Predictors of Relapse and Survival Following Autologous Stem Cell Transplant in Patients with Diffuse Large B-Cell Lymphoma

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Background

- Although the majority of patients with diffuse large B-cell lymphoma (DLBCL) can be cured with intensive chemotherapy and rituximab, 30-40% of patients will be refractory to or relapse after first line treatment. For these patients, the current standard of care is salvage chemotherapy followed by high-dose chemotherapy and autologous stem cell transplantation (ASCT).
- Prior studies have largely examined clinical risk factors associated with higher risk of relapse after ASCT; however, there is limited data integrating both pathologic and molecular features.

Objective

- We aimed to identify high-risk features associated with relapse after ASCT using a combination of clinical, molecular, pathologic, and transplant characteristics.

Methods

- We retrospectively analyzed the medical records of 235 adult patients with DLBCL who underwent ASCT at our two institutions from 2010 to 2020 **(Table 1).** Patients with primary CNS lymphoma, primary mediastinal B-cell lymphoma, or Burkitt lymphoma were excluded. We analyzed demographics, clinical characteristics, cell of origin (COO) by immunohistochemistry (IHC), fluorescence in-situ hybridization (FISH) testing, and treatment/transplant characteristics.
- The primary endpoints were 3-year progression-free survival (PFS) and overall survival (OS) from ASCT. The Kaplan-Meier method was used to estimate survival, with univariate and multivariate Cox proportional hazards regression performed to identify factors associating with PFS and OS.

Table 1: Characteristics

Characteristic	Number (Percent)
Median age at ASCT (years)	61 (range 25-75)
Age <60	131/235 (56%)
Age ≥60	104/235 (44%)
Male sex	149/235 (63%)
Stage at diagnosis	
I-II	46/234 (20%)
III-IV	188/234 (80%)
Extranodal involvement	
Yes	174/234 (74%)
No	60/234 (26%)
R-IPI at diagnosis	
0-3	163/195 (84%)
4-5	32/195 (16%)
Prior indolent lymphoma	
Yes	71/235 (30%)
No	164/235 (70%)
Cell of origin (COO) by IHC	
Germinal center (GCB)	115/191 (60%)
Non-GCB	76/191 (40%)
Double/triple-hit lymphoma (DHL)	
Yes	35/158 (22%)
No	123/158 (78%)
Double-expressor lymphoma	
Yes	14/57 (25%)
No	43/57 (75%)
Disease category	
Primary refractory	29/178 (16%)
Early relapse (<12 mo)	71/178 (40%)
Late relapse (≥12 mo)	78/178 (44%)
Median lines of treatment	2 (range 1-5)
1-2 lines	196/235 (83%)
≥3 lines	39/235 (17%)
Disease status at ASCT	
CR	154/234 (66%)
PR	76/234 (32%)
SD/PD	4/234 (2%)
Conditioning regimen	
BEAM	165/235 (70%)
Cy/TBI	47/235 (20%)
Other	23/235 (10%)

Figure 1: PFS and OS by COO and disease status

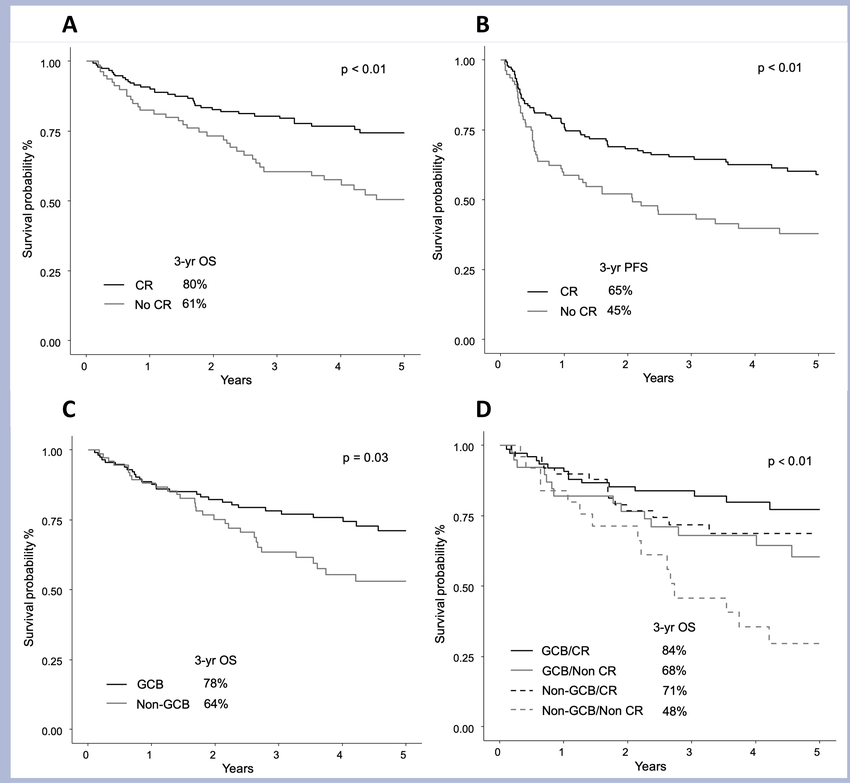

Figure 1. Kaplan Meier plots showing: **A)** OS by disease status at transplant. **B)** PFS by disease status at transplant. **C)** OS by cell of origin. **D)** OS by cell of origin and disease status at transplant.

Results

- With median follow-up of 5.2 years from time of ASCT, 98 patients (42%) relapsed and 78 (33%) died. 3-year PFS and OS were 58% (95% CI 51-64%) and 74% (95% CI 67-79%), respectively.
- In univariate analysis, factors associated with worse PFS and worse OS included 3 or more lines of treatment pre-ASCT (p<0.01 for both) and non-CR at ASCT (p<0.01 for both) **(Figure 1A and B).** Transformed disease was also associated with worse PFS (p=0.03).
- In multivariate analysis, non-CR at ASCT remained significant (HR 2.22, 95% CI 1.26-3.90, p<0.01) for worse OS, along with non-GCB COO (HR 1.81, 95% CI 1.03-3.18, p=0.04) and age >60 at ASCT (HR 1.92, 95% CI 1.06-3.47, p=0.03) **(Figure 1C)**. Stratifying by COO and disease status at transplant, 3-year OS was best in the GCB/CR group (84%, 95% CI 73-90%), while worse but similar in the GCB/non-CR and non-GCB/CR groups (68%, 95% CI 51-80% and 71%, 95% CI 56-83%, respectively) **(Figure 1D).** The non-GCB/non-CR group had the worst 3-year OS (48%, 95% CI 27-67%).
- No individual factors beyond CR/non-CR at ASCT were associated with worse 3-year PFS.
- Notably, DHL/THL patients (77% of whom were in CR at time of ASCT) had similar PFS (p=0.08) and OS (p=0.30) to non-DHL/THL patients, suggesting that response to therapy may be more prognostic than high-risk molecular features alone.

Conclusions

- This analysis indicated that factors associated with OS after ASCT were disease status at time of transplant and COO, with non-GCB patients not in CR having the poorest outcomes. GCB patients not in CR were still able to be cured by ASCT at a high rate. Molecular rearrangements including DHL/THL were not prognostic, although interpretation may be limited by the modest number of DHL/THL patients.
- These findings may inform which patients should undergo ASCT, while the highest risk group may be better treated with alternatives including novel targeted agents or chimeric antigen receptor cell therapy.

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