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Clinical implications of early blood transfusion after kidney transplantation

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Pre-transplantation red blood cell transfusion (RBCT) is a well-recognized cause of allosensitization. However, the effects of RBCT after kidney transplantation remain controversial. This study evaluates the impacts of RBCT within the first 30 days post-transplantation (early RBCT) with regard to long-term patient and graft outcomes. We retrospectively analyzed 785 patients who underwent HLA- and ABO-compatible kidney transplantation between 2014 and 2020. Patients were categorized based on whether they received early RBCT. Overall, 18.9% of patients received early RBCT. On multivariable analysis, early RBCT was independently associated with increased risks of all-cause mortality (hazard ratio, 2.264; 95% CI 1.186–4.324; *P* = 0.013) and death-censored graft loss (hazard ratio, 1.995; 95% CI 1.045–3.810; *P* = 0.036). Cumulative incidence of antibody-mediated rejection was significantly higher in the early RBCT group (*P* = 0.024). In the sensitivity analysis, the early RBCT significantly increased the risk of patient mortality (*P* = 0.017), death-censored graft loss (*P* = 0.018) and antibody-mediated rejection (*P* = 0.05), regardless of the donor profile. Early post-transplantation RBCT was associated with increased risks of all-cause mortality, graft loss, and antibody-mediated rejection, highlighting the need for reconsideration of transfusion practices following kidney transplantation.

Keywords Allosensitization, Graft survival, Kidney donor profile index, Kidney transplantation, Transfusion

At the time of kidney transplantation, the majority of patients with end-stage kidney disease have anemia secondary to reduced endogenous erythropoietin production and iron deficiency[1]. Anemia often worsens in the early post-transplantation period for various reasons, including intraoperative blood loss, allograft dysfunction, and the effects of immunosuppressive therapy[2]. Consequently, red blood cell transfusion (RBCT) is frequently administered as an effective and immediate intervention in the early post-transplantation period, with 20–60% of transplant recipients receiving post-transplantation RBCT[3–6].

While the risks of alloimmunization associated with pre-transplantation RBCT are well-established[7,8], the implications of RBCT during the immunosuppressed, post-transplantation period are less clear[9]. The impact of RBCT on graft outcomes has been the subject of considerable debate, with previous studies reporting conflicting results[4–6,10]. This leads to considerable variability in RBCT practices across different transplantation centers and between different physicians, which is further compounded by the absence of a standardized target hemoglobin level for post-transplantation RBCT. The ongoing evolution of immunosuppressive therapies and changing indications for RBCT also add to the complexity of this issue[11–13]. Moreover, continuing advances in solid-phase assays and refinement of the criteria for diagnosing antibody-mediated rejection (AMR) further highlight the pressing need to explore the effects of post-transplantation RBCT considering contemporary clinical practices and emerging medical evidence[14,15].

The objective of this study was to evaluate the clinical implications of RBCT within the first month after kidney transplantation with regard to patient survival, graft survival, and biopsy-proven rejection.

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Results

Baseline characteristics

After applying the inclusion and exclusion criteria, 785 patients were included in this study, 148 (18.9%) of whom received early RBCT (within 1 month after transplantation). Baseline characteristics are summarized in Table 1. No significant differences were observed between the early RBCT and no RBCT groups regarding recipient and donor age, number of HLA mismatches, and proportion of re-transplantation. Recipients in the early RBCT group were more frequently female, had a longer duration of pre-transplantation dialysis, and more frequently received a deceased donor graft, compared to those in the no RBCT group. The proportion of patients receiving anti-thymocyte globulin induction was significantly higher in the early RBCT group (44.6% vs. 19.0%, $P<0.001$). While there were no statistical differences in peak PRA for HLA class I, peak PRA for HLA class II tended to be higher in the early transfusion group ($P=0.032$). The median follow-up duration of the entire study population was 66 months (IQR, 44.0–86.0 months).

Transfusion characteristics

A total of 469 packed red blood cells were administered to 148 recipients within 1 month after kidney transplantation. The median number of packed red blood cells among transfused recipients was 2 (IQR, 1.0–3.0), and the median time from transplantation to the first RBCT was 5.0 days (IQR, 2.0–12.0 days). Although pre-transplantation hemoglobin levels were comparable between the two groups, the lowest hemoglobin level during the first month after transplantation was significantly lower in the early RBCT group than in the no RBCT group (9.6 ± 1.2 vs. 7.6 ± 1.0 g/dL, $P<0.001$).

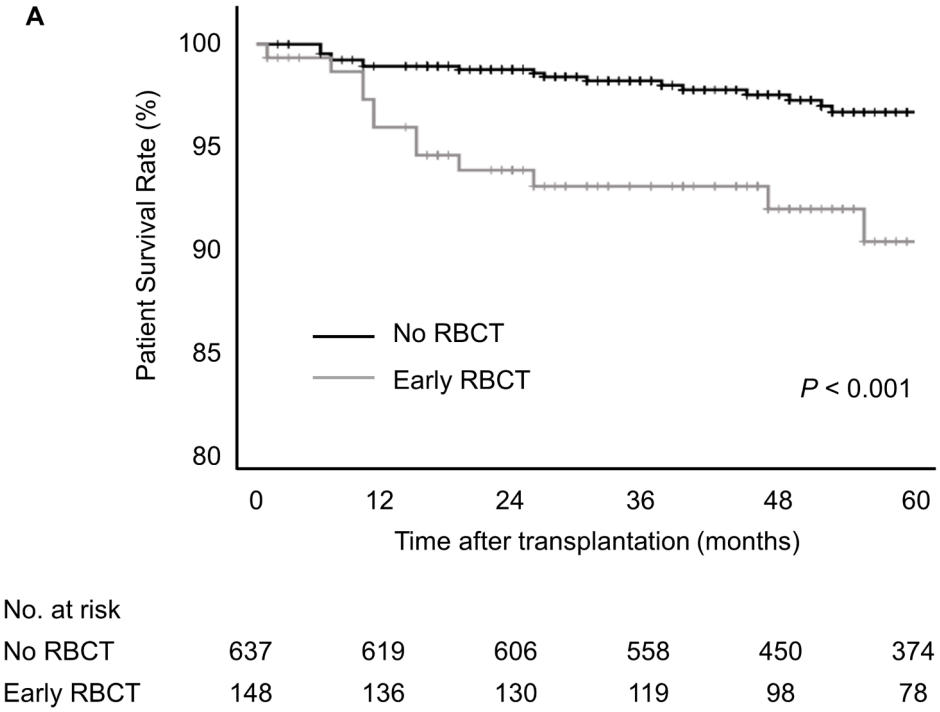
To investigate independent risk factors for requiring early RBCT after transplantation, we conducted multivariable logistic regression analysis (Table S2). Recipient age, diabetes mellitus, body mass index, re-transplantation, dialysis vintage, and intraoperative RBCT did not exhibit significant associations with early RBCT after transplantation. In contrast, female recipient, lower pre-transplantation hemoglobin levels, and anti-thymocyte globulin induction were identified as significant risk factors associated with early RBCT.

Graft and patient outcomes

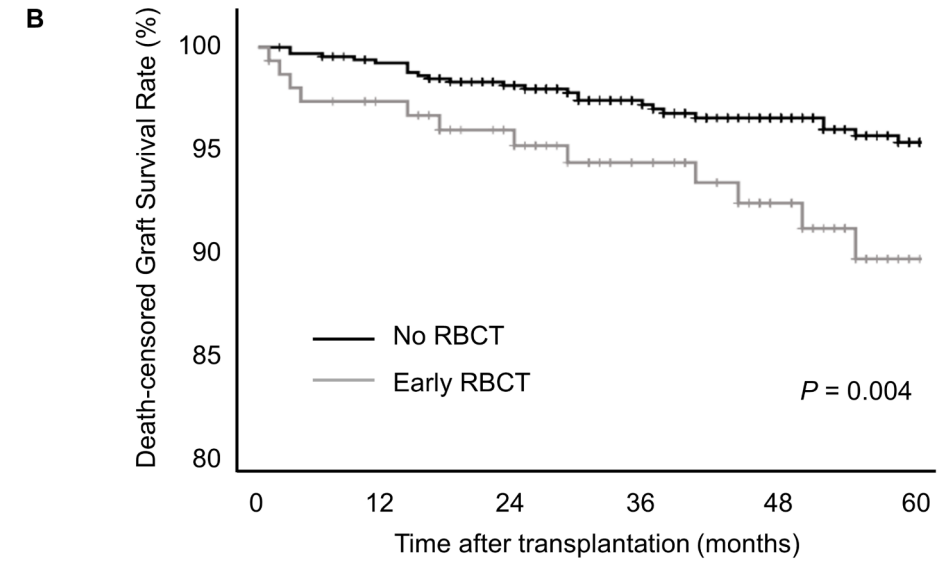
During the follow-up period, 43 (5.5%) of the 785 patients died, and 44 (5.6%) experienced death-censored graft loss. As depicted in Fig. 1, both patient survival and death-censored graft survival were significantly lower in the early RBCT group than in the no RBCT group. The 1-year, 3-year, and 5-year patient survival rates were 95.8%, 92.3%, and 87.4% for the early RBCT group and 98.7%, 97.6%, and 96.2% for the no RBCT group ($P<0.001$). Multivariable Cox regression analysis confirmed the independent association between early RBCT and higher all-cause mortality (adjusted hazard ratio [aHR], 2.264; 95% confidence interval [CI], 1.186–4.324; $P=0.013$; Table 2). Additionally, the amount of transfused packed red blood cells was associated with an increased risk of all-cause mortality when assessed as continuous variable (aHR, 1.130; 95% CI, 1.084–1.177; $P<0.001$). The

	No early RBCT ($n=637$)	Early RBCT ($n=148$)	*P* value
Age (yr; mean ± SD)	48.7 ± 11.9	50.2 ± 11.5	0.177
Female, *n* (%)	240 (37.7%)	74 (50.0%)	0.006
Re-transplant, *n* (%)	49 (7.7%)	12 (8.1%)	0.865
HLA mismatch (mean ± SD)	2.8 ± 1.7	2.9 ± 1.5	0.384
Dialysis vintage (m; median, IQR)	6.0 (1.0–74.0)	56.0 (3.3-112.3)	< 0.001
Pre-transplant Hb (mg/dL; mean ± SD)	11.0 ± 1.5	10.8 ± 1.4	0.279
Lowest Hb during 1 month post-KT (mg/dL; mean ± SD)	9.6 ± 1.2	7.6 ± 1.0	< 0.001
Deceased donor, *n* (%)	206 (32.3%)	84 (56.8%)	< 0.001
Donor age (yr; mean ± SD)	44.9 ± 12.9	46.6 ± 15.1	0.166
Female donor, *n* (%)	313 (49.1%)	70 (47.3%)	0.687
Induction			< 0.001
ATG, *n* (%)	138 (19.0%)	78 (44.6%)	
Basiliximab, *n* (%)	516 (81.0%)	82 (55.4%)	
Tacrolimus, *n* (%)	632 (99.2%)	146 (98.6%)	0.622
Peak PRA for HLA class I, *n* (%)			0.183
0%	417 (65.7%)	89 (60.5%)	
1–50%	159 (25.0%)	37 (25.2%)	
51–100%	59 (9.3%)	21 (14.3%)	
Peak PRA for HLA class II, *n* (%)			0.032
0%	447 (70.4%)	88 (59.9%)	
1–50%	119 (18.7%)	34 (23.1%)	
51–100%	69 (10.9%)	25 (17.0%)	

Table 1. Baseline characteristics. *ATG* anti-thymocyte globulin, *Hb* hemoglobin, *HLA* human leukocyte antigen, *KT* kidney transplant, *PRA* panel reactive antibody, *RBCT* red blood cell transfusion.



No. at risk						
No RBCT	637	619	606	558	450	374
Early RBCT	148	136	130	119	98	78



No. at risk						
No RBCT	637	619	605	557	449	374
Early RBCT	148	136	130	119	98	78

Fig. 1. The Kaplan-Meier curves for (**A**) patient survival and (**B**) death-censored graft survival in the early RBCT and no RBCT groups. *RBCT* red blood cell transfusion.

1-year, 3-year, and 5-year death-censored graft survival rates were 97.3%, 94.4%, and 89.8% for the early RBCT group and 99.4%, 97.1%, and 95.6% for the no RBCT group ($P = 0.004$). Early RBCT was significantly associated with an increased risk of death-censored graft loss on multivariable analysis (aHR, 1.995; 95% CI, 1.045–3.810; $P = 0.036$; Table S1). Infection was the most common cause of death in both groups, followed by malignancy and cardiovascular disease (Table S5). The most common cause of graft failure was rejection, accounting for 51.9% of the graft failure cases in the no early RBCT group and 53.8% in the early RBCT group (Table S6).

Factors	Univariable		Multivariable	
	cHR (95% CI)	*P* value	aHR (95% CI)	*P* value
Age (for 1 year increase)	1.075 (1.041–1.109)	< 0.001	1.073 (1.035–1.114)	< 0.001
Female	0.383 (0.184–0.799)	0.011	0.290 (0.133–0.634)	0.002
Diabetes mellitus	2.055 (1.121–3.769)	0.020	1.934 (0.950–3.938)	0.069
Re-transplantation	1.869 (0.789–4.431)	0.155	2.242 (0.929–5.408)	0.072
Dialysis duration (for 1 month increase)	1.009 (1.005–1.012)	< 0.001	1.007 (1.001–1.012)	0.026
HLA mismatch	1.316 (1.080–1.603)	0.006	1.428 (1.133-1.800)	0.003
ATG induction	4.362 (2.390–7.959)	< 0.001	1.777 (0.842–3.750)	0.131
Deceased donor KT	5.262 (2.652–10.439)	0.006	2.627 (0.957–7.206)	0.061
Donor age (for 1 year increase)	1.021 (0.996–1.047)	0.095	0.991 (0.968–1.014)	0.424
Female donor	1.082 (0.595–1.968)	0.796		
Early RBCT	3.022 (1.640–5.571)	< 0.001	2.264 (1.186–4.324)	0.013

Table 2. Risk factor assessment for all-cause mortality. *aHR* adjusted hazard ratio, *ATG* anti-thymocyte globulin, *cHR* crude hazard ratio, *CI* confidence interval, *HLA* human leukocyte antigen, *KT* kidney transplantation, *RBCT* red blood cell transfusion.

Biopsy-proven allograft rejection

A total of 245 biopsy-proven allograft rejection episodes (134 AMR and 111 TCMR) occurred in 165 recipients. The median time to the first biopsy-proven allograft rejection was 5 months (IQR, 2.0–23.0). Cumulative incidence for AMR was significantly higher in the early RBCT group than in the no RBCT group ($P = 0.024$; Fig. S1), whereas cumulative incidence for TCMR between the two groups was not significantly different ($P = 0.641$). Multivariable analysis confirmed the independent association between early RBCT and the development of AMR (aHR, 1.655; 95% CI, 1.054–2.598; $P = 0.029$). Number of HLA mismatches (aHR, 1.352; 95% CI, 1.181–1.547; $P < 0.001$) and donor age (aHR, 1.019; 95% CI, 1.002–1.036; $P = 0.027$) were also identified as independent risk factors for AMR.

Graft renal function

Mean eGFR values at various time points in the two groups are shown in Fig. S2. Mean eGFR at 1 month after kidney transplantation was significantly lower in the early RBCT group (58.2 ± 28.3 vs. 68.2 ± 21.0 mL/min/1.73 m^2, $P < 0.001$). Mean eGFR was not significantly different between groups at 3 months post-transplantation and thereafter.

Sensitivity analysis

To address potential selection bias due to the inclusion of patients in poor condition in the transfusion group or those receiving kidneys from suboptimal donor, we performed a 1:2 propensity score matching for sensitivity analysis based on the recipient sex, recipient age, donor type (Living or Deceased donor) and the donor profile (Kidney donor profile index; KDPI or Living kidney donor profile index; LKDPI). This analysis resulted in a cohort of 398 kidney transplant recipients. 269 patients (68.1%) received early red blood cell transfusion (RBCT), while 139 patients (31.9%) did not (Table S3). The matched group revealed differences only in preoperative hemoglobin levels and use of antithymocyte globulin. No statistical differences were observed in other variables including the patients' comorbidities, Estimated post-transplant survival score (EPTS), and donor profiles.

Patient survival and death-censored graft survival were considerably lower in the early RBCT group compared to the no RBCT group. The survival rates of patients at 1 year, 3 years, and 5 years were 94.9%, 91.9%, and 89.7% in the RBCT group, while in the no RBCT group, they were 97.4%, 96.6%, and 96.2%, respectively ($P = 0.017$; Fig. S3a). The death-censored graft survival rates at 1 year, 3 years, and 5 years were 97.0%, 96.1%, and 93.9% for the early RBCT group, compared to 98.9%, 98.4%, and 98.4% for the no RBCT group ($P = 0.018$; Fig. S3b). Also, cumulative incidence for AMR was higher in the early RBCT group compared to the no RBCT group ($P = 0.05$; Fig. S4),

Importantly, in risk analyses, early RBCT was independently associated with an increased risk of death-censored graft loss, as shown by multivariable regression analysis (aHR 0.502; 95% CI, 1.150–2.372; $P = 0.007$; Table S4). Number of HLA mismatch also showed the risk, but types of induction agents were not associated with patient outcome.

Discussion

We had hypothesized that early red blood cell transfusion (RBCT) after kidney transplantation would be associated with adverse outcomes, including increased risks of all-cause mortality, graft loss, and antibody-mediated rejection. In this single-center study of 785 kidney transplant recipients, we investigated the clinical implications of early RBCT after transplantation. Our results revealed a significant, dose-dependent association between early RBCT and increased risk of all-cause mortality. Patients receiving early RBCT also had a higher

risk of death-censored graft loss and AMR, compared to those who did not receive early RBCT. However, no significant associations were observed between early RBCT and TCMR or graft renal function after the first post-transplantation month. These results underscore the nuanced associations between early RBCT and specific clinical outcomes following kidney transplantation. Because donor profile was expected to affect posttransplantation outcomes, we performed subgroup analysis for sensitivity analysis. In the subgroup analysis, the early RBCT significantly increased the risk of patient mortality, death-censored graft loss and antibody-mediated rejection, regardless of the donor profile.

Pre-transplantation RBCT is a well-recognized risk factor for developing anti-HLA antibodies[7,8]. To mitigate this risk, considerable efforts have been made to minimize pre-transplantation RBCT and to use leukocyte-depleted blood products[7,16]. Nevertheless, the effects of RBCT during the post-transplantation period, particularly during the period of intense immunosuppressive therapy, remain controversial[4–6,17,18]. In addition to the risk of alloimmunization, both anemia severe enough to require RBCT and RBCT itself may have detrimental effects, especially in the clinical setting of major surgery. Although a substantial proportion (20–60%) of kidney transplant recipients receive post-transplant RBCT, research on the long-term clinical implications of post-transplantation RBCT remains limited. Our study aimed to comprehensively investigate the associations between early post-transplantation RBCT on various long-term outcomes.

Perioperative RBCT has been linked to higher mortality following major surgery[19,20]. This association is secondary not only to preoperative anemia or intraoperative bleeding but also to complications induced by RBCT itself, such as acute lung injury, circulatory overload, infection, and immunosuppression[21]. Kidney transplant recipients commonly experience anemia, leading to widespread use of RBCT in the early post-transplant period[3–6,21]. However, the impact of post-transplant RBCT on patient survival remains controversial, and there is a lack of clear indications for RBCT in this setting.

In the current large-scale study of recent kidney transplant recipients, we found that 18.9% of recipients received early RBCT after transplantation, and receiving early RBCT was associated with a dose-dependent increase in all-cause mortality. These findings align with those of a previous single-center study, which also identified a dose-dependent relationship between post-transplantation RBCT and all-cause mortality[17]. However, this prior study included RBCT at any time after transplantation and did not provide specific indications for RBCT. Recent national cohort data from Korea also demonstrated a dose-dependent association between RBCT during hospitalization and all-cause mortality but did not distinguish between intraoperative and postoperative RBCT[22]. Overall, the findings of our study and others underscore the need to reconsider the effects of RBCT through further in-depth investigations into the specific effects of post-transplant RBCT on kidney transplantation outcomes.

Our results revealed that postoperative RBCT was also significantly associated with not only mortality but also death-censored graft survival in the current study. Previous research on the impact of RBCT on graft outcomes has produced mixed results, with some studies reporting negative effects and others finding no significant impact[4–6,17]. These inconsistencies may be attributed to variations in transfusion practices over time and between institutions and practitioners, as well as a lack of clear transfusion guidelines. Our study, with its more recent and uniform cohort, provides updated insights that may be used to inform current transfusion protocols and highlights the need for a cautious approach to postoperative RBCT in the context of kidney transplantation.

We identified early postoperative RBCT as an independent risk factor for developing AMR, but not TCMR. This association, while not proof of causality, offers a plausible explanation for the observed decrease in death-censored graft survival in our cohort. It suggests that RBCT specifically affects humoral immunity[23]. Moreover, previous studies have linked postoperative RBCT with the development of *de novo* donor-specific antibodies, further supporting the potential immunological implications of RBCT[4,9]. Together, our findings, although retrospective and requiring careful interpretation, underscore the need to revisit current transfusion practices in kidney transplantation.

Although the Kidney donor profile index (KDPI) or Living kidney donor profile index (LKDPI) scores are a well-known predictor for post-transplant outcomes[24,25], previous researches have not investigated the post-transplantation outcomes after transfusion while considering the donor profile[5,6,10,17]. Our research is significant in that we discovered transfusion remains a risk factor affecting patient outcomes even under similar donor profile conditions.

Furthermore, although multiple prior studies have shown that comorbidities like cardiovascular disease represent the leading cause of death in kidney transplant recipients with a functioning allograft[26,27], there was no difference in the rates of comorbidities, including hypertension, diabetes, and cardiovascular disease, between the two recipient groups (Table S3). When comparing ETPS in the matched group, we found no difference between the two groups.

Even after matching, there remained differences in pre-operative hemoglobin levels and ATG use between the two groups. Despite previous studies showing that the use of ATG increases anemia[28], we did not see such an association in our data. Our risk factor analysis confirmed that ATG did not act as a risk factor for patient survival or graft outcomes. Therefore, the fact that transfusion impacted outcomes in both groups where post-transplant survival was expected to be similar offers an important insight that previous studies have not demonstrated.

This study has several limitations that deserve consideration. Firstly, the relationship between RBCT and poor outcomes may only be an association, as causation cannot be confirmed because of the retrospective design of this study. Future prospective studies with clear indications for RBCT are required to more conclusively determine the effects of early RBCT. Secondly, protocol biopsies were not routinely obtained in all patients, so episodes of subclinical rejection may have been missed. Nevertheless, we meticulously examined all indicated biopsies, and allograft rejection episodes were analyzed using the latest Banff criteria. The lack of donor-specific antibody (DSA) data analysis is another limitation of our study. Although our findings suggest a potential link between

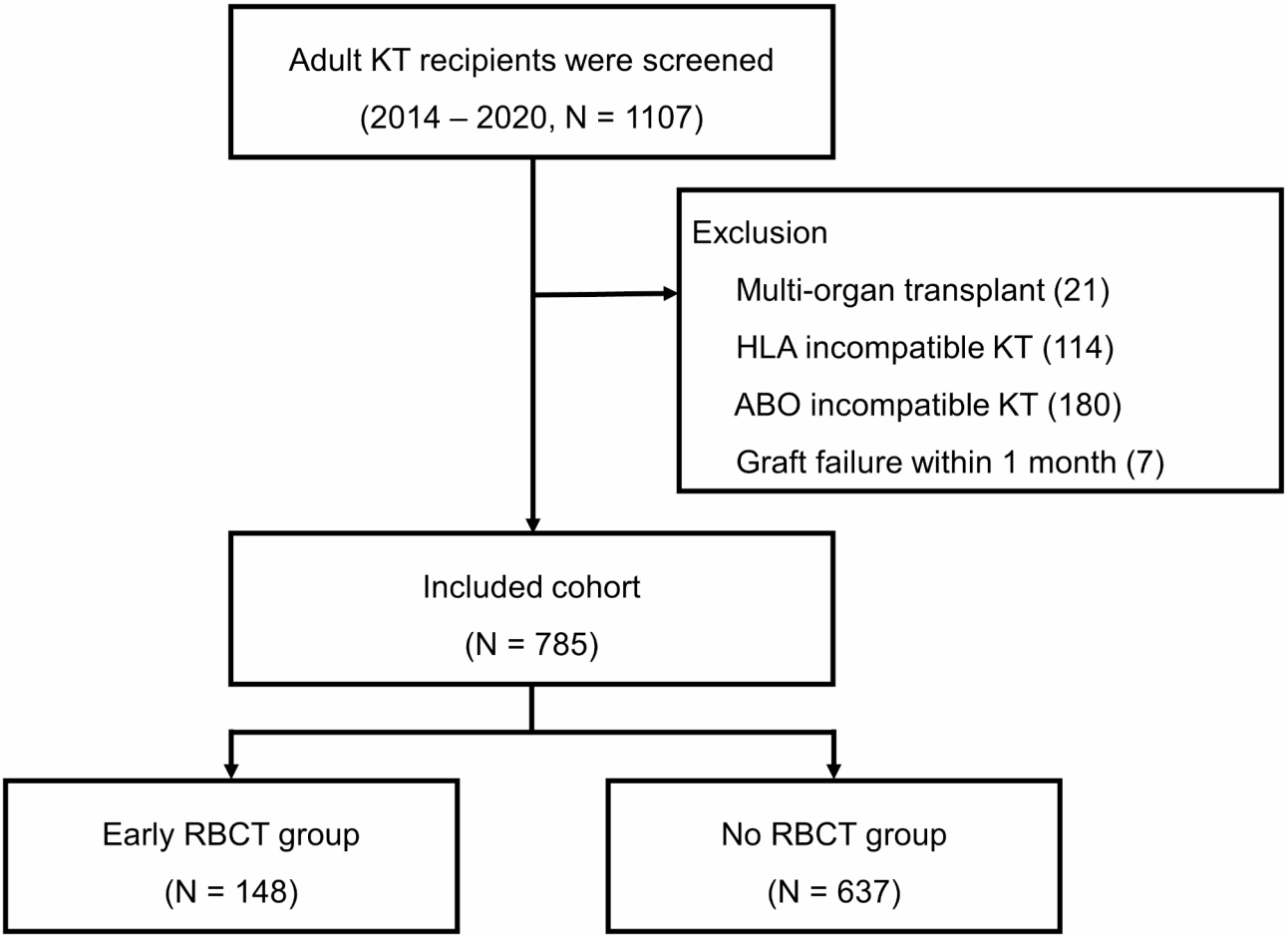


Fig. 2. Study flow. *HLA* human leukocyte antigen, *KT* kidney transplantation, *RBCT* red blood cell transfusion

transfusion and *de novo* DSA, we were unable to analyze *de novo* DSA development comprehensively. Regular postoperative DSA follow-up only began in 2019 due to changes in insurance coverage policies. Although peak PRA for HLA class II was higher in the early transfusion group, it is necessary to confirm whether this actually led to a higher occurrence of DSA. Furthermore, we do not have information on HLA types of blood donors, which makes it difficult to attribute any *de novo* DSA directly to transfusion.

In conclusion, our findings highlight a significant association between early post-transplantation RBCT and increased risk of all-cause mortality, death-censored graft failure, and AMR in kidney transplant recipients. These results warrant a critical reassessment of RBCT practices in the post-transplantation setting and emphasize the urgent need for further research and updated evidence-based clinical guidelines regarding transfusion practices.

Methods

Study design and participants

We screened consecutive adults who underwent kidney transplantation between January 2014 and December 2020 at Severance Hospital, Seoul, Republic of Korea. We excluded patients who underwent multi-organ transplantation, received HLA- and/or ABO-incompatible kidneys, or experienced graft loss or death within 1 month after transplantation. After excluding ineligible patients, 785 recipients were included in this study (Fig. 2).

To perform sensitivity analysis, all patients' KDPI[29] or LKDPI[30] scores were collected, and a total of 398 matched cohorts were created.

All study procedures were conducted in accordance with the Declaration of Helsinki and were approved by the Institutional Review Board of Severance Hospital (4-2022-1073). Informed consent was waived by the Institutional Review Board of Severance Hospital because of the study's retrospective design.

Exposure

The main study exposure was "early RBCT", which was defined as transfusion of packed red blood cells within 30 days after transplantation, starting on postoperative day 1. We selected this timeframe based on existing literature suggesting that a significant proportion of blood transfusions occur during the first month post-transplantation[3,4]. Patients were categorized into two groups: those who received early RBCT and those who did not. Throughout the study period, our institution exclusively used leukocyte-depleted packed red blood cells for

transfusions. Data regarding transfusions were confirmed by comprehensively reviewing the blood bank records and each patient's chart. RBCT decisions were guided by a general target hemoglobin level of 7.0 g/dL, although transfusion decisions were ultimately left to the discretion of the attending physician, who considered several other factors, such as the presence of heart disease, abnormal vital signs, or bleeding tendency.

Immunosuppression

Immunosuppressants were prescribed according to the standard protocol at our institution[31]. Most patients received induction therapy with basiliximab or anti-thymocyte globulin (Thymoglobulin©; Sanofi-Aventis, Boston, USA). Thymoglobulin was preferred in high-risk transplant recipients, such as those who underwent deceased donor kidney transplantation or received old-to-young grafts. Maintenance immunosuppression consisted of tacrolimus, prednisolone, and mycophenolate mofetil (MMF). The initial tacrolimus dosage was 0.1 mg/kg orally twice daily, with subsequent doses titrated to maintain a trough concentration of 5–8 ng/mL. The initial dose of intravenous methylprednisolone was 500–1000 mg, which was gradually reduced and converted to oral prednisolone (5–10 mg/day) during the first 3 weeks after transplantation. The initial dose of MMF was 1.0 g/day, which was subsequently adjusted to minimize adverse events (e.g., gastrointestinal side effects, neutropenia). Both complement-dependent cytotoxicity crossmatch (CDC) and flow cytometry (FXM) crossmatching methods were used for all patients. For Deceased donor kidney transplantation (DDKT) patients, crossmatching was performed the day before or on the day of surgery. For Living donor kidney transplantation (LDKT) patients, blood samples from the recipient and donor were submitted together for testing approximately three days before transplantation.

Study endpoints and definitions

The primary study endpoint was patient survival. The secondary endpoints included death-censored graft survival, biopsy-proven allograft rejection, and graft renal function. Patient survival was calculated from the date of transplantation to the date of death, loss to follow-up, or December 31, 2022 (the end of the study follow-up). Death-censored graft loss was defined as the return to dialysis or the need for re-transplantation. Graft survival was calculated from the date of transplantation to the date of graft loss or December 31, 2022.

Renal biopsies were performed in patients with acute allograft dysfunction, which was defined as a > 30% increase in serum creatinine level above baseline or proteinuria of > 500 mg/day. Allograft biopsy samples were processed using light, immunofluorescent, and electron microscopy. All allograft rejections were confirmed by biopsy and classified as AMR or T-cell mediated rejection (TCMR) according to the most recent Banff criteria at the time of the biopsy[32]. Cases of mixed rejection (in which AMR and TCMR occurred simultaneously) were analyzed as AMR. Estimated glomerular filtration rate (eGFR) was calculated using the Chronic Kidney Disease Epidemiology Collaboration equation [33].

Statistical analysis

Depending on the type of variable, data were expressed as frequency, mean ± standard deviation, or median and interquartile range (IQR). Continuous variables were compared using Student's t-test and Mann-Whitney test and categorical variables were compared using Chi-square or Fisher's exact test. Multivariable logistic regression analysis was performed with early RBCT as the outcome variable. Patient survival, graft survival, and cumulative incidence of biopsy-proven allograft rejections were analyzed using Kaplan-Meier curves and the log-rank test. Associations between early RBCT and time-to-event outcomes were evaluated using Cox proportional hazard models, which included the following covariates: sex, age, dialysis duration, diabetes mellitus, re-transplantation, induction agent (anti-thymocyte globulin vs. basiliximab), type of donor (living vs. deceased), early RBCT, number of HLA mismatches, donor age, and donor sex. Clinically significant variables and variables with a p value ≤ 0.2 in univariable analyses were introduced in multivariable regression models. For sensitivity analysis, propensity score matching analysis was performed by matching donor profiles.

Statistical analyses were performed using SPSS software (version 26.0; SPSS Inc., Chicago, IL, USA; www.ibm.com/analytics/spss-statistics-software) and R (version 3.6.3; R Foundation for Statistical Computing, Vienna, Austria; www.R-project.org). All tests were performed two-tailed, and p values < 0.05 were considered significant.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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References

1. Fishbane, S. & Spinowitz, B. Update on anemia in ESRD and earlier stages of CKD: Core curriculum 2018. *Am. J. Kidney Dis.* **71**, 423–435 (2018).
2. Vanrenterghem, Y. et al. Prevalence and management of anemia in renal transplant recipients: A European survey. *Am. J. Transplant.* **3**, 835–845 (2003).
3. Scornik, J. C., Schold, J. D., Bucci, M. & Meier-Kriesche H.-U. Effects of blood transfusions given after renal transplantation. *Transplantation* **87**, 1381–1386 (2009).
4. Ferrandiz, I. et al. Impact of early blood transfusion after kidney transplantation on the incidence of donor-specific anti-HLA antibodies. *Am. J. Transplant.* **16**, 2661–2669 (2016).
5. Khedjat, K. et al. Post-transplantation early blood transfusion and kidney allograft outcomes: A single-center observational study. *Transpl. Int.* **35**, 10279 (2022).

6. Daloul, R., Braga, J. R., Diez, A., Logan, A. & Pesavento, T. Early posttransplant blood transfusion and risk for worse graft outcomes. *Kidney Int. Rep.* **6**, 986–994 (2021).
7. Leffell, M. S. et al. Red blood cell transfusions and the risk of allosensitization in patients awaiting primary kidney transplantation. *Transplantation* **97**, 525–533 (2014).
8. Scornik, J. & Meier-Kriesche, H. U. Blood transfusions in organ transplant patients: mechanisms of sensitization and implications for prevention. *Am. J. Transplant.* **11**, 1785–1791 (2011).
9. Hassan, S. et al. Shared alloimmune responses against blood and transplant donors result in adverse clinical outcomes following blood transfusion post–renal transplantation. *Am. J. Transplant.* **19**, 1720–1729 (2019).
10. Gaiffe, E. et al. Early post-transplant red blood cell transfusion is associated with an increased risk of transplant failure: A nationwide French study. *Front. Immunol.* **13**, 854850 (2022).
11. Halloran, P. F. Immunosuppressive drugs for kidney transplantation. *N. Engl. J. Med.* **351**, 2715–2729 (2004).
12. Carson, J. L. et al. Red blood cell transfusion: 2023 AABB international guidelines. *JAMA* **330**, 1892–1902 (2023).
13. Babitt, J. L. et al. Controversies in optimal anemia management: Conclusions from a kidney disease—improving global outcomes (KDIGO) conference. *Kid. Int.* **99**, 1280–1295 (2021).
14. Zhang, R. Donor-specific antibodies in kidney transplant recipients. *Clin. J. Am. Soc. Nephrol.* **13**, 182–192 (2018).
15. Loupy, A., Mengel, M. & Haas, M. Thirty years of the International banff classification for allograft pathology: The past, present, and future of kidney transplant diagnostics. *Kid. Int.* **101**, 678–691 (2022).
16. Karpinski, M. et al. Leukocyte reduction of red blood cell transfusions does not decrease allosensitization rates in potential kidney transplant candidates. *J. Am. Soc. Nephrol.* **15**, 818–824 (2004).
17. Massicotte-Azarniouch, D. et al. Blood transfusion and adverse graft-related events in kidney transplant patients. *Kid. Int. Rep.* **6**, 1041–1049 (2021).
18. Sullivan, H. C. & Gebel, H. M. Hurts so good: uncovering the relationship between blood transfusions and allograft outcome. *Kid. Int. Rep.* **6**, 875–877 (2021).
19. Glance, L. G. et al. Association between intraoperative blood transfusion and mortality and morbidity in patients undergoing noncardiac surgery. *J. Am. Soc. Anesthesiologists* **114**, 283–292 (2011).
20. Wu, W. C. et al. Operative blood loss, blood transfusion, and 30-day mortality in older patients after major noncardiac surgery. *Ann. Surg.* **252**, 11–17 (2010).
21. Rohde, J. M. et al. Health care–associated infection after red blood cell transfusion: A systematic review and meta-analysis. *Jama* **311**, 1317–1326 (2014).
22. Lee, K. et al. The association between peri-transplant RBC transfusion and graft failure after kidney transplantation: a nationwide cohort study. *J. Clin. Med.* **10**, 3750 (2021).
23. Refaai, M. A. & Blumberg, N. Transfusion immunomodulation from a clinical perspective: An update. *Expert Rev. Hematol.* **6**, 653–663 (2013).
24. Kim, H. J. Clinical relevance of the living kidney donor profile index in Asian kidney transplant recipients. *Korean J. Transpl.* **36**, 140–140 (2022).
25. Dahmen, M. et al. Validation of the kidney donor profile index (KDPI) to assess a deceased donor's kidneys' outcome in a European cohort. *Sci. Rep.* **9**, 11234 (2019).
26. Ojo, A. et al. Long-term survival in renal transplant recipients with graft function. *Kid. Int.* **57**, 307–31326 (2000).
27. Rangaswami, J. et al. Cardiovascular disease in the kidney transplant recipient: epidemiology, diagnosis and management strategies. *Nephrol. Dialysis Transpl.* **34**, 760–773 (2019).
28. Chang, Y. et al. Clinical risk factors associated with the post-transplant anemia in kidney transplant patients. *Transpl. Immunol.* **38**, 50–53 (2016).
29. Rao, P. S. et al. A comprehensive risk quantification score for deceased donor kidneys: the kidney donor risk index. *Transplantation* **88**, 231–236 (2009).
30. Massie, A. B. et al. A risk index for living donor kidney transplantation. *Am. J. Transplant.* **16**, 2077–2084 (2016).
31. Lee, J. et al. The recovery status from delayed graft function can predict long-term outcome after deceased donor kidney transplantation. *Sci. Rep.* **7**, 13725 (2017).
32. Loupy, A. et al. *The Banff 2019 Kidney Meeting Report (I): Updates on and Clarification of Criteria for T cell–and antibody-mediated Rejection* (Wiley Online Library, 2020).
33. Inker, L. A. et al. New creatinine-and cystatin C–based equations to estimate GFR without race. *N. Engl. J. Med.* **385**, 1737–1749 (2021).

Author contributions

M.K. and J.L. drafted the manuscript. M.K., H-H.K., and J.L. conceived and designed the study. S.H.Y., M.C., H.J.K., H.W.K., J.Y., B.S.K., K.H.H., M.S.K., and J.L. collected the data. M.K. and J.L. performed the statistical analysis and interpreted the data. All authors read and approved the final version of the manuscript.

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Declarations

Competing interests

The authors declare no competing interests.

Additional information

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