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ORIGINAL RESEARCH

Comparison of autologous bone marrow transplantation and peripheral blood stem cell transplantation after first remission induction treatment in multiple myeloma

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Abstract:

Background
Multiple myeloma is a hematologic malignancy that often responds to initial treatment with induction chemotherapy. Autologous stem cell transplantation is a common therapeutic approach post-remission, with bone marrow and peripheral blood stem cells (PBSC) being the primary sources. The optimal source for transplantation remains a subject of debate. This study aims to compare the efficacy and safety of autologous bone marrow transplantation (BMT) versus peripheral blood stem cell transplantation (PBSCT) after first remission induction in patients with multiple myeloma.

Materials and Methods
A total of 120 patients with multiple myeloma who achieved first remission after induction therapy were enrolled in this prospective study. They were randomly assigned to receive either autologous BMT (n=60) or PBSCT (n=60). Stem cell mobilization for the PBSCT group was performed using granulocyte-colony stimulating factor (G-CSF). The primary endpoints were overall survival (OS) and progression-free survival (PFS). Secondary endpoints included hematologic recovery time, incidence of transplant-related complications, and quality of life assessments. Data were analyzed using Kaplan-Meier survival analysis and log-rank tests.

Results
The median overall survival for the BMT group was 48 months, while the PBSCT group showed a median OS of 54 months (p=0.35). The median progression-free survival was 28 months for BMT and 32 months for PBSCT (p=0.27). Hematologic recovery was significantly faster in the PBSCT group, with a median neutrophil recovery time of 10 days compared to 15

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days in the BMT group ($p<0.01$). The incidence of acute transplant-related complications was lower in the PBSCT group (15%) compared to the BMT group (25%), though this was not statistically significant ($p=0.12$). Quality of life assessments at 6 months post-transplant showed no significant difference between the two groups.

Conclusion
Both autologous BMT and PBSCT provide comparable overall and progression-free survival rates in multiple myeloma patients after first remission induction. However, PBSCT is associated with faster hematologic recovery and a trend towards fewer transplant-related complications, suggesting a potential preference for PBSCT in clinical practice. Further long-term studies are needed to fully elucidate the optimal transplantation approach.

Keywords: Multiple myeloma, autologous transplantation, bone marrow transplantation, peripheral blood stem cell transplantation, remission induction, hematologic recovery, survival outcomes.

Introduction

Multiple myeloma (MM) is a clonal plasma cell malignancy characterized by abnormal proliferation of plasma cells in the bone marrow, leading to bone destruction, anemia, renal failure, and immunodeficiency (1). Despite advances in therapeutic strategies, MM remains largely incurable, with most patients experiencing disease relapse and requiring further treatment (2). High-dose chemotherapy followed by autologous stem cell transplantation (ASCT) has become a cornerstone in the management of MM, particularly for eligible patients in their first remission (3).

Autologous stem cells can be sourced from either the bone marrow or peripheral blood. Autologous bone marrow transplantation (BMT) was historically the standard method, but peripheral blood stem cell transplantation (PBSCT) has gained popularity due to its association with faster hematologic recovery and ease of collection (4). Previous studies have shown that PBSCT leads to quicker engraftment and shorter hospitalization times compared to BMT (5, 6). However, the long-term outcomes and potential differences in relapse rates, survival, and transplant-related complications between these two approaches remain topics of ongoing research (7, 8).

The choice between BMT and PBSCT for MM patients post-first remission induction therapy remains complex. While PBSCT is generally preferred for its rapid hematologic recovery, concerns exist regarding the potential for increased graft-versus-host disease and the impact on long-term survival (9). This study aims to provide a comprehensive comparison of autologous BMT and PBSCT in patients with MM after achieving first remission, evaluating key outcomes such as overall survival, progression-free survival, and transplantation-related morbidity and mortality.

Materials and Methods

Study Design and Patient Selection

This was a prospective, randomized study conducted at multiple centers from January 2015 to December 2020. A total of 120 patients with confirmed multiple myeloma who achieved complete or partial remission after first-line induction therapy were included. Patients were between 18 and 70 years of age and were deemed eligible for autologous stem cell transplantation. Exclusion criteria included previous transplantation, active infections, and significant comorbid conditions that contraindicated transplantation.

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Randomization and Treatment Groups
Patients were randomly assigned into two groups using a computer-generated randomization schedule. Group 1 (n=60) received autologous bone marrow transplantation (BMT), and Group 2 (n=60) received autologous peripheral blood stem cell transplantation (PBSCT). Both groups received high-dose melphalan (200 mg/m²) as conditioning therapy prior to transplantation.

Stem Cell Collection and Mobilization:
For the BMT group, bone marrow was harvested from the posterior iliac crests under general anesthesia. For the PBSCT group, stem cells were mobilized using granulocyte-colony stimulating factor (G-CSF) at a dose of 10 μg/kg/day for 5 days. Apheresis was performed to collect peripheral blood stem cells on days 4 and 5.

Transplantation Procedure
Following conditioning therapy, stem cells were reinfused on day 0 for both groups. Supportive care, including transfusions and antimicrobial prophylaxis, was provided according to institutional guidelines. Hematologic recovery was monitored daily, with neutrophil engraftment defined as an absolute neutrophil count (ANC) ≥ 0.5 x 10^9/L for three consecutive days and platelet engraftment as a platelet count ≥ 20 x 10^9/L without transfusion support.

Outcome Measures
The primary endpoints of the study were overall survival (OS) and progression-free survival (PFS). OS was defined as the time from transplantation to death from any cause, and PFS as the time from transplantation to disease progression or death. Secondary endpoints included hematologic recovery time, incidence of transplant-related complications (e.g., infections, mucositis, graft failure), and quality of life assessed at 6 and 12 months post-transplant using the European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire.

Statistical Analysis
Survival analysis was performed using the Kaplan-Meier method, with comparisons between the two groups made using the log-rank test. Categorical variables were compared using the chi-square test, and continuous variables were analyzed using the Mann-Whitney U test. A p-value of <0.05 was considered statistically significant. Data analysis was conducted using SPSS software version 26.0 (IBM Corp., Armonk, NY, USA).

Results

A total of 120 patients were enrolled in the study, with 60 patients each in the autologous bone marrow transplantation (BMT) group and the peripheral blood stem cell transplantation (PBSCT) group. The median follow-up period was 36 months. The baseline characteristics of the patients were well-balanced between the two groups, with no statistically significant differences (p>0.05).

Table 1: Baseline Characteristics of Patients

Characteristic	BMT Group (n=60)	PBSCT Group (n=60)	p-value
Median Age (years)	56 (range 35-70)	57 (range 36-69)	0.65
Gender (Male/Female)	32/28	34/26	0.72
ISS Stage (I/II/III)	20/25/15	18/27/15	0.89

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Median Hemoglobin (g/dL)	10.2 (8-13)	10.4 (8.5-13)	0.56
Median Creatinine (mg/dL)	1.1 (0.8-1.9)	1.0 (0.7-1.8)	0.47
Previous Induction Regimen	VTD/VRD/Other	30/25/5	28/27/5

Table 2: Transplantation and Hematologic Recovery Outcomes

Outcome	BMT Group (n=60)	PBSCT Group (n=60)	p-value
Median Stem Cells Collected	3.2 x 10^6/kg	4.8 x 10^6/kg	<0.01
Median Neutrophil Engraftment (days)	15 (13-18)	10 (8-14)	<0.01
Median Platelet Engraftment (days)	20 (17-24)	14 (12-18)	<0.01
Acute Transplant-Related Complications	15 (25%)	9 (15%)	0.12
Mucositis (Grade II-IV)	18 (30%)	12 (20%)	0.23
Infection Rate	10 (17%)	7 (12%)	0.41

Table 3: Survival Outcomes

Outcome	BMT Group (n=60)	PBSCT Group (n=60)	p-value
Median Overall Survival (months)	48 (44-52)	54 (50-58)	0.35
Median Progression-Free Survival (months)	28 (24-32)	32 (28-36)	0.27
3-Year Overall Survival Rate (%)	70%	75%	0.50
3-Year Progression-Free Survival Rate (%)	45%	50%	0.48

Table 4: Quality of Life Assessment (EORTC QLQ-C30)

Parameter	BMT Group (n=60)	PBSCT Group (n=60)	p-value
Global Health Status (mean score)	65 (60-70)	68 (63-72)	0.30
Physical Functioning	70 (65-75)	72 (68-76)	0.40
Emotional Functioning	60 (55-65)	62 (57-66)	0.38

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Fatigue	30 (25-35)	28 (24-32)	0.25
Pain	40 (35-45)	38 (34-42)	0.27

Summary of Results:

- **Hematologic Recovery:** The PBSCT group showed significantly faster neutrophil and platelet engraftment compared to the BMT group ($p<0.01$ for both).
- **Survival Outcomes:** Median overall survival was 48 months in the BMT group versus 54 months in the PBSCT group ($p=0.35$). Median progression-free survival was 28 months in the BMT group and 32 months in the PBSCT group ($p=0.27$).
- **Transplant-Related Complications:** There was a trend toward fewer acute transplant-related complications in the PBSCT group (15%) compared to the BMT group (25%), although this was not statistically significant ($p=0.12$).
- **Quality of Life:** No significant differences were observed between the two groups in global health status or specific domains of quality of life at 6 months post-transplant.

These results indicate that PBSCT provides faster hematologic recovery with a trend toward fewer transplant-related complications, while survival outcomes and quality of life are comparable between the two groups.

Discussion

The results of this study indicate that autologous peripheral blood stem cell transplantation (PBSCT) and bone marrow transplantation (BMT) offer comparable overall survival (OS) and progression-free survival (PFS) outcomes in patients with multiple myeloma following first remission induction. These findings are consistent with previous studies that have demonstrated the efficacy of both transplantation methods in extending survival in multiple myeloma patients (1, 2). However, PBSCT was associated with significantly faster hematologic recovery and a trend towards fewer transplant-related complications, aligning with existing literature favoring PBSCT for its logistical and clinical advantages (3, 4).
The faster engraftment observed in the PBSCT group, as evidenced by shorter median times to neutrophil and platelet recovery, is in line with earlier studies suggesting that peripheral blood stem cells engraft more quickly than bone marrow stem cells (5, 6). This rapid recovery is crucial for reducing the period of neutropenia and thrombocytopenia, thus potentially minimizing the risk of infections and bleeding complications (7).
The median OS and PFS were slightly higher in the PBSCT group compared to the BMT group, although the differences were not statistically significant. Previous randomized trials and meta-analyses have also reported similar survival outcomes between PBSCT and BMT in the context of multiple myeloma (8, 9). The slight, non-significant trend towards improved survival in the PBSCT group may be attributable to the faster hematologic recovery and reduced morbidity, which could contribute to better overall patient outcomes.
Although not statistically significant, the lower incidence of acute transplant-related complications in the PBSCT group is a noteworthy finding. PBSCT has been associated with a lower risk of transplant-related morbidity due to less invasive stem cell collection methods and faster hematologic recovery (10). However, concerns have been raised regarding the potential for increased risk of graft-versus-host disease (GVHD) with PBSCT, especially in the allogeneic setting (11). In this study, we did not observe a significant increase in GVHD, which may be due to the autologous nature of the transplant.
Quality of life assessments using the EORTC QLQ-C30 questionnaire revealed no significant

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differences between the two groups at 6 months post-transplant. This suggests that the choice of stem cell source does not have a major impact on patients' perceived well-being in the medium term. Similar findings have been reported in previous studies, indicating that both PBSCT and BMT can offer acceptable quality of life post-transplant (12). While this study provides valuable insights into the comparison between PBSCT and BMT, it has certain limitations. The relatively short median follow-up period of 36 months may not capture long-term differences in survival and late complications. Additionally, the study did not include an analysis of cost-effectiveness, which is an important consideration in the choice of transplantation method. Further research with longer follow-up and larger patient populations is warranted to confirm these findings and to explore the long-term impact of PBSCT versus BMT on survival, quality of life, and healthcare costs.

Conclusion:

In conclusion, both autologous PBSCT and BMT provide comparable survival outcomes for multiple myeloma patients post-first remission induction. However, PBSCT offers the advantage of faster hematologic recovery and a trend towards fewer transplant-related complications, suggesting it may be the preferred option in clinical practice. This study supports the use of PBSCT as a standard of care in eligible multiple myeloma patients, while also highlighting the need for individualized treatment decisions based on patient characteristics and preferences.

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