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Hematopoietic Stem Cell Transplantation - Comorbidity Index in Patients with Multiple Myeloma for Autologous Transplantation: A Valuable Tool for Predicting Overall Survival

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Abstract

Introduction: The scoring system of the hematopoietic cell transplantation comorbidity index (HCT-CI) was used in patients with Multiple Myeloma (MM) undergoing ASCT, and it could predict progress-free survival and overall survival.
The primary endpoint of our study is to determine the ideal cut-off value for the HCT-CI score, which can be effective in showing overall survival in patients with MM undergoing ASCT.
Methods: The X-tile model was used to determine the cut-off values of the HCT-CI score. Survival probabilities were calculated by using the Kaplan-Meier estimator. Univariate and multivariate analysis was performed using Cox proportional hazard regression model.
Findings: By using the X-tile model according to the HCT-CI score, patients were divided into 2 categories according to OS: HCT-CI Score ≤6 as low-risk (n:93, 81.6%), HCT-CI score >6 as high-risk (n:21, 18.4%).
The median duration of survival could not be reached for the low-risk group and the entire cohort, but it was 22 months for high-risk patients. One-year and 2-year OS rates were 96.7% and 86.9% in the low-risk group; 69.9% and 40.3% in the high-risk group ($p<0.001$), respectively. In multivariate regression analysis, only being >70 years old and HCT-CI >6 were found to be significant with an HR 3.718 and 5.543, respectively.
Discussion: HCT-CI score >6 can aid physicians to decide ASCT in MM patients and predict the overall survival of patients. Since similar survival times can be achieved with current combination therapies (monoclonal antibodies, etc.) in these patients, ASCT may not be considered.

Keywords: ***Multiple Myeloma (MM), Autologous Stem Cell Transplantation (ASCT), Hematopoietic stem cell transplantation - comorbidity index (HCT-CI), survival***

Introduction

High-dose therapy with autologous stem cell transplantation (ASCT) is an effective treatment for patients with Multiple Myeloma (MM) who are eligible for transplantation [1]. Importantly, determination of eligible candidates requires pre-transplant evaluation of comorbidities. Eligibility for transplantation varies depending on the underlying hematologic disease; different countries apply particular transplant eligibility, as well as different transplant centers in the same country. Choosing the appropriate patient for transplantation and anticipating issues that may occur during ASCT is still a paramount problem for patients of all ages; when it can be done, various studies [2,3] have stated that favorable results have been obtained with ASCT even in elderly patients with MM.

The scoring system of the hematopoietic cell transplantation comorbidity index (HCT-CI), developed by Sorror [4] to show early non-relapse mortality (NRM) in patients undergoing allogeneic stem cell transplant, was also used in patients undergoing ASCT and included patients with MM. Although it does not effectively show transplant-related early mortality in MM patients, some studies [5,6] in the past years have shown that it could predict progress-free survival (PFS) and overall survival (OS).

As research conducted in the current treatment era utilizes many new medications, we intended to evaluate the impact of medical comorbidities on the outcome of MM patients undergoing ASCT using the HCT-CI. The primary endpoint of our study is to determine the ideal cut-off value for the HCT-CI score, a value that can be effective in showing overall survival in patients with MM who are treated with ASCT. The secondary endpoints are comparing the patients' characteristics and comorbidities before ASCT, transplant outcomes, and overall survival according to the cut-off value determined by HCT-CI.

Materials & Methods

The files of all MM patients who underwent high-dose melphalan with ASCT between January 2015 and December 2020 were retrospectively scanned and all database collecting was approved by the local ethics committee. All protocols, experimental studies, and clinical trials involving human subjects were approved by the ethics committee of the institution before the study began, and that the protocols conformed to the ethical guidelines of the 1975 Helsinki Declaration.

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Treatments were selected by the hematologist, who made the diagnosis of the patients, according to the current international guidelines (NCCN, ESMO, etc.), labels, and practices. Multiple Myeloma panel tests (serum biochemistry, serum protein electrophoresis, serum plasma, and spot urine immune electrophoresis, serum plasma free light chain kappa/lambda, and 24-hour urine total light chain kappa/lambda), beta-2 microglobulin analysis, and whole-body 18-Fluorodeoxyglucose using positron emission tomography (PET-CT) were performed in the pre-transplant setting in all patients included in the study. ECOG performance scores, ISS stages were recorded before transplantation.

All patients were assigned an HCT-CI score based on the criteria reported by Sorror et al4 before transplantation (**Supplementary Table 1**). If data concerning particular medical comorbidity were not available for an individual, then in all instances it was assumed that no abnormality was present, and the scores were applied accordingly.

Melphalan was administered at doses of 200 mg/m² or 140 mg/m² as a conditioning regimen on day -2 according to the measurements of creatinine clearance (CrCl) and the patients' ages. Left ventricular ejection fractions (EF%) were measured by transthoracic echocardiography and FEV-1, FVC, and PEF25-75 values were measured with spirometry before transplantation. All patients received levofloxacin for bacterial prophylaxis, fluconazole for fungal prophylaxis, and valaciclovir for viral prophylaxis starting from day -2. All these prophylaxes were continued up to +30 days of transplantation. Neutrophil engraftment is defined as the first day of three consecutive days where the neutrophil count (absolute neutrophil count) is 500 cells/mm3 or greater. Platelet engraftment is defined as 20.000/mm3 unsupported by a platelet transfusion.

After discharge, they were followed up in the outpatient clinic once a week during the first month. Afterward, monitoring of complete blood count and biochemical tests (urea, creatinine, ast, alt, ldh, etc.) every 2-3 weeks was employed, depending on their clinical condition. Myeloma panel tests and PET-CT imaging were repeated with all patients at the end of the third month after transplantation. Post-transplant response status was determined by comparing the results obtained on day 100 after transplantation with those obtained prior to transplantation. All patients who survived had at least a 100-day follow-up.

Statistical Method

The X-tile model (Version 3.6.1) was used to determine the cut-off values of the HCT-CI score. Survival curves were plotted using the Kaplan-Meier method, and differences among the individual groups were defined using the log-rank test.

Descriptive statistics, frequency, and percentage were used to summarize the characteristics of the study population. Group comparisons were done using the Mann-Whitney U test, chi-square test, and Fisher exact test. Survival probabilities were calculated by using the Kaplan-Meier estimator, point-wise comparison, and log-rank analysis were used to analyze the survival of different groups. Univariate and multivariate analysis was performed using Cox proportional hazard regression model. Variables analyzed included HCT-CI (>2, and >6), age (>65 years, and >70 years), ECOG, gender, myeloma subgroup, ISS stage, melphalan dose, and biochemical parameters (albumin, LDH, creatinine, B2-microglobulin at the time of transplantation). Univariate Cox regression was done for variable selection at a .05 significance level was used to identify covariates; multivariate Cox regression analysis was performed with all significant covariates. IBM SPSS Version 25 was used for statistical analysis.

Results

Patients Characteristics

Between January 2015 and December 2020, 114 patients who had ASCT in concordance with a diagnosis of MM were included in the study. There was a predominance of males, with 64 patients (56.1%) examined and the median age was 61 years (26-76). Median HCT-CI score was 4 for all patients (0-11). The distribution of patients due to the HCT-CI score is given in Figure 1, and the distribution of comorbidities among patients between the groups was given in table 1. The most common comorbidities were pulmonary disease (44.7%), psychiatric disturbances (41.2%), diabetes/steroid-induced hyperglycemia (31.6%), peptic ulcer (29.8%), and priory infection (22.8%).

X-tile Modelling & Group Comparisons

By using the X-tile model according to the HCT-CI score, patients were divided into 2 categories according to OS: HCT-CI Score ≤6 as low-risk (n:93, 81.6%), HCT-CI score >6 as high-risk (n:21, 18.4%).

According to the new risk score, men were predominantly in the low-risk group (55 patients, 59.1%) and the majority of patients in the high-risk group were female (12 patients, 57.1%). Median ages were 58 (26-76), and 66 (35-72) in the low-risk and high-risk groups, respectively. The number of patients with an ECOG score of zero showed a significant difference between the groups (50 patients (53.8%) in low-risk vs. 2 patients (9.5%) in high-risk groups, p:<0.001). The number of patients with left ventricular ejection fraction (LVEF) above 50% was similar between the groups (89 patients (95.7%) in the low-risk group vs. 19 patients (90.5%) in the high-risk group, respectively), but there were statistically significantly more patients with estimated glomerular filtration rate (eGFR) below 60 ml/min/1.73 m2 in the high-risk group (10 patients, 47.6%) than low-risk group (21 patients, 22.6%) (p:0.020).

Myeloma subgroups, ISS stages of patients, pre-transplant and post-transplant response rates were similar among both groups. Although a decreased tendency was observed without significant statistical difference in stem cell mobilization success with G-CSF in the high-risk group (p: 0.255), in most of the patients it was successfully mobilized with G-CSF: 84 patients (90.3%) in the low-risk group, and 17 patients (81%) in the high-risk group, respectively. As expected, melphalan dose reduction was performed more frequently in the high-risk group (10 patients in the high-risk group (47.6%), and 24 patients in the low-risk group (25.8%), p: 0.048) (**Table 2**).

With regard to the post-transplant complications presenting on the 100th-day after the transplantation, death due to septic shock was observed in one patient from each risk group, while death due to cardiorenal toxicity was observed in one patient in the high-risk group. Renal toxicity and hepatobiliary toxicities were more frequent in high-risk patients (p:0.020, HR: 3.72, 95% CI: 1.236 - 11.244), but cardiac toxicity, pulmonary toxicity, bleeding, and deep vein thrombosis were comparable between groups (**Table 3**). The median time for neutrophil and platelet engraftments were also similar. For neutrophil engraftment, 11 days in the low-risk group and 11.5 days in the high-risk group, respectively. For platelet engraftment, 12 days in the low-risk group and 13.5 days in the high-risk group, respectively. The requirement for red blood cell (RBC) and platelet transfusion was higher in the high-risk group (2 vs. 3 in RBC transfusion, 3 vs. 5 in platelet transfusion, p:0.001 and p:0.003, respectively). Median length of stay in hospital was 21 days in the high-risk group and 18 days in the low-risk group (p:0.021).

Survival Analysis

Median follow-up of patients was 21 months (0-79). The median duration of survival could not be reached for the low-risk group and the entire cohort, but it was 22 months for high-risk patients. One-year and 2-year OS rates were 96.7% and 86.9% in the low-risk group; 69.9% and 40.3% in the high-risk group (p<0.001), respectively (**Figure 2**).

In univariate cox-regression analysis, being >70 years old, HCT-CI >6, ECOG >0, reduced melphalan dose, and creatinine levels of patients before ASCT were found to be significant in terms of increased OS. In multivariate regression analysis, only being >70 years old and HCT-CI >6 were found to be significant with an HR 3.718 (p: 0.011, 95% CI: 1.344 – 10.291) and 5.543 (p: 0.001, 95% CI: 2,072 – 14,833), respectively (**Supplementary Table 2**).

In univariate cox-regression analysis, HCT-CI score > 2 was also found to be significant in terms of OS with an HR 3.457 (p:0.023, 95% CI: 1.19 – 10.043) when compared with HCT-CI ≤2. Considering this information, patients were divided into 3 risk groups for OS according to their HCT-CI scores: 0-2 (Very low-risk), 3-6 (low risk), and >6 (high-risk). The median OS of patients was 58 months in low-risk patients, and 22 months in high-risk patients; while it could not be reached in the very low-risk group. One-year and 2-year OS of patients were 100% and 89.9% in the very low-risk group; 94.2% and 84.6% in the low-risk group; 69.9% and 40.3% in the high-risk group (**Figure 3**). While HCT-CI score between 2-6 appeared to be associated with worse OS compared to HCT-CI 0-1 score, but it did not reach statistical significance (p: 0.182, HR: 2.18, 95% CI: 0.694 – 6.849) in cox-regression analysis. HCT-CI Score >6 had a statistically significantly worse OS compared to both HCT-CI scores of 0-2 and 3-6 (with an HR 8.7, p:<0.001, 95% CI 2.74 – 27.6; HR 4, p:0.001, (95% CI 1.7 – 9.34).

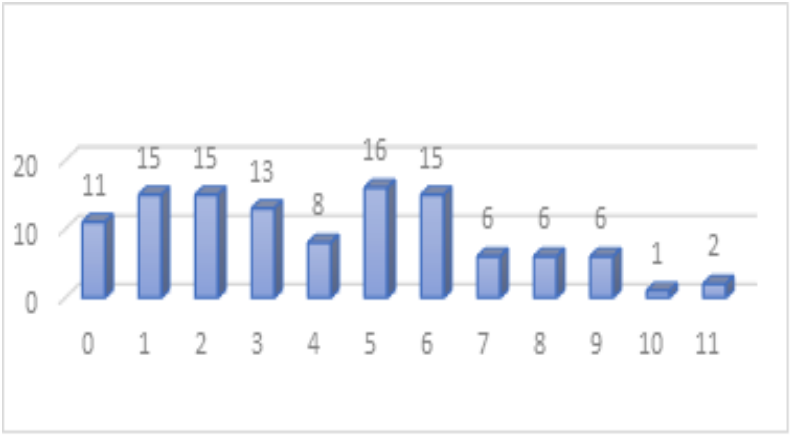

Figure 1: Distribution of Patients due to HCT-CI Score

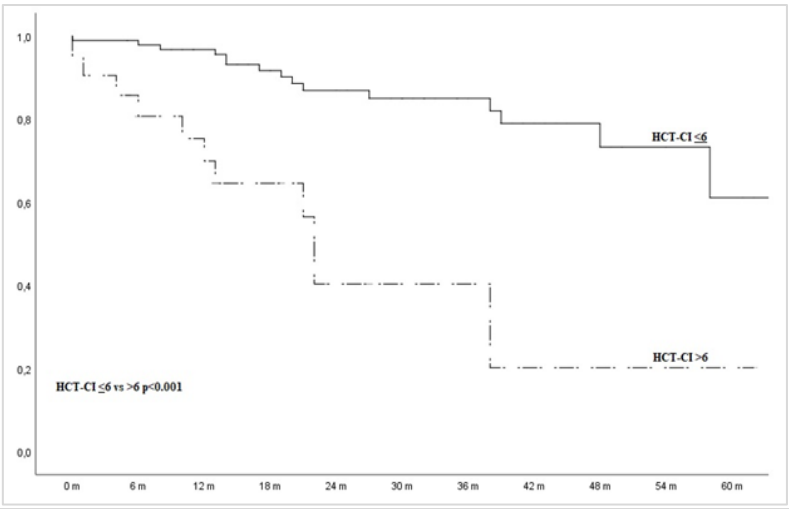

Figure 2: OS according to risk groups calculated from HCT-CI score (low risk vs. high-risk)

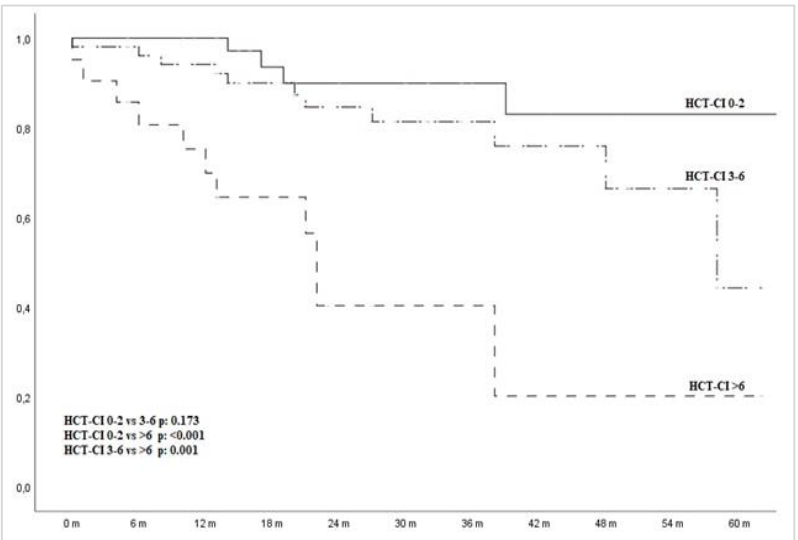

Figure 3: OS according to 3 risk groups calculated from HCT-CI score (very low-risk vs. low-risk vs. high-risk)

Table 1: Distribution of comorbidities among patients between the groups

	All Patients	HCTCI ≤6	HCT-CI >6	p
Psychiatric Disturbance	47 (41.2%)	33 (35.5%)	14 (66.7%)	**0,009**
Peptic Ulcer	34 (29.8%)	21 (22.6%)	13 (61.9%)	**0,000**
Heart Valve Disease	21 (18.4%)	12 (12.9%)	9 (42.9%)	**0,003**
Pulmonary Disease	51 (44.7%)	34 (36.6%)	17 (81%)	**0.000**
Diabetes / Steroid induced hyperglysemia	36 (31.6%)	24 (25.8%)	12 (57.1%)	**0,005**
Infection	26 (22.8%)	19 (20.4%)	7 (33.3%)	0,250
Renal Disease	9 (7.9%)	3 (3.2%)	6 (28.6%)	**0,001**
Cardiac Disease	17 (14.9%)	12 (12.9%)	5 (23.8%)	0,305
Arrhytmia	5 (4.4%)	1 (1.1%)	4 (19%)	**0,004**
Hepatic Disease	21 (18.4%)	17 (18.3%)	4 (19%)	1,000
Prior Solid Tumor	9 (7.9%)	4 (4.3%)	5 (23.8%)	**0,010**
Inflammatory Bowel Disease	0 (0%)	0 (0%)	0 (0%)	
Cerebrovascular Disease	1 (0.9%)	1 (1.1%)	0 (0%)	1,000
Obesity	10 (8.8%)	5 (5.4%)	5 (23.8%)	**0,018**
Rheumatologic Disease	2 (1.8%)	1 (1.1%)	1 (4.8%)	0,336

Table 2: Patients & Disease & Treatment characteristics between groups

	All Patients	HCTCI ≤6	HCT-CI >6	p
HCT-CI	4 (0-11)	3 (0-6)	8 (7-11)	**0,000**
Male (n,%)	64 (56.1%)	55 (59.1%)	9 (42.9%)	0,174
Age (years, range)	61 (26-76)	58 (26-76)	66 (35-72)	0,410
18-39	8 (7%)	7 (7.5%)	1 (4.8%)	0,395
40-49	15 (13.2%)	14 (15.1%)	1 (4.8%)	
50-59	34 (29.8%)	28 (30.1%)	6 (28.6%)	
60-65	9 (7.9%)	7 (7.5%)	2 (9.5%)	
66-69	25 (12.9%)	17 (18.3%)	8 (38.1%)	
70-80	23 (20.2%)	20 (12.5%)	3 (14.3%)	
ISS				
Stage I	54 (47.4%)	48 (51.6%)	6 (28.6%)	0,080
Stage II	25 (21.9%)	17 (18.3%)	8 (38.1%)	
Stage III	35 (30.7%)	28 (30.1%)	7 (33.3%)	
Myeloma Subgroups				
IgG	76 (67.9%)	63 (68.5%)	13 (65%)	0,460
IgA	22 (19.6%)	18 (19.6%)	4 (20%)	
Light Chain	9 (8%)	6 (6.5%)	3 (15%)	
Other	5 (4.5%)	5 (5.4%)	-	
Lines of Chemotherapy	1 (1-5)	1 (1-3)	1 (1-5)	0,973
Response Before Transplant				
CR	17 (14.9%)	15 (16.1%)	2 (9.5%)	0,634
VGPR	64 (56.1%)	53 (57%)	11 (52.4%)	
PR	32 (28.1%)	24 (25.8%)	8 (38.1%)	
SD	1 (0.9%)	1(1.1%)	-	
ECOG				
0	52 (45.6%)	50 (53.8%)	2 (9.5%)	**0,000**
≥1	62 (54.4%)	43 (46.2%)	19 (90.5%)	
LVEF				
≥%50	108 (94.7%)	89 (95.7%)	19 (90.5%)	0,305
<%50	6 (5.3%)	4 (4.3%)	2 (9.5%)	
eGFR				
≥60 ml/dk	83 (72.8%)	72 (77.4%)	11 (52.4%)	**0,020**
< 60 ml/dk	31 (27.2%)	21 (22.6%)	10 (47.6%)	
Stem Cell Mobilization				
G-CSF	101 (88.6%)	84 (90.3%)	17 (81%)	0,077
Cyclo & G-CSF	9 (7.9%)	5 (5.4%)	4 (19%)	
Plerixafor & G-CSF	4 (3.5%)	4 (4.3%)	-	
Melphalan Dose				
<200 mg/m2	34 (29.8%)	24 (25.8%)	10 (47.6%)	0,048
200 mg/m2	80 (70.2%)	69 (74.2%)	11 (52.4%)	
Hospital Stay	18 (13-64)	18 (13-36)	21 (14-64)	**0,021**

Table 3: Outcomes of patients after ASCT

	All Patients	HCTCI ≤6	HCT-CI >6	p
TRM	3 (2.6%)	1 (1.1%)	2 (9.5%)	0,087
Febrile Neutropenia	61 (53.5%)	47 (50.5%)	14 (66.7%)	0,181
Renal Toxicity	18 (15.8%)	11 (11.8%)	7 (33.3%)	**0,023**
Cardiac Toxicity	7 (6.1%)	5 (5.4%)	2 (9.5%)	0,611
Pulmonary Toxicity	1 (0.9%)	1 (1.1%)	0	1,000
Hepatobiliary Toxicity	25 (21.9%)	16 (17.2%)	9 (42.9%)	**0,018**
Bleeding	11 (9.6%)	7 (7.5%)	4 (19%)	0,117
Deep Vein Trombosis	7 (6.7%)	5 (5.9%)	2 (10.5%)	0,609
Hospital Stay	18 (13-64)	18 (13-36)	21 (14-64)	**0,021**
Neutrophil Engraftment	11 (5-25)	11 (10-25)	11.5 (5-22)	0,323
Platelet Engraftment	12 (9-32)	12 (9-27)	13.5 (9-32)	0,542
RBC Transfusion	2 (0-19)	2 (0-8)	3 (0-19)	**0,001**
Platelet Transfusion	3 (1-35)	3 (1-13)	5 (1-35)	**0,003**
Response After Transplant				
CR	37 (33.9%)	32 (35.2%)	5 (27.8%)	0,186
VGPR	67 (61.5%)	55 (60.4%)	12 (66.7%)	
PR	2 (1.8%)	2 (2.2%)	-	
SD	3 (2.7%)	2 (2.2%)	1 (5.6%)	

Discussion

ASCT is a safe and effective treatment with durable outcomes in appropriately selected patients. We used HCT-CI score, which is normally used to show early mortality in allogeneic stem cell transplantation, to demonstrate the effects of comorbidities on overall survival in patients with MM undergoing ASCT. As expected, comorbidities were numerous in patients with the high-risk disease according to HCT-CI; myeloma subgroups, disease stage, and pre-transplant and post-transplant response rates were similar between groups. Renal and hepatobiliary toxicities after ASCT were seen more frequently, and also the need for platelet and red blood cell transfusions were performed more in high-risk patients.

Age >70 years old, and HCT-CI >6 had a significant effect on OS. Also, when compared as 3 groups according to risk score (very low risk, low risk, and high-risk), OS was significantly shorter in high-risk patients. While there was a tendency for short OS in low-risk patients compared with very low-risk patients, this difference was not statistically significant.

The largest study showing the effects of HCT-CI score on OS in 1154 MM patients was conducted by Saad et al. in 2014 [5] They reported that in univariate analysis, the patients with HCT-CI score 1 to 2 had a worse OS with an HR 1.37, and HCT-CI > 2 with an HR 1.5 when compared with an HCT-CI score of 0. In multivariate analysis, HCT-CI score >0 had an HR 1.33 (p:0.04) when compared with HCT-CI score 0. In another study, Jaglowski et al.[7] reported that there was no statistical difference between groups with HCT-CI scores <3 vs ≥3 (p:0.92). Obiozor et al.[8] also reported that HCT-CI score >2 also appeared to be associated with worse OS compared with HCT-CI 0-1, but the difference did not reach statistical significance (HR 1.311, 95% CI: 0.72 to 2.76), similar to patients with HCT-CI score between 2-6 in our study. We found that all patients with an HCT-CI >2 had a worse OS with an HR 3.45 than patients with a score ≤2; however, this difference was mostly due to the patients with HCT-CI >6, not from those with an HCT-CI between 3-6 (with an HR 8.7 compared to an HCT-CI score 0-2 p<0.001, and HR 4 compared to HCT-CI score 3-6 p:0.001).

In our study, we reported that the 2-year OS of patients with HCT-CI score 0-2 was 89.9%. In Saad's study [5], it was 89%, and only in patients with an HCT-CI score 0. In patients with an HCT-CI score 1-2, it was 84%. We reported that patients with higher HCT-CI scores (between 3-6) had a 2-year OS 84.6%. HCT-CI score did not influence OS in patients age >65 years at the time of transplant in Saad's study [5], but HCT-CI score >6 influence OS in all age groups in our study (data not shown). When comparing the comorbidities of patients between two studies, it was observed that pulmonary dysfunction (44.7% vs 22.6%), psychiatric disturbances (41.2% vs. 12.2%), diabetes/steroid-induced hyperglycemia (31.6% vs 13.7%), peptic ulcus (29.8% vs 2.5%), and all other comorbidities were higher in our study. In both studies, melphalan dose was reduced similarly in about 26-28% of patients, especially with high HCT-CI scores. Although HCT-CI scores were higher, and comorbidities were more frequent; in our study, the overall survival in patients with HCT-CI score ≤6 was similar to patients with an HCT-CI score between 0-2 in Saad's study. It was speculated to be due to the fact that OS has improved significantly in patients with Multiple Myeloma. This is driven by better biological insights into the disease, implementation of more sensitive tests and technologies leading to earlier detection of relapse disease, access to better combination therapies, and increased access to supportive care measures [6]. So now, high-risk patients could be defined as patients with HCT-CI score >6.

In Saad's study [5], there was no difference in OS among patients who received reduced melphalan dose. In our study, reduced melphalan was associated with worse outcomes in univariate cox-regression analysis, but not in multivariate analysis. TRM was similar in both studies (1-2%). Saad also reports that age >65 years did not influence OS as similar with our study, although we found that age >70 years influence OS with an HR 3.7. For myeloma subgroups, although IgA myeloma is traditionally associated with poorer outcomes, it was not shown to influence OS in both studies.

Not only overall survival was short, but also treatment-related toxicities were more common in high-risk patients. Labonte and colleagues in their study [9] report that patients with HCT-CI score ≥1 had severe organ toxicity 2.5 times higher than patients with HCT-CI score 0. Also, parallel with our study, high-risk patients had more pulmonary and hepatotoxicity comparing with the low-risk patients (with an HR 3.7).

The median time to neutrophil and platelet engraftment were 11 days (5-25) and 12 days (9-32) in all patients and were similar to other studies [2,3,9,10]. Joseph et al.[10] reported that median red blood cell (RBC) transfusion in MM patients was 2 units comparable with our study, but median platelet transfusion was 1 unit, lower than our study (median 3 units). This difference was due to the difference in bleeding complications between the two studies (3% and 9.6%, respectively).

Waszczuk-Gajda in her study [11] reported about the infection complications in 1374 patients with MM that 336 of 1374 patients (24.4%) had infection episodes during ASCT, but Gil et

al.[12] reported that 56 of 64 patients with MM had infection complications during neutropenia after ASCT. Febrile neutropenia was observed in 53.5% of our patients, with a tendency to occur more frequently in high-risk patients. Different rates of febrile neutropenia in these studies and our study may be related to the different comorbidity rates of the patients in these studies.

The median length of hospital stay was higher in high-risk patients than in low-risk patients in our study (21 days vs. 18 days). Labonte [9] also reported that patients with high HCT-CI scores had 5.34 times higher risk for prolonged length of inpatient care beyond 18 days, similar to our study. Joseph et al.[10] also report a median of 16 days of inpatient hospital care, similar to our low-risk patients.

Limitations

The retrospective design of the study is by itself a limitation. Our study included patients treated over the past decade with heterogenous induction regimens (vincristine-doxorubicin-dexamethasone, bortezomib-cyclophosphamide-dexamethasone, bortezomib-thalidomide-dexamethasone, etc.) and variable use of maintenance therapy, thereby affecting the overall survival homogeneity. Since the genetic makeup of most of our patients was unknown, including genetic analyzes in our study was not possible. We could also not make any comments about the progress-free survival for most of the patients due to the lack of information beyond 100 days post-transplant.

Conclusion

Successful results in studies conducted with both the elderly and patients with comorbidities showed that ASCT can be a treatment option for people of all ages with MM, as long as an accurate patient selection can be done. HCT-CI score >6 can aid physicians in making this tough decision and predict both the overall survival of patients and treatment-related toxicity incidence. Since similar survival times can be achieved with current combination therapies (monoclonal antibodies, etc.) in these patients, ASCT may not be considered. Randomized controlled studies are needed on this subject. Also, there is still a need to develop a scoring system that can be easily performed and can be more effective in showing morbidity and mortality in MM patients.

Declarations of interest

None

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