



Review Article

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**CRITERIA FOR THE SELECTION OF PATIENTS WITH LYMPHOMAS FOR
AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION**

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Abstract. Autologous hematopoietic stem cell transplantation (AH SCT) is a well-established standard treatment for patients with relapsed or refractory lymphomas. However, optimal patient selection remains critical to maximize therapeutic benefit while minimizing treatment-related mortality (TRM). This article aimed to systematically examine the current evidence on criteria guiding patient selection for AH SCT in lymphoma. Chemosensitivity, performance status, disease type and remission status, organ function, Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI) score, and positron emission tomography/computed tomography (PET/CT) response assessment constitute the core selection criteria. Disease-specific nuances are identified across Hodgkin lymphoma (HL), diffuse large B-cell lymphoma (DLBCL), follicular lymphoma (FL), mantle cell lymphoma (MCL), and T-cell lymphoma. Individualized, multidimensional patient selection integrating disease biology, functional status, comorbidity burden, and body composition is essential to optimize outcomes in the era of emerging novel therapies.

Keywords: autologous hematopoietic stem cell transplantation, lymphoma, patient selection, chemosensitivity, HCT comorbidity index, treatment-related mortality, novel therapies.

Introduction. Lymphomas, encompassing Hodgkin lymphoma (HL) and the heterogeneous group of non-Hodgkin lymphomas (NHL), represent one of the most prevalent categories of hematologic malignancies worldwide. Collectively, they account for a substantial proportion of cancer diagnoses, with NHL alone ranking as the seventh most common cancer globally. Despite significant advances in frontline chemoimmunotherapy regimens, a considerable proportion of patients experience disease relapse or demonstrate primary refractory disease following initial treatment. Epidemiological data indicate that approximately 20–30% of patients with NHL and roughly 15% of patients with HL will relapse after first-line therapy, presenting a formidable clinical challenge that necessitates effective salvage strategies (McBride et al., 2017).

Autologous hematopoietic stem cell transplantation (AH SCT) has been established as the standard of care for patients with chemosensitive relapsed or refractory lymphoma for over three decades. The conceptual foundation of AH SCT rests on a two-step therapeutic approach: the administration of high-dose chemotherapy (HDC) designed to eradicate residual malignant cells that have survived prior treatment, followed by the infusion of previously collected autologous hematopoietic stem cells to rescue and restore normal hematopoietic function. This approach leverages the dose-response relationship of cytotoxic chemotherapy, delivering myeloablative doses that would otherwise result in irreversible marrow failure (Savani et al., 2015). The landmark PARMA trial established the superiority of HDC followed by AH SCT over conventional salvage chemotherapy alone for chemosensitive relapsed aggressive NHL, demonstrating significant improvements in both event-free survival and overall survival. Since then, AH SCT has become deeply integrated into treatment algorithms for multiple lymphoma subtypes.

However, the clinical reality is that not all patients with relapsed or refractory lymphoma derive equal benefit from AH SCT. The procedure carries inherent risks, including treatment-related mortality (TRM) estimated at 2–5% in contemporary series, prolonged immunosuppression, organ toxicity from conditioning regimens, and infectious complications. When patients are inappropriately selected—particularly those with chemorefractory disease, severe comorbidities, or poor functional status—the risks of AH SCT may substantially outweigh the potential benefits, leading to

increased TRM without meaningful improvements in disease control or overall survival (Rosenthal et al., 2024). Consequently, the identification of robust, evidence-based criteria for patient selection has become a central concern in transplant hematology.

The landscape of lymphoma therapy has evolved considerably in recent years with the introduction of chimeric antigen receptor T-cell (CAR-T) therapy, bispecific antibodies, antibody-drug conjugates such as brentuximab vedotin, and immune checkpoint inhibitors. These novel agents have expanded the therapeutic armamentarium for relapsed and refractory lymphoma, in some cases offering alternatives to AHST or redefining the patient populations most likely to benefit from transplantation. This evolving therapeutic context underscores the need for a contemporary analysis of selection criteria, ensuring that patients are directed to the most appropriate therapy based on their individual disease characteristics and clinical profile (McBride et al., 2017; Savani et al., 2015).

The objective of this article is to analyze the multidimensional criteria that guide patient selection for AHST across the major lymphoma subtypes. By synthesizing current guidelines from major transplantation societies, recent clinical evidence, and emerging predictive biomarkers, this work aims to provide a comprehensive framework for clinicians navigating the complex decision-making process surrounding AHST candidacy in lymphoma.

Research methods. This study existing literature on patient selection criteria for AHST in lymphoma. The methodology was selected as the most appropriate approach given the broad scope of the topic, which spans multiple lymphoma subtypes, diverse selection criteria, and evolving therapeutic paradigms. Unlike a systematic review with a narrowly defined research question, this article aimed to provide a comprehensive synthesis of clinical guidelines, observational studies, and landmark trials that collectively inform transplant candidacy decisions.

The literature search was conducted across multiple electronic databases, clinical practice guidelines and consensus statements from the European Society for Blood and Marrow Transplantation (EBMT), the American Society for Blood and Marrow Transplantation (ASBMT), and the National Marrow Donor Program (NMDP) were reviewed. The search employed a combination of Medical Subject Headings and free-text terms, including: “autologous HSCT,” “lymphoma,” “patient selection,”

“chemosensitivity,” “HCT comorbidity index,” “Hodgkin,” “non-Hodgkin,” “DLBCL,” “follicular lymphoma,” and “mantle cell lymphoma.”

Inclusion criteria encompassed studies addressing AHSCT selection criteria in adult lymphoma patients, clinical practice guidelines from recognized transplantation societies, randomized controlled trials, prospective and retrospective cohort studies, and meta-analyses published between 1998 and 2025. Exclusion criteria comprised pediatric-only studies, studies focused exclusively on allogeneic hematopoietic stem cell transplantation (unless containing relevant comparative data with AHSCT), single case reports, and publications not available in the English language. The reference lists of identified articles were manually screened to identify additional relevant studies. Data were synthesized qualitatively and organized according to thematic categories corresponding to the principal domains of patient selection.

Results and Discussion. Core Universal Selection Criteria. Chemosensitivity stands as the single most important criterion in determining candidacy for AHSCT across all lymphoma subtypes. Patients must demonstrate a meaningful response—defined as either a complete remission (CR) or partial remission (PR)—to salvage chemotherapy prior to proceeding with transplantation. The rationale is straightforward: if the lymphoma does not respond to conventional-dose salvage chemotherapy, the probability of disease eradication with high-dose conditioning is exceedingly low. Primary refractory disease, defined as absence of response to salvage regimens, is generally considered a contraindication to AHSCT. Furthermore, the depth of response prior to transplantation is a powerful prognostic determinant. In a large cohort study of DLBCL patients, those achieving CR before AHSCT demonstrated a five-year overall survival (OS) of 74.9%, compared to 47% for patients achieving only PR ($p = 0.008$). PET/CT-confirmed CR, reflecting metabolic complete response, is associated with the most favorable outcomes (Rosenthal et al., 2024).

Performance status constitutes another fundamental selection criterion. The Karnofsky Performance Score (KPS) of 70 or greater is generally required for AHSCT eligibility, corresponding to an Eastern Cooperative Oncology Group (ECOG) performance status of 0–2. Low KPS is associated with worse post-transplant outcomes, including impaired mobility, reduced self-care capacity, and higher TRM. It is important to emphasize that chronological age alone is not a contraindication to AHSCT. Rather,

functional status—as assessed by validated performance scales and comprehensive geriatric assessment in older patients—is the primary determinant. Studies have demonstrated that selected patients aged 60 years and older can safely undergo AHSCT with acceptable outcomes. A prospective study of 47 older lymphoma patients (median follow-up 50 months) demonstrated that quality of life, encompassing physical, social, and emotional well-being, was preserved following AHSCT (Lemieux et al., 2020).

Adequate organ function is a prerequisite for tolerating the myeloablative conditioning regimen. Standard thresholds include a left ventricular ejection fraction (LVEF) of 40–50% or greater, pulmonary diffusion capacity for carbon monoxide (DLCO) of 50% of predicted or greater, creatinine clearance of 50 mL/min or greater, and hepatic transaminases no more than twice the upper limit of normal. Additionally, the bone marrow should be free of extensive lymphoma infiltration to ensure adequate stem cell mobilization and engraftment (Savani et al., 2015).

The Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI) is a validated tool specifically designed to predict non-relapse mortality (NRM) risk in transplant candidates. The index assigns weighted scores to a range of comorbid conditions, with aggregate scores of 0, 1–2, and 3 or greater stratifying patients into low, intermediate, and high NRM risk categories, respectively. The HCT-CI should be employed as a complement to clinical assessment and functional status evaluation, not as a substitute for individualized clinical judgment. Integrated use of performance status, organ function parameters, and the HCT-CI enables a comprehensive risk assessment that guides transplant decision-making (Savani et al., 2015).

Body Composition and Novel Predictors

In recent years, body composition assessment has emerged as a promising independent predictor of transplant outcomes. Sarcopenia, defined as reduced skeletal muscle mass and function, has garnered particular attention in the AHSCT setting. A study of lymphoma patients undergoing AHSCT demonstrated a sarcopenia prevalence of 34.6% among transplant candidates. Sarcopenic patients exhibited significantly worse disease control, with a three-year progression-free survival (PFS) of 59% compared to 84% in non-sarcopenic patients ($p = 0.02$). Although no statistically significant difference in overall survival was observed, the marked disparity in PFS

suggests that sarcopenia independently influences disease control following transplantation (Sumransub et al., 2022a).

The skeletal muscle index (SMI), derived from routine pre-transplant computed tomography imaging at the level of the third lumbar vertebra, provides an objective, non-invasive, and reproducible measure of muscle mass. This approach is particularly attractive because CT imaging is already performed as part of standard pre-transplant staging, requiring no additional procedures or costs. Notably, in cohorts where sarcopenia was assessed, conventional predictors such as KPS and HCT-CI did not stratify outcomes with the same discriminatory power, suggesting that body composition captures an independent dimension of physiological reserve not reflected by standard assessment tools (Leal et al., 2024).

The practical implications of these findings are twofold. First, CT-based sarcopenia assessment should be considered for integration into the standard pre-AHST evaluation, providing additional prognostic information that may influence selection decisions. Second, for patients identified as sarcopenic who remain otherwise suitable AHST candidates, structured pre-habilitation programs incorporating exercise training and nutritional optimization may potentially mitigate the adverse prognostic impact of reduced muscle mass, although prospective validation of this approach is needed.

Disease-Specific Selection Criteria

Hodgkin Lymphoma. Autologous hematopoietic stem cell transplantation has been the standard of care for patients with relapsed or refractory Hodgkin lymphoma following successful salvage chemotherapy. The standard indication is chemosensitive first relapse or primary refractory disease that demonstrates response to salvage regimens. Critically, AHST is not indicated for patients in first complete remission (CR1) who achieve PET-negative status after frontline therapy, as these patients do not derive additional benefit from transplant consolidation. Similarly, patients with primary refractory disease who demonstrate no response whatsoever to salvage chemotherapy should not proceed to AHST (Perales & Ahmed, 2024).

The standard treatment algorithm involves salvage chemotherapy with regimens such as ifosfamide, carboplatin, and etoposide (ICE); dexamethasone, high-dose

cytarabine, and cisplatin (DHAP); or gemcitabine, dexamethasone, and cisplatin (GDP), followed by PET/CT response assessment and subsequent AHST for patients achieving CR or PR. The BEAM conditioning regimen (carmustine, etoposide, cytarabine, and melphalan) remains the most widely used preparative regimen for HL. A recent study evaluating the PEAM regimen, in which cisplatin is substituted for carmustine, demonstrated comparable efficacy with shorter neutrophil engraftment time (10 versus 12 days) and improved gastrointestinal tolerability, offering a potential alternative particularly in settings where carmustine availability is limited (Acosta-Maldonado et al., 2024).

The therapeutic landscape for relapsed and refractory HL has been transformed by the introduction of brentuximab vedotin and immune checkpoint inhibitors, including pembrolizumab and nivolumab. These agents have demonstrated substantial activity in the relapsed/refractory setting, and their incorporation into treatment algorithms has reduced the overall utilization of AHST in HL. In the current era, AHST is primarily indicated for patients who are refractory to or relapse after brentuximab vedotin and/or checkpoint inhibitor therapy, or for patients in resource-limited settings where access to novel agents is constrained (McBride et al., 2017; Perales & Ahmed, 2024).

Diffuse Large B-Cell Lymphoma

Diffuse large B-cell lymphoma is the most common aggressive NHL subtype, and AHST has traditionally been the standard of care for patients with chemosensitive first relapse or primary refractory disease responding to salvage therapy. The strongest indication is for patients who achieve CR after salvage chemotherapy. Importantly, AHST is not indicated for patients in first complete remission (CR1), as multiple studies have demonstrated that upfront consolidation with AHST does not improve overall survival in any International Prognostic Index (IPI) risk group. For patients with primary refractory disease achieving only PR after salvage, the role of AHST is controversial, and CAR-T cell therapy has emerged as the preferred approach in this population (Rosenthal et al., 2024).

Key prognostic factors that inform selection at the time of transplant evaluation include the quality of response to salvage therapy (CR versus PR), the presence of extranodal disease at relapse (hazard ratio 2.35, $p = 0.005$ for inferior outcomes), age-

adjusted IPI greater than 2 at the time of salvage, and PET/CT-confirmed metabolic CR. A comparative analysis of AHST and CAR-T cell therapy in the relapsed/refractory DLBCL setting demonstrated that among chemosensitive patients achieving CR, AHST was associated with a two-year OS of 69% compared to 47% for CAR-T ($p = 0.004$), supporting AHST as the preferred approach when CR is achieved after salvage. In contrast, CAR-T therapy is preferred for patients achieving only PR or for those with chemorefractory disease (Rosenthal et al., 2024). Peripheral blood is the standard stem cell source for AHST in DLBCL, and tandem autologous transplantation is not recommended based on current evidence.

Follicular Lymphoma

Follicular lymphoma, the most common indolent NHL subtype, presents distinct considerations for AHST candidacy. The European Society for Blood and Marrow Transplantation Lymphoma Working Party (EBMT-LWP) consensus does not recommend AHST in CR1 to consolidate first remission outside of clinical trial protocols. The primary indications for AHST in FL include chemosensitive first relapse, particularly early relapse occurring within 24 months of initial therapy (a recognized adverse prognostic feature), poor response to initial treatment, and histological transformation to high-grade lymphoma (López-Guillermo et al., 2013).

AHST has been demonstrated to extend both progression-free survival and overall survival in the relapsed FL setting. However, relapse remains the primary cause of treatment failure following AHST, reflecting the inherent biology of this indolent but incurable disease. By comparison, allogeneic hematopoietic cell transplantation offers lower relapse rates, attributable to the graft-versus-lymphoma immunologic effect, but at the cost of substantially higher non-relapse mortality. The choice between autologous and allogeneic approaches must therefore be individualized based on patient age, comorbidity burden, donor availability, and disease kinetics (Kahl et al., 2011; López-Guillermo et al., 2013).

Mantle Cell Lymphoma and T-Cell Lymphoma

Mantle cell lymphoma occupies a unique position in the AHST landscape. Unlike most other lymphoma subtypes, AHST is recommended as consolidation in first complete or partial remission (CR1/PR1) for younger, fit patients with MCL. This

recommendation is based on evidence demonstrating that AHSC consolidation in CR1 significantly improves progression-free survival compared to conventional chemotherapy alone. Additionally, chemosensitive relapse remains a valid indication for AHSC in MCL patients who did not receive transplant consolidation upfront (Savani et al., 2015).

T-cell lymphomas, including T-cell lymphoblastic lymphoma (T-LBL), present additional complexity. AHSC is recommended in CR1 for standard-risk T-cell lymphoma patients, whereas allogeneic transplantation is preferred for patients not achieving CR1 or those with high-risk disease features. A comparative study of AHSC and matched sibling donor allogeneic transplantation (MSD-HSCT) in T-LBL patients in CR1 demonstrated comparable outcomes, with three-year OS of 62.8% and 64.4%, respectively ($p = 0.929$), suggesting that AHSC is a reasonable option in this context given its lower procedure-related toxicity. For Burkitt lymphoma, AHSC is considered in first remission for high-risk patients and in chemosensitive first or subsequent relapse (Zhang et al., 2023; Savani et al., 2015).

Contraindications to AHSC in Lymphoma

Absolute contraindications to AHSC in lymphoma are well defined and include chemorefractory disease demonstrating no response to salvage chemotherapy, uncontrolled active infection (bacterial, fungal, or viral), severe uncontrolled comorbid disease such as New York Heart Association Class III or IV heart failure or active hepatitis with significant hepatic dysfunction, ECOG performance status of 3 or greater that is not correctable with supportive measures, and inability to collect an adequate number of hematopoietic stem cells, defined as a CD34-positive cell dose below 2×10^6 per kilogram of recipient body weight (Savani et al., 2015).

Relative contraindications require individualized assessment and include advanced age (greater than 70 years) in the context of a high HCT-CI score, significant pulmonary compromise with DLCO below 40% of predicted, prior mediastinal radiotherapy with resultant reduced diffusion capacity, HIV infection with detectable viral load, and major psychiatric illness that may interfere with treatment compliance and post-transplant follow-up. These relative contraindications do not categorically preclude AHSC but necessitate careful risk-benefit analysis conducted collaboratively between the transplant team and the patient.

A particularly important clinical scenario is post-AHSCT relapse. A second autologous transplantation is generally not recommended for patients who relapse following a prior AHSCT, as the likelihood of durable response is low. Instead, these patients should be evaluated for allogeneic hematopoietic stem cell transplantation or CAR-T cell therapy, which offer alternative mechanisms of disease control including graft-versus-lymphoma effect and targeted immunotherapy, respectively (Savani et al., 2015).

The evidence reviewed in this article demonstrates that optimal patient selection for AHSCT in lymphoma is a multidimensional process requiring the integration of disease biology, chemosensitivity, performance status, organ function, comorbidity burden as quantified by the HCT-CI, body composition parameters, and disease subtype-specific criteria. No single criterion operates in isolation; rather, the transplant decision emerges from the composite assessment of multiple interrelated variables. Chemosensitivity remains the foundational requirement, without which the probability of meaningful benefit from AHSCT is negligible. Upon this foundation, the clinician must layer assessments of physiological fitness, organ reserve, and comorbidity to determine whether the individual patient can safely tolerate the rigors of myeloablative conditioning and the subsequent period of aplasia and immune reconstitution.

The therapeutic paradigm for relapsed and refractory lymphoma is undergoing a profound transformation. The emergence of CAR-T cell therapy, bispecific antibodies, and immune checkpoint inhibitors is progressively redefining the role of AHSCT, particularly for DLBCL and HL. For DLBCL, the demonstration that CAR-T therapy offers superior outcomes compared to AHSCT in the chemorefractory or partial-response setting has led to a stratified approach in which the quality of response to salvage therapy determines the preferred consolidation modality. For HL, the incorporation of brentuximab vedotin and checkpoint inhibitors into earlier lines of therapy has reduced the pool of AHSCT-eligible patients while simultaneously identifying a more clearly defined population of patients who remain candidates for transplantation (Perales & Ahmed, 2024; Rosenthal et al., 2024).

In resource-limited settings, where access to CAR-T therapy and novel biologic agents may be constrained by availability and cost, AHSCT remains the most accessible curative-intent therapy for chemosensitive relapsed lymphoma. Selection criteria in

these contexts must be adapted to local capacity, with emphasis on robust pre-transplant assessment using universally available tools such as performance status evaluation, basic organ function testing, and the HCT-CI. The development of alternative conditioning regimens, such as PEAM, further enhances the feasibility of AHSCT in resource-constrained environments.

Emerging biomarkers of post-transplant outcomes add another dimension to patient selection. The observation that high levels of proliferating regulatory T cells (Ki67-positive Tregs) at day 28 post-AHSCT are associated with significantly worse five-year OS (42% versus 75%, $p = 0.01$) suggests that immune reconstitution dynamics may serve as early indicators of transplant failure, potentially enabling risk-adapted post-transplant interventions (Sumransub et al., 2022b). While these findings are not yet incorporated into standard selection algorithms, they illustrate the direction toward more biologically informed decision-making.

Several questions remain unresolved and merit investigation in prospective studies. These include the optimal timing of AHSCT versus CAR-T cell therapy in the evolving treatment landscape, the potential role of measurable residual disease (MRD) and circulating tumor DNA (ctDNA) monitoring as dynamic selection tools that can inform transplant timing and candidacy, and the value of structured pre-habilitation programs for sarcopenic patients identified during pre-transplant evaluation.

Conclusion. Chemosensitivity remains the cornerstone of patient selection for AHSCT in lymphoma. Complete remission achieved after salvage chemotherapy, confirmed by PET/CT imaging, predicts the most favorable transplant outcomes across all lymphoma subtypes. Upon this foundation, disease subtype-specific indications, organ function parameters, the HCT-CI, performance status, and emerging metrics such as body composition and sarcopenia assessment provide complementary information that collectively guides individualized transplant decisions.

The expanding therapeutic landscape, characterized by the integration of CAR-T cell therapy, bispecific antibodies, and immune checkpoint inhibitors into lymphoma treatment algorithms, is progressively refining the indications for AHSCT. Rather than diminishing the relevance of transplantation, these advances are sharpening the identification of patients most likely to benefit, moving toward a more targeted patient population defined by chemosensitivity, physiological fitness, and disease-specific

prognostic features. In resource-limited settings, AHSCT retains a central role as the most broadly accessible curative-intent modality for chemosensitive relapsed lymphoma.

Future research should prioritize the prospective integration of MRD assessment, ctDNA monitoring, and body composition analysis into selection algorithms. Large-scale, real-world registry studies are needed to guide decision-making in the era of novel therapies, particularly to define the optimal sequencing of AHSCT and CAR-T cell therapy. Ultimately, the goal is to ensure that every patient receives the therapy most likely to provide durable disease control while preserving quality of life—an objective that demands continued refinement of the evidence-based, multidimensional selection framework described herein.

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