A retrospective study of treatment and outcomes of patients with lymphoma undergoing hematopoietic stem cell transplantation

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Research Article

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Abstract

Purpose

Early evaluation of symptoms and taking appropriate preventive measures can improve outcomes for patients with lymphoma undergoing hematopoietic stem cell transplantation. This study was conducted to examine the treatment and outcomes of patients with lymphoma undergoing hematopoietic stem cell transplantation.

Methods

Patients with lymphoma (n=64) undergoing SCT at a university hospital between June 15, 2018 and June 15, 2020 were selected for retrospective study. The medical treatments of patients were obtained from the records on the Hospital Information Management System database. The study was reported following the STROBE checklist. Standard deviation, arithmetic mean, frequency, percentage test, t-test, chi-square, Fisher's exact test, Mann-Whitney U test, Independent t-test, and multivariate logistic regression analysis were used to analyze the data.

Results

The mean age of patients was 48.25±16.93. Although relapse developed in 26 patients with lymphoma, remission was achieved in 38 patients. The incidence of skin graft-versus-host disease (GVHD) symptoms in patients with relapse was found to be significantly higher than in patients in remission. The most common symptoms seen in patients undergoing stem cell transplantation were oral mucositis, febrile neutropenia, and anemia. Most patients were found to receive oral care, antibiotic treatment, and granulocyte-colony stimulating factor (G-CSF) treatment following SCT.

Conclusions

Patients experienced severe symptoms due to HSCT, and necessary treatment was applied for the symptoms. Further clinical studies must determine the symptoms and patient outcomes associated with SCT.

Introduction

Lymphoma is an important health problem due to disease-and treatment-related complications and the development of treatment-bound secondary cancers [1–3]. According to the World Health Organization (WHO) data, the incidence of lymphoma is 8.1%, and the mortality rate is 3.3% [4]. According to Center for International Blood & Marrow Transplant Research (CIBMTR) data, 22,729 stem cell transplantations (SCTs) are performed in the United States each year [5]. When the two-year survival of patients with lymphoma is examined, it is seen that there is an approximately 57% variance [6].

One of the treatment types applied as a standard of care for treating lymphoma, particularly in cases with a poor prognosis, is SCT. Autologous SCT or allogeneic SCT is performed in the selected cases. In autologous SCT, cells are obtained from the person's own body, whereas in allogeneic SCT, cells are obtained from a donor [7] Patients with lymphoma may experience many symptoms and syndromes such as anemia, febrile neutropenia, thrombocytopenia, and graft-versus-host disease (GVHD) during hematopoietic stem cell transplantation (HSCT) [8, 9]. Additionally, some complications accompany the symptoms since the care provided to patients in SCT units is critical. Complications such as malnutrition and movement problems because of prolonged bed rest may reduce patients' perception and adversely affect their outcomes [1, 10].

Severe symptoms/complications experienced by patients with lymphoma may adversely affect the quality of healthcare services and lead to life-threatening problems [10–12]. Therefore, it is essential for nurses working in SCT units to follow up on the treatment and outcomes of patients with lymphoma frequently [8, 13]. HSCT is among the treatment approaches that prolong the life of patients with lymphoma, improve their quality of life, achieve remission success and reduce the incidence of relapse [11, 14]. Although SCT contributes positively to the recovery process of patients with lymphoma, it causes patients to face many social, economic, and psychological problems [15, 16]. Patients experience many symptoms depending on the disease and treatment process, and in this case, their life processes are affected and the satisfaction from life is prevented [3, 9].

It is predicted that educational interventions for patients with lymphoma can be planned and their comfort can be achieved by determining the symptoms that they experience and examining the treatment and patient outcomes [13, 17]. In this process, nurses should evaluate the findings of complications effectively and comprehensively to identify the symptoms early and increase the quality of care [2, 9, 18]. Additionally, it is thought that nurses' evaluation of treatment processes and patient outcomes will help determine the content of care and counseling programs to be offered to patients, choosing treatment and care programs specific to them, increasing their compliance with care and treatment goals, controlling the negative effects of the disease and treatments, and improving their outcomes. Therefore, this study was planned to evaluate the treatment and outcomes of patients with lymphoma undergoing HSCT.

Methods

Study design

A retrospective study design was used. All patients with lymphoma undergoing HSCT at a university hospital between June 15, 2018 and June 15, 2020 were selected for the study. This hospital has an SCT unit and an average of 100 hematology patients are admitted for SCT annually. The STROBE control checklist was used to report the results (Supplementary File 1).

Setting and participants

Patients who were aged 18 years and over, were diagnosed with lymphoma, undergoing SCT, and had a complete Hospital Information Management System (HIMS) record were included in the study. HIMS is the abbreviation of the general name given to a software group used to processing all medical patient data. Repeated admissions were not taken into account in the study, and each patient's admission was independently examined. No sampling procedure was applied. All patients with lymphoma who were hospitalized in the stem cell unit between the study dates were included in the study. In this study, data from 74 patients with lymphoma were obtained. Five patients younger than 18 years (7.3%) and five patients with incomplete HIMS data (7.3%) were excluded from the study. Therefore, patients with lymphoma (n = 64) who undergoing HSCT and met the inclusion criteria were included in the study. The rate of reaching the sample was determined as 86.5%.

Data collection

In this study, a patient information form was used in line with data on the HIMS database. The data of patients were retrieved from the database by using Structured Query Language (SQL) scripts, which is a structured query language, with the help of the Hospital Information Processing personnel. The retrieved data were arranged on Microsoft Excel software. Accordingly, the demographic characteristics of patients with lymphoma, their medical history (diagnosis, metastasis status, presence of chronic disease), medical treatment processes (type of SCT, treatment method, treatment protocol), symptoms experienced during hospitalization, and patient outcomes (data for relapse and remission) were recorded on a Microsoft Excel file.

Data analysis

The Shapiro-Wilk test was used to test the normality of the data. Continuous variables were given with mean ± SD for normally distributed data and median (min-max) for non-normally distributed data. Categorical variables were expressed as frequencies (n) and percentages (%). Pearson chi-square test and Fisher’s exact test were used for the analysis of categorical variables. Mann-Whitney U test was performed for non-parametric comparisons of continuous data while an Independent t-test was used for parametric comparisons. Multivariate logistic regression analysis was used to determine the independent predictors of recurrence. The significant variables in the univariate analysis were included in the multivariate model. The results of the model were reported with odds ratios (OR) and corresponding 95% confidence intervals (95% CIs). Statistical analysis was performed with IBM SPSS Statistics for Windows, Version 23.0 (IBM Corp., Armonk, NY). A two-sided p-value less than 0.05 was considered statistically significant.

Ethics

Written approval was obtained from the Clinical Research Ethics Committee of a University Hospital (26.08.2020/606) and from the hospital where the study was conducted. The study was conducted following the Declaration of Helsinki. The data obtained were kept confidential.

Results

Patient characteristics

The mean age of patients included (n = 64) in the study was 48.25 ± 16.93 years, 78.1% were male, and 56.3% were single, 40.6% of them had Diffuse Large B-Cell Lymphoma (DLBCL), and 25% had Hodgkin Lymphoma (HL). The median time of diagnosis was 24 (min-max: 5–54) months. Metastasis was seen in 18 (28.1%) of patients with lymphoma. Of the patients, 93.8% had undergone autologous SCT, and 84.4% had undergone SCT once. While most patients received only chemotherapy (75%), 25% received both chemotherapy and radiotherapy. The median count of cures was 4 (min-max: 2–7), hospital stay was 23 (min-max: 16–43) days, and remission was 18 (min-max: 4–36) months. Relapse was found in 26 (40.6%) of patients with lymphoma, while remission was achieved in 38 (59.4%) patients. The rate of DLBCL (61.5%) diagnosis in patients with relapse was significantly higher than that in patients in remission (26.3%) (p = 0.046). The rate of autologous SCT (100% and 84.6%) in patients with remission and the rate of allogeneic SCT (15.4% and 0%) in patients with relapse were significantly higher (p = 0.024). We observed that the application of the Tiotepa + Carmustine treatment protocol (21.1%) was higher in patients in remission than in patients with relapse (0%) (p = 0.045). The count of cures (Mean Rank = 37.39) applied in patients in remission was higher than in patients with relapse (Mean Rank = 25.35; p = 0.008) (Table 1).

Table 1
Patient characteristics

Variables	All patients	Relapse	Remission	p
Number of patients (%)	64	26(40.6)	38(59.4)	-
Age (year), *mean ± SD*	48.25 ± 16.93	47.46 ± 17.22	48.79 ± 16.94	0.761
Gender, *n(%)*				
Female	14(21.9)	6(23.1)	8(21.1)	0.847
Male	50(78.1)	20(76.9)	30(78.9)	
Marital status, *n(%)*				
Married	28(43.8)	10(38.5)	18(47.4)	0.481
Single	36(56.3)	16(61.5)	20(52.6)	
Diagnosis, *n(%)*				
Hodgkin lymphoma	16(25.0)	4(15.4)[a]	12(31.6)[a]	**0.046**
Diffuse large B-cell lymphoma	26(40.6)	16(61.5)[a]	10(26.3)[b]	
Foliküler lymphoma	10(15.6)	4(15.4)[a]	6(15.8)[a]	
Primer central nervous system lymphoma	8(12.5)	2(7.7)[a]	6(15.8)[a]	
T-cell lymphoma	4(6.3)	0(0)[a]	4(10.5)[a]	
Diagnosis time (months), *median (min-max)*	24(5–54)	24(5–42)	24(8–54)	0.701
Metastasis status, *n(%)*	18(28.1)	10(38.5)	8(21.1)	0.128
Chronic disease, *n(%)*	20(31.3)	8(30.8)	12(31.6)	0.945
Diabetes mellitus	16(25)	8(30.8)	8(21.1)	0.378
Hypertension	6(9.4)	4(15.4)	2(5.3)	0.213
Hypothyroidism	4(6.3)	0(0)	4(10.5)	0.140
Type of stem cell transplantation, *n(%)*				
Autologous	60(93.8)	22(84.6)	38(100)	**0.024**
Allogenic	4(6.3)	4(15.4)	0(0)	
Number of stem cell transplantation, *n(%)*				
1	54(84.4)	16(61.5)	38(100)	**< 0.001**
2	10(15.6)	10(38.5)	0(0)	
Treatment method, *n(%)*				
Chemotherapy	48(75.0)	20(76.9)	28(73.7)	0.769
Chemotherapy + Radiotherapy	16(25.0)	6(23.1)	10(26.3)	
Treatment protocol, *n(%)*				
BEAM	36(56.3)	16(61.5)[a]	20(52.6)[a]	**0.045**
BCNU	14(21.9)	8(30.8)[a]	6(15.8)[a]	
Ifosfamide + Carboplatin + Etoposide	6(9.4)	2(7.7)[a]	4(10.5)[a]	
Thiotepa + Carmustine	8(12.5)	0(0)[a]	8(21.1)[b]	
Count of cure, *median (min-max)*	4(2–7)	4(2–6) Mean Rank = 25.35	4(3–7) Mean Rank = 37.39	**0.008**
Length of hospital stay (day), *medyan(min-maks)*	23(16–43)	24(16–43)	22(18–29)	0.309
Remission period (months), *median (min-max)*	18(4–36)	-	18(4–36)	-

Independent t-test, Mann-Whitney U test, Pearson chi-square test, Fisher's exact test. Different lowercase letters in a row indicate a statistically significant difference between groups.

Insert Table 1 here

Symptoms experienced after SCT

The most common post-transplantation symptoms in patients who undergoing SCT were oral mucositis (78.1%), febrile neutropenia (68.8%), and anemia (56.3%). The incidence of skin GVHD (53.8%) symptoms in patients with relapse was found to be significantly higher than in patients in remission (10.5%) ($p < 0.001$) (Table 2).

Table 2
Symptoms experienced after SCT

Symptoms, n(%)	All patients (n = 64)	Relapse (n = 26)	Remission (n = 38)	p
Oral mucositis	50(78.1)	22(84.6)	28(73.7)	0.367
Febrile neutropenia	44(68.8)	20(76.9)	24(63.2)	0.243
Anemia	36(56.3)	16(61.5)	20(52.6)	0.481
Oral intake disorder	30(46.9)	12(46.2)	18(47.4)	0.924
Pain	22(34.4)	12(46.2)	10(26.3)	0.101
Secretion	20(31.3)	8(30.8)	12(31.6)	0.945
Skin GVHD	18(28.1)	14(53.8)	4(10.5)	**< 0.001**
Thrombocytopenia/bleeding	18(28.1)	10(38.5)	8(21.1)	0.128
Nausea	16(25.0)	8(30.8)	8(21.1)	0.378
Dyspnea	16(25.0)	4(15.4)	12(31.6)	0.142
Vomiting	14(21.9)	6(23.1)	8(21.1)	0.847
Pneumonia	12(18.8)	4(15.4)	8(21.1)	0.747
Cough	12(18.8)	2(7.7)	10(26.3)	0.101
Low IGg	12(18.8)	4(15.4)	8(21.1)	0.747
Diarrhea	8(12.5)	4(15.4)	4(10.5)	0.705
GIS GVHD	2(3.1)	2(7.7)	0(0)	0.161

Pearson chi-square test, Fisher's exact test. Skin GVHD: Skin Graft-Versus-Host Disease, GIS GVHD: Gastrointestinal System Graft-Versus-Host Disease

Insert Table 2 here

Treatments applied after SCT

Most of the patients received oral care (96.9%), antibiotic treatment (93.8%), and granulocyte-colony stimulating factor (G-CSF) (71.9%) treatment after SCT. Additionally, it was determined that patients received antipyretic (55.6%), erythrocyte transfusion (53.1%), antifungal (53.1%), or antiviral (53.1%) treatments. We observed that the rate of receiving antifungal (69.2%), analgesic (69.2%), and anticoagulant (46.2%) treatment after SCT in patients with relapse was significantly higher (respectively: 42.1%, 26.3%, and 15.8%) than in patients in remission (respectively: $p = 0.033$; $p = 0.001$; $p = 0.008$) (Table 3).

Table 3
Treatments applied after SCT

Treatments, n(%)	All patients (n = 64)	Relapse (n = 26)	Remission (n = 38)	p
Oral care	62(96.9)	24(92.3)	38(100)	0.161
Antibiotic	60(93.8)	26(100)	34(89.5)	0.140
G-CSF	46(71.9)	20(76.9)	26(68.4)	0.457
Antipyretic	35(55.6)	15(60.0)	20(52.6)	0.565
Erythrocyte transfusion	34(53.1)	16(61.5)	18(47.4)	0.265
Antifungal	34(53.1)	18(69.2)	16(42.1)	**0.033**
Antiviral	34(53.1)	16(61.5)	18(47.4)	0.265
Nutritional	32(50.0)	16(61.5)	16(42.1)	0.127
Analgesics	28(43.8)	18(69.2)	10(26.3)	**0.001**
Antiemetics	20(31.3)	10(38.5)	10(26.3)	0.303
Platelet transfusion	18(28.1)	10(38.5)	8(21.1)	0.128
Anticoagulant	18(28.1)	12(46.2)	6(15.8)	**0.008**
Oxygen	16(25.0)	4(15.4)	12(31.6)	0.142
Nebula	16(25.0)	4(15.4)	12(31.6)	0.142
IVIG	10(15.6)	2(7.7)	8(21.1)	0.181

Pearson chi-square test, Fisher's exact test, IVIG: Intravenous Immunoglobulin G Therapy, G-CSF: Granulocyte Colony Stimulating Factor

Insert Table 3 here

Symptoms experienced after SCT according to patients' demographic characteristics

According to the study findings, the rate of febrile neutropenia (78.3% and 44.4%; p = 0.015) and secretion (39.1% and 1.1%; p = 0.037) in patients aged 18–64 years and oral intake disorder (88.9% and 30.4%; p < 0.001) in patients aged 65–74 were significantly higher after SCT. The incidence of febrile neutropenia (80% and 28.6%) in male patients and oral intake disorder (71.4% and 40%) in female patients were found to be statistically higher (p = 0.001; p = 0.037). Diarrhea (18.2%) was seen more common in patients without chronic diseases (0%) than in patients with chronic disease (p = 0.049). Oral mucositis was higher in patients with DM (100% and 70.8%; p = 0.014), and the rate of pain (41.7% and 12.5%; p = 0.038) was higher in patients without DM. Anemia (100% and 51.7%; p = 0.031), skin GVHD (66.7% and 24.1%; p = 0.048), and thrombocytopenia/bleeding (66.7% and 24.1%; p = 0.048) rates were found to be higher in patients with hypertension (Table 4).

Table 4
Symptoms experienced after SCT according to patients' demographic characteristics

	Age			Gender			Chronic diseases			DM		
Symptoms, n(%)	**18–64**	**65–74**	**p**	**Female**	**Male**	**p**	**No**	**Yes**	**p**	**No**	**Yes**	**p**
Oral mucositis	36(78.3)	14(77.8)	0.999	10(71.4)	40(80.0)	0.485	34(77.3)	16(80.0)	0.999	34(70.8)	16(100)	**0.**
Febrile neutropenia	36(78.3)	8(44.4)	**0.015**	4(28.6)	40(80.0)	**0.001**	30(68.2)	14(70.0)	0.884	34(70.8)	10(62.5)	0.
Anemia	24(52.2)	12(66.7)	0.293	10(71.4)	26(52.0)	0.195	22(50.0)	14(70.0)	0.135	26(54.2)	10(62.5)	0.
Oral intake disorder	14(30.4)	16(88.9)	**< 0.001**	10(71.4)	20(40.0)	**0.037**	20(45.5)	10(50.0)	0.736	22(45.8)	8(50.0)	0.
Pain	18(39.1)	4(22.2)	0.200	4(28.6)	18(36.0)	0.755	18(40.9)	4(20.0)	0.103	20(41.7)	2(12.5)	**0.**
Secretion	18(39.1)	2(11.1)	**0.037**	2(14.3)	18(36.0)	0.193	16(36.4)	4(20.0)	0.191	16(33.3)	4(25.0)	0.
Skin GVHD	12(26.1)	6(33.3)	0.554	2(14.3)	16(32.0)	0.315	10(22.7)	8(40.0)	0.230	10(20.8)	8(50.0)	0.
Thrombocytopenia/bleeding	16(34.8)	2(11.1)	0.070	4(28.6)	14(28.0)	0.999	14(31.8)	4(20.0)	0.384	14(29.2)	4(25.0)	0.
Nausea	10(21.7)	6(33.3)	0.352	6(42.9)	10(20.0)	0.095	12(27.3)	4(20.0)	0.757	14(29.2)	2(12.5)	0.
Dyspnea	8(17.4)	8(44.4)	0.051	4(28.6)	12(24.0)	0.736	8(18.2)	8(40.0)	0.117	10(20.8)	6(37.5)	0.
Vomiting	8(17.4)	6(33.3)	0.190	6(42.9)	8(16.0)	0.062	12(27.3)	2(10.0)	0.193	14(29.2)	0(0)	**0.**
Pneumonia	8(17.4)	4(22.2)	0.726	0(0)	12(24.0)	0.054	8(18.2)	4(20.0)	0.999	10(20.8)	2(12.5)	0.
Cough	10(21.7)	2(11.1)	0.483	0(0)	12(24.0)	0.054	8(18.2)	4(20.0)	0.999	10(20.8)	2(12.5)	0.
Low IGg	10(21.7)	2(11.1)	0.483	0(0)	12(24.0)	0.054	8(18.2)	4(20.0)	0.999	10(20.8)	2(12.5)	0.
Diarrhea	4(8.7)	4(22.2)	0.206	2(14.3)	6(12)	0.999	8(18.2)	0(0)	**0.049**	8(16.7)	0(0)	0.
GIS GVHD	2(4.3)	0(0)	0.999	0(0)	2(4)	0.999	0(0)	2(10)	0.094	0(0)	2(12.5)	0.

Pearson chi-square test, Fisher's Exact test.

Insert Table 4 here

Symptoms experienced after SCT according to patients' clinical characteristics

The rate of thrombocytopenia/bleeding (55.6%) after SCT was higher in patients without metastasis than in patients with metastasis (17.4%) (p = 0.004). The rate of pain (100% and 30%; p = 0.012), skin GVHD (100% and 23.3%; p = 0.005), and GIS GVHD (50% and 0%; p = 0.003) was statistically higher in patients undergoing allogeneic SCT. Anemia (63% and 20%; p = 0.016) was higher in patients undergoing SCT once, and diarrhea (40% and 7.4%; p = 0.016) and GIS GVHD (20% and 0%; p = 0.022) were higher in patients undergoing two transplants. Oral mucositis (87.5% and 50%) was found to be statistically higher in patients who received only chemotherapy, and the rate of dyspnea (50% and 16.7%) was higher in patients who received both chemotherapy and radiotherapy (p = 0.004 and p = 0.016) (Table 5).

Table 5
Symptoms experienced after SCT according to patients' clinical characteristics

	Metastasis status			Type of SCT			Number of SCT			Treatment method	
Symptoms, n(%)	**No**	**Yes**	**p**	**Autologous**	**Allogeneic**	**p**	**1**	**2**	**p**	**Chemotherapy**	**Ch + Ra**
Oral mucositis	14(77.8)	36(78.3)	0.999	48(80.0)	2(50.0)	0.206	40(74.1)	10(100)	0.101	42(87.5)	8(5
Febrile neutropenia	14(77.8)	30(65.2)	0.384	40(66.7)	4(100)	0.300	36(66.7)	8(80.0)	0.486	30(62.5)	14(
Anemia	12(66.7)	24(52.2)	0.293	34(56.7)	2(50.0)	0.999	34(63.0)	2(20.0)	**0.016**	24(50.0)	12(
Oral intake disorder	6(33.3)	24(52.2)	0.174	30(50.0)	0(0)	0.116	26(48.1)	4(40.0)	0.738	24(50.0)	6(3
Pain	6(33.3)	16(34.8)	0.913	18(30.0)	4(100)	**0.012**	18(33.3)	4(40.0)	0.726	14(29.2)	8(5
Secretion	6(33.3)	14(30.4)	0.822	20(33.3)	0(0)	0.300	16(29.6)	4(40.0)	0.712	14(29.2)	6(3
Skin GVHD	2(11.1)	16(34.8)	0.070	14(23.3)	4(100)	**0.005**	16(29.6)	2(20.0)	0.712	14(29.2)	4(2
Thrombocytopenia/bleeding	10(55.6)	8(17.4)	**0.004**	18(30.0)	0(0)	0.570	14(25.9)	4(40.0)	0.448	14(29.2)	4(2
Nausea	2(11.1)	14(30.4)	0.197	16(26.7)	0(0)	0.564	14(25.9)	2(20.0)	0.999	12(25.0)	4(2
Dyspnea	4(22.2)	12(26.1)	0.999	16(26.7)	0(0)	0.564	14(25.9)	2(20.0)	0.999	8(16.7)	8(5
Vomiting	2(11.1)	12(26.1)	0.315	14(23.3)	0(0)	0.568	12(22.2)	2(20.0)	0.999	10(20.8)	4(2
Pneumonia	4(22.2)	8(17.4)	0.726	10(16.7)	2(50.0)	0.157	10(18.5)	2(20.0)	0.999	8(16.7)	4(2
Cough	4(22.2)	8(17.4)	0.726	12(20.0)	0(0)	0.999	10(18.5)	2(20.0)	0.999	6(12.5)	6(3
Low IGg	4(22.2)	8(17.4)	0.726	10(16.7)	2(50.0)	0.157	8(14.8)	4(40.0)	0.082	8(16.7)	4(2
Diarrhea	4(22.2)	4(8.7)	0.206	8(13.3)	0(0)	0.999	4(7.4)	4(40.0)	**0.016**	6(12.5)	2(1
GIS GVHD	0(0)	2(4.3)	0.999	0(0)	2(50.0)	**0.003**	0(0)	2(20.0)	**0.022**	2(4.2)	0(0

Pearson chi-square test, Fisher's Exact test.

Insert Table 5 here

The count of cures and the length of hospital stay in patients according to the symptoms experienced after SCT

The count of cures in patients who had anemia seen (Mean rank = 36.83) after SCT was significantly higher than compared to patients without anemia (Mean rank = 26.93) (p = 0.027). The median count of cures was 4 in patients (min-max: 3–7) without diarrhea and 4 in patients with diarrhea (min-max: 2–6), and this difference was found to be statistically significant (p = 0.002). It was determined that the length of hospital stay (22 [min-max: 18–43]) was shorter in patients who had febrile neutropenia (24.5 [min-max: 16–29]) (p = 0.021). Likewise, patients who had secretions had a significantly shorter hospital stay (21 [min-maks: 18–29]) than compared to patients without secretions (23.5 [min-max: 16–43]) (p = 0.036). Hospital stay was statistically significantly longer in patients without thrombocytopenia/bleeding than compared to patients with thrombocytopenia/bleeding (24 [min-max: 16–43] and 22 [min-max: 18–26]; p = 0.031) (Table 6).

Table 6
The count of cures and the length of hospital stay in patients according to the symptoms experienced after SCT

		Count of cure		Length of hospital stay	
Symptoms	**n**	**Median (min-max)**	**p**	**Median (min-max)**	**p**
Oral mucositis					
No	14	4(3–6)	0.293	22(16–43)	0.452
Yes	50	4(2–7)		23(18–29)	
Febrile neutropenia					
No	20	4.5(3–7)	0.238	24.5(16–29)	**0.021**
Yes	44	4(2–6)		22(18–43)	
Anemia					
No	28	4(2–6)	**0.027**	23.5(18–29)	0.935
Yes	36	4(3–7)		23(16–43)	
Oral intake disorder					
No	34	4(3–6)	0.888	22(18–43)	0.387
Yes	30	4(2–7)		24(16–29)	
Pain					
No	42	4(3–7)	0.148	23(18–28)	0.999
Yes	22	4(2–6)		22(16–43)	
Secretion					
No	44	4(3–7)	0.937	23.5(16–43)	**0.036**
Yes	20	4(2–6)		21(18–29)	
Skin GVHD					
No	46	4(2–7)	0.533	23(18–29)	0.548
Yes	18	4(3–6)		23(16–43)	
Thrombocytopenia/bleeding					
No	46	4(2–7)	0.473	24(16–43)	**0.031**
Yes	18	4(3–6)		22(18–26)	
Nausea					
No	48	4(2–7)	0.746	23(18–43)	0.925
Yes	16	4(3–6)		23.5(16–29)	
Dyspnea					
No	48	4(2–6)	0.113	23(18–43)	0.708
Yes	16	4(3–7)		24(16–29)	
Vomiting					
No	50	4(2–7)	0.812	23(18–43)	0.922
Yes	14	4(3–6)		24(16–29)	
Pneumonia					
No	52	4(2–7)	0.472	23(16–29)	0.072
Yes	12	4(3–5)		26(18–43)	
Cough					
No	52	4(2–7)	0.172	23(16–43)	0.333

Mann-Whitney U test.

		Count of cure		Length of hospital stay	
Yes	12	4(3–4)		21(18–29)	
Low IGg					
No	52	4(2–7)	0.640	23(16–43)	0.809
Yes	12	4(3–6)		22.5(18–29)	
Diarrhea					
No	56	4(2–7)	**0.002**	23(16–43)	0.713
Yes	8	3(3–4)		23(20–24)	
Mann-Whitney U test.					

Insert Table 6 here

Discussion

In our study results, the vast majority of patients were treated with chemotherapy and the BEAM protocol and had a long hospital stay (Table 1). It is thought that the length of hospital stay is long because the SCT process is a difficult treatment option and patients experience various symptoms related to transplantation. It was determined that chemotherapy and the BEAM protocol were often applied in SCT [14, 19, 20], and that prolonged hospitalization times were observed [21]. The reason for examining the treatments was to increase the awareness of nurses applying chemotherapy protocols about patients with lymphoma undergoing SCT. In our findings, the count of cures applied to patients in remission was found to be significantly higher. It is recommended to examine the effectiveness of the count of chemotherapy cures in further studies.

In our study, it was found that patients with lymphoma undergoing SCT frequently experienced oral mucositis, febrile neutropenia, and anemia. Also, the frequency of symptoms experienced in the remission group was higher than that in the relapse group (Table 2). Nurses should provide patients with education on the prevention and management of symptoms and monitor their symptoms frequently in line with individual needs. It is important to use evidence-based guidelines in patient care, especially on symptom management. Additionally, with the developing technology, the need for programs that can support distance communication between patients and healthcare professionals and provide distance symptom management in emergencies is increasing.

In our study findings, the incidence of skin GVHD was found to be significantly higher in patients with relapse (Table 2). The reasons for this situation may be related to the diversity of SCT, disease progression, and the coexistence of more than one symptom. In SCT, it is necessary to be careful about the risks that may be caused by GVHD, as it increases the mortality and relapse rate. In a study, it was stated that GVHD increased the relapse status [22, 23], and the severity of symptoms experienced along with GVHD increased. In another study, it was reported that the BEAM protocol could be used as an alternative treatment option in the process of curing GVHD. Additionally, it was stated that the burden of other symptoms decreased rapidly during the recovery phase of GVHD [24]. In a systematic review, oral mucositis was reported in 79.7% of patients who received high-dose chemotherapy before SCT [25]. In a meta-analysis investigating the risk factors for febrile neutropenia in patients with lymphoma undergoing autologous SCT and were followed up as inpatient and outpatient, the risk of febrile neutropenia was found to be significantly lower in patients undergoing outpatient SCT compared to the inpatient group ($p < 0.001$) [26]. GVHD appears to be a common symptom. For this reason, nurses should educate patients with lymphoma on the early signs of GVHD during the SCT process, consider the possibility of relapse in patients who come to the clinic with GVHD and provide appropriate nursing care for their symptoms associated with severe immunological reactions and organ dysfunction due to GVHD.

Patients were found to most frequently receive oral care, antibiotics, G-CSF, antipyretic, erythrocyte transfusion, antifungal, and antiviral treatments for the symptoms after SCT. Antifungal, analgesic, or anticoagulant treatments for patients with relapse were found to be significant compared with patients in remission (Table 3). As a result of the study examining the prophylaxis of febrile neutropenia in patients with lymphoma undergoing autologous SCT, it was reported that the use of G-CSF was beneficial in terms of infection risks that may occur in patients and contributes to the reduction of the burden of other symptoms [27]. It was stated that febrile neutropenia was among the most common reasons for hospitalization in patients undergoing autologous SCT and that the use of antibiotics increased patients' quality of life and reduced hospital admissions [28]. In our study results, it was found that there were similarities between the symptoms experienced by patients with lymphoma and the treatments applied. Oral mucositis, febrile neutropenia, and anemia symptoms were among the reasons for using the treatments applied accordingly. Patients diagnosed with lymphoma undergoing SCT should be educated by nurses about side effects related to treatment practices and they should be followed up for these side effects.

In our study, it was found that febrile neutropenia was significantly more common in the 18–64 age group, and oral intake impairment was found to be significantly higher in patients with lymphoma in the 65–74 age group (Table 4). As a result of autologous SCT applied to elderly patients with lymphoma by Sun et al., it was stated that patients between the ages of 70 and 79 often experienced thrombocytopenia [29]. Oral intake disorder due to old age is an expected symptom, and this symptom may increase further after SCT. In line with these findings, patients with lymphoma should be provided with nursing care, considering the age group characteristics and age-related changes.

Febrile neutropenia was significantly higher in male patients and oral intake impairment was significantly higher in female patients in terms of symptoms observed after SCT by gender (Table 4). The prevalence of anemia and nutrition-related symptoms in females and infection-related symptoms and low IGg in males after SCT is noteworthy. It is recommended that symptoms experienced by gender should be compared in studies with larger sample groups.

In this study, oral mucositis in all patients with lymphoma and DM and pain and vomiting symptoms in patients without DM was significantly higher (Table 4). Considering the findings, such as delay in the wound healing process in diabetes and decrease in neuropathy-related pain sensation, nursing care and symptom management of patients with diabetes and lymphoma should be strengthened. In this study, anemia, skin GVHD, and thrombocytopenia symptoms were found to be significantly higher in patients with hypertension (Table 4). Long-term and continuous follow-up is necessary so that health professionals can apply appropriate and timely treatment to patients [30]. In line with these findings, it is thought that continuous comprehensive evaluation of patient's health status will improve their outcomes, as they experience various symptoms based on their age groups and chronic disease status. It is recommended that investigate the causal relationships between hypertension and diabetes and symptoms seen after SCT in further studies.

In our study, the incidence of thrombocytopenia/bleeding after SCT was significantly higher in lymphoma patients with metastasis (Table 5). It is important to educate patients with lymphoma with metastasis, particularly in terms of thrombocytopenia/bleeding symptoms, which is one of the most vital symptoms, and to follow up with them closely. The study findings indicated that the symptoms of pain, skin GVHD, and GIS GVHD were more intense in patients with allogeneic SCT (Table 5). In the study by Peng et al., (2021) it was reported that patients undergoing allogeneic SCT most frequently experienced GVHD, infection, and bleeding symptoms. In one study, it was stated that the symptoms seen in patients varied depending on treatment options and metastasis status, while it was reported that the count of SCTs did not cause any change in symptoms experienced them [20]. In another study, it was reported that patients most frequently experienced febrile neutropenia symptoms after intense chemotherapy [21]. It can be said that as the count of SCTs increases, the symptoms experienced by patients increase, as well. For this reason, patients must be supported by nurses in symptom management in every process of SCT. In our findings, oral mucositis was significantly higher in patients treated with chemotherapy alone, and dyspnea was significantly higher in those treated with both chemotherapy and radiotherapy. Additionally, it was found that febrile neutropenia, anemia, pain, and cough symptoms were more common in patients who received both chemotherapy and radiotherapy (Table 5). Patients with lymphoma should be provided with nursing care, particularly in terms of symptoms, such as oral mucositis, dyspnea, febrile neutropenia, anemia, pain, and cough, considering the type of treatment applied and the area of radiotherapy.

In our study results, it was found that the symptoms of anemia and diarrhea observed in patients after SCT were associated with the count of cures. Additionally, it was determined that patients with febrile neutropenia and secretion symptoms had a short hospital stay. Patients with thrombocytopenia/bleeding symptoms had a longer hospital stay (Table 6). In a study, it was reported that the most common symptoms experienced by patients after intensive chemotherapy were febrile neutropenia, oral mucositis, and nausea/vomiting. Chuang et al. stated that patients' length of stay varied by the count of cures [31]. Oral mucositis and febrile neutropenia are the most common symptoms during the follow-up of the symptoms of patients with lymphoma and they affect the hospitalization process [26]. It is thought that it is important to educate patients to prevent febrile neutropenia and thrombocytopenia/bleeding, which are the most vital risks for patients with lymphoma, and these symptoms should be a health care priority in patients after SCT. It is necessary to make an early diagnosis of symptoms of patients with lymphoma as expected symptoms of intensive chemotherapy protocols, initiate an effective treatment as soon as possible and perform evidence-based nursing interventions. Thus, it is thought that the symptom load of patients can be alleviated in a short time, the length of hospital stay may be shortened, and their comfort, well-being, quality of life, and life span can be increased.

Limitations

This study has several limitations. The study data were obtained retrospectively from the HIMS database. Also, all 74 patients could not be included in the study due to incomplete data in some patients' medical records.

Conclusion

Oral mucositis, febrile neutropenia, anemia, GVHD, oral intake disorder, and pain are common symptoms, and oral care, antibiotics, or G-CSF treatments are most common treatments for patients with lymphoma undergoing SCT. Nurses should provide education on prevention and management of symptoms, maintain patient care in line with evidence-based guidelines after SCT. It is important to control and manage vital symptoms such as bleeding due to febrile neutropenia and thrombocytopenia in patients with lymphoma very well in terms of length of hospital stay, quality of life, and life expectancy. Additionally, it is recommended to conduct further clinical studies on topics such as the count of chemotherapy cures and the effect of chronic diseases on the frequency of symptoms and patient outcomes in patients with lymphoma undergoing SCT. Today, with the developing technology, the need for programs that can support distance communication between patients and healthcare professionals and provide distance symptom management in emergencies is increasing.

Declarations

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Author contributions

All authors contributed to the study's conception and design. Material preparation, data collection, and analysis were performed by [Merve Gozde Sezgin] and [Hicran Bektas]. The first draft of the manuscript was written by [Merve Gozde Sezgin] and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Ethics declarations

Ethics approval

Not applicable.

Availability of data and material: (data transparency)

Not applicable.

Code availability: (software application or custom code)

Not applicable.

Consent to participate

Not applicable.

Consent for publication

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Conflict of interest

The authors declare no competing interests.

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