Hospital Readmissions Among Hematopoietic Cell Transplantation (HCT) Recipients

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ABSTRACT

Background: Hematopoietic cell transplantation (HCT) is a highly specialized, complex and resource-intensive procedure that requires significant post-transplant care. Although there are significant efforts to maximize graft survival, there are still risks of complications, some of which require hospitalizations. The objectives of this study were to quantify the rate of rehospitalization post HCT, as well as to characterize the reasons for these readmissions.

Methods: Patients who received an HCT between Jan 2009 and Sept 2013 were identified in the Premier hospital database using ICD-9 codes. First HCT procedure was defined as the index event. The frequency and reasons for hospital readmission were identified during the 12-months post-HCT hospitalization using discharge record documentations.

Results: Of the study population (n=4393; mean age: 50.4 years), 57.9% were male and 91.2% adults. Most patients received HCT (36.8% allogeneic) in urban (94.4%), large (⩾600 beds: 66.5%), teaching hospitals (87.6%). There were 157 deaths in the index HCT hospitalization that were excluded, resulting in 4236 patients for this evaluation. Approximately 38% of these HCT recipients had a hospital readmission for any cause during the 12 months post HCT hospitalization, with 65.6% occurring within the first 3 months post-HCT hospitalization. Readmissions were most frequently related to opportunistic infections (25.8%), followed by graft-versus-host disease (13.7%), renal impairment (11.1%), and neutropenia (10.0%). Readmission of patients with high severity APR-DRG levels of 3 (22.3%) and 4 (19.1%) were the most frequent (severity of illness level rated 1–4: minor, moderate, major, and extreme).

Conclusions: HCT recipients are at significant risk of complications during the first few months after transplant until reconstitution of immune system function. Opportunistic infection-related rehospitalizations are common and can require high intensity of care and resources. Future strategies that minimize the risks of these infections can have significant clinical and economic advantages.

INTRODUCTION

- Hematopoietic cell transplantation (HCT) is a potentially curative therapy for certain malignant and non-malignant diseases that are often fatal. However, opportunistic infections represent a significant obstacle to the success of HCT.[1]
- Owing to the need for extended immunosuppressive therapy, HCT recipients are at a high risk for opportunistic infections, which can lead to hospital readmission.[2,3]
- Bejanyan *et al*. reported a rate of 39% for 30-day readmission post HCT, with infection during index hospitalizations for HCT associated with a two-fold greater risk for 30-day readmission.[2]
- Another study of 1141 patients with HCT reported that 28% of patients were readmitted within 30 days of discharge and 43% by Day 100.[3] In this latter study, infection during the index hospitalization for HCT was a significant risk factor for hospital readmission.[3]
- Double-stranded (ds)DNA virus infections, such as those with cytomegalovirus (CMV) and varicella zoster virus (VZV), are of particular concern among HCT recipients, as they can be associated with severe complications, including pneumonia, gastroenteritis/colitis, hepatitis, and death.[1]
- Although some studies provide information on the prevalence of opportunistic infections during hospitalization among patients with HCT, there is scant literature available on the potential for hospital readmission among HCT recipients and the frequency of readmissions related to opportunistic infections occurring post HCT.

OBJECTIVES

- The objectives of this study were to quantify the frequency of hospital readmission post HCT and to characterize the reasons for these readmissions.

METHODS

Study population

- Patients who received 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 HCT. The first HCT procedure was defined as the index event.

Demographics and clinical characteristics

- Patient demographics, including age, sex, US region of residence, race, health plan type, urban/rural hospital, hospital teaching status, and hospital size; and clinical characteristics, including Charlson Comorbidity Index (CCI) score and All Patient Refined-Diagnosis Related Group (APR-DRG) severity of illness level were evaluated during a 12-month baseline period.
  - The CCI is a commonly used method of estimating the 1-year mortality for a patient with certain comorbid conditions. The CCI is a weighted score based on the occurrence of 19 specific diseases diagnosed during the baseline period prior to, as well as on, the index date.
  - The APR-DRG is a methodology designed to categorize patients into similar disease categories and to identify them by severity level. There are four different levels of severity: Level 1 – minor, Level 2 – moderate, Level 3 – major, Level 4 – extreme.

Outcome measurements

- The frequency and causes of hospital readmissions were evaluated during a 12-month follow-up period after the HCT index hospitalization using hospital discharge records. The causes of hospital readmissions were categorized as:
  - readmission for any cause
  - graft-versus-host disease (GVHD)-related readmission
  - renal impairment-related readmission
  - neutropenia-related readmission
  - post-transplant lymphoproliferative disorder-related readmission
  - opportunistic infection-related readmission, including readmissions related to viral, bacterial, and fungal infections
  - dsDNA virus infection-related readmission
    - CMV infection-related readmission
    - BK virus infection-related readmission
    - adenovirus infection-related readmission
    - other dsDNA virus infection-related readmission.
      - Other dsDNA virus infections included those of human papilloma virus, human herpes virus types 6 or 7, VZV, Epstein–Barr virus, and herpes simplex virus.

RESULTS

- Of patients who received HCT (n=4393; mean age: 50.4 years), 36.8% received allogeneic HCT, 57.9% were male, and 8.8% were <18 years of age (**Table 1**).
- The majority (53.9%, n=2370) of patients who received HCT had a CCI score of 1–2. The proportions of patients with APR-DRG illness severity level 1, 2, 3, and 4 were 46.6%, 34.6%, 11.0%, and 7.8%, respectively (**Table 2**).
- During the index hospitalization, 1841 patients (41.9%) had a diagnostic code for opportunistic infection in their discharge records.
- During the index hospitalization among the overall population with HCT, 7.3% (n=319) of patients had dsDNA virus infections, and among those who received allogeneic HCT, 13.4% (n=216) had dsDNA virus infections.
- During index HCT hospitalizations 157 deaths occurred, resulting in a population of 4236 post-discharge patients.

Table 1. Demographics of HCT study population.

Demographic		HCT study population N=4393	
Age (years)	Mean	50.4	
	Standard deviation	18.6	
	Median	56.0	
		n	%
Age group (years)	0–20	450	10.2
	21–40	591	13.5
	41–50	614	14.0
	51–60	1136	25.9
	⩾61	1602	36.5
Adult/pediatric	Adult (⩾18 years)	4007	91.2
	Pediatric (<18 years)	386	8.8
Transplant type	Allogeneic HCT	1617	36.8
	Autologous HCT	2776	63.2
Sex	Female	1848	42.1
	Male	2545	57.9
US region	Midwest	602	13.7
	Northeast	2027	46.1
	South	1543	35.1
	West	221	5.0
Race	Black	577	13.1
	Hispanic	74	1.7
	Other	964	21.9
	White	2778	63.2
Urban/rural hospital	Rural	244	5.6
	Urban	4149	94.4
Teaching status	No	545	12.4
	Yes	3848	87.6
Number of beds	<200	243	5.5
	200–399	594	13.5
	400–599	635	14.5
	⩾600	2921	66.5

HCT, hematopoietic cell transplantation.

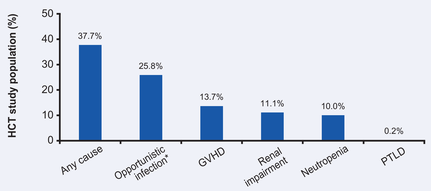
Table 2. Clinical characteristics of the HCT study population.

Clinical characteristic		N=4393	
CCI	Mean	2.75	
	Standard deviation	1.75	
	Median	2.00	
		n	%
CCI group	0	278	6.3
	1–2	2370	53.9
	3–4	1262	28.7
	⩾5	483	11.0
APR-DRG severity level	1 – Minor	2049	46.6
	2 – Moderate	1519	34.6
	3 – Major	484	11.0
	4 – Extreme	341	7.8

APR-DRG, All Patient Refined-Diagnosis Related Group; CCI, Charlson Comorbidity Index; HCT, hematopoietic cell transplantation.

- Among the patients who survived the index HCT hospitalization, 37.7% (n=1595) had a hospital readmission for any cause during the follow-up period. Non-infection-related readmissions were most frequently due to GVHD (13.7%, n=579), renal impairment (11.1%, n=470), and neutropenia (10.0%, n=422; **Figure 1**).
- Among the patients who survived the index HCT hospitalization, 25.8% (n=1091) had hospital readmissions related to opportunistic infections, which include viral, bacterial, and fungal infections (**Figure 1**). Among the patients who survived the index HCT hospitalization, 8.2% (n=349) had hospital readmissions related to dsDNA virus infections. The frequency of hospital readmissions related to opportunistic infections and dsDNA virus infections are not mutually exclusive, as patients may have had both dsDNA and other non-dsDNA virus opportunistic infections.

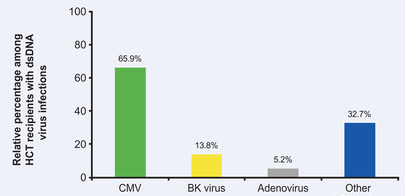
Figure 1. Frequency of hospital readmissions in patients who were alive after the index HCT categorized by cause.



*Opportunistic infection-related readmissions include readmissions related to viral, bacterial, and fungal infections. Patients may have multiple readmissions or readmission with multiple diagnoses. Thus, the categories of readmissions are not mutually exclusive.
GVHD, graft-versus-host disease; HCT, hematopoietic cell transplantation; PTLD, post-transplant lymphoproliferative disorder.

- Of the hospital readmissions related to opportunistic infections, 32.0% (n=349) were related to dsDNA virus infections. Of the patients with hospital readmissions related to dsDNA virus infections, 65.9% (n=230) had infections with CMV, 13.8% (n=48) with BK virus, 5.2% (n=18) with adenovirus, and 32.7% (n=114) had other dsDNA virus infections (**Figure 2**).

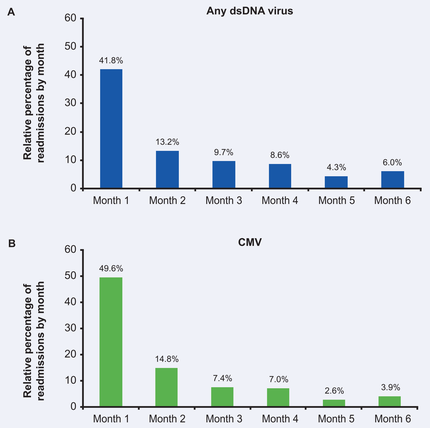
Figure 2. Relative percentage of hospital readmissions related to dsDNA virus types among HCT recipients with any dsDNA virus infection-related readmissions.



*Other dsDNA virus infections included those of human papillomavirus, human herpes virus types 6 or 7, varicella zoster virus, Epstein–Barr virus, and herpes simplex virus.
CMV, cytomegalovirus; dsDNA, double-stranded DNA; HCT, hematopoietic cell transplantation.

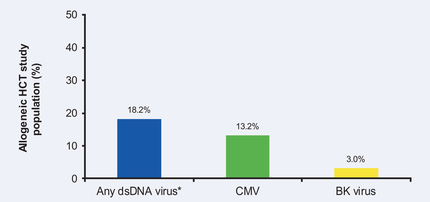
- Among patients with any dsDNA virus infection, CMV infection, and BK virus infection, 41.8%, 49.6%, and 56.3%, respectively, had hospital readmissions within the first month after hospital discharge (**Figure 3**). Over half (55.6%) of readmissions related to adenovirus infections were within the first 3 months post-HCT hospitalization.
- Among the surviving study population with allogeneic HCT, hospital readmission rates related to dsDNA virus infections were high (**Figure 4**).
- Readmission of patients with high-severity APR-DRG levels of 3 – major severity (22.3%) and 4 – extreme severity (19.1%) were the most frequent (**Figure 5**).

Figure 3. Relative percentage* of monthly hospital readmissions related to (A) any dsDNA virus infection, (B) CMV infection, and (C) BK virus infection during the follow-up period for Months 1–6.



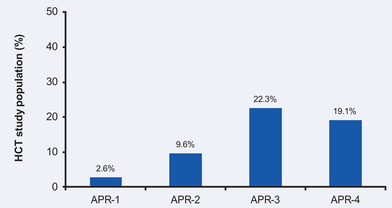
*Relative percentage refers to the percentage of hospital readmissions among patients with such related readmissions in the follow-up period.
CMV, cytomegalovirus; dsDNA, double-stranded DNA.

Figure 4. Frequency of hospital readmissions related to dsDNA virus types among recipients of allogeneic HCT.



*Hospital readmissions related to infections with cytomegalovirus and BK virus are subsets of those related to infections with any dsDNA virus.
CMV, cytomegalovirus; dsDNA, double-stranded DNA; HCT, hematopoietic cell transplantation.

Figure 5. Frequency of hospital readmissions categorized by APR-DRG severity of illness level.



APR-DRG severity level rated 1–4: minor, moderate, major, and extreme.
APR-DRG, All Patient Refined-Diagnosis Related Group; HCT, hematopoietic cell transplantation.

LIMITATIONS

Patients with virus infections were identified using ICD-9 diagnosis codes in the study and those with less severe virus infections might not have been coded with the ICD-9 diagnosis codes during hospitalization. Thus, prevalence of virus infections are most likely an underestimate of the actual prevalence.

CONCLUSIONS

- **Hospital readmissions related to opportunistic infections were observed to be relatively common among patients post HCT.**
- **Approximately one in three hospital readmissions related to opportunistic infections were due to dsDNA virus infections, with CMV infections being the most common.**
- **Hospital readmissions due to dsDNA virus infections were high among patients who received allogeneic HCT.**
- **Medications used to treat CMV infections are frequently associated with side effects of neutropenia and renal impairment, which were among the top three causes of non-opportunistic infection-related hospital readmissions of patients with HCT.[4]**
- **The majority of hospital readmissions among HCT recipients were categorized as major or extreme severity, according to the APR-DRG severity level of illness.**
- **Future strategies that minimize the risks of these infections may have significant clinical and economic advantages.**

REFERENCES

1. Marr KA. *Hematology Am Soc Hematol Educ Program* 2012;2012:265–70.
2. Bejanyan N *et al*. *Biol Blood Marrow Transplant* 2012;18:874–80.
3. Spring L *et al*. *Biol Blood Marrow Transplant* 2015;21:509–16.
4. Bacigalupo A *et al*. *Exper Rev Anti Infect Ther* 2012;10:1249–64.

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DISCLOSURES

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