Biol Blood Marrow Transplant 23 (2017) 1641–1645

Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

Evaluation of Performance Status and Hematopoietic Cell Transplantation Specific Comorbidity Index on Unplanned Admission Rates in Patients with Multiple Myeloma Undergoing Outpatient Autologous Stem Cell Transplantation

Cynthia Obiozor [1], Dipti P. Subramaniam [2], Clint Divine [1], Leyla Shune [1], Anurag K. Singh [1], Tara L. Lin [1], Sunil Abhyankar [1], G. John Chen [2], Joseph McGuirk [1], Siddhartha Ganguly [1,*]

[1] *Division of Hematologic Malignancy and Cellular Therapeutics, University of Kansas Medical Center, Kansas City, Kansas*
[2] *Division of Health Services Research, Office of Scholarly, Academic, and Research Mentoring, University of Kansas Medical Center, Kansas City, Kansas*

Article history:
Received 27 March 2017
Accepted 2 June 2017

Key Words:
Multiple myeloma
Autologous stem cell transplantation
Outpatient transplantation
Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI)

A B S T R A C T

Although outpatient autologous stem cell transplantation (ASCT) is safe and feasible in most instances, some patients undergoing planned outpatient transplantation for multiple myeloma (MM) will need inpatient admission for transplantation-related complications. We aim to evaluate the difference, if any, between outpatient and inpatient ASCT cohorts of MM patients in terms of admission rate, transplantation outcome, and overall survival. We also plan to assess whether the Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI) and Karnofsky Performance Status (KPS) can predict unplanned admissions after adjusting for confounding factors. Patients with MM (n = 448) who underwent transplantation at our institution between 2009 and 2014 were included in this retrospective analysis. Patients were grouped into 3 cohorts: cohort A, planned inpatient ASCT (n = 216); cohort B, unplanned inpatient admissions (n = 57); and cohort C, planned outpatient SCT (n = 175). The statistical approach included descriptive, bivariate, and survival analyses. There were no differences among the 3 cohorts in terms of type of myeloma, stage at diagnosis, time from diagnosis to transplantation, CD34 cell dose, engraftment kinetics, and 100-day response rates. Serum creatinine was higher and patients were relatively older in both the planned inpatient (median age, 62 years; range, 33 to 80 years) and unplanned (median age, 59 years; range, 44 to 69 years) admission cohorts compared with the outpatient-only cohort (median age, 57 years; range, 40 to 70 years) ($P < .05$). Performance status (cohort A: median, 90%; range, 60% to 100%; cohort B: 80%, 50% to 100%; cohort C: 80%, 60% to 100%) was lower ($P < .05$) and HCT-CI score (cohort A: median, 1.78; range, 0 to 8; cohort B: 2.67, 0 to 9; cohort C: 2.16, 0 to 7) was higher ($P < .004$) in both inpatient groups compared with the planned outpatient cohort. With a median follow up of 5 years, poor performance status (KPS <70%) appeared to be associated with worse survival ($P < .002$). HCT-CI >2 also appeared to be associated with worse outcomes compared with HCT-CI 0 to 1, the the difference did not reach statistical significance (hazard ratio, 1.41l 95% confidence interval, 0.72 to 2.76). Only 1 patient out of 448 died from a transplantation-related cause. Outpatient transplantation for myeloma is safe and feasible. In our experience, one-third of the patients undergoing outpatient transplantation needed to be admitted for transplantation-related toxicities. Patients in this group had lower preexisting KPS and higher HCT-CI scores. Whether planned admission for this group would have prevented unplanned admissions and undue stress on patients and the healthcare system should be tested in a prospective manner.

INTRODUCTION

Even in this era of novel therapies, autologous stem cell transplantation (ASCT) improves progression-free survival for eligible patients with newly diagnosed multiple myeloma (MM) [1]. Customarily, ASCT for patients with MM had been performed in the inpatient setting, owing to safety concerns. Several studies now have shown that outpatient transplantation is safe, cost-effective, and feasible [2,3]. Ideal candidates for outpatient ASCT are patients with good

Financial disclosure: See Acknowledgments on page 1644.

* Correspondence and reprint requests: Siddhartha Ganguly, MD, FACP, Division of Hematologic Malignancies and Cellular Therapeutics, University of Kansas Health Systems, 2330 Shawnee Mission Parkway, Suite 210, Westwood, KS 66205.
E-mail address: sganguly@kumc.edu (S. Ganguly).

http://dx.doi.org/10.1016/j.bbmt.2017.06.001
1083-8791/

performance status, few or no comorbidities, and a good social support system. As it stands, there is no general consensus regarding the eligibility criteria for outpatient versus inpatient ASCT. Historically, physicians' clinical judgment is used to allocate patients who are eligible for transplantation and identify those appropriate for outpatient versus inpatient ASCT.

The Hematopoietic Cell Transplantation Comorbidity Index (HCT-CI) designed by Sorror et al. [4] is an index encompassing 17 different categories of pretransplantation comorbidities. The HCT-CI score provides information with regard to assessment of graft-versus-host disease, nonrelapse mortality (NRM), and survival risks that a patient is likely to face after allogeneic hematopoietic cell transplantation (HCT). Although the HCT-CI is most appropriate in the allogeneic setting [5], Saad et al. [6] tested the utility of HCT-CI as a predictor of NRM and survival in patients with MM undergoing ASCT. In that study, outcomes of 1156 patients from the database of Center for International Blood and Marrow Transplant Research (CIBMTR) were analyzed retrospectively. Although a higher HCT-CI score was not predictive of NRM, it was associated with inferior survival ($P < .05$).

Many centers have established a multidisciplinary team approach to manage outpatient ASCT for patients with MM. Planned inpatient transplantation is typically reserved for older patients, patients with a poor KPS score, and patients with associated comorbidities. Although outpatient ASCT is feasible and safe in most instances, some patients will still require unplanned inpatient admission for transplantation-related toxicities. Identifying at-risk patients beforehand may help avoid unplanned admissions.

The primary objective of this study was to examine whether in patients with MM, those with a low KPS score and a high HCT-CI score have higher rates of unplanned admissions and regimen-related toxicities compared with fit patients. The secondary objective was to evaluate the difference between outpatient and inpatient ASCT in patients with MM in terms of transplantation characteristics and health outcomes.

MATERIALS AND METHODS

This study is a retrospective chart review design of patients with MM who underwent ASCT at the University of Kansas Medical Center between 2009 and 2014. Patients were grouped into 3 cohorts: cohort A, planned inpatient ASCT; cohort B, unplanned inpatient admission post-ASCT; and cohort C, planned outpatient ASCT.

Most of our patients who undergo outpatient ASCT and come from out of town stay at the American Cancer Society–provided Hope Lodge throughout the duration of the transplantation procedure until count recovery. Patients undergoing outpatient ASCT present daily to the outpatient clinic/infusion center, which is open daily, including weekends and major holidays. In our main medical center, the Cancer Treatment Outpatient (CTO) unit accepts patients after hours and overnight for short-term evaluation for symptoms or issues that cannot be resolved over the telephone. The CTO is monitored by nursing staff with supervision from physicians. In most circumstances, patients are encouraged to bypass emergency department visits.

In terms of the statistical approach, a descriptive analysis was performed to ascertain mean/median and standard deviation/range for continuous variables and proportions and frequencies for categorical variables. Next, comparisons among the cohorts were determined, using the chi-square test and analysis of variance to evaluate the differences. Then Cox regression analysis was performed to determine the difference in survival times between cohorts based on the HCT-CI. Kaplan-Meier analysis was used to identify differences in survival estimates between cohorts, based on their performance status. A P value < .05 was considered to indicate statistical significance. Statistical analyses were done using SPSS version 23.0 (IBM, Armonk, NY).

RESULTS

A total of 448 patients with MM underwent ASCT at the University of Kansas Medical Center between 2009 and 2014. These patients were grouped into 3 cohorts for analysis: cohort A (planned inpatient ASCT), with a total of 216 patients; cohort B (unplanned inpatient admission post-ASCT), with 57 patients; and cohort C (planned outpatient ASCT), with 175 patients.

Our findings demonstrate that serum creatinine was higher and patients were relatively older in cohort A compared with cohort C (median age, 62 years [range, 33 to 80 years] versus 57 years [range, 40 to 70 years]; $P < .05$] (Table 1). Performance status was lower (cohort A: median, 90%; range, 60% to 100%; cohort B: 80%, 50% to 100%; cohort C: 80%, 60% to 100%) ($P < .05$) and HCT-CI score was higher (cohort A: median, 1.78; range, 0 to 8; cohort B: 2.67, 0 to 9; cohort C: 2.16, 0 to 7) ($P < .004$) in both inpatient cohorts compared with the planned outpatient-only cohort (Table 1). A higher dose of melphalan (200 mg/m^2 versus 140 mg/m^2) was used more often in cohort C compared with cohort A (Table 2).

Reasons for planned inpatient transplantation were primarily older age (≥70 years; 20%), high serum creatinine level (23%), psychosocial issues (16%), and associated comorbidities (41%) (Table 3).

One-third of patients undergoing outpatient transplantation required admission for transplantation-related toxicities. Neutropenic fever (20%) and gastrointestinal (GI) toxicity (17%) were the 2 most common reasons for unplanned admissions (Table 4). The most frequent day for unplanned admission was day +7 after stem cell infusion, and the average length of stay was 7 days (range, 1 to 18 days). The most frequent reasons for a length of stay exceeding the median were intravenous antibiotic administration and ongoing failure to thrive. Approximately 30% of patients in the inpatient cohorts and 59% of those in the outpatient cohort (via the clinic or CTO) received intravenous antibiotics for neutropenic fever.

Almost all patients in each cohort required platelet transfusion (median, 2 transfusions; range, 0 to 9). The platelet transfusion threshold was <10,000/μL. Red cell transfusion was less frequent (median, 0; range, 0 to 6). The red cell transfusion threshold was hemoglobin <7 g/dL.

There was no difference among the 3 cohorts in terms of type of myeloma (IgG versus non-IgG or light chain), stage at diagnosis, disease status at 100 days post-transplantation, time from diagnosis to first transplantations, CD34 cell infused dose, or time to engraftment (granulocyte and platelet). With a median follow-up of 5 years, an HCT-CI >2 appeared to be associated with worse survival compared with an HCT-CI of 0 to 1, but the difference did not reach statistical significance (hazard ratio, 1.41; 95% confidence interval, 0.72 to 2.76] (Figure 1), indicating that HCT-CI had no significant effect on survival in this study cohort. On the other hand, poor performance status (KPS <70%; $P = .002$) appears to be associated with lower survival (Figure 2).

DISCUSSION

At the time of our analysis, the median duration of follow-up was >5 years. Our results show that one-third of the patients undergoing outpatient transplantation required admission for transplantation-related toxicities. Of the 448 eligible charts reviewed, only 1 cardiac related death was reported in the planned inpatient cohort, proving that outpatient transplantation is safe and feasible.

Based on institutional policy, planned inpatient admission and lower dosage of melphalan (140 mg/m^2) were normally used for patients age >70 years and patients with a serum creatinine concentration >2.0 mg/dL [7]. Creatinine value measured at the time of evaluation for transplantation and consent was used to adjust melphalan dosing. Thus,