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OBESITY DOES NOT PRECLUDE SAFE AND EFFECTIVE MYELOABLATIVE HEMATOPOIETIC CELL TRANSPLANTATION (HCT) FOR ACUTE MYELOID LEUKEMIA (AML) IN ADULTS

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Abstract

The incidence of excessive adiposity is increasing worldwide and is associated with numerous adverse health outcomes. We compared outcomes by body mass index (BMI) for adult patients with acute myeloid leukemia (AML) who underwent autologous (auto, n=373), related donor (RD, n=2041), or unrelated donor (URD, n=1801) allogeneic myeloablative hematopoietic cell transplantation (HCT) using marrow or peripheral blood stem cells reported to the Center for

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International Blood and Marrow Transplant Research (CIBMTR) from 1995-2004. Four weight groups by BMI (kg/m^2) were defined: underweight < 18; normal 18 – 25; overweight >25 – 30; and obese > 30. Multivariable analysis referenced to the normal weight group showed an increased risk of death for underweight patients in the RD group (RR, 1.92; 95% CI, 1.28-2.89; P = 0.002) but not in the URD group. There were no other differences in outcomes among the other weight groups within the other HCT groups. Overweight and obese patients enjoyed a modest decrease in relapse incidence, though this did not translate into a survival benefit. Small numbers of patients limit the ability to better characterize the adverse outcomes seen in the underweight RD but not the underweight URD allogeneic HCT patients. Obesity alone should not be considered a barrier to HCT.

Keywords

Hematopoietic cell transplantation; obesity; outcomes; acute myeloid leukemia

INTRODUCTION

Obesity remains an increasingly prominent and challenging international health issue, particularly in the developed world(1-7). Excessive adiposity has been associated with a number of medical complications including cardiovascular disease and diabetes that could adversely impact outcomes for hematopoietic cell transplantation (HCT) for acute myeloid leukemia (AML)(6,8,9). AML is often optimally treated with HCT and in some cases, affords the best opportunity for long-term disease free survival. Recently, it was demonstrated that even in the intermediate-risk setting, allogeneic HCT (alloHCT) improves overall survival compared to other approaches(10). However, there has been concern that obese and overweight patients may not have equivalent outcomes when compared to those of normal weight. To date, transplant outcomes for patients with AML based on BMI have not been well-characterized.

In 2004, we published results from an observational study performed by the Center for International Blood and Marrow Transplantation Research (CIBMTR) for patients undergoing autologous HCT (autoHCT) for lymphoma(11). In that study, we showed that obese patients fared at least as well as patients with normal body mass index. The purpose of this study was to explore the impact of BMI in a different disease setting and in the context of allogeneic transplantation to understand if the previous observations regarding obesity apply.

PATIENTS AND METHODS

Data Sources

The CIBMTR is a research affiliation of the International Bone Marrow Transplant Registry (IBMTR), Autologous Blood and Marrow Transplant Registry (ABMTR) and the National Marrow Donor Program (NMDP) established in 2004 that comprises a voluntary working group of more than 450 transplantation centers worldwide that contribute detailed data on consecutive allogeneic and autologous hematopoietic SCT to a Statistical Center at the Medical College of Wisconsin in Milwaukee and the NMDP Coordinating Center in Minneapolis. Participating centers are required to report all transplants consecutively; compliance is monitored by on-site audits. Patients are followed longitudinally, with yearly follow-up. Computerized checks for discrepancies, physicians' review of submitted data and on-site audits of participating centers ensure data quality. Observational studies conducted by the CIBMTR are performed in compliance with the Privacy Rule (HIPAA) as a Public Health Authority, and in compliance with all applicable federal regulations pertaining to the protection of human research participants as determined by continual review of the Institutional Review Boards of the National Marrow Donor Program and the Medical College of Wisconsin since 1985.

Patients

Our study inclusion criteria included all patients with AML who received a first allogeneic marrow or peripheral stem cell graft HCT from a related donor (RD alloHCT) or an unrelated donor (URD alloHCT) or received an autoHCT between 1995 and 2004 and reported to the CIBMTR. Patients whose transplant center reported myeloablative conditioning (as determined by the transplant center) and whose disease status prior to transplant was reported as primary induction failure (PIF), first or second complete remission (CR1, CR2) or first relapse were included in this study. For the autologous cohort, recipients of purged grafts (n=55) were excluded. A total of 4,735 patients met these initial selection criteria. We further excluded 520 patients (74 autologous; 305 RD, 141 URD) from teams with inadequate follow-up or inconsistent reporting over the study period in order to reduce selection and reporting bias of patients. To ensure that the research patients were representative of all registered patients in the CIBMTR database, demographics and relapse and survival rates between research and registered patients were compared and no differences were noted.

The final study population included 1,801 and 2,041 patients who received an URDalloHCT or RDalloHCT, respectively, and 373 patients who underwent autoHCT. Patients were divided into groups based on body mass index (BMI) calculated from weight at the time of transplantation. Weight groups were defined according to consensus weight designations by the World Health Organization(12) and the National Heart Lung and Blood Institute Expert Panel(13) as follows: underweight, BMI <18 kg/m^2; normal, BMI 18 to 25 kg/m^2; overweight, BMI >25 to 30 kg/m^2; and obese, BMI >30 kg/m^2. Obese (BMI >30 to 34) and morbidly obese groups (BMI ≥ 35) were combined for all analyses after confirmation of the lack of significant outcomes differences when analyzed separately (see section on overall survival-multivariate analysis for details).

Data Collection

All missing or inconsistent data at the time of data file preparation were queried. Unavailable data from the transplant centers was treated as missing in the analysis. Cytogenetics data at the time of diagnosis or prior to transplantation were queried if not previously reported. Cytogenetic data were available for 79% of patients. Follow-up was updated for all patients in the data file. The median follow-up by transplant type and the completeness of follow-up index at 3 years(14) were 74 months and 94% for RD alloHCT, 58 months and 86% for URD alloHCT, and 85 months and 80% for autoHCT, respectively.

Study End Points

Primary end points were overall survival (OS), transplant-related mortality (TRM), relapse, and leukemia-free survival (LFS). OS was defined as time to death from any cause; surviving patients were censored at time of last follow-up. TRM was defined as death within the first 28 days of transplantation from any cause or death in continuous complete remission at any subsequent time point. Relapse was defined as the time to onset of clinical or hematologic recurrence, disease progression, or persistent disease. For relapse, patients with persistent disease were considered events at day 28. LFS was defined as survival in continuous complete remission of primary disease; disease relapse or persistence, or deaths were considered as events.

Secondary end points studied included rates of primary neutrophil and platelet engraftment, grade II-IV acute graft-versus-host disease (GVHD), and chronic GVHD. Neutrophil engraftment was defined as the time to achieve a sustained absolute neutrophil count ≥500 cells/μL for three consecutive days. Time to platelet engraftment was defined as time to achieve a platelet count of 20,000/μL, evaluable at 7 days from the last platelet transfusion.

Acute and chronic GVHD were graded by the transplant center according to standard criteria (15,16).

Statistical Analysis

Patient-, disease-, and transplant-related factors were compared among the four BMI groups by using the Chi-squared test for categorical variables and the Kruskal-Wallis test for continuous variables. Univariate probabilities LFS and OS were estimated by using the Kaplan-Meier method(17). The log rank test was used for comparing survival curves. Probabilities of TRM, relapse, neutrophil engraftment, platelet engraftment, acute and chronic GVHD were estimated by using cumulative incidence to allow for competing risks. In the multivariate analyses we used Cox proportional hazards regression models separately for each donor type. Models were constructed to compare the outcomes among the four BMI groups, with normal BMI used as the baseline group, while adjusting for all covariates listed in the demographics tables (Table 1). A model was built for each primary outcome of interest as a dependent variable and all the relevant exposure variables as explanatory variables. A main effect term for the four BMI groups was forced into the model. The proportional hazards assumption for all the variables was examined by using time-varying covariates, but violations of this assumption were not detected. Interactions between weight groups and other significant explanatory variables were explored but none were found significant. The models were adjusted for the geographical region of the patient (US, Canada, Europe, Asia, Australia/New Zealand, Mideast/Africa, Central/South America) using a stratified Cox model to account for imbalances in the BMI groups by region. Bonferroni corrections were applied to allow adjustment for multiple comparisons between each weight group and the normal weight group. A P value <. 0167 was therefore considered statistically significant, whereas the P values for inclusion in the final models of all other potentially confounding covariates were set at <.05. Comparisons of all secondary outcomes were limited to univariate comparisons.

RESULTS

Patient Characteristics

Patients included in this analysis were age 18 years or older, with AML in first or second complete remission (CR), in first relapse, or with primary induction failure after initial therapy who underwent HCT between 1995-2004, inclusive. A total of 4,215 patients were evaluated in this study. Comparisons of patient-, disease-, and transplant-related characteristics among the weight groups are listed in Table 1. Because of low numbers of patients in the underweight arm for those undergoing autoHCT (n=5), this group was omitted from analysis. With respect to the key risk characteristics of age, Karnofsky performance status (KPS) < 90, disease status at transplant, cytogenetic risk group, and, for unrelated allogeneic transplants, donor matching, no differences among the normal weight, overweight, and obese groups were observed. For the underweight group, there were some differences compared to the normal weight group for the RD alloHCT group (more primary induction failures [PIF] and first relapses: 38% vs 28%, respectively) and for the URD alloHCT group (median age: 26 vs 40; KPS <90: 58 vs 32%; and well-matched donor(18): 18 vs 39%, respectively). Table 2 summarizes the rates of neutrophil and platelet engraftment according to BMI group and transplant type. Hematopoietic recovery was similar among all BMI groups.

Overall Survival-Univariate Analysis

Figure 1 shows Kaplan-Meier estimates of OS by transplant type and weight group. For the RD alloHCT group, probabilities of OS in the univariate analysis were similar between the normal (63% [95% CI, 60%-66%]), and overweight (60% [95% CI, 56%-64%]) groups, slightly worse in the obese group (52% [95% CI, 47%-58%]), and markedly worse in the underweight group (38% [95% CI, 22%-55%]) at 1 year. Corresponding OS probabilities at 5

years were 47% (95% CI, 44%-50%), 44% (95% CI, 40%-49%), 37% (95% CI, 31%-43%), and 19% (95%CI, 6%-35%), respectively. For the URD alloHCT and the autoHCT groups, there were no statistically significant differences among the weight groups.

Overall Survival-Multivariate Analysis

In multivariate analysis (Table 3) in the RD alloHCT setting, with normal weight patients as the reference, the underweight group had a higher risk of mortality (RR, 1.92; 95% CI, 1.28-2.89; P = .002); there were no differences among the normal, overweight, and obese groups. The morbidly obese group (BMI ≥ 35) was analyzed separately for OS versus the normal weight group: RD group n=118, RR=1.05 (0.81-1.35), p=0.733; URD group: n=170, RR=1.11 (0.91-1.35), p=0.317. Other factors associated with higher risks of mortality were age >50 years, KPS <90%, and disease stage worse than first remission at transplantation; CSA +/− other, T cell depletion for GVHD prophylaxis (CSA/MTX as the reference group); high risk cytogenetics (normal cytogenetics as reference); and use of TBI. For the URD alloHCT and autoHCT groups, there were no differences in overall survival among the weight groups.

Transplant-Related Mortality

Point wise probabilities of TRM are summarized in Table 2. In multivariable analysis in the RD alloHCT setting, the underweight group experienced a relative risk (RR) of TRM of 2.23 (95% CI: 1.17-4.25; P =0.014) compared to the normal weight group. There were no differences among the other weight groups. Other significant variables increasing the risk of TRM were age >40, KPS <90, GVHD prophylaxis with CSA +/− other or T cell depletion, and a disease status of primary induction failure at transplant. A favorable factor was year of transplant between 2000 and 2004 (versus 1995 to1999). In the URD alloHCT and autoHCT settings, there were no differences among the BMI groups.

Relapse

Table 2 summarized the univariate probabilities of leukemia relapse by BMI group at each transplant type. In multivariate analysis, in the RD alloHCT setting, the underweight group had a higher risk of relapse compared to the normal weight group, with a RR of 2.06 (95% CI, 1.20-3.54, P = 0.009). There were no differences in the other weight groups. Interestingly, similar to the previous study of autoHCT for lymphoma, the relative risk of relapse was reduced for the URD alloHCT overweight (RR 0.82, 95% CI 0.68-0.99, P = 0.044) and obese (RR 0.76, 95% CI 0.0.60-0.96, P = 0.022) groups, though this difference did not translate into a survival benefit. There were no differences among the weight groups in the autoHCT group (underweight was excluded, n=5).

Leukemia-Free Survival

In multivariate analysis, LFS was worse in the RD alloHCT setting for the underweight group (RR 2.07, 95% CI 1.36-3.13, P = <0.001). Otherwise, no other differences were observed for any other groups in any other setting.

Acute and Chronic Graft-versus-Host Disease (GVHD)

The rates of acute and chronic GVHD by transplant type are summarized in Table 2. No statistically significant differences were observed among the weight groups in either allo HCT setting for either type of GVHD.

DISCUSSION

In this contemporary, retrospective, large study in AML patients, we demonstrated that obesity as defined by BMI at time of transplantation does not correlate with worse survival outcomes

but that underweight recipients of RD allo HCT have shorter survival compared to patients within the normal BMI range. Similar to our previous study in patients with lymphoma, the current study demonstrates that obesity does not appear to represent a significant barrier to successful HCT for AML.

The impact of obesity on transplant outcomes remains controversial. The HCT-specific comorbidity index developed by Sorror et al included obesity (BMI >35kg/m^2) as one of the components to predict non-relapse mortality at 2 years(19). This study included 708 patients in the training set who underwent allogeneic HCT for several indications; of these, 2% were obese. The data in this analysis predate the collection of HCT-CI-specific information initiated by CIBMTR in 2007 so no direct comparison is possible. However, transplant-related mortality in our study was not significantly higher in obese AML patients compared to normal weight patients, regardless of the donor type.

In the previous lymphoma study, we observed poorer outcomes in one of the underweight groups. Interestingly, poorer survival outcomes were observed in underweight patients in the RD allo HCT group but not the URD alloHCT group. Because of the small numbers of patients in the RD alloHCT group, there is some imbalance compared to the other weight groups with respect to disease status at time of transplantation with disproportionately more PIF/relapse and CR2 patients, though it is not clear how much this finding accounts for the difference in leukemia-free and overall survival. Such an imbalance of disease status was not seen in the underweight URD alloHCT group. It is noteworthy that the underweight RD alloHCT group had a similar KPS ($P = 0.353$) and cytogenetic risk ($P = 0.327$) compared to the other weight groups; these important factors do not appear to account for the difference in survival. It may also be that the higher risk of the URD alloHCT procedure masks important but less obvious risks associated with being underweight whereas in the related donor HCT setting, such risks become manifest. Small numbers of patients and lack of available data pertinent to nutritional status such as serum albumin or TPN use limit the ability to better characterize this observation in underweight patients. Moreover, the analysis does not account for unknown biological factors not included in the model that may be influencing outcomes in the underweight RD allo HCT group.

An important limitation of this study is that any conditioning regimen dose adjustments for overweight and obesity used by the various transplant centers could not be assessed from the CIBMTR data. Since chemotherapy dosing in the conditioning regimen may be based on actual weight or adjusted ideal body weight, clinical outcomes may have been confounded by whether dose adjustments were made for patients with high BMI. There is currently no accepted standard conditioning regimen dose adjustment schema based on weight and various methodologies are used, as was ascertained by Grigg and colleagues(20). A small study of AML patients undergoing autoHCT without dose adjustment has previously suggested that some adjustment may be beneficial, as the lack of conditioning regimen dose adjustment in that study resulted in unacceptable treatment-related mortality(21).

Similar to our previous study in lymphoma, the current study demonstrates that obesity does not appear to represent a significant barrier to successful HCT in AML. This conclusion must be tempered, however, with the acknowledgment that the patients who received myeloablative HCT were likely selected by their transplant centers, and were deemed to be “fit” to withstand the rigors of HCT. The limitations of pre-transplant co-morbidity data within the CIBMTR database preclude an assessment of this issue. Thus, the caveat is that it appears that overweight and obese patients have similar outcomes to normal weight patients when they otherwise appear to be eligible HCT candidates. Obesity alone, however, should not preclude HCT when appropriate for the treatment of AML.

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REFERENCES

1. Al Rashdan IR, Nesef YA. Prevalance of Overweight, Obesity, and Metabolic Syndrome Among Adult Kuwaitis: Results From Community-based National Survey. Angiology. 2009
2. Chen CM. Overview of obesity in Mainland China. Obes Rev 2008;9(Suppl 1):14–21. [PubMed: 18307694]
3. Kosti RI, Panagiotakos DB. The epidemic of obesity in children and adolescents in the world. Cent Eur J Public Health 2006;14:151–159. [PubMed: 17243492]
4. Low S, Chin MC, Deurenberg-Yap M. Review on epidemic of obesity. Ann Acad Med Singapore 2009;38:57–59. [PubMed: 19221672]
5. Misra A, Khurana L. Obesity and the metabolic syndrome in developing countries. J Clin Endocrinol Metab 2008;93:S9–30. [PubMed: 18987276]
6. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999-2004. JAMA 2006;295:1549–1555. [PubMed: 16595758]
7. Oguz A, Temizhan A, Abaci A, et al. Obesity and abdominal obesity; an alarming challenge for cardio-metabolic risk in Turkish adults. Anadolu Kardiyol Derg 2008;8:401–406. [PubMed: 19103534]
8. Flegal KM, Graubard BI, Williamson DF, Gail MH. Cause-specific excess deaths associated with underweight, overweight, and obesity. JAMA 2007;298:2028–2037. [PubMed: 17986696]
9. Guh DP, Zhang W, Bansback N, Amarsi Z, Birmingham CL, Anis AH. The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. BMC Public Health 2009;9:88. [PubMed: 19320986]
10. Koreth J, Schlenk R, Kopecky KJ, et al. Allogeneic stem cell transplantation for acute myeloid leukemia in first complete remission: systematic review and meta-analysis of prospective clinical trials. JAMA 2009;301:2349–2361. [PubMed: 19509382]
11. Navarro WH, Loberiza FR Jr. Bajorunaite R, et al. Effect of body mass index on mortality of patients with lymphoma undergoing autologous hematopoietic cell transplantation. Biol Blood Marrow Transplant 2006;12:541–551. [PubMed: 16635789]
12. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser 2000;894:i–xii. 1–253. [PubMed: 11234459]

13. 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. [PubMed: 9813653]
14. Clark TG, Altman DG, De Stavola BL. Quantification of the completeness of follow-up. Lancet 2002;359:1309–1310. [PubMed: 11965278]
15. Glucksberg H, Storb R, Fefer A, et al. Clinical manifestations of graft-versus-host disease in human recipients of marrow from HL-A-matched sibling donors. Transplantation 1974;18:295–304. [PubMed: 4153799]
16. Shulman HM, Sullivan KM, Weiden PL, et al. Chronic graft-versus-host syndrome in man. A long-term clinicopathologic study of 20 Seattle patients. Am J Med 1980;69:204–217. [PubMed: 6996481]
17. Kaplan E. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958;53:457–481.
18. Weisdorf D, Spellman S, Haagenson M, et al. Classification of HLA-matching for retrospective analysis of unrelated donor transplantation: revised definitions to predict survival. Biol Blood Marrow Transplant 2008;14:748–758. [PubMed: 18541193]
19. 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. [PubMed: 15994282]
20. Grigg A, Harun MH, Szer J. Variability in determination of body weight used for dosing busulphan and cyclophosphamide in adult patients: results of an international survey. Leuk Lymphoma 1997;25:487–491. [PubMed: 9250819]
21. Meloni G, Proia A, Capria S, et al. Obesity and autologous stem cell transplantation in acute myeloid leukemia. Bone Marrow Transplant 2001;28:365–367. [PubMed: 11571508]

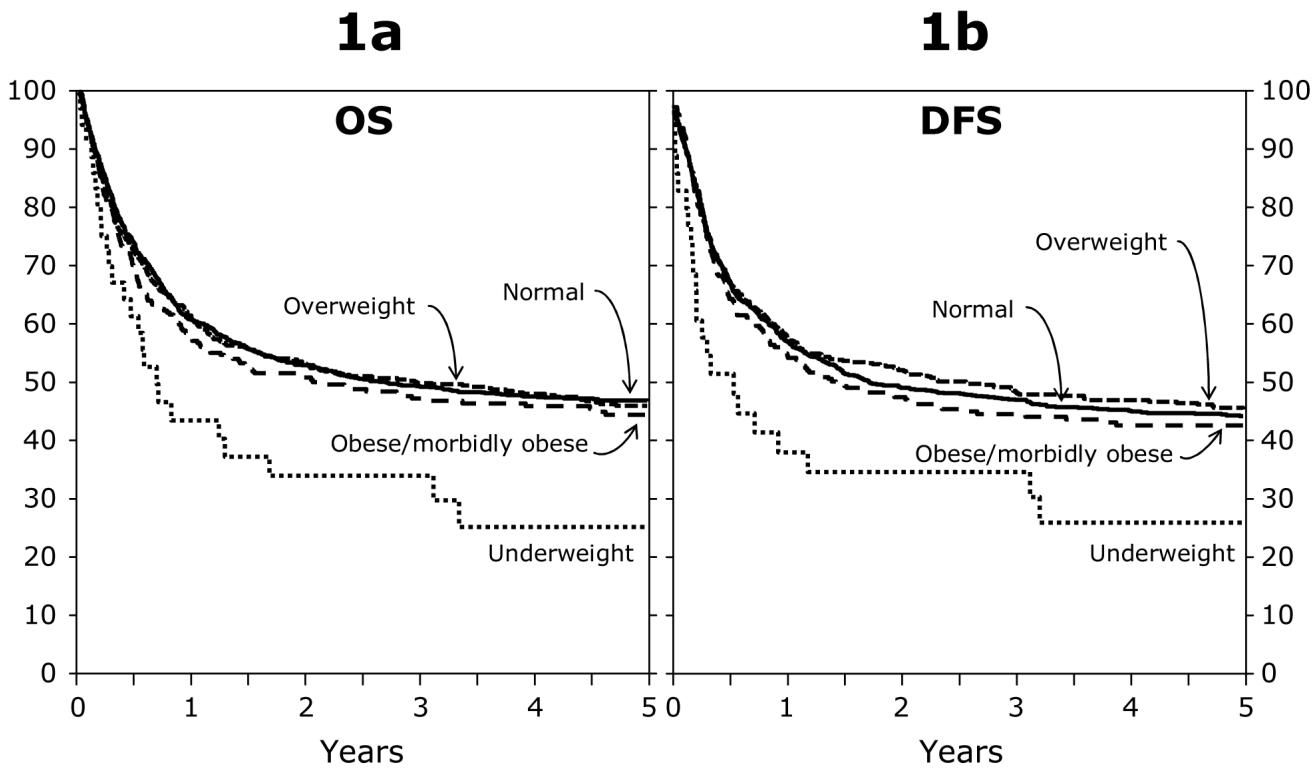

Figure 1.

a. Adjusted probability of overall survival among BMI groups for patients (≥ 18 years) after an RD alloHCT for AML between 1995 and 2004.

1b. Adjusted probability of disease free survival among BMI groups for patients (≥ 18 years) after an RD alloHCT for AML between 1995 and 2004

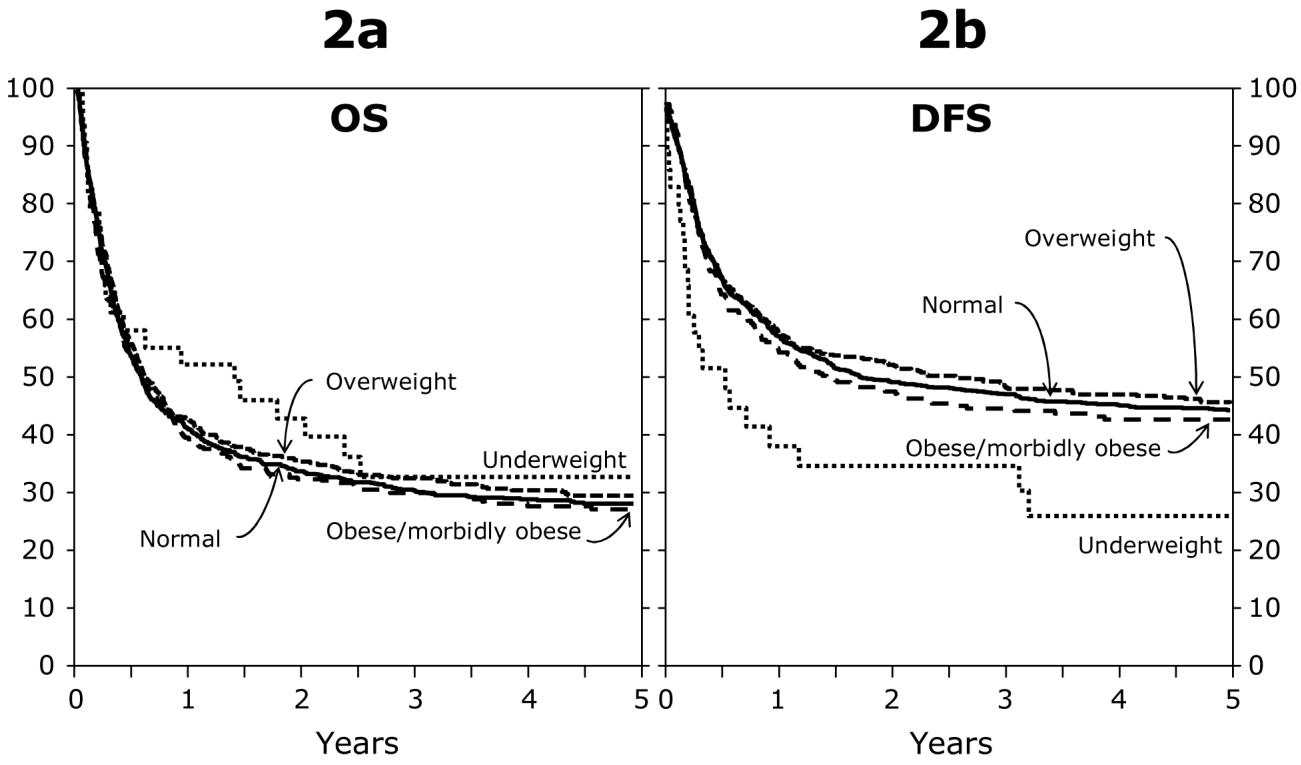

Figure 2.

a. Adjusted probability of overall survival among BMI groups for patients (≥ 18 years) after an URD alloHCT for AML between 1995 and 2004.

2b. Adjusted probability of disease free survival among BMI groups for patients (≥ 18 years) after an URD alloHCT for AML between 1995 and 2004.

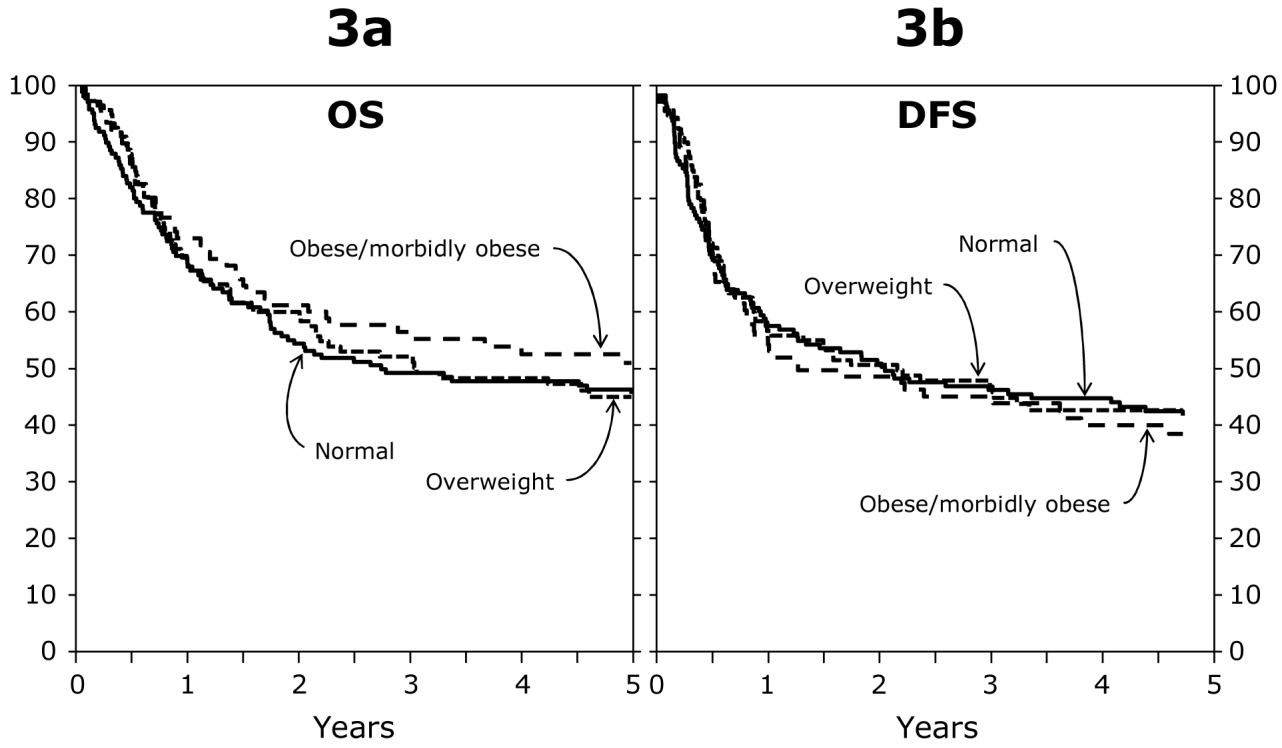

Figure 3.

a. Adjusted probability of overall survival among BMI groups for patients (≥ 18 years) after an autologous HCT for AML between 1995 and 2004.

3b. Adjusted probability of disease free survival among BMI groups for patients (≥ 18 years) after an autologous HCT for AML between 1995 and 2004.

Table 1

Characteristics of patients with age ≥18 years, who underwent a myeloablative bone marrow or peripheral blood transplantation for AML, reported to the CIBMTR between 1995 and 2004

Characteristics of patients	Total N (%)	Underweight N (%)	Normal N (%)	Overweight N (%)	Obese/Morbidly Obese (N %)	P-value[c]
Autologous						
Number of patients	373	-	169	119	85	
Age, median (range), years	46 (18-71)	-	42 (18-71)	50 (19-71)	49 (18-70)	0.001
Male sex	183 (49)	-	74 (43)	73 (61)	36 (42)	0.005
Karnofsky score≥ 90	285 (76)	-	128 (76)	92 (77)	65 (77)	0.989
Disease status at transplant		-				0.069
PIF/1st Relapse	27 (7)	-	14 (8)	9 (8)	4 (5)	
CR1	247 (68)	-	122 (74)	68 (59)	57 (67)	
CR2	92 (25)	-	30 (18)	38 (33)	24 (28)	
Cytogenetics		-				0.049
Favorable risk	66 (18)	-	33 (20)	16 (13)	17 (20)	
Intermediate risk	204 (54)	-	83 (49)	75 (63)	46 (55)	
High risk	30 (8)	-	15 (9)	6 (5)	9 (11)	
Unknown[a]	73 (20)	-	38 (22)	22 (18)	13 (15)	
Peripheral blood Graft	308 (83)	-	141 (83)	95 (80)	72 (85)	
Total body irradiation	98 (97)	-	47 (94)	31 (100)	20 (100)	0.206
Lung shielding for TBI	24 (6)	-	9 (5)	8 (7)	7 (8)	0.663
Year of Transplant		-				0.045
1995-1999	271 (73)	-	130 (77)	88 (74)	53 (62)	
2000-2004	102 (27)	-	39 (23)	31 (26)	32 (38)	
Median follow-up, (range), months	85 (3-148)	-	87 (3-148)	80 (8-139)	72 (12-137)	
HLA-match Sibling Donor Allogeneic						
Number of patients	2041	32	1178	552	279	
Age, median (range), years	39 (19-67)	36 (19-54)	37 (18-67)	43 (18-67)	43 (18-64)	<0.001
Male sex	1065 (52)	13 (41)	603 (51)	323 (59)	126 (45)	0.001
Karnofsky score≥ 90	1398 (69)	19 (59)	811 (69)	389 (70)	179 (64)	0.353
Disease status at transplant						<0.001

Characteristics of patients	Total N (%)	Underweight N (%)	Normal N (%)	Overweight N (%)	Obese/Morbidly Obese (N %)	P-value[c]
PIF/1st Relapse	572 (28)	12 (38)	322 (27)	744 (26)	94 (34)	
CR1	1172 (57)	11 (34)	693 (59)	331 (60)	137 (49)	
CR2	297 (15)	9 (28)	163 (14)	77 (14)	48 (17)	
AML Cytogenetics						0.327
Favorable risk	223 (11)	3 (9)	132 (11)	56 (10)	32 (11)	
Intermediate risk	1078 (53)	15 (47)	614 (52)	290 (53)	159 (57)	
High risk	275 (13)	8 (25)	158 (13)	79 (14)	30 (11)	
Unknown[a]	465 (23)	6 (19)	274 (23)	127 (23)	58 (21)	
Year of Transplant						0.124
1995-1999	1300 (64)	17 (53)	769 (65)	350 (63)	164 (59)	
2000-2004	741 (36)	15 (47)	409 (35)	202 (37)	115 (41)	
Bone marrow graft	1004 (49)	12 (38)	605 (51)	262 (47)	125 (45)	
Total body irradiation	873 (98)	12 (100)	522 (98)	231 (98)	108 (97)	0.851
Lung shielding for TBI	506 (25)	9 (28)	328 (28)	115 (21)	54 (19)	0.001
GVHD Prophylaxis						0.084
T-cell depletion	105 (5)	--	56 (5)	31 (6)	18 (6)	
CNI + MTX ± other	1555 (76)	24 (75)	904 (77)	427 (77)	200 (72)	
Other	381 (19)	8 (25)	218 (18)	94 (17)	61 (22)	
Median follow-up (range), months	74 (2-152)	83 (24-142)	74 (2-152)	81 (3-149)	73 (3-152)	
Unrelated Donor Allogeneic						
Number of patients	1801	33	864	529	375	
Age, median (range), years	40 (18-70)	26 (18-52)	37 (18-65)	42 (18-70)	42 (19-68)	<0.001
Male sex	954 (53)	14 (42)	430 (50)	320 (60)	190 (51)	<0.001
Karnofsky score ≥ 90	1102 (61)	14 (42)	520 (60)	339 (64)	229 (61)	0.008
Disease status at transplant						<0.001
PIF/1st Relapse	729 (41)	14 (42)	368 (43)	421 (40)	133 (36)	
CR1	549 (30)	14 (42)	268 (31)	172 (33)	95 (25)	
CR2	523 (29)	5 (15)	228 (26)	143 (27)	147 (39)	
Cytogenetics at diagnosis						0.020
Favorable risk	191 (11)	3 (9)	88 (10)	40 (8)	60 (16)	
Intermediate risk	897 (50)	17 (51)	438 (51)	275 (52)	167 (47)	

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Characteristics of patients	Total N (%)	Underweight N (%)	Normal N (%)	Overweight N (%)	Obese/Morbidly Obese (N %)	P-value[c]
Unfavorable risk	378 (21)	9 (27)	188 (22)	111 (21)	70 (19)	
Unknown[a]	335 (19)	4 (12)	150 (17)	103 (19)	78 (21)	
Year of Transplant						0.074
1995-1999	747 (41)	16 (48)	383 (44)	205 (39)	143 (38)	
2000-2004	1054 (59)	17 (52)	481 (56)	324 (61)	232 (62)	
Bone marrow Graft	1295 (72)	25(76)	629 (73)	383 (72)	258 (69)	
TBI Conditioning	150 (8)	7 (21)	83 (10)	45 (9)	15 (4)	0.040
Lung shielding for TBI	150 (8)	7 (21)	83 (10)	45 (9)	15 (4)	<0.001
GVHD Prophylaxis						0.247
T-cell depletion	227 (13)	3 (9)	101 (12)	62 (12)	61 (16)	
CNI +MTX ± other	1359 (75)	30 (91)	664 (77)	400 (76)	265 (71)	
Other	215 (12)	-	99 (11)	67 (12)	49 (13)	
HLA Match status[b]						<0.001
Well matched	699 (39)	6 (18)	314 (36)	202 (38)	177 (47)	
Partially matched	643 (36)	14(42)	315 (36)	193 (36)	121 (32)	
Mismatched	297 (16)	5 (15)	143 (17)	86 (16)	63 (17)	
Missing HLA data	162 (9)	8 (24)	92 (11)	48 (9)	14 (4)	
Median follow-up, (range), months	58 (3-149)	57 (31-119)	60 (4-149)	54 (4-146)	51 (3-136)	

Abbreviations: HLA= human leukocyte antigen; GVHD=graft versus host disease; CNI = calcineurin inhibitors, MTX = methotrexate, PIF=primary induction failure; CR1=first complete remission; CR2=second complete remission.

[a] Unknown cytogenetics includes patients not tested for cytogenetics or, have insufficient cytogenetic information to categorize or have non evaluable metaphases.

[b] HLA Match status: Well matched was defined as no known disparity at HLA A,B,C,DRB1, partially matched as one locus known or likely disparity with their donors and mismatched as ≥2 locus disparity.

[c] Chi-square p-value was calculated for categorical values

Table 2

Univariate probabilities of patients ≥ 18 years of age who received a myeloablative bone marrow or peripheral blood transplantation for AML, from a related donor, reported to the CIBMTR between 1995 and 2004

Outcome event	Total N (eval)	Underweight	Normal	Overweight	Obese/morbidly obese	P-value[a]
Autologous						
Transplant-related mortality[b]	364					
@ 1 year		-	5 (2-9)%	4 (1-9) %	5 (1-11) %	0.973
@ 3 years		-	6 (3-10) %	6 (3-11) %	6 (2-13) %	0.998
Relapse[c]	364					
@ 1 year		-	36 (29-44) %	45 (36-54) %	38 (28-49)%	0.341
@ 3 years		-	46 (38-54) %	53 (44-62) %	47 (36-58)%	0.506
Neutrophil Recovery[c]	365					
@ 60 days		-	96 (92-99) %	98 (95-100)%	95 (90-99) %	0.417
Platelet engraftment[c]	357					
@ 100 days		-	78 (72-84) %	83 (75-89) %	86 (77-92) %	0.345
Related Donor Allogeneic						
Transplant-related mortality[b]	2008					
@ 1 year		29 (15-46) %	17 (15 -19) %	21 (18-25) %	25 (16-31)%	0.007
@ 3 years		29 (15-46) %	21 (18-23) %	25 (22-29) %	30 (24-35) %	0.010
Relapse[c]	2008					
@ 1 year		39 (23-56) %	24 (21-26) %	22 (18-25) %	26 (21-31) %	0.214
@ 3 years		42 (25-59) %	30 (27-32) %	27 (23-31) %	31(26-37) %	0.288
Neutrophil engraftment[c]	2026					
@ 60 days		94 (83-99) %	96 (95-97) %	95 (94-97) %	96 (93-98) %	0.916
Platelet engraftment[c]	1962					
@ 100 days		72 (55-86) %	86 (84-88) %	82 (79-86) %	79 (74-84) %	0.011
Chronic GVHD[b]						
@ 1 year		19 (7-34) %	36 (34-39) %	36 (32-40) %	32 (27-38) %	0.053
Acute GVHD[b]						
Grades 2-4 @100 days	1953	16 (6-31) %	29 (27-32) %	34 (30-38) %	36 (30-42) %	0.007
Unrelated Donor Allogeneic						

Outcome event	Total N (eval)	Underweight	Normal	Overweight	Obese/morbidly obese	P-value[a]
Transplant-related mortality[b]	1779					
@ 1 year		22 (10-38) %	32 (28-35) %	35 (31-39) %	43 (38-48) %	0.001
@ 3 years		28 (14-45) %	36 (32-39) %	40 (35-44) %	46 (41-51) %	0.003
Relapse[b]	1779					
@ 1 year		31 (17-48) %	31 (28-34) %	26 (23-30) %	22 (18-27) %	0.010
@ 3 years		44 (27-61) %	36 (33-39) %	31 (27-35) %	25 (21-29) %	<0.001
Neutrophil engraftment[b]	1797					
@ 60 days		97 (85-100)%	91 (89-93) %	91 (88-93) %	91 (88-94) %	0.520
Platelet engraftment[b]	1768					
@ 100 days		67 (50-82) %	69 (66-72) %	69 (65-73) %	65 (61-70) %	0.668
Chronic GVHD[b]	1787					
@ 1 year		38 (22-55) %	32 (29-36) %	36 (32-41) %	34 (29-38) %	0.502
Acute GVHD[b]	1773					
Grades 2-4 @100 days		48 (31-66) %	44 (41-47) %	46 (42-50) %	50 (45-55) %	0.228

Abbreviations: GVHD= graft vs. host disease

[a] Point-wise p-value unless otherwise noted.

[b] Probabilities of relapse, treatment-related mortality, engraftment and GVHD were calculated using the cumulative incidence.

Table 3

Multivariable analysis of AML patients ≥18 years of age who received a bone marrow or peripheral blood transplant between 1995 and 2004, reported to the CIBMTR

HCT Type	Normal	Underweight	Overweight	Obese	Overall P-value
Autologous	n=164	n=5	n=112	n=81	
Death		--	0.98 (0.70-1.38)	0.89 (0.61-1.29)	
			(p=0.925)	(p=0.532)	P^{overal}=0. 809
Treatment failure		--	0.98 (0.70-1.38)	0.12 (0.78-1.59)	
			(p=0.919)	(p=0.542)	$P^{overall}$=0.768
Relapse		--	1.11 (0.76-1.62)	1.19 (0.81-1.75)	
			(p=0.574)	(p=0.363)	$P^{overall}$=0.649
TRM		--	0.79 (0.33-1.91)	0.97 (0.37-2.52)	
			(p=0.606)	(p=0.953)	$P^{overall}$=0.861
Related Allogeneic	n=1176	n=32	n=553	n=275	
Death		1.92 (1.28-2.89)	1.05 (0.91-1.21)	1.16 (0.97-1.38)	
		(p=0.002)	(p=0.532)	(p=0.109)	$P^{overall}$=0.008
Treatment failure		2.07 (1.36-3.13)	0.97 (0.84-1.12)	1.09 (0.91-1.31)	
		(p= <0.001)	(p= 0.720)	(p=0.330)	$P^{overall}$=0.005
Relapse		2.06 (1.20-3.54)	0.87 (0.71-1.05)	0.96 (0.75-1.23)	
		(p=0.009)	(p=0.146)	(p=0.757)	$P^{overall}$=0.020
TRM		2.23 (1.17-4.25)	1.12 (0.90-1.38)	1.27 (0.97-1.66)	
		(p=0.014)	(p=0.304)	(p=0.081)	$P^{overall}$=0.040
Unrelated Allogeneic	n=846	n=31	n=523	n=368	
Death		0.86 (0.56-1.33)	0.96 (0.84-1.09)	1.04 (0.89-1.21)	
		(p=0.496)	(p=0.502)	(p=0.621)	$P^{overall}$=0.683
Treatment failure		0.91 (0.60-1.38)	0.93 (0.82-1.06)	0.99 (0.86-1.15)	
		(p=0.652)	(p=0.284)	(p=0.931)	$P^{overall}$= 0.716
Relapse		1.04 (0.60-1.78)	0.82 (0.68-0.99)	0.76 (0.60-0.96)	
		(p=0.893)	(p=0.044)	(p=0.022)	$P^{overall}$= 0.059
TRM		0.85 (0.44-1.66)	1.03 (0.86-1.24)	1.16 (0.96-1.41)	

HCT Type	Normal	Underweight	Overweight	Obese	Overall P-value
		(p=0.635)	(p=0.712)	(p=0.129)	$p_{overall}$=0.439

Abbreviations: -- = not done due to insufficient number of pts; treatment failure = death or recurrence of disease; TRM = treatment related mortality