Frequency of Hospital Readmissions Post Allogeneic Hematopoietic Cell Transplantation

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INTRODUCTION

- While potentially curative for some life-threatening diseases, allogeneic hematopoietic cell transplantation (allo-HCT) is a complex and resource-intensive procedure that creates a significant burden for patients and healthcare systems.
- Because of the need for extended immunosuppressive therapy, allo-HCT recipients are at a high risk for opportunistic infections, including double-stranded DNA (dsDNA) viral infections, which can lead to hospital readmission.[1-3]
- A chart review of 100 patients who underwent HCT in the year 2000 reported that 51% of the population had at least one hospital readmission after HCT, and among patients who had an infection within a month prior to HCT, there was an associated 50% mortality rate.[4]
- A separate study of 618 allo-HCT recipients (1990–2009) reported a 39% rate of hospital readmission within 30 days post allo-HCT, and an association between infections during initial hospitalizations and readmission.[2]
- Considering the changes in practice patterns and advances in allo-HCT, it is important to evaluate the rate of readmission using a more recent data source among a larger study population.
- The objectives of this study were to examine the rates of hospital readmissions post allo-HCT and the reasons for the readmissions.

METHODS

Study population

- Patients who received allo-HCT between January 2009 and September 2013 were identified from the Premier hospital database based on having an International Classification of Diseases, Ninth Revision Clinical Modification (ICD-9-CM) code for allo-HCT on hospital discharge records. The first allo-HCT procedure was defined as the initial hospitalization event.

Demographics and clinical characteristics

- Demographics and clinical characteristics were evaluated using available records in the database during the initial hospitalization and the 12 months prior to hospitalization for allo-HCT.
  - Clinical characteristics included the Charlson Comorbidity Index (CCI) score and the All Patient Refined Diagnosis Related Group (APR-DRG) illness severity level.
    - The CCI is a method used commonly to assess the overall comorbidity levels of patients. It is a weighted score based on the diagnosis of 19 specific diseases.
    - APR-DRG is a method designed to group patients into similar disease categories based on disease severity. There are four different levels of severity: Level 1–Minor, Level 2–Moderate, Level 3–Major, Level 4–Extreme.

Outcome measurements

- The rates of hospital readmissions up to 12 months post allo-HCT for any cause and rates of hospital readmissions for selected clinically important reasons, based on primary or secondary ICD-9-CM diagnosis codes on hospital discharge records, were evaluated. Evaluated reasons for hospital readmissions included:
  - opportunistic infection (related to viral, bacterial, and fungal infections)
    - dsDNA viral infections
  - graft-versus-host disease (GVHD)
  - renal impairment
  - neutropenia
  - post-transplant lymphoproliferative disorder (PTLD),
- Among allo-HCT recipients with documented opportunistic infections, we identified rates of documented dsDNA viral infections during the initial allo-HCT hospitalizations. The rate of documented dsDNA viral infections was specifically evaluated, as the associated morbidity and mortality are significant among allo-HCT recipients.[1,5] dsDNA viral infections were categorized as "any dsDNA viral infection" or as one of the following:
  - cytomegalovirus (CMV) infection
  - BK virus (BKV) infection
  - adenovirus (AdV) infection
  - human papilloma virus (HPV) infection
  - human herpes virus (HHV) 6 or 7 infection
  - varicella zoster virus (VZV) infection
  - Epstein–Barr virus (EBV) infection
  - herpes simplex virus (HSV) infection.

RESULTS

- Of patients who received allo-HCT (n=1617), the mean age was 42.5 years, 17.9% were <18 years of age, and 57% were male (**Table 1**).

Table 1. Patient demographics

	N=1617	
Age (years)		
Mean (SD)	42.5 (20.7)	
Median	48	
	n	**%**
Adults/children		
Adult (≥18 years old)	1328	82.1
Child (<18 years old)	289	17.9
Sex		
Female	696	43.0
Male	921	57.0
US region		
Midwest	133	8.2
Northeast	909	56.2
South	554	34.3
West	21	1.3
Race/ethnicity		
White	1026	63.5
Black	179	11.1
Hispanic	37	2.3
Other	375	23.2
Health plan		
Commercial-Managed Care	1046	64.7
Medicaid	282	17.4
Medicare	208	12.9
Others	81	5.0
Urban/rural hospital		
Rural	92	5.7
Urban	1525	94.3
Teaching hospital		
No	57	3.5
Yes	1560	96.5
Number of beds		
<200	127	7.9
200–399	140	8.7
400–599	180	11.1
≥600	1170	72.4

SD, standard deviation.

- Approximately three-quarters of patients received allo-HCT in large hospitals (≥600 beds) (**Table 1**).
- The mean CCI score was 2.3, indicating a relatively low number of comorbid conditions per patient (**Table 2**).
- During initial hospitalizations for allo-HCT, greater than one-third (37.1%) of the study population had major and extreme illness severity levels, as indicated by the APR-DRG level (**Table 2**).

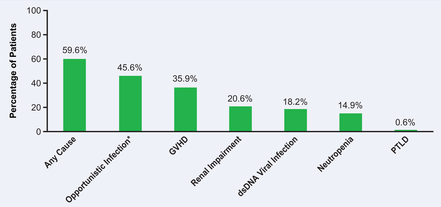
Table 2. Clinical characteristics of patients

	N=1617	
CCI		
Mean (SD)	2.3 (1.7)	
Median	2	
	n	**%**
CCI group		
0	257	15.9
1–2	830	51.3
3–4	415	25.7
≥5	115	7.1
APR-DRG severity level		
1–Minor	466	28.8
2–Moderate	551	34.1
3–Major	263	16.3
4–Extreme	337	20.8

APR-DRG, All Patient Refined Diagnosis Related Group; CCI, Charlson Comorbidity Index; SD, standard deviation.

- During initial allo-HCT hospitalizations, 118 deaths occurred, resulting in a study population of 1499 allo-HCT patients to be followed for up to 12 months post-transplant.
- Among this cohort, 59.6% (n=893) had a hospital readmission for any cause within the 12 months following the initial allo-HCT hospitalization (**Figure 1**).
  - Of patients with readmissions, 45.2% had readmissions that occurred within 1 month and 74.7% occurred within 3 months of discharge from the initial allo-HCT hospitalization.
  - Readmissions most frequently involved opportunistic infections (45.6%, n=683), followed by GVHD (35.9%, n=538) (**Figure 1**).
    - Among patients with readmissions involving opportunistic infections, 40.0% (n=273) were documented as dsDNA viral infections.
    - Among patients with readmissions related to GVHD, 57.1% (n=307) had readmissions with a diagnosis of either chronic or acute GVHD. The remaining patients (42.9%, n=231) had readmissions with a diagnosis of unspecified GVHD.
  - Among the 1499 allo-HCT patients, 14.9% (n=224) had readmissions related to neutropenia (**Figure 1**).
    - Among these patients, 10.7% (n=24) and 7.6% (n=17) had readmissions with diagnoses of drug-induced and infection-related neutropenia, respectively.

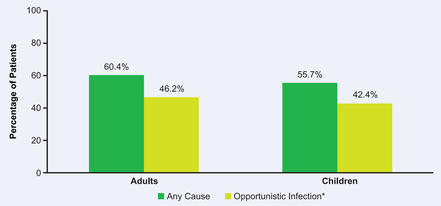
Figure 1. Rates of hospital readmissions in the 12-month period following initial hospitalization for allogeneic hematopoietic cell transplantation: selected clinically important reasons



*Opportunistic infections include viral, bacterial, and fungal infections.
Patients may have had multiple readmissions or readmission with multiple diagnoses. Thus, the categories of readmissions are not mutually exclusive.
dsDNA, double-stranded DNA; GVHD, graft-versus-host disease; PTLD, post-transplant lymphoproliferative disorder.

- Rates of readmissions for any cause among adults and children were 60.4% and 55.7%, respectively; rates of readmissions involving opportunistic infections were 46.2% and 42.4%, respectively (**Figure 2**).

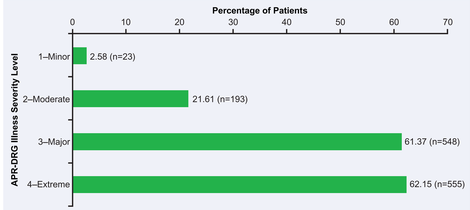
Figure 2. Rates of hospital readmissions for any cause and opportunistic infections among adults (>18 years of age) and children (≤18 years of age) in the 12-month period following initial hospitalization for allogeneic hematopoietic cell transplantation



*Opportunistic infection includes viral, bacterial, and fungal infections.

- Among patients with readmissions (n=893), 61.4% (n=548) and 62.2% (n=555) had readmissions that were classified as having APR-DRG major and extreme illness severity, respectively (**Figure 3**).

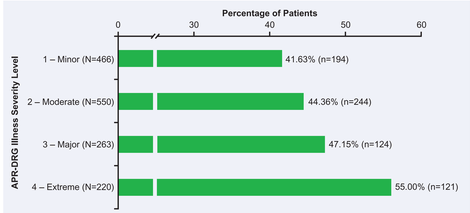
Figure 3. Patients with hospital readmissions (n=893) by the APR-DRG associated with the readmissions



Individual patients may be counted towards more than one APR-DRG severity category, owing to multiple readmissions.
APR-DRG, All Patient Refined Diagnosis Related Group.

- These readmissions were further evaluated by the initial allo-HCT hospitalization APR-DRG severity of illness level:
  - Patients with different initial hospitalization illness severity levels had similar rates of any-cause readmissions in the follow-up period (1–Minor: 58.8%, 2–Moderate: 58.4%, 3–Major: 59.3%, 4–Extreme: 64.6%, p=0.4375).
  - However, rates of readmissions for opportunistic infections did differ among patients with different initial hospitalization illness severity levels (1–Minor: 41.6%, 2–Moderate: 44.4%, 3–Major: 47.2%, 4–Extreme: 55.0%, p=0.0098; **Figure 4**).

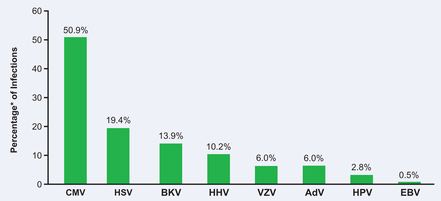
Figure 4. Patients with opportunistic infections* by initial hospitalization APR-DRG illness severity level readmitted within the 12 months following initial hospitalization for allogeneic hematopoietic cell transplantation



*Opportunistic infection includes viral, bacterial, and fungal infections.
APR-DRG, All Patient Refined Diagnosis Related Group.

- As documented by ICD-9-CM codes, 13.4% (n=216; mean age: 35.0 years) of the study population had documented dsDNA viral infections during the initial allo-HCT hospitalization.
  - The most frequently documented dsDNA viral infections were CMV (50.9%, n=110), followed by HSV (19.4%, n=42), and BK virus (13.9%, n=30) (**Figure 5**).
  - dsDNA viral infections were documented in 11.1% of adults (≥18 years of age) and 23.5% of children, of which approximately 50.7% and 51.5% were CMV infections, respectively.
  - Approximately 1 out of 3 patients (108/337) with an Extreme level of illness severity had documented dsDNA viral infection during the initial hospitalization (1–Minor: 1.5%, n=7/466; 2–Moderate: 8.4%, n=46/551; 3–Major: 20.9%, n=55/263; 4–Extreme: 32.1%, n=108/337; p<0.0001).
  - Of the 216 HCT recipients with dsDNA viral infections, 17.1% (n=37) died during the initial hospitalization. Among the remaining 179 patients, more than half (53.6%, n=96) had at least one hospital readmission during the follow-up period.

Figure 5. dsDNA viruses reported among patients with at least one dsDNA viral infection during the initial hospitalization



*Percentages are calculated as the number of patients with each type of dsDNA viral infection divided by the total number of patients with any dsDNA viral infection (n=216). Patients may have more than one type of dsDNA viral infection and thus the sum of such percentages may be greater than 100%.
AdV, adenovirus; BKV, BK virus; CMV, cytomegalovirus; EBV, Epstein–Barr virus; HHV, human herpes virus; HPV, human papilloma virus; HSV, herpes simplex virus; VZV, varicella zoster virus.

LIMITATIONS

- Identification of opportunistic infections, including dsDNA viral infections, was based on hospital discharge ICD-9-CM diagnosis codes, and therefore it is likely that the infection rates estimated in this study may represent a potential underestimate of the prevalence rates of such conditions.
- While the Premier hospital database contains information from a large number of hospitals across the US, it may not be representative of all types of transplant centers. In this study, approximately three-quarters of allo-HCT recipients received their transplant in large hospitals (≥600 beds). Thus, the study findings may not be representative of all allo-HCT transplant recipients, especially among those who received allo-HCT in smaller hospitals.

CONCLUSIONS

- **In this study population, more than half of patients who received allo-HCT had at least one hospitalization in the 12 months following their initial allo-HCT hospitalization, with three-quarters of readmissions occurring within the first 3 months after discharge.**
- **This cohort of allo-HCT recipients had high rates of readmissions involving opportunistic infections, of which dsDNA viral infections accounted for 40%.**
- **Allo-HCT recipients with greater illness severity during the initial allo-HCT hospitalization were more likely to have readmissions with documented opportunistic infections in the follow-up period.**

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DISCLOSURES

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