Original Article

Quality of Life Assessment with EORTC QLQ in Patients with Hodgkin Lymphoma: Multicenter Study

Hodgkin Lenfoma Hastalarında EORTC QLQ ile Yaşam Kalitesi Değerlendirmesi: Cok Merkezli Calışma

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ABSTRACT

Aim: The aim of our study is to obtain data on the quality of life (QoL) in Hodgkin lymphoma (HL) patients in a representative sample of the general population of Turkey with the help of the EORTC QLQ-C30 and QLQ-HL27 questionnaires.

Material and Methods: A total of 68 patients from seven different centers diagnosed with HL between 2018-2020 were included in the study. The questionnaires were answered cross-sectionally by the patient under the control of a physician in the centers participating in the study.

Results: Out of 68 patients, 42.6% (n=29) were female and 57.4% (n=39) were male. The ages of the patients ranged from 18 to 74 years, with a mean of 42.10±16.62 and with a median value of 40 years. There was no significant difference between age subgroups in terms of QLQ-C30 global health status/ QoL, functional or symptom scales and HL27 SB, PC, EI and WF scores (p>0.05, for all). It was determined that the constipation scores of females were higher than the scores of males (p=0.041). No statistically significant difference was found in terms of HL27 SB, PC, EI and WF sub-dimension scores according to gender (p>0.05).

Conclusions: There was only a statistically significant difference in terms of QLQ-C30 constipation sub-dimension scores according to gender. The constipation scores of females were higher than the scores of men. More detailed and large population studies are needed to reveal the effectiveness of QoL assessment in HL patients.

Keywords: Hodgkin lymphoma, EORTC QLQ-C30, QLQ-HL27, quality of life

ÖZET

Amaç: Çalışmamızın amacı, EORTC QLQ-C30 ve QLQ-HL27 anketleri yardımıyla Türkiye genelini temsil eden bir örneklemde Hodgkin lenfoma (HL) hastalarında yaşam kalitesi hakkında veri elde etmekti.

Gereç ve yöntemler: 2018-2020 yılları arasında, HL tanısı almış yedi farklı merkezden toplam 68 hasta çalışmaya dahil edildi. Anketler, araştırmaya katılan merkezlerde hekim kontrolünde hasta tarafından yanıtlandı.

Bulgular: 68 hastanın %42.6'sı (n=29) kadın, %57.4'ü (n=39) erkekti. Hastaların yaşları 18 ile 74 arasında değişmekte olup, ortalama 42.10±16.62 ve ortanca değeri 40 idi. QLQ-C30 global sağlık

First Received: 29.08.2021, Accepted: 01.01.2022 doi: 10.5505/aot.2022.25991 durumu/ yaşam kalitesi, fonksiyonel veya semptom skalaları ve HL27 SB, PC, EI ve WF skorları açısından yaş alt grupları arasında anlamlı fark yoktu (tümü için, p>0.05). Kadınların kabızlık puanlarının erkeklere göre daha yüksek olduğu belirlendi (p=0.041). Cinsiyete göre HL27 SB, PC, EI ve WF alt puanları açısından istatistiksel olarak anlamlı fark bulunmadı (p>0.05).

Sonuc: Cinsiyete göre sadece QLQ-C30 kabızlık alt puanları açısından istatistiksel olarak anlamlı bir fark vardı. Kadınların kabızlık puanları erkeklerin puanlarından daha yüksekti. HL hastalarında QoL değerlendirmesinin etkinliğini ortaya çıkarmak için daha ayrıntılı ve geniş popülasyon çalışmalarına ihtiyaç olduğu görülmektedir.

Anahtar sözcükler: Hodgkin lenfoma, EORTC QLQ-C30, QLQ-HL27, yaşam kalitesi

Introduction

Hodgkin lymphoma (HL) is a rare B-cell malignant neoplasm. Its incidence in the population is 2.3/100.000. The classic HL (CHL) subtype (95%) is the most common, while the nodular lymphocyte-predominant HL (NLPHL) subtype is less common (5%) [1, 2].

Although the incidence of HL is higher between the ages of 20-40, it shows a second peak at the age of 55 and above. There are no clearly defined risk factors for the development of HL, but familial factors, viral exposures. and immunosuppression are thought to be involved [3].

Initial treatment for patients diagnosed with HL is based on the histological features of the disease, the stage of presentation, and the presence of poor prognostic factors. Combined therapy modalities, which include radiotherapy (RT) to the affected area, usually followed by shortened chemotherapy regimens, are applied in early-stage HL patients. In con-trast, patients with advanced HL usually receive long-term, combination chemotherapy regimens, and radiation therapy is used only in selected cases. For patients diagnosed with HL with relapsed or refractory disease, salvage chemotherapy followed by high-dose chemotherapy and autologous stem cell transplantation is the standard of care [2]. The current standard treatment of HL disease is the adriamycin, bleomycin, vinblastine, dacarbazine (ABVD) protocol.

Due to the high survival rate in HL patients with successful treatment options, the evaluation of the quality of life (QoL) has gained importance in this patient group [4]. These patients are at risk for long-term physical and psychological side effects after their treatment [5]. Patients cured after HL therapy could have pain, fatigue, sexual, psychosocial, cognitive emotional or problems [5-7]. As an example, persistent fatigue is increased 2.5-3 times in HL patients compared to the normal population, it is seen in up to 40% of patients after treatment and may occur even years after successful treatment [8].

The European Organization for Research and Treatment of Cancer (EORTC) aimed to develop an integrated and modular approach to assessing the quality of life (QoL) of cancer patients. A basic QoL questionnaire called "EORTC QLQ-C30" consisting of 30 questions is used. In addition, EORTC QLQ-HL27 is a special questionnaire consisting of 27 questions and adjusted to evaluate the QoL in HL patients [9]. In our study, both questionnaires were presented to the patients in the Turkish language.

The aim of our study is to obtain data on QoL in HL patients in a representative sample of the general population of Turkey with the help of the EORTC QLQ-C30 and QLQ-HL27 questionnaires. Interpretation of these data will help to improve the patient's QoL by allowing timely appropriate intervention for the symptoms caused by the disease or chemotherapy. In our study, we aimed to evaluate the effect of the disease and the primary systemic treatment on QoL in HL patients.

Material and Methods

A total of 68 patients from seven different centers diagnosed with HL between 2018 and 2020 were included in our study. The questionnaires were answered crosssectionally by the patient under the control of a physician in the centers participating in the study. Written consent was obtained from all patients with HL, using an informed consent The QLQ-C30, the core OoL form. questionnaire of the EORTC, and the QLQ-HL27, the lymphoma module specific for HL patients, were used. Version 3.0 of the EORTC QLQ-C30 has 30 questions and three sections: functional scales, symptom scales, and global health status/ QoL. Functional scales are physical, role, emotional, cognitive and social functioning. The symptom scales are dyspnea, insomnia, appetite loss, nausea and vomiting, constipation, diarrhea, fatigue, pain and financial difficulties [9]. The reliability and validity of the Turkish version of the EORTC QLQ-C30 have been proven [10]. EORTC QLQ-HL27 includes 4 sections and 27 questions on HL and treatment-related disease symptoms, side effects of treatment, body image, and future perspective [9].

Ethical committee approval was received (Approval date and number: Istanbul Medipol University, 2020, 228).

Statistical analysisNCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program was used for statistical analysis. Descriptive statistical methods (mean, standard deviation, median, frequency, percentage, minimum, maximum) were used while evaluating the study data. conformity of the quantitative data to the normal distribution was tested with the Shapiro-Wilk test and graphical examinations. The Mann-Whitney U test was used

for comparisons between two groups of quantitative variables that did not show normal distribution, and the Kruskal-Wallis test was used for comparisons between more than two groups. The Cronbach alpha coefficient was used to determine the internal consistency levels of the scales. Statistical significance was accepted as p<0.05.

Results

Out of 68 patients, 42.6% (n=29) were female and 57.4% (n=39) were male. The ages of the patients ranged from 18 to 74 years, with a mean of 42.10±16.62 and with a median value of 40 years. The disease type was nodular sclerosing in 45.6% (n=31), mixed cellular in 36.8% (n=25), lymphocyte rich in 11.8% (n=8), lymphocyte-poor in 1.5% (n=1) and lym-phocyte predominant in 4.4% (n=3) of patients. The general distributions, mean and me-dian values of the scale subscores are shown in Table 1.

There was no significant difference between age subgroups in terms of QLQ-C30 global health status/ QoL, functional or symptom scales (p>0.05). Also, no statistically significant difference was found between age subgroups in terms of HL27 SB, PC, EI and WF scores (p>0.05) (Table 2).

gender According breakdown, statistically significant difference was found in terms of QLQ-C30 constipation scores between males and females (p=0.041). It was determined that the constipation scores of females were higher than the scores of males. No statistically significant difference was found in terms of HL27 SB, PC, EI and WF sub-dimension scores according to gender (p>0.05) (Table 3).

There was no significant difference between stage subgroups in terms of QLQ-C30 global health status/ QoL, functional or symptom scales (p>0.05). Also, no statistically significant difference was found between age

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	59.6 (24.3)	58.3	0.0 (1.5)	100.0 (8.8)	0.699	0.823
Functional Scales						
Physical Functioning	61.3 (27)	60.0	0.0 (0)	100.0 (11.8)	0.666-0.791	0.877
Role Functioning	67.9 (30.9)	66.7	0.0 (2.9)	100.0 (39.7)	0.766	0.867
Emotional Functioning	60.2 (29.4)	66.7	0.0 (2.9)	100.0 (13.2)	0.676-0.775	0.870
Cognitive Functioning	67.4 (29.1)	66.7	0.0 (1.5)	100.0 (29.4)	0.556	0.714
Social Functioning	61.8 (29.7)	66.7	0.0 (2.9)	100.0 (25)	0.696	0.820
Symptom Scales						
Fatigue	47.1 (30.8)	44.4	0.0 (13.2)	100.0 (5.9)	0.798-0.827	0.902
Nausea and vomiting	25.2 (27.8)	16.7	0.0 (42.6)	100.0 (1.5)	0.545	0.699
Pain	40.9 (32.5)	33.3	0.0 (23.5)	100.0 (7.4)	0.640	0.779
Dyspnea	38.7 (35.3)	33.3	0.0 (36.8)	100.0 (11.8)	-	-
Sleep disturbance	42.2 (36.7)	33.3	0.0 (33.8)	100.0 (16.2)	-	-
Appetite loss	33.3 (38.2)	16.7	0.0 (50)	100.0 (14.7)	-	-
Constipation	27 (33.2)	0.0	0.0 (52.9)	100.0 (7.4)	-	-
Diarrhea	14.7 (24)	0.0	0.0 (67.6)	100.0 (1.5)	-	-
Financial difficulties	49 (33.8)	66.7	0.0 (25)	100.0 (13.2)	-	-
QLQ-HL27						
SB	36.9 (24)	38.9	0.0 (4.4)	100.0 (0)	0.329-0.763	0.808
PC	39 (28.4)	33.3	0.0 (13.2)	100.0 (2.9)	0.534-0.814	0.848
EI	37.5 (26.8)	38.9	0.0 (8.8)	100.0 (0)	0.704-0.806	0.908
WF	43.7 (25.2)	45.5	0.0 (4.4)	100 (0)	0.282-0.784	0.881

Table 2. Evaluation of scale scores according to age subgroups

Parameters\Age Subgroup	<65 (n=60)	≥ 65 (n=8)	n
	Median (Min, Max)	Median (Min, Max)	р
QLQ-C30			
Global Health Status/QoL	58.33 (0, 100)	70.83 (33.33, 100)	0.421
Functional Scales	60 (6.67, 100)	53.33 (33.33, 100)	0.731
Physical Functioning	66.67 (0, 100)	75 (0, 100)	0.889
Role Functioning	66.67 (0, 100)	58.33 (16.67, 83.33)	0.416
Emotional Functioning	83.33 (0, 100)	50 (33.33, 100)	0.217
Cognitive Functioning	66.67 (0, 100)	58.33 (33.33, 100)	0.770
Symptom Scales			
Fatigue	44.44 (0, 100)	55.56 (0, 77.78)	0.977
Nausea and vomiting	16.67 (0, 100)	25 (0, 83.33)	0.705
Pain	33.33 (0, 100)	41.67 (0, 83.33)	0.915
Dyspnea	33.33 (0, 100)	66.67 (0, 100)	0.557
Sleep disturbance	33.33 (0, 100)	50 (0, 100)	0.968
Appetite loss	0 (0, 100)	50 (0, 100)	0.485
Constipation	0 (0, 100)	50 (0, 100)	0.077
Diarrhea	0 (0, 100)	0 (0, 66.67)	0.746
Financial difficulties	66.67 (0, 100)	66.67 (0, 66.67)	0.557
QLQ-HL27			
SB	38.89 (0, 88.89)	33.33 (0, 83.33)	0.939
PC	33.33 (0, 100)	54.17 (0, 83.33)	0.667
El	38.89 (0, 94.44)	38.89 (5.56, 72.22)	0.970
WF	46.97 (0, 96.97)	45.45 (3.03, 78.79)	0.607

Mann-Whitney U test was used

Table 3. Evaluation of scale scores according to gender

Parameters\ Gender	Female (n=29)	Male (n=39)	n	
	Median (Min, Max)	Median (Min, Max)	р	
QLQ-C30				
Global Health Status/QoL	58.33 (0, 100)	58.33 (8.33, 100)	0.413	
Physical Functioning	60 (13.33, 100)	60 (6.67, 100)	0.672	
Role Functioning	66.67 (33.33, 100)	83.33 (0, 100)	0.480	
Emotional Functioning	66.67 (0, 100)	66.67 (0, 100)	0.794	
Cognitive Functioning	66.67 (0, 100)	83.33 (16.67, 100)	0.262	
Social Functioning	66.67 (0, 100)	66.67 (0, 100)	0.648	
Symptom Scales				
Fatigue	55.56 (0, 100)	44.44 (0, 100)	0.321	
Nausea and vomiting	16.67 (0, 100)	16.67 (0, 83.33)	0.785	
Pain	50 (0, 100)	33.33 (0, 100)	0.477	
Dyspnea	33.33 (0, 100)	33.33 (0, 100)	0.500	
Sleep disturbance	66.67 (0, 100)	33.33 (0, 100)	0.106	
Appetite loss	0 (0, 100)	33.33 (0, 100)	0.679	
Constipation	33.33 (0, 100)	0 (0, 100)	0.041*	
Diarrhea	0 (0, 66.67)	0 (0, 100)	0.379	
Financial difficulties	66.67 (0, 100)	66.67 (0, 100)	0.531	
QLQ-HL27				
SB	44.44 (5.56, 88.89)	38.89 (0, 83.33)	0.567	
PC	41.67 (0, 100)	33.33 (0, 100)	0.579	
El	33.33 (0, 83.33)	38.89 (0, 94.44)	0.911	
WF	48.48 (0, 87.88)	45.45 (0, 96.97)	0.687	

Mann-Whitney U test was used

Table 4. Evaluation of scale scores according to stages

Parameters\ Stages	Stage 1&2 (n=27)	Stage 3&4 (n=41)	
	Median (Min, Max)	Median (Min, Max)	_ р
QLQ-C30			
Global Health Status/QoL	58.33 (0, 100)	58,33 (16.67, 100)	0.668
Physical Functioning	60 (6.67, 100)	66.67 (20, 100)	0.880
Role Functioning	66.67 (33.33, 100)	66.67 (0, 100)	0.569
Emotional Functioning	75 (0, 100)	58,33 (8.33, 100)	0.457
Cognitive Functioning	83.33 (0, 100)	66.67 (16.67, 100)	0.509
Social Functioning	66.67 (0, 100)	50 (0, 100)	0.788
Symptom Scales			
Fatigue	44.44 (0, 100)	44.44 (0, 100)	0.668
Nausea and vomiting	0 (0, 66.67)	16.67 (0, 100)	0.210
Pain	33.33 (0, 100)	33.33 (0, 100)	0.559
Dyspnea	33.33 (0, 100)	33.33 (0, 100)	0.520
Sleep disturbance	33.33 (0, 100)	33.33 (0, 100)	0.710
Appetite loss	0 (0, 100)	33.33 (0, 100)	0.108
Constipation	33.33 (0, 100)	0 (0, 100)	0.395
Diarrhea	0 (0, 100)	0 (0, 66.67)	0.784
Financial difficulties	66.67 (0, 100)	66.67 (0, 100)	0.405
QLQ-HL27			
SB	33.33 (0, 83.33)	, 83.33) 38.89 (0, 88.89)	
PC	33.33 (0, 100)	50 (0, 100)	0.439
EI	33.33 (0, 88.89)	44.44 (0, 94.44)	0.269
WF	42.42 (0, 84.85)	48.48 (0, 96.97)	0.598

Mann Whitney U Test was used

Table 5. Evaluation of scale scores according to HL subtypes

Parameters\ Disease Subtype	(n=31)		Other (n=12)	_ p
			Median (Min, Max)	
QLQ-C30				
Global Health Status/QoL	58.33 (16.67, 100)	58.33 (0, 100)	66.67 (16.67, 100)	0.684
Physical Functioning	66.67 (6.67, 100)	60 (13.33, 100)	63.33 (6.67, 100)	0.871
Role Functioning	66.67 (0, 100)	66.67 (0, 100)	66.67 (33.33, 100)	0.997
Emotional Functioning	66.67 (16.67, 100)	50 (0, 100)	75 (0, 100)	0.418
Cognitive Functioning	83.33 (16.67, 100)	66.67 (0, 100)	66.67 (16.67, 100)	0.540
Social Functioning	66.67 (33.33, 100)	66.67 (0, 100)	58.33 (16.67, 100)	0.633
Symptom Scales				
Fatigue	44.44 (0, 88.89)	55.56 (0, 100)	44.44 (33.33, 100)	0.148
Nausea and vomiting	16.67 (0, 83.33)	16.67 (0, 100)	8.33 (0, 66.67)	0.689
Pain	33.33 (0, 100)	66.67 (0, 100)	41.67 (0, 100)	0.528
Dyspnea	33.33 (0, 100)	33.33 (0, 100)	50 (0, 100)	0.346
Sleep disturbance	33.33 (0, 100)	33.33 (0, 100)	33.33 (0, 100)	0.415
Appetite loss	0 (0, 100)	33.33 (0, 100)	0 (0, 100)	0.340
Constipation	0 (0, 66.67)	0 (0, 100)	16.67 (0, 100)	0.760
Diarrhea	0 (0, 66.67)	0 (0, 100)	0 (0, 33.33)	0.861
Financial difficulties	66.67 (0, 100)	66.67 (0, 100)	50 (0, 100)	0.360
QLQ-HL27				
SB	38.89 (0, 83.33)	44.44 (0, 88.89)	36.11 (11.11, 72.22)	0.695
PC	33.33 (0, 91.67)	33.33 (0, 100)	41.67 (8.33, 100)	0.514
El	38.89 (0, 83.33)	33.33 (0, 88.89)	41.67 (5.56, 94.44)	0.928
WF	45.45 (0, 87.88)	45.45 (0, 87.88)	46.97 (0, 96.97)	0.574

Kruskal-Wallis test was used

subgroups in terms of HL27 SB, PC, EI and WF scores . (p>0.05) (Table 4).

There was also no significant difference between HL subtypes in terms of QLQ-C30 global health status/ QoL, functional or symptom scales; of HL27 SB, PC, EI and WF scores (p>0.05) (Table 5).

Discussion

Our study is the first from Turkey to evaluate QoL using QLQ-C30 and QLQ-HL27 in a large and multi-center HL patient group. There is limited information on the use of QLQ subtypes in hematological malignancies and no clear evidence for their effectiveness. In a recent study from 2020 [10], healthrelated QoL (HRQoL) was evaluated using the EORTC QLQ-C30 in a total of 515 hematological malignancies diagnosed with leukemia, lymphoma and multiple myeloma over the age of 18 years. Of the 515 patients included in the study, 46.6% were diagnosed with lymphoma, 34% with leukemia and 19.4% with multiple myeloma; 70.9% of them were with advanced-stage or high risk. Anxiety rate was 15.1% and depression 12.8%. While the mean global health status score was found to be 59.6 in our study, it was found to be 59.2 in this study. In our study, there was no significant difference between age subgroups, stages and disease subtypes in terms of the global health scores/QoL.

In an HL cohort from 2020 [11], patients with advanced HL, 5-year HL-survivors and the general population were compared with each other. Patients reported worse HRQoL scores than survivors across most functional scales and symptom scales. These scores varied as a function of gender but not age. Survivors' HRQoL reports were comparable to the ones of the general population. In addition, even though the QoL scores of HL patients are worse than the general population, they improve over the years.

In another study from Turkey in 2020 [12], in a group of 121 chronic myeloid leukemia patients, who had used a tyrosine kinase inhibitor (TKI) for at least 3 months, the effectiveness of QLQ-C30 and QLQ-CML24 was examined. While the median age of the patients was 53, there was no difference in global health status scores between patients who received different TKIs. In the QLQ-CML24 module, the most common symptom was fatigue with 58.7%; there was no significant difference between the TKI groups in terms of the effect on activities of daily living. In our study in the HL patient group, the median age was 40, and there was no significant difference between the groups we formed in terms of QLQ-C30 and QLQ-HL27 parameters. A statistically significant difference was found only in terms of QLQconstipation sub-dimension scores according to gender (p=0.041). Another major study [13] included adults aged 18 years and older who had completed treatment for a hema-tological malignancy and were at 1 to 5 years post-treatment. In a total of 131 patients with a mean age of 66, being advanced age was found to be associated with poor QoL. Males reported better physical functioning, fewer pain symptoms, and less insomnia compared to females. While the median age of the study was 66, 77.9% of them were diagnosed with lymphoma (B-cell). In our study, the only difference between males and females was consti-pation. The median age was 40 years due to the younger age group of HL. In another study involving 490 patients from 40 different centers with a diagnosis of multiple myeloma, which is seen as a disease of the older age group [14], the median age was 71 and the mean global health status score was 49.4. In the patient group followed in the no-treatment interval, the global health status scores and functional scores were better and fewer symptoms were observed.

In another MM cohort, a total of 445 patients were evaluated; a high global health status /QoL score has been shown to be associated with good treatment response and fewer side effects; it was also observed that an increase in the score was significantly associated with longer treatment [15]. In our study, the fact that the general health status scores and QLQ-C30 or HL27 parameters did not differ significantly in patients who were with more advanced stages and needed longer treatment should be considered as an important result. According to MM, which is a disease of advanced age; it is important in terms of treatment tolerance in HL where young age is dominant.

There are also limitation points of this study. The most important one is the fact that validity and reliability study of the EORTC QLQ-HL27 was not done in Turkish language.

Another important points were the limited patient population and statistical analysis, which became difficult especially when subgroups were established.

As a result, this study is the first from our country to evaluate the QLQ-C30 and QLQ-HL27 questionnaires, especially in a relatively young patient population com-pared to other hematologic malignancies of literature. There was no significant differ-ence between age, gender and stage subgroups in terms of OLO-C30 and QLQ-HL27 sub-parameters. There was only a statistically significant difference in terms of QLQ-C30 constipation subdimension scores according to gender. The constipation scores of females were higher than the scores of men. More detailed and large population studies are needed to reveal the effectiveness of QoL assessment in HL patients.

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