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Autologous stem cell transplantation in multiple myeloma at Chris Hani Baragwanath Academic Hospital

Authors:
Vedanand Rawoo[1]
Moosa Patel[1]
Atul B. Lakha[1]
Vinitha Philip[1]
Muhammed F. Waja[1]

Affiliations:
[1]Department of Medicine, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

Corresponding author:
Moosa Patel,
moosa.patel@wits.ac.za

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Background: Autologous stem cell transplantation (ASCT) is the standard of care for multiple myeloma (MM), even in the era of novel therapeutic agents. Data regarding ASCT outcomes in MM is lacking in South Africa.

Aim: To assess the impact of ASCT on MM at a public health facility.

Setting: Clinical Haematology Unit, Chris Hani Baragwanath Academic Hospital, Johannesburg.

Methods: A retrospective analysis of MM patients who received ASCT over 19 years.

Results: Fifty-one patients received ASCT as part of their treatment schedule. While 41 patients received a single transplantation, 10 patients underwent a salvage transplantation after relapsing. Most of the patients (74.5%) had a delayed transplantation. The median overall survival (OS) was 57 months for the entire group, 32 months in the early transplantation group and 58.5 months in the delayed transplantation group, with no statistical difference between the early and delayed groups (p = 0.12) and among the different International Staging System groups (p = 0.71). The median time for disease relapse after the first ASCT was 30 months.

Conclusion: Autologous stem cell transplantation is an important consolidation treatment modality for MM in the South African public health sector as it prolongs survival. Greater access to novel agents during induction and relapse is advocated in the South African public health sector to further improve the outcomes that are currently seen with ASCT.

Contribution: This study adds to the limited body of knowledge pertaining to ASCT in MM in the African continent.

Keywords: multiple myeloma; autologous stem cell transplantation; melphalan; South Africa; consolidation; ASCT; high-dose therapy.

Introduction

Multiple myeloma (MM) is a clonal plasma cell neoplasm that contributes to approximately 1% of all cancers worldwide and 10% of all haematological cancers.[1] The median age of patients at diagnosis is 65 years in the United States (US) and 72 years in Europe.[2] In contrast, previous studies performed at our institution have shown that patients are diagnosed 5-10 years earlier.[3,4]

Following induction therapy, high-dose therapy (HDT) with melphalan, followed by an autologous stem cell transplantation (ASCT) rescue, has superseded conventional chemotherapy as the current standard treatment for newly diagnosed MM patients since the two seminal studies performed in the 1980s, confirming the superiority of high-dose melphalan and ASCT in achieving better outcomes.[5,6] Longer progression-free survival (PFS), treatment-free intervals and better quality of life are all associated with the use of early ASCT.[7] These benefits, however, did not translate into improved overall survival (OS) when compared to delayed transplantation given at disease relapse. Thus, delayed ASCT is a safe alternative in the current MM treatment landscape of novel therapies.[8,9] Patients with high-risk MM have more aggressive disease, more rapid progression and more complications as compared to patients with standard-risk MM. These patients therefore benefit enormously from early upfront ASCT, ideally within 12 months of diagnosis.[10]

A cut-off age of 65 years has traditionally been used as an entry criterion for ASCT in most clinical trials.[11,12] Recent studies have shown a significant benefit of ASCT in patients at least 70 years old with minimal comorbidities and a good performance status (PS). These patients achieved similar

anti-myeloma benefits without an increase in transplant-related mortality (TRM) and relapse rate and had improved PFS as compared to their younger-aged counterparts.[13,14,15] A tandem ASCT is defined as a pre-planned second ASCT within 2 to 3 months of the first ASCT. The benefits of this practice in improving survival outcomes, as shown by clinical trials, have been conflicting. The greatest benefit of tandem ASCT was appreciated in patients who had at least one adverse cytogenetic abnormality, particularly deletion of chromosome 17p, in whom the mortality risk is reduced after receiving a tandem ASCT.[9,16] However, the role of tandem ASCT in the current era of novel agents is less convincing, even in patients with high-risk cytogenetics. There is a good chance that the use of two novel agents in induction therapy has reduced the need for a tandem ASCT.[17]

The majority of patients experience a relapse of MM, despite consolidation and/or maintenance therapy after their first ASCT. Many factors determine the choice of treatment after each relapse. These include the timing of the relapse, the response to prior therapy, the severity of the relapse and the PS of the patient. Novel agents used to treat relapsed MM, despite showing a modest survival benefit, are subject to high levels of chemotherapy resistance, which ultimately leads to refractory disease.[18] There is evidence to suggest that salvage ASCT to treat relapsed or progressive MM after a first ASCT is an attractive option, as it is related to an improved PFS and OS and is associated with very low non-transplant mortality rates.[18,19] Salvage ASCT is most effective in patients who had a longer duration of response after their first ASCT, a good baseline PS and who have access to novel agents to be used for maintenance therapy. Immunotherapy with chimeric antigen receptor-T (CAR-T) cells and bispecific cells is the latest treatment modality that has shown great promise in the setting of refractory or relapsed disease but its use in newly diagnosed MM is still being investigated.[20]

Data that are related specifically to ASCT and its outcomes in MM patients in a South African context are sparse. Most studies performed locally have explored the patient and disease characteristics and analysed outcomes in MM patients, with a few focussing on treatment modalities.[3,4,21,22] This retrospective analysis was undertaken to assess the patient profiles, disease characteristics, response and complications related to HDT and ASCT in a state hospital in Johannesburg, South Africa (SA).

Methods

This retrospective study included all the patients who had a confirmed diagnosis of MM and had received at least one ASCT at the Clinical Haematology Unit, Department of Medicine, Chris Hani Baragwanath Academic Hospital (CHBAH) in Johannesburg, SA between 01 January 2003 and 31 December 2021 (i.e., over a 19-year period).

Clinical, radiological and most of the laboratory data were obtained from patients' hospital files kept at the Clinical Haematology Unit. Additional data regarding bone marrow studies and cytogenetics, including fluorescence-in situ hybridisation, was accessed from the National Health Laboratory Service's online Labtrak System (Trackcare, Intersystems, Cambridge, Massachusetts, United States). The diagnosis of MM was based on a combination of clinical, radiological and laboratory features including serum and/or urine protein electrophoresis, serum free light chain assay, immunofixation and bone marrow aspirate and trephine examination. The study period was divided into two equal halves, January 2003 to June 2012 and July 2012 to December 2021. This was done in order to compare some of the outcomes in the latter half of the study, where there was an increasing trend and greater access to a limited number of novel agents and newer induction chemotherapy regimens. Survival outcomes were analysed based on a number of variables, including the International Staging System (ISS) criteria in MM,[23] the induction chemotherapy regimen, the disease response status at the time of ASCT, the timing of ASCT and the maintenance chemotherapy agent used.

All patients in the study received a single dose of intravenous etoposide 400 mg as the mobilisation agent for a peripheral blood stem cell harvest. It was administered approximately 10–12 days before the harvest and 1 week before granulocyte-colony stimulating factor (G-CSF) (filgrastim 5 µg/kg twice daily for 5 days) was given. Melphalan was used as the consolidation chemotherapy regimen in all patients. Most of the patients (80%) received a total dose of 200 mg/m^2 of melphalan, usually administered as a 100 mg/m^2 intravenous infusion over 30 min – 60 min for two consecutive days. Neutrophil engraftment after ASCT was defined as the number of days for the absolute neutrophil count (ANC) to improve to more than 0.5×10^9/L for three consecutive days. Platelet engraftment was defined as the time taken, in days, for the platelet count to improve to greater than 20×10^9/L, without the need for any platelet transfusion for at least 7 days.

Disease response was assessed after induction chemotherapy and at 6 months after ASCT and was defined according to the International Myeloma Working Group criteria.[24] The response criteria used in this review were mostly based on serum and urine electrophoresis and immunofixation findings, along with clinical and imaging data. Most patients did not have a bone marrow aspirate and trephine biopsy repeated as a routine investigation after their induction phase or ASCT. Overall survival was defined as the time, in months, from the date of initial diagnosis of MM to the time of death or last follow-up. Finally, TRM was defined as death because of any transplantation-related cause, other than disease relapse and was assessed up to 100 days post-ASCT.

Statistical analysis

Categorical data were analysed and presented as frequencies and percentages for the overall study and were also stratified by period (January 2003–June 2012 and July 2012–December 2021). To test for statistical significance for categorical

measures stratified by period, Chi-Square test analysis or Fisher's test was used. Continuous measures were assessed using medians and inter-quartile ranges (IQRs) as well as means and standard deviations and were compared non-parametrically and parametrically using the Kruskal–Wallis test and student t-test, respectively. All statistical analyses were conducted in SAS Enterprise Guide, version 7.1 (SAS Institute, Cary, North Carolina, United States). Kaplan–Meier curves were used to compare survival outcomes, whenever feasible, between different groups.

Ethical considerations

Ethics approval was obtained from the Human Research Ethics Committee of the University of the Witwatersrand, Johannesburg. The ethical clearance number is M210739. Access to patients' records was obtained after getting consent from the Head of the Clinical Haematology Unit, the Head of the Department of Internal Medicine and the Chief Executive Officer of CHBAH. No patient informed consent was required because of the retrospective nature of the study. Patient-identifying data were kept anonymous and safeguarded in a password protected Microsoft Excel® spreadsheet.

Results

Baseline characteristics

Out of a total of 691 newly diagnosed MM patients, 51 (7.4%) received an ASCT at our institution during the study period. Three patients who had received an ASCT in the private sector, and were subsequently following up at our facility, were excluded from the study. Gender-wise, 30 (58.8%) patients were female and the male: female ratio was 1: 1.43. The median age at presentation was 54 years (IQR 34–62). The majority of the patients (86.3%) were of 'black African' ethnicity. The baseline Eastern Cooperative Oncology Group (ECOG) performance score was ≤ 1 in 76.5% of the patients (Table 1).

The most common comorbidity was hypertension (n = 33, 64.7%), followed by diabetes mellitus (n = 10, 19.6%). 7.8% of the cohort had some form of renal impairment at diagnosis, which did not require acute renal replacement therapy and was reversible with conservative measures. Three (5.9%) of the patients were human immunodeficiency virus (HIV) seropositive. All of them were virologically suppressed before their ASCT.

The most prevalent MM subtype was IgG myeloma (66.7%), followed by the light chain variant (27.4%). Data regarding the cytogenetic profile were available for 15 cases, of whom 80% had standard-risk disease. Of the three cases with high-risk features, one had t(4;14), one t(14;20) and one del 17p.

Induction chemotherapy

Data regarding the induction chemotherapy regimen were available for 47 patients. Most of these induction regimens consisted of modified cyclophosphamide, vincristine, adriamycin and dexamethasone (CVAD) (85.1%), one patient was treated with Velcade (bortezomib), thalidomide and dexamethasone (VTD), one with melphalan and prednisone and five patients (10.6%) required more than one induction regimen before ASCT (Figure 1). The mean number of induction chemotherapy cycles required to achieve at least a partial response (PR) before ASCT was 9.5 (with a median of 8 cycles). At the time of ASCT, eight (15.7%) patients had achieved complete response (CR), 12 (23.5%) were in very good partial response (VGPR) and 31 (60.8%) in PR (Figure 2).

Mobilisation

All patients received a single dose of 400 mg of intravenous etoposide (at an outpatient setting). This was followed by inpatient administration of G-CSF (filgrastim 5 µg/kg twice daily) for 5 days (commencing 1 week after etoposide administration). The median $CD34^+$ yield obtained for ASCT was 9.83 × 10^6/kg (IQR 2–36) (Table 2). While 17 (36.2%) patients underwent a single apheresis session, 21 (44.7%) had two apheresis sessions and 9 (19.1%) had three sessions to obtain the desired yield.

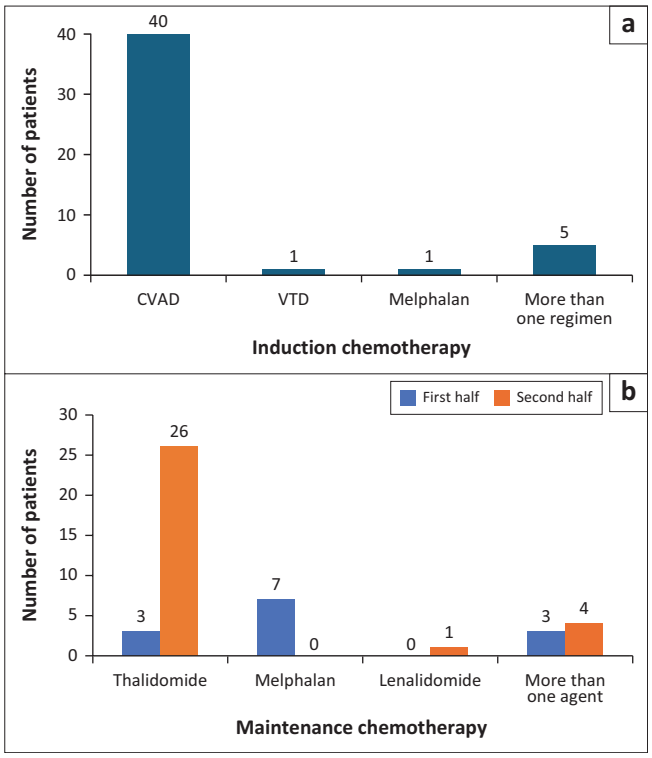
High-dose therapy- autologous stem cell transplantation

Melphalan was used as the conditioning regimen in all the patients in the study. Most of the patients (80%) received a total dose of 200 mg/m^2 of melphalan, usually administered as a 100 mg/m^2 intravenous infusion over 30 min – 60 min for two consecutive days. Neutrophil engraftment after high-dose melphalan occurred after a median of 11 days

TABLE 1: Patient and disease characteristics at diagnosis.

Parameter	*n*	%	Median	Range
Gender				
Male	21	41.2	-	-
Female	30	58.8	-	-
Age at diagnosis (years)	-	-	54.0	47–57
Eastern Cooperative Oncology Group performance status				
0	6	11.8	-	-
1	33	64.7	-	-
2	10	19.6	-	-
3	2	3.9	-	-
International Staging System stage (n = 41)				
I	13	32.0	-	-
II	13	32.0	-	-
III	15	36.0	-	-
Multiple myeloma subtype				
IgG	34	66.7	-	-
IgA	3	5.9	-	-
Light chain myeloma	14	27.4	-	-
Cytogenetic profile (n = 15)				
Low/intermediate risk	12	80.0	-	-
High risk	3	20.0	-	-
HIV seropositivity	3	5.9	-	-
β^2 microglobulin (mg/L)	-	-	4.9	2.7–8.6
Albumin (g/L)	-	-	35.0	31–41.5
Paraprotein (g/L)	-	-	38.0	24.7–61.9
Haemoglobin (g/L)	-	-	9.7	8.2–11.1
Bone marrow plasma cells (%)	-	-	28.0	3.0–95

Ig, Immunoglobulin; HIV, human immunodeficiency virus.



CVAD, cyclophosphamide, vincristine, adriamycin, dexamethasone; VTD, Velcade (bortezomib), thalidomide, dexamethasone.

FIGURE 1: Induction (a) and maintenance chemotherapy (b) in patients who received autologous stem cell transplantation.

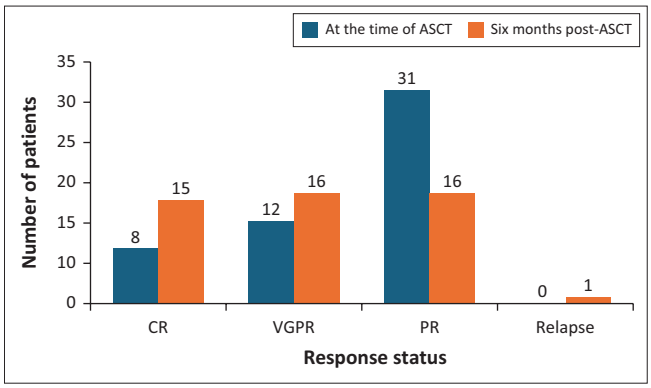
(IQR 3–14). Platelet engraftment took place after a median of 10 days (IQR 6–15) (Table 2).

In all, 41 patients received a single ASCT. The 10 patients who received a second ASCT had done so as a salvage strategy following relapse after the first ASCT. Most of the patients (74.5%) had a delayed ASCT (i.e., more than 12 months after being diagnosed). The median time between diagnosis and the first ASCT was 17 months (IQR 6–72), with a mean of 23.2 months for the entire cohort. There was no difference in OS when a delayed approach to ASCT was adopted ($p = 0.12$).

Early complications from HDT encountered within the first 2 weeks were mostly related to myelosuppression. While 90.2 % (n = 46) of the patients developed grade IV neutropenia, 14 (33.3%) and 23 (54.8%) patients developed World Health Organization grades III and IV thrombocytopenia, respectively. Anaemia was seen in 52.9% of patients. Gastrointestinal side effects were seen in 39.2% of cases.

Maintenance chemotherapy

Thalidomide monotherapy was given to 29 (65.9%) patients, melphalan to 7 (15.9%) patients, lenalidomide to 1 patient in the latter half of the study and different maintenance agents to 7 patients. Significantly more patients were on thalidomide in the second period because of its increased availability in the latter part of the study (Figure 1). Six patients did not receive any maintenance agent; four of them demised before any maintenance therapy could be started and the remaining two patients were lost to follow up shortly after ASCT. Thalidomide and melphalan were given for a median of 32.5 months (IQR 5–103) and 11 months (IQR 5–53), respectively.



ASCT, Autologous stem cell transplantation, CR, complete response; VGPR, very good partial response; PR, partial response.

FIGURE 2: Disease response after induction chemotherapy and six months after autologous stem cell transplantation.

TABLE 2: Characteristics of high-dose therapy-autologous stem cell transplantation in our cohort.

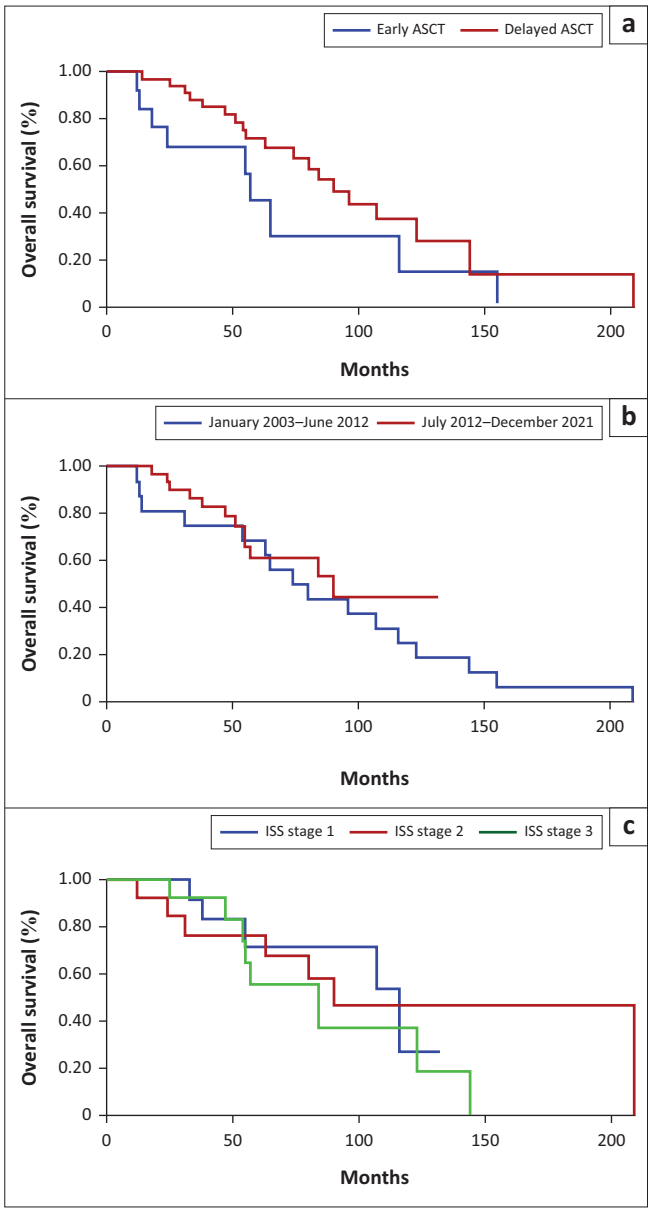
Parameter	*n*	%	Median	Range
$CD34^+$ yield (x 10^6/kg)	-	-	9.83	2.0–36
Melphalan dose				
200 mg/m²	41	80.4	-	-
Total dose of 250 mg – 350 mg	9	17.6	-	-
Total dose of 170 mg	1	2.0	-	-
Time to neutrophil engraftment (days)	-	-	11.00	3.0–14
Time to platelet engraftment (days)	-	-	10.00	6.0–15
Single ASCT	41	80.4	-	-
Salvage ASCT	10	19.6	-	-
Timing of ASCT (months)				
Early	13	25.5	-	-
Delayed	38	74.5	-	-
Overall survival (months)	-	-	-	-
Early ASCT	-	-	32.00	12–155
Delayed ASCT	-	-	58.50	14–209

ASCT, autologous stem cell transplantation; CD, cluster of differentiation; HDT, high-dose therapy.

Outcomes

The median OS in our patient population was 57 months (IQR 12–209) from the time of diagnosis. Twenty-nine patients (56.9%) had demised or presumed dead as per their last visit notes. All the patients from the first half of the study and 33.3% from the latter half of the study had demised. Of the patients who demised, 18 (62.1%) showed evidence of disease relapse. Of the remaining eight patients who died and who did not show disease relapse, four had sepsis, one had fulminant heart failure, one died from complications related to multiple other comorbidities and two died of unknown causes.

In terms of the ISS stage, the median OS for patients in stages I, II and III were 55 months, 82 months and 55 months, respectively.



Note: Kaplan-Meier survival estimates.

ASCT, autologous stem cell transplantation; ISS, International Staging System.

FIGURE 3: Overall survival according to (a), timing of autologous stem cell transplantation; (b), the two time periods of the study and (c), international staging system staging.

Out of the 22 patients who were alive at the conclusion of the study, 2 (9.1%), 5 (22.7%) and 10 (45.5%) were in PR, VGPR and CR, respectively. Four (18.2%) had evidence of disease relapse. The disease response status after ASCT was not clearly defined or not available for four patients (7.8%).

At 6 months after the first ASCT, 19 (37.2%) patients had a favourable response; 3 had improved from PR to CR, 11 from PR to VGPR and 5 from VGPR to CR status (Figure 2). Twenty-seven patients (52.9%) stayed in their pre-ASCT response status: 13 in PR, 7 in VGPR and 7 in CR. One patient relapsed from a pre-ASCT PR status. The response status of four patients could not be interpreted at 6 months as three had demised prior to that and one patient defaulted further follow up appointments soon after his ASCT.

The median OS in the early ASCT group was 32 months compared to 58.5 months for the delayed ASCT group. Survival data were compared between the two halves of the study. A 5-year predicted survival analysis for the second half of the study could not be performed because of the small number of patients. Survival between the two groups was not statistically significant (p = 0.45). Furthermore, no statistical significance was found when survival trends were compared between the different ISS staging groups and between the early and delayed ASCT groups (p-values of 0.71 and 0.12, respectively) (Figure 3).

Twenty-three patients relapsed at some point after their ASCT in this study. The median time for relapse after the first ASCT was 30 months. While 69.6% of the patients relapsed after the first ASCT, 30.4% of the relapsed patients had done so after their second ASCT.

Discussion

This study looked at the patient and disease characteristics and the outcomes associated with ASCT in the management of MM patients at a South African public health sector Clinical Haematology Centre. To our knowledge, ASCT is not a commonly available treatment option in many centres across the African continent when compared to higher-income countries. Autologous stem cell transplantation still has an important role in the treatment of newly diagnosed MM and has been shown in several trials to be associated with improved PFS and OS, both before and after the introduction of the novel induction agents and the anti-CD38 monoclonal antibody daratumumab.[8,25,26,27]

The mean number of transplants per year in this review was 2.68. This contrasts with the number of ASCT offered in Europe and the US, where ASCT is offered to most eligible patients eligible for it.[28] The new standard of care in terms of induction treatment is a quadruplet combination, including daratumumab, an immunomodulatory drug, a proteasome inhibitor and dexamethasone.[1] In our study, most of the patients received a VAD-based regimen (85.1%), which used to be one of the standard induction approaches before the introduction of the novel agents. Induction therapy with novel agents such as lenalidomide, thalidomide and bortezomib have been shown to be associated with better survival outcomes in a number of clinical trials.[26,29,30] At our institution, these agents have been scarcely used as induction agents, mostly because of difficulties in accessing them owing to their expensive cost. Bortezomib is still largely unavailable across the public sector in SA and thalidomide, which was more readily available to our patients, was used mostly as maintenance therapy. With novel agents, three to four induction cycles are recommended to achieve an acceptable level of response before considering ASCT. This limits exposure of the bone marrow to the myelosuppressive effects of the therapy used.[31,32] In our study, the median number of induction chemotherapy cycles was eight. The reasons for requiring a longer induction period were likely because of the inferior effectiveness of the chemotherapy regimens,

compared to novel agent-based therapy, to achieve at least a PR status prior to ASCT. In addition, some patients received more than one induction regimen, as and when more suitable induction drugs became available later, which resulted in prolonged periods of induction chemotherapy to achieve the desired initial response, prior to ASCT.

Cyclophosphamide (3 g/m^2 – 4 g/m^2) alone or combined with etoposide, yields significantly more stem cells than growth factor–only mobilisation.[33] In our setting, the mobilisation agent used in all patients was etoposide. This was combined with G-CSF (e.g., filgrastim) to improve the yield at apheresis. The use of cyclophosphamide was not common practice in our study. This is likely because of prior exposure to cyclophosphamide in some of the induction regimens and the effectiveness of etoposide in achieving the desired stem cell yield prior to ASCT.

The median age at diagnosis in our patient population was 54 years, with the oldest transplanted patient being 62 years of age, which was in line with the standard for ASCT at the time.[11,34] The choice of younger patients was important for several reasons. Most (86.3%) of the patients had at least one comorbidity. In addition, the majority of our patients came from a disadvantaged socioeconomic background and some of them had to travel long distances for their treatment and appointments. This required a younger, fit patient who would be able to come for regular visits and tolerate the high doses of chemotherapy drugs with their potential associated side effects.

In our setting, the amount of stem cells reinfused was > 2 × 10^6 $CD34^+$ cells/kg as most patients had an adequate amount of stem cells collected. The practice at our institution was to split the collected stem cells into two aliquots, for a possible tandem or salvage second ASCT. The median engraftment times for the ANC and platelets were 11 and 10 days, respectively, which was comparable to the study carried out by Bashir et al., where they also used melphalan 200 mg/m^2 as the conditioning regimen.[35] The Cape Town study performed by Novitzky et al., showed slightly longer engraftment times of 13 and 17 days for the ANC and platelets, respectively.[22]

Early ASCT compared to a delayed strategy has been shown to have better PFS but not OS.[8,36] The median OS in our patient cohort who received an early ASCT within 12 months of diagnosis was 32 months compared to 58.5 months for patients who received a delayed ASCT (> 12 months after admission). This was non-significant ($p = 0.12$) and confirms the fact that a delayed approach was safe, effective and feasible in our patient population, having not impacted adversely on the OS. Many factors accounted for delays in patients receiving an ASCT. Some patients, after counselling, were uncertain and unwilling to commit to the procedure despite agreeing to it and having already had a stem cell harvest. At times, the ASCT had to be postponed because of the unavailability of melphalan and/or growth factors. In addition, at times, there were unplanned delays on the part of the Clinical Haematology Unit, based on the availability of the clinical and nursing staff. Furthermore, most of our patients underwent a single ASCT, and it was generally not common practice to perform tandem ASCT. Salvage ASCT in suitable patients is a feasible and effective treatment option among patients after failure of a first ASCT.[18,19] Out of the 10 patients who received a salvage ASCT at our institution, 2 displayed high-risk cytogenetics (one had del 17p, one t[4;14]) and 2 standard-risk cytogenetics.

Overall survival in the era before ASCT was usually less than 18 months with conventional chemotherapy.[37] The median OS in our cohort of patients was 57 months (range: 12–209 months). Parallels could be drawn with another study whereby a VAD regimen was used in 79 patients before they received their ASCT after a median time of 6 months after diagnosis. The median OS in that cohort of patients was 66 months.[38] Two retrospective studies from our centre and looking at newly diagnosed MM patients, regardless of whether they received treatment or not, showed inferior survival rates.[3,4] The initial study showed an OS of 28.3 months with a lower median survival of 15.5 months. In the second study of 289 patients, the median OS was 15.9 months. This shows the clear benefit that MM treatment, including ASCT, had in prolonging our patients' survival. There was no statistically significant impact of ASCT when the OS between the two halves of the study was compared ($p = 0.45$). However, the predicted OS over a longer time-period in the latter half of the study could not be calculated because of the smaller number of patients. This might have been a useful piece of information to assess the impact of novel agents, which were being increasingly used towards the end of the study, on survival. In terms of the disease stage, patients in ISS stage I survive longer than patients in either stage II or III (median OS of 111, 66 and 45 months, respectively) after receiving an ASCT.[23] These findings were different in our study, with median OS times of 55 months, 82 months and 55 months for ISS stages I, II and III, respectively. Again, these skewed findings might not have reflected the true outcome in our study as the predicted survival times could not be ascertained because the number of patients in each of the above ISS subgroups analysed was too small to reach statistical significance and, moreover, because of the wide variability in the ASCT times throughout the study.

The retrospective nature and the small sample size were limiting factors in our study. There were several patients for whom important data regarding disease staging, induction chemotherapy regimen and maintenance therapy were missing. Moreover, a significant proportion (19.6%) of patients were lost to follow up after their ASCT, which hindered us from carrying out more robust survival analyses and may have affected our OS findings. Finally, a large proportion of the patients did not have cytogenetic results available to risk-stratify their disease and guide management accordingly.

Conclusion

Autologous stem cell transplantation in a South African public health sector setting is advocated currently as it is feasible and is associated with improved survival. The routine and more widespread introduction of novel agents at a public health sector setting is likely to impact favourably on an improved quality of response to induction therapy by allowing a larger number of patients to be offered ASCT as consolidation therapy and by further giving us a broader choice of drugs which could be used as maintenance therapy. Delayed ASCT did not impact unfavourably in our patient population in terms of OS despite the reasons mentioned earlier for the delay. Therefore, such an approach may still be useful until novel agents become a reality in the South African public health sector setting, which will then allow for more patients to be subjected to an earlier ASCT. This should be followed by more optimal maintenance therapy with a view to decreasing the number of relapses and improving the OS of patients with MM.

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Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contributions

The design and conceptualisation of the study was provided by M.P. Data collection, analysis and write-up of the manuscript were carried out by V.R. Revision and final approval of the manuscript as well as expert guidance and critical feedback were provided by the V.R., A.B.L., V.P. and M.F.W.

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Data availability

Data supporting the findings of this study are available from the corresponding author, M.P., on request.

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