High-Risk Centers and the Benefits for Lower-Risk Transplants

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ABSTRACT

Objectives: Allogeneic hematopoietic cell transplantation (HCT) is the transplantation of stem cells from a donor and an effective treatment for many hematologic malignancies. We sought to compare allogeneic HCT survival outcomes and hazard of death among US centers that treat higher-risk patients versus those in centers that do not perform lower-risk HCT procedures.

Study Design: We utilized 2008 to 2010 Center for International Blood and Marrow Transplant Research data. We categorized patients into 4 risk categories that align with factors shown in the literature to be associated with HCT survival. We stratified centers into those that do and do not conduct high-risk pre-transplant HCT.

Methods: To further evaluate the association between pre-transplant mortality risk and HCT survival by transplant center, we examined the association between risk category score and hazard of death using Cox proportional hazard modeling.

Results: There were 12,436 HCT recipients at 147 transplant centers. Of the 147 centers, 74 performed HCT for patients ranging from the lowest risk category to the highest category, and 73 centers performed only lower-risk HCT. Adjusting for all other factors, lower-risk patients that underwent transplants in lower- or higher-risk centers had a similar relative hazard of death ($P \leq .05$).

Conclusions: Low-risk patients had similar survival outcomes irrespective of whether they underwent transplant at higher- or lower-risk centers. Patient and payer policy implications could include initiatives that reduce travel for low-risk patients. Similarly, HCT center administrators and providers that manage higher-risk patients need not expect commensurate benefits in survival for lower-risk patients.

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Hematopoietic cell transplantation (HCT) is a complex treatment procedure for various hematologic malignancies and other conditions that are often otherwise incurable. Each year, approximately 17,000 patients receive HCTs in the United States. This number has been steadily increasing since 2000[1] due to advances in transplantation over the last several decades that have resulted in an increasing number of healthcare facilities that are more willing to perform more complex and higher-risk transplants. Although mortality is a useful measure of transplant center quality, comparing outcomes among centers is challenging if estimates do not take differences in transplant populations into account.[2,3] For instance, centers that perform transplants on a relatively larger percentage of high-risk patients with an intrinsically higher risk of mortality may be potentially perceived as poor performers compared with centers that perform transplants on a lower percentage of such patients.

Patient risk can affect overall center performance in several ways. Variation in HCT patient characteristics in centers that treat higher-risk patients could deplete human and financial resources for lower-risk patients. Alternatively, establishing processes to successfully manage high-risk patients could benefit lower-risk patients as well, thereby increasing quality and lowering the procedural mortality for all patients. There is a well-documented body of HCT literature indicating that certain patient characteristics—such as human leukocyte antigen (HLA) matching, comorbidities, age, and Karnofsky performance score—are determinants of a patient's pre-transplant risk level and survival rates.[4-18]

In this paper we explore the effects on survival for lower-risk HCT patients undergoing transplant at HCT centers that do or do not perform high-risk transplants. We hypothesized that there were demonstrably superior survival results for low- and moderate-risk patients as transplant centers continue to explore new clinical successes with higher-risk

Take-Away Points

We sought to compare allogeneic hematopoietic cell transplantation (HCT) survival outcomes and hazard of death among US centers that treat higher-risk patients versus lower-risk centers that do not. Low-risk patients had similar survival outcomes regardless of whether they had a transplant performed at higher- or lower-risk centers. HCT center administrators and managers need not expect that the performance of higher-risk HCT provides benefits in survival for lower-risk patients.

- Lower-risk patients who underwent transplants in either lower- or higher-risk centers had a similar relative hazard of death.
- There should be a reduction in policy emphasis on Centers of Excellence for lower-risk patients.
- We expect that health plans will increasingly use risk-stratified types of data to encourage lower-risk patients to restrict travel and receive comparable care at local transplant centers.

patients. Specifically, we focused on potential spillover effects and benefits of higher-risk HCT performance on the low-risk patient population within the same centers. We seek to evaluate differences in outcomes among lower-risk HCT patients by risk-stratifying centers that perform HCT in high-risk patients versus centers that do not perform high-risk HCT.

METHODS

Data Source

The data were obtained from the statistical center of the Center for International Blood and Marrow Transplant Research (CIBMTR), located at the Medical College of Wisconsin in Milwaukee, and from the National Marrow Donor Program. The CIBMTR is partially supported by Grant U24-CA76518 from the National Institutes of Health, and by the Health Resources and Services Administration (HRSA). CIBMTR is composed of a voluntary working group of more than 450 transplantation centers worldwide that contribute detailed data on consecutive HCT to its Statistical Center. In addition, the CIBMTR holds the contract for the Stem Cell Therapeutic Outcomes Database part of the C.W. Bill Young Transplantation Program from the HRSA. As part of this program, all transplant centers in the United States are mandated to report clinical outcomes data for HCT to the CIBMTR. We obtained a de-identified data set from the CIBTMR. The analysis has not been reviewed by the CIBMTR. Our study was deemed exempt from review by the Human Subjects Committee of the University of Minnesota's Institutional Review Board.

Patients

Our cohort included patients 18 years or older who received transplants between January 1, 2008, and December 31, 2010, for whom data were reported to the CIBTMR. We excluded patients missing any of the 4 risk category (RC) criteria (N = 406 patients; see below for RC derivation) and centers that reported only 1 transplant from 2008 to 2010 (N = 15 centers).

Derivation of the Patient Risk Categories

The literature indicates that several patient characteristics are clinically important to the long-term survival of HCT recipients. To determine patient risk, we chose 4 characteristics that have been consistently reported across studies to be associated with survival following HCT: age at transplant, HLA match status, Karnofsky performance score, and comorbidities.[4-17] We used binary risk indicators for the 4 patient characteristics to create a risk score for overall mortality that ranged from 0 to 4. Table 1 is a summary of characteristics included in the RCs.

Transplant recipients older than 40 years (score of 1) were considered to be higher risk than younger individuals (score of 0).[5] The Karnofsky performance status is used to determine the recipient's functional status and can range from 0 to 100. A Karnofsky performance score of 90 to 100 categorizes patients with the ability to carry on normal activity prior to transplant. CIBMTR codes Karnofsky performance score as a dichotomous variable of 90-100 (score of 0) and ≤80 (score of 1). Coexisting disease is a binary category of diseases collected by CIBMTR. CIBMTR codes HCT patients with any of 18 comorbidities as coexisting disease present (score of 1). Patients with no coexisting disease were scored as 0. The HLA match status of donors describes the degree of immunologic similarity between recipients and donors. HLA 8/8 match, well-matched unrelated, and HLA-matched HCTs were all scored as 0; any mismatched unrelated (HLA 6/8, or 7/8 matched, partially matched, or mismatched) or mismatched-related HCTs were scored as 1. Prior to consolidating related and unrelated transplant groups within our RC, we created separate RCs for each transplant group and independently verified our models for each group.

We considered patients with all 4 risk components—HLA mismatch, coexisting disease, age ≥40, and Karnofsky performance score <80—to be the highest pre-transplant risk within our analytical cohort (scored with an RC of 4). Conversely, transplant recipients with an RC score of 0—HLA match, no coexisting disease, aged <40, and Karnofsky performance score ≥90—were considered to have the lowest risk within our cohort. Patients with an RC score of 1 or 2 and 3 were considered to have moderate pre-HCT risk.

Overall survival for patients with scores of 1 and 2 were similar but different enough from a score of 3. We therefore combined scores 1 and 2 into a single group. We had a total of 4 risk groupings, including risk scores of 0, combined 1 and 2, 3, and 4. Although the data we received from CIBTMR were dichotomous and only broadly identified coexisting disease, HLA match, and Karnofsky performance score as either present or absent, we confirmed that our RCs were illustrative of distinct patient risk. Using Kaplan-Meier methods, we found that the difference in survival probability for our RCs was significant and observed distinct differences among all 4 groups (Figure 1). We tested different age cut-offs to ensure that our risk assumptions did not change our results. Given that our cut-off has been supported by the literature[6] and that using other cut-offs in age does not change the magnitude and direction of our results, we found it beneficial to classify age as a binary variable. We also tested each of the RCs independently in our models to ensure that all individual components of the risk score behaved similarly. Under all assumptions, conclusions remain unchanged.

Table 1. Summary of Characteristics Included in the Risk Categories

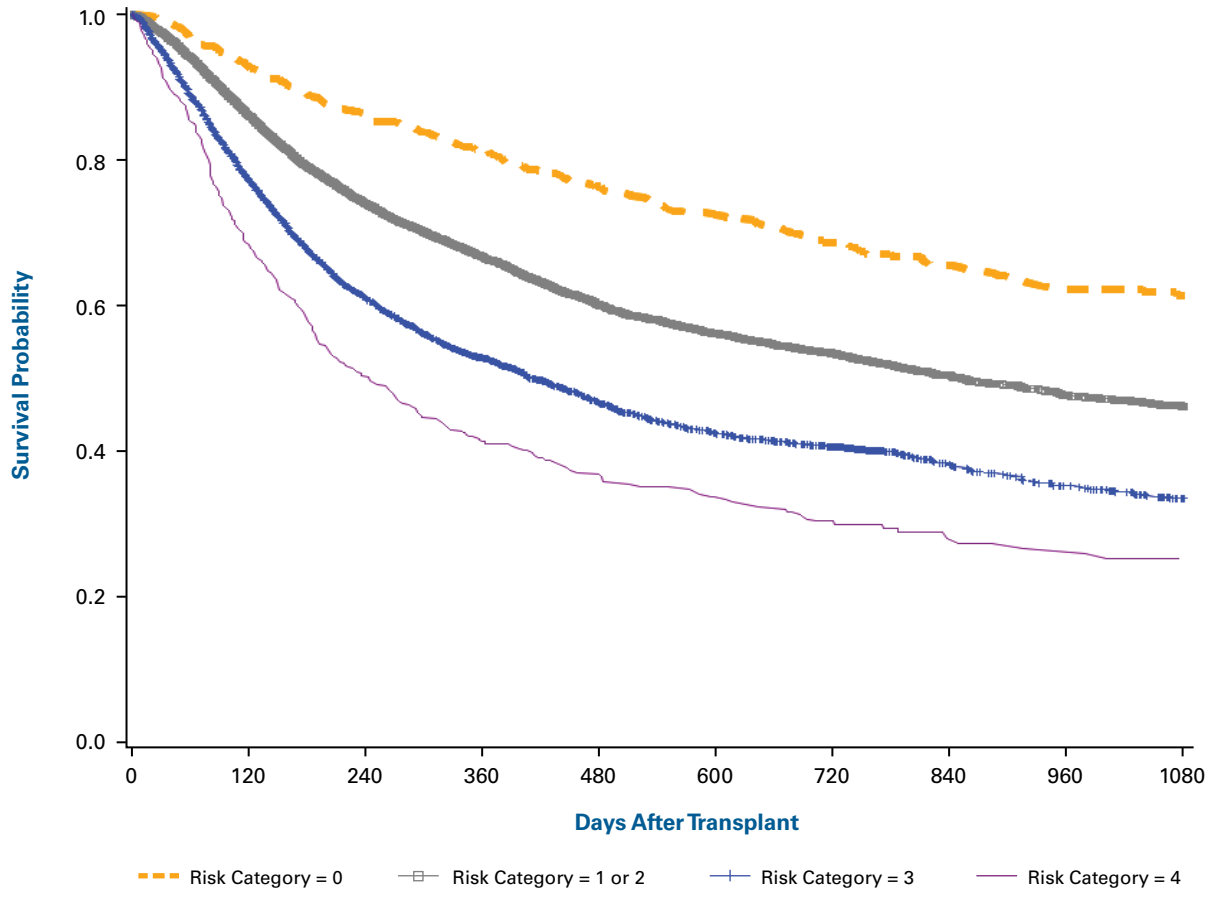
High Risk (risk category score= 4) HCT for any patients with all of the following:	Low Risk (risk category score= 0) No HCT for any patients with all of the following:
Age >40 years	
Coexisting disease	
HLA mismatch	
Karnofsky performance status score at transplant (10 to 80)	

HCT indicates hematopoietic cell transplantation; HLA, human leukocyte antigen.

Center Characteristics

Based on our pre-HCT patient risk score categories, we categorized centers into either high- or low-risk. Centers that performed HCTs with only lower-risk patients (defined as risk scores = 0-3) were considered to be low-risk centers. Of the 147 centers, 73 (N = 1984 transplants)

Figure 1. Unadjusted Kaplan Meier Overall 3-Year Mortality Estimates by Risk Categories for All Transplant Centers (2008-2010)



performed only lower-risk HCT. There were 74 high-risk centers, categorized as any center that performed HCT for patients with the highest RC score of 4 (N = 6864 transplants). We recorded other center characteristics that included a high-volume center indicator for centers conducting more than the mean number of transplants across the 3 years of observation. To adjust for possible high-risk center effects and the inclusion of unrelated donors in our cohort, a transplant center and related/unrelated donor indicator was added to all multivariate models as frailty variables. We also adjusted for region using the 10 HHS regions.

Statistical Analysis

We evaluated differences in center RCs and patient characteristics across all years. After assessing this unadjusted relationship, we evaluated the association between our RCs and 3-year hazard of death using Kaplan-Meier methods and Cox proportional hazards modeling. Kaplan-Meier methods were used to estimate unadjusted 3-year cumulative mortality across the RCs for our entire cohort, for a bifurcated cohort of centers that performed high-risk transplants, and for transplant centers that did not perform high-risk transplants within our analytical period. Three separate multivariable Cox models were used to compare the impact of pre-transplant risk factors independently for high- and low-risk centers and a combined model for all centers. Within the overall combined model, patients from high- and low-risk centers were included together. The model adjusted for patient factors and included a bivariate high-risk center indicator (yes/no) and a higher-risk unrelated donors indicator.

In all models, we performed several sensitivity analyses to ensure that the observed effects were not a product of our RCs and modeling decisions. We compared models that included each risk component measured separately to verify that there was statistical benefit to the creation and inclusion of our risk scores. Prior to consolidating related and unrelated transplant groups within our RC, we created separate RCs for each transplant group and independently verified our models for each group. We conducted sensitivity analyses utilizing the Sorror comorbidity score, an alternative comorbidity score for HCT, which did not produce different results.[11] In addition, we restricted our analysis to the largest disease groups—acute myeloid leukemia (AML), acute lymphoblastic leukemia, non-Hodgkin lymphoma, Hodgkin lymphoma—to uncover broader trends. We created a more conservative cut-off point to define high-risk centers (eg, ≥5% high-risk patients treated) to ensure that we discovered no changes in our findings. We also conducted separate survival analyses with the use of hierarchical linear models to verify that accounting for transplant recipients being nested in centers did not produce results of different magnitude or direction. Under all assumptions, conclusions remain unchanged. SAS version 9.3 (SAS Institute, Cary, North Carolina) was used for all analyses. *P* values were 2-sided with a level of significance of ≤.05.

RESULTS

Our total cohort included 12,436 allogeneic transplants conducted in 147 centers. Over half of our patient cohort was aged 40 or older, and 36% of our cohort was determined to need special care to carry on normal activity prior to transplantation (Karnofsky performance scoring <80). Nearly 66% of our population was classified by CIBMTR to have coexisting disease prior to transplant (Table 2).

Table 2. Basic Characteristics of Related and Unrelated Transplants in High- and Low-Risk Centers (2008-2010)

Demographic Characteristics	Total All Centers	High-Risk Centers (74 centers)		Low-Risk Centers (73 centers)		
	n	n	%	n	%	*P*
Gender						
Male	7218	6049	58	1169	59	.386
Female	5218	4403	42	815	41	
Race						
Non-Hispanic white	10,230	8701	83	1529	77	<.0001
Hispanic	976	758	7	218	11	
Black	666	506	5	160	8	
Other/multiple/unknown	564	487	5	77	4	

(continued)

Table 2. Basic Characteristics of Related and Unrelated Transplants in High- and Low-Risk Centers (2008-2010) *(continued)*

Demographic Characteristics	Total All Centers	High-Risk Centers (74 centers)		Low-Risk Centers (73 centers)		
	n	n	%	n	%	*P*
Age, years						
18-29	1562	1183	11	379	19	<.0001
30-39	1392	1167	11	225	11	
40-49	2487	2095	20	392	20	
50-59	3893	3287	32	606	31	
60-69	2847	2489	24	358	18	
70+	255	231	2	24	1	
Transplant year						
2008	3764	3182	30	582	29	.422
2009	4149	3493	34	656	33	
2010	4523	4523	36	746	38	
Disease group						
Acute myelogenous leukemia and myelodysplastic disorders	6026	5101	49	925	46	<.0001
Acute lymphoblastic leukemia	1523	1229	12	294	15	
Other leukemia and myeloproliferative syndromes	1736	1496	14	240	12	
Non-Hodgkin lymphoma and Hodgkin lymphoma	2147	1830	18	344	17	
Other malignancy	565	493	5	72	4	
Severe aplastic anemia	320	248	2	72	4	
Other nonmalignant disease	92	55	1	37	2	
Coexisting disease						
Absent	4516	3564	34	952	48	<.0001
Present	7920	6888	66	1032	52	
Karnofsky score						
90-100	7997	6526	62	1471	74	<.0001
≤80	4439	3926	38	513	26	
HLA matching status						
Matched unrelated	5131	4356	76	775	80	<.0001
Mismatched unrelated	1597	1390	24	207	20	
HLA matching status						
Matched related	5176	4211	89	965	96	<.0001
Mismatched related	532	495	11	37	4	
Patients by risk category						
0	798	586	6	212	11	<.0001
1 or 2	8168	6698	64	1462	74	
3	3059	2749	26	310	16	
4	419	419	4	–	–	
Center volume (mean)						
Low-volume center (<55 transplants)	1285	436	4	849	43	
High-volume center (≥55 transplants)	11,151	10,016	96	1135	57	

HLA indicates human leukocyte antigen.
By definition, low-risk centers do not perform hematopoietic cell transplantation for patients with a risk category of 4.

Characteristics by Type of Center: Disease Groups and Volume Differences

The distribution of AML and myelodysplastic syndromes (MDS) from 2008 to 2010 represented the largest cohort of patients receiving HCT in both types of centers. In high-risk centers, 5101 (49%) of the patient population had AML and MDS while the patient population of low-risk centers had 47% of patients (N = 925) with AML and MDS (Table 2).

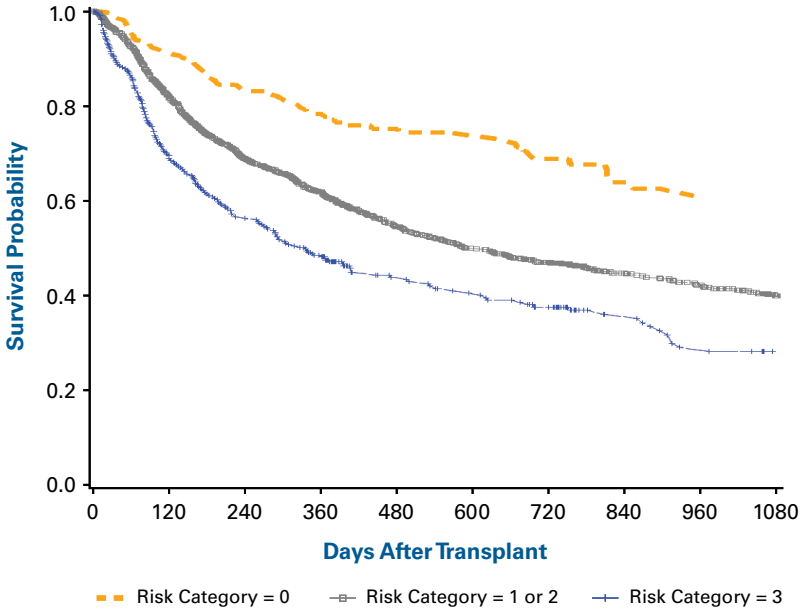
High-risk centers were generally higher-volume centers. The mean HCT volume per center performed from 2008 to 2010 was 85 transplants (range = 2-529 transplants). The mean transplant volume per center in high-risk centers was 141 transplants, while low-volume centers had a mean transplant volume per center of 27 transplants from 2008 to 2010. Higher volume in high-risk centers was not driven by high-risk patients. Instead, high-risk centers primarily focused on the lowest and moderate-risk population (RCs = 0, 1, and 2).

Association Between Risk Category and Mortality

Unadjusted Kaplan-Meier mortality estimates showed significantly higher 3-year overall mortality among patients whose RC = 4 (Figure 1). When we stratified high- and low-risk transplant centers, we found the Kaplan-Meier mortality estimates unchanged (Figure 2A and 2B). Specifically, our estimates showed that patients with RC = 0 had the lowest 3-year overall mortality, while the high-risk group (RC = 4) had significantly higher mortality. We also found similar 3-year survival results for low-risk patients in high-risk centers (62% survival probability) and low-risk patients in low-risk centers (61% survival probability).

After adjusting for race, sex, year of transplant, broad disease categories (Table 3), and region, we found that our pre-transplant risk groups were all significantly associated with higher relative hazard of death (adjusted hazard ratio [HR], 1.72 [95% CI, 1.51-1.96] for RC = 1 or 2 vs 0; adjusted HR, 2.55 [95% CI, 2.22-2.92] for RC = 3 vs 0; and adjusted HR, 3.37 [95% CI, 2.83-4.01] for RC = 4 vs 0). In all centers, race, hematological condition, and volume were all associated with 3-year relative hazard of death (P <.05 for all).

Figure 2A. Adult Unrelated and Related Overall Survival in Low-Risk Centers by Risk Category (2008-2010)



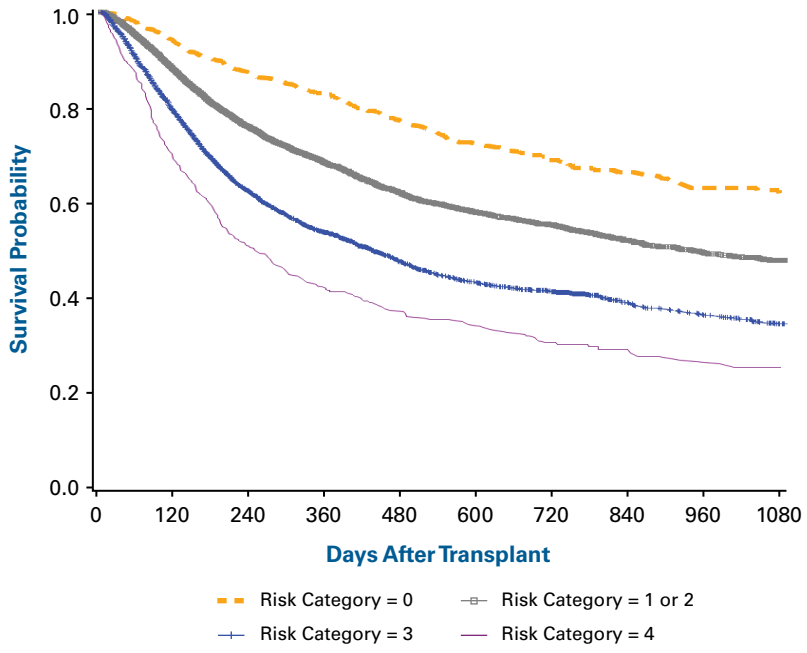
	Time 0	240 Days	365 Days	1080 Days
Risk Category = 0 Number at Risk	212	176	165	147
Survival Probability		83%	78%	61%
Risk Category = 1 or 2 Number at Risk	1462	1003	892	722
Survival Probability		69%	61%	39%
Risk Category = 3 Number at Risk	310	174	147	114
Survival Probability		56%	48%	23%

When we stratified centers by risk type, we observed similar patterns. In high-risk centers, after adjusting for race, sex, year of transplant, and broad disease categories, our pre-transplant risk groups were all significantly associated with relative hazard of death relative to risk score = 0 (adjusted HR, 1.6 [95% CI, 1.40-1.90] for RC = 1 or 2 vs 0; adjusted HR, 2.46 [95% CI, 2.11-2.88] for RC = 3 vs 0; and adjusted HR, 3.2 [95% CI, 2.67-3.90] for RC = 4 vs 0).

In our cohort of lower-risk centers, after adjusting for race, sex, year of transplant, and broad disease categories, we found that our pre-transplant risk groups were all significantly associated with higher relative hazard of death (adjusted HR, 1.97 [95% CI, 1.52-2.55] for RC = 1 or 2 vs 0; adjusted HR, 2.77 [95% CI, 2.07-3.70] for RC = 3 vs 0).

We conducted several additional sensitivity analyses. We created a more conservative cut-off point to define high-risk center (≥5% high-risk patients treated) and test-

Figure 2B. Adult Unrelated and Related Overall Survival in High-Risk Centers by Risk Categories (2008-2010)



	Time 0	240 Days	365 Days	1080 Days
Risk Category = 0 Number at Risk	586	510	482	411
Survival Probability		87%	82%	62%
Risk Category = 1 or 2 Number at Risk	6698	5041	4533	3802
Survival Probability		75%	68%	48%
Risk Category = 3 Number at Risk	2749	1689	1462	1180
Survival Probability		61%	53%	31%
Risk Category = 4 Number at Risk	419	210	172	131
Survival Probability		50%	41%	20%

ed additional age cut-offs (aged 50+ and 55+ years). The changes had no appreciable effect on the direction or magnitude of the study's findings.

DISCUSSION

The last several decades have witnessed a remarkable expansion of HCT use both in the United States and globally. Although half of the cohort of centers we examined continue to explore new clinical successes with higher-risk patients, this does not translate to demonstrably superior results for low- and moderate-risk patients. We sought to illustrate potential center-level benefits of performing high-risk HCT for overall center performance. However, in contrast to our hypothesis, we did not find any significant differences or advantages for lower-risk patients in high-risk centers. Instead, we observed that lower-risk patients who receive transplants in low-risk centers have comparable survival outcomes to lower-risk patients who receive transplants in high-risk centers. We believe that HCT care processes have been standardized, routinized, and disseminated to the point that the learning and improvement that derives from performing higher-risk HCT volume is no longer a major factor in improving outcomes for lower-risk patients. Low-risk patients had similar survival outcomes regardless of whether they received transplants at higher- or lower-risk centers. Patient and payer policy implications could include initiatives that reduce travel for low-risk patients.

Our study builds upon previous ones that examined the implications of pre-transplant risk on overall survival. Much of the literature has focused on validating various pre-HCT risk groupings. Our RC score allowed us to stratify low- and high-risk centers and to explore differences in survival for lower-risk HCT patients. Although higher-volume centers were more likely to perform higher-risk transplants, higher-risk volume did not drive overall patient volume in higher-risk centers. Instead, our results indicate that higher-risk centers focused most of their HCT procedures on the lower-risk population. Research has previously shown that providers with more experience ("learning by doing") produce better outcomes. Although the surgical literature has shown a direct relationship between procedure volume and survival,[20-27] our results illustrate the apparent lack of any comparative advantage for low-risk patients to seek care from high-risk centers. Their mortality is similar whether they receive transplants at low- or high-risk facilities. The fact that larger, higher-volume centers appeared to be more likely to take on pre-transplant risk cannot simply be a product of clinical expertise for all HCT. If

Table 3. Factors Associated with 3-Year Relative Hazard of Death Among HCT Patients by Center Category, Cox Proportional Hazard Models, Hazard Ratio, 95% CI

	Model 1: All Centers		Model 2: High-Risk Centers Only		Model 3: Low-Risk Centers Only	
Characteristics	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***	**HR (95% CI)**	***P***
Risk categories						
0	Referent		Referent		Referent	
1 or 2	1.72 (1.51-1.96)	<.0001	1.63 (1.40-1.90)	<.0001	1.97 (1.52-2.55)	<.0001
3	2.55 (2.22-2.93)	<.0001	2.46 (2.11-2.88)	<.0001	2.77 (2.07-3.70)	<.0001
4	3.37 (2.84-4.01)	<.0001	3.23 (2.67-3.90)	<.0001	–	–
Gender						
Male	Referent		Referent		Referent	
Female	0.91 (0.87-0.96)	.001	0.92 (0.87-0.98)	.006	0.87 (0.76-0.99)	.04
Race						
Non-Hispanic white	Referent		Referent		Referent	
Hispanic	1.06 (0.95-1.16)	.29	1.07 (0.96-1.20)	.23	1.01 (0.81-1.24)	.97
Black	1.16 (1.04-1.29)	.01	1.06 (0.93-1.20)	.41	1.55 (1.25-1.93)	<.0001
Other/multiple/unknown	0.99 (0.87-1.13)	.92	0.96 (0.83-1.11)	.61	1.22 (0.87-1.69)	.24
Transplant year						
2008	Referent		Referent		Referent	
2009	1.02 (0.93-1.06)	.98	0.98 (0.91-1.05)	.51	1.12 (0.96-1.30)	.16
2010	1.01 (0.94-1.08)	.84	0.99 (0.92-1.06)	.79	1.09 (0.93-1.28)	.28
Disease group						
Acute myelogenous leukemia and myelodysplastic disorders	Referent		Referent		Referent	
Acute lymphoblastic leukemia	0.99 (0.95-1.08)	.86	0.96 (0.88-1.05)	.38	1.13 (0.95-1.36)	.19
Other leukemia and myeloproliferative syndromes	0.76 (0.70-0.83)	<.0001	0.75 (0.68-0.81)	<.0001	0.85 (0.69-1.04)	.11
Non-Hodgkin lymphoma and Hodgkin lymphoma	0.82 (0.77-0.89)	<.0001	0.82 (0.76-0.89)	<.0001	0.87 (0.72-1.03)	.12
Other malignancy	0.92 (0.82-1.05)	.24	0.93 (0.81-1.05)	.25	0.93 (0.66-1.29)	.65
Severe aplastic anemia	0.54 (0.45-0.68)	<.0001	0.64 (0.51-0.80)	.0001	0.29 (0.17-0.52)	<.0001
Other nonmalignant disease	0.62 (0.44-0.90)	.01	0.71 (0.44-1.15)	.16	0.53 (0.30-0.92)	.03
Center volume						
Low volume	Referent		Referent		Referent	
High volume	1.20 (1.10-1.32)	<.0001	1.33 (1.17-1.52)	<.0001	1.18 (1.02-1.36)	.02
Donor indicator						
Related donor indicator	Referent		Referent		Referent	
Unrelated donor indicator	1.15 (1.09-1.21)	<.0001	1.14 (1.08-1.21)	<.0001	1.20 (1.06-1.37)	.005
Risk indicator						
Low-risk center indicator	Referent					
High-risk center indicator	1.14 (1.05-1.23)	.002	–		–	

HCT indicates hematopoietic cell transplantation; HR, hazard ratio.
Adjusted for risk categories, gender, race, year of transplant, disease group, center volume, donor indicator (related vs unrelated) and region of transplant. Model 1 adjusted with low- and high-risk center indicator.

volume were indeed a surrogate for HCT expertise, we would expect higher-risk centers to have superior outcomes for all RCs.

It is possible for health plans to overvalue facilities that treat higher-risk patients by expecting substantial survival gains for the lower-risk patients treated at these centers.

Our findings demonstrate that the distinction between risk-taking centers and lower-risk centers is simply that a portion of their procedure volume has higher pre-transplant risk, not that they perform all other transplants with equal dexterity. Our results point to the fact that higher-volume centers attract a full range of pre-transplant risk recipients to their centers, and that there are other unmeasured factors that are common in both large and small centers that provide similar outcomes. For lower-risk patients, this is an important distinction that can help guide their decision whether to receive their transplant at a low-risk or high-risk center and to expect similar rates of survival. Recent research has suggested that HCT survival for lower-risk patients in nonaccredited centers to be comparable to survival in accredited centers.[27]

More research is needed to determine if designated Centers of Excellence (CoE) and accredited centers offer substantial benefits over HCT centers not certified as a CoE for lower-risk or less complex patients. This finding has important policy implications. Health plans frequently collect data on hospital performance, but they do not frequently stratify data to provide patients and health plan managers with the net benefits of treatment based on specific patient risk levels. As with reporting and use of physician-level performance data, we expect that health plans will increasingly use risk-stratified data to encourage lower-risk patients to restrict travel to receive comparable HCT care.

Limitations

Although our study provides further insight into the relationship between risk stratification and HCT center-specific survival, we acknowledge data-related limitations. The data we received from CIBMTR did not include post transplant complications. It is unclear if post transplant complications are attenuated by receiving a transplant in a low- or high-risk center. Additionally, our analysis only included 3 years of data. This limited our ability to measure an RC trend over time or observe centers that crossed over from being low-risk centers to high-risk centers or vice versa. We are limited by the fact that CIBMTR broadly identifies coexisting disease as either present or absent and because patient inclusion within an RC may be a construct of a center's willingness to both over- and undercode the presence of a coexisting disease. We tested our RCs with and without the inclusion of coexisting disease in our models and did not observe results of different magnitude or direction. Despite these data limitations, we believe that our RC groups provide practical benefit for clinicians and patients alike to stratify centers into RCs.

CONCLUSIONS

The Stem Cell Therapeutic and Research Act of 2005 was passed to establish a more transparent transplant outcomes research environment for clinicians and HCT recipients. Novel and rapid innovative clinical approaches have expanded HCT to a more complex case mix of patients. Still, our results show HCT remains associated with significant mortality for all pre-transplant RCs and that there is indeed no difference among centers when stratified for risk. However, the broader explanation of a center's specific HCT survival rate remains complex, requiring a deeper understanding of the causal mechanisms involved in individual transplant centers and finding specific factors that could be introduced to all centers to improve outcomes. While our work begins this stratification process, our results suggest the need for additional research using longitudinal data and corresponding methods to investigate the factors that more broadly predict the characteristics of superior centers and improve survival for all levels of pre-transplant risk.

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