, 78 (46%) were female and 90 (54%) were male. The median age was 64 (22-84). Seventy-six (45.2%) of the respondents were below the age of 65, and 92 (54.8%) were 65 years and above. A total of 142 of

the questionnaires (84%) were answered by the patients themselves and 26 (16%) by their relatives.

No statistically significant difference was found in terms of QLQ-C30 global health status/QoL, cognitive functioning, dyspnea, constipation, diarrhea, and financial difficulty scores according to gender subgroups (p>0.05). A statistically significant difference was found in QLQ-C30 physical functioning, role functioning, emotional functioning, social functioning, fatigue, nausea and vomiting, pain, sleep disturbance, and appetite loss scores according to gender subgroups (respectively, p<0.001, p=0.001, p=0.010, p=0.002, p<0.001, p=0.036, p<0.001, p=0.013, p=0.011). It was determined that the physical functioning, role functioning, emotional functioning, social functioning, and nausea and vomiting scores of the females were higher than the males, while the scores of fatigue, pain, sleep disturbance, and appetite loss were lower

(Table 1). When Cronbach's alpha values, which show the internal consistency of the questions in the QLQ-C30 scale, are examined; it is seen that it varies between 0.497 and 0.924. Although the Cognitive Functioning dimension has low reliability, the high reliability of the other dimensions and the Global Health Status/QoL score indicates that the QLQ-C30 scale is highly reliable. Cronbach's alpha values that can be calculated for Symptom Scales vary between 0.760 and 0.806; accordingly, our scale is quite reliable Cronbach's alpha values that can be calculated for the QLQ-MY20 also vary between 0.763 and 0.865; accordingly, our scale is highly reliable (Table 1).

There was no statistically significant difference in MY20 body image scores according to gender subgroups (p>0.05). A statistically significant difference was found in terms of MY20 future perspective, disease symptoms and side effects of treatment scores according to gender

Table 1. General distribution of scale scores						
	Mean (SD)	Median	Floor (%)	Ceiling (%)	Item own-scale correlations*	Reliability (Cronbach's α)
QLQ-C30						
Global Health Status/QoL	57.8 (26.7)	62.5	0 (4.3)	100 (10.5)	0.859	0.924
Functional scales						
Physical functioning	52.2 (26.6)	53.3	0 (3)	100 (1.2)	0.582-0.745	0.854
Role functioning	63.8 (36.1)	66.7	0 (10.3)	100 (37.6)	0.799	0.887
Emotional functioning	67.9 (27.7)	75.0	0 (0.6)	100 (17.8)	0.688-0.806	0.894
Cognitive functioning	74.1 (24.7)	83.3	0 (1.9)	100 (29)	0.333	0.497
Social functioning	64.8 (33)	66.7	0 (9.2)	100 (28.8)	0.711	0.830
Symptom scales						
Fatigue	52.1 (28.2)	44.4	0 (4.8)	100 (9.1)	0.628-0.702	0.806
Nausea and vomiting	14.8 (23.9)	0.0	0 (61.1)	100 (2.5)	0.627	0.760
Pain	40.9 (31.9)	33.3	0 (22.4)	100 (8.5)	0.672	0.804
Dyspnea	21.1 (29.1)	0.0	0 (57.3)	100 (5.5)	-	-
Sleep disturbance	33.1 (36.6)	33.3	0 (44.1)	100 (16.1)	-	-
Appetite loss	29 (34.3)	33.3	0 (48.8)	100 (11.1)	-	-
Constipation	28.5 (32)	33.3	0 (45.3)	100 (8.8)	-	-
Diarrhea	17.3 (26.6)	0.0	0 (63)	100 (4.3)	-	-
Financial difficulties	39.5 (36.7)	33.3	0 (36.6)	100 (16.1)	-	-
QLQ-MY20						
Functional Scales						
Future perspective	40.8 (27.4)	44.4	0 (9.1)	100 (4.3)	0.557-0.632	0.763
Body image	26.7 (28.7)	33.3	0 (43.2)	100 (5.6)	-	-
Symptom scales						
Disease symptoms	31.9 (25.6)	25.0	0 (9.1)	100 (2.4)	0.636-0.765	0.865
Side effects of treatment	30.3 (19.8)	29.6	0 (1.8)	90 (0.6)	0.253-0.735	0.838
SD: Standard deviation, QoL: Quality of life, QLQ-MY20: Quality of Life Questionnaire Multiple Myeloma Module, QLQ-C30: Quality of Life Questionnaire Consisting of 30 Questions						

subgroups (p=0.045, p=0.018, p=0.008, respectively). It was determined that the scores of females were lower than the scores of males (Table 2).

Patients in the age subgroup <65 years had better scores of physical functioning (p=0.01), while patients in the age subgroup ≥65 years had better scores of fatigue (p=0.04) (Table 3).

No statistically significant difference was found in terms of QLQ-C30 global health status/QoL, role functioning, social functioning, nausea, and vomiting, dyspnea, sleep disturbance, constipation and diarrhea scores according to the respondents (p>0.05). It was determined that there was a statistically significant difference in QLQ-C30 physical functioning, emotional functioning, cognitive functioning, fatigue, pain, appetite loss and financial difficulty scores according to the respondents (p=0.009, p=0.001, p=0.010, p=0.009, p=0.002, p=0.006, p=0.013, respectively). It was determined that physical functioning, emotional functioning, cognitive functioning scores of patients was higher than relatives, while the scores of fatigue, pain, appetite loss and financial difficulties were lower (Table 4).

No statistically significant difference was found in terms of MY20 future perspective, body image, disease symptoms and side effects of treatment scores according to the respondents (p>0.05). A statistically significant difference was found in terms of MY20 future perspective, disease symptoms and side effects of treatment scores according to the respondents (p=0.006, p=0.014, p=0.008, respectively). It was determined that the scores of patients were lower than the scores of relatives (Table 4).

DISCUSSION

The number of studies evaluating the QoL using valid scales for MM is limited.[12] In Turkey, there is no large-scale multicenter study evaluating only the QoL of patients with MM. In our study, we had the opportunity to analyze the QoL parameters in patients with MM from the country, which has different sociocultural characteristics compared with Western countries.

The EORTC QLQ-MY20 questionnaire used in our study includes questions specific to MM and questions used in general cancer patients. Thus, it allows the evaluation of the

Table 2. Evaluation of scale scores according to gender subgroups			
Parameters\Gender subgroup	Female [median (min-max)]	Male [median (min-max)]	p value
QLQ-C30	**n=78**	**n=90**	
Global Health Status/QoL	66.67 (0, 100)	58.33 (0, 100)	0.842
Physical functioning	66.67 (0, 100)	40 (0, 93.33)	**<0.001***
Role functioning	83.33 (0, 100)	58.33 (0, 100)	**0.001***
Emotional functioning	83.33 (8.33, 100)	70.83 (0, 100)	**0.010***
Cognitive functioning	83.33 (33.33, 100)	83.33 (0, 100)	0.140
Social functioning	83.33 (0, 100)	58.33 (0, 100)	**0.002***
Symptom scales			
Fatigue	33.33 (0, 100)	66.67 (0, 100)	**<0.001***
Nausea and vomiting	0 (0, 100)	0 (0, 100)	**0.036***
Pain	33.33 (0, 100)	50 (0, 100)	**<0.001***
Dyspnea	0 (0, 100)	0 (0, 100)	0.802
Sleep disturbance	16.67 (0, 100)	33.33 (0, 100)	**0.013***
Appetite loss	0 (0, 100)	33.33 (0, 100)	**0.011***
Constipation	33.33 (0, 100)	33.33 (0, 100)	0.345
Diarrhea	0 (0, 100)	0 (0, 100)	0.603
Financial difficulties	33.33 (0, 100)	33.33 (0, 100)	0.083
QLQ-MY20			
Future perspective	33.33 (0, 100)	44.44 (0, 100)	**0.045***
Body image	33.33 (0, 100)	33.33 (0, 100)	0.842
Disease symptoms	22.22 (0, 94.44)	33.33 (0, 100)	**0.018***
Side effects of treatment	23.33 (0, 77.78)	33.33 (0, 90)	**0.008***
QoL: Quality of life, QLQ-MY20: Quality of Life Questionnaire Multiple Myeloma Module, QLQ-C30: Quality of Life Questionnaire Consisting of 30 Questions, min-max: Minimum-maximum			

Table 3. Evaluation of scale scores according to age subgroups

Parameters-Age subgroup	<65 [median (min-max)]	≥65 [median (min-max)]	p value
QLQ-C30	**n=76**	**n=92**	
Global Health Status/QoL	58.33 (0-100)	66.67 (0-100)	0.565
Physical functioning	60 (0-100)	46.67 (0-93.3)	**0.01***
Role functioning	75 (0-100)	66.67 (0-100)	0.366
Emotional functioning	83.33 (8.33-100)	75 (0-100)	0.272
Cognitive functioning	83.33 (0-100)	83.33 (0-100)	0.148
Social functioning	66.67 (0-100)	66.67 (0-100)	0.713
Symptom scales			
Fatigue	44.44 (0-100)	55.56 (0-100)	**0.040***
Nausea and vomiting	0 (0-100)	0 (0-100)	0.426
Pain	33.33 (0-100)	33.33 (0-100)	0.095
Dyspnea	0 (0-100)	0 (0-100)	0.928
Sleep disturbance	33.33 (0-100)	33.33 (0-100)	0.427
Appetite loss	0 (0-100)	33.33 (0-100)	0.201
Constipation	33.33 (0-100)	33.33 (0-100)	0.154
Diarrhea	0 (0-100)	0 (0-100)	0.374
Financial difficulties	33.33 (0-100)	33.33 (0-100)	0.361
QLQ-MY20			
Future perspective	61.11 (0-100)	55.56 (0-100)	0.698
Body image	66.67 (0-100)	66.67 (0-100)	0.397
Disease symptoms	22.22 (0-94.44)	27.78 (0-100)	0.922
Side effects of treatment	25.93 (3.33-80)	27.78 (0-90)	0.928

QoL: Quality of life, QLQ-MY20: Quality of Life Questionnaire Multiple Myeloma Module, QLQ-C30: Quality of Life Questionnaire Consisting of 30 Questions, min-max: Minimum-maximum

effects of MM on the QoL, unlike general cancer patients. The content of the EORTC QLQ-MY20 was drawn from an extensive literature search through interviews with patients in various countries and with healthcare professionals experienced for treating patients with MM. The content of the module was created based on the issues that are not objectively measured but frequently reported by patients and examined in various clinical trials. Detailed interviews with patients provided a thorough understanding of the problems experienced by patients with myeloma and the impact of the disease as they perceived it in their lives. This led to the production of a questionnaire covering the most severe symptoms and problems most commonly experienced by patients during diagnosis, treatment and follow-up processes. Additionally, the questionnaire encompasses the most serious and most frequent side effects of standard treatments given to patients with MM.[12]

Although myeloma patients are treated with different chemotherapy agents and regimens, the side effects of conventional chemotherapy and steroids may negatively affect the health-related QoL of patients for a longer time. This is why the module focuses on the expected side effects of conventional chemotherapy and steroids. The myeloma module and EORTC QLQ-C30 are also suitable for monitoring patients after bisphosphonate studies or high-dose chemotherapy.[12]

In our study, QoL data from patients with MM in the Turkish population were obtained by creating the Turkish version of the QLQ-30/MY-20 questionnaires. Our results were validated with the QLQ-30/MY-20 questionnaires by applying Cronbach validation. Thus, it has been shown that the Turkish version of the QLQ-30/MY-20 questionnaires is a reliable and valid questionnaire that shows the QoL in patients with MM and can be used in clinical studies.

When the results of the survey were evaluated in an overview, it was seen that the QoL was significantly affected. Particularly, it was shown that the symptomatic scales were more affected than the functional scales. Here, it was emphasized how important the management of treatment-related side effects and the adequate administration of appropriate symptomatic treatment in terms of the patient's QoL in the holistic treatment management.

Table 4. Evaluation of scale scores according to the respondents			
Parameters\Respondents	Patients [median (min-max)]	Relatives [median (min-max)]	p value
QLQ-C30	n=142	n=26	
Global Health Status/QoL	66.67 (0, 100)	50 (0, 100)	0.348
Physical functioning	53.33 (0, 100)	33.33 (0, 100)	**0.009***
Role functioning	66.67 (0, 100)	33.33 (0, 100)	0.070
Emotional functioning	79.17 (8.33, 100)	50 (0, 91.67)	**0.001***
Cognitive functioning	83.33 (0, 100)	66.67 (16.67, 100)	**0.010***
Social functioning	66.67 (0, 100)	66.67 (0, 100)	0.137
Symptom scales			
Fatigue	44.44 (0, 100)	66.67 (0, 100)	**0.009***
Nausea and vomiting	0 (0, 100)	16.67 (0, 100)	0.220
Pain	33.33 (0, 100)	66.67 (0, 100)	**0.002***
Dyspnea	0 (0, 100)	0 (0, 100)	0.696
Sleep disturbance	33.33 (0, 100)	33.33 (0, 100)	0.066
Appetite loss	0 (0, 100)	33.33 (0, 100)	**0.006***
Constipation	33.33 (0, 100)	33.33 (0, 100)	0.240
Diarrhea	0 (0, 100)	0 (0, 100)	0.429
Financial difficulties	33.33 (0, 100)	66.67 (0, 100)	**0.013***
QLQ-MY20			
Future perspective	33.33 (0, 100)	55.56 (11.11, 100)	**0.006***
Body image	33.33 (0, 100)	33.33 (0, 100)	0.317
Disease symptoms	22.22 (0, 100)	38.89 (0, 100)	**0.014***
Side effects of treatment	25.93 (0, 90)	37.04 (3.33, 81.48)	**0.008***
QoL: Quality of life, QLQ-MY20: Quality of Life Questionnaire Multiple Myeloma Module, QLQ-C30: Quality of Life Questionnaire Consisting of 30 Questions, min-max: Minimum-maximum			

In the subgroup analysis of the survey results, differences were observed in the QoL perceptions of the patients and their relatives. Especially in the symptomatic scale evaluation, it was concluded that the relatives of the patients had a more negative perception than the patients themselves. Considering these data, it was concluded that the relatives of the patients should be more elaborately evaluated and emotionally supported.

Moreover, although there were more positive results in terms of functional QoL in females compared with males, more negative results were observed in terms of symptoms. In a Croatian study by Ficko et al.[8], females demonstrated poorer performance in terms of symptoms such as fatigue, pain, dyspnea, and insomnia; whereas males functionally showed a better performance. Similarly, in studies of German, Norwegian, and Slovenian origin, males filled in a less symptomatic and better QoL questionnaire in all scales.[13,14] Although these results do not correspond to our study in terms of functional scales, they show similarities in terms of symptoms. When evaluated according to age groups, worse performance scores were found in elderly patients on symptom scales, such as fatigue. These findings are also similar to the results of studies conducted in Norwegian, Slovenian and German societies.[13-15]

In a study by Strasser-Weippl and Ludwig[16], high symptom and low functional scale scores were obtained in patients with active disease at the beginning of primary treatment; indeed, this supports the previously reported data on serious and significantly impaired QoL in patients with MM.[17,18] In the same study, it was stated that initial pain and fatigue are the most negative symptoms. In the study of Strasser-Weippl and Ludwig[16], additional evidence was obtained that the physical and psychosocial dimensions of QoL were significantly impaired at baseline in patients with MM compared with the healthy control population. Additionally, the same study showed that low initial psychosocial QoL was associated with poor prognosis. It was found that this relationship was independent of the somatic parameters of the disease and did not disappear with the treatment effects in the disease process. Although the results of our study were similar in general, the psychosocial status of our patients at the beginning of the treatment was not determined during the survey.

New drugs have significantly improved response rates in patients with MM and prolonged survival.[19] Despite this improvement in the QoL of patients, which is one of the main goals of MM treatment, the disease is still not curable.[16] Some studies have shown that there is a significant deterioration in the QoL of patients with myeloma even at the time of diagnosis.[20] Simultaneously, initial QoL may be associated with prognosis, but it is unclear whether this relationship is independent of other strong prognostic factors in MM.[21]

Study Limitations

Since it was a cross-sectional study, we did not have the opportunity to analyze survival and prognosis. The lack of follow-up data in our study, the fact that the questioning was not repeated over time, and that it contains cross-sectional data can be expressed as the limitation points.

CONCLUSION

MM continues to be a disease on which several studies have been conducted and new treatment agents are developed every day. Considering the survival advantage obtained with effective agents despite their incurable nature, patients have a longer life expectancy; however, targeted therapies come with serious long-term side effects. Considering the use of these drugs as long-term maintenance therapy, the importance of QoL in MM patients becomes clear again. In our country, where socio-cultural differences are intense between regions, it is inevitable that studies covering a wide geographical area are needed both to determine the effect on the QoL and to plan the improvements that can be made in this regard.

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Ethics

Ethics Committee Approval: The study were approved by the İstanbul Medipol University Ethical Committee (date: 03/22/2019, approval number: 217). The experimental procedures were based on the Declaration of Helsinki and relevant institutional regulations.

Informed Consent: Informed consent was obtained as written forms from all of our patients for publish.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Concept: A.İ.G., Design: A.İ.G., İ.S., V.B.E., Ö.G.S., Data Collection or Processing: A.İ.G., İ.S., V.B.E., M.H.D., İ.İ., R.E., A.T., V.K., İ.N.K.E., Z.E.A., Z.N.T., E.N.T., Ö.G.S., Analysis or Interpretation: A.İ.G., Ö.G.S., Literature Search: A.İ.G., İ.S., Ö.G.S., Writing: A.İ.G., İ.S., Ö.G.S.

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