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Blood transfusions and pulmonary complications after hematopoietic cell transplantation

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Abstract

BACKGROUND—Transfusion of blood products is an essential component of the hematopoietic cell transplantation (HCT) process. Blood transfusion carries several risks including, but not limited to, lung injury. The effect of transfusions on lung complications after HCT has not been previously investigated.

STUDY DESIGN AND METHODS—We retrospectively studied 215 adult allogeneic HCT recipients at the University of Minnesota and examined the association between transfusion of blood components and development of lung complications after HCT. Patients without lung complications were used as the control group.

RESULTS—A total of 113 (58%) of the patients developed lung injury events before Day 180 after HCT. Six-month survival was significantly lower in the lung event group (52%) versus the controls (78%; $p = 0.01$). Patients who eventually developed lung events received more transfusion episodes per week in the first month after HCT (median, 4.3 vs. 2.7 for controls), platelet units per week (3.5 vs. 2.0), and RBC units per week (1.8 vs. 1.4; $p < 0.01$) for all. In a multivariable analysis, each additional transfusion before Day +30 was associated with a 2.7% higher risk of lung complication (95% confidence interval, 0.8–4.8; $p = 0.01$), adjusting for time to engraftment, conditioning intensity, and donor type. Blood utilization increased after the lung event and remained high for several months relative to controls.

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CONFLICT OF INTEREST

The authors have disclosed no conflicts of interest.

SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article at the publisher's website

CONCLUSION—Our data suggest that transfusion of blood products is associated with and may further complicate lung complications after HCT. Cautious use of blood components in the post HCT period is recommended.

Pulmonary complications after allogeneic hematopoietic cell transplantation (HCT) are major contributors to posttransplant morbidity and mortality and decreased quality of life.^{1–13} Factors reported to increase the risks of pulmonary complications include myeloablative preparative regimens, high-dose total body irradiation (TBI), age greater than 40, acute graft-versus-host disease (GVHD), or transplants for acute leukemia or myelodysplastic syndrome.^{2,6} Additionally, all HCT patients receive large numbers of blood and platelet (PLT) transfusions.¹⁴ Blood transfusions, mainly PLTs and plasma, are associated with acute and delayed pulmonary complications,^{15,16} especially in critically ill patients.^{17,18} These pulmonary complications may be broadly defined or specific such as in transfusion-related acute lung injury (TRALI).^{17–21} The pathophysiologic mechanism of TRALI is thought to be a two-hit model in which factors activate or sensitize the pulmonary endothelium and then transfusion of plasma-containing products such as PLTs provide human leukocyte antigen (HLA) antibodies that interact with the recipient's neutrophils leading to the adverse lung event, TRALI.^{22,23} In HCT or patients with neutropenia, the pathophysiologic mechanism of transfusion-associated pulmonary complications is not so clear. These patients experience many events including drug or radiation toxicity, infections, or systemic inflammatory cascades that can sensitize the pulmonary endothelium. In addition, PLT products contain a variety of cytokines including proinflammatory factors.^{24,25} PLT transfusions may thereby directly contribute to pulmonary complications in HCT recipients. To examine this pathophysiologic relationship, we studied blood utilization in adult HCT recipients to identify any direct association between transfusion therapy and pulmonary complications.

MATERIALS AND METHODS

We reviewed the blood product utilization of 215 consecutive adult HCT patients at the University of Minnesota between January 2008 and December 2012. Twenty patients were excluded for the following reasons: offspring or twin donor (n = 11), lung complications before transplant (n = 4), or incomplete transfusion data (n = 5) leaving 195 for analysis. Blood utilization was quantitated as the total number of transfusion episodes and the number of transfusion episodes per week. Transfusion of any dose of each unique component (red blood cells [RBCs], plasma, or PLTs) in 1 day was counted as one transfusion episode. Blood products were supported from the American Red Cross.

Patients with pulmonary complications were identified through the University of Minnesota Blood and Marrow Transplant database, which prospectively records clinical and laboratory information on all patients transplanted at our center. Pulmonary complications were categorized as acute respiratory distress syndrome/idiopathic pneumonia syndrome (ARDS/IPS), diffuse alveolar hemorrhage (DAH), bacterial pneumonia, fungal pneumonia, viral pneumonia, pneumonia not otherwise specified (NOS), pulmonary edema, and other. These diagnostic categories were based on our detailed review of the transplant database. If

necessary, the serious episodes were further characterized by detailed retrospective review of the medical record and all relevant microbiologic, virologic, and pathologic studies.

Definition of lung events

The diagnostic criteria, incidence, and outcomes of non-infectious lung events occurring later than Post-HCT Day 80 have been reported²⁶ and similar data review was performed for all lung events during the study period. Infections were determined based on data obtained through bronchoscopy and bronchoalveolar lavage, lung biopsy or autopsy (if available), microbiology data, and the treating physician's notes. Review of the infectious work-up included information from cytologic and pathologic analyses with conventional staining, culture, and available testing for bacteria, acid fast Bacilli, *Legionella* species, fungus, and *Pneumocystis carinii*; shell vial culture, routine culture, enzyme-linked immunosorbent assay, and polymerase chain reaction as available for cytomegalovirus (CMV), respiratory syncytial virus, and other respiratory viruses; immunofluorescence staining for CMV, herpes simplex virus, varicella zoster virus, respiratory syncytial virus, parainfluenza virus, influenza virus, adenovirus, and *Legionella*; and cultures for *Mycoplasma* and chlamydia. Fungal pneumonia was diagnosed based on the European Organization for Research and Treatment of Cancer published criteria.²⁷

Previously described definitions for the different syndromes within the noninfectious lung complications were used. All patients underwent a bronchoalveolar lavage to exclude infection. Bronchiolitis obliterans (BO) was diagnosed based on a moderate to severe obstructive pattern on pulmonary function tests: forced expiratory volume in 1 second of less than 80% and forced expiratory volume in 1 second/forced vital capacity of less than 70% of the predicted value along with typical findings on high-resolution computed tomography. These included areas of decreased attenuation of lung parenchyma, expiratory air trapping, and subsegmental or segmental bronchial dilatation. Lung biopsy confirmation was required to establish diagnosis of BO and the histopathologic criteria used included obliteration of the airway lumen of terminal bronchioles due to granulation tissue containing peribronchial, bronchial, and perivascular mononuclear infiltrates.^{28,29} Bronchiolitis obliterans syndrome (BOS) was diagnosed based on the same clinical criteria, but without histologic confirmation. Bronchiolitis obliterans with organizing pneumonia (BOOP) was diagnosed based on the presence of a ventilatory defect, decreased diffuse lung capacity for carbon monoxide, and normal expiratory flow with imaging findings of peripherally distributed patchy air space consolidation and nodular opacities and, if available, biopsy results for confirmation.^{30,31} IPS was diagnosed based on exclusion of infectious etiology, presence of multilobar infiltrates, severe restrictive pattern on spirometry, and lung biopsy results if obtained.³² DAH was diagnosed by the acute onset of alveolar infiltrates and hypoxemia with a progressively bloodier alveolar lavage on bronchoscopy.³³ Rare pulmonary complications of noninfectious etiology include pneumothorax, ARDS, pulmonary fibrosis, pulmonary embolism, and pulmonary vascular events. Patients with the different syndromes of late-onset noninfectious pulmonary complications were classified into four groups: BO, BOS, or BOOP (BO/BOS/BOOP); IPS or ARDS (IPS/ARDS); DAH (DAH); and rare entities (other).

Blood utilization data were obtained from hospital blood bank records and were merged with the clinical transplant database for analysis. Our blood and marrow transplant program transfusion policy suggests that prophylactic PLT transfusions were administered to non-bleeding patients at a pretransfusion trigger of less than $10 \times 10^9/L$ unless additional risks of bleeding (e.g., mucositis, plasma coagulation disorder, sepsis) are present. Treatment of therapeutic bleeding followed World Health Organization guidelines. RBC transfusions were administered for a hemoglobin level of less than 8 g/dL. All blood products were irradiated before transfusion to prevent transfusion-associated GVHD and all cellular blood products were leukoreduced within 72 hours of collection to prevent alloimmunization and transmission of CMV and to limit white blood cell (WBC)-associated transfusion reactions. The mean age of transfused blood products was RBCs 22.7 days (maximum allowable, 42 days), plasma 1.5 days after thaw (maximum allowable, 5 days), and PLTs 4 days (maximum allowable, 5 days).

Statistical analysis

Characteristics of patients who had a lung complication were compared to contemporaneous HCT controls using a two-sided Wilcoxon rank-sum test for continuous variables and Fisher's exact test for categorical variables. Kaplan-Meier estimations were used to calculate survival from time of transplant, which was compared between groups using Cox regression with a time-dependent covariate for those with a lung complication. Surviving patients were followed for at least 13 months (median, 41 months).

Transfusions were analyzed as densities (number of episodes or units per week) over time periods of interest to account for differential time on study and summarized with standard descriptive measures including medians, ranges, and boxplots. For boxplots (see figures), the thick horizontal line represents the median, which is surrounded by a box representing the interquartile range (IQR). Observations outside or very far outside the IQR are represented by dashed lines and dots, respectively. Two-sided Wilcoxon rank-sum tests evaluated differences in group distributions of transfusion density, and paired Wilcoxon signed-rank tests evaluated changes before and after the complication onset.

To investigate whether transfusion burden could independently associate with the likelihood of having a pulmonary complication, we considered early transfusion density, defined as transfusions per week from transplant to complication onset, up to a maximum of Day 30 for both event and control groups. There were similar numbers of deaths in both the control (three deaths) and lung complication (five deaths) groups before Day 30. The effects of factors on early transfusion density were modeled using multivariable linear regression with a log link function. The effects of early transfusion density and other factors on the odds of ever having a lung complication were modeled using multivariable fine and gray regression, considering death as a competing risk. Factors included were sex, conditioning intensity, age, CMV serostatus, donor type, and disease risk. Because age and conditioning intensity were confounded with each other, only one could be included in a given model, the choice of which did not impact the transfusion effect estimate. Number of transfusions and neutrophil engraftment were included as time-dependent covariates in the fine and Gray model.

RESULTS

The demographic characteristics of the patients are shown in Table 1. Of the 195 patients, 113 (58%) experienced a pulmonary complication before Day 180. The remaining 82 patients served as the control cohort. Of the 113 patients with lung events, 81 (72%) were related to infection and the most common were bacterial and fungal pneumonia and pneumonia NOS (Table S1, available as supporting information in the online version of this paper). Only three patients had ARDS/IPS.

There were no differences between patient groups in sex, CMV serostatus, donor source, stem cell source, or disease risk (Table 1). The groups differed in age, time to engraftment, conditioning intensity, and survival (Table 1). Patients in the study group were more likely to have received TBI-containing myeloablative conditioning compared to those in the control group who more often received low-dose TBI and reduced-intensity conditioning (RIC). Patients with lung events had significantly poorer survival at 6 months (52%) compared with the control group (78%, $p = 0.01$) and a shorter median survival (209 day vs. 775 days) as well ($p = 0.01$).

Early transfusions and likelihood of lung complications

We analyzed the blood utilization in the pulmonary complication group preceding the date of onset of the complication. To form a suitable comparison group, we considered blood utilization in the control group until Day +30 after HCT (since the median onset of pulmonary complication was Day +24 after HCT). In the lung complication group, transfusions were counted until the date of onset of complication or until Day +30 if onset was later than Day +30. In the period immediately after HCT, but before onset of lung complications, patients who eventually had a lung complication averaged more transfusion episodes per week (median, 4.3 vs. 2.7 for controls; $p < 0.01$), more PLT units per week (median, 3.5 vs. 2.0; $p < 0.01$), and more RBC units per week (median, 1.8 vs. 1.4; $p < 0.01$) compared to the control group. Median plasma units per week were 0 for both groups (Fig. 1).

In multivariable regression we evaluated whether this early transfusion burden was associated with likelihood of developing a pulmonary complication. Each additional transfusion was associated with a 2.6% higher risk of pulmonary complications (95% confidence interval [CI], 0.8–4.8; $p = 0.01$). Myeloablative conditioning with TBI (hazard ratio [HR], 1.7 vs. RIC; $p = 0.01$) also had increased risk of developing a pulmonary complication. Early engraftment (HR, 0.7; $p = 0.29$) was not significant independent of conditioning intensity.

Transplant-related factors predictive of early transfusion burden

Factors predictive of increased transfusion burden before Day +30 were receiving HCT from an umbilical cord blood (UCB) donor (HR, 1.7 vs. sibling; $p < 0.01$), or myeloablative conditioning with TBI (HR, 1.6 vs RIC; $p < 0.01$). CMV status recipient–/donor– (both donor and recipient are CMV negative) had fewer episodes per week (HR, 0.7 vs R+; $p =$

0.02; Table 2). Similar trends were observed when analyzing the number of RBC or PLT units transfused instead of number of transfusion episodes (data not shown).

Blood utilization in the week before and after a lung event

For the 113 patients with a pulmonary complication, there were significantly fewer transfusion episodes in the week before the lung event compared with the week after the onset of the pulmonary complication (Fig. S1, available as supporting information in the online version of this paper). This was true for patients with either bacterial, fungal, or pneumonia NOS, but not for patients with ARDS, DAH, pulmonary edema, viral pneumonia, or other (Fig. S1).

During the week preceding the lung event, the median total of transfusions was five compared to seven transfusions the week after onset of the pulmonary complication ($p < 0.01$; Table S2, available as supporting information in the online version of this paper). PLT transfusions increased substantially in the week after the onset of the pulmonary complication in patients with bacterial pneumonia (5–11 units) and increased slightly in the other groups. The number of transfusions leading to the week of the lung event are shown in Table S2.

Patients with DAH received the largest number of PLT transfusions (11 units) in the week before onset of the pulmonary complication, but surprisingly, this decreased (3 units) in the week after complication onset. There were no significant differences ($p = 0.12$) in the number of RBC units given to those with different types of pulmonary complications (each subgroup median RBC units ranged from 2 to 4).

A few patients with pulmonary complications received very large numbers of PLT and plasma transfusions. For instance, in eight patients with DAH, the maximum number of PLT transfusions was 30, bacterial pneumonia 29, pneumonia NOS 33, and pulmonary edema 33 (Table 3). In the DAH group, the maximum number of plasma units transfused in the week before onset of the pulmonary complication was 21, bacterial pneumonia 17, and ARDS/IPS 15.

Long-term blood utilization

Finally, we analyzed factors that were significantly associated with longer term increased blood utilization, up to Day 180 (Table S3, available as supporting information in the online version of this paper), including transfusion before and after a lung event. All subtypes of pulmonary complications had more transfusion episodes than the control group, especially ARDS/IPS, DAH, bacterial pneumonia, and pulmonary edema, which all averaged 2.6 or more times the number of transfusion episodes per week ($p < 0.01$). Other factors associated with higher transfusion density were myeloablative conditioning with TBI (1.4-fold higher than RIC, $p = 0.02$) and having a UCB donor (1.7-fold higher than sibling donor, $p < 0.01$). The higher transfusion burden associated with UCB donors has been previously described and is likely related to slower engraftment.¹⁴ The number of transfusion episodes was not affected by age or disease risk. Associations were similar when analyzing the number of RBC and PLT units infused instead of the number of transfusion episodes. Multivariable analysis was precluded for plasma units since the majority of patients did not receive any

plasma. RBC and PLT usage continued to be higher in the complication group, even well after most lung events had occurred (Table 4).

DISCUSSION

Patients who undergo HCT require frequent transfusion of blood components as part of their therapy.¹⁴ Transfusion of blood products is associated with adverse lung events in nontransplant patients and contributes to morbidity and mortality in the HCT population.^{15,16} Our data indicate that despite advances in supportive care, patients with pulmonary complications had poor survival. Importantly for this analysis, they received more transfusions preceding the onset of the lung event, had more transfusions after the onset of the lung event, and had worse survival than controls.

Patients with pulmonary complications received more transfusions than patients with no pulmonary adverse events (AEs) during the entire 180-day study period (Table 4), and there was a further increase in transfusions after the pulmonary AEs. We cannot determine whether transfusions had a direct causative role in the pulmonary AEs, yet the transfusion burden in the weeks preceding the lung events were greater than in the controls.

Blood products may contain inflammatory substances that could accentuate pulmonary dysfunction or increase its clinical consequences. PLT concentrates contain cytokines and proinflammatory mediators that interact with a number of cell types, including endothelial cells and WBCs, and thus could potentially have an adverse impact on patients with damaged endothelium or pulmonary vascular damage.^{34–38} While the cytokines in the transfused blood products can be linked to lung injury such as TRALI, their impact on causing lung infections is not clear. The association between increased transfusion burden and lung complications can be related to the concomitant reduced ability of the marrow to produce fully functional WBCs aimed at preventing infections.

Aged blood products have been linked to increased risks of transfusion-related lung injuries through several mechanisms including soluble mediators such as bioactive lipids and CD40L that accumulate during storage of RBCs and PLTs and biochemical changes in the aging RBCs leading to increase in the RBC proinflammatory properties.³⁹ One limitation of our analysis is that we did not have the data for the age of each blood product to determine if that was of any significance. Another limitation of this analysis is the lack of comparison of baseline (pretransplant) pulmonary function between the control group and the complication group. Of note, noninfectious inflammatory syndromes, ARDS/IPS, were only 2.7% of lung complications in this study, with the majority of lung complications being infectious (71.7%) or pulmonary edema (15%).

In the week preceding the onset of the pulmonary AE, patients with ARDS and DAH had the largest total blood and PLT use. For patients with DAH, after the event PLT use decreased by at least 8 units in four patients, increased from 9 to 46 in one, and was relatively unchanged in three. The decrease in PLT usage among some DAH patients after the event was not anticipated and cannot be fully explained.

These data suggest that extensive transfusion use may be associated with and possibly further complicate pulmonary injuries after HCT. Therefore, we suggest caution regarding excessive transfusion in HCT recipients. Additionally, techniques such as leukoreduction^{24,40} and storage of PLTs in additive solutions instead of plasma to limit the proinflammatory stimuli associated with transfusion may limit the morbidity and mortality of pulmonary injury after allogeneic HCT.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

ABBREVIATIONS

AE(s)	adverse event(s)
ARDS/IPS	acute respiratory distress syndrome/idiopathic pneumonia syndrome
BO	bronchiolitis obliterans
BOOP	bronchiolitis obliterans with organizing pneumonia
BOS	bronchiolitis obliterans syndrome
DAH	diffuse alveolar hemorrhage
HCT	hematopoietic cell transplantation
HR	hazard ratio
IQR	interquartile range
NOS	not otherwise specified
RIC	reduced-intensity conditioning
TBI	total body irradiation
UCB	umbilical cord blood

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Fig. 1. Transfusion density during the first 30 days by group and blood product.

TABLE 1

Demographic factors and transplant outcomes after HCT *

	Pulmonary complication group (n = 113)	Control group (n = 82)	p value
Demographic factors			
Age (years) at transplant			
Median (range)	41 (18–68)	49 (19–69)	<0.01
18–39	52 (46)	13 (16)	
40–54	36 (32)	41 (50)	
55–69	25 (22)	28 (34)	
Sex			
Male	64 (57)	48 (59)	0.88
Female	49 (43)	34 (41)	
CMV serostatus			
R+	74 (65)	48 (59)	0.72
R–/D–	24 (21)	23 (28)	
R–/D+	10 (9)	7 (9)	
Unknown	5 (4)	4 (5)	
Disease type			
ALL	16 (14)	6 (7)	0.09
AML	32 (28)	32 (39)	
CML	7 (6)	2 (2)	
Other leukemia	5 (4)	1 (1)	
Myelodysplasia	16 (14)	6 (7)	
Non-Hodgkin’s lymphoma	10 (9)	16 (20)	
Hodgkin’s lymphoma	7 (6)	4 (5)	
Myeloproliferative disease	6 (5)	1 (1)	
Other malignancy	9 (8)	9 (11)	
Nonmalignant	5 (5)	5 (6)	
Donor source			
Sibling	37 (33)	32 (39)	0.20
Unrelated donor	9 (8)	2 (2)	
UCB	67 (59)	48 (59)	
Stem cell source			
Marrow	12 (11)	4 (5)	0.27
PBSC	34 (30)	30 (37)	
UCB	67 (59)	48 (59)	
Disease risk [‡]			
High risk	69 (61)	50 (61)	0.99
Standard risk	44 (39)	32 (39)	
Conditioning intensity			
TBI with myeloablative	57 (50)	21 (26)	<0.01
TBI with RIC	52 (46)	53 (65)	

	Pulmonary complication group (n = 113)	Control group (n = 82)	p value
No TBI	4 (4)	8 (10)	
<i>Transplant outcomes</i>			
Neutrophil engraftment			
Days to engraftment, median (IQR)	17.0 (11–25)	13.5 (7–18)	<0.01
Engrafted	106 (94)	80 (98)	
Died before engraftment	7 (6)	2 (2)	
Survival			
Alive at 6 months (95% CI)	52% (43%–61%)	78% (67%–86%)	<0.01
Survival (months), median (95% CI)	7 (4–15)	25 (13, NE)	

* Data are reported as number (%).

† Standard risk includes AML/ALL in CR1 or CR2 and CML in CP1. High risk is all others.

ALL = acute lymphoblastic leukemia; AML = acute myeloid leukemia; CML = chronic myeloid leukemia; CMV = cytomegalovirus; NE = not estimable; R/D = recipient/donor; PBSCs = peripheral blood stem cells.

TABLE 2

Factors associated with transfusion density^{*}

Risk factor	Relative transfusion density	95% CI	p value
Intercept	3.1		
CMV serostatus			
R+	1.0		
R-/D-	0.7	0.6–1.0	0.03
R-/D+	0.9	0.6–1.3	0.45
Donor type			
Sibling	1.0		
UCB	1.6	1.2–2.1	< 0.01
Unrelated donor	1.3	0.8–2.1	0.27
Age at HCT (years) [†]			
18–39	1.3	1.0–1.5	0.02
40–69	1.0		

^{*} Multivariable linear regression; Shown is the relative change in early transfusion density (number of episodes per week) through day 30. The intercept estimates the expected transfusion density for a patient in the reference categories (lacking all higher risk factors). Effects were similar when considering PLT or RBC units instead of total episodes (data not shown).

[†] In a separate model that substituted conditioning intensity for age, TBI with myeloablative conditioning had 1.6 times the expected early transfusion density (95% CI, 1.3–1.9; p < 0.01) compared to RIC.

TABLE 3

Transfusions in the pulmonary complications group 1 week preceding and 1 week after the event

Subgroup	1 week before event			1 week after event		
	Mean	Median	Maximum	Mean	Median	Maximum
All patients (n = 113)						
Transfusion episodes	5.5	5	18	7.1	7	20
PLT units	6.3	4	33	8.9	6	48
Plasma units	0.6	0	21	0.7	0	17
RBC units	2.3	2	8	2.6	2	8
ARDS/IPS (n = 3)						
Transfusion episodes	10.0	11	13	10.0	11	18
PLT units	8.7	10	10	15.5	16	29
Plasma units	5.0	0	15	0.3	0	1
RBC units	3.0	2	6	3.0	4	5
DAH (n = 8)						
Transfusion episodes	8.3	9	18	6.4	3	19
PLT units	12.5	11	30	10.8	3	46
Plasma units	2.8	0	21	2.6	0	11
RBC units	4.0	4	8	2.6	2	8
Other (n = 4)						
Transfusion episodes	3.5	4	7	5.5	6	9
PLT units	1.9	2	4	5.2	5	10
Plasma units	0.0	0	0	0.0	0	0
RBC units	2.0	2	4	1.5	2	2
Bacterial pneumonia (n = 27)						
Transfusion episodes	6.2	6	13	9.4	10	20
PLT units	7.6	5	29	12.5	11	48
Plasma units	0.8	0	17	0.4	0	10
RBC units	2.2	2	6	3.1	4	7
Fungal pneumonia (n = 26)						
Transfusion episodes	4.5	4	13	5.9	5	14

Subgroup	1 week before event			1 week after event		
	Mean	Median	Maximum	Mean	Median	Maximum
PLT units	4.7	3	15	6.5	4	21
Plasma units	0.2	0	4	0.4	0	8
RBC units	1.8	2	6	2.5	2	8
Pneumonia NOS (n = 19)						
Transfusion episodes	5.1	4	14	7.2	8	16
PLT units	5.6	4	33	8.4	6	46
Plasma units	0.3	0	6	0.6	0	6
RBC units	2.2	2	6	3.0	2	6
Pulmonary edema (n = 17)						
Transfusion episodes	5.8	6	14	7.2	7	14
PLT units	6.0	3	33	8.6	8	26
Plasma units	0.0	0	0	1.4	0	17
RBC units	2.8	2	6	2.7	2	6
Viral pneumonia (n = 9)						
Transfusion episodes	3.2	2	13	4.2	2	14
PLT units	4.3	1	25	4.6	1	18
Plasma units	0.0	0	0	0.0	0	0
RBC units	1.2	2	3	1.1	0	4

TABLE 4

Transfusions before Day 30, Days 31–60, and Days 61–180

Time interval after transplantation	Median	
	Complication group (n = 113)	Control group (n = 82)
Days 0–30		
Transfusion episodes	22.00	11.00
PLT units	21.00	8.00
Plasma units	0.00	0.00
RBC units	8.00	6.00
Days 31–60 *		
Transfusion episodes	12.50	1.00
PLT units	10.50	0.00
Plasma units	0.00	0.00
RBC units	4.00	2.00
Days 61–180 *		
Transfusion episodes	7.00	0.00
PLT units	5.00	0.00
Plasma units	0.00	0.00
RBC units	4.00	0.00

* Excluding patients who died before Day 31 or Day 61, respectively.