Early Posttransplant Blood Transfusion and Risk for Worse Graft Outcomes

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Introduction: Blood transfusion is a risk factor for allosensitization. Nevertheless, blood transfusion posttransplant remains a common practice. We evaluated the effect of posttransplant blood transfusion on graft outcomes.

Methods: We included nonsensitized, first-time, kidney-alone recipients transplanted between 1 July 2015 and 31 December 2017. Patients were grouped based on receiving blood transfusion in the first 30 days posttransplant. The primary end point was a composite outcome of biopsy-proven acute rejection, death of any cause, or graft failure in the first year posttransplant. Secondary outcomes included the individual components of the primary outcome and the cumulative incidence of *de novo* donor-specific antibodies (DSAs).

Results: Two hundred seventy-three patients were included. One hundred twenty-seven (47%) received blood transfusion. Patients in the transfusion group were more likely to be older, have had a deceased donor, and have received induction with basiliximab. There was no difference between groups in the composite primary outcome (adjusted hazard ratio = [HR] 1.34; 95% confidence interval [CI], 0.83–2.17; $P =$ 0.23). The cumulative incidence of *de novo* DSAs during the first year posttransplant was similar between groups (12.8% transfusion vs. 10.9% no transfusion, $P = 0.48$).

Conclusion: Early transfusion of blood products in kidney transplant recipients receiving induction with lymphocyte depletion was not associated with an increased hazard of experiencing acute rejection, death from any cause, or graft loss.

S ensitization to human leukocyte antigens (HLAs) remains a critical obstacle to successful transplantation.[1–7] Over the last decade, there has been a significant effort by the transplant community to prevent and control the production of HLA antibodies before and after organ transplantation.

Pregnancy, blood product transfusion, and previous organ transplantation have been associated with the development of HLA sensitization. Kidney transplant candidates are at particularly increased risk for sensitization from blood transfusion because of the high prevalence of anemia associated with kidney disease.[8] Exposure to HLA antigens on the surface of red blood cells and leukocytes has been associated with not only the development of new anti-HLA antibodies but also an increase in the breadth of the preexisting antibody profile, measured by calculated panel reactive antibody.[9,10] The use of leukocyte-reduced blood products does not seem to eliminate such a risk.[11–13] International guidelines for the management of anemia in patients with chronic kidney disease have been established to standardize anemia treatment and promote a reduction in blood transfusion.[14] These guidelines explicitly call for avoiding the administration of blood products in patients eligible for organ transplantation.

This universal consensus regarding the need to avoid blood products in kidney transplant candidates does not extend into similar cautionary calls in the posttransplant setting. Blood product transfusions are used frequently in transplant recipients, especially in the early posttransplant period. Such a difference in clinical practice might stem from the presumption that the risk for allosensitization after transfusion of blood products is mitigated by concomitant use of immunosuppressive induction and maintenance drugs.[15]

To date, only a few retrospective studies have evaluated the immunologic safety of posttransplant

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blood transfusion. These reports had conflicting results in terms of the risk for acute rejection and graft and patient survival.[16–20] Therefore, we aimed to evaluate whether the transfusion of blood products was indeed associated with an increased risk for acute rejection, graft loss, or death by any cause in nonsensitized kidney transplant recipients on maintenance immuno-suppressive therapy.

METHODS

Study Design and Participants
This was a retrospective cohort study that included nonsensitized adults who received either a deceased or a living donor kidney transplant at our center between 1 July 2015 and 31 December 2017. We excluded patients who had any historic evidence of HLA sensiti-zation defined as calculated panel reactive antibody >0% and/or panel reactive antibody class I or class II >0%, had a previous organ transplantation, or had a kidney transplantation combined with other solid organ.

The clinical and research activities being reported are consistent with the Principles of the Declaration of Istanbul as outlined in the Declaration of Istanbul on Organ Trafficking and Transplant Tourism.

Main Exposure
The main exposure was a transfusion of any blood product performed within 30 days after trans-plantation. We chose this definition based on published literature suggesting that the majority of blood trans-fusions occur within the first month after trans-plantation.[16,17] Only leukocyte-reduced blood products are used for transfusion in kidney transplant recipients at our center. Patients were divided into 2 groups: (1) early posttransplant transfusion and (2) no early transfusion. A blood transfusion was confirmed based on a review of records from the blood bank and indi-vidual patients' chart review. For patients who received multiple blood transfusions, the date of the first transfusion was used to categorize study participants.

Immunosuppressive Therapies
Most patients received induction therapy with a lymphocyte-depleting agent, either thymoglobulin or alemtuzumab, in compliance with our center's proto-col. In a minority of patients, an interleukin 2 receptor antagonist (basiliximab) was used. All patients had early steroid withdrawal by day 7 posttransplant un-less the patient was on chronic prednisone therapy before transplant. Maintenance immunosuppression was achieved with variable dual immunosuppressive therapy combinations including a calcineurin

inhibitor, mammalian target of rapamycin inhibitors, antimetabolites, and/or belatacept therapy.

Outcomes
The primary outcome was the composite of biopsy-proven acute rejection, death of any cause, or graft loss in the first 12 months after transplant. Secondary outcomes included the individual components of the composite outcome and the cumulative incidence of developing *de novo* DSAs during the first year after transplant. A rejection episode was defined as any episode of biopsy-proven acute cellular, antibody-mediated, mixed, or borderline cellular rejection of the transplanted kidney according to the Banff 2013 histopathologic classification. All biopsies were for cause. Graft loss was defined as a return to dialysis or retransplantation at any time after the initial transplant episode. DSAs were identified using Luminex solid phase assay (One Lambda, Canoga Park, CA) with a mean fluorescence intensity cutoff of 1000. Posttrans-plant DSA screening was performed on a for-cause basis.

Statistical Analysis
A descriptive analysis was performed comparing baseline characteristics between the exposure groups. Continuous variables were expressed as median (25th–75th percentile) and compared with the Mann-Whitney *U* test. Categoric variables were expressed as the ab-solute number (proportion) and compared using the chi-square statistic. To avoid immortal time bias when defining time-based exposure groups, we used a land-mark design.[21] The landmark was set at 30 days after the date of the renal transplantation. Patients who died before 30 days were excluded. Outcomes were assessed from day 30 after transplant until the end of follow-up on 30 June 2019. We used inverse probability of treatment weighting (IPTW) with weights derived from the propensity score to estimate the effect of transfusion in recipients of a kidney transplantation on the hazard of the composite outcome.[22] The propensity score was created using a logistic regression model for the predicted probability of receiving a blood trans-fusion as a function of 25 variables (Supplementary Appendix S1). IPTW-weighted adjusted survival curves and the log-rank test were used to compare outcomes between groups according to the exposure.[23] Log-rank tests were used to evaluate the occurrence and time to an event between the transfusion and no transfusion group. We used the IPTW-weighted Cox proportional hazard model to calculate adjusted HRs with associated 95% Wald CIs for the transfusion group using no transfusion as the reference category. Additionally, the cumulative incidence function was

used to evaluate the incidence of *de novo* DSAs, treating death of any cause as a competing event.[24] A 2-sided $P < .05$ was considered statistically significant. All analyses were performed with SAS University Edition software (SAS Institute Inc, Cary, NC).

Ethics Approval

Institutional research board approval was obtained from The Ohio State University Biomedical Sciences Institutional Review Board (2018H0510) before the initiation of data collection.

RESULTS

Study Cohort

We identified 598 kidney recipients between 2015 and 2017. The application of the inclusion and exclusion criteria resulted in a cohort of 274 individuals (Figure 1). One patient died with a functioning graft within 1 month of transplant and was excluded due to the landmark analysis. There was no other graft loss or loss to follow-up within the first month after transplant. In total, 273 patients were included in the final analysis.

Baseline Clinical Characteristics

Of 273 individuals, 127 (47%) received at least 1 blood product transfusion (33 receiving only intraoperative transfusion, 69 receiving only postoperative transfusion, and 25 receiving both intraoperative and postoperative transfusion), and 146 (53%) did not receive blood products within 1 month after transplantation. Of the 127 individuals who had a transfusion, 6 (5%) received both platelets and packed red blood cells. The median hemoglobin at the time of

Figure 1. Study diagram. ‡Includes any historic PRA class I or class II or calculated panel reactive antibody > 0% before transplant. *Patient died of suicide 9 days posttransplant. PRA, panel reactive antibody.

transfusion was 7.1 g/dl (25th–75th percentile = 6.7–7.5). The median time to transfusion after transplantation was 4.5 days (25th–75th percentile = 2.0–15.0). The most common indication for blood transfusion was an acute drop in hemoglobin to a level below 8 g/dl or asymptomatic anemia with hemoglobin < 7 g/dl. Approximately 63% of patients received a blood transfusion within the first week posttransplantation, and 65% received multiple blood transfusions on several days. The median number of transfused blood products units was 2 (25th–75th percentile = 1–3). Patients were followed for a median time of 1024 days (25th–75th percentile = 824–1258).

Patients who received blood product transfusion were older, received more deceased donors, and had a higher creatinine at 1 month posttransplant. More patients in the transfusion group were discharged on maintenance immunosuppressive therapy with a combination of a calcineurin inhibitor and antimetabolites compared with a combination of a calcineurin inhibitor and a mammalian target of rapamycin inhibitor in the no transfusion group (Table 1).
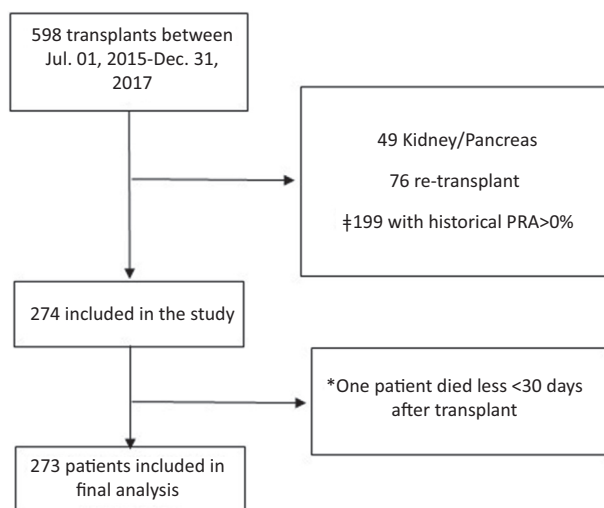
Primary Outcome

The primary outcome occurred in 26 patients (20.5%) in the transfusion group and in 11 patients (7.5%) in the no transfusion group (Table 2). Compared with no transfusion, individuals who received a transfusion in the early period after transplantation had a statistically significant higher hazard of experiencing biopsy-proven acute rejection, death from any cause, or graft loss according to the unadjusted analysis (HR = 2.91; 95% CI, 1.44–5.89; $P < .05$). However, in the IPTW-weighted analysis, blood transfusion was not associated with an increased risk for the composite outcome of biopsy-proven acute rejection, death from any cause, or graft failure (IPTW HR = 1.34; 95% CI, 0.83–2.17; $P = 0.233$) (Figure 2).

Secondary Outcomes of Death, Allograft Survival, and Acute Rejection

A total of 5 individuals (3.9%) who received a transfusion and 2 (1.4%) who did not receive a transfusion died during the first year after transplant. The most common cause of death was sepsis (n = 3). There were 2 suicides (including the patient who died during the 30-day transfusion window). There was no statistically significant difference in the risk for death from any cause between both groups (unadjusted HR = 2.90; 95% CI, 0.56–14.95; $P = 0.20$; IPTW weighted HR = 1.04; 95% CI, 0.31–3.52, $P = 0.95$) (Figure 3).

A total of 16 patients experienced acute rejection in the first 30 days after transplant (Supplementary Table S1). The cumulative incidence of acute

Table 1. Baseline characteristics of the overall study cohort by transfusion within 30 days posttransplantation

Variable	N (%) or median (25th–75th)			P value
	Overall (N = 273)	Transfusion (n = 127)	No transfusion (n = 146)	
Recipient characteristics				
Age, median (25th–75th)	55 (43–62)	57 (47–63)	52 (40–61)	0.0127
Female sex, n (%)	78 (29)	41 (32)	37 (25)	0.2280
Race, n (%)				0.5402
White	197 (72)	90 (71)	107 (73)	
Black	56 (21)	30 (24)	26 (18)	
Asian	5 (2)	2 (2)	3 (2)	
Others	15 (5)	5 (4)	10 (7)	
Cause of ESRD, n (%)				0.1473
Diabetes	92 (34)	52 (41)	40 (27)	
Hypertension	70 (26)	29 (23)	41 (28)	
IgA nephropathy	21 (8)	7 (6)	14 (10)	
Polycystic kidney disease	17 (6)	6 (5)	11 (8)	
Other	73 (27)	33 (26)	40 (27)	
Year of transplant, n (%)				0.2542
2015	59 (22)	33 (26)	26 (18)	
2016	114 (42)	51 (40)	63 (43)	
2017	100 (37)	43 (34)	57 (39)	
Organ donor type, n (%)				0.0005
Living	113 (41)	37 (29)	76 (52)	
Deceased brain death	122 (45)	67 (53)	55 (38)	
Deceased cardiac death	38 (14)	23 (18)	15 (10)	
Total HLA mismatches,[a] n (%)				0.6841[b]
0	42 (15)	18 (14)	24 (16)	
1	3 (1)	1 (1)	2 (1)	
2	15 (5)	4 (3)	11 (8)	
3	41 (15)	19 (15)	22 (15)	
4	60 (22)	30 (24)	30 (21)	
5	71 (26)	33 (26)	38 (26)	
6	41 (15)	22 (17)	19 (13)	
DR mismatches, n (%)				0.4985
0	64 (23)	26 (20)	38 (26)	
1	118 (43)	59 (46)	59 (40)	
2	91 (33)	42 (33)	49 (34)	
Donor/recipient CMV status, n (%)				0.7064
D−/R−	71 (26)	37 (30)	34 (24)	
D+/R−	75 (28)	35 (28)	40 (28)	
D−/R+	47 (18)	21 (17)	26 (18)	
D+/R+	75 (28)	32 (26)	43 (30)	
Induction, n (%)				0.0173
ATG	250 (91)	115 (91)	135 (92)	
ATG and basiliximab	7 (3)	4 (3)	3 (2)	
Basiliximab	8 (3)	7 (6)	1 (1)	
Alemtuzumab	8 (3)	1 (1)	7 (5)	
Maintenance immunosuppression, n (%)				0.0041
CNI/antimetabolites	68 (25)	40 (31)	28 (19)	
CNI/mTORi	174 (64)	67 (53)	107 (73)	
mTORi/antimetabolites	27 (10)	17 (13)	10 (7)	
Belatacept	4 (1)	3 (2)	1 (1)	
AlloScreen checked in the first year after transplant, n (%)	214 (78)	102 (80)	112 (77)	0.6605
Number of AlloScreen tests performed in the first year, median (25th–75th)	3 (2–5)	3 (2–5)	3 (2–5)	0.8818
30-day creatinine, median (25th–75th)	1.71 (1.41–2.32)	1.81 (1.39–3.04)	1.65 (1.43–2.07)	0.0259
180-day creatinine, median (25th–75th)	1.62 (1.26–1.94)	1.62 (1.21–1.93)	1.62 (1.30–1.96)	0.7726
365-day creatinine, median (25th–75th)	1.51 (1.25–1.91)	1.51 (1.22–1.97)	1.50 (1.27–1.91)	0.7246
30-day eGFR, median (25th–75th)	43.01 (30.50–55.85)	40.10 (22.99–55.85)	44.63 (34.58–55.96)	0.0105
180-day eGFR, median (25th–75th)	47.13 (37.56–59.48)	46.94 (37.59–59.60)	47.53 (37.38–58.85)	0.6882

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Table 1. (Continued)

	N (%) or median (25th–75th)			
Variable	Overall (N = 273)	Transfusion (n = 127)	No transfusion (n = 146)	P value
365-day eGFR, median (25th–75th)	48.81 (36.73–61.95)	47.61 (36.22–61.44)	48.92 (36.82–63.40)	0.4395
Donor characteristics				
Age, median (25th–75th)	42 (30–50)	44 (33–52)	41 (29–49)	0.1268
Female sex, n (%)	126 (46)	58 (46)	68 (47)	0.9036

[a]Total HLA mismatch for loci A, B, and DR.
[b]P value based on asymptotic chi-square due to the extensive calculations required for an exact test with this variable.
CMV, cytomegalovirus; CNI, calcineurin inhibitor; D, donor; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; HLA, human leukocyte antigen; IgA, immunoglobulin A; mTORi, mammalian target of rapamycin inhibitor; R, receptor.

rejection was higher in the transfusion group in the unadjusted analysis (16.4% in transfusion and 5.5% in no transfusion, $P < 0.05$) but not in the IPTW-weighted analysis (IPTW weighted 12.4% in transfusion and 8.3% in no transfusion, $P = 0.11$) (Figure 4a). Death-censored graft failure was similar between the groups (unadjusted 1.6% in transfusion and 0.7% no transfusion, $P = 0.49$; IPTW weighted 1.0% in transfusion and 0.8% no transfusion, $P = 0.79$) (Figure 4b).

Secondary Outcomes of DSAs

The majority of patients (78%) had at least 1 AlloScreen (LABScreen, One Lambda) test checked during the first year posttransplantation. There was no difference between the 2 groups in the number of patients who had an AlloScreen test completed (transfusion 80% vs. no transfusion 77%, $P = 0.66$) or the median numbers of

AlloScreen tests performed (median [25th–77th percentile] = 3 [2–5], $P = 0.88$).

Among patients who received a transfusion, 19 individuals developed *de novo* DSAs by the end of the first year compared with 17 in the no transfusion group. There was no significant difference in the cumulative incidence of *de novo* DSAs between the groups (unadjusted 15.0% in transfusion and 11.6% in no transfusion, $P = 0.38$; IPTW weighted 12.8% in transfusion and 10.9% in no transfusion, $P = 0.48$) (Figure 4c). There was also no significant difference in the DSA class between groups for individuals who developed *de novo* DSAs (Table 2). HLA locus specificity and the mean fluorescence intensity of *de novo* DSAs are listed in Supplementary Tables S2 and S3. Additionally, in patients who had an AlloScreen checked in the first year posttransplant, a similar proportion of patients developed non-DSA HLA antibodies in both groups (transfusion 30% vs. no transfusion 23%, $P = 0.29$).

Table 2. 1-year study outcomes, number of events according to transfusion in the early posttransplant period, hazard ratio with Wald 95% confidence intervals using no transfusion within 30 days as reference, and summary of donor-specific antibody (DSA) type

			Unadjusted		IPTW	
Outcome	Transfusion (n = 127)	No transfusion (n = 146)	Hazard ratio (95% confidence interval) or cumulative incidence (%)	Cox or Gray P value	Hazard ratio (95% confidence interval) or cumulative incidence (%)	Cox or Gray P value
Primary outcome, n (%)						
Death from any cause, graft loss, or any type of rejection	26 (20.5)	11 (7.5)	2.91 (1.44–5.89)	0.0030	1.34 (0.83–2.17)	0.2269
Secondary outcomes, n (%)						
Death from any cause	5 (3.9)	2 (1.4)	2.90 (0.56–14.95)	0.2032	1.04 (0.31–3.52)	0.9517
Biopsy-proven rejection	21 (16.5)	8 (5.5)	Yes: 16.4% No: 5.5%	0.0052	Yes: 12.4% No: 8.3%	0.1137
Cellular	16 (76.2)	6 (75.0)				
Antibody mediated	1 (4.8)	1 (12.5)				
Mixed	0 (0.0)	0 (0.0)				
Borderline	4 (19.0)	1 (12.5)				
Graft loss	2 (1.6)	1 (0.7)	Yes: 1.6% No: 0.7%	0.4904	Yes: 1.0% No: 0.8%	0.7877
De novo DSAs	19 (15.0)	17 (11.6)	Yes: 15.1% No: 11.5%	0.3832	Yes: 12.8% No: 10.9%	0.4790
DSA type, n (%)			Exact χ^2 P value			
Class I	5 (20)	3 (9)	0.3895			
Class II	14 (56)	23 (72)				
Class I and II	6 (24)	6 (19)				

IPTW, inverse probability of treatment weighting.
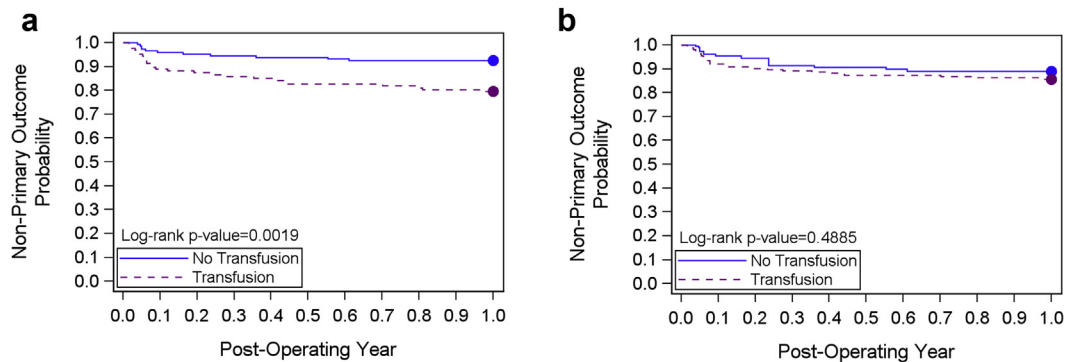
Figure 2. (a) Unadjusted survival curves and (b) inverse probability of treatment–weighted survival curves for the probability of not having the primary outcome.

DISCUSSION

In this single-center study of 273 nonsensitized kidney transplant recipients, we examined whether early transfusion of blood products was associated with worse clinical outcomes and allosensitization. Our data revealed that the transfusion of blood products within the first 30 days after transplantation was not associated with an increased rate of the composite primary outcome of biopsy-proven acute rejection, death from any cause, or graft loss in comparison with patients who did not receive an early blood transfusion. Additionally, early posttransplant transfusion of blood products was not associated with an increased incidence of *de novo* DSAs.
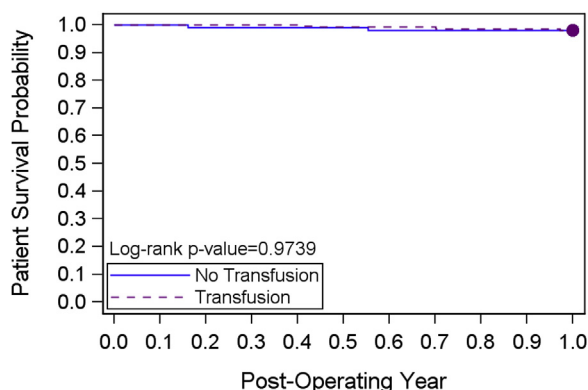
Interestingly, patients who received transfusion had a higher serum creatinine at 30 days posttransplantation. This could be a reflection of the higher number of deceased donors in this group. A worse graft function during the first month posttransplant could also explain the slower recovery of blood counts and the higher need for transfusion in this group.

Our study results are consistent with some of the previously published reports. Scornik et al.[17] examined the effect of transfusion in 746 kidney and kidney pancreas transplant recipients. They reported a

Figure 3. Inverse probability of treatment–weighted survival curves for the probability of the occurrence of no death of any cause.

comparable frequency of posttransplant transfusion in 45% of the patients, with 80% of the transfusions occurring in the first month posttransplantation. Similar to our study, Scornik et al. found the incidence of rejection and graft loss to be similar between patients who did or did not receive blood products. Additionally, in a subset of 199 recipients who were tested for posttransplant antibodies, the incidence of DSA did not differ between transfused and non-transfused patients. Interestingly, patients included in this report received non–leukocyte-depleted blood products. Such products carry a theoretically higher potential for alloimmunization because of the higher content of white blood cells. However, it is worth noting that Scornik et al. used the less sensitive FlowPRA assay for DSA detection, which might have affected the accuracy of their DSA data.

In another report, Verghese et al.[18] examined a cohort of 482 pediatric kidney transplant recipients and found patient survival, risk for acute rejection, and DSA-free survival to be similar in patients who received blood transfusion compared with those who did not. In a subcohort of 134 pediatric recipients who received DSA testing using solid-phase, single antigen bead assay, blood transfusion was not associated with an increased risk for antibody mediated rejection or *de novo* DSAs. In this study, similar to our study, patients received lymphocyte-depleting induction therapy.

Our findings contrast with 2 recent reports. In a study by Ferrandiz et al.,[16] blood transfusion given within 12 months from transplant was associated with an increased risk for antibody-mediated rejection and *de novo* DSA formation in the first year after transplantation. The discrepancy compared with our results could be potentially explained by differences in the use of induction therapy and study design. In our study, 97% of patients received lymphocyte-depleting induction therapy versus 9.2% in the report by Ferrandiz et al.; lymphocyte depletion therapy has been shown to decrease the risk for biopsy-proven acute
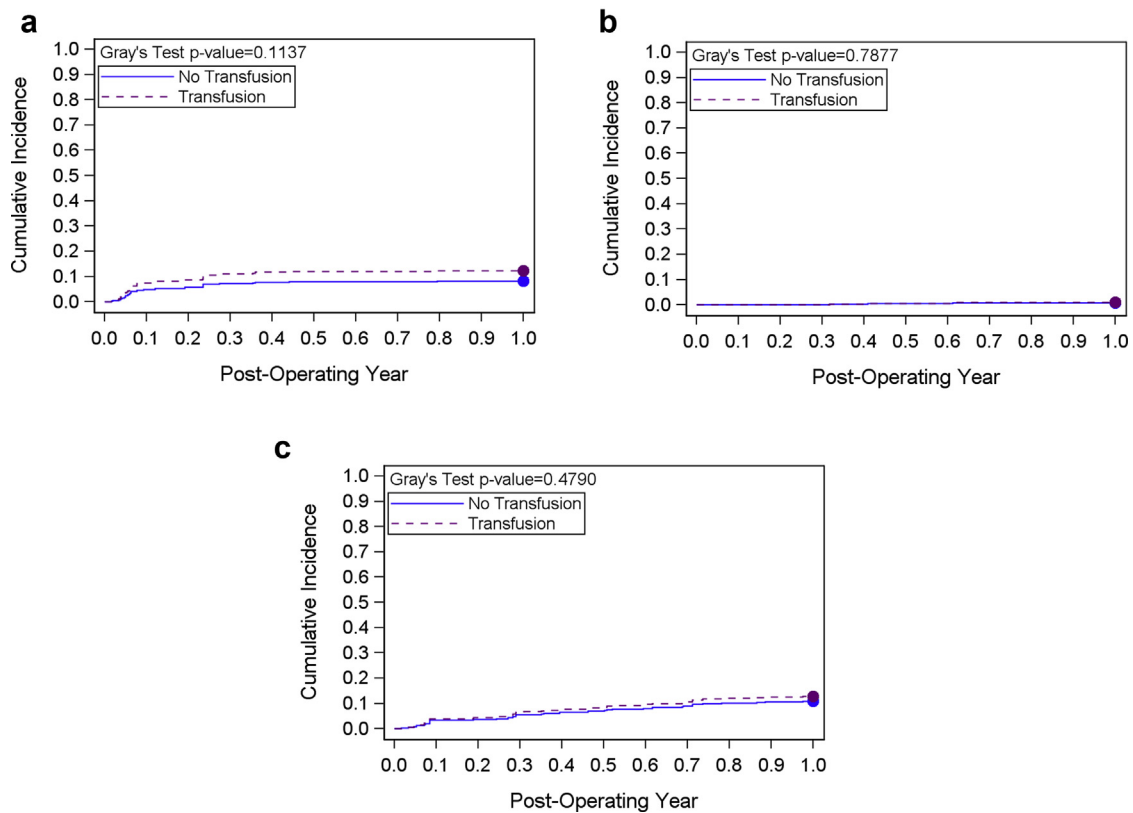
Figure 4. Inverse probability of treatment–weighted cumulative incidence, with death as a competing event of (a) rejection, (b) death censored graft failure, and (c) cumulative incidence of *de novo* DSA.

rejection[25,26] and might have provided additional protection against transfusion-induced allosensitization. Additionally, Ferrandiz *et al.* included patients who received blood products beyond the first month posttransplant (up to 1 year), during which time the intensity of immunosuppressive therapies tends to decrease.

Similarly, a more recent study by Hassan *et al.*[20] found posttransplant blood transfusion to be associated with a higher risk of allograft failure, all rejection, and *de novo* DSA formation. Their study also suggested that posttransplant blood transfusion could evoke *de novo* DSAs. The majority of kidney transplant recipients in this study received lymphocyte depletion with alemtuzumab followed by single-agent maintenance therapy with tacrolimus. The use of tacrolimus monotherapy represents a strategy of immunosuppression minimization. The combination of alemtuzumab with immunosuppression therapy minimization has been clearly associated with inferior allograft outcomes and an increased risk for chronic allograft injury.[27,28] The use of such an immunosuppressive regimen might have made recipients of blood transfusion more susceptible to allosensitization from the blood product and contributed to the inferior outcomes noted in the blood transfusion group. Additionally, in this study, 86 recipients had HLA typing of at least 1 blood donor. Forty-six of these

patients developed *de novo* DSAs. Interestingly, transfusion-specific antibodies for the blood donor HLA antigens occurred mainly in patients who also developed DSAs (40/46, 87%) compared with patients who remained DSA free (3/40, 7.5%). Patients who developed *de novo* DSAs had the traditional risk factors associated with increased alloimmunization compared with the DSA-negative group such as younger age, higher proportion of simultaneous kidney-pancreases recipients, and higher degree of donor-recipient HLA mismatch. Such observation suggests that the development of transfusion-specific antibodies similar to the development of DSAs was the result of under-immunosuppression rather than the trigger that evoked *de novo* DSA production.

The current potent immunosuppressive therapies are capable of averting an alloimmune response to the large load of allo-HLA antigens carried on the tissues of the renal allografts. It seems reasonable that these immunosuppressive therapies will be equally effective in obviating a similar alloimmune response to the allogenic HLA antigens presented on the surface of blood products. Hence, we agree with the presumption that exposure to allo-HLA antigens in the context of blood transfusion does not lead to allosensitization if it occurred under the condition of adequate immunosuppressive therapies.

Our study has several strengths. First, we included only nonsensitized patients to avoid the confounding effect of pretransplant sensitization on graft outcomes and risk for rejection. Second, we used a landmark analysis to estimate unbiased survival probabilities conditional on exposure to a blood product, whereas previous studies have used a naive analysis neglecting the perils of time-dependent exposures. Third, we used IPTW using the propensity score to adequately adjust for the inherent treatment bias in nonrandomized observational studies.

Nevertheless, our study also has limitations that deserve consideration. First, the enrollment of nonsensitized patients decreased our sample size substantially. As a consequence, we observed wide CIs around the point estimates affecting the precision of our findings. Additionally, the inclusion of nonsensitized patients only might limit the applicability of our findings to patients with established pretransplant sensitization. Previous reports have suggested that blood transfusion might have a stronger sensitizing effect in patients with previous exposure to alloantigens.[15] Second, patients underwent for-cause rather than routine DSA screening. This might have reduced the detected incidence of *de novo* DSAs among study participants. Lastly, our study evaluated the risks associated with early perioperative blood transfusion and might not necessarily extend to blood transfusion received later in the posttransplant period.

In summary, in recipients of a kidney-only transplant, early transfusion of blood products was not associated with an increased hazard of experiencing biopsy-proven acute rejection, death from any cause, or graft loss nor was it associated with an increased cumulative incidence of *de novo* DSAs in comparison with patients who did not receive a blood transfusion. Despite increased exposure to non–self-HLA antigen on blood products, our study supports the notion that the risk for alloimmunization related to blood transfusion in the early perioperative period is probably small when lymphocyte depletion and modern immunosuppression maintenance regimens are used.

DISCLOSURE

All the authors declared no competing interests.

AUTHOR CONTRIBUTIONS

RD was the principle investigator and participated in the research design, data collection, data analysis, and writing of the manuscript. JRB participated in statistical analysis and writing manuscript. AD participated in writing and reviewing the manuscript. AL participated in statistical analysis and writing the manuscript. TP participated in writing and reviewing the manuscript.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Appendix S1. Variables included in propensity score IPTW
Table S1. Rejection, death, and graft loss prior to 30-day landmark
Table S2. HLA loci in patients who developed DSA within a year
Table S3. Summary of HLA loci MFI for patients who developed DSA within a year

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