Biol Blood Marrow Transplant 25 (2019) e33–e38

Biology of Blood and Marrow Transplantation

journal homepage: www.bbmt.org

Impact of Obesity on Clinical Outcomes of Elderly Patients Undergoing Allogeneic Hematopoietic Cell Transplantation for Myeloid Malignancies

Ensi Voshtina[1], Aniko Szabo[2], Mehdi Hamadani[3,4], Timothy S. Fenske[3], Anita D'Souza[3,4], Saurabh Chhabra[3], Wael Saber[3,4], William R. Drobyski[3], Parameswaran Hari[3,4], Nirav N. Shah[3,*]

[1] *Department of Medicine, Medical College of Wisconsin, Milwaukee, Wisconsin*
[2] *Division of Biostatistics, Medical College of Wisconsin, Milwaukee, Wisconsin*
[3] *Division of Hematology and Oncology, Medical College of Wisconsin, Milwaukee Wisconsin*
[4] *Center for International Bone Marrow Transplant Research, Milwaukee Wisconsin*

Article history:
Received 14 July 2018
Accepted 29 August 2018

Key Words:
Allogeneic transplantation
Myeloid malignancy
Obesity

A B S T R A C T

Allogeneic hematopoietic cell transplantation (allo-HCT) is a high-risk treatment option for patients with hematologic malignancies. Advanced age and obesity can impact outcomes after allo-HCT. Previous registry studies of all age groups found that obesity does not affect outcomes. However, obesity can accelerate age-related decline in physical function and exacerbate comorbid conditions in older patients. Studies evaluating the effect of obesity on elderly patients undergoing allo-HCT are lacking. We performed a retrospective analysis of 86 nonobese (body mass index [BMI] <30) and obese (BMI ≥ 30) patients age ≥ 60 years who underwent allo-HCT for myeloid malignancies between January 2010 and June 2015. We found no significant between-group differences in mean age, sex, comorbid conditions, cytogenetic risk, disease indication for transplantation, or donor type. The median overall survival (OS) was 36 months for the BMI <30 group and 24 months for the BMI ≥ 30 group ($P = .55$). The median progression-free survival (PFS) was 10.1 months in the BMI <30 group and 13.6 months in the BMI ≥ 30 group ($P = .93$). There were no significant between-group differences in acute graft-versus-host disease (GVHD) and cumulative incidence of chronic GVHD at 1 year post-transplantation. Among patients admitted for transplantation, the mean length of stay was 25 days in the BMI <30 group and 26 days in the BMI ≥ 30 group ($P = .64$). The rate of readmission within 30 days of discharge was significantly higher in the BMI ≥ 30 group (34% versus 16%; $P = .045$). Our data reveal that in these elderly patients with myeloid malignancies undergoing allo-HCT, clinical outcomes, including OS, PFS, and GVHD, were not affected by obesity. Thus, in elderly patients, obesity should not preclude consideration for curative allo-HCT and does not portend worse outcomes after allo-HCT.

INTRODUCTION

Myeloid malignancies, such as acute myelogenous leukemia (AML) and myelodysplastic syndrome (MDS), are potentially life-threatening diseases of the elderly, occurring mostly in the seventh to eighth decades of life [1,2]. The general approach to treatment is a form of induction chemotherapy followed by consideration of allogeneic hematopoietic cell transplantation (allo-HCT) as consolidation therapy in selected patients considered to have high-risk disease and to be fit for transplantation. Historically, allo-HCT was reserved for young patients with an acceptable performance status, but with the adoption of reduced-intensity and nonmyeloablative conditioning regimens, along with improved supportive care measures, the application of this procedure has been extended to older patients with more comorbid conditions [3]. Several large studies have demonstrated the long-term efficacy and safety of allo-HCT in older patients while suggesting that age is not an independent risk factor for survival post-transplantation [4-8].

One comorbidity given particularly close consideration before allo-HCT is obesity. Obesity is defined in several ways, but one commonly accepted definition is body mass index (BMI) ≥ 30 kg/m^2 [9]. It is often associated with other comorbid conditions, such as cardiovascular diseases and diabetes, and has been associated with increased mortality [10-13]. Approximately 40% of patients age 65 to 74 years in the United States are classified as obese according to the Centers for Disease Control and Prevention criteria; thus, obesity is often encountered during the allo-HCT evaluation [14]. Obesity can disproportionally affect older patients as it exacerbates the age-related decline in physical

Financial disclosure: See Acknowledgments on page e37.
* Correspondence and reprint requests: Nirav N. Shah, 9200 W Wisconsin Avenue, Milwaukee, WI 53226.
E-mail address: nishah@mcw.edu (N.N. Shah).

https://doi.org/10.1016/j.bbmt.2018.08.031
1083-8791/

function and is an important cause of disability in older adults [15]. Obesity also impacts the development of malignancy. A US population-based study using BMI and cancer incidence data estimated that in 2012, 28,128 new cancer cases in males and 72,266 cases in females were attributable to excess BMI [16]. There is sufficient evidence to suggest associations between higher BMI and an increased risk of various specific cancers, including gastrointestinal malignancies, breast cancer, and multiple myeloma [17]; however, the association between elevated BMI and reported poorer prognosis after cancer diagnosis and treatment has been consistent only in patients with breast cancer [18−20].

In the context of allo-HCT, obesity and its associated conditions can be a barrier to a successful procedure. A validated risk assessment tool, the HCT-specific comorbidity index (HCT-CI) [21], is commonly used to predict the outcome of allo-HCT in terms of risk of death from transplantation complications (nonrelapse mortality [NRM]). Sorror et al [21] found that obesity (which they defined as BMI >35) had a high predictive hazard ratio (HR) for 2-year NRM. Under this system, BMI >35 accounts for a comorbidity with a weighted score of 1 and is considered a marker of worse survival. However, the impact of obesity on outcomes after allo-HCT for hematologic malignancies remains unclear, and other studies have found no correlation with worse survival [22,23]. In the present study, we aimed to evaluate the effect of obesity on outcomes in older patients (age ≥60 years) undergoing allo-HCT for myeloid malignancies and compare these patients' outcomes with those of nonobese counterparts of the same age group.

METHODS

Study Design

We performed a retrospective, single-center analysis using our institutional database for allo-HCT from the Blood and Marrow Transplant Program at the Medical College of Wisconsin. The study was approved by the Institutional Review Board of Froedtert and the Medical College of Wisconsin.

Patient Population

The patient population consisted of adult patients with myeloid malignancies (AML, MDS, or MPN), age ≥60 years, who underwent unrelated or related donor allo-HCT between January 2010 and June 2015.

Data Sources and Data Elements

Our data were abstracted from inpatient and outpatient electronic medical record. Demographic data collected included age at transplantation, sex, weight and BMI at day of admission, disease indication for allo-HCT, type of graft donor (sibling or unrelated donor), HLA matching, and outpatient versus inpatient transplant. Comorbid conditions, such as history of diabetes mellitus (DM), hypertension (HTN), cerebrovascular accident (CVA), chronic kidney disease (CKD), and coronary artery disease (CAD), were abstracted from the patient's problem list. Pretransplantation disease status was based on the bone marrow biopsy percentage of blasts measured immediately before allo-HCT. The type of conditioning was identified as either myeloablative (MAC) or reduced intensity (RIC) based on consensus criteria [24]. Chemotherapy dosing followed standard protocol at our institution, which is based on adjusted body weight (actual body weight plus a 40% difference between actual and ideal body weight) for agents other than fludarabine, which is always dosed based on actual body weight. Laboratory values measured at allo-HCT included WBC, hemoglobin, and platelet count. For patients with AML, cytogenetic risk stratification at diagnosis was calculated on modified European Leukemia Net recommendations [25]. For patients with MDS, risk stratification was done according to the Revised International Prognostic Scoring System score at diagnosis [26]. For all patients, HCT-CI scores including and excluding obesity were calculated [21], and a Karnofsky Performance Status (KPS) score was obtained from chart review. The KPS is a standard measurement of cancer patients' ability to perform ordinary tasks and is scored from 0 to 100 [27]. Acute graft-versus-host disease (aGVHD) was defined as GVHD occurring at <100 days after allo-HCT; chronic GVHD (cGVHD), as GVHD occurring at ≥100 days.

Statistical Analysis

Patients were stratified by BMI ≥30 or <30. Descriptive statistics were used to measure baseline characteristics, for which comparative analyses were done using 2 and Fisher's exact tests. The Kaplan-Meier method was used to calculate overall survival (OS) and progression-free survival (PFS), which were estimated from the date of allo-HCT to death, progression, or last follow-up. The log-rank test was used to compare OS and PFS between the BMI ≥30 and BMI <30 groups. Univariate and multivariate analyses were performed to determine the effect of patient-level variables on OS using a

Table 1
Patient Characteristics

Characteristic	BMI <30 kg/m^2(N = 45; 52%)	BMI ≥30 kg/m^2(N = 41; 48%)	*P* Value
Baseline characteristics			
Age at HCT, yr, mean	66	64	.10
Male sex, n (%)	26 (58)	23 (56)	.88
Weight, kg, mean	76	101	<**.01**
KPS ≥90, n (%)	25 (56)	27 (66)	.33
HCT-CI score ≥3, n (%)			
Including obesity	13 (29)	30 (73)	<**.01**
Excluding obesity	13 (29)	25 (61)	<**.01**
DM, n (%)	15 (33)	18 (44)	.31
HTN, n (%)	24 (53)	25 (61)	.48
History of CVA, n (%)	2 (4)	0	.17
History of CKD, n (%)	5 (11)	1 (2)	.12
History of CAD, n (%)	5 (11)	8 (20)	.28
≥5% blasts, n (%)	9 (20)	3 (7)	.12
WBC at HCT, K/μL, median	2.7	3.5	.07
Hemoglobin at HCT, K/dL, median	9.8	10	.93
Platelets at HCT, K/μL, median	83	122	.51
Myeloablative conditioning, n (%)	13 (29)	19 (46)	.09
Matched related transplant, n (%)	17 (38)	20 (49)	.30
7/8 HLA-matched transplant, n (%)	0 (0)	3 (7)	.10
Outpatient HCT, n (%)	6 (13)	4 (10)	.74
Disease indication, n (%)			.77
AML	26 (58)	27 (66)	
MDS	16 (35)	12 (29)	
MPN	3 (7)	2 (5)	
Cytogenetic risk, n (%)			.36
Good	9 (20)	13 (32)	
Intermediate	20 (44)	13 (32)	
Poor	16 (36)	15 (36)	

Significant *P* values are in bold type.

Cox proportional hazards model. $P \leq .05$ was considered to indicate statistical significance. A secondary analysis was performed among patients with BMI <30 and BMI>35 using the same methods detailed above. Statistical analyses were performed using Stata version 13.1 (StataCorp, College Station, TX).

RESULTS

We identified 86 patients who met the inclusion criteria; patient characteristics are summarized in Table 1. Of these, 41 patients (48%) had a BMI ≥30 and 45 (52%) had a BMI <30. In the BMI ≥30 group, 15 patients had a BMI >35 (range, 30 to 49). The median age at transplantation was 66 years in both groups. There were no significant differences in mean age, sex, cytogenetic risk (good, intermediate, or poor), disease indication (AML, MDS, or MPN), donor (related or unrelated), and KPS score ≥90 between the 2 groups. Presence of comorbid conditions, such as DM, HTN, CKD, CVA, and CAD, were similar in the 2 groups. MAC was provided to 19 patients in the BMI ≥30 group (46%) and to 13 patients (29%) in the BMI <30 group (*P* = .09). Three patients in the BMI ≥30 group had a <8/8-matched unrelated donor. GVHD prophylaxis included tacrolimus and short-course methotrexate in all patients except 1, who received post-transplantation cyclophosphamide. The 3 patients with a <8/8 match received anti-thymocyte globulin in addition to tacrolimus. Pretransplantation bone marrow biopsy revealed >5% blasts in 3 patients (7%) in the BMI ≥30 group and 9 patients (20%) in the BMI <30 group (*P* = .12). Significantly more patients in the BMI ≥30 group had an HCT-CI score ≥3 (30 versus 13; *P* < .01). After excluding obesity (BMI >35 as in the HCI-CI model), the percentage of patients with an HCT-CI ≥3 remained higher in the BMI ≥30 group (61% versus 29%; *P* < .01).

Clinical outcome data are reported in Table 2. The median OS was 36 months in the BMI <30 group and 24 months in the BMI ≥30 group (Figure 1A), but the difference was not statistically significant (*P* = .55). The median PFS was 10.1 months in the BMI <30 group and 13.6 months in the ≥30 group (*P* = .93) (Figure 1B). aGVHD occurred in 16 patients (36%) in the BMI <30 group, compared with only 8 patients (20%) in the BMI ≥30 group (*P* = .10). The 1-year cumulative incidence of cGVHD was 56% in the BMI ≥30 group versus 38% in the BMI <30 group (*P* = .09). Among the patients admitted for transplantation (n = 76), the mean length of stay was 25 days in BMI <30 group and 26 days in the BMI ≥30 group (*P* = .64). More patients in the BMI ≥30 group were readmitted within 30 days of discharge (34% versus 16%; *P* = .045).

Regression analyses were performed to identify predictors for OS. In univariate analysis, only poor-risk cytogenetics was associated with worse OS (HR, 2.63; 95% confidence interval [CI], 1.12 to 6.18; *P* = .03) (Table 3). Selected variables were then included in a multivariate analysis (Table 3). In this analysis, poor-risk cytogenetics remained a predictor for increased risk for death, but BMI had no bearing on OS (HR, 1.17; 95% CI, 0.58 to 2.35; *P* = .66).

We then performed a secondary analysis by comparing outcomes between patients with BMI >35 (n = 15), which correlates with severe obesity [28], and patients with BMI <30 (n = 45) to examine whether outcomes were worse in patients at the extremes of weight. Again, we found no between-group differences in patient variables, including age, sex, KPS score, presence of comorbid conditions (DM, HTN, CVA, CKD, and CAD), intensity of conditioning, indication for HCT, and disease status before transplantation. There were more patients with HCT-CI ≥3 in the BMI >35 group (*P* < .01), but this did not hold true when we excluded the point for obesity (*P* = .21). There were no between-group differences in aGVHD or cumulative incidence of cGVHD at 1 year. Interestingly, in the >35 BMI group, the length of stay among hospitalized patients was longer (median, 28 days versus 25 days; *P* = .16) and more patients were readmitted within 30 days of HCT (47% versus 16%; *P* = .01). The median OS and PFS was not reached in the BMI >35 group, and values were not statistically different from those of the BMI <30 group (Figure 2A and B). In multivariate analysis, BMI >35 was not associated with worse OS (HR, 0.75; 95% CI, 0.43 to 1.32; *P* = .32) (Table 4).

DISCUSSION

Allo-HCT is a high-risk treatment offered to patients with hematologic malignancies with a curative intent. What was once limited to younger patients with matched sibling donors is now offered to patients as old as 80 years with a variety of donor options. With an aging population and the increased frequency of myeloid diseases in patients age ≥60 years, the use of allo-HCT is increasing in this age group [29]. At the same time, the proportion of patients who are obese or severely obese has increased. Obesity hastens age-related decline and is a factor used to evaluate patients before transplantation [15,21]. In this study, we evaluated outcomes among older patients with and without obesity and found that obesity at time of allo-HCT does not correlate with worse survival outcomes and should not represent a barrier to successful allo-HCT in appropriately selected elderly patients. In particular, our findings held true regardless of our BMI cutoff (30 or 35), with a median survival of almost 2 years.

Two large Center for International Blood and Marrow Transplant Research observational studies explored the effect of obesity on transplantation outcomes across all age groups, and both studies found that obesity does not impair outcomes after HCT. The first, by Navarro et al [22], studied 4215 patients with AML who underwent allo-HCT, using an even number of related and unrelated donors. Patients were divided into 4 weight groups by BMI: underweight, <18; normal weight, 18 to 25; overweight, >25 to 30; and obese, >30. The median age was 40 for the unrelated donor allo-HCT group and 39 for the related donor allo-HCT group, representing a significantly younger cohort compared with ours. They found significantly worse treatment failure, relapse, treatment-related mortality, and OS in the underweight group compared with the normal weight group. In contrast, patients in the obese BMI group did not have significantly worse survival outcomes than normal-weight patients. In the second study, Vogl et al [30] studied the outcomes of 1087 patients who underwent autologous HCT for multiple myeloma. Patients were divided into groups based on BMI: normal weight, 18.5 to 25; overweight, 25 to 30; obese, 30 to 35; and severely obese, >35. These authors also found that BMI had no significant effect on survival outcomes, including PFS, OS, progression/relapse, and NRM. Our study was different in that it evaluated the effect of obesity in older allo-HCT recipients, who may be at greater risk of obesity-related diseases.

Other studies have shown a correlation between pretransplantation BMI and post-transplantation complications. GVHD is a major complication of allo-HCT. Hyperglycemia during the neutropenic period has been associated with a significantly increased risk of grade II-IV aGVHD and NRM [31]. Increased BMI and obesity are known to be associated with hyperglycemia and thus may increase the risk of aGVHD. However, our results do not show a higher incidence of aGVHD in elderly obese patients compared with nonobese elderly patients. The 1-year cumulative incidence of cGVHD was higher in obese patients, although the

Table 2
Clinical Outcomes

Outcome	BMI <30 kg/m²(N = 45; 52%)	BMI ≥30 kg/m²(N = 41; 48%)	*P* Value
OS, mo, median	36	24	.55
PFS, mo, median	10.1	13.6	.93
Relapse post-HCT, n (%)	21 (47)	13 (32)	.16
30-day readmission, n (%)	7 (16)	14 (34)	**.045**
aGVHD, n (%)	16 (36)	8 (20)	.10
1-year cumulative incidence of chronic GVHD, n (%)	17 (38)	23 (56)	.09
Intensive care unit transfer, n (%)	2 (4)	2 (5)	.92
Length of stay, d, mean	25	26	.64

Significant *P* values are in bold type.

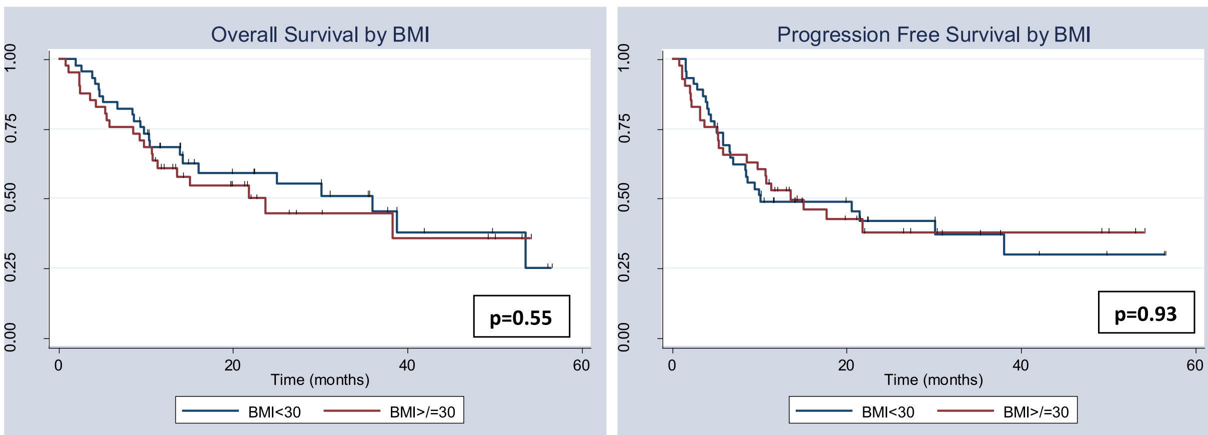

Figure 1. OS (A) and PFS (B) in the BMI <30 and BMI ≥30 groups.

Table 3
Univariate and Multivariate Analyses for OS, BMI <30 versus BMI ≥30

Covariate	Univariate Analysis			Multivariate Analysis		
	HR	95% CI	*P* Value	HR	95% CI	*P* Value
BMI >30	1.20	.66-2.19	.56	1.17	.58-2.35	.66
>5% BM blasts at HCT	.37	.11-1.20	.10	.50	.14-1.72	.27
Myeloablative conditioning	.94	.51-1.75	.85	.95	.51-1.78	.88
Poor-risk cytogenetics	2.63	1.12-6.18	**.03**	2.57	1.08-6.11	**.03**
HCT-CI >3 excluding obesity	.89	.48-1.64	.72	.94	.46-1.90	.86

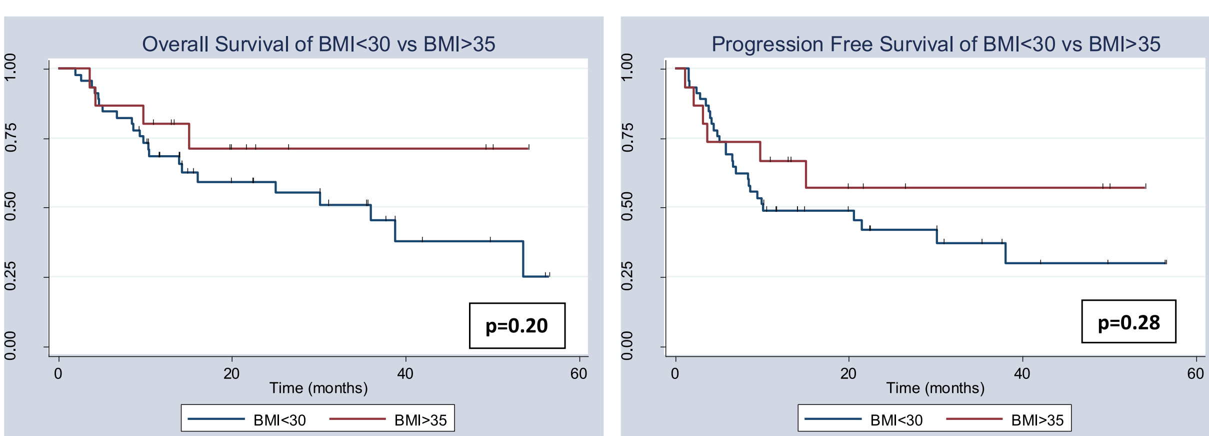

Figure 2. OS (A) and PFS (B) in the BMI <30 and BMI ≥35 groups.

difference was not statistically significant. The same group of researchers also found an association between obesity and increased risk of infection [32]. This may be due to related comorbidities associated with obesity, such as diabetes, which has been linked to impaired cell-mediated immune response and higher infection rates [33]. Our

Table 4
Multivariate Analyses for OS (BMI <30 versus BMI ≥35)

Covariate	Multivariate Analysis		
	HR	95% CI	*P* Value
BMI >35	.75	.43-1.32	.32
>5% BM blasts at HCT	.38	.09-1.69	.20
Myeloablative conditioning	.60	.25-1.43	.25
Poor-risk cytogenetics	1.42	.98-2.05	.06
HCT-CI >3, excluding obesity	.80	.27-2.31	.68

analysis of patient outcomes showed equivalent numbers of intensive care unit transfers and mean length of stay in our elderly obese patients with a BMI ≥30 and our nonobese elderly patients suggesting no increased risk of post-HCT complications due to obesity. However, patients with a BMI ≥30 were more likely to be readmitted to the hospital, and patients in the highest BMI group (>35) showed a trend toward longer length of hospital stay. This trend could be related to an increased incidence of obesity-related comorbidities and obesity-related illnesses. The higher rate of comorbidities was evident in our finding of a statistically significant HCT-CI score ≥3 in our elderly patients with a BMI ≥30 even after excluding 1 point for obesity.

In terms of transplantation-related outcomes, similar to other studies, here patients with poor-risk cytogenetics were found to have poorer OS. Interestingly, in our cohort, the presence of increased blasts did not adversely affect survival outcomes. The significance of this finding is limited by our small sample size, however. Although nonmyeloablative or reduced-intensity conditioning regiments have been developed to reduce NRM in elderly patients and those with significant comorbidities [34,35], more than one-third of all patients in our ≥60 year old cohort were able to tolerate myeloablative conditioning, and independent of BMI, the intensity of conditioning was not associated with an increased risk of mortality. This finding is consistent with larger studies that have found no statistically significant differences in survival outcomes after allo-HCT by the type of conditioning [36,37].

Our study has several limitations. This retrospective analysis is limited by the accuracy of the documentation retrieved from the medical record. As a single-center analysis, it is subject to institutional biases in the patient population that might not reflect the general population. In addition, our sample size was limited to cases available in our database. A larger study through the transplant registries would be useful to confirm our findings and overcome these limitations. Finally, although we tried to account for possible confounders with multivariate analysis, we might not have considered all possible variables that affect outcomes.

In conclusion, the present study demonstrates that obese elderly patients undergoing allo-HCT did not experience inferior outcomes compared with nonobese elderly allo-HCT recipients, regardless of the BMI cutoff for obesity used (30 or 35). BMI >30 was associated with increased rehospitalization within 30 days of discharge after allo-HCT. Severely obese (BMI >35) patients showed trends toward longer duration of hospitalization and a higher rate of readmissions within 30 days of discharge after transplantation. Hospital-based measures may be implemented to identify these higher-risk patients to reduce the risk of readmission and length of stay. In a patient age ≥60 years, elevated BMI should not impact the consideration of a curative intent allo-HCT if he or she is otherwise appropriate for transplantation.

ACKNOWLEDGMENTS

Conflict of interest statement: There are no conflicts of interest to report.

REFERENCES

1. Howlader N, Noone AM, Krapcho M, et al., eds. *SEER Cancer Statistics Review, 1975-2014*. Bethesda, MD: National Cancer Institute; 2017.
2. Ma X, Does M, Raza A, Mayne ST. Myelodysplastic syndromes: incidence and survival in the United States. *Cancer*. 2007;109:1536–1542.
3. Slavin S, Nagler A, Naparstek E, et al. Nonmyeloablative stem cell transplantation and cell therapy as an alternative to conventional bone marrow transplantation with lethal cytoreduction for the treatment of malignant and nonmalignant hematologic diseases. *Blood*. 1998;91:756–763.
4. Federmann B, Faul C, Meisner C, Vogel W, Kanz L, Bethge WA. Influence of age on outcome after allogeneic hematopoietic cell transplantation: a single center study in patients aged ≥60. *Bone Marrow Transplant*. 2015;50:427–431.
5. Sorror ML, Sandmaier BM, Storer BE, et al. Long-term outcomes among older patients following nonmyeloablative conditioning and allogeneic hematopoietic cell transplantation for advanced hematologic malignancies. *JAMA*. 2011;306:1874–1883.
6. Brunner AM, Kim HT, Coughlin E, et al. Outcomes in patients age 70 or older undergoing allogeneic hematopoietic stem cell transplantation for hematologic malignancies. *Biol Blood Marrow Transplant*. 2013;19:1374–1380.
7. Muffly L, Pasquini MC, Martens M, et al. Increasing use of allogeneic hematopoietic cell transplantation in patients aged 70 years and older in the United States. *Blood*. 2017;130:1156–1164.
8. Shah NN, Ahn KW, Litovich C, et al. Outcomes of Medicare-age eligible NHL patients receiving RIC allogeneic transplantation: a CIBMTR analysis. *Blood Adv*. 2018;2:933–940.
9. Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults—The Evidence Report. National Institutes of Health. *Obes Res* 1998;(6 Suppl 2):51S–209S.
10. Flint AJ, Rexrode KM, Hu FB, et al. Body mass index, waist circumference, and risk of coronary heart disease: a prospective study among men and women. *Obes Res Clin Pract*. 2010;4:e171–e181.
11. Lee IM, Manson JE, Hennekens CH, Paffenbarger RS Jr. Body weight and mortality: a 27-year follow-up of middle-aged men. *JAMA*. 1993;270:2823–2828.
12. Hu FB, Manson JE, Stampfer MJ, et al. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. *N Engl J Med*. 2001;345:790–797.
13. Chan JM, Rimm EB, Colditz GA, Stampfer MJ, Willett WC. Obesity, fat distribution, and weight gain as risk factors for clinical diabetes in men. *Diabetes Care*. 1994;17:961–969.
14. Fakhouri TH, Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of obesity among older adults in the United States, 2007-2010. *NCHS Data Brief* 2012;(106):1–8.
15. Villareal DT, Chode S, Parimi N, et al. Weight loss, exercise, or both and physical function in obese older adults. *N Engl J Med*. 2011;364:1218–1229.
16. Arnold M, Pandeya N, Byrnes G, et al. Global burden of cancer attributable to high body mass index in 2012: a population-based study. *Lancet Oncol*. 2015;16:36–46.
17. Lauby-Secretan B, Scoccianti C, Loomis D, Grosse Y, Bianchini F, Straif K. Body fatness and cancer—viewpoint of the IARC Working Group. *N Engl J Med*. 2016;375:794–798.
18. Goodwin PJ. Obesity and breast cancer outcomes: how much evidence is needed to change practice? *J Clin Oncol*. 2016;34:646–648.
19. Schmitz KH, Neuhouser ML, Agurs-Collins T, et al. Impact of obesity on cancer survivorship and the potential relevance of race and ethnicity. *J Natl Cancer Inst*. 2013;105:1344–1354.
20. Chlebowski RT, Blackburn GL, Thomson CA, et al. Dietary fat reduction and breast cancer outcome: interim efficacy results from the Women's Intervention Nutrition Study. *J Natl Cancer Inst*. 2006;98:1767–1776.
21. Sorror ML, Maris MB, Storb R, et al. Hematopoietic cell transplantation (HCT)-specific comorbidity index: a new tool for risk assessment before allogeneic HCT. *Blood*. 2005;106:2912–2919.
22. Navarro WH, Agovi MA, Logan BR, et al. Obesity does not preclude safe and effective myeloablative hematopoietic cell transplantation (HCT) for acute myelogenous leukemia (AML) in adults. *Biol Blood Marrow Transplant*. 2010;16:1442–1450.
23. Nikolousis E, Nagra S, Paneesha S, et al. Allogeneic transplant outcomes are not affected by body mass index (BMI) in patients with haematological malignancies. *Ann Hematol*. 2010;89:1141–1145.
24. Bacigalupo A, Ballen K, Rizzo D, et al. Defining the intensity of conditioning regimens: working definitions. *Biol Blood Marrow Transplant*. 2009;15:1628–1633.
25. Döhner H, Weisdorf DJ, Bloomfield CD. Acute myeloid leukemia. *N Engl J Med*. 2015;373:1136–1152.
26. Greenberg PL, Tuechler H, Schanz J, et al. Revised international prognostic scoring system for myelodysplastic syndromes. *Blood*. 2012;120:2454–2465.

27. Schag CC, Heinrich RL, Ganz PA. Karnofsky performance status revisited: reliability, validity, and guidelines. *J Clin Oncol*. 1984;2:187–193.
28. Physical status: the use and interpretation of anthropometry. Report of a WHO Expert Committee. *World Health Organ Tech Rep Ser*. 1995;854:1–452.
29. D'Souza A, Lee S, Zhu X, Pasquini M. Current use and trends in hematopoietic cell transplantation in the United States. *Biol Blood Marrow Transplant*. 2017;23:1417–1421.
30. Vogl DT, Wang T, Pérez WS, et al. Effect of obesity on outcomes after autologous hematopoietic stem cell transplantation for multiple myeloma. *Biol Blood Marrow Transplant*. 2011;17:1765–1774.
31. Fuji S, Kim SW, Mori S, et al. Hyperglycemia during the neutropenic period is associated with a poor outcome in patients undergoing myeloablative allogeneic hematopoietic stem cell transplantation. *Transplantation*. 2007;84:814–820.
32. Fuji S, Kim SW, Yoshimura K, et al. Possible association between obesity and posttransplantation complications including infectious diseases and acute graft-versus-host disease. *Biol Blood Marrow Transplant*. 2009;15:73–82.
33. Geerlings SE, Hoepelman AI. Immune dysfunction in patients with diabetes mellitus (DM). *FEMS Immunol Med Microbiol*. 1999;26:259–265.
34. Chakraverty R, Peggs K, Chopra R, et al. Limiting transplantation-related mortality following unrelated donor stem cell transplantation by using a nonmyeloablative conditioning regimen. *Blood*. 2002;99:1071–1078.
35. Ho AY, Pagliuca A, Kenyon M, et al. Reduced-intensity allogeneic hematopoietic stem cell transplantation for myelodysplastic syndrome and acute myeloid leukemia with multilineage dysplasia using fludarabine, busulphan, and alemtuzumab (FBC) conditioning. *Blood*. 2004;104:1616–1623.
36. Sorror ML, Sandmaier BM, Storer BE, et al. Comorbidity- and disease status-based risk stratification of outcomes among patients with acute myeloid leukemia or myelodysplasia receiving allogeneic hematopoietic cell transplantation. *J Clin Oncol*. 2007;25:4246–4254.
37. Blaise D, Vey N, Faucher C, Mohty M. Current status of reduced-intensity conditioning allogeneic stem cell transplantation for acute myeloid leukemia. *Haematologica*. 2007;92:533–541.