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Transplant Center Characteristics And Survival After Allogeneic Hematopoietic Cell Transplantation In Adults

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Abstract

Allogeneic hematopoietic cell transplantation (alloHCT) is a highly specialized procedure. We surveyed adult transplant centers in the United States (US) and then used data reported to the Center for International Blood and Marrow Transplant Research (CIBMTR) (2008–2010) to evaluate associations of center volume, infrastructure, and care delivery models with survival post

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AUTHOR CONTRIBUTIONS

Study concept and design: All authors
Acquisition, analysis, or interpretation of data: All authors
Drafting of manuscript: Majhail, Mau, Le-Rademacher
Critical revision of manuscript for important intellectual content: All authors
Statistical analysis: Mau, Chitphakdithai, Le-Rademacher, Logan
Administrative, technical or material support: Majhail, Mau, Denzen
Study supervision: Majhail

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alloHCT. Based on their 2010 alloHCT volume, centers were categorized as low-volume (≤40 alloHCTs; N=42 centers, 1,900 recipients) or high-volume (>40 alloHCTs; N=41 centers, 9,637 recipients). 100-day survival was 86% (95% CI, 85–87%) in high-volume compared to 83% (95% CI, 81–85%) in low-volume centers (difference 3%; P<0.001). One-year survival was 62% (95% CI, 61–63%) and 56% (95% CI, 54–58%), respectively (difference 6%; P < 0.001). Logistic regression analyses adjusted for patient and center characteristics; alloHCT at high-volume centers (odds ratio [OR] 1.32; P<0.001) and presence of a survivorship program dedicated to HCT recipients (OR 1.23; P=0.009) were associated with favorable 1-year survival compared to low-volume centers. Similar findings were observed in a CIBMTR validation cohort (2012–2014); high-volume centers had better 1-year survival (OR 1.24, P<0.001). Among US adult transplant centers, alloHCT at high-volume centers and at centers with survivorship programs is associated with higher 1-year survival.

Keywords

Hematopoietic stem cell transplantation; Overall survival; Center factors; Care delivery models; Provider factors; Volume

INTRODUCTION

Allogeneic hematopoietic cell transplantation (alloHCT) is a highly specialized and complex but standard medical procedure for hematologic cancers and other diseases.[1] The practice of alloHCT varies among transplant centers, including variation in patient selection, transplantation regimens, supportive care practices, and the management of post-transplant complications.[2–7] Additionally, infrastructure and care delivery models differ substantially among centers.[8–11] This variation in center practices, experience and resources may influence recipient outcomes.

Few studies have examined the association of transplant center characteristics with survival after HCT.[12–16] A 1992 study from the Center for International Blood and Marrow Transplant Research (CIBMTR), an international HCT clinical outcomes registry, showed higher risk of treatment failure in centers that transplanted fewer than six patients annually.[12] A followup study in 2001 that used survey information from United States (US) transplant centers and their patient outcomes data showed that clinical severity of patients and physician case load was associated with 1-year mortality.[13] Retrospective studies from Europe have also suggested an association between center volume and alloHCT survival.[14, 15] We conducted a study to examine the association of center characteristics with alloHCT outcomes in a period during which substantive changes in indications and practice and advances in transplantation techniques and supportive care have occurred.[1, 17, 18] The utilization of this procedure is increasing due to expanding indications, transplantation in older patients, and the routine use of alternative donors. Furthermore in the current era, all US centers must report outcome data on their alloHCT procedures to the CIBMTR. Hence, we surveyed adult HCT centers in the US and then used their patient data reported to the CIBMTR to evaluate associations of center volume, infrastructure, personnel and care delivery models with survival after alloHCT.

METHODS

Data Source

US transplant centers were identified from the CIBMTR.[1] Centers contribute detailed data on consecutive HCTs to a Statistical Center at the Medical College of Wisconsin in Milwaukee and the National Marrow Donor Program (NMDP) in Minneapolis. Patients are followed longitudinally with yearly follow-up. Computerized checks for errors, physician review of submitted data, and on-site audits of participating centers ensure data quality. The CIBMTR also administers the Stem Cell Therapeutic Outcomes Database, a component of the C.W. Bill Young Transplantation Program, through a contract with the Health Resources and Services Administration.[19] Under the purview of this law, transplant centers in the US are required to report data for all alloHCT recipients to the CIBMTR, including complete followup through 1-year post-transplantation. The CIBMTR performs an annual center-specific survival analysis (CSA) and reports risk-adjusted 1-year survival for first alloHCT for each center.[20, 21] Observational studies by the CIBMTR are performed in compliance with the Privacy Rule (HIPAA) as a Public Health Authority and with all applicable federal regulations pertaining to the protection of human research participants as determined by continuous review of the Institutional Review Board (IRB) of the NMDP.

Transplant Center Survey

The development, administration and results of the US HCT center survey were reported previously.[8] Briefly, a 42-item web-based instrument directed towards transplant center medical directors was administered in 2012. The survey inquired about four broad domains of center characteristics: (1) Physician and healthcare provider characteristics (number of transplant physicians and advanced practice providers (APPs), nurse staffing ratio, and other personnel); (2) Transplant unit structure and resources (inpatient and outpatient facilities, stem cell processing facilities, Foundation for the Accreditation of Cellular Therapies (FACT) accreditation status, emergency call structure, and enrollment of patients on clinical trials); (3) Care delivery structure and models (composition of inpatient and outpatient clinical teams and models of care, critical care support, and transition of care); and (4) Medical center characteristics (center location, teaching status, hospital size, National Cancer Institute Comprehensive Cancer Center (NCI CCC) designation, and patient population treated). The survey was conducted under guidance of the NMDP IRB.

We identified 115 centers that had reported alloHCT data primarily on adult patients (age ≥18 years at transplantation) at the time of survey administration, among which seven were deemed ineligible (inactive at time of survey administration [N=1] or reported no alloHCT in the preceding three years [N=6]). Overall, 85/108 eligible centers responded (response rate 79%).

Patient Data

Patient clinical and outcomes information were obtained from the 2012 CSA dataset that includes first alloHCT recipients at US centers transplanted between January 2008 and December 2010. Two centers that responded to the survey had submitted incomplete patient data to the CIBMTR and were excluded. The remaining 83 centers included in the analysis

had reported data on 11,634 first alloHCT recipients during the three-year time period. The analysis considered patients who died within the first 12 months or who were alive with ≥11 months of follow-up; 97 patients who were alive with <11 months of follow up were excluded.[20] Thus, our final analysis consisted of center characteristics information on 83 transplant centers and patient data on 11,537 recipients.

Statistical Analysis

Descriptive analyses using Fisher's or Chi-square tests for categorical variables and T-tests for continuous variables were conducted to determine the distribution of patient and center characteristics. The primary outcomes for our study were overall survival at 100-days and at 1-year after transplantation. Survival was estimated from the date of transplantation. Kaplan Meier method was used to estimate survival probabilities at 100-day and at 1-year.

Random effect logistic regression models were used to identify center and provider characteristics associated with 100-day and 1-year survival. Of note, since the primary endpoints were survival at fixed time points (100-day and 1-year post transplant, with complete follow-up on all patients out to each time point), logistic regression was used rather than a time-to-event Cox model. To minimize the confounding effects between center case mix and center- and provider-level characteristics, all regression models included patient-level characteristics using the same set of patient-level variables considered for the risk adjustment in the 2012 CIBMTR center-specific analysis (the methodology for the CSA was described previously.[20]) These variables included recipient age group, recipient race, Karnofsky performance score, disease group, chemotherapy sensitivity (non-Hodgkin lymphoma and Hodgkin lymphoma only), recipient cytomegalovirus status, time from diagnosis to transplant for acute leukemia, donor type, graft type, HLA match (bone marrow and peripheral blood stem cell grafts only), intensity of conditioning regimen, donor age group at transplant (unrelated donor only), donor/recipient sex match (bone marrow and peripheral blood stem cell donors only), prior autologous transplant, HCT comorbidity index score group,[22] and year of transplantation. All variables used in the CSA (listed above) except for year of transplantation were deemed clinically important and were included in the models regardless of statistical significance. Transplant year was included only in the model for 100-day survival, where it reached statistical significance.

The effects of all center characteristics were evaluated one at a time as well as in the presence of other center characteristics to minimize the effect of multicollinearity due to high correlation between some center characteristics. As annual center transplant activity can vary, to provide a simple categorization for center volume, we classified transplant centers based on their overall alloHCT activity reported during the last year of the CSA dataset used for our analysis (i.e., calendar year 2010). Of note, there was good correlation between center alloHCT volume over the entire 3-year period and their volume in 2010 (R=0.96). Without knowledge of a transplant volume cut-point associated with survival, we evaluated categories of several sizes and ultimately a dichotomous categorization of 40 alloHCT/year was determined the optimal cut-point using the maximum likelihood approach based on 1-year survival.[23] Coincidentally, this cut-point was close to the median number of alloHCT reported by surveyed centers in 2010 (median 39). Furthermore, we confirmed the

cut-point by reviewing a spline fit of the effect of alloHCT volume on 1-year survival. During the 2008–2010 time period, 1,900 patients received HCT at centers reporting ≤40 alloHCT in 2010 ('low-volume'; N=42 centers), while 9,637 recipients were reported by centers with >40 alloHCT ('high-volume'; N=41 centers). All logistic regression models included random effects for transplant center to account for potential correlation of outcome among patients within the same center.

Our analysis revealed an association between center volume and survival (see Results). To specifically validate this finding, we evaluated the effect of center volume on 1-year survival in a subsequent cohort of patients reported by adult transplant centers that were included in the 2016 CSA dataset (first alloHCT reported between 2012 and 2014). Centers were considered irrespective of whether they had been included in the initial analysis (N=107 centers, 14,659 alloHCT recipients), and centers were categorized using the same volume threshold (≤40 vs. >40 alloHCT in 2014). Logistic regression analysis for 1-year overall survival was performed adjusting for patient characteristics that were considered in the 2016 CSA and including random effects for transplant center.

Analyses were conducted using the SAS statistical software (SAS Institute, Cary, NC). All P-values reported are two sided and a P-value of <0.05 was considered significant.

RESULTS

Center Characteristics

As noted in Methods, 79% of the 108 eligible centers responded to our survey. Compared to responding centers, non-responding centers reported lower total HCT activity in 2010 (median 46 vs. 101 for responding centers [P<0.01]) and had lower 1-year survival for their alloHCT recipients (56%, vs. 62% for responding centers [P<0.01]). Table 1 provides characteristics of 83 centers included in the analysis. Resources, personnel, and models of inpatient and outpatient care delivery and discharge practices addressed by the survey varied among centers in both categories.

Patient Characteristics

Table 2 describes characteristics of patients who received alloHCT from 2008–2010 at the 83 transplant centers included in the analysis. Although statistically significant differences were observed in the distribution of several recipient characteristics, in general these differences were small. The characteristics of patients treated at low- and high-volume centers were mostly similar.

Center Characteristics and Patient Survival

Table 3 presents results of univariate analysis for 1-year survival for each center characteristic. Table 4 describes the results of random effect logistic regression models evaluating the associations of center characteristics with 100-day and 1-year overall survival. For the 100-day model, only center volume was found to be significantly associated with the outcome; the odds of survival were 41% higher in patients who received alloHCT at high-volume compared to low-volume centers (odds ratio 1.41; 95% CI, 1.16–1.72; P <0.001).

Center volume was also associated with 1-year survival with 32% higher odds of survival among patients transplanted at high-volume centers (odds ratio 1.32; 95% CI, 1.13–1.55; P <0.001). Among other center characteristics tested in the model (see Table 1), the only factor significantly associated with 1-year survival was the presence of a dedicated survivorship program for HCT recipients (odds ratio 1.23; 95% CI, 1.05–1.43; P=0.009). The standard deviation (SD) of the random center effect in this model was 0.24, indicating that a 1 SD increase in the residual center effect corresponds to an odds ratio for 1 year survival of 1.27, similar in magnitude to the effect of high-volume center or of presence of a dedicated survivorship program.

Figure 1A describes the effect of center volume on 1-year survival. The survival probability at 100-days was 86% (95% confidence intervals [CI], 85–87%) for patients transplanted at high volume centers compared to 83% (95% CI, 81–85%) for patients who received HCT at low volume centers (survival difference = 3%; 95% CI, 1–5%; P <0.001). The unadjusted survival probability at 1-year for the two center categories was 62% (95% CI, 61–63%) and 56% (95% CI, 54–58%), respectively (survival difference 6% [95% CI, 3–9%], P<0.001). We performed additional analyses to evaluate center size as deciles of center volume which confirmed the association with 1-year survival and validated our cutpoint of 40 alloHCT for classifying centers as low- and high-volume (Figure 1B). Figure 1C highlights center level variation in 1-year survival based on center volume.

Validation Analysis

A similar association between center volume and 1-year survival was observed in a cohort of alloHCT recipients reported by adult transplant centers from 2012–2014 (Figure 1D). In random effect logistic regression analysis, patients transplanted at centers that performed >40 alloHCT in 2014 had higher odds of 1-year survival (odds ratio 1.27 [95% CI, 1.10–1.46], P<0.001 compared to low-volume centers); 1-year survival was 68% (95% CI, 67–68%) and 65% (95% CI, 64–67%), respectively (P=0.017). Of note, the general better survival in the more recent validation cohort was not surprising since improvement in outcomes of alloHCT over time has been well described.[17, 24, 25].

DISCUSSION

Among alloHCT recipients transplanted at adult transplant centers in the US, center volume was associated with 100-day and 1-year survival. In addition, the presence of a survivorship program dedicated to HCT recipients was associated with 1-year survival. We did not identify an association between survival and other physician and healthcare provider characteristics, transplant unit structure and resources, care delivery structure and models, or medical center characteristics included in our survey.

A variety of provider and hospital factors have been investigated as potential modulators of quality of health care, though most research has focused on the volume-outcome relationship.[26–29] Studies generally suggest that higher provider and hospital volumes are associated with better outcomes for specific surgical procedures and medical conditions.[28, 30–34] However, the mechanisms of the volume-outcome relationship are not fully understood, and volume may serve as a proxy for structural factors and quality measures.

[35, 36] We designed our study to address this limitation of existing research in the context of alloHCT. Similar to prior studies,[12–14, 37] we identified center volume as a significant predictor for survival. However, we were not able to identify specific center structural factors and care delivery models besides the availability of a survivorship program that may explain this association.

The interpretation and implications of our findings have to be considered in the context of the complexity of center volume-survival relationship. For example, should the threshold for alloHCT volume identified in our analysis be the basis for transplant center accreditation (e.g., by FACT/JACIE)? We caution against using our threshold as a benchmark for qualifying individual centers on survival for several reasons. First, the cut point of >40 alloHCT/year is a statistical threshold based on the aggregate dataset that was used for analysis. The magnitude of survival difference between the two center volume categories was relatively small and there was variation in 1-year alloHCT survival among centers. Not all low volume programs had suboptimal survival and vice versa. We queried centers on a comprehensive list of center characteristics, however, we may not have captured nuances such as team interactions, allocation of resources, institutional support, patient care priorities, center expertise and experience, catchment area characteristics and referral and clinical practice patterns that may affect outcomes. Furthermore, we did not have information on patient related variables such as socioeconomic status and distance of residence from the transplant center which have been shown to be associated with alloHCT outcomes.[38, 39] There are patient-related issues that need to be considered in any policy discussions about limiting and centralizing transplant care to selected centers (e.g., by volume) given the potential to accentuate healthcare disparities and limit access.[39, 40] The other question that can be raised is whether volume reflects the expertise to provide care for more complex transplant patients. For example in one study, 1- and 3-year survival for autologous transplantation was higher in centers that also performed alloHCT.[37] Overall, our study emphasizes the need for continued exploration of the volume-survival relationship for alloHCT – to better identify factors that drive this association so that relevant best-practices can be translated to centers that are low-volume or have suboptimal survival and to inform policy decisions that can balance patient access with care at centers with optimal survival.

Our findings should encourage centers to dedicate resources towards setting up programs that focus on health maintenance, preventive care and followup of alloHCT recipients. Several barriers to care after patients are discharged from the transplant center (typically around day 100 after HCT) have been described, and coordinated survivorship care may enhance long-term patient outcomes beyond 1 year after transplantation.[11, 41, 42] We acknowledge that presence of survivorship clinic may be a surrogate for other center resources and characteristics that were not captured on our survey. We also recognize the variability in the organization of survivorship clinics that currently exist at transplant centers and optimizing care models for HCT survivors is an area of active research.[43, 44] Centers can use guidelines for long-term followup and tools such as treatment summary and survivorship care plans to establish a foundation for coordinated patient-centric survivorship care.[44–48]

Our study has the limitations of an observational registry based analysis. In addition, we did not take into account autologous HCT experience and volumes, since reporting of

autologous HCT activity is voluntary and is not included in the annual center survival analysis. However, we did find good correlation between alloHCT and total transplant volume for included centers. We developed our survey using a systematic process that included qualitative feedback from center medical directors;[8] however, we recognize that a survey cannot completely capture the complexity of transplant center structure, resources and experience. We did not include pediatric centers in our analysis since their practice of transplantation and center resources are substantially different from adult centers. We did not find an association between center accreditation and outcomes that has been previously described,[14, 16] possibly because nearly all centers included in our analysis were FACT accredited. Since the CSA dataset only included information on overall survival, we are not able to describe causes of death, relapse and complications.

In summary, our study validates the association of alloHCT volume and center survival and highlights the value of a dedicated program for coordinating the care of HCT survivors. Additional research is being planned using qualitative methods to better understand transplant center characteristics that may explain the volume-outcome relationship that we have demonstrated, especially focusing on characteristics that may be generalizable and transferable to centers with the aim of improving alloHCT outcomes across the board.

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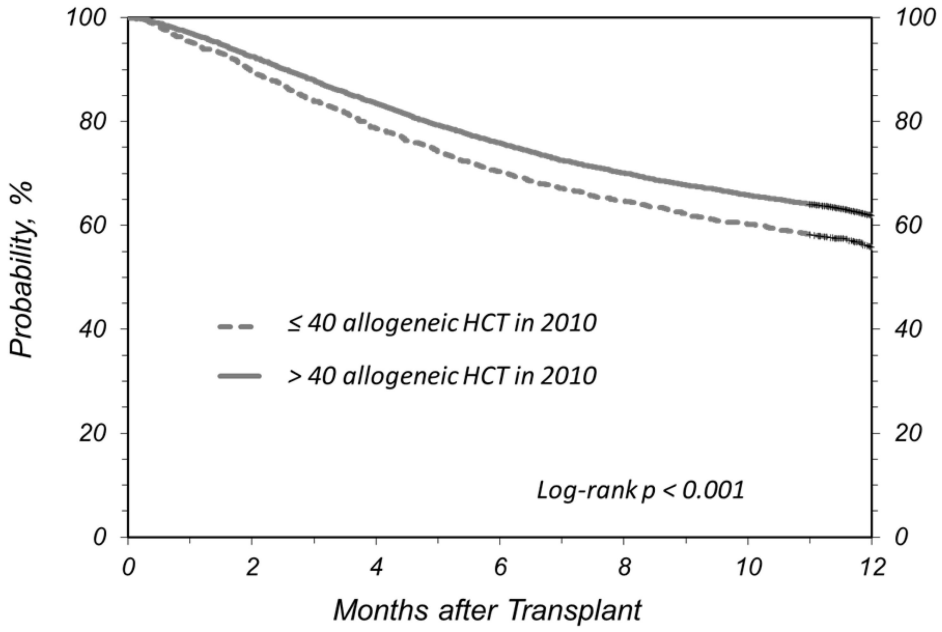
(A)



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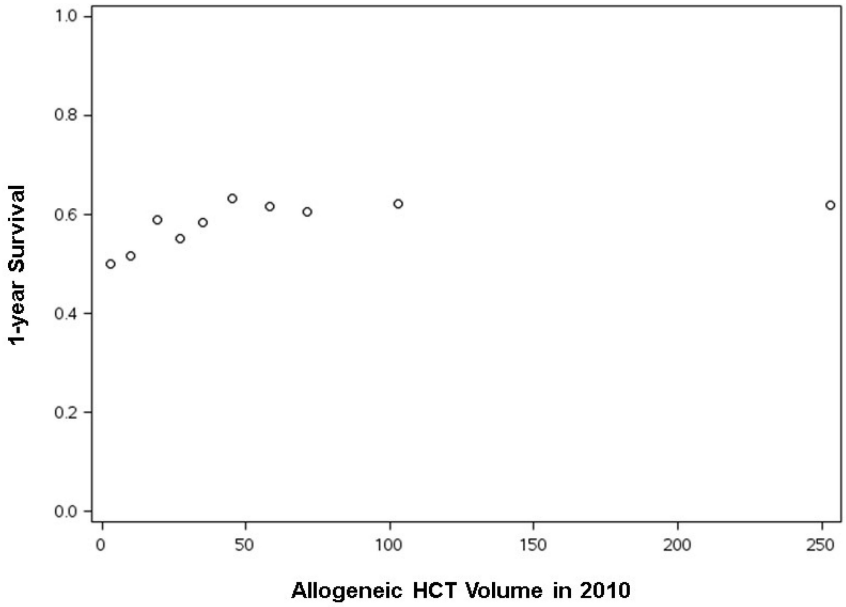

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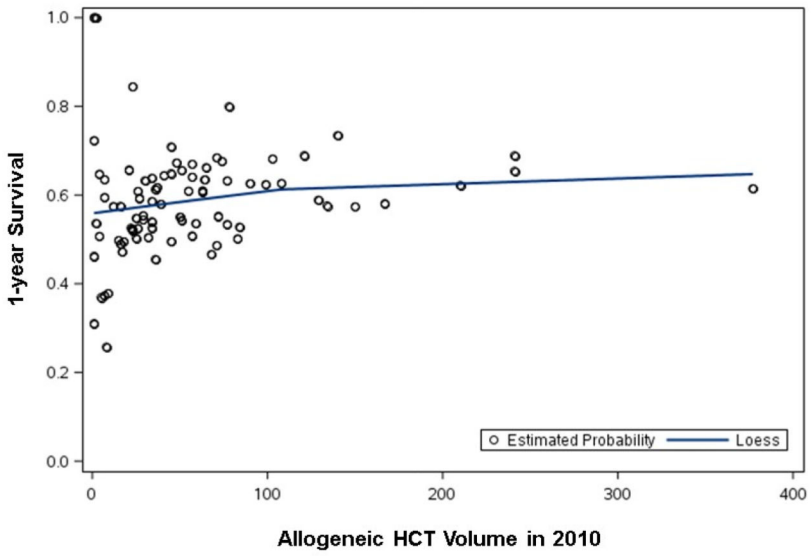

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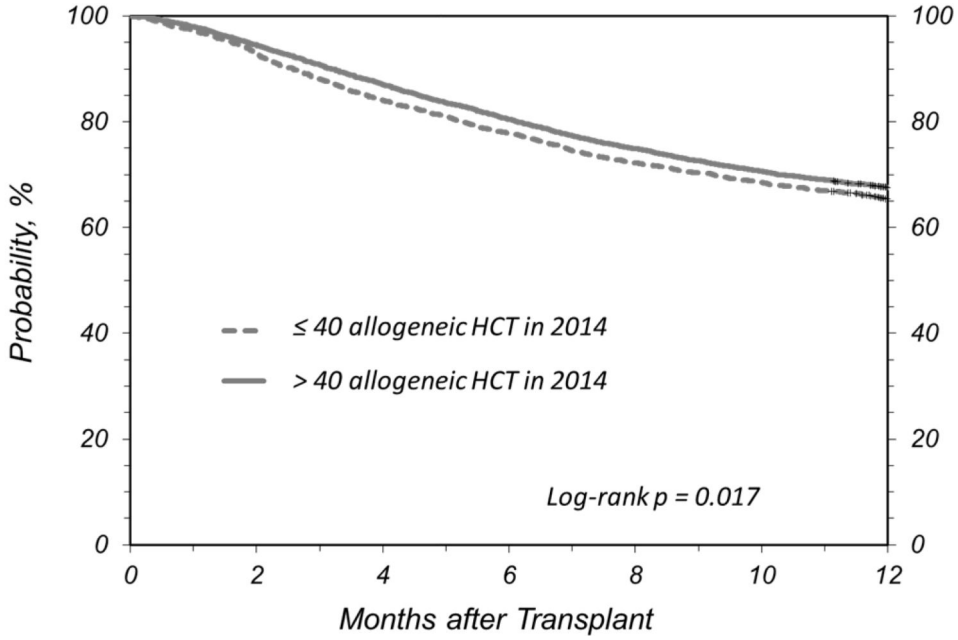

Figure 1:

(a) Unadjusted survival probability by transplant center volume for alloHCT reported by adult transplant centers to the CIBMTR between 2008 and 2010 (categories based on alloHCT performed in 2010), (b) Adjusted probability of 1-year survival by deciles of transplant center alloHCT volume reported to the CIBMTR between 2008 and 2010, (c) Scatter plot of adjusted probability of 1-year survival and transplant center alloHCT volume reported to the CIBMTR between 2008 and 2010 (the line represents the LOESS smoothing function applied to the scatterplot), and (d) Validation analysis showing unadjusted survival

probability by center volume for alloHCT reported by adult transplant centers to the CIBMTR between 2012 and 2014 (categories based on alloHCT performed in 2014)

Table 1:

Center characteristics

Characteristic	Center volume*		
	≤ 40 alloHCT N (%)	> 40 alloHCT N (%)	P-Value
Number of centers	42	41	
Affiliation with teaching hospital			0.020
No	12 (28.6)	3 (7.3)	
Yes	30 (71.4)	38 (92.7)	
Ownership status			0.214
Government	14 (33.3)	8 (19.5)	
Private	28 (66.7)	33 (80.5)	
Hospital size (inpatient beds)			0.043
<500	18 (42.9)	12 (29.3)	
500–999	19 (45.2)	23 (56.1)	
≥1000	5 (11.9)	6 (14.6)	
NCI Comprehensive Cancer Center			0.001
No	31 (73.8)	15 (36.6)	
Yes	11 (26.2)	26 (63.4)	
EHR in inpatient and/or outpatient area			0.676
No	4 (9.5)	2 (4.9)	
Yes	38 (90.5)	39 (95.1)	
Inpatient beds exclusively dedicated to HCT			0.324
No	3 (7.1)	3 (7.3)	
Yes	39 (92.9)	38 (92.7)	
Separate outpatient clinic for HCT patients			0.359
No	17 (40.5)	12 (29.3)	
Yes	25 (59.5)	29 (70.7)	
Stem cell processing lab on site/campus			0.156
No	7 (16.7)	2 (4.9)	
Yes	35 (83.3)	39 (95.1)	
FACT accreditation for allogeneic HCT			0.055
No	5 (11.9)	0	
Yes	37 (88.1)	41 (100.0)	
Participation in cooperative group clinical trials			0.007
No	12 (28.6)	2 (4.9)	
Yes	30 (71.4)	39 (95.1)	

Characteristic	Center volume*		
	≤ 40 alloHCT N (%)	> 40 alloHCT N (%)	P-Value
Patients enrolled on IRB approved protocols			0.016
None	4 (9.5)	0	
<25%	20 (47.6)	14 (34.2)	
25–49%	7 (16.7)	18 (43.9)	
≥50%	11 (26.2)	9 (22.0)	
Affiliated with hematology-oncology fellowship program			0.006
No	14 (33.3)	3 (7.3)	
Yes	28 (66.7)	38 (92.7)	
Long-term follow-up or survivorship program			0.359
No	30 (71.4)	25 (61.0)	
Yes	12 (28.6)	16 (39.0)	
Graft-versus-host disease clinic			0.049
No	38 (90.5)	30 (73.2)	
Yes	4 (9.5)	11 (26.8)	
Average inpatient nurse-patient ratio			0.048
≤1:2	15 (35.7)	5 (12.2)	
1:3	22 (52.4)	29 (70.7)	
≥1:4	5 (11.9)	7 (17.1)	
FTE transplant clinical coordinators			<0.001
≤1	8 (19.1)	1 (2.4)	
2–3	28 (66.7)	8 (19.5)	
4–6	6 (14.3)	23 (56.1)	
≥7	0	9 (22.0)	
FTE pharmacists			<0.001
≤1	27 (64.3)	7 (17.1)	
2–3	14 (33.3)	26 (63.4)	
≥4	1 (2.4)	8 (19.5)	
FTE psychosocial clinicians			<0.001
≤1	26 (61.9)	5 (12.2)	
2–3	16 (38.1)	28 (68.3)	
≥4	0	8 (19.5)	
Median number of attending physicians (IQR)	4 (3–5)	8 (6–12)	
Median number of APPs (IQR)	2 (1–5)	8 (5–14)	
Clinical effort of majority of HCT physicians			0.007
See HCT patients only	7 (16.7)	14 (34.2)	

Characteristic	Center volume*		
	≤ 40 alloHCT N (%)	> 40 alloHCT N (%)	P-Value
See HCT and hematologic oncology patients	28 (66.7)	27 (65.9)	
See HCT and general oncology patients	7 (16.7)	0	
Provider responsible for after hour calls			0.652
Attending physician	23 (54.8)	27 (65.9)	
Fellow	14 (33.3)	10 (24.4)	
Other providers (e.g., hospitalists, APPs)	5 (11.9)	4 (9.8)	
Primary team for patients on ventilator			0.700
HCT team	3 (7.1)	4 (9.8)	
Critical care team	15 (35.7)	11 (26.8)	
Co-managed by HCT and critical care teams	24 (57.1)	26 (63.4)	
Primary unit for ventilator patients			0.183
HCT unit	6 (14.3)	11 (26.8)	
Critical care unit	36 (85.7)	30 (73.2)	
Physician care model in first 100 days			0.013
Same physician inpatient and outpatient	10 (23.8)	1 (2.4)	
>1 physician inpatient and same outpatient	22 (52.4)	29 (70.7)	
>1 physician inpatient and outpatient	10 (23.8)	11 (26.8)	
Outpatient care model till day 100 for most patients			0.133
Seen by attending physician	24 (57.1)	23 (56.1)	
Seen by APPs and staffed with physician	18 (42.9)	14 (34.2)	
Seen by APPs independently	0	4 (9.8)	
Discharge practice for most patients without complications			0.712
Varies from provider to provider	25 (59.5)	25 (61.0)	
Co-followed with referring oncologist	8 (19.1)	10 (24.4)	
Patients are not discharged from transplant center	9 (21.4)	6 (14.6)	

Abbreviations: HCT – hematopoietic cell transplantation; NCI – National Cancer Institute; EHR – electronic health record; FACT: Foundation for the Accreditation of Cellular Therapy; IRB – Institutional Review Board; IQR – interquartile range; APPs – advanced practice providers; FTE – full time equivalent

*Based on allogeneic hematopoietic cell transplant volume reported to the CIBMTR in 2010

Table 2.

Characteristics of adult allogeneic hematopoietic cell transplantation recipients from centers that responded to the survey

Characteristic	Center size*		P-value
	≤ 40 alloHCT N (%)	> 40 alloHCT N (%)	
Number of centers	42	41	
Number of recipients	1900	9637	
Recipient age group			0.457
< 40 years	466 (24.6)	2236 (23.2)	
40 to 59 years	961 (50.6)	4946 (51.3)	
≥ 60 years	473 (24.9)	2455 (25.5)	
Recipient race			<0.001
Non-Hispanic White	1501 (79.0)	7828 (81.2)	
Hispanic	170 (9.0)	769 (8.0)	
Black/African American	166 (8.7)	524 (5.4)	
Other	63 (3.3)	516 (5.4)	
Karnofsky performance score			<0.001
90 to 100	1120 (59.0)	5972 (62.0)	
<90	732 (38.5)	3173 (32.9)	
Unknown	48 (2.5)	492 (5.1)	
Diagnosis			
Acute myeloid leukemia	762 (40.1)	3572 (37.1)	
Acute lymphoblastic leukemia	248 (13.1)	1114 (11.6)	
Chronic myeloid leukemia	85 (3.6)	366 (3.8)	
Chronic lymphocytic leukemia	86 (4.5)	598 (6.2)	
Other leukemia	12 (<1)	96 (1.0)	
Myelodysplastic syndromes	224 (11.8)	1093 (11.3)	
Myeloproliferative diseases	66 (3.5)	292 (3.0)	
Non-Hodgkin lymphoma	228 (12.0)	1481 (15.4)	
Hodgkin lymphoma	53 (2.8)	296 (3.1)	
Plasma cell disorders	67 (3.5)	448 (4.7)	
Other malignancy	1 (<1)	12 (<1)	
Severe aplastic anemia	57 (3.0)	208 (2.2)	
Other non-malignant diseases	11 (<1)	61 (<1)	
Donor type			<0.001
Unrelated donor	1066 (56.1)	5636 (58.5)	
Matched sibling	748 (39.4)	3331 (34.6)	
Syngeneic	18 (<1)	52 (<1)	
Other related	68 (3.6)	618 (6.4)	

Characteristic	Center size*		P-value
	≤ 40 alloHCT N (%)	> 40 alloHCT N (%)	
Graft type			0.064
Bone marrow	232 (12.2)	1310 (13.6)	
PBSC ± bone marrow	1533 (80.7)	7544 (78.3)	
Cord blood ± others	135 (7.1)	783 (8.1)	
Prior autologous transplant			0.210
No	1672 (88.0)	8379 (87.0)	
Yes	228 (12.0)	1258 (13.1)	
HCT comorbidity index score			<0.001
0	834 (43.9)	3696 (38.4)	
1–2	501 (26.4)	2710 (28.1)	
≥ 3	529 (27.8)	3010 (31.2)	
Data not collected	36 (1.9)	221 (2.3)	
Year of transplant			0.040
2008	575 (30.1)	2966 (30.8)	
2009	609 (32.1)	3316 (34.4)	
2010	716 (37.8)	3355 (34.8)	

Abbreviations: alloHCT – allogeneic hematopoietic cell transplantation; HCT – hematopoietic cell transplantation; CR – complete remission; PIF – primary induction failure; HLA – human leukocyte antigen; PBSC – peripheral blood stem cell; IQR – interquartile range

*Based on alloHCT volume reported to the CIBMTR in 2010

Table 3:

Univariate analysis of center characteristics and 1-year survival

	Centers, N	Patients, N	1-year survival, %	P-value*
Affiliation with teaching hospital				0.724
No	15	807	60.7	
Yes	68	10730	61.0	
Ownership status				0.580
Government	22	2748	59.3	
Private	61	8789	61.5	
Hospital size (inpatient beds)				0.624
<500	30	3705	63.0	
500–999	42	6240	60.4	
≥1000	11	1592	58.4	
NCI Comprehensive Cancer Center				0.295
No	46	3731	59.2	
Yes	37	7806	61.8	
EHR in inpatient and/or outpatient area				0.725
No	6	477	60.2	
Yes	77	11060	61.0	
Inpatient beds exclusively dedicated to HCT				0.327
No	6	473	56.7	
Yes	77	11064	61.2	
Separate outpatient clinic for HCT patients				0.581
No	29	2752	60.2	
Yes	54	8785	61.2	
Stem cell processing lab on site/campus				0.852
No	9	641	61.5	
Yes	74	10896	60.9	
FACT accreditation for allogeneic HCT				0.766
No	5	93	58.1	
Yes	78	11444	61.0	
Participation in cooperative group clinical trials				0.832
No	14	538	60.4	
Yes	69	10999	61.0	
Patients enrolled on IRB approved protocols				0.471
None	4	120	52.5	
<25%	34	2895	60.7	

	Centers, N	Patients, N	1-year survival, %	P-value*
25–49%	25	5274	60.6	
≥50%	20	3248	62.1	
Affiliated with hematology-oncology fellowship program				0.994
No	17	893	61.9	
Yes	66	10644	60.9	
Long-term follow-up or survivorship program				0.005
No	55	5941	58.0	
Yes	28	5596	64.1	
Graft-versus-host disease clinic				0.013
No	68	7577	59.4	
Yes	15	3960	64.0	
Average inpatient nurse-patient ratio				0.247
≤1:2	20	1520	62.7	
1:3	51	7833	61.7	
≥1:4	12	2184	57.1	
FTE transplant clinical coordinators				0.034
≤1	9	302	64.9	
2–3	36	2385	56.3	
4–6	29	5561	62.4	
≥7	9	3289	61.5	
FTE pharmacists				0.048
≤1	34	2123	57.2	
2–3	40	6440	61.1	
≥4	9	2974	63.4	
FTE psychosocial clinicians				0.011
≤1	31	1656	56.3	
2–3	44	6284	60.3	
≥4	8	3597	64.4	
Clinical effort of majority of HCT physicians				0.220
See HCT patients only	21	4912	62.4	
See HCT and hematologic oncology patients	55	6475	60.0	
See HCT and general oncology patients	7	150	52.7	
Provider responsible for after hour calls				0.090
Attending physician	50	7485	62.4	
Fellow	24	2691	58.6	
Other providers (e.g., hospitalists, APPs)	9	1361	58.1	

	Centers, N	Patients, N	1-year survival, %	P-value*
Primary team for patients on ventilator				0.448
HCT team	7	970	56.0	
Critical care team	26	3042	60.5	
Co-managed by HCT and critical care teams	50	7525	61.8	
Primary unit for ventilator patients				0.563
HCT unit	17	3228	59.4	
Critical care unit	66	8309	61.6	
Physician care model in first 100 days				0.546
Same physician inpatient and outpatient	11	344	56.0	
>1 physician inpatient and same outpatient	51	7699	60.0	
>1 physician inpatient and outpatient	21	3494	63.4	
Outpatient care model till day 100 for most patients				0.236
Seen by attending physician	47	5907	59.7	
Seen by APPs and staffed with physician	32	4929	62.2	
Seen by APPs independently	4	701	63.3	
Discharge practice for most patients without complications				0.383
Varies from provider to provider	50	7474	61.2	
Co-followed with referring oncologist	18	2873	61.9	
Patients are not discharged from transplant center	15	1190	57.2	

Abbreviations: alloHCT – allogeneic hematopoietic cell transplantation; HCT – hematopoietic cell transplantation; NCI – National Cancer Institute; EHR – electronic health record; FACT: Foundation for the Accreditation of Cellular Therapy; IRB – Institutional Review Board; FTE – full time equivalent

*P-value for univariate random effect logistic regression analysis

Table 4.

Center characteristics associated with 100-day and 1-year overall survival on multivariable analysis

Characteristic	N		Odds Ratio*† (95% CI)	P-value
	Patients	Centers		
100-day survival				
Center volume				
≤ 40 alloHCT in 2010	1900	42	1	
> 40 alloHCT in 2010	9637	41	1.41 (1.16–1.72)	<0.001
1-year survival				
Center volume				
≤ 40 alloHCT in 2010	1900	42	1	
> 40 alloHCT in 2010	9637	41	1.32 (1.13–1.55)	<0.001
Long-term followup/survivorship program				
No	5941	55	1	
Yes	5596	28	1.23 (1.05–1.43)	0.009

Abbreviations: alloHCT – allogeneic hematopoietic cell transplantation; CI – confidence intervals

*Odds ratio of being alive at 100-days or 1-year; odds ratio >1 indicates better odds of survival

†Adjusted for the following patient-level variables that were considered for risk-adjustment in the 2012 CIBMTR center-specific survival analysis: recipient age, recipient race/ethnicity, Karnofsky performance score at transplant, prior autologous transplant, recipient cytomegalovirus status, hematopoietic cell transplant comorbidity index score, disease stage, interval from diagnosis to transplant for acute myeloid leukemia and acute lymphoblastic leukemia, chemotherapy sensitivity for non-Hodgkin lymphoma and Hodgkin lymphoma, graft type, donor type HLA match, donor age for unrelated bone marrow or peripheral blood stem cell recipients, donor recipient sex match for bone marrow or peripheral blood stem cell recipients, conditioning regimen intensity for leukemia and year of transplant; transplant year was also included in the model for 100-day survival (additional information on variables included in the analysis is available at http://www.cibmtr.org/Meetings/Materials/CSOAForum/Pages/index.aspx)