İstanbul Med J 2026; 27(3): 268-74
DOI: 10.4274/imj.galenos.2026.91961

Real-World Outcomes of Allogeneic Hematopoietic Stem Cell Transplantation in Lymphoma Patients: A Single-Center Study

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ABSTRACT

Introduction: Lymphomas are heterogeneous hematological malignancies, and despite effective frontline therapies, a subset of individuals develops relapsed or refractory disease. Autologous hematopoietic stem cell transplantation (HSCT) remains the standard approach; however, outcomes are poor after relapse. Allogeneic HSCT (Allo-HSCT) offers a potentially curative graft-vs.-lymphoma effect, but its use has declined due to toxicity and the emergence of novel therapies. Thus, its role in modern lymphoma management remains to be elucidated.

Methods: This retrospective investigation was performed at a single center. Patients with hodgkin lymphoma (HL) and non-HL who had undergone Allo-HSCT between January 2008 and May 2025 were evaluated for clinical characteristics, treatment outcomes, and survival parameters. A total of 25 patients were included in the study.

Results: Among the evaluated variables, only febrile neutropenia (FEN) was significantly associated with a higher mortality and shorter overall survival (OS), while other clinical and demographic factors showed no significant association. $CD34^+$ cell dose demonstrated limited predictive value for mortality (area under the curve: 0.654); the cohort's median OS was 6 months.

Conclusion: FEN emerged as the only clinical factor significantly correlated with increased mortality and with inferior OS, whereas other demographic and transplantation-related variables had no significant impact. $CD34^+$ cell dose demonstrated limited discriminative ability in predicting mortality, suggesting that post-transplant infectious complications may play a pivotal role in patient outcomes.

Keywords: Lymphoma, Allogeneic hematopoietic stem cell transplantation, survival, $CD34^+$ cell, febril neutropenia

Introduction

Lymphomas are hematological neoplasms characterized by significant clinical and biological heterogeneity (1). According to data from 2025, 89,070 lymphoma cases were reported. Lymphoma is classified as the second most frequently diagnosed malignancy among adolescents, in consideration of 19% of cases (2).

Lymphoid neoplasms arise from cells that normally differentiate into T or B lymphocytes. They are classified, according to their cellular origin, as either B-cell or T-cell neoplasms. Hodgkin lymphoma (HL) is a subtype of lymphoma characterized by the presence of neoplastic Reed-Sternberg cells and typically presents with cervical or supraclavicular lymphadenopathy. In contrast, non-HL (NHL) consists of a cohort of neoplastic abnormalities of the reticuloendothelial system, distinguished by systemic symptoms and clinical manifestations (3,4).

The primary treatment for classical HL consists of a combination of chemotherapy and radiotherapy. Autologous hematopoietic stem cell transplantation (HSCT) plays a critical association with the management of relapsed or refractory (R/R) classical HL (5). In contrast, Allogeneic HSCT (Allo-HSCT) in HL is generally reserved for medically eligible individuals who relapse after autologous HSCT and demonstrate only a partial response (PR) or progressive disease (PD) following immune checkpoint inhibition (6,7).

Most NHLs are initially treated with chemotherapy, and the majority of patients achieve remission following first-line therapy (8,9). However, a subset of individuals either relapse following complete response (CR) or exhibit resistance to initial treatment. In patients with R/R NHL, autologous HSCT is commonly employed (10,11). In contrast, Allo-HSCT is rarely used in (R/R)NHL due to its significant treatment-related toxicity and the availability of alternative therapeutic options (12).

This study was presented as an oral presentation at the 14th Annual Meet the Experts of Transplantation and Myeloma: EBMT and TCT Symposium, held in Istanbul, Türkiye, on May 8–9, 2026.

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Cite this article as: Sarıcı A, Kaya E, Kuku İ, Erkurt MA, Berber İ, Hidayet E, et al. Real-world outcomes of Allogeneic hematopoietic stem cell transplantation in lymphoma patients: a single-center study. İstanbul Med J. 2026; 27(3): 268-74

Received: 01.04.2026
Accepted: 13.07.2026
Publication Date: 03.08.2026

Methods

This retrospective analysis, carried out at one institution, processed the clinical information from patients with HL and NHL who were cared for with Allo-HSCT at the Adult Stem Cell Transplantation Unit of İnönü University Turgut Özal Medical Center between January 2008 and May 2025. Clinical characteristics, treatment outcomes, overall survival (OS), progression-free survival, and prognostic factors have been evaluated through a retrospective analysis of electronic medical records.

Ethical approval for this study was obtained from the Institutional Ethics Committee from the İnönü University Health Sciences Non-Interventional Ethics Committee (approval number: 2025/7665, date: April 30, 2025). The study was conducted between May 28, 2025, and August 28, 2025. This retrospective study was conducted using anonymized patient data in accordance with the principles of the Declaration of Helsinki. As this was a retrospective study, individual informed consent was not obtained from the patients.

Information retrieved from medical records included mobilization strategies, time to neutrophil and platelet engraftment, harvested $CD34^+$ cell yield, and the number of chemotherapy cycles administered prior to autologous HSCT. Neutrophil recovery was defined as the attainment of an absolute neutrophil count greater than 0.5×10^9/L for three successive days in the absence of granulocyte colony-stimulating factor support. Platelet recovery was defined as the attainment of a platelet count exceeding 20×10^9/L without transfusion support.

The number of therapy lines received for the disease, conditioning regimens prior to HSCT, use of maintenance therapy after transplantation, and whether a second HSCT was performed were recorded.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). Summary statistics were presented as number and percentage (n, %) for categorical variables, and as mean ± standard deviation [mean ± standard deviation (SD)] and median (minimum-maximum) for continuous variables.

The Mann-Whitney U test was applied to compare two groups. Categorical variables were compared using the Pearson chi-square test, with Fisher's exact test applied when appropriate. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the predictive value of CD34 for mortality. OS was assessed by the Kaplan-Meier method and compared using the log-rank test. Statistical significance was defined as $p<0.05$.

Results

The comparison of sociodemographic and hospital-based variables of individuals grouped by mortality status is presented in Table 1. The comparative analysis showed no statistically significant differences in age, sex, underlying disease type, number of prior chemotherapy lines and cycles, number of transplant procedures, conditioning regimen, pre-

Table 1. Association of sociodemographic and clinical variables with mortality

Variables	Total (n,%) n=25	Alive (n,%) n=11	Dead (n,%) n=14	p
Age				
Mean ± SD	39±11	38±13	39±10	0.701[a]
Median (min-max)	40 (19-63)	39 (20-63)	41 (19-54)	
Sex				
Female	9 (36)	4 (36)	5 (36)	1.000[b]
Male	16 (64)	7 (64)	9 (64)	
Primary disease				
NHL	14 (84)	6 (55)	8 (57)	1.000[b]
HL	11 (16)	5 (45)	6 (43)	
Number of prior chemotherapy lines before HSCT				
1	7 (28)	4 (36)	3 (21)	0.875[b]
2	9 (36)	4 (36)	5 (36)	
3	9 (36)	3 (28)	6 (43)	
Number of chemotherapy cycles prior to HSCT				
Mean ± SD	8.8±4	8.4±4.4	9±4.1	0.700[a]
Median (min-max)	8 (2-18)	8 (3-18)	10 (2-16)	
Number of HSCT				
2	22 (88)	10 (91)	12 (86)	1.000[b]
3	3 (12)	1 (9)	2 (14)	
Conditioning regime				
BU-CY	1 (4)	0 (0)	1 (7)	0.913[b]
BU-CY-E	15 (60)	6 (55)	9 (65)	
BEAM	4 (16)	2 (18)	2 (14)	
Other	5 (20)	3 (27)	2 (14)	

Table 1. Continued

Variables	Total (n,%) n=25	Alive (n,%) n=11	Dead (n,%) n=14	p
Pre-HSCT PLT				
Mean ± SD	118.5±59.7	127±57	112±63	0.701[a]
Median (min-max)	120 (20-226)	120 (53-226)	111 (20-207)	
Neutrophil engraftment time				
Mean ± SD	17±4.7	15,7±3,5	19±6	0.173[a]
Median (min-max)	16.5 (10-30)	15 (10-22)	20 (11-30)	
PLT engraftment time				
Mean ± SD	17.2±7.7	15.9±6.2	18.8±9.4	0.755[a]
Median (min-max)	14.5 (8-35)	13 (8-26)	17 (10-35)	
Disease status before HSCT				
Complete response	10 (40)	6 (55)	4 (30)	0.532[b]
Partial response	8 (32)	3 (27)	5 (35)	
Progression	7 (28)	2 (18)	5 (35)	
Occurrence of FEN				
No	10 (40)	7 (63)	3 (21)	0.049[b]
Yes	15 (60)	4 (37)	11 (79)	
Duration of hospitalization				
Mean ± SD	25.7±20.1	21.8±6.7	28.7±26.2	0.805[a]
Median (min-max)	23 (7-112)	23 (10-33)	22.5 (7-112)	
100-day all-cause mortality				
No	17 (68)			0.273[a]
Yes	8 (32)			
Second ASCT				
No	22 (88)	10 (91)	12 (86)	1.000[b]
Yes	3 (12)	1 (9)	2 (14)	
IPI score				
0	6 (24)	4 (36)	2 (14)	0.555[b]
1	10 (40)	4 (36)	6 (43)	
2	7 (28)	3 (28)	4 (29)	
3	2 (8)	0 (0)	2 (14)	
CD34+ cell count				
Mean ± SD	9.1±7.4	11.2±9.4	7.3±5.1	0.202[a]
Median (min-max)	7.1 (2.3-36.3)	7.5 (2.3-36.3)	5.2 (2.8-22.4)	
Follow-up duration (months)				
Mean ± SD	23.4±27.5	50.1±20.3	2.4±1.9	<0.001[a]
Median (min-max)	6 (1-75)	50 (14-75)	1.5 (1-7)	

[a]: Independent t-test, [b]: Pearson chi square test, [c]: Fisher's exact test, p<0.05 statistically significant. SD: Standard deviation, min–max: Minimum-maximum, NHL: Non-Hodgkin lymphoma, HL: Hodgkin lymphoma, HSCT: Hematopoietic stem cell transplantation, BU-CY: Busulfan–cyclophosphamide, BU-CY-E: Busulfan-cyclophosphamide–etoposide, BEAM: Carmustine, etoposide, cytarabine, and melphalan, PLT: Platelet, FEN: Febrile neutropenia, ASCT: Autologous stem cell transplantation, IPI: International Prognostic index

transplant platelet levels, time to neutrophil and platelet engraftment, and pre-transplant disease status (all p>0.05).

The occurrence of febrile neutropenia (FEN) was significantly associated with mortality, with an increased mortality rate observed in those presenting with FEN compared with those who did not (78.6% vs. 21.4%; p=0.049). These findings indicate that FEN may be an important predictor of mortality (Figure 1).

Patients who survived had a significantly longer follow-up duration compared to those who died (50.09±20.30 months vs. 2.42±1.98 months; p<0.001).

Collectively, these results indicate that among the variables examined, only the development of FEN and follow-up duration were significantly associated with mortality, whereas other clinical and demographic variables was not found to significantly influence mortality.

Table 2 shows the diagnostic performance of CD34 levels for discriminating mortality, evaluated by ROC analysis. According to the analysis, the area under the curve for CD34 was 0.654 (95% confidence interval: 0.422-0.886), suggesting a limited but statistically significant ability of CD34 to predict mortality (p=0.049).

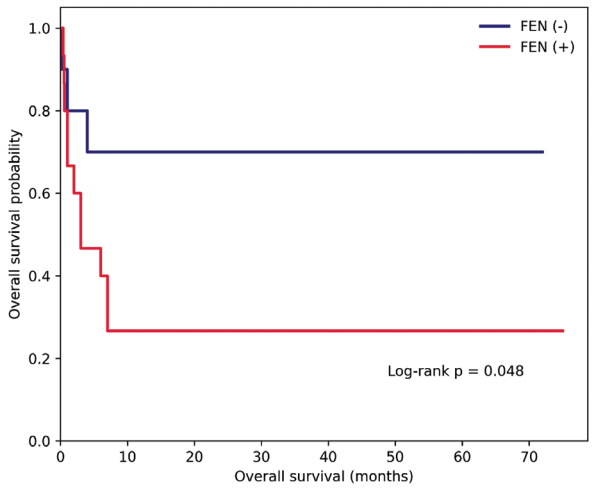

Figure 1. Comparable findings were observed between the groups with respect to length of hospital stay, second autologous transplantation status, IPI score, and CD34^{+} cell dose (all p>0.05). FEN: Febrile neutropenia

The most appropriate cut-off point was determined as ≤7.30, at which CD34 demonstrated a sensitivity of 61.5% and a specificity of 54.5% for the prediction of mortality.

In Table 3, OS outcomes were evaluated using Kaplan-Meier analysis. The median OS in the overall population was 6.00 months (0.0-12.52).

OS did not differ significantly with respect to sex; primary disease type; number of chemotherapy lines and cycles prior to transplantation; number of transplants; platelet count; neutrophil and platelet engraftment times; pre-transplant disease status; presence of a second autologous transplant; IPI score; and CD34 level (all p>0.05).

However, OS differed significantly depending on the development of FEN (p=0.048). The median OS in patients who developed FEN was 3.00 months (1.14-4.85), whereas the median OS was not estimable in those who did not develop FEN. This finding indicates that the development of FEN was associated with poorer OS.

Table 2. Assessment of the discriminative ability of CD34 for mortality

Variables	AUC	%95 CI	Cut-off	Sensitivity (%)	Specificity (%)	p
CD34	0.654	0.422–0.886	≤7.30	61.5	54.5	0.049

AUC: Area under the curve, CI: Confidence interval

Table 3. Comparison of overall survival among patients

Variables	Median (month) (%95 CI)	p
General	6 (0-1.5)	
Sex		
Female	1 (-)	0.702
Male	6 (0.1-11.8)	
Primary disease		
NHL	4 (0-11.3)	0.930
HL	6 (-)	
Number of prior chemotherapy lines before HSCT		
1	- (-)	0.666
2	7 (4.1-9.9)	
3	3 (0.1-5.9)	
Number of chemotherapy cycles prior to HSCT		
<8	7 (-)	0.673
>8	4 (0.2-7.7)	
Number of HSCT		
2	6 (-)	0.899
3	4 (2.4-5.6)	
Pre-HSCT PLT		
<120	6 (0-12.7)	0.953
>120	4 (-)	
Neutrophil engraftment time		
<16.5	- (-)	0.592
>16.5	- (-)	

Table 3. Continued

Variables	Median (month) (%95 CI)	p
PLT engraftment time		
<14.5	- (-)	0.412
>14.5	6 (0-14.7)	
Disease status before HSCT		
Complete response	- (-)	0.365
Partial response	2 (0-4.7)	
Progression	3 (0-8)	
Occurrence of FEN		
No	- (-)	0.048
Yes	3 (1.1-4.8)	
Second ASCT		
No	6 (-)	0.899
Yes	4 (2.4-5.6)	
IPI score		
0	- (-)	0.478
1	4 (0-8.6)	
2	7 (0-19.8)	
3	2 (-)	
CD34+ cell count		
<7.3	3 (0-10)	0.416
>7.3	- (-)	

Kaplan-Meier analysis and the log-rank test were used. A p value <0.05 was considered statistically significant. CI: Confidence interval, NHL: Non-Hodgkin lymphoma, HL: Hodgkin lymphoma, HSCT: Hematopoietic stem cell transplantation, PLT: Platelet, FEN: Febrile neutropenia, ASCT: Autologous stem cell transplantation, IPI: International Prognostic Index

No statistically significant differences were observed for the other variables; variations in median survival were apparent across some subgroups but did not reach statistical significance. Overall, only FEN was significantly associated with OS among the variables analyzed.

Discussion

In our study evaluating the outcomes of our Allo-HSCT patients, most sociodemographic and clinical variables—including age, sex, disease characteristics, treatment-related factors, engraftment parameters, and $CD34^+$ cell dose—had no statistically significant association with mortality or OS. In contrast, the development of FEN emerged as the only clinically relevant predictor of both increased mortality and shorter OS, highlighting its potential role as a key adverse prognostic indicator. Although $CD34^+$ cell dose demonstrated modest discriminative ability for mortality in ROC analysis, it did not translate into a difference in survival. Additionally, patients with longer follow-up were more likely to survive, as expected. Overall, these findings suggest that infectious complications, rather than baseline clinical or transplant-related variables, may exert a greater influence on outcomes in this cohort.

Rivas et al. (13) reported a multicenter analysis of 113 patients with R/R HL who received Allo-HSCT. Patients in CR had significantly improved OS and PFS (both $p \leq 0.001$) and lesser non-relapse mortality (NRM) ($p=0.04$). CR was emerged as an independent factor associated with improved OS and PFS in multivariate analysis (13).

Sureda et al. (14) analyzed 78 relapsed HL patients undergoing Allo-HSCT. NRM was 8% at day 100 and 15% at 1 year. PFS rates were 48% and 24% at 1 and 4 years, whereas OS rates were 71% and 43%. Pre-transplant CR was significantly associated with better outcomes (14).

Mercadal et al. (15) analyzed 53 recipients with B-cell NHL who underwent Allo-HSCT. Patients had a median follow-up of 72 months, with a median of 3 prior treatment lines. The 3-year PFS rate was 55%, OS was 63% and GRFS rates was 55% (15).

Doocey et al. (12) reported outcomes in 44 patients with R/R aggressive NHL undergoing Allo-HSCT. Participants had a mean age of 40 years. Five-year event-free survival (EFS) was 43, and OS was 48%. Grade III–IV acute graft-vs.-host disease proved to be the only significant predictor of both OS and EFS and was associated with poorer survival (12).

Goldberg et al. (16) retrospectively reported the results of 34 participants with NHL who had undergone Allo-HSCT at a single center. The mean follow-up duration among survivors was 45 months. The 2-year OS rate was 0.61. A Ki-67 expression ≤25% was found to be associated with superior OS ($p<0.01$), and HSCT performed in CR was associated with a reduced cumulative risk of events ($p=0.04$) (16).

Tarella et al. (17) evaluated Allo-HSCT in patients with R/R B-cell NHL, encompassing 285 transplant procedures in 281 patients. Patients had a median age at HSCT of 50 years; 94 were female. At transplantation,

47.7% were in CR, 22.3% in PR, 10.6% in SD, and 19.4% in PD. The median follow-up among survivors was 8.7 years. PFS rates at 3 and 9 years were 43.7% and 39.3%, respectively; OS rates were 50.4% and 46.6%. Pre-transplant CR was a favorable predictor of both PFS and OS (17).

Kami et al. (18) evaluated outcomes of Allo-HSCT in recipients with adult T-cell leukemia/lymphoma. The estimated 1-year OS and PFS rates were 53±30% and 45±29%, in that order (18).

Berning et al. (19) investigated 135 patients with natural killer/T-cell lymphoma who underwent Allo-HSCT. The study population had a median age of 43. After a median follow-up of 4.8 years, the 3-year PFS and OS rates were 48.6% and 55.6%, respectively. Multivariate analysis demonstrated that a shorter interval (0-12 months) from disease identification to Allo-HSCT and transplantation performed outside CR/PR were associated with poorer PFS (19).

Rigacci et al. (20) retrospectively analyzed 165 patients with NHL who underwent Allo-HSCT. Post-HSCT, CR and PR were achieved in 72 and 9 patients, respectively, with an OS rate of 49%. Rapid disease progression following HSCT was documented in 84 patients. Multivariate analysis identified remission status prior to transplantation as the only independent predictor of both OS and PFS (20).

Freytes et al. (21) analyzed 114 lymphoma patients undergoing Allo-HSCT and reported a 3-year cumulative incidence of disease progression of 52% and treatment-related mortality of 22%. Achievement of CR at transplant and the use of total body irradiation in patients with NHL were associated with reduced progression events and improved OS (21).

Further multicenter studies with larger patient cohorts, including real-world data, are needed to better define the role of allo-HSCT, particularly in patients with lymphoma.

Study Limitations

Several limitations should be acknowledged in this study. The study's retrospective design and single-center setting may predispose the study to selection bias and restrict the generalizability of the results. Second, the limited sample size may have constrained the power to detect subtle associations, potentially explaining the lack of statistically significant results for certain variables. Third, potential confounding factors—such as differences in supportive care practices, infection management, donor characteristics, and conditioning regimen intensity—could not be fully controlled. In addition, missing or incomplete data inherent to retrospective record-based analyses may have affected the accuracy of some variables. The heterogeneity of the patient population, including both HL and NHL cases with varying disease stages and prior treatment exposures, may also have influenced the outcomes. Finally, the relatively short follow-up period for some patients, particularly those who experienced early mortality, limits assessment of long-term survival outcomes.

Conclusion

FEN was the sole independent predictor significantly associated with increased mortality and reduced OS after Allo-HSCT in patients with HL and NHL. Other clinical variables, including $CD34^+$ cell dose, showed no significant impact. These findings highlight the critical role of infection management in improving outcomes.

Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from the Institutional Ethics Committee from the İnönü University Health Sciences Non-Interventional Ethics Committee (approval number: 2025/7665, date: April 30, 2025).

Informed Consent: This retrospective study was conducted using anonymized patient data in accordance with the principles of the Declaration of Helsinki. As this was a retrospective study, individual informed consent was not obtained from the patients.

Footnotes

Authorship Contributions: Surgical and Medical Practices - İ.K., İ.B.; Concept - E.K., M.A.E., G.V.Ç.; Design - İ.K., İ.B.; Data Collection or Processing - A.S., İ.K., İ.B., G.V.Ç.; Analysis or Interpretation - A.S., E.K., M.A.E., E.H.; Literature Search - A.S., İ.B., E.H., G.V.Ç.; Writing - A.S., İ.K., E.H.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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