

# Autologous stem cell transplantation in an older adult population

Over the past decade there has been a remarkable progress in the treatment of multiple myeloma (MM) and non-Hodgkin lymphoma (NHL). Nevertheless, autologous stem cell transplant (ASCT) remains an integral part of the care for patients with MM, and one of few curative options for patients with relapsed/refractory (R/R) NHL. Historically, an arbitrary age of 65 has been used to determine patient's eligibility for ASCT. This stems from the fact that the majority of prospective studies evaluating efficacy of ASCT in MM have excluded patients >65 years old.<sup>1</sup> Currently, nearly half of new diagnoses of MM and NHL are >75 years old.<sup>2,3</sup> However, the data on safety and efficacy of ASCT patients >75 years remains limited.

Racial minorities remain severely underrepresented in cancer clinical trials, thus limiting the generalizability of clinical cancer research to these populations.<sup>4</sup> Data on ASCT in elderly minority patients has to our knowledge not yet been reported. In this letter we present results of a retrospective study showing comparable transplant related mortality in minority patients >75 years old as compared to those aged 55-66 years old.

We conducted a retrospective cohort study comparing ASCT outcomes in patients >75 years old and 55-65 years old for the diagnosis of MM or NHL, who were conditioned with either melphalan or BEAM (carmustine, etoposide, cytarabine, melphalan) respectively. Patients were selected from an internal database which has all ASCT performed at our center between 2005-2021. The study group included patients >75 years old. The control group included patients 55-65 years old that were matched to the study group patients by sex and date of transplant. Electronic medical records were reviewed to gather data. The primary outcomes were admission mortality, length of stay, time to white blood cell (WBC) and platelet engraftment, incidence of neutropenic fever, positive blood culture, intensive care unit (ICU) admission, and 30-day rehospitalization rate. Secondary outcome were 1- and 5-year mortality rates. Patients with no follow-up post ASCT and ASCT prior to 1- and 5-year follow-up were excluded from analysis. Admission mortality and long-term survival probability were calculated using log rank test. Continuous data was reported as medians and interquartile ratios (IQR) and analyzed using Wilcoxon rank sum test. Significance was denoted by  $\alpha=0.05$ .

Between 12/2005 and 3/2021, there were 43 patients >75 years old who underwent ASCT for MM or NHL. Data collection was censored on 4/2/22. Table 1 summarizes patient characteristics at index ASCT. Twenty-four (55.8%)

patients were female. The median age in the study group was 77.1 (range, 76.2-77.9) years old and 61.9 (range, 57.4-63.0) years old in the control group. Both groups predominantly included minority patients: 55.8% and 46.5% were Spanish/Hispanic/Latino and 25.6% and 14.0% were Afri-

**Table 1.** Patient characteristics.

	Study	Control
N	43	43
Female, N (%)	24 (55.8)	24 (55.8)
Age, median (IQR)	77.1 (76.2-77.9)	61.9 (57.4-63.0)
Performance status, N	28	31
100	5	2
90	14	16
80	5	7
70	3	3
60	1	3
Minority, N (%)		
Spanish/Hispanic/Latino	24 (55.8)	20 (46.5)
African American	11 (25.6)	6 (14.0)
Non-minority*, N (%)	8 (18.6)	17 (39.5)
Medicaid insurance**, N (%)		
Minority	12/33 (36.4)	20/25 (80.0)
Non-minority	0	9/13 (69.2)
Auto-HSCT indication		
Multiple myeloma, N (%)	34 (79.1)	33 (76.7)
Upfront	28 (82.4)	24 (72.7)
Relapsed/refractory	6 (17.6)	9 (27.3)
Melphalan dose, N (%)		
200 mg/m <sup>2</sup>	5 (14.7)	28 (84.8)
140 mg/m <sup>2</sup>	19 (55.9)	5 (15.6)
100 mg/m <sup>2</sup>	9 (26.5)	0
50 mg/m <sup>2</sup>	1 (2.9)	0
Lymphoma, N (%) ***	9 (20.9)	10 (23.3)
DLBCL	7 (77.8)	7 (70.0)
Other	2 (22.2)	3 (30.0)
Upfront	4 (44.4)	6 (60.0)
Relapsed/refractory	5 (55.6)	4 (40.0)
Prior auto-HSCT for relapsed disease, N (%)	1 (2.3)	2 (4.6)

Auto-HSCT: autologous hematopoietic stem cell transplant; IQR: interquartile ratio; DLBCL: diffuse large B-cell lymphoma. \*Non-minority patients include those with ethnicity other than Spanish/Hispanic/Latino and those without documented Race/Ethnicity. \*\* In the study group: 1/43 patient had unknown insurance status, 39/42 had Medicare coverage, of 11/39 had dual Medicare/Medicaid coverage, 1/42 patient only had Medicaid coverage and 2/42 had commercial insurance. In the control group: 5 had unknown insurance status, 24/38 had only Medicaid coverage, 5/38 had dual Medicare/Medicaid coverage, 1/38 had only Medicare, 8/38 had commercial insurance. \*\*\*All patients with lymphoma received BEAM (carmustine, etoposide, cytarabine, melphalan) conditioning.

can American, in the study and control groups, respectively. MM was the most common indication for auto-HSCT comprising 34 (79.1%) and 33 (76.1%) patients in the study and control groups, respectively.

Table 2 outlines patient outcomes. Admission mortality did not differ significantly between the groups, with only one death in the control group ( $P=0.083$ ). The length of stay was comparable at 18 (range, 17-22) days and 19 (range, 16-20) days ( $P=0.2$ ) for study and control groups, respectively. Time to WBC engraftment in the study group was 12 (range, 11-12) days and 11 (range, 11-12) days in the control group ( $P=0.032$ ). Time to platelet engraftment in the study group was 14 (range, 12-15) days and 12 (range, 11-14) days in the control group ( $P=0.014$ ). Although time to both WBC and platelet engraftment was significantly

longer in the study group, the clinical significance of this finding is questionable, especially as it did not significantly prolong length of stay. There was no significant difference between incidence of neutropenic fever, or between incidence of positive blood cultures in patients with neutropenic fever. There was a non-statistically significant increase in the rate of ICU admissions in the study (4/43) versus control group (0/43) ( $P=0.12$ ). The 30-day re-hospitalization rate was comparable between the two groups ( $P=0.68$ ).

In the study group, two patients died within 1 year of ASCT (day +360 and +133) translating into 1-year mortality of 4.9% (2/41). Five-year survival was 53.8% (14/26). In the control group, one patient died on day +26 of ASCT translating into 1-year mortality of 2.8% (1/36). Five-year sur-

**Table 2.** Outcomes.

	Study	Control	P value
Admission mortality, N (%)	0	1 (2.3)	0.083
Minority	0	0	
Non-minority	0	1/1	
LOS - days, median (IQR)	18 (17-22)	19 (16-20)	0.2
Minority	18 (16-20.5)	17 (16.3-20)	
Non-minority	19.5 (17.75-28.25)	18 (16-19)	
Days to WBC engraftment, median (IQR)	12 (11-12)	11 (11-12)	<b>0.032</b>
Minority	12 (11-12)	11 (11-12)	
Non-minority	12 (12-12.3)	11 (10-12)	
Days to Plt engraftment, median (IQR)	14 (12-15)	12 (11-14)	<b>0.014</b>
Minority	13.5 (12-15)	13 (11.5-14)	
Non-minority	15 (14-22.8)	12 (11-13)	
Neutropenic fever, N (%)	22 (51.2)	27 (62.8)	0.38
Positive blood culture, N (%*)	7 (31.8)	11 (40.7)	0.56
Minority	17/35	15/26	
Non-minority	5/8	12/1	
ICU admission, N (%)	4 (9.3)	0	0.12
Minority	4/35	0	
Non-minority	0/8	0	
30-day readmission, N (%)	4 (9.3)	2 (4.8)	0.68
Minority	3/35	1/25	
Non-minority	1/8	1/17	
1-year survival, N (%)**	39/41 (95.1)	35/36 (97.2)	1
Minority	32/33	21/22	
Non-minority	7/8	14/14	
5-year survival, N (%)***	14/26 (53.8)	13/24 (54.2)	1
Minority	13/22	9/15	
Non-minority	1/4	4/9	

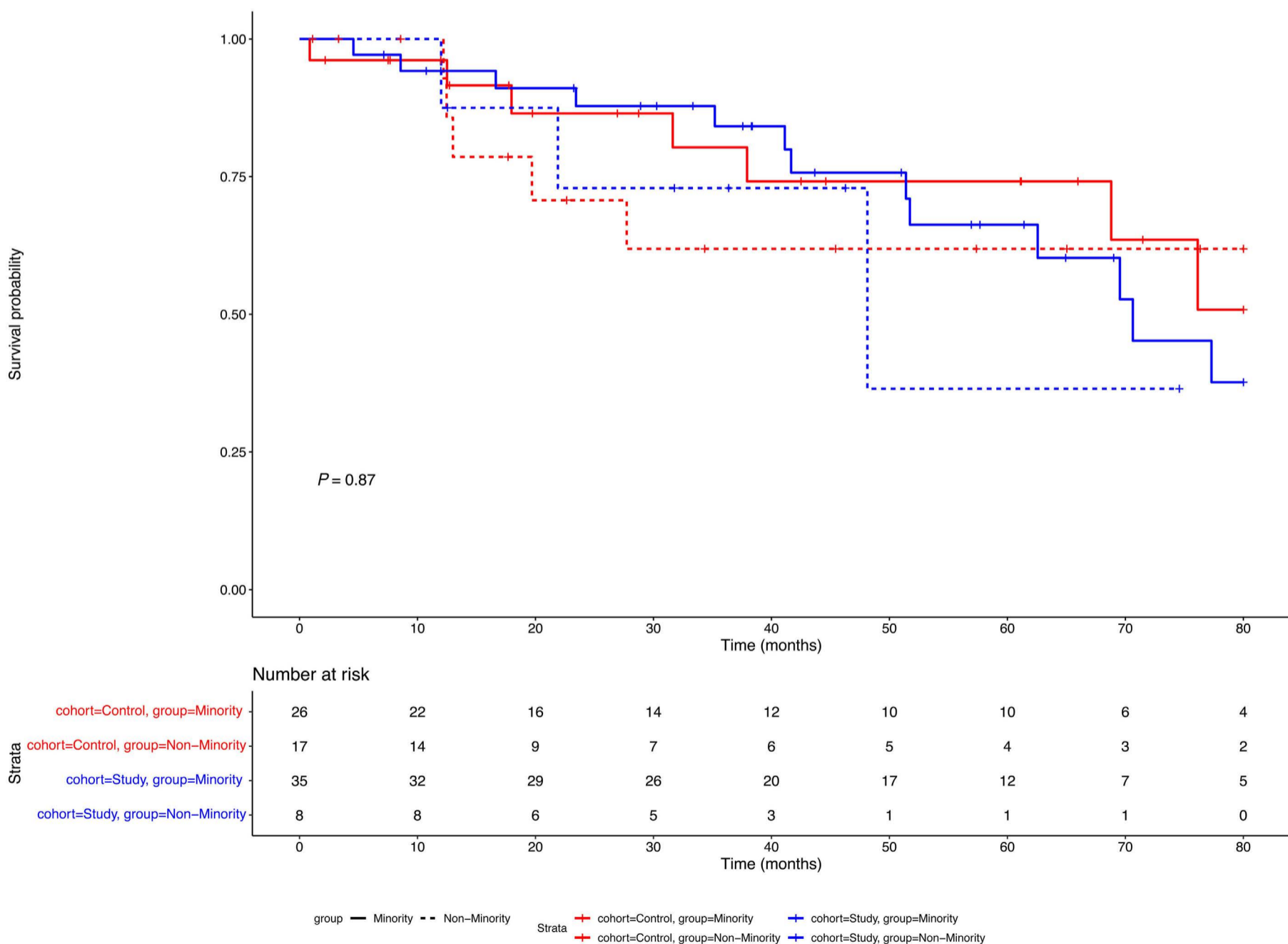
LOS: length of stay; WBC: white blood cells; Plt: platelets; ICU: intensive care unit; ASCT: autologous stem cell transplant. Minority subgroup includes African American and Spanish/Hispanic/Latino patients. \*Percent of those with neutropenic fever. \*\*Only includes patients with transplant >1 year ago and with follow-up after 1 year post-ASCT. Study group: 2 patients were excluded from analysis: 1 patient was lost to follow-up prior to the 1 year mark and 1 patient had ASCT <1 year ago. Control group: 7 patients were excluded from analysis: 5 patients were lost to follow-up prior to the 1 year mark and 2 patients had ASCT <1 year ago. \*\*\*Only includes patients with ASCT >5 years ago and with follow-up after 5 years post ASCT. Study group: 17 patients excluded from analysis: 6 patients were lost to follow up prior to the 5 year post ASCT follow-up; 11 patients had ASCT <5 years ago. Control group: 19 patients were excluded from analysis: 8 patients were lost to follow-up prior to the 5 year post ASCT follow up; 11 patients had ASCT <5 years ago.

vival was 54.2% (13/24) (Figure 1).

The treatment landscape for elderly patients with both MM and NHL has dramatically improved in recent years. However, ASCT remains a significant contributor to improved outcomes in the elderly population with MM, and one of the few options for long term disease control for patients with R/R NHL.<sup>5-10</sup> The main concern related to ASCT in the elderly has historically been transplant-related mortality (TRM). With the improvement of supportive care, TRM rates in elderly patients have been declining. Our finding of 0% TRM is similar to that of prior reports in this age category.<sup>7,11</sup> Additionally, in our study we observed a comparable 5-year mortality rate for elderly patients and their younger counterparts, despite a 15-year age difference.

In contrast to above-mentioned reports, our elderly cohort includes 80% patients from racial minority groups, predominantly Hispanic or African American. Studies have shown that Hispanics and African Americans are far less likely to undergo ASCT, despite an abundance of data

showing similar or better outcomes.<sup>12,13</sup> Our study is the first to our knowledge to address the outcomes for elderly minority patients undergoing ASCT. It is worth noting that in the two large reports comparing outcomes of ASCT in minorities and Caucasians with MM, the upper age limit in minority cohorts was 75 years old, while Caucasian cohorts included patients up to age of 80.<sup>12,14</sup> Similar to patients with MM, favorable outcomes for elderly patients with NHL receiving ASCT with BEAM conditioning have been reported, with no reports in the literature on minority elderly patients.<sup>15</sup> This is of clinical importance as various studies have shown that minority patients with NHL have worse outcomes compared to Caucasians.<sup>16,17</sup> This data suggests that elderly minority patients have two separate variables contributing to a decreased chance of being offered ASCT. 26.4% of the Bronx's population lives below the poverty line.<sup>18</sup> Montefiore Medical Center is one of the largest providers of Medicaid and Medicare in New York State. Analysis of National Cancer Database (NCDB) showed that ASCT improved survival for MM patients from



**Figure 1. Overall survival.** Survival probability of individual patient cohorts was plotted against time with control groups marked in blue and study groups marked in red.

all economic backgrounds, but uninsured patients or those with Medicaid had significantly lower overall survival.<sup>19</sup> Similar trends have been observed with in patients with NHL.<sup>20</sup>

This study has limitations such as retrospective design, small sample size, variability in minority proportion, and melphalan dosing discrepancy between the groups.

Our study is one of the few to demonstrate the safety of ASCT in patients >75 years old and the only study to evaluate ASCT in a predominantly minority elderly population. We did not find a statistically significant increase in 100-day transplant related mortality in patients > 75 years old compared to patients 55-65 years old. Older patients and those younger than 65 years old appear to have comparable 5-year mortality.

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### Disclosures

No conflicts of interest to disclose.

### Contributions

KF and MG developed the study concept and design; KF and TJ collected data, performed statistical analysis and drafted the manuscript; MG supervised the study and critically revised the manuscript; RE and CP identified study patients; KP performed statistical data analysis; JM, AL, FK, FJ, KG, AN, MA, KF, AdC, RB, DB, MP, CP, KG, RAS, NK, ASi, IM, NS, AV, IB and MG coordinated patient care and follow-up.

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### Data-sharing statement

The data that support the findings of this study are available upon request.

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