HİTİT MEDICAL JOURNAL
HİTİT ÜNİVERSİTESİ TIP FAKÜLTESİ DERGİSİ

e-ISSN: 2687-4717 Cilt|Volume: 7 • Sayı|Issue: 3 - Ekim|October 2025

Analysis of Predictors of Progression-free Survival and Early Response in Young Adult Classical Hodgkin Lymphoma

Genç Erişkin Klasik Hodgkin Lenfomada Progresyonsuz Sağkalım ve Erken Yanıt Öngörücülerinin Analizi

Tuğcan Alp Kırkızlar[1] | Erge Karadağ[2] | Ahmet Yiğitbaşı[1] | Onur Kırkızlar[1] Elif Gülsüm Ümit[1] | Ahmet Muzaffer Demir[1]

[1]Trakya University Faculty of Medicine, Department of Internal Medicine, Division of Hematology, Edirne, Türkiye
[2]Trakya University Faculty of Medicine, Department of Internal Medicine, Edirne, Türkiye

Sorumlu Yazar | Correspondence Author
Tuğcan Alp Kırkızlar
tugcanalp82@hotmail.com
Address for Correspondence: Trakya University Faculty of Medicine, Department of Internal Medicine, Division of Hematology, 22030, Edirne, Türkiye.

Makale Bilgisi | Article Information
Makale Türü | Article Type: Araştırma Makalesi | Research Article
Doi: https://doi.org/10.52827/hititmedj.1652673
Geliş Tarihi | Received: 11.03.2025
Kabul Tarihi | Accepted: 13.05.2025
Yayım Tarihi | Published: 13.10.2025

Atıf | Cite As
Alp Kırkızlar T, Karadağ E, Yiğitbaşı A, Kırkızlar O, Ümit EG, Demir AM. Analysis of Predictors of Progression-free Survival and Early Response in Young Adult Classical Hodgkin Lymphoma. Hitit Medical Journal 2025;7(3):341-349. https://doi.org/10.52827/hititmedj.1652673

Hakem Değerlendirmesi: Alan editörü tarafından atanan en az iki farklı kurumda çalışan bağımsız hakemler tarafından değerlendirilmiştir.
Etik Beyanı: Çalışma için 21/10/2024 tarihinde Trakya Üniversitesi Tıp Fakültesi Girişimsel Olmayan Araştırmalar Etik Kurulu'ndan onay alınmıştır. Karar no: 17/09.
İntihal Kontrolleri: Evet (iThenticate)
Çıkar Çatışması: Yazarlar çalışma ile ilgili çıkar çatışması beyan etmemiştir.
Şikayetler: hmj@hitit.edu.tr
Katkı Beyanı: Fikir/Hipotez: TAK, OK, AMD; Tasarım: TAK, OK, EGÜ, AMD, EK; Data Collection/Data Processing: TAK, EK, AY; Veri Analizi: TAK, EK, AY; Makalenin Hazırlanması: TAK, EK, AY, OK, EGÜ, AMD.
Hasta Onamı: Tüm hastalardan yazılı bilgilendirilmiş onam ve yayın için izin alınmıştır.
Finansal Destek: Bu çalışma ile ilgili herhangi bir finansal kaynaktan yararlanılmamıştır.

Peer Review: Evaluated by independent reviewers working in the at least two different institutions appointed by the field editor.
Ethical Statement: Approval for the study was obtained from the Trakya University Faculty of Medicine Non-Interventional Research Ethics Committee on 21/10/2024. Decision no: 17/09.
Plagiarism Check: Yes (iThenticate)
Conflict of Interest: The authors declared that, there are no conflicts of interest.
Complaints: hmj@hitit.edu.tr
Authorship Contribution: Idea/Hypothesis: TAK, OK, AMD; Design: TAK, OK, EGÜ, AMD, EK; Data Collection/Data Processing: TAK, EK, AY; Data Analysis: TAK, EK, AY; Manuscript Preparation: TAK, EK, AY, OK, EGÜ, AMD.
Informed Consent: Written informed consent and consent for publication was obtained from the patients.
Financial Disclosure: There are no financial funds for this article.

Analysis of Predictors of Progression-free Survival and Early Response in Young Adult Classical Hodgkin Lymphoma

ABSTRACT

Objective: Classical Hodgkin lymphoma (HL) is a common malignancy among adolescents and young adults (AYA). As this age group has biological, clinical, and psychosocial differences compared to other age groups, it is referred to as the AYA group. The present study aimed to evaluate young adult patients diagnosed with classical HL at our center and identify predictors of complete response (CR) at interim evaluation and progression-free survival (PFS).

Material and Method: Patients aged 18-39 years diagnosed with classical HL who were treated and followed up at our center between 2015 and 2023 were retrospectively analyzed.

Results: The median age of 54 patients was 30 years, and 53.7% were female. Nodular sclerosis was the most common subtype, observed in 61.1% of cases. At diagnosis, 48.1% of patients were in the early stage, while 51.9% were in the advanced stage. Among early-stage patients, 53.8% were categorized as unfavorable risk, whereas 46.4% and 7.1% of advanced-stage patients were classified as intermediate and high risk, respectively. In the first-line treatment, 92.6% of patients were treated with the ABVD protocol. At the interim evaluation, the CR rate was 66.1%, while the CR rate at the end of treatment was 88%. The mortality rate was 3,7% during a median follow-up of 47.5 months. The mean overall survival was 107.4 months. The mean PFS was 83.5 months, with no statistically significant difference between the early CR and non-CR groups (*p=0.197*). When the predictors of PFS and CR at interim assessment were analyzed in multivariate analyses, no significant variables were found.

Conclusion: In our study, our results are similar to the literature, and the survival and response rates in the patient population, almost all of whom were on the ABVD protocol, are also encouraging. Despite analyzing potential predictors of PFS and early CR for guiding treatment and follow-up, no significant factors were identified. Furthermore, achieving early CR did not significantly impact PFS.

Keywords: Hodgkin disease, Progression-free survival, Young adults.

ÖZET

Amaç: Klasik Hodgkin lenfoma (HL) ergen-genç erişkin yaş grubunda (AYA) sık görülen bir malignitedir. Bu yaş grubu diğer yaş gruplarına göre biyolojik, klinik ve psikososyal farklılıklara sahip olduğundan AYA grubu olarak ifade edilmektedir. Biz de bu çalışmayla merkezimizdeki genç erişkin grupta Klasik HL tanılı olgularımızı değerlendirmeyi, ara değerlendirmede tam yanıtın (CR-erken yanıt) ve progresyonsuz sağkalım (PFS) öngörücülerini belirlemeyi amaçladık.

Gereç ve Yöntem: 2015-2023 tarihleri arasında merkezimizde klasik HL tanısı alarak tedavi ve izlemi yapılan 18-39 yaş grubundaki hastalar retrospektif olarak incelendi.

Bulgular: Elli-dört hastanın ortanca yaşı 30 yıl ve %53,7'i kadındı. En sık alt tip nodüler sklerozan olup olguların %61,1'inde görüldü. Tanı anında, hastaların %48,1'i erken evredeyken %51,9'u ileri evreydi. Erken evre hastaların %53,8'i olumsuz risk grubundayken ileri evre hastaların %46,4've %7,1'i orta ve yüksek riske sahipti. İlk sıra tedavide hastaların %92,6'sına ABVD protokolü uygulanmıştı. Ara değerlendirmede CR oranı %66,1 iken tedavi sonunda CR oranı %88 idi. Ortanca 47,5 aylık izlem sürecinde mortalite oranı %3,7 idi. Ortalama toplam sağkalım süresi 107.4 aydı. Ortalama PFS süresi 83,5 ay olup, erken yanıt sağlanan ve sağlanamayan gruplar arasında istatiksel fark bulunmadı (*p=0.197*). PFS ve ara değerlendirmede CR öngörücüleri multivariate analizlerde incelendiğinde anlamlı değişken saptanmadı.

Sonuç: Çalışmamızda sonuçlarımız literatürle benzerlik göstermekte olup, tamamına yakınına ABVD protokolü uygulanan hasta grubumuzda sağkalım ve tedavi yanıt oranları da yüz güldürücüdür. Hastaların tedavi yaklaşımı ve izleminde katkı sağlayabilecek PFS ve erken CR öngörücüleri incelenmiş ancak anlamlı değişkenler saptanamamıştır. Bunun yanında erken CR sağlanmasının PFS farkı anlamlı bulunmamıştır.

Anahtar Sözcükler: Genç erişkin, Hodgkin hastalığı, Progresyonsuz sağkalım.

Introduction

Hodgkin lymphoma (HL) is a lymphoid malignancy classified into two main groups based on morphology and immunophenotype: classical and nodular lymphocyte predominant. Classical Hodgkin lymphoma accounts for approximately 90% of all HL cases. It includes four subtypes: 'nodular sclerosis,' 'lymphocyte-rich,' 'lymphocyte-depleted,' and 'mixed cellularity.' While different types and subtypes of HL have a bimodal age distribution or peak in different age groups, overall HL peaks in the 15-35 and over 55 age groups (1-3).

The National Cancer Institute (NCI) defines the 15–39 age group as adolescents and young adults (AYA), considering their distinct pathogenesis, treatment, and psychosocial characteristics. This concept, widely accepted, is also applied to solid tumors and some hematological malignancies, particularly acute lymphoblastic leukemia. The highest incidence of HL occurs in the AYA group. Although there is extensive literature on the management and treatment of older HL patients, research specific to the AYA group remains limited (4-6).

From a treatment point of view, pediatric or adult protocols can be used for this age group, but the results of the studies are controversial. In our country, adult-based protocols are generally preferred for young adults. According to guidelines, initial treatment with the ABVD chemotherapy protocol (adriamycin, vinblastine, dacarbazine, bleomycin) is recommended, except in selected cases of advanced-stage disease. Depending on interim assessment responses, options include dose-reduced or bleomycin-excluded protocols (AVD: adriamycin, vinblastine, dacarbazine), combination with radiotherapy, or intensified treatments (BEACOPP: bleomycin, etoposide, doxorubicin, cyclophosphamide, vinblastine, procarbazine, prednisone), or second-line therapies (7).

In our study, we aimed to evaluate epidemiological, clinical, and treatment outcomes of AYA patients diagnosed with classical HL at our center and to identify predictors of early complete response (CR) and progression-free survival (PFS).

Material and Method

This retrospective study was conducted on patients aged 18–39 years newly diagnosed with classical Hodgkin lymphoma (HL) at the Trakya University Faculty of Medicine, Department of Hematology, between January 2015 and December 2023. The study was performed in compliance with the principles of the Declaration of Helsinki and approved by the Trakya University Faculty of Medicine Non-Interventional Clinical Research Ethics Committee (TÜTF-GOBAEK 2024/417). All of the patients' data were obtained from both electronic and hand-written medical records. Fifty-four patients aged 18–39 years who had been diagnosed with classical HL and whose treatments and evaluations were conducted at our center were included in the study. Patients with classical HL subtypes—'nodular sclerosis,' 'lymphocyte-rich,' 'lymphocyte-depleted,' and 'mixed cellularity'—based on morphological and immunophenotypical evaluations were included. However, nodular lymphocyte predominant HL was considered a separate entity and excluded (3). Data on patients' age, sex, date of diagnosis, B symptoms, morphological and immunohistochemical findings, disease subtypes, presence of extranodal disease, bulky disease, bone marrow involvement, laboratory parameters (hemoglobin, leukocyte, lymphocyte, lactate dehydrogenase (LDH), albumin, and erythrocyte sedimentation rate (ESR) levels, imaging studies (ultrasound (US), computed tomography (CT), positron emission tomography/CT (PET/CT), magnetic resonance imaging (MRI)), lymph node/tissue/bone marrow biopsy evaluations, treatments received, and treatment responses were collected. Staging was performed using the Lugano classification, derived from the Ann Arbor staging system, based on PET/CT imaging findings (8,9). The presence of B symptoms was defined as fever >38°C within the past month, recurrent night sweats, or unintended weight loss exceeding 10% of body weight in the previous six months. Extranodal involvement was classified as limited to nodal-adjacent or closely proximal extranodal sites or as widespread extranodal involvement. Bulky disease was defined as abdominal lymph nodes or masses ≥10 cm in greatest dimension, or mediastinal masses ≥10 cm or exceeding one-third of the thoracic transverse diameter as determined by CT, MRI or US (8,9). Bone marrow involvement was assessed

through morphological and immunohistochemical analyses of unilateral bone marrow aspiration and biopsy samples. Prognosis was assessed using the European Organisation for Research and Treatment of Cancer (EORTC) unfavorable factors for stage I-II patients and the International Prognostic Score-7 (IPS-7) for stage III-IV patients (10,11).

During first-line treatment, clinical, laboratory and PET/CT imaging evaluations were conducted for interim assessment after 2–4 cycles and for end-of-treatment assessment upon planned treatment completion. Response status was classified according to the Lugano response criteria, based on metabolic response assessed using the Deauville score (a 5-point scale) from PET/CT reports. Complete response (CR) was defined as a Deauville score of 1–3 in nodal or extranodal sites, with or without a residual mass. Partial response (PR) was defined as a score of 4 or 5 with reduced uptake compared to baseline and residual mass(es) of any size. Stable disease (SD) was defined as a score of 4 or 5 with no significant change in uptake from baseline. Progressive disease (PD) was defined as a score of 4 or 5 with increased uptake from baseline and/or the presence of new FDG-avid foci consistent with disease. Relapsed disease was defined as the recurrence of the disease in existing or new foci confirmed through morphological and immunohistochemical analysis after achieving CR, while primary refractory disease was defined as a lack of CR or PR to initial therapy. For first-line treatment, patients received the ABVD protocol (doxorubicin, vinblastine, dacarbazine, bleomycin) or the A-AVD protocol (brentuximab vedotin, doxorubicin, vinblastine, dacarbazine) in cases of advanced-stage disease, known pulmonary pathology, or pulmonary involvement with impaired pulmonary function tests. Autologous hematopoietic stem cell transplantation (AHSCT) was performed in cases of relapse or primary refractory disease where chemosensitivity was demonstrated following salvage therapy.

Patients were followed until their last outpatient visit or death. Progression-free survival (PFS) was defined as the time from treatment initiation to disease progression. Overall survival (OS) was calculated from the date of diagnosis to the last follow-up or death.

All statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS, version 26, 2019). Continuous variables were expressed as mean and median values, while categorical variables were expressed as percentages. Overall survival (OS) and progression-free survival (PFS) analyses, as well as group comparisons, were conducted using Kaplan-Meier and log-rank survival analyses. A *p-value of <0.05* was considered statistically significant. Logistic regression analysis was used to evaluate predictors of complete response (CR) at interim evaluation, while Cox regression analysis assessed predictors of progression-free survival (PFS). Variables with p-values of 0.20 or less in univariate analyses were included in multivariate analyses. Variables with *p-values of <0.05* in multivariate analyses were considered statistically significant. A comprehensive set of clinical and laboratory variables—including age, sex, disease subtype, stage at diagnosis, presence of B symptoms, extranodal involvement, bulky disease, splenomegaly, bone marrow involvement, hemoglobin level, leukocyte and lymphocyte counts, serum albumin, lactate dehydrogenase (LDH), erythrocyte sedimentation rate (ESR), and first-line treatment regimen—was included in the analysis to evaluate their potential as predictors of complete response and progression-free survival (PFS). For PFS, interim and end-of-treatment response assessments were also incorporated into the analysis.

Results

Among the 54 patients aged 18–39, 53.7% were female, and the median age was 30 years. The distribution of classical Hodgkin lymphoma subtypes was as follows: nodular sclerosis (61.1%), mixed cellularity (25.9%), lymphocyte-rich (11.1%), and lymphocyte-depleted (1.9%). At diagnosis, 18.6% of the patients were stage IV according to the Lugano classification, and 29.6% presented with B symptoms. Splenomegaly was present in 27.8%, bulky disease in 5.6%, extranodal involvement in 16.7%, and bone marrow involvement in 5.5% of patients. For patients in stages I and II (26 patients, 48.1%), EORTC risk assessment categorized 46.2% as favorable risk and 53.8% as unfavorable risk. In advanced-stage patients (stages III and IV) categorized by IPS-7, 46.5% were low risk, 46.4% medium risk and 7.1% high risk. At

diagnosis, the median erythrocyte sedimentation rate was 35.5 mm/hour, LDH level was 243.5 U/L, albumin level was 4.15 g/dL, leukocyte count was 9.750/mm^3, lymphocyte count was 1.540/mm^3 and hemoglobin level was 11.9 g/dL (Table I).

Table I. Distribution Characteristics of 54 Newly Diagnosed Patients with Classical Hodgkin Lymphoma Aged 18-39 Years

Variable	
Age (median) (n:54)	30 years (min-max:18-39 years)
Sex (n:54) (%)	Female: 53,7 Male: 46,3
Subtype of classical Hodgkin Lymphoma (n:54) (%)	Nodular sclerosis: 61,1 Lymphocyte-rich: 11,1 Lymphocyte-depleted: 1,9 Mixed cellularity: 25,9
Stage of disease based on the Lugano classification (n:54) (%)	I: 7,4 II: 40,7 III: 33,3 IV: 18,6
B symptoms (n:54) (%)	29,6
Extranodal involvement (n:54) (%)	16,7
Bulky disease (n:54) (%)	5,6
Splenomegaly (n:54) (%)	27,8
Bone marrow involvement (n:54) (%)	5,5
Median hemoglobin level (n:54)	11,95 g/dL (7,4-17,4)
Median leukocyte level (n:54)	9.750/mm3 (1.010-26.920)
Median lymphocyte level (n:54)	1.540/mm3 (190-3.400)
Median albumin level (n:54)	4,15 g/dL (2,6-5)
Median lactate dehydrogenase level (n:54)	243,5 U/L (122-763)
Median erythrocyte sedimentation rate level (n:54)	35,5 mm/hour (2-109)
Risk assessment based on EORTC (n: 26) (%)	Favourable: 46,2 Unfavourable: 53,8
Risk assessment based on IPS-7 (n: 28) (%)	0: 3,6 1: 14,3 2: 28,6 3: 32,1 4: 14,3 5: 7,1
First-line treatment (n:54) (%)	ABVD: 92,6 A-AVD: 7,4
Complete response with first-line treatment (n:54) (%)	88,9
Median follow-up time (n:54) (month)	47,5 (7-112)
Mean PFS time (n:54) (month)	83,5 (±5,15) (%95CI)
Mortality rate (n:54) (%)	3,7

EORTC: European Organisation for Research and Treatment of Cancer; IPS-7: International Prognostic Score-7; ABVD: Adriamycin, Bleomycin, Vinblastine, Dacarbazine; A-AVD: Brentuximab vedotin, Adriamycin, Vinblastine, Dacarbazine; PFS: Progression-free survival.

Initial treatment involved the ABVD protocol (adriamycin, vinblastine, dacarbazine, bleomycin) in 92.6% of patients, while the remaining patients received the A-AVD protocol (brentuximab vedotin, adriamycin, vinblastine, dacarbazine) per the specified indications. Interim evaluations after 2–4 courses of first-line treatment revealed complete response (CR) in 61.1%, partial response (PR) in 35.2%, and stable disease (SD) in 3.7% of patients. End-of-first-line treatment assessments showed CR in 88.9% of patients, while 11.1% had SD or progressive disease (PD). Two patients received radiotherapy. Six patients were considered to have primary refractory disease and four patients experienced relapse.

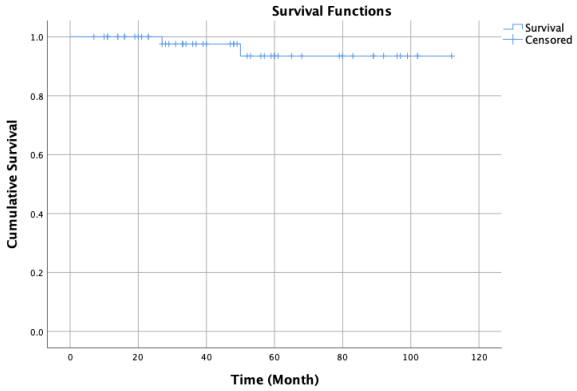

Figure I. Kaplan-Meier Survival Plot for the Entire Patient Group

Second-line treatments included brentuximab-ICE (ifosfamide, carboplatin, etoposide) in five patients, ICE in four patients, and brentuximab-bendamustine combination in one patient. These therapies achieved CR in eight patients, PR in one patient, SD in one patient and PD in one patient. Of the patients who achieved CR after second-line treatment, seven underwent autologous hematopoietic stem cell transplantation (AHSCT) and one declined. Three remaining patients received single-agent brentuximab, nivolumab, or nivolumab-brentuximab. Three patients required ≥4 lines of treatment.

During follow-up, of the eight patients who underwent AHSCT, one was evaluated as having PD at the 3-month follow-up, and another relapsed at the 9-month follow-up. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) was performed in one patient. Over a median follow-up of 47.5 months, two patients died: one due to complications following allo-HSCT and the other, a primary refractory disease

patient, from COVID-19 Pneumonia.

Kaplan-Meier survival analysis revealed a mean overall survival (OS) of 107.4 (±3.16) months (95% CI), with the median OS not reached (Figure I). The mean progression-free survival (PFS) was 83.5 (±5.15) months. When comparing groups with and without CR at interim evaluation using Kaplan-Meier log-rank analysis, the mean PFS was 88.10 (±5.63) months in the CR group and 64.40 (±7.23) months in the non-CR group, although this difference was not statistically significant (*p=0.197*, Figure II).

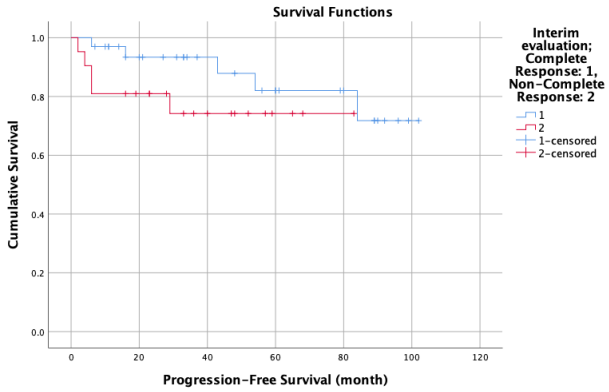

Figure II. Progression-free Survival Kaplan-Meier (log-rank) Analysis Plot of Patients with and without Complete Response at Interim Assessment

Logistic regression analysis assessed variables predictive of achieving CR at interim evaluation. In univariate analysis, male gender, higher hemoglobin levels, and receiving ABVD therapy were associated with increased CR rates (*p=0.041, p= 0.073, p=0.160,* respectively). However, these factors lost significance in multivariate analysis (*p=0.116, p=0.556, p=0.179,* respectively).

Factors predictive of PFS were evaluated using Cox regression analysis. In univariate analysis, lymphocyte-depleted subtype and A-AVD therapy were associated with shorter PFS (*p=0.030, p=0.042,* respectively). These factors lost significance in multivariate analysis (*p=0.329 and p=0.328,* respectively).

Discussion

Hodgkin lymphoma (HL) accounts for 10% of all lymphomas in developed countries. According to data from the United States, the median age at diagnosis is 39 years, with the highest incidence observed in the 20–34 age group (12). For the adolescent and young adult (AYA) group, representing the most frequently affected age range, differences in epidemiological, clinical, and treatment approaches have been proposed to result in distinct disease courses. Compared to studies on older age groups in HL, the literature focusing on the AYA group remains limited.

In a single-center study by Zawati et al. comparing AYA (15–39 years) and adult (≥40 years) classical HL patients in terms of epidemiological, clinical, and treatment outcomes, a total of 112 HL patients were included, of whom 66 represented the AYA group and 46 the adult group. The AYA group had a median age of 27.5 years, and 61% were male. Among these patients, 58% had the nodular sclerosing subtype, and 33% had the mixed cellularity subtype. Furthermore, 72% of the patients were stage II (46%) and III (26%), with B symptoms present in 54% of cases at diagnosis (13). The Pediatric Health Information System database was used to analyse age-related differences in HL in another study by Kendel et al. 3.034 patients aged 0-39 years were included, with 58% in the 15-39 age group. The median age in this age group was 17.2 years. Gender distribution analysis showed that males predominated in younger age groups, while females became more prevalent as age increased. For the 15-39 age range, 52% of the patients were female. Regarding subtype distribution, 66% of patients had the nodular sclerosis subtype, while 5% had the mixed cellularity subtype (14).

A 2021 study using Surveillance, Epidemiology, and End Results (SEER) data analyzed 15.889 patients aged 15-39 years who had survived at least five years post-diagnosis between 1980 and 2009. This study evaluated age, ethnicity, and socioeconomic status. Among these patients, 50% were male, and the median age at diagnosis was 27 years. Approximately half of the patients were stage II at diagnosis, while 12.8% were stage IV (15). The results from our clinic, which included patients aged 18 years and older, revealed a median age of 30 years—slightly higher than that reported in the literature for populations aged 15 years and above. Furthermore, the female predominance of 53.7% observed in our study aligns with similar findings reported by Kendel et al. In terms of subtype distribution, the nodular sclerosis subtype accounted for 61.1% of cases, and 40.7%

of patients were stage II at diagnosis, aligning with trends reported in previous studies.

In the adolescent and young adult (AYA) age group, there are differences in treatment protocols, with pediatric- or adult-based approaches showing varying outcomes and long-term effects. These differences continue to be debated. Supporting the efficacy of adult protocols, the 2006 study by Foltz et al evaluated HL patients between 1981 and 2004. The study compared treatment outcomes of the ABVD protocol, an adult regimen, in 16-21 and 22-45 age groups, concluding similar efficacy. 10-year progression-free survival (PFS) rates were 77% and 80%, respectively, and overall survival (OS) rates for limited disease were 96% in both groups, while in advanced disease they were 88% and 86%, respectively (16). Similarly, the German Hodgkin Study Group's 2009 comparison of 15-20 and 21-45 age groups reported similar survival outcomes (17). However, both studies lacked comparisons with pediatric regimens and assessments of long-term complications. Conversely, studies advocating pediatric-based treatments suggest superior outcomes. Although differences in case distribution between groups, staging, and response assessment criteria are noted, a 2017 study contrasting pediatric and adult protocols did not align with prior findings. In the 17-21 age group, five-year survival to treatment failure was 85% with pediatric protocols but only 68% with adult protocols. Comparing the 17-21 and 22-45 age groups treated with adult regimens, survival to treatment failure was lower in the younger group, at 68% versus 76%, demonstrating a disadvantage for younger patients treated with adult protocols (5). In the study by Marr et al. comparing 55 pediatric patients <18 years and 154 young adults aged 18-25 years, all treated with ABVD, no significant differences in sex, subtype, tumour burden or risk assessment distributions were found between the groups. They concluded that ABVD is an effective treatment (18). In Zawati et al.'s study comparing AYA and adult HL patients, 62% of the AYA group received ABVD, 21% BEACOPP and 3% MOPP-ABVD as initial treatment. With a median follow-up of 51 months, the complete response (CR) rate with initial therapy was 74%. Mortality was 20%, and relapse and refractory disease occurred in 39% of patients. The study highlighted that adolescent patients presented with more advanced diseases at diagnosis, necessitating more intensive therapies (13). In our study, the complete response (CR) rate to initial treatment was approximately 90%, with 93% of patients receiving the ABVD regimen. Over a median follow-up of 47.5 months, 18.5% of patients were classified as having either primary refractory or relapsed disease. In comparison, Zawati et al. reported a primary refractory/relapsed disease rate of 39% in the 15–39-year age group based on data from Tunisia, with a median follow-up of 51 months (13). Meanwhile, Marr et al. observed a lower rate of 19.8% in the 18–25-year age group in a Canadian cohort, with a longer median follow-up of 67 months (18). Notably, this latter finding aligns more closely with the rate observed in our study. These discrepancies may be partly attributable to differences in patient demographics—particularly ethnic background—as well as variations in follow-up duration, age group classifications and treatment approach across studies.

Regarding mortality, the study by Kendel et al, which included a detailed analysis of chemotherapy agents, treatment complications, and supportive care, reported that approximately 70% of patients received alkylating agents, vinca alkaloids, and anthracyclines, while 55% were treated with bleomycin. However, no data on treatment outcomes were included, and the overall mortality rate was reported as 1%, without specifying the causes (14). A study using Surveillance, Epidemiology, and End Results (SEER) data of HL patients surviving five years after diagnosis reported a median follow-up of 9,4 years (15). In our study, the mean overall survival (OS) was 8.95 years, and the mortality rate was 3.7%. Among the two patients who died, one had achieved complete response but succumbed to complications of allo-HSCT two years after diagnosis, while the other, with primary refractory disease, died from an infection four years after diagnosis, despite partial disease control.

Additionally, we analyzed potential predictors of early complete response (CR) and progression-free survival (PFS). However, no significant predictive variables were identified in the multivariate analyses. To the best of our knowledge, there are currently no published data specifically addressing early predictors

of CR in this context, and our findings did not reveal any such factors. Data on predictors of event-free survival (EFS) and PFS in the adolescent and young adult (AYA) population also remain limited. Although the underlying mechanisms contributing to relapse in Hodgkin lymphoma (HL) are not fully understood, several well-established adverse prognostic factors—such as advanced stage at diagnosis, bulky disease, extranodal involvement, presence of B symptoms, and suboptimal early treatment response—are thought to increase the risk of relapse. In a study by Zawati et al. focusing on AYA patients, advanced stage was identified as the primary predictor of inferior EFS, while treatment with the ABVD regimen was associated with improved EFS (13). Similarly, in another study evaluating patients aged 6 to 25 years, Ann Arbor stage IV disease, presence of bulky disease, and B symptoms were identified as prognostic factors for PFS in univariate analysis (18). In contrast to these findings, our study identified the lymphocyte-depleted histological subtype and treatment with A-AVD as being associated with shorter PFS in univariate analysis; however, these variables did not retain statistical significance in the multivariate model. This discrepancy may be attributed to the specific age range of 18–39 years, potential ethnic variation, or the limited number of patients included in the study.

Limitations of our study include its retrospective nature, which may have resulted in incomplete assessment of B symptoms, and some patients discontinuing follow-up or transferring to other centers.

In conclusion, our study focused on the 18-39 age group, a cohort with limited data in the HL literature. The epidemiological distribution in our study is consistent with the existing literature. Furthermore, the response rates and mean survival observed in patients primarily treated with the ABVD protocol support its efficacy as a treatment. However, our analysis did not identify any predictors of prolonged PFS or early CR.

References

1. Medeiros LJ, Greiner TC. Hodgkin's disease. Cancer 1995;75:357-369.

2. Campo E, Jaffe ES, Cook JR, et al. The International Consensus Classification of Mature Lymphoid Neoplasms: a report from the Clinical Advisory Committee. Blood 2022;140:1229-1253.

3. Alaggio R, Amador C, Anagnostopoulos I, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. Leukemia 2022;36:1720-1748.

4. Jachimowicz RD, Engert A. The challenging aspects of managing adolescents and young adults with Hodgkin's lymphoma. Acta Haematol 2014;132:274-278.

5. Henderson TO, Parsons SK, Wroblewski KE, et al. Outcomes in adolescents and young adults with Hodgkin lymphoma treated on US cooperative group protocols: An adult intergroup (E2496) and Children's Oncology Group (COG AHOD0031) comparative analysis. Cancer 2018;124:136-144.

6. Bhuller KS, Zhang Y, Li D, et al. Late mortality, secondary malignancy and hospitalisation in teenage and young adult survivors of Hodgkin lymphoma: report of the Childhood/Adolescent/Young Adult Cancer Survivors Research Program and the BC Cancer Agency Centre for Lymphoid Cancer. Br J Haematol 2016;172:757-768.

7. Akay OM, Birtaş Ateşoğlu E, Mehtap Ö, Salim O. Hodgkin Lenfoma. Türk Hematoloji Derneği Lenfoma Tanı ve Tedavi Kılavuzu içinde, Galenos Yayınevi, İstanbul 2020, 2-23.

8. Lister TA, Crowther D, Sutcliffe SB, et al. Report of a committee convened to discuss the evaluation and staging of patients with Hodgkin's disease: Cotswolds meeting. J Clin Oncol 1989;7:1630-1636.

9. Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. J Clin Oncol 2014;32:3059-3068.

10. André MPE, Girinsky T, Federico M, et al. Early Positron Emission Tomography Response-Adapted Treatment in Stage I and II Hodgkin Lymphoma: Final Results of the Randomized EORTC/LYSA/FIL H10 Trial. J Clin Oncol 2017;35:1786-1794.

11. Hasenclever D, Diehl V. A prognostic score for advanced Hodgkin's disease. International Prognostic Factors Project on Advanced Hodgkin's Disease. N Engl J Med 1998;339:1506-1514.

12. https:// www.seer.cancer.gov. Cancer stat facts/Hodgkin lymphoma (Last access: 18.03.2025)

13. Zawati I, Adouni O, Finetti P, et al. Adolescents and young adults with classical Hodgkin lymphoma in northern Tunisia: insights from an adult single-institutional study. Cancer Radiother 2020;24:206-214.

14. Kendel NE, Stanek JR, Willen FK, Audino AN. Characterizing age-related differences in Hodgkin lymphoma in children, adolescents and young adults. Pediatr Hematol Oncol

2024;41:336-345.
15. Berkman AM, Andersen CR, Puthenpura V, et al. Impact of Race, Ethnicity, and Socioeconomic Status over Time on the Long-term Survival of Adolescent and Young Adult Hodgkin Lymphoma Survivors. Cancer Epidemiol Biomarkers Prev 2021;30:1717-1725.
16. Foltz LM, Song KW, Connors JM. Hodgkin's lymphoma in adolescents. J Clin Oncol 2006;24:2520-2526.
17. Eichenauer DA, Bredenfeld H, Haverkamp H, et al. Hodgkin's lymphoma in adolescents treated with adult protocols: a report from the German Hodgkin study group. J Clin Oncol 2009;27:6079-6085.
18. Marr KC, Connors JM, Savage KJ, Goddard KJ, Deyell RJ. ABVD chemotherapy with reduced radiation therapy rates in children, adolescents and young adults with all stages of Hodgkin lymphoma. Ann Oncol 2017;28:849-854.