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Clinical outcomes of autologous stem cell transplantation in multiple myeloma: A single-center experience

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Abstract

Despite the widespread integration of novel therapeutic agents, autologous stem cell transplantation (ASCT) remains a cornerstone of treatment for transplant-eligible patients with multiple myeloma (MM). While randomized trials have established its efficacy, real-world data are essential for evaluating outcomes and prognostic factors in routine clinical practice. This study aimed to assess clinical characteristics, transplant-related outcomes, and survival in MM patients undergoing ASCT at a single center. We retrospectively analyzed 112 MM patients who underwent ASCT. Baseline clinical and laboratory features, induction regimens, transplant-related variables, and response rates were evaluated. Progression-free survival (PFS) and overall survival (OS) were estimated using the Kaplan–Meier method, and prognostic factors were analyzed using Cox proportional hazards regression models. The median age was 60 years, with 21.4% of patients aged over 65 years. Following bortezomib-based induction therapy, the majority of patients achieved very good partial response or better before ASCT. By day 100 post-transplant, the overall response rate exceeded 90%, with complete response achieved in 33% of patients. The median PFS was 23.8 months, while the median OS was not reached. International Staging System (ISS) stage II–III disease and a pre-transplant response of partial response or less were independently associated with inferior PFS and OS. Our real-world data confirm that ASCT continues to provide substantial clinical benefit in the era of novel agents. Depth of response prior to transplantation and disease stage at diagnosis remain the most important determinants of long-term survival outcomes.

Keywords: multiple myeloma, autologous stem cell transplantation, progression free survival, overall survival

1. Introduction

Multiple myeloma (MM) is a clonal plasma cell malignancy characterized by marked biological heterogeneity and a highly variable clinical course. Although MM accounts for approximately 1–2% of all malignancies and nearly 17% of hematologic cancers, its management remains challenging due to frequent relapses and the development of treatment resistance over time (1).

For more than three decades, high-dose chemotherapy followed by autologous stem cell transplantation (ASCT) has represented a central therapeutic strategy for transplant-eligible patients with MM (2). The introduction of proteasome inhibitors and immunomodulatory agents has substantially improved response rates and survival outcomes. Rather than diminishing the role of ASCT, these agents have enhanced its effectiveness by enabling deeper responses prior to transplantation and more durable disease control thereafter (3). Despite ongoing debate regarding the necessity of ASCT in the era of novel therapies, current evidence continues to support its role as an integral component of frontline treatment for eligible patients (4).

While randomized controlled trials have established the efficacy of ASCT, their findings often reflect selected patient populations managed under highly standardized conditions. Real-world data are therefore essential to assess treatment outcomes in routine clinical practice, where patient characteristics, comorbidities, and treatment sequencing may differ substantially. Single-center studies, in particular, provide valuable insight into institutional practices and outcome patterns (5). In this context, we present our single-center experience with ASCT in patients with MM treated in the era of novel induction agents, focusing on treatment responses, progression-free survival (PFS), overall survival (OS), and prognostic factors influencing post-transplant outcomes.

2. Materials and Methods

2.1. Study Design and Patients

This retrospective, single-center study included patients diagnosed with MM according to International Myeloma Working Group (IMWG) criteria (6) who underwent ASCT between 2019 and 2023 at the Ondokuz Mayıs University, Department of Hematology. A total of 112 patients aged ≥18 years with complete clinical, laboratory, radiological, and bone marrow data and regular post-transplant follow-up at our center were included in the analysis. Patients undergoing tandem or allogeneic transplantation, those with primary plasma cell leukemia, and patients lacking adequate follow-up data were

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excluded. The median follow-up duration from ASCT to last contact or death was 14 months (range 4–40).

2.2. Clinical and Laboratory Evaluation

Baseline demographic characteristics, disease-related features, laboratory parameters, and radiological findings were recorded. Disease staging was performed using the International Staging System (ISS) (7). The Revised ISS was not applied due to incomplete cytogenetic data.

Treatment response was assessed according to the International Myeloma Working Group (IMWG) response criteria(6). Patients achieving complete response (CR), very good partial response (VGPR), or partial response (PR) were classified as responders.

2.3. Transplantation and Follow-up

Data regarding induction regimens, stem cell mobilization strategies, conditioning therapy, infused $CD34^+$ cell dose, engraftment kinetics, and transplant-related complications were collected. Progression-free survival (PFS) was defined as the time from ASCT to disease progression or death from any cause, whichever occurred first. Overall survival (OS) was defined as the time from ASCT to death or last follow-up.

2.4. Statistical Analysis

Statistical analyses were performed using IBM SPSS version 20.0. Categorical variables were summarized as numbers and percentages, and continuous variables as mean ± standard deviation or median (minimum–maximum), as appropriate. Comparisons between categorical variables were performed using Pearson's chi-square test or Fisher's exact test. Continuous variables were compared using Student's t-test or the Mann–Whitney U test based on data distribution. Survival analyses were conducted using the Kaplan–Meier method, and factors associated with survival outcomes were evaluated using Cox proportional hazards regression analysis. Variables with $p<0.10$ in univariable analyses were entered into the multivariable Cox regression model. A p-value <0.05 was considered statistically significant.

3. Results

A total of 112 patients with MM who underwent ASCT were included in the analysis. Baseline clinical and disease characteristics of the study population are summarized in Table 1.

Table 1. Disease characteristics and baseline findings of the study population (n=112)

Variable	Value
Age, years	57.9 ± 7.7 (median 60; range 39–71)
Age >65 years, n (%)	24 (21.4)
Sex, n (%)	
Male	63 (56.3)
Female	49 (43.8)
Paraprotein subtype, n (%)	
IgG	69 (61.6)
IgA	24 (21.4)
Free light chain	19 (17.0)
Renal impairment at diagnosis, n (%)	21 (18.8)
Lytic bone lesions, n (%)	88 (78.6)
Hypercalcemia at diagnosis, n (%)	14 (12.5)
ISS stage, n (%)	
Stage I	59 (52.7)
Stage II	28 (25.0)
Stage III	25 (22.3)
Bone marrow cellularity, %	59.8 ± 17.7
Bone marrow fibrosis grade, n (%)	
Grade 0	86 (76.8)
Grade 1	23 (20.5)
Grade 2	2 (1.8)
Grade 3	1 (0.9)

Induction regimens and pre-transplant response rates are presented in Table 2. The majority of patients received bortezomib-based induction therapy, and most achieved at least a VGPR prior to transplantation.

Table 2. Induction therapy and pre-transplant response

Variable	Value
Induction regimen, n (%)	
VCD	70 (62.5)
VCD → VRd	22 (19.6)
VTd	16 (14.3)
VRd	4 (3.6)
Median induction cycles	4 (range 3–8)
Radiotherapy before ASCT, n (%)	17 (15.2)
Pre-transplant response, n (%)	
Complete response (CR)	27 (24.1)
Very good partial response (VGPR)	74 (66.1)
Partial response (PR)	9 (8.0)
Stable disease (SD)	1 (0.9)
Progressive disease (PD)	1 (0.9)
Salvage therapy before ASCT (KRd), n (%)	11 (9.8)

Transplant-related characteristics, mobilization approaches, engraftment kinetics, and early post-transplant outcomes are summarized in Table 3. Median neutrophil and platelet engraftment occurred on days 11 and 13, respectively. By day 100 after ASCT, most patients achieved CR or VGPR. During follow-up, disease relapse was observed in 45.5% of patients.

Table 3. Transplant characteristics and early post-transplant outcomes

Variable	Value
Mobilization regimen, n (%)	
G-CSF	86 (76.8)
G-CSF + plerixafor	22 (19.6)
G-CSF + cyclophosphamide	4 (3.6)
Median collection days	2
Median collected CD34+ cells (×10⁶/kg)	4.66 (range 2.67–24.9)
Conditioning regimen, n (%)	
Melphalan 200 mg/m²	88 (78.6)
Melphalan 140 mg/m²	24 (21.4)
Mean infused CD34+ cells (×10⁶/kg)	4.8 ± 2.67
Median neutrophil engraftment, days	11
Median platelet engraftment, days	13
Day-100 response, n (%)	
CR	37 (33.0)
VGPR	66 (58.9)
PR	2 (1.2)
PD	7 (6.3)
Relapse during follow-up, n (%)	51 (45.5)

The median PFS was 23.8 months. Estimated 2-year and 5-year PFS rates were 78.2% and 61.6%, respectively (Fig. 1). Median OS was not reached, with estimated 2-year and 5-year OS rates of 99.1% and 88.6%, respectively (Fig. 2).

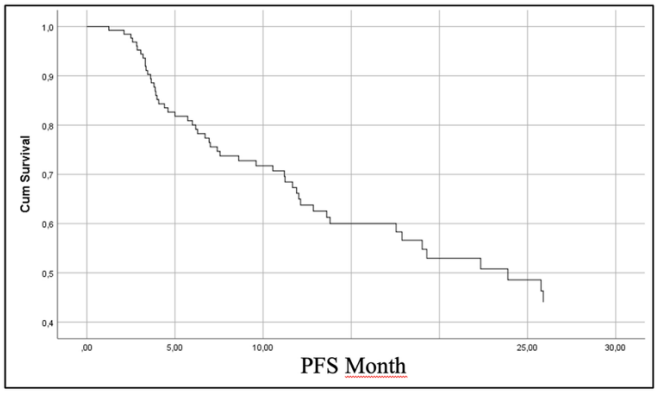

Fig. 1. Kaplan–Meier Curve for Progression-Free Survival
Kaplan–Meier analysis demonstrating progression-free survival (PFS) in patients with multiple myeloma following autologous stem cell transplantation. The median PFS was 23.8 months.

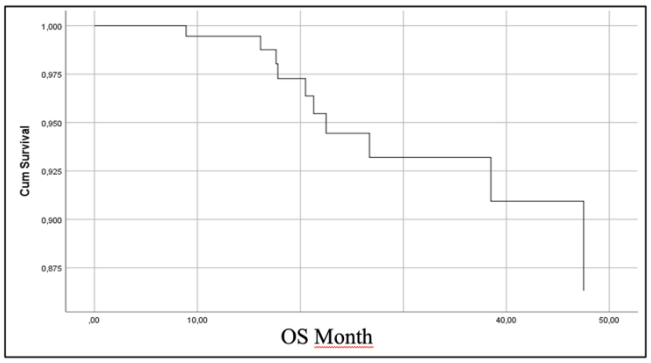

Fig. 2. Kaplan–Meier Curve for overall survival
Kaplan–Meier analysis demonstrating overall survival (OS) in patients with multiple myeloma following autologous stem cell transplantation. Median overall survival was not reached during the follow-up period.

In Cox regression analyses, pre-transplant response status and ISS stage were independently associated with both PFS and OS. Patients with a pre-transplant response of PR or worse and those with ISS stage II–III disease demonstrated significantly inferior survival outcomes (Table 4).

Table 4. Cox Regression analysis for survival outcomes

A. Progression-free survival

Variable	HR	95% CI	p
Pre-transplant response (≤PR vs ≥VGPR)	2.24	1.12–4.46	0.022
ISS stage (II–III vs I)	1.83	1.05–3.21	0.034

B. Overall Survival

Variable	HR	95% CI	p
Pre-transplant response (≤PR vs ≥VGPR)	4.40	1.46–13.27	0.008
ISS stage (II–III vs I)	4.93	1.03–23.66	0.046

4. Discussion

The therapeutic landscape of MM has evolved substantially with the introduction of proteasome inhibitors and immunomodulatory drugs (4). Although these advances have improved depth of response and survival, they have also raised questions regarding the continued role of ASCT in the era of proteasome inhibitor and IMiD based induction therapies of highly effective induction regimens (8). Our single-center, real-world experience supports the feasibility and real-world outcomes of ASCT in transplant-eligible patients, demonstrating that relapse remains common and that transplantation continues to provide meaningful clinical benefit in eligible patients.

In our cohort, response rates exceeded 90% at day 100 post-transplant, consistent with outcomes reported in contemporary ASCT series utilizing bortezomib and lenalidomide-based induction therapies. Importantly, depth of response prior to ASCT emerged as a key determinant of survival. Patients who failed to achieve at least VGPR before transplantation experienced significantly inferior PFS and OS. This finding reinforces the concept that pre-transplant chemosensitivity is a

critical predictor of post-transplant outcomes, as demonstrated in multiple prior studies (9-11).

Prior large scale studies have consistently demonstrated that the International Staging System (ISS) retains robust prognostic value in newly diagnosed multiple myeloma. In the original ISS validation study including more than 10,000 patients, Greipp et al. showed that increasing ISS stage was associated with progressively inferior overall survival, independent of treatment strategy, including high-dose therapy and autologous stem cell transplantation (7). Subsequent large cohort analyses in the modern treatment era have confirmed that higher ISS stages continue to predict shorter progression-free and overall survival, underscoring the persistent impact of baseline disease burden despite therapeutic advances (12, 13).

Disease stage at diagnosis, assessed using the ISS, also retained prognostic significance in our analysis. Despite the increasing adoption of the Revised ISS, our findings highlight the continued utility of conventional ISS staging in real-world settings where complete cytogenetic data may not be available. Inferior outcomes observed in patients with ISS stage II–III disease were consistent with previous large-scale studies, underscoring the persistent impact of baseline disease burden on long-term prognosis (12, 13).

Several studies have challenged the traditional view that advanced age represents a barrier to autologous stem cell transplantation (ASCT) in multiple myeloma. Large registry based and retrospective analyses have demonstrated that selected older patients can safely undergo ASCT with response rates and survival outcomes comparable to those of younger cohorts, provided that biological fitness rather than chronological age guides patient selection (14, 15). In our cohort, chronological age did not adversely affect response rates or survival, supporting current recommendations that emphasize physiological fitness over age alone when considering ASCT eligibility.

Renal impairment, another historically adverse prognostic factor in multiple myeloma, has also shown a diminishing impact in the era of novel agents. Previous studies have reported that bortezomib-based induction therapy can lead to rapid disease control and significant improvement in renal function, thereby attenuating the negative prognostic influence of renal dysfunction (16, 17). Consistent with these findings, renal involvement at diagnosis did not significantly affect post-transplant response or survival outcomes in our study, suggesting that effective upfront therapy may overcome the historical survival disadvantage associated with renal impairment.

Regarding transplant-related variables, infused $CD34^+$ cell dose and engraftment kinetics did not translate into differences in long-term disease control once an adequate minimum stem cell threshold was achieved. Prior evidence indicates that $CD34^+$ cell dose is primarily linked to the tempo of hematologic recovery-particularly neutrophil and platelet engraftment-rather than sustained post-transplant survival outcomes in large MM transplant cohorts (18). In parallel, bone marrow fibrosis did not emerge as a significant prognostic factor for post-transplant outcomes in our cohort, which is consistent with contemporary data suggesting that fibrosis is more relevant to certain disease biology patterns (e.g., association with extramedullary disease) than to transplant efficacy itself (19).

Although disease relapse was observed in nearly half of our cohort during follow-up (45.5%), the median overall survival (OS) was not reached. At 5 years, the estimated OS rate remained high at 88.6%, despite a median progression-free survival (PFS) of 23.8 months. This dissociation between PFS and OS reflects a fundamental shift in the treatment paradigm of multiple myeloma in the era of novel agents. Large contemporary studies have demonstrated that the availability of effective salvage therapies—including second-generation proteasome inhibitors, immunomodulatory drugs, anti-CD38 monoclonal antibodies, and cellular or bispecific immunotherapies—has significantly prolonged post-relapse survival. In multiple real-world and registry-based analyses, median post-relapse survival now exceeds 4–5 years, even among patients experiencing early disease recurrence (1, 8, 20).

Consistent with these observations, our data suggest that modern salvage strategies can effectively compensate for disease recurrence after ASCT, leading to sustained long-term survival. Consequently, PFS and OS appear increasingly decoupled in contemporary multiple myeloma management, with OS now reflecting not only the durability of first remission but also the cumulative benefit of sequential, highly active therapies delivered over the disease course.

This study has limitations inherent to its retrospective design, single-center setting, and relatively limited follow-up duration. Additionally, minimal residual disease assessment and comprehensive cytogenetic profiling were not available for all patients. Nonetheless, the consistency of our findings with previously published data supports their validity. Importantly, the absence of a non-transplant comparator group limits the ability to infer causal survival benefit from ASCT, and our findings should therefore be interpreted as observational real-world outcomes rather than comparative effectiveness results.

In conclusion, our real-world experience confirms that ASCT remains a cornerstone of MM management in the era of proteasome inhibitor and IMiD based induction therapies of highly effective induction regimens. Depth of pre-transplant response and ISS stage at diagnosis continue to be the most reliable predictors of post-transplant outcomes. While emerging therapies such as anti-CD38 monoclonal antibodies, CAR T-cell therapies, and bispecific antibodies are rapidly reshaping treatment paradigms, our results support the continued integration of ASCT as an effective consolidation

strategy until long-term data from these novel approaches are fully established.

Conflict of interest

The authors declared no conflict of interest.

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None to declare.

Authors' contributions

Concept: A.N.G., E.K. Design: A.N.G.; E.K., Data Collection or Processing: A.N.G.; E.K., Analysis or Interpretation: A.N.G.; E.K., Literature Search: A.N.G.; E.K., Writing: A.N.G.; E.K.

Ethical Statement

This study was approved by the Ondokuz Mayıs University Clinical Research Ethics Committee (Approval No: B.30.2.0DM.0.20.08/214; Decision No: 2023/135) and was conducted in accordance with the Declaration of Helsinki and its later amendments.

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