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Original Article

# Outcomes of Autologous Hematopoietic Stem Cell Transplantation in Elderly Multiple Myeloma Patients: A Single-Center Analysis

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SUMMARY

*Background:* Multiple myeloma (MM) predominantly affects older adults, and as the population ages, the incidence of MM is rising. Autologous stem cell transplant (ASCT) is a standard treatment for eligible MM patients, but its application in elderly patients is limited due to comorbidities and increased treatment-related risks. This study evaluated the outcomes of ASCT in elderly MM patients at a single center in Taiwan.

*Methods:* This retrospective study included 32 MM patients who underwent ASCT at MacKay Memorial Hospital, Tamsui branch, Taiwan, between May 2016 and May 2024. Patients were divided into two age groups: < 65 years (22 patients, younger patients) and ≥ 65 years (10 patients, elderly patients). Clinical data, survival outcomes (overall survival [OS] and progression-free survival [PFS]), and adverse events were analyzed for statistical comparison.

*Results:* At a median follow-up of 45 months, the median OS for the entire cohort was not reached, with no significant difference between age groups (84 months in the younger group and not reached in the elderly group, p = 0.924). Median PFS was 19 months for the younger group and 36 months for the elderly group (p = 0.754). Among the most common adverse events were fever (71.9%), infection (56.3%), and diarrhea (78.1%). Younger patients had significantly higher rates of fever (86.4%) and infection (95.5%) compared to elderly patients (40% and 40%, respectively).

*Conclusion:* This study suggests that ASCT provides comparable survival outcomes for elderly and younger MM patients. Fewer and milder complications in the elderly group also suggested that age alone should not preclude elderly patients from ASCT. Further research is needed to refine treatment strategies for elderly MM patients.



## 1. Background

Multiple myeloma (MM) is a plasma cell malignancy primarily affecting older adults, with the median age at diagnosis being 66 years.[1] As the global population ages, the incidence of MM is expected to rise, with a growing proportion of patients aged 65 and older. This demographic shift underscores the increasing importance of tailoring treatment strategies to meet the specific needs of elderly MM patients, particularly in the context of autologous stem cell transplantation (ASCT).[2–4]

Elderly patients with MM face unique challenges due to the high prevalence of comorbidities, frailty, and an increased susceptibility to therapy-related toxicities.[5] While ASCT is a cornerstone of MM treatment, offering significant survival benefits, its application in the elderly population is often limited by the physical demands of the procedure and the higher risk of treatment-related complications.

In response to these challenges, advances in non-intensive therapies, including the use of novel agents such as thalidomide, lenalidomide, and bortezomib, have improved treatment outcomes for elderly patients by reducing toxicity while enhancing efficacy.[6,7] The development of newer therapies, including immunotherapies like CD38 monoclonal antibodies, bispecific antibodies, and chimeric antigen receptor (CAR) T cell therapy therapies, offers additional therapeutic options.[7,8] However, the effectiveness and safety of these therapies in elderly and frail patients remain areas of active investigation.[9,10]

When comparing elderly patients to younger cohorts, it is evident that younger patients tend to have better overall survival (OS) and progression-free survival (PFS), primarily due to a lower burden of comorbidities and a generally better performance status at diagnosis.[11] Given these differences, it is crucial to refine treatment approaches for elderly patients, ensuring that they receive appropriate, personalized care based on their unique clinical profiles.

In this study, we aim to evaluate the outcomes of ASCT in elderly MM patients at a single center in Taiwan. By presenting real-world data, we hope to contribute valuable insights that can help optimize treatment strategies and improve outcomes for this growing patient population.

## 2. Patients and methods

This retrospective study was conducted at MacKay Memorial Hospital (MMH), focusing on newly diagnosed MM patients who un-

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derwent frontline ASCT after adequate induction therapy with triplet therapy (bortezomib, thalidomide, dexamethasone) between 2016 and 2024. At least partial response after induction therapy is required. The study was approved by the Institutional Review Board of MacKay Memorial Hospital (Approval Number: 24MMHIS046e). Eligibility criteria included a confirmed diagnosis of MM, completion of ASCT, and availability of comprehensive clinical data. Patients with incomplete or missing data were excluded from the analysis.

Patient data were captured from electronic medical records, including demographics, clinical characteristics (age, gender, ECOG performance status, International Staging System (ISS) stage, cytogenetics, and immunoglobulin subtype), treatment details (induction therapy regimen, stem cell mobilization, and ASCT procedure), and outcomes (OS, PFS, and adverse events). The definition of high-risk cytogenetics is the chromosomal abnormalities including t(4;14) t(14;16) t(14;20) Del(17p).

### 2.1. Statistical analysis

Descriptive statistics were used to summarize patient characteristics and treatment outcomes. Categorical variables were compared using the Chi-square test or Fisher's Exact Test, while continuous variables were compared using the Mann-Whitney U test for non-parametric data. OS was defined as the time from diagnosis to death from any cause or the last known follow-up date. PFS was defined as the time from ASCT to disease progression, death, or the last known follow-up date. Kaplan-Meier survival curves were generated for both OS and PFS, and group differences were assessed using the log-rank test. The hazard ratios (HR) for OS and PFS were calculated using the Mantel-Haenszel method and log-rank test. Besides, Cox-regression test was also applied to evaluate the effect of imbalanced characteristics on the survival. All figures and statistical analyses were performed by Prism version [10.1.1 (270), November 21, 2023] (GraphPad Software, San Diego, CA). Statistical significance was defined as a p-value of less than 0.05 in two-sided tests.

## 3. Results

### 3.1. Patient characteristics

Between May 2016 and May 2024, a total of 32 MM patients underwent ASCT at MacKay Memorial Hospital. The majority of these patients were male (58.8%) (Table 1). Patient characteristics were divided into two age groups: < 65 years (22 patients) and ≥ 65 years (10 patients). The median age was 61 years (range: 47 to 73 years) for the entire cohort, with a higher median age of 69 years in the older group. The gender distribution differed significantly between groups (p = 0.0496), with 50% males in the younger group versus 90% in the older group. ECOG performance status did not differ significantly between groups (p = 0.635), with most patients having an ECOG score of 1 (65.6%). The ISS staging showed that 50% of patients were stage III, with no significant age-related differences (p = 0.192). High-risk cytogenetics were observed in 9.4%, with a slightly higher proportion in the older group (p = 0.224). Most patients had immunoglobulin G (IgG) subtype (59.4%), and induction therapy was predominantly using the bortezomib, thalidomide, and dexamethasone (VTd) regimen (90.6%), with no significant differences between age groups (p = 0.471).

**Table 1**
Clinical characteristics of 32 multiple myeloma patients undergoing autologous hematopoietic stem cell transplantation.

| | Number | % | Age < 65 | % | Age ≥ 65 | % | p-value** |
|---|---|---|---|---|---|---|---|
| Patients | 32 | | 22 | 68.8% | 10 | 31.3% | |
| Age, year | | | | | | | < 0.001 |
| Median (range) | 61 (47–73) | | 61 (47–64) | | 69 (65–73) | | |
| Gender, n (%) | | | | | | | 0.049 |
| Male | 20 | 58.8% | 11 | 50.0% | 9 | 90.0% | |
| ECOG, n (%) | | | | | | | 0.635 |
| 0 | 9 | 28.1% | 5 | 22.7% | 4 | 40.0% | |
| 1 | 21 | 65.6% | 15 | 68.2% | 6 | 60.0% | |
| 2 | 1 | 3.1% | 1 | 4.5% | 0 | 0.0% | |
| 3 | 1 | 3.1% | 1 | 4.5% | 0 | 0.0% | |
| ISS, n (%) | | | | | | | 0.192 |
| I | 8 | 25.0% | 4 | 18.2% | 4 | 40.0% | |
| II | 7 | 21.9% | 6 | 27.3% | 1 | 10.0% | |
| III | 16 | 50.0% | 12 | 54.5% | 4 | 40.0% | |
| Unknown | 1 | 3.1% | 0 | 0.0% | 1 | 10.0% | |
| High risk*, n (%) | 3 | 9.4% | 1 | 4.5% | 2 | 20.0% | 0.224 |
| Subtype, n (%) | | | | | | | 0.316 |
| IgG | 19 | 59.4% | 15 | 68.2% | 4 | 40.0% | |
| IgA | 9 | 28.1% | 5 | 22.7% | 4 | 40.0% | |
| Light chain only | 4 | 12.5% | 2 | 9.1% | 2 | 20.0% | |
| Induction therapy, n (%) | | | | | | | 0.471 |
| VTD | 29 | 90.6% | 19 | 86.4% | 10 | 100.0% | |
| VRD | 2 | 6.3% | 2 | 9.1% | 0 | 0.0% | |
| VCD | 1 | 3.1% | 1 | 4.5% | 0 | 0.0% | |
| Average Melphalan dose, mg/m$^2$ | 196.27 | | 197.03 | | 194 | | 0.694 |
| Engraftment, day | | | | | | | |
| Myeloid, median (range) | 11 (9–13) | | 11 (9–13) | | 11 (9–12) | | 0.449 |
| Platelet, median (range) | 17 (14–30) | | 17 (14–20) | | 17 (14–30) | | 0.654 |

* The high risk is defined by cytogenetic chromosome study including t(4;14) t(14;16) t(14;20) Del(17p).
** Categorical variables were compared using the Chi-square test or Fisher's Exact Test, while continuous variables were compared using the Mann-Whitney U test for non-parametric data. p-value < 0.05 means significant difference between 2 groups.
D, dexamethasone; ECOG, Eastern Cooperative Oncology Group performance status; Ig, immunoglobin; ISS, The international staging system; R, lenalidomide; T, thalidomide; V, bortezomib.

### 3.2. Transplant outcomes

The median follow-up times of overall, < 65 and ≥ 65 years old patients were 67, 45 and 64 months respectively. The median OS and PFS for the entire cohort were not reached and 24 months (95% CI: 18.0–29.9 months), respectively. Kaplan-Meier survival curves for OS and PFS are shown in Figures 1 and 2.

The median OS for patients < 65 years was 84 months, while for those ≥ 65 years, it was not reached. However, survival curves for both age groups were not significantly different (p = 0.924, HR = 0.93, 95% CI = 0.18–4.83), indicating similar outcomes (Figure 1). The median PFS was 19 months for patients < 65 years and 36 months for patients ≥ 65 years, with no significant difference between groups (p = 0.229, HR = 0.57, 95% CI = 0.23–1.42) (Figure 2). The Cox regression test was performed for the multiple variables impact (due to the imbalance from gender and stage 1 disease) on the survival time analysis. The result showed that both variables: male gender and stage 1 disease did not show statistically significant impact on the survival analysis. (male gender: HR = 1.53, p = 0.567; stage 1 disease: HR = 0.379, p = 0.313). The result implied that the imbalance variables may confound the survival in the 2 groups, but in this study the impact was not significant.

### 3.3. Adverse events

Adverse events were documented in 71.9% of patients, with the most common being fever (71.9%), infection (56.3%), and diarrhea (78.1%) (Table 2). Younger patients (< 65 years) had a higher incidence of severe adverse events, particularly infection (95.5%) and fever (86.4%). In contrast, older patients (≥ 65 years) had fewer and

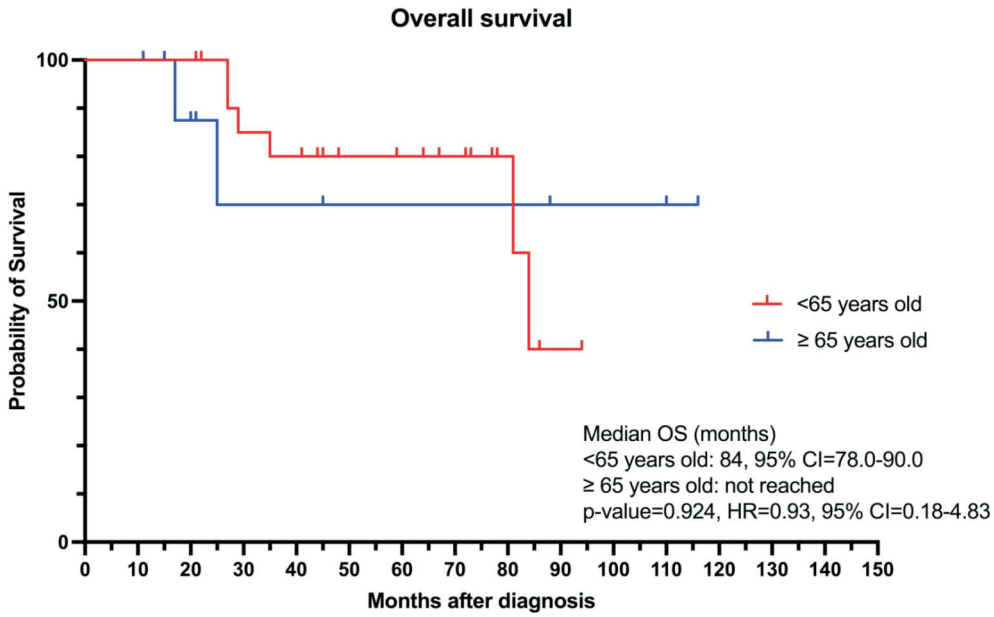


**Figure 1.** Overall survival of multiple myeloma patients undergoing autologous hematopoietic stem cell transplantation with stratification based on two age groups: < 65 years old and ≥ 65 years old.

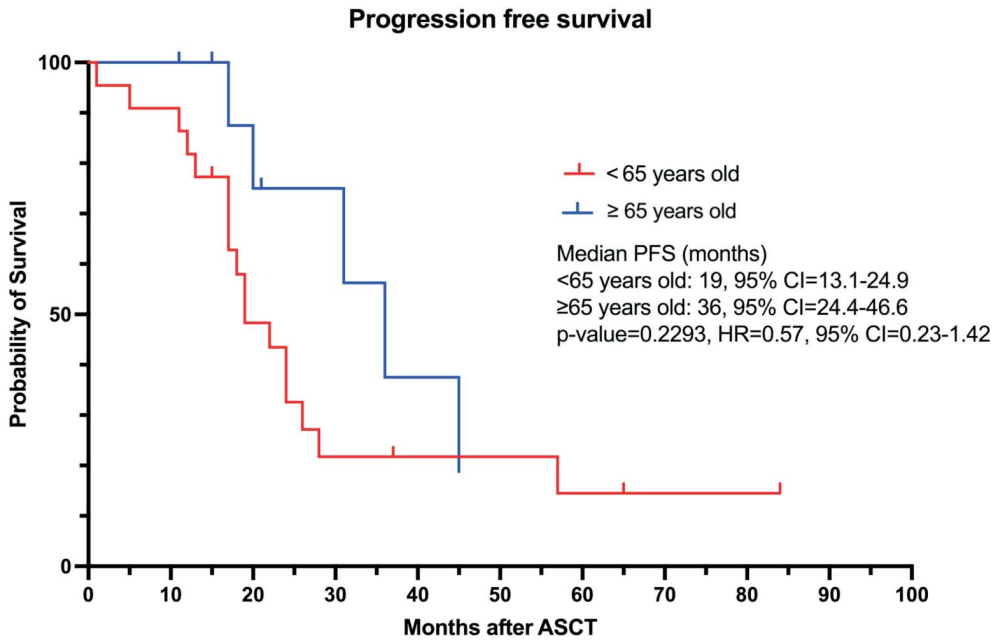


**Figure 2.** Progression-free survival of multiple myeloma patients undergoing autologous hematopoietic stem cell transplantation with stratification based on two age groups: < 65 years old and ≥ 65 years old.

**Table 2**
Adverse events in 32 multiple myeloma patients undergoing autologous hematopoietic stem cell transplantation.

| | Total (n = 32) | % | < 65 (n = 22) | % | ≥ 65 (n = 10) | % | p-value |
|---|---|---|---|---|---|---|---|
| Fever, n | 23 | 71.9% | 19 | 86.4% | 4 | 40.0% | 0.012 |
| Infection, n | 18 | 56.3% | 21 | 95.5% | 4 | 40.0% | 0.001 |
| Oral mucositis, n | | | | | | | |
| All grade | 9 | 28.1% | 6 | 27.3% | 3 | 30.0% | > 0.99 |
| Grade I/II | 9 | 28.1% | 6 | 27.3% | 3 | 30.0% | > 0.99 |
| Grade III/IV | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | > 0.99 |
| Bleeding events, n | 5 | 15.6% | 5 | 22.7% | 0 | 0.0% | 0.155 |
| Diarrhea | | | | | | | |
| All grade | 25 | 78.1% | 19 | 86.4% | 6 | 60.0% | 0.165 |
| Grade I/II | 22 | 68.8% | 17 | 77.3% | 5 | 50.0% | 0.217 |
| Grade III/IV | 3 | 9.4% | 2 | 9.1% | 1 | 10.0% | > 0.99 |
| Nausea and vomiting | | | | | | | |
| All grade | 25 | 78.1% | 15 | 68.2% | 10 | 100.0% | 0.069 |
| Grade I/II | 25 | 78.1% | 15 | 68.2% | 10 | 100.0% | 0.069 |
| Grade III/IV | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | > 0.99 |
| AST/ALT elevation | | | | | | | |
| All grade | 6 | 18.8% | 4 | 18.2% | 2 | 20.0% | > 0.99 |
| Grade I/II | 6 | 18.8% | 4 | 18.2% | 2 | 20.0% | > 0.99 |
| Grade III/IV | 0 | 0.0% | 0 | 0.0% | 0 | 0.0% | > 0.99 |
| RBC transfusion, unit | | | | | | | > 0.99 |
| Median (range) | 0 (0–8) | | 0 (0–8) | | 0 (0–0) | | |
| Platelet transfusion, unit | | | | | | | > 0.99 |
| Median (range) | 2 (1–8) | | 2 (1–8) | | 2 (1–6) | | |

* Categorical variables were compared using the Chi-square test or Fisher's Exact Test, while continuous variables were compared using the Mann-Whitney U test for non-parametric data. p-value < 0.05 means significant difference between 2 groups.
ALT, alanine aminotransferase; AST, aspartate aminotransferase; RBC, red blood cell.

milder complications. Significant differences were found in fever (p = 0.012) and infection (p = 0.001), with younger patients experiencing higher rates of both. Fever affected 86.4% of patients < 65 years versus 40% of those ≥ 65 years, and infection was observed in 95.5% of younger patients compared to 40% of older patients. No significant age-related differences were observed for oral mucositis, nausea/vomiting, or liver enzyme elevations (p = 1 for mucositis and liver enzymes; p = 0.069 for nausea/vomiting). Similarly, no significant differences in bleeding events or diarrhea were found (p = 0.155 and p = 0.165, respectively). The median number of red blood cell and platelet transfusions was similar across both age groups.

## 4. Discussion

Our study provides valuable insights into the outcomes of ASCT in elderly MM patients, highlighting the feasibility and challenges of ASCT in this age group in Taiwan. The comparison between younger (< 65 years) and older (≥ 65 years) patients underscores important differences in clinical characteristics, treatment outcomes, and adverse events, providing a deeper understanding of how age affects ASCT outcomes. In our cohort, the median OS was not reached for the elderly group. This finding may be influenced by the relatively small sample size (10 patients in the ≥ 65 group), which limits statistical power. Nevertheless, the comparable survival outcomes suggest that ASCT can provide substantial survival benefits to elderly patients when properly selected.[12] The result of our analysis shows that in selected elderly patients ASCT may also provide partly survival benefits and the adverse events are acceptable. Our results align with previous studies by Pawlyn et al. and Klein et al., which reported that ASCT can be both safe and effective for elderly patients, provided that they are fit enough for the procedure.[4,13] Our study underscores the importance of considering individual patient profiles over chronological age when evaluating eligibility for ASCT in MM patients. This observation is further supported by studies such as those by Abdallah et al. and Belotti et al., which advocate for a more nuanced approach to patient selection based on functional status and comorbidities.[4,13–20]

The comparison between the < 65 and ≥ 65 age groups revealed that no significant differences was observed in terms of both OS and PFS. This is consistent with findings from other studies demonstrating that younger MM patients typically achieve better survival outcomes due to fewer comorbidities and a better overall health status at diagnosis.[21,22] In contrast, elderly patients tend to have more comorbidities, poorer performance status and may struggle with the intensity of ASCT, which can negatively affect both treatment efficacy and survival. However, despite the challenges, our data indicate that elderly patients who are appropriately selected for ASCT can achieve outcomes comparable to younger patients, especially when modern induction therapies like VTd are used.[23] These findings underscore the importance of careful patient evaluation and personalized treatment plans to maximize outcomes for elderly MM patients.

It is noteworthy that adverse events were more common in younger patients in our study, particularly fever and infection. These findings are consistent with the results of previous studies that younger patients may experience more intense treatment-related complications, possibly due to more aggressive treatment regimens and a higher intensity of post-transplant care.[24,25] On the other hand, the elderly group had fewer and milder complications, reflecting the lower intensity of their treatment regimens and possibly a more cautious approach to managing adverse events. Interestingly, the incidence of other complications, such as nausea, vomiting, oral mucositis, and liver enzyme elevations (aspartate aminotransferase/alanine transaminase), was similar across both age groups, suggesting that these events are less dependent on age and may be more related to the transplant procedure itself, rather than patient age. This is in contrast to other studies where elderly patients were found to have higher rates of certain adverse events, such as infections and treatment-related toxicity.[26] Our findings, however, suggest that with careful monitoring and supportive care, the incidence of severe complications in elderly MM patients can be minimized.

While ASCT remains the standard of care for eligible MM patients, recent advances in non-intensive therapies and immunotherapy have led to improvements in outcomes, particularly in elderly patients. The introduction of novel agents like lenalidomide, bortezomib, and thalidomide has revolutionized treatment, reducing the toxicity associated with traditional regimens and improving survival.[27,28] In addition, newer immunotherapies, including monoclonal antibodies such as daratumumab, and bispecific antibodies, offer promising options for elderly patients who may not tolerate intensive therapies as well.[26,29,30]

Recent studies have shown that these newer agents, when used as part of induction or maintenance therapy, can improve response rates and reduce the need for intensive treatments like ASCT, especially in elderly patients with significant comorbidities.[31,32] However, the applicability of these newer therapies in elderly MM patients remains an area of ongoing research, and the long-term effects of combining these therapies with ASCT need further investigation.[33]

Our study underscores the importance of individualized treatment plans for elderly MM patients, focusing on a comprehensive health assessment and careful risk stratification to identify patients who are likely to benefit from ASCT.[34] Future research should explore the role of non-intensive therapies and immunotherapies in elderly MM patients, particularly in combination with ASCT, to improve outcomes while minimizing toxicity.[35] Moreover, studies should assess the long-term effects of ASCT in elderly patients, as well as the role of emerging immunotherapies in managing relapse and minimizing post-transplant complications.[36]

Our study has several limitations. The retrospective design and small sample size of the elderly cohort (n = 10) limit the generalizability of our findings. Furthermore, the lack of randomized controls and potential selection bias means that caution should be taken when interpreting these results. For example, more male gender and ISS stage 1 were observed in the ≥ 65 year-old patient. Another limitation is the imbalance of follow up time between the < 65 year-old and ≥ 65 year-old patient. The survival estimates may be artificially better in the group with shorter follow-up time because the enough events (deaths) may not be observed if the follow-up time is too short. However, despite these limitations, the study provides valuable data on the outcomes of ASCT in elderly MM patients and reinforces the need for individualized treatment strategies based on patient age, comorbidities, and disease stage.

In conclusion, our study supports the use of ASCT as an effective treatment for elderly MM patients, with comparable survival outcomes to younger cohorts when patients are appropriately selected. Advances in non-intensive therapies and immunotherapies offer promising alternatives and can be integrated into treatment regimens to reduce toxicity and improve outcomes. Ongoing research is essential to refine treatment strategies and explore new therapeutic options to further enhance survival and quality of life for elderly MM patients.

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## Conflicts of interest

We declare that there are no conflicts of interest relevant to this study.

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