Original papers

Quality of life in patients with lymphoproliferative neoplasms at diagnosis and after the first-line treatment

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Abstract

Background. The assessment of the quality of life (QoL) in hematology-oncology patients is extremely important. The disease and anti-cancer therapy can cause adverse effects, directly impacting the physical and mental condition of the patient and indirectly influencing their social and professional situation. Therefore, a properly performed QoL assessment should take into account all of these aspects. Moreover, QoL assessment has a prognostic value in regard to treatment success and prognosis; therefore, the improvement in the QoL is often one of the goals of therapy.

Objectives. To identify the changes in QoL during therapy in patients with lymphoproliferative neoplasms.

Materials and methods. Forty-six hematology-oncology patients participated in this prospective single-center study. Their QoL was analyzed at 2 time points (before and after the first-line treatment). For this purpose, the EORTC QLQ-C30 questionnaire was used. All statistical analyses were performed using the STATISTICA v. 13 software. A value of $p < 0.05$ was considered statistically significant.

Results. The study included patients with multiple myeloma (MM; 47.8%), non-Hodgkin lymphoma (NHL; 28.3%) and chronic lymphocytic leukemia (CLL; 23.9%). After the first line of treatment, patients perceived their overall QoL as slightly better than before starting the treatment, with an average increase of 1.94. Statistically significant differences were observed in physical and emotional functioning as well as fatigue, pain, dyspnea, appetite, and constipation.

Conclusions. In patients with lymphoproliferative neoplasms, after the first-line treatment, an improvement in an overall QoL and level of functioning, as well as a reduction in the severity of symptoms were observed.

Key words: quality of life, chemotherapy, lymphoproliferative neoplasms

Background

Lymphoproliferative neoplasms consist of a diverse group of diseases,[1] in which those with the highest global incidence rate include: non-Hodgkin lymphoma (NHL; 2.8%), leukemia (2.5%) and multiple myeloma (MM; 0.9%). The above diseases accounted for 2.6%, 3.1% and 1.2% of deaths in 2020, respectively.[2]

Non-Hodgkin lymphoma is a heterogeneous group of lymphatic system neoplasms, representing a wide spectrum of diseases with various aggressiveness. These neoplasms can originate from peripheral B lymphocytes (85–90%), T lymphocytes or natural killer cells.[3,4] Clinically, NHL is divided into indolent lymphomas and aggressive lymphomas, according to the proliferation rate of the neoplastic cell and timing of the symptom onset.[5] In highly developed countries, the most common leukemia in adults is chronic lymphocytic leukemia (CLL). This neoplasm is characterized by an increased number of circulating, immunocompetent, small, mature, monoclonal B lymphocytes with typical morphology and immunophenotypes within the peripheral blood.[6,7] In turn, MM is a cytogenetically heterogeneous clonal proliferative disorder of atypical plasma cells, characterized by multifocal bone marrow involvement and specific secondary organ symptoms.[8,9]

Due to the remarkable progress made in the treatment of hematological malignancies (HMs) and significant improvements in the survival rates of patients, it is necessary to adopt a more chronic treatment model for these diseases. Thus, the improvement in the patient's quality of life (QoL) is becoming more and more important.[10] Quality of life is a multidimensional phenomenon covering various domains of human life; therefore, despite many years of analysis, no unambiguous definition of this concept has been achieved.

In medical science, the most commonly used definition of QoL was published in 1995 by the World Health Organization (WHO). According to the WHO, QoL is an individual's perception of their life position in the context of the culture and value systems in which they live, in relation to individual goals, expectations, standards, and fears. This concept includes following elements: physical and emotional health, level of independence, social relationships, personal beliefs, and the relationship of these elements to important environmental characteristics. All aspects must be evaluated in order for a comprehensive, personal QoL assessment to be performed. Moreover, this definition draws the attention to the fact that QoL is a subjective concept that includes both positive and negative aspects of human life.[11]

The concept of health-related quality of life (HRQoL) is equally important, the definition of which is patient-oriented and, above all, functional. Health-related quality of life represents the sum of the daily functional abilities in a patient's life in 4 domains: physical and professional activity, mental functioning, social interactions, and somatic experiences. At the same time, it should be noted that HRQoL is a multifactorial parameter assessed by the patient and can change during the course and treatment of the disease.[12]

Considering the above, the assessment of QoL in hematology-oncology patients in connection with the diagnosis and treatment is extremely important. Both the disease and the anti-cancer therapy can cause adverse effects that directly impact the physical and mental conditions of a patient, and can indirectly influence their social and professional situation. Thus, a properly performed QoL assessment should take into consideration all of these aspects. Moreover, the QoL has a prognostic value with regard to treatment success and prognosis; therefore, the improvement in QoL is often one of the goals of patient therapy.[13]

The QoL analyses can be carried out using various methods, the most common of which are questionnaires. The questionnaires should be characterized by high validity and reliability. Moreover, the questionnaire cannot simply focus on a single domain, as it would not constitute an accurate QoL assessment.[14,15]

The available questionnaires can be divided into:

- general (generic), which are used both in healthy and sick individuals with various clinical diseases;
- detailed (specific), designed to assess a particular disease based on its specific elements – spheres of functioning or factors resulting from the disease;
- mixed, containing the elements of a general questionnaire and those intended for a specific disease.[16]

According to the results of a systematic review of QoL research in medicine and health sciences, the most frequently used general questionnaires were: SF-36, EQ-5D and WHOQOL-BREF. At the same time, among specific questionnaires, the EORTC QLQ-C30 questionnaire is most frequently used.[13] On the other hand, mixed questionnaires are often prepared specifically for a clinical trial and are used solely for this purpose (ad hoc).[16]

The EORTC QLQ-C30 questionnaire (v. 3.0) was developed by the Quality of Life Research Group of the European Organization for Research and Treatment of Cancer (EORTC). Its basic version (core) is a standardized tool intended for oncological patients regardless of the form, type and location of the tumor.[17] However, separate modules for the assessment of QoL related to specific primary tumor sites were also developed.[14] Among HMs, the module for the assessment of QoL in MM patients (QLQ-MY20)[18] is fully validated. On the other hand, the modules for patients with Hodgkin lymphoma (HL; QLQ-HL27), high- or low-grade NHL (HG/LG-NHL; QLQ-NHL-HG29 and QLQ-NHL-LG20, respectively), CLL (QLQ-CLL17),[19] and chronic myeloid leukemia (CML; QLQ-CML24)[20,21] are currently in the final stages of development. The results of previous research suggest that the EORTC QLQ-C30 and its modifications are reliable tools for the assessment of QoL in hematology-oncology patients.[10,22]

Objectives

Individual problems revealed during the QoL assessment may lead to the modification of the treatment or rehabilitation regimen in order to improve the health condition of the patient. Therefore, our study aimed to identify the QoL in patients with lymphoproliferative neoplasms before and after the first line of treatment.

Materials and methods

The presented results are part of a larger research project carried out in the years 2017–2019 at Department of Hematology and Cancer Prevention in Chorzów, Poland. The study protocol was approved by the Bioethical Committee of the Medical University of Silesia in Katowice, Poland, under the resolutions No. KNW/0022/KB1/4/17 and KNW/0022/KBI/4/I/17/19.

Adults with a confirmed diagnosis of CLL, NHL or MM who were receiving an intensive treatment program were eligible for the study. Patients who had previously undergone cancer therapy and those with an active acute or chronic infection, a systemic connective tissue disease, an implanted pacemaker, or a significant clinical burden, were excluded from the study. The inclusion criteria were met by a total of 58 patients, 8 of whom refused to participate and 4 died. The final analysis consisted of 46 people who were monitored twice during their hospitalization:

– after diagnosis, before starting therapy;
– after the first line of treatment, while assessing its effect.

In this study, the standardized EORTC QLQ-C30 questionnaire (v. 3.0) was used to assess the QoL of cancer patients. The questionnaire contains questions regarding the impact of the disease on different areas of a patient's life (physical, role, emotional, cognitive, and social functioning), the occurrence of symptoms (fatigue, nausea and vomiting, pain, dyspnea, insomnia, appetite loss, constipation, and diarrhea), financial difficulties, and an overall assessment of QoL (Table 1).[17]

For each question, the respondent must choose 1 answer. For 28 of the questions, the answers are given on a 4-point Likert-type scale (1 – never, 2 – sometimes, 3 – often, 4 – very often) and assess the intensity of the analyzed parameters. The last 2 questions evaluate the general health of the patient on a 7-point scale (from 1 – very bad to 7 – excellent). Patients completed the questionnaires by themselves. If a question arose, they could ask the researcher for an explanation.

After collecting the responses, a raw score was calculated for each of the abovementioned 15 questionnaire items. Next, a linear transformation was performed to obtain a score in a range from 0 to 100. The conversion of the results to a 100-point scale was made according to the EORTC guidelines.[23] Of note, a higher score on the functional scales means better functioning and a higher response for general health corresponds to a better QoL. The situation is different when interpreting the symptom scales, where a higher score indicates

Table 1. Description of questions included in the EORTC QLQ-C30 questionnaire (own elaboration based on the studies)[19,24]

Scale	Abbreviation	Item numbers	Number of items	Item range*
Functional scales				
Physical functioning	PF	1–5	5	3
Role functioning	RF	6, 7	2	3
Emotional functioning	EF	21–24	4	3
Cognitive functioning	CF	20, 25	2	3
Social functioning	SF	26, 27	2	3
Symptom scales				
Fatigue	FA	10, 12, 18	3	3
Nausea and vomiting	NV	14, 15	2	3
Pain	PA	9, 19	2	3
Symptom items				
Dyspnea	DY	8	1	3
Insomnia	SL	11	1	3
Appetite loss	AP	13	1	3
Constipation	CO	16	1	3
Diarrhea	DI	17	1	3
Financial difficulties	FI	28	1	3
Global health status/QoL	QL	29, 30	2	6

* Item range indicates the difference between the possible maximum and minimum response to individual items. EORTC QLQ-C30 – European Organisation for Research and Treatment of Cancer quality of life questionnaire; QoL – quality of life.

a higher level of symptom burden.[17,23] Additionally, each patient answered questions concerning sociodemographic data: gender, education, year of birth, place of residence, and a subjective assessment of health.

The normality of the distribution was assessed using the Shapiro–Wilk test. The Pearson's χ^2 test was performed to compare qualitative variables, while quantitative variables before and after treatment were compared using the Wilcoxon signed-rank test. A value of $p < 0.05$ was considered statistically significant. The analyses were performed using the STATISTICA v. 13 software (TIBCO Software Inc., Palo Alto, USA). The graphic design and supplementary calculations were performed using Microsoft Excel 2016 (Microsoft Corp., Redmond, USA).

The research followed the principles outlined in the Declaration of Helsinki for all human or animal research. In addition, for investigations involving human subjects, informed consent was obtained from the participants involved.

Results

The general characteristics of the study group are presented in Table 2. The youngest patient was 19 years old and the oldest was 81 years old. The median age of the respondents was 62 years, and the mean age was 59.5 (±15.3 years). Men (65.0%) constituted a much greater percentage, with a slight majority of patients having secondary education (34.8%). Most of the patients lived in a city (91.3%) with their families (89.1%). The presence of more than 2 comorbidities (including hypertension, type 2 diabetes or prostatic hyperplasia) was reported in 60.9% of patients.

The most common hematology-oncology diagnosis was MM (Fig. 1). All patients enrolled in the study received chemotherapy or chemoimmunotherapy for a mean duration of 118 (±48.8) days. Most of the patients, before starting the treatment (84.8%) and after the first line of treatment (91.3%), described their health as good or very good (Fig. 2). In the case of this parameter, there was no statistically significant difference (χ^2 test; p = 0.3775).

After ending the first line of treatment, patients perceived their overall QoL to be slightly better than before starting the treatment, with an average increase of 1.94. For all functional scales, the results in the 2nd observation period increased, which means a better level of patient functioning. Statistically significant changes were demonstrated in the physical and emotional functioning parameters (Table 3).

In the case of symptom scales, most of the results decreased, which indicates a lower intensity of symptoms. At the same time, respondents indicated the occurrence

Table 2. General characteristics of the study group

Parameters	Value
Age [years], mean (±SD)	59.5 (±15.3)
Age [years], median (range)	62 (19–81)
Time duration of treatment [days], mean (±SD)	118 (±48.8)
Gender	
Female, n (%)	16 (35.0)
Male, n (%)	30 (65.0)
Education	
Primary, n (%)	6 (13.0)
Basic vocational, n (%)	14 (30.4)
Secondary, n (%)	16 (34.8)
Higher, n (%)	10 (21.8)
Place of residence	
City, n (%)	42 (91.3)
Village, n (%)	4 (8.7)
Living with the family	
Yes, n (%)	41 (89.1)
No, n (%)	5 (10.9)
Multiple diseases	
Yes, n (%)	28 (60.9)
No, n (%)	18 (39.1)

SD – standard deviation.

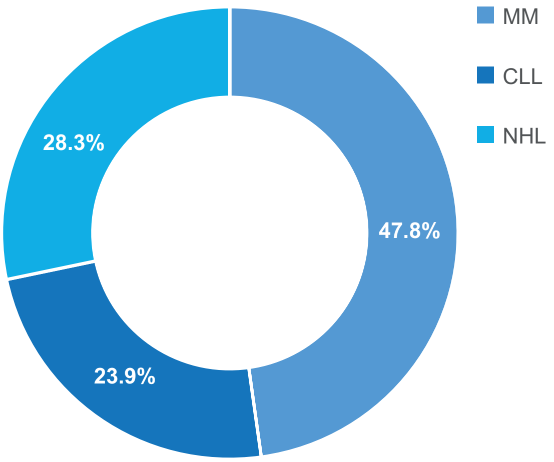

Fig. 1. Incidence of lymphoproliferative neoplasms in the study group

MM – multiple myeloma; CLL – chronic lymphocytic leukemia; NHL – non-Hodgkin lymphoma.

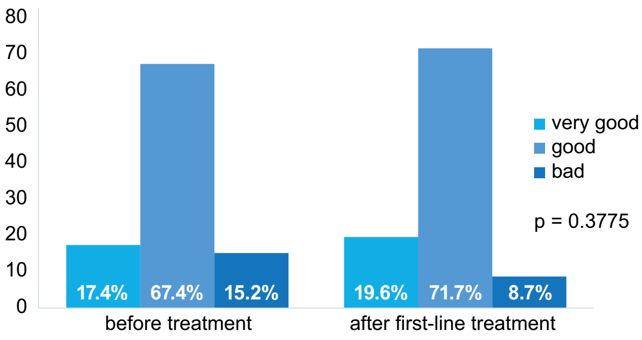

Fig. 2. Self-assessment of patients' health before and after the first-line treatment

Table 3. Parameters of the quality of life and functional scales before and after the first-line treatment

Scale	Before treatment				After first-line treatment				p-value*
	M ±SD	Me	Q1	Q3	M ±SD	Me	Q1	Q3	
QL	60.74 ±15.95	58.33	50.00	75.00	62.68 ±16.73	58.33	58.33	175.00	0.1224
PF	81.59 ±14.14	80.00	80.00	86.67	88.55 ±15.76	93.33	86.67	100.00	0.0004
RF	69.20 ±24.84	66.67	66.67	100.00	72.07 ±22.76	75.00	66.67	100.00	0.1006
EF	71.38 ±12.99	75.00	66.67	83.33	83.88 ±12.47	83.33	83.33	91.67	0.0003
CF	82.97 ±17.39	83.33	66.67	100.00	84.78 ±14.83	83.33	83.33	100.00	0.1219
SF	72.83 ±16.98	66.67	66.67	83.33	74.07 ±18.13	75.00	66.67	100.00	0.1337

* Wilcoxon test; M – mean; SD – standard deviation; Me – median; Q1 – 1st quartile; Q3 – 3rd quartile; QL – global health status/quality of life (QoL); PF – physical functioning; RF – role functioning; EF – emotional functioning; CF – cognitive functioning; SF – social functioning.

Table 4. Parameters of symptom scales and items before and after the first-line treatment

Scale	Before treatment				After first-line treatment				p-value*
	M ±SD	Me	Q1	Q3	M ±SD	Me	Q1	Q3	
FA	21.26 ±18.27	11.11	11.11	22.22	32.13 ±16.27	33.33	22.22	33.33	0.0004
NV	9.42 ±12.98	0.00	0.00	16.67	11.44 ±15.37	0.00	0.00	16.67	0.4445
PA	25.14 ±14.15	22.22	16.67	50.00	10.94 ±13.03	0.00	0.00	33.33	0.0002
DY	18.12 ±26.02	0.00	0.00	33.33	9.42 ±12.95	0.00	0.00	0.00	0.0001
SL	15.94 ±18.24	0.00	0.00	33.33	11.59 ±18.88	0.00	0.00	33.33	0.3612
AP	23.91 ±24.00	33.33	0.00	33.33	12.42 ±15.17	0.00	0.00	33.33	0.0003
CO	18.12 ±16.79	33.33	0.00	33.33	8.70 ±14.80	0.00	0.00	33.33	0.0116
DI	11.59 ±17.52	0.00	0.00	33.33	9.97 ±17.48	0.00	0.00	0.00	0.4567
FI	8.87 ±12.80	0.00	0.00	33.33	11.32 ±14.27	0.00	0.00	33.33	0.1821

* Wilcoxon test; M – mean; SD – standard deviation; Me – median; Q1 – 1st quartile; Q3 – 3rd quartile; FA – fatigue; NV – nausea and vomiting; PA – pain; DY – dyspnea; SL – insomnia; AP – appetite loss; CO – constipation; DI – diarrhea; FI – financial difficulties.

of fatigue and nausea/vomiting more often after the first line of treatment. The average values regarding financial difficulties also increased. Statistically significant differences were observed for fatigue, pain, dyspnea, appetite loss, and constipation (Table 4).

Discussion

The results of a systematic review on QoL in patients with HMs indicate that these diseases negatively affect the overall QoL. The deterioration in quality was found in all domains of life, both in terms of physical and mental health, as well as the social and professional aspects. Fatigue was the most common physical symptom. A decrease in sexual activity and cognitive functions were also noted.[24] At the same time, our research shows that the overall QoL of hematology-oncology patients improved slightly after the end of the first-line treatment. Cancer is a disease that can negatively affect one's perception of QoL through changes in many aspects of life, the lack of acceptance and the need to adapt to a new and not yet fully understood situation. In our patients, the results of the initial follow-up, which was at the time of diagnosis and initiation of anti-cancer treatment, identified additional stress and a sense of danger and uncertainty in their responses. After completing therapeutic measures, their approach to the disease, and thus also QoL, changed positively. Similar results were obtained by the authors who conducted a longitudinal cohort study in 102 adult oncology patients, performing 3 evaluations (before the administration of the 1st, 2nd and the 3rd/last cycle of chemotherapy), whose QoL was slightly better at the end of treatment.[25] Patients treated with a hematopoietic stem cell transplant showed much better QoL at 3 months after the procedure compared to the baseline period (71.39 ±12.32 compared to 60.00 ±13.20).[26] Also, in patients with acute myeloid leukemia (AML) after induction chemotherapy, the global QoL increased compared to the time of diagnosis (65.5 ±21.0 compared to 49.3 ±26.3).[10] A similar trend was noted in patients with CML, which continued for 2 years from the baseline period.[27] Inverse results were obtained in patients with acute leukemias[28] and MMs.[29] These differences may result from a number of variables, including study size, type and stage of cancer, treatment, adverse effects, and the period of observation.

Interestingly, the improvements in QoL of patients may also be influenced by the favorable changes observed in their diet, as reported in a systematic review by Govindaraju et al. These authors searched 8 databases for publications on the correlation between the use of specific eating patterns and QoL or health status in patients with an average age ≥60 years old. In the majority of analyzed studies, the use of rational eating patterns (e.g., the Mediterranean diet) was associated with a better self-esteem and QoL in one or more aspects of life.[30]

Based on our analysis, the functional aspects with the greatest changes were seen in the physical and emotional state of the respondents. There was a significant improvement in the physical domain during the observation period (88.55 ±15.76 compared to 81.59 ±14.14). Therefore, it can be concluded that after completing the first-line therapy, everyday activities were less difficult for patients. A slight increase in this parameter was also shown after induction chemotherapy in 255 patients with AML.[10] The same trend was noted after 3, 6, 12, 18, and 24 months in patients with CML.[27] A different result was obtained in patients with newly diagnosed acute leukemias, in whom a significant deterioration of physical functions was observed after the administration of induction chemotherapy. At the same time, when comparing the results for both described groups, it should be noted that patients with AML and acute lymphoblastic leukemia had much lower values in this domain even before the treatment (70.68 ±20.75 compared to 81.59 ±14.14).[28] Patients with MM had an even greater decrease in physical functioning before the treatment (53.9 ±26.3), and it dropped significantly 3 months after chemotherapy (38.9 ±21.3).[29] Conflicting results were obtained in patients with diffuse large B-cell lymphoma, CLL and AML. During the follow-up after the 2nd treatment cycle, the value of physical functioning was 69.67 ±18.16. It slightly decreased (68.89 ±21.81) after the 1st month, and then increased substantially (80.35 ±18.52) 6 months after the end of therapy.[31]

In our study, changes in role and social functioning also slightly improved during the 2nd follow-up period. This means that patients felt slightly less restricted in their work and hobbies, as well as in their family and social life. This is an ambiguous result, which seems to be the outcome of a better organization in this sphere of life, where, despite hospital stays or adverse effects related to the treatment, patients remained professionally and socially active. Similar results were obtained by Salas et al., who showed that patients examined before the last cycle of chemotherapy had better results in terms of role and social functioning.[25] An upward trend in these domains was also shown in patients observed over 3 periods – after the 2nd treatment cycle and at the 1st and 6th month after its completion.[31] Interestingly, in German observations conducted among 109 patients with HMs, the mean values in both spheres were much lower (37.4 ±37.6 for role functioning and 43.9 ±36.8 for social functioning).[32]

It is possible that due to the changes described above, there were significant differences in the emotional domain, assessed in terms of mental tension, worry, irritation, and depression. As shown by the results of a cross-sectional study conducted among 87 patients with HMs, a disorder in this sphere of life significantly affects one's global QoL.[33] Similar conclusions were reached by other authors who showed that patients with more stress had worse QoL.[32] In our study, patients experienced negative emotions more often during the diagnosis period, likely due to the state of uncertainty about their future and a high level of mental tension. Of course, therapy can also evoke such emotions, but the appropriate support from family, friends and medical staff can reduce their severity. In addition, the treatment aimed at improving a patient's health, which they are aware of, should have a positive effect on the results. Improvements in this parameter were also observed after the completion of induction chemotherapy in patients with AML,[10] CML[27] and MM.[29] The same trend was also shown in patients after the hematopoietic stem cell transplant.[25] Also, comparing the data of hematology-oncology patients after the 2nd treatment cycle and after its completion, the values of emotional functioning significantly increased.[31] However, different results were shown in patients with acute leukemias, in whom the implementation of induction chemotherapy was associated with a significantly negative impact on emotional functioning.[28]

When analyzing cognitive functioning defined by difficulties in focusing attention and remembering, slightly better values were observed in patients during the 2nd period of observation (84.78 ±14.83 compared to 82.97 ±17.39). This may be due to a lower emotional burden which is consistent with the results reported by other authors.[10,31] Interestingly, in a study conducted in patients with AML and acute lymphoblastic leukemia, the baseline results in this sphere of life were higher (91.09 ±15.37) and slightly decreased (88.33 ±21.60) after the treatment. However, these subjects were younger (mean age: 33.03 ±15.4 years).[28] A significant decrease in this domain was observed in patients with MM after induction chemotherapy compared to the period before its implementation (57.3 ±28.1 and 78.0 ±27.1, respectively).[29]

The greatest changes in symptom severity were observed in fatigue, pain, dyspnea, loss of appetite, and constipation. Of these symptoms, only the severity of fatigue, described as the need to rest and feeling of weakness, increased significantly during the 2nd stage of our study (21.26 ±18.27 compared to 32.13 ±16.27). The remaining symptoms decreased significantly in their severity. Among other symptoms, the intensity of nausea and vomiting increased slightly, while insomnia and diarrhea decreased in intensity. This may be largely due to the fact that patients often received medications to alleviate the adverse effects of therapy. Divergent results were obtained in patients with acute leukemia who, after the 1st administration of induction chemotherapy, noticed an increase in all the described symptoms, except for dyspnea.[28] Different results were seen in a study of patients treated for diffuse large B-cell lymphoma, CLL and AML. The severity of fatigue, nausea and vomiting, insomnia, loss of appetite, constipation, and diarrhea decreased during the period from the 2nd treatment cycle to a month after its completion, while the intensity of pain and dyspnea increased during this time.[31] On the other hand, patients with AML after the completion of induction chemotherapy showed a lower intensity of all these symptoms, except for constipation.[10] Interestingly, the authors of a prospective study of 124 patients with CML reported that the baseline severity of fatigue was an independent predictor of achieving a greater molecular response.[27]

In our study, during the 2nd follow-up, patients more often chose a higher value in the dimension of financial difficulties. This could be related to both the costs of absenteeism at work and the treatment itself. Other authors obtained similar results in this aspect of life.[26,28] However, different results were seen in patients with MM, in which this value decreased significantly 3 months after chemotherapy compared to the period before the treatment (14.7 ±28.9 compared to 41.3 ±41.1).[29]

In summary, assessing the QoL in hematology-oncology patients is extremely important for many clinical reasons. Both the disease itself and the applied anti-cancer therapy may cause adverse effects that directly affect the patient's physical and mental health, indirectly influencing their social and professional situation. At the same time, QoL has a prognostic value in terms of treatment success and prognosis; therefore, the assessment of this parameter should be conducted during early stages of clinical management. Certain types of interventions, such as physical programs and psychotherapy can help in improving the QoL.[24,34]

Limitations

Our study has several limitations. The basic element is the relatively small size of the study group, as well as a wide range of patient ages and their clinical and therapeutic heterogeneity. This also closely correlates with the limitation in the ability to conduct detailed statistical analyses. Moreover, this was a single-center study and the obtained results may not reflect that of the population.

Conclusions

After the 1st line of treatment, patients perceived their overall QoL to be slightly better compared to the diagnostic period.

During the 2nd evaluation period, the results for all functional scales increased, indicating a better level of patient functioning. Additionally, significant changes took place in the physical and emotional spheres.

Most of the values on the symptom scales during the 2nd period of the study significantly decreased, which indicates a lower intensity of symptoms. Additionally, significant differences were seen in pain, dyspnea, appetite loss, and constipation.

After the end of treatment, an increase in the intensity of symptoms was seen in fatigue as well as nausea and vomiting. At this time, patients also experienced financial difficulties more often.

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