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Incidence and Causes of Hospital Readmission in Pediatric Patients after Hematopoietic Cell Transplantation

David Stephen Shulman [1,*], Wendy B. London [2], Dongjing Guo [3], Christine N. Duncan [2], Leslie E. Lehmann [4]

[1] Department of Pediatrics, Boston Children's Hospital, Boston, Massachusetts
[2] Dana-Farber Cancer Institute/Boston Children's Hospital, Boston, Massachusetts
[3] Division of Pediatric Hematology-Oncology, Dana-Farber Cancer Institute/Boston Children's Hospital, Boston, Massachusetts
[4] Pediatric Stem Cell Transplantation Center, Dana-Farber Cancer Institute/Boston Children's Hospital, Boston, Massachusetts

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A B S T R A C T

Allogeneic (allo) and autologous (auto) hematopoietic cell transplantation (HCT) provide the potential to cure otherwise fatal diseases but they are resource-intense therapies. There is scant literature describing the burden of hospital readmission in the critical 6-month period of immunosuppression after HCT. We report the incidence, causes, and outcomes of readmission in the 6 months after day 0 of HCT and in the 30 days after hospital discharge. This study is an institutional review board–approved retrospective medical record review of children who underwent HCT at a single institution. Between January 1, 2008 and December 31, 2011, 291 children underwent HCT at our institute. Of these, 140 patients were excluded because they were not followed primarily at our institute for the first 6 months after transplantation, 14 patients were excluded because they died during their initial hospitalization, and 1 patient was excluded because the initial hospitalization was longer than 6 months. Of the remaining 136 patients, 63% had at least 1 readmission. Of the patients who underwent allo-HCT, 78% were readmitted, in contrast to 38% of auto-HCT patients ($P < .001$). For the 206 readmissions, the mean length of hospital stay was 10.7 days (range, 1 to 129). Seventy-two percent of auto-HCT patients were initially readmitted for fever, and 46% ultimately had a source identified. No risk factors for readmission were found in the auto-HCT group. Fifty-two percent of allo-HCT patients were readmitted for fever and 28% of these patients ultimately had an identified source. Gastrointestinal-related problems accounted for 30% of primary readmissions among allo-HCT patients. Patients with an unrelated donor had a trend towards increased rates of 30-day readmission ($P = .06$) and were more likely to have a second readmission ($P = .002$). Patients who were cytomegalovirus (CMV) positive before transplantation were more likely to be readmitted ($P = .02$). The majority of children who undergo HCT are readmitted during the critical 180 days after transplantation. Readmission is much more common among allo-HCT patients, in particular those with unrelated donors and CMV-positive serologies before transplantation. Fever is the most common cause of readmission in these patients, and serious infections are identified in a significant portion of patients. These findings and future research in this area will help improve both patient education and resource utilization.

BACKGROUND

Hematopoietic cell transplantation (HCT) provides potentially curative therapy for many neoplastic, hematologic, metabolic, and immunodeficiency diseases. Allogeneic HCT (allo-HCT) and autologous HCT (auto-HCT) are associated with significant risk, given the high toxicity of conditioning regimens and the prolonged period of immune suppression after transplantation. There is an extensive literature demonstrating that innate immunity, including epithelial barriers, monocytes, granulocytes, and macrophages, recover within weeks; B cell and CD8 T cell function recover over a period of months; and CD4 T cell function may take years after transplantation to normalize [1,2]. The pace of recovery varies by the type of conditioning a patient receives, donor source, and the type of cells utilized for the transplantation. After autologous transplantation, the pace of immune reconstitution would be expected to be more rapid given the lack of

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* Correspondence and reprint requests: David Stephen Shulman, MD, Boston Children's Hospital, 300 Longwood Ave, Boston, MA 02115.
E-mail address: davidsshulman@gmail.com (D.S. Shulman).

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allogeneic effect and need for immunosuppressive medications, but the specific timeline has not been clearly delineated [3]. Neutropenia typically resolves in 14 to 21 days after transplantation, but there are laboratory and functional changes in the immune system for much longer [2,3]. In allogeneic transplantations, the use of peripheral blood stem cells hastens T cell reconstitution when compared with bone marrow, but the risk of infection remains high for at least 1 year after HCT [4]. When umbilical cord blood is used as the stem cell source, transplanted cells are naïve, and thus T cell–mediated cellular immunity in particular is deficient for months after transplantation [5,6]. Even as immune cell counts recover, relative immunodeficiency persists as the reconstituted T and B cell subsets likely do not hold the breadth of antigen identification seen in a normal immune system. Children receiving HCT are typically discharged soon after neutrophil engraftment—defined as an absolute neutrophil count greater than 500 cells/high power field for 3 consecutive days—but months before full immune reconstitution. Thus, there is an ongoing risk of complications and consequent readmission, which will likely vary among patient groups given the heterogeneity of the population.

Overall, 6.5% of children admitted to general children's hospitals are readmitted within 30 days of discharge, and the highest rates of readmission are in children with neoplasms [7]. Readmission rates after stem cell transplantation would be expected to be greater than that seen in general pediatric oncology patients—as high as 50% in 1 small pediatric series—yet there is a paucity of data about this population [8]. Adult and pediatric patients likely have different post-transplantation courses given the types of disease seen in adults and the burden of comorbidities; nevertheless, this population may provide insight into the pediatric HCT population. Among adult patients undergoing allo-HCT, 39% were readmitted within 30 days, most commonly for fever or infection. Receiving total body irradiation, use of an unrelated donor, and acquiring an infection during the index hospitalization were shown to be risk factors for readmission [9].

A better understanding of the incidence, causes, and risk factors for readmission in children undergoing HCT may improve quality of care and outcomes. Potential initiatives include improvement in predischarge patient education, different approaches to prophylactic antibiotics, or use of long-term central venous access. Additionally, such information would inform resource allocation and identify high-risk populations requiring close monitoring and follow-up. A study of pediatric cardiothoracic surgery patients—another group at high risk of readmission—showed that a firm understanding of the risk factors for readmission could inform quality improvement measures in the postoperative period [10].

In this study, we describe the incidence, causes, risk factors, and outcomes of hospital readmission in a large pediatric HCT program at a tertiary freestanding pediatric hospital. Readmissions were evaluated in the critical 6 months after day 0 of transplantation, during which time significant immune suppression persists. Given that the standard metric for assessing readmissions after hospitalization is 30 days from discharge, we also report 30-day readmission data. We hypothesized that the readmission rates would be higher among children undergoing allo-HCT compared with those undergoing auto-HCT, and that graft-versus-host disease (GVHD) and complications occurring during initial hospitalization may be risk factors for readmission during the 180 days after transplantation. Furthermore, we hypothesized that readmission in itself may have prognostic impact on outcomes at 1 year.

METHODS

Patients and Data Collection

This study is an institution review board–approved retrospective medical record review of 291 consecutive children who underwent HCT between January 1, 2008 and December 31, 2011 at the Dana-Farber/Boston Children's Hospital Cancer Center (Figure 1). Of these, 140 patients (75%, n = 106, allo-HCT; 25%, n = 34, auto-HCT) were excluded because they were not followed exclusively at the Dana-Farber for 6 months after discharge from the primary hospital admission (index hospitalization), and 14 patients (71%, n = 10, allo-HCT; 29%, n = 4, auto-HCT) were excluded because they died during their initial hospitalization. One allo-HCT patient was hospitalized for more than 6 months after day 0 of hospitalization and was consequently omitted from analysis. Hospital records were reviewed for the remaining 136 patients from the day of admission for HCT to 6 months after the day of transplantation. Of the 136 included patients, 65% received allo-HCT (n = 88) and 35% underwent auto-HCT (n = 48). From the index hospitalization we recorded age at transplantation, gender, underlying disease, transplantation type (auto, allo), donor relation (related, unrelated), time to neutrophil count > 500, presence of GVHD during initial hospitalization for allo-HCT patients, presence of infection (bacterial, viral, or fungal), whether there was an admission to the intensive care unit (ICU) after transplantation, and whether the patient was readmitted to our hospital within 6 months after transplantation (6-month readmission) and/or within 30 days from discharge from the index hospitalization (30-day readmission). Patients who underwent planned tandem transplantations were reported beginning from the date of the last transplantation. Planned readmissions, such as those for antibody therapy or scheduled elective surgeries, were not classified as readmissions.

All allo-HCT patients and/or donors who were IgG positive for cytomegalovirus (CMV) before HCT were screened weekly for viral reactivation by antigen testing or quantitative PCR.

In our practice, criteria for discharge after HCT include the following: (1) neutrophil engraftment, (2) no active infections, and (3) no active GVHD. The majority of patients are discharged with a central line. Before discharge, all patients and their families undergo a formalized discharge teaching session with a dedicated clinical nurse specialist, which includes discussion of readmission criteria (fever, diarrhea, cough, etc). In addition, all patients have nutrition consultation during HCT and at the time of discharge.

For those patients readmitted, additional information was collected, including the number of readmissions within 6 months from the day of transplantation (day 0), the cause of readmission, the length of readmission, transfer to the ICU during readmission, and documented infection during readmission.

For all patients, 100-day, 6-month, and 1-year overall mortality, transplantation-related mortality (TRM) data, and survival data were collected.

Statistical Analysis

The readmission rate was calculated by taking the total number of patients with at least 1 readmission in the given time period and dividing by the 136 patients reviewed; a 95% confidence interval (CI) was placed on this rate. Risk factors for readmission, including age, positive blood culture, transplantation type, donor type, and GVHD at time of discharge, were analyzed with univariate Fisher's exact test and a multivariate logistic regression model. To assess the impact of readmission on mortality, Kaplan-Meier curves of overall survival (OS), were plotted for all patients, by readmission versus no readmission, and a log-rank test comparison of the curves was performed. OS point estimates are at 1 year ± standard error. OS was calculated starting from the time of transplantation until death from any cause or until last contact if the patient did not die. A logistic regression model was used to test if readmission was associated with 1-year mortality. Logistic regression models were used to assess the prognostic impact of age, positive blood culture during readmission, and transplantation type on second readmission, and Cox proportional hazard regression models assessed the effect of these factors on time to second readmission. The same methods were used to address the impact of peak fever at readmission, positive blood culture during readmission, age and donor type on second readmission, and time to second readmission. Cumulative incidence of TRM, with adjustment for death from other causes, was calculated according to the methods of Kalbfleish and Prentice [11].

RESULTS

Readmission Rates

For the 136 patients in our study, 41% (n = 56) were readmitted within 30 days of discharge from their primary transplantation hospitalization; 52% (n = 46) of allo-HCT patients and 21% of auto-HCT patients (n = 10) ($P < .01$). In

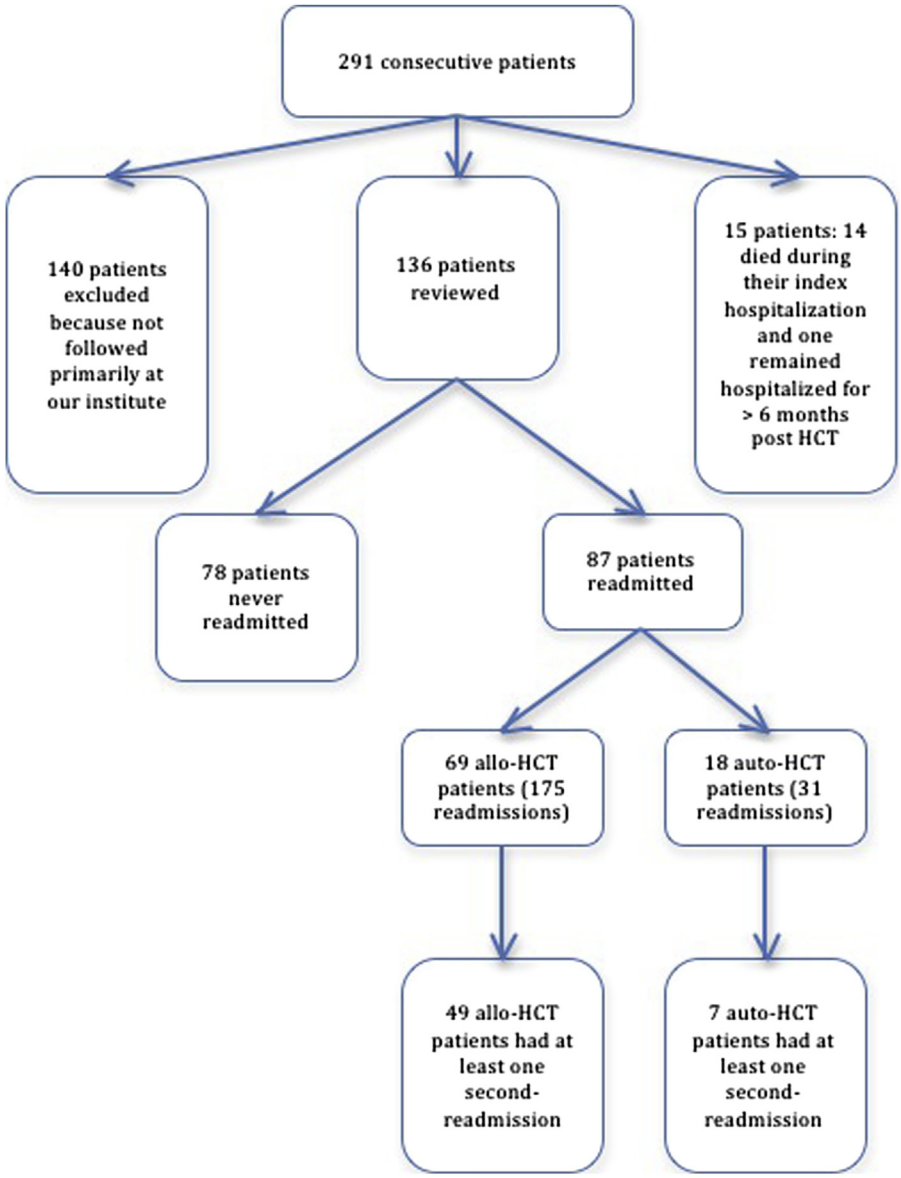

Figure 1. CONSORT diagram of the determination of the analytic cohort and their 6-month readmission status.

the 6-month period after day 0 of transplantation, 63% (n = 87) of patients had at least 1 readmission; 78% (n = 69) of the allo-HCT cohort and 38% (n = 18) of auto-HCT patients ($P < .001$) (Table 1). Of the 87 readmitted patients, 64% (n = 56) had a second readmission: 71% (n = 49) of allo-HCT patients and 39% (n = 7) of auto-HCT patients ($P = .01$) (Table 1). There were a total of 206 readmissions in this patient population over the 6 months after day 0 of transplantation, with an average length of hospitalization of 10.7 days (range, 1 to 129).

All subsequent results will be reported on readmission data from the 6 months after day 0 of transplantation, unless otherwise specified. Figure 1 describes the absolute numbers of patients and readmissions reviewed in the study.

Auto-HCT Patients

Of the 48 auto-HCT patients, the average age was 8 years (range, 6 months to 20 years) and the average length of hospitalization after transplantation day 0 was 25 days (range, 9 to 77). Of the 18 readmitted auto-HCT patients, the

Table 1
Readmission Rates in Auto- and Allo-Transplantation Patients

Outcome	All Patients		Allo-Transplantation		Auto-Transplantation		
	No. Evaluable	Rate, % (95% CI)	No. Evaluable	Rate, % (95% CI)	No. Evaluable	Rate, % (95% CI)	*P* Value
30-d readmission	56 of 136	41 (33-49)	46 of 88	52 (42-63)	10 of 48	21 (9-32)	<.01
6-mo readmission	87 of 136	63 (56-72)	69 of 88	78 (70-87)	18 of 48	38 (24-51)	<.01
Second readmission	56 of 87	64 (54-74)	49 of 69	71 (60-82)	7 of 18	39 (16-61)	.01

Table 2
Risk Factors for Readmission in Auto- and Allo-HCT Patients

Risk Factors	30-d Readmission			6-mo Readmission		
	No	Yes	*P* Value*	No	Yes	*P* Value*
All patients						
Transplantation type						
Allo	42	46	<.0001	19	69	<.0001
Auto	38	10		30	18	
Age						
≤13 yr	59	39	.70	37	61	.60
>13 yr	21	17		12	26	
Positive blood culture during transplantation hospitalization						
Yes	29	20	1.00	20	29	.50
No	51	36		29	58	
ICU stay during transplantation hospitalization						
Yes	9	9	.40	8	10	.40
No	71	47		41	77	
Allo-HCT						
Donor type						
Related	16	9	.06	6	19	.70
Unrelated	26	37		13	50	
Age						
≤13 yr	33	30	.20	16	47	.30
>13 yr	9	16		3	22	
GVHD at time of discharge						
Yes	4	5	1.00	4	5	.10
No	38	41		15	64	
Positive blood culture during transplantation hospitalization						
Yes	15	15	.80	10	20	.06
No	27	31		9	49	
CMV status						
Positive	16	22	.40	4	34	.02
Negative	25	24		14	35	
Equivocal	1	0		1	0	
ICU stay during transplantation hospitalization						
Yes	5	8	.60	4	9	.50
No	37	38		15	60	
Auto-HCT						
Age						
≤13 yr	26	9	.20	21	14	.70
>13 yr	12	1		9	4	
Positive blood culture during transplantation hospitalization						
Yes	14	5	.50	10	9	.40
No	24	5		20	9	
ICU stay during transplantation hospitalization						
Yes	4	1	1.00	4	1	.60
No	34	9		26	17	

mean time from discharge to readmission was 35 days (range, 2 to 86). Seventy-two percent (n = 13) presented with fever. Forty-six percent of patients with fever (n = 6) ultimately had an identified infectious source: *Staphylococcus* non-*aureus* bacteremia (n = 3), *Escherichia coli* bacteremia (n = 1), *Acinetobacter* bacteremia (n = 1), and *Pantoea*/*Shewanella* bacteremia (n = 1). Two patients were admitted for identified infections without an antecedent fever: viral stomatitis and herpes zoster. Of the 3 other patients without fever, 1 was readmitted for vomiting, 1 for poor weight gain, and 1 for gastric tube malfunction.

Age, admission to the ICU, and positive blood culture during primary admission were not significant predictors of readmission on univariate or multivariate analysis among auto-HCT patients (Table 2).

Of the 18 auto-HCT patients who were readmitted, 7 had at least 1 additional readmission, for a total of 13 second readmissions among this population and an average of 1.72 (range, 1 to 4, 95% CI, 1.19 to 2.26) subsequent readmissions. There were 4 readmissions for fever: 2 patients were found to have *Klebsiella pneumoniae* bacteremia and a source was not identified in the remaining 2. One patient had a gastric tube site cellulitis without antecedent fever. One patient had 3 subsequent readmissions for hypertension and pericardial effusion and 1 had 3 subsequent readmissions for malnutrition. One patient was admitted for hyperkalemia and the last for lethargy.

At 1 year after transplantation, 2 auto-HCT patients had died—1 from relapsed primitve neuroectodermal tumor on day 304 after transplantation and 1 in an auto accident 101 days after transplantation for Hodgkin lymphoma. No auto-HCT patients died of treatment-related causes.

Allo-HCT Patients

Of the 88 allo-HCT patients, the average age was 9 years (range, 2 months to 22 years), the average length of hospitalization after transplantation day 0 was 39 days (range, 16 to 177), and the mean time from discharge to readmission was 30 days (range, 2 to 127). Fifty-two percent (n = 36) of patients had a fever at time of readmission; of these, a source was ultimately identified in 28% (n = 10). Of the 10 patients, 4 were bacteremic: 1 patient died of *Klebsiella* septic shock, the remaining blood cultures grew *Staphylococcus* non-*aureus*, *Mycobacterium fortuitum*, and *Enterobacter cloacae*. Five had viral infections (2 CMV viremia, 1 CMV colitis, 1 Epstein-Barr viremia, 1 adenovirus viremia), and 1 had radiologic sinusitis. The remaining 72% of patients who presented with fever did not have an identified source of infection. Of the 33 patients without fever, 11 patients were readmitted for gastrointestinal (GI) problems: 1 had GI GVHD, 1 had poor weight gain, 2 had dehydration, 1 was in preparation for a GI cleanout before colonoscopy, and the remainder had vomiting and diarrhea. There were 7 patients readmitted with infections without antecedent fever, including 4 with CMV reactivation detected on routine screening, 1 with orbital cellulitis, 1 with a presumed central venous line site infection, and 1 with sinusitis. Remaining causes of readmission were varied.

Although donor type (unrelated versus related) was not statistically significantly predictive of 6-month readmission, there was a trend towards increased rates of 30-day readmission for patients with unrelated donors in comparison to those with related donors ($P = .06$). Patients who were CMV-IgG positive before transplantation had a statistically significant higher 6-month readmission rate than patients whose CMV status was negative or equivocal ($P = .02$). Age, GVHD at time of discharge, and positive blood culture during index hospitalization did not predict hospital readmission among allo-HCT patients (Table 2).

Of the 69 allo-HCT patients who were readmitted, 49 had at least 1 additional readmission, and the average number of readmissions among all 69 patients was 2.54 (range, 1 to 8, 95% CI, 2.15 to 2.92). There were a total of 106 subsequent readmissions among this population, and 45% (n = 49) were for fever, with a fever source identified in 37% (n = 18). The most commonly identified organisms were CMV (n = 5), *Clostridium difficile* (n = 3) and *Staphylococcus* non-*aureus* bacteremia (n = 3). Of the 57 nonfever second readmissions, 18 were for complaints referable to the GI system, 11 were for respiratory complaints, 4 were for electrolyte abnormalities, 3 for central venous line malfunctions, and in the remaining 23, causes were varied.

Allo-HCT patients who had an unrelated donor had 6.3 (95% CI, 2.0 to 20.0) times greater odds of having second readmission within 6 months after transplantation than allo-HCT patients who had a related donor ($P = .002$).

At 1 year after transplantation, 7 allo-HCT patients had died from treatment-related causes and 6 patients had died of progressive disease. Of the 7 patients succumbing to treatment-related causes, 2 died of multiorgan failure, 2 died

of respiratory failure, 2 died of GVHD, and 1 died of *Klebsiella* sepsis.

Overall Mortality

One-year OS was 89% ± 3% (n = 136); 96% ± 3% for auto-HCT (n = 48) and 85% ± 4% for allo-HCT (n = 88). Patients who were not readmitted within 30 days from discharge or within 6 months of transplantation day 0 had lower all-cause mortality. Patients readmitted within 30 days had 1-year OS of 84% ± 5% compared with 92% ± 3% for those not readmitted ($P = .10$) (Figure 2A). Patients readmitted within 6 months of transplantation had a 1-year OS of 85% ± 4% compared with those who were not at 96% ± 3% ($P = .052$) (Figure 2B). Overall survival for auto-HCT was 94.1% ± 5.7% and 96.6% ± 3.4% for patients readmitted within 6 months of transplantation and those who were not, respectively ($P = .70$) (Figure 2C). Allo-HCT patients who were readmitted within 6 months had an OS of 82.3% ± 4.6% compared with those who were not 94.7% ± 5.1% ($P = .20$) (Figure 2D). Patients who required ICU level care during their readmission had a 57% ± 12% 1-year survival compared with 92% ± 3% for those not admitted to the ICU ($P < .0001$). Age, type of transplantation, and positive blood culture were not found to be significant predictors of OS.

The overall 1-year cumulative incidence of TRM was 6.2% ± 2.1% (n = 136); 5.2% ± 2.5% for those not readmitted within 1 month of discharge (n = 80) versus 7.7% ± 3.7% for those readmitted within 1 month of discharge (n = 56) ($P = .60$) (Figure 3A). The 1-year cumulative incidence of TRM was 4.2% ± 2.9% for those not readmitted within 6 months of transplantation (n = 49) versus 7.3% ± 2.9% for patients readmitted within 6 months of transplantation (n = 87) ($P = .50$) (Figure 3B).

DISCUSSION

Readmission after HCT is very common in the pediatric population, far exceeding the average readmission rates among hospitalized general pediatric patients. At our institute, 63% of all HCT patients were readmitted at least once in the 6 months after transplantation. Such information may prove beneficial to families preparing for transplantation as well as at the time of discharge, in addition to informing resource allocation for this population. We found readmission to be common in the first 30 days after discharge from transplantation. This data has not been reported previously and may be useful for future comparative quality improvement initiatives as 30-day readmission is easy to capture and serves as a standard metric across many diseases. However, the focus of this study was readmissions in the 6 months after day 0 of transplantation, the time of greatest perturbation of immunologic function.

After transplantation, 38% of children receiving auto-HCT were readmitted, which— although significantly lower than for allo-HCT patients—is still substantial. Fever was commonly the cause of readmission. Forty-six percent of auto-HCT patients presenting with fever ultimately had

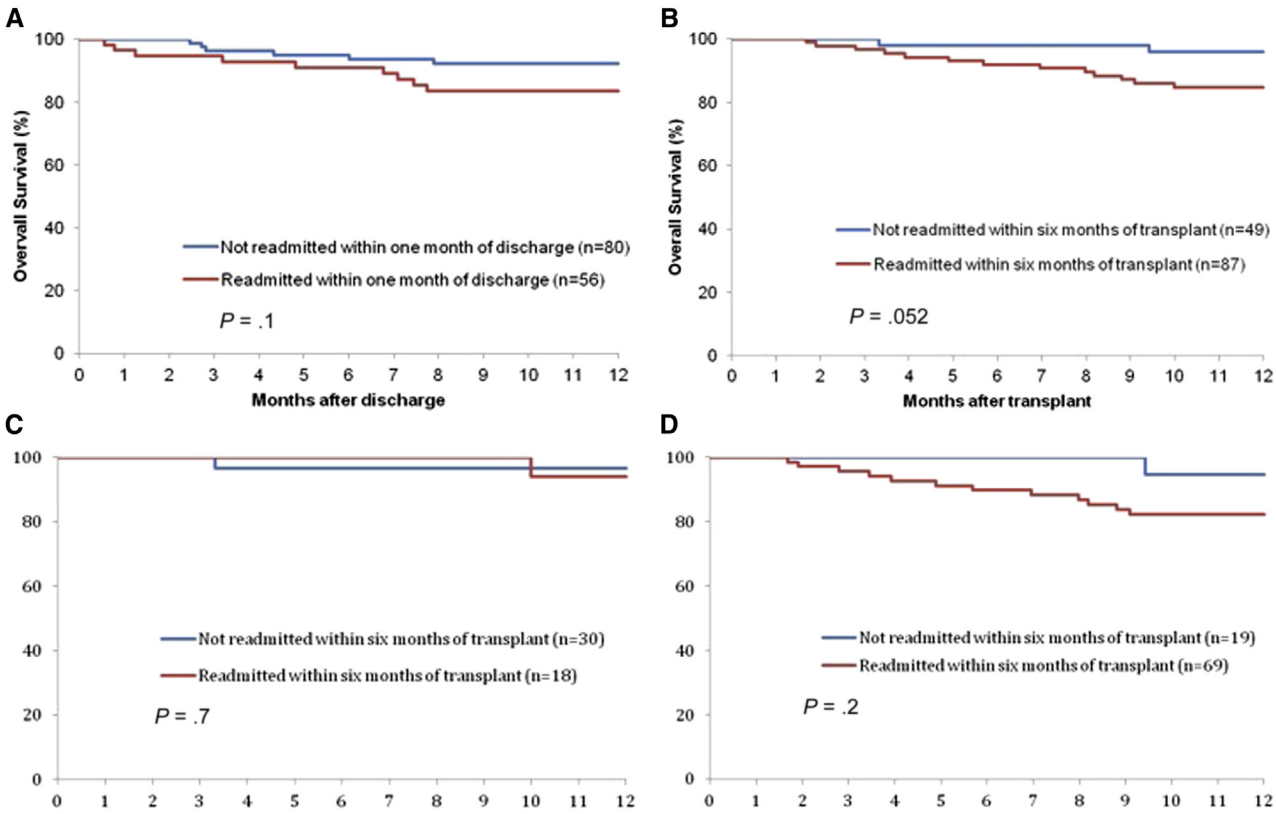

Figure 2. (A) Kaplan-Meier curves of OS, starting from the time of post-transplantation hospital discharge, by readmission within 30 days: not readmitted (n = 80) versus readmitted within 1 month of discharge (n = 56) ($P = .10$). (B) Kaplan-Meier curves of OS, starting from the time of post-transplantation hospital discharge, by readmission within 6 months: not readmitted (n = 49) versus readmitted within 6 months of transplantation (n = 87) ($P = .052$). (C) Kaplan-Meier curves of OS in auto-HCT patients, starting from the time of post-transplantation hospital discharge, by readmission within 6 months: not readmitted (n = 30) versus readmitted within 6 months of transplantation (n = 18) ($P = .70$). (D) Kaplan-Meier curves of OS in allo-HCT patients, starting from the time of post-transplantation hospital discharge, by readmission within 6 months: not readmitted (n = 19) versus readmitted within 6 months of transplantation (n = 69) ($P = .20$).

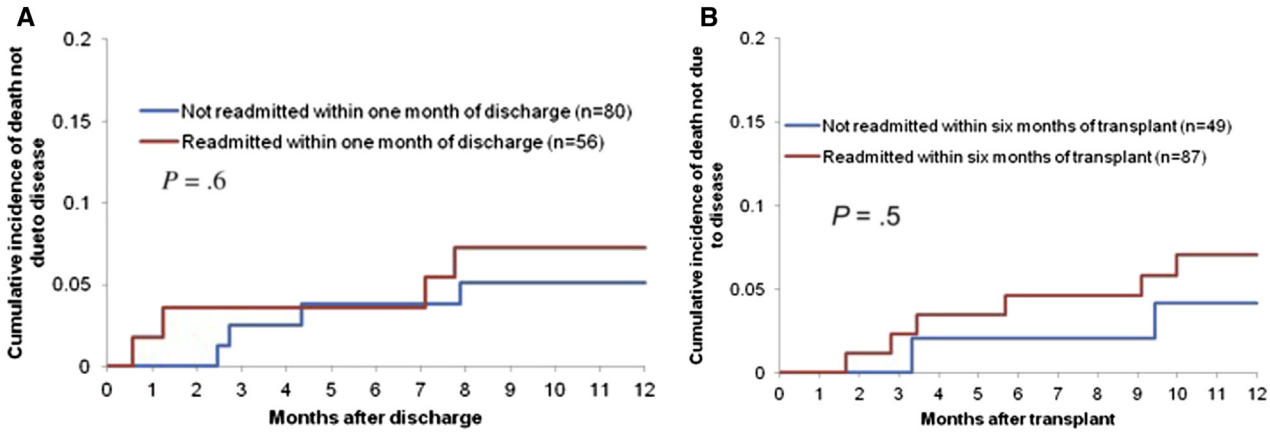

Figure 3. (A) Curves of the cumulative incidence of transplantation-related mortality (TRM), starting from the time of transplantation, by readmission within 30 days: not readmitted (n = 80) versus readmitted within 1 month of transplantation (n = 56) ($P = .60$). (B) Curves of the cumulative incidence of transplantation-related mortality (TRM), starting from the time of transplantation, by readmission within 6 months: not readmitted (n = 49) versus readmitted within 6 months of discharge (n = 87) ($P = .50$).

either a positive culture or a clinical diagnosis of infection, suggesting that these patients will likely continue to require periods of inpatient care after transplantation and that preemptive antibiotic therapy is necessary. The second most common cause of readmission was a nutritional problem. Neither age nor factors related to the primary hospitalization (ICU admission, bacteremia) could be identified as risk factors for the auto-HCT population.

Among allo-HCT patients, 52% were readmitted within 30 days of discharge, a rate much higher than reported in the adult HCT literature [9]. Of the children readmitted after allo-HCT, 52% had fever at readmission; a source was identified in 28% suggesting admission and preemptive antibiotic therapy are essential for patients presenting with fever. GI complaints were the second most common cause of readmission. In the allogeneic setting, such complaints often warrant an inpatient evaluation. GVHD and infectious colitis must be distinguished from more benign causes. In addition, concerns regarding absorption of oral medications and hydration status may prompt a hospital admission.

Allo-HCT patients were more likely to have a subsequent readmission than auto-HCT patients, with an average of 2.53 readmissions. Thus, those readmitted are likely to be readmitted multiple times and deserve careful monitoring after discharge form the first readmission. Fever and infection were the most common causes of second readmission among allo-HCT patients. Allo-HCT patients with unrelated donors had 6.3 times greater odds of subsequent readmissions than those with related donors. Positive pretransplantation CMV serologies carried increased odds of readmission in the allo-HCT population and may be an area worth further evaluation in terms of prophylaxis or increased surveillance.

Patients readmitted within 6 months of transplantation day 0 had worse 1-year OS. Roughly one half of allo-HCT deaths in our study were the result of TRM, the causes of which were varied. We did not find evidence to support an association of readmission with the incidence of TRM; however, this may be due in part to the small sample size. Patients who were readmitted to an ICU carried significantly worse odds of survival at 1 year. We were limited in identifying additional risk factors for death because of small sample size and low power.

We identified nutritional and GI-related problems as a significant cause of readmission in our population, a potentially preventable complication of transplantation. Such readmission could potentially be prevented through a predischarge nutritional care model, including nutritionist consults and nutritional discharge follow-up plan. A similar process in patients hospitalized for asthma demonstrated that implementation of a well-informed standardized care plan at the time of discharge could reduce readmissions [12].

Fever was the most common cause of readmission in our study and a challenging complaint in terms of attempting to reduce readmissions among HCT patients. In our study, 46% of auto-HCT and 28% of allo-HCT patients presenting with fever were found to have either a bacterial infection or viremia, supporting the notion that fever must be taken seriously in this patient population and include hospital admission with prophylactic antibiotics. Infectious complications after allogeneic transplantation are known to be common and our rates of bacteremia are comparable to other centers [13]. Further research should focus on elucidating robust risk factors for true infection among all children presenting with fever. For example, there is a rich body of literature on the management of febrile infants—a population in which 5% to 7% of those with fever have a serious bacterial infection—that has demonstrated safe protocols for empiric management of these patients [14,15]. Multicenter studies may be able to identify similar risk factors among HCT patients and provide evidence for standardized protocols based on presenting symptoms and laboratory data. Alternative strategies may focus on the need to decrease fever and infections after transplantation, potentially including early removal of central venous access and/or prophylactic antibiotic regimens. Nevertheless, patient education should continue to focus on informing parents of the importance of recognizing fever and seeking urgent care in such circumstances.

A limitation of our analysis is that the patient population was limited to the subset of patients who either were referred from outside institutions and remained local for 6 months after treatment, or to those who were initially local to our institute. Examining readmissions for patients who were referred for transplantation and received subsequent follow-up elsewhere would increase the generalizability of our results. Of note, the proportion of allogeneic transplantation patients appears comparable between the excluded population and studied population; 75% and 65%, respectively. Given that our data represent the experience of

only 1 institute, we are unable to assess whether there is significant cross-institute variability in readmission rates, which might elucidate best and worst practices in transplantation. As this was a retrospective chart review, there is the possibility for ascertainment bias. The sicker patients may have been more likely to remain local after transplantation, compared with patients in better health who may have traveled home for follow-up.

In summary, readmission, including subsequent readmissions, is a common problem in pediatric stem cell transplantation, and families and staff should be prepared for this possibility in the time after transplantation. Ideally, we would be able to predict those patients at high risk of readmission. However, at this time our data demonstrate that allo-HCT patients are the cohort most likely to be readmitted and that positive pretransplantation CMV titers or having an unrelated donor may carry an increased risk of readmission and second readmission. Given the high proportion of patients with fever who subsequently have an identified source, fever should continue to trigger hospital readmission and empiric antibiotics in this population. GI complaints, including malnutrition, are another common trigger for readmission. It may be possible to decrease readmission rates in this group through education and outpatient support by a nutritional team. Readmission may indicate worse OS and, thus, warrants closer monitoring of this population. Future efforts should focus on a multicenter study to further examine causes and predictors of readmission.

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