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Influence of storage time and amount of red blood cell transfusion on postoperative renal function: an observational cohort study

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ABSTRACT

Introduction: To identify the impact of storage time and amount of transfused red blood cell units on renal function.

Methods: Consecutive transfused patients (n = 492), undergoing cardiac surgery at a single centre and receiving at least one red blood cell unit, were pooled in different groups depending on storage time and amount of transfusion.

Results: Altogether 2,133 red blood cell units were transfused (mean age 21.87 days). Pre- and intraoperative data were similar between groups. Postoperative serum creatinine ($p < 0.01$), glomerular filtration rate ($p < 0.01$), and urea ($p < 0.01$) showed a significant correlation with the amount of transfused red blood cell units, but not with storage time. Acute kidney insufficiency (creatinine values greater than 2.0 mg/dl or a duplication of the preoperative value) developed in 29 % of patients and was associated with red blood cell mean age ($p = 0.042$), absolute age ($p = 0.028$), and amount of transfused ($p < 0.01$) units. Acute kidney failure requiring renal replacement therapy occurred in 9.6 % of patients and was associated with the amount of transfusion ($p < 0.01$).

Conclusions: Worsening of renal function after cardiac surgery is associated with storage time and amount of transfused red blood cell units. Acute kidney insufficiency was defined as serum creatinine values greater than 2.0 mg/dl or a duplication of the preoperative value (baseline). Acute kidney failure was defined as becoming dependent upon dialysis.

Keywords: *storage time, red cell, cardiac surgery, kidney insufficiency, kidney failure.*

INTRODUCTION

Red blood cell (RBC) units are typically available for transfusion as early as 3-4 days after collection and with modern preservation techniques solutions can be administered up to 42 days after collection (1).

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Despite these "milestones" of transfusion medicine, stored blood is subject to several functional and mechanic changes. These reversible and irreversible changes, known as "storage lesion", start in about two to three weeks of storage-time (2). During storage, erythrocytes undergo corpuscular changes, including depletion of 2,3-diphosphoglycerate and adenosine triphosphate, increased rigidity, a progressive depletion of nitric oxide, and a significant increase in abnormally shaped RBCs (1, 3-7). Furthermore, cytokines that accumulate with

storage of RBCs are associated with transfusion-mediated systemic inflammatory reactions and higher risk of bacterial infections (8). Many studies propose that the amount and the storage time of transfused RBC units are associated with reduced survival and significantly increased risk of postoperative complications like prolonged intubation, renal failure, septicaemia or sepsis, multi-organ failure, and other serious complications (1, 4, 9-15). In postoperative patients (above all in cardiac surgery patients) there are many particular situations (like low cardiac index, hypovolemia, long cardiopulmonary circulation and atrial fibrillation) which cause compromised renal function. In that moment the concomitant RBC transfusion further worsen renal function. Therefore, it is mandatory to analyse specific organ function. The extent of perioperative renal impairment ranges from subclinical injury to established renal failure requiring dialysis. Acute renal failure affects 1-5 % of cardiac surgery patients and remains a major cause of morbidity and mortality (3, 8, 16-25). Therefore, the purpose of this retrospective observational cohort study was to focus on the impact of storage time and amount of transfused red blood cells on renal function.

METHODS

In the period between January 2009 and January 2010, 961 patients underwent cardiac surgery at the Clinic for Thoracic, Cardiac and Vascular Surgery of Würzburg University Hospital and 492 (51.2 %) were transfused. The following perioperative data were collected: sex, age, body mass index, emergency operation, diabetes mellitus, chronic obstructive pulmonary disease, operation type, cardio-pulmonary bypass time, aortic-cross-clamp time, storage time of RBCs in days, amount of transfused RBCs, serum creatinine, glomerular filtration rate (GFR) and urea starting preoperatively until postoperative day two. Patients were pooled in different groups depending on storage time (group 1 – group 6) and amount of RBC transfusions (group 7 and 8). Group 1 (mean age of all transfused RBCs ≤14 days); group 2 (mean age of all transfused RBCs > than 14 days); group 3 (only one RBC unit was transfused, age ≤14 days); group 4 (only one RBC unit was transfused, age > 14 days); group 5 (only RBCs older than14 days); group 6 (only RBCs younger than 14 days); group 7 (five or less RBC units, regardless of storage time); group 8 (more than 5 RBC units, regardless of storage time). Patients who needed renal replacement therapy treatment in the postoperative period were registered.

All data were taken retrospectively from the central hospital computer and the blood-bank database. All laboratory values were registered until day 2 after surgery. The following inclusion criteria were defined: male or female patients aged 18 years or older, transfusion of at least one (or more) buffy-coat depleted red blood cell unit, and cardiac surgery (coronary-artery bypass grafting (CABG), valve surgery, or a combination of CABG and valve surgery, or surgery on the thoracic aorta). Exclusion criteria were defined as follows: immunosuppressive therapy, concurrent immunological disease, and preoperative signs of inflammation. Emergency was not defined as an exclusion criteria. The management of transfusion (transfusion-trigger) was defined as a haemoglobin value < 8.0 g/dl in combination with at least one of the following: urine output < 100 ml/hour, and/or SvO2 < 65 %, and/or lactate > 3.0 mmol/l, and/or PaO2 < 60 mmHg or SaO2 < 90 %. Obtaining approval of the local Ethics Committee was not applicable due to the retrospective nature of the study.

Definitions. Kidney insufficiency and kidney failure were defined according to Society of Thoracic Surgery (www.sts.org) itemized on the National Database Definition Clarification of the STS (1).

Acute kidney insufficiency was defined as serum creatinine values greater than 2.0 mg/dl or a duplication of the preoperative value (baseline). Acute kidney failure was defined as becoming dependent upon renal replacement therapy. Pathological creatinine value was defined as greater than 1.1 mg/dl. Pathological glomerular filtration rate (GFR) was defined as less than 60 ml/min. Pathological urea value was defined as greater than 50 mg/dl.

Statistical analysis. Statistical analysis was performed by an independent statistician. The results were summarized in a database and evaluated with the statistic program SPSS (18.0). A p-value < 0.05 was deemed to be statistically significant. Descriptive statistics with continuous variables are reported as numbers and percentages of answered questions for categorical variables. A group overview was also prepared for nominal-scaled variables. To determine differences in these values, the Chi-square test of independence was performed. For ratio-scaled variables a descriptive overview of the eight groups was prepared. The eight groups were then analysed with the Mann-Whitney U test for significant differences. If the variable was binomial (e.g. gender) Fisher's exact test was calculated. Data were processed and analysed while preserving anonymity.

Table 1 - *Mean age of the red blood cells units according to the different groups.*

	Mean age of the red blood cells [days]
Group 1	11,5 ± 8,2
Group 2	23,7 ± 5,6
Group 3	10,9 ± 2,9
Group 4	22,8 ± 6,1
Group 5	10,9 ± 2,0
Group 6	21,4 ± 5,9
Group 7	10,9 ± 4,8
Group 8	26,4 ± 5,7

Group 1 (mean age of all transfused RBC ≤ 14 days); group 2 (mean age of all transfused RBCs > than 14 days); group 3 (only one RBC was transfused, age ≤14 days); group 4 (only one RBC was transfused, age >14 days); group 5 (only RBCs older than14 days); group 6 (only RBCs younger than 14 days); group 7 (five or less RBC units, regardless of storage time); group 8 (more than 5 RBC units, regardless of storage time). RBC = red blood cell.

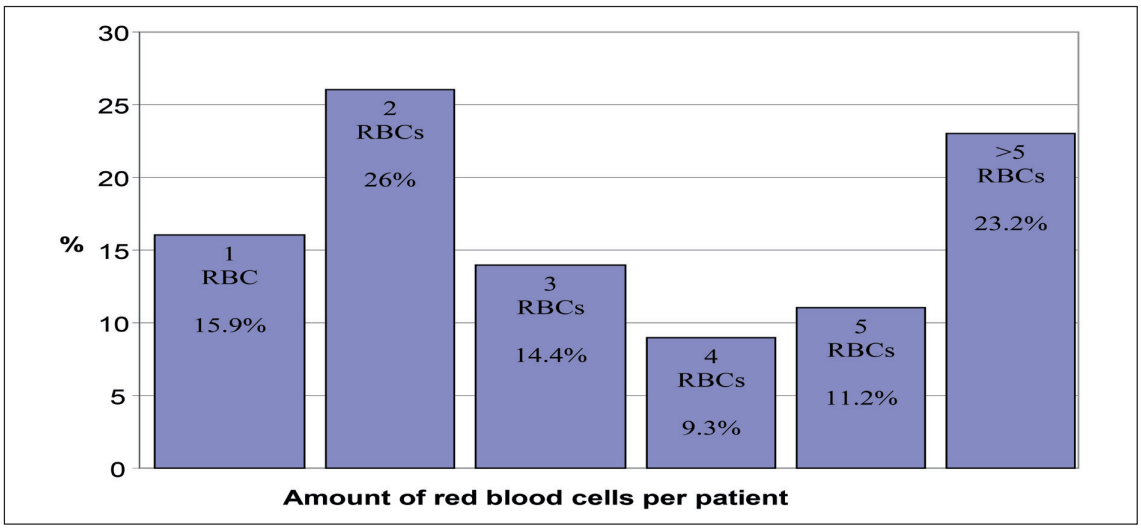

Figure 1 - *Percentage of patients receiving 1, 2, 3, 4, 5 red blood cell units or more than 5. RBC = red blood cell.*

Table 2 - *Demographic and clinical parameters in the different groups.*

	Group 1 88/492 (17.9%)	Group 2 404/492 (82.1%)	p	Group 3 63/492 (12.8%)	Group 4 429/492 (87.2%)	p
Male	65/88 (73.9%)	258/404 (63.9%)	n.s.	64/63 (73%)	277/429 (64.6%)	n.s.
Age [years]	66.55 ± 11.1	68.55 ± 9.9	n.s.	67.98 ± 16.8	68.22 ± 14.8	n.s.
BMI > 35 [kg/m^2]	13/88 (14.7%)	49/404 (12.1%)	n.s.	12/63 (19%)	50/429 (11.6%)	n.s.
Emergency	12/88 (13.6%)	47/404 (12.1%)	n.s.	10/63 (15.8%)	56/429 (13%)	n.s.
D.M.	24/88 (27.2%)	109/404 (26.9%)	n.s.	18/63 (28.5%)	115/429 (26.8%)	n.s.
COPD	9/88 (10.2%)	31/404 (7.6%)	n.s.	7/63 (11.1%)	33/429 (7.6%)	n.s.
CABG Valve Combination Aorta	51/88 (57.9%) 12/88 (13.6%) 20/88 (22.7%) 5/88 (5.6%)	212/404 (52.4%) 83/404 (20.5%) 86/404 (21.2%) 23/404 (5.6%)	n.s. n.s. n.s. n.s.	49/63 (77.7%) 4/63 (6.3%) 8/63 (12.6%) 2/63 (3.1%)	279/429 (65%) 49/429 (11.4%) 80/429 (18.6%) 21/429 (4.8%)	n.s. n.s. n.s. n.s.
CPB [min]	121.9 ± 42.9	132.1 ± 49.8	n.s.	119.2 ± 38.4	122.9 ± 44.1	n.s.
ACC [min]	92.1 ± 32.4	93.5 ± 37.6	n.s.	88.9 ± 30.8	89.2 ± 39.4	n.s.
	Group 5 63/492 (12.8%)	**Group 6 314/492 (63.8%)**	**p**	**Group 7 378/492 (76.8%)**	**Group 8 114/492 (23.2%)**	**p**
Male	46/63 (73%)	200/314 (63.7%)	n.s.	251/378 (66.4%)	72/114 (64%)	n.s.
Age [years]	67.98 ± 11.8	68.56 ± 15.5	n.s.	67.6 ± 16.4	70.18 ± 14.9	n.s.
BMI > 35 [kg/m^2]	12/63 (19%)	38/314 (12.1%)	n.s.	54/378 (14.2%)	13/114 (11.4%)	n.s.
Emergency	11/63 (17.4%)	39/314 (12.4%)	n.s.	55/378 (14.5%)	14/114 (14%)	n.s.
D.M.	18/63 (28.5%)	83/314 (26.4%)	n.s.	103/378 (27.2%)	30/114 (26.3%)	n.s.
COPD	7/63 (11.1%)	26/314 (8.2%)	n.s.	31/378 (8.2%)	9/114 (7.8%)	n.s.
CABG Vavle Combination Aorta	48/63 (76.1%) 5/63 (7.9%) 21/63 (33.3%) 4/63 (6.3%)	166/314 (52.8%) 50/314 (15.9%) 88/314 (28%) 10/314 (3.1%)	n.s. n.s. n.s. n.s.	191/378 (50.5%) 79/378 (20.8%) 95/378 (25.1%) 13/378 (3.4%)	46/114 (40.3%) 17/114 (14.9%) 20/114 (17.5%) 3/114 (2.6%)	n.s. n.s. n.s. n.s.
CPB [min]	122.5 ± 41.9	130.1 ± 39.5	n.s.	128.1 ± 38.7	131.2 ± 39.1	n.s.
ACC [min]	90.6 ± 29.5	88.2 ± 31.2	n.s.	89.5 ± 38.1	92.1 ± 40.5	n.s.

BMI = body mass index, D.M. = Diabetes mellitus, COPD = chronic obstructive pulmonary disease, CABG = coronary artery bypass grafting, CPB = cardio-pulmonary bypass, ACC = aortic cross clamp, n.s. = not significant

Table 3 - *Preoperative serum creatinine, glomerular filtration rate, and urea values according to the different groups.*

	Group 1 88/492(17.9%)	Group 2 404/492(82.1%)	p	Group 3 63/492 (12.8%)	Group 4 429/492 (87.2%)	p
Creatinine	1.10 ± 0.5	1.24 ± 0.6	n.s.	1.15 ± 0.7	1.22 ± 0.5	n.s.
GFR	58.41 ± 23.1	58.38 ± 19.9	n.s.	54.56 ± 23.4	58.80 ± 18.1	n.s.
Urea	45.49 ± 22.5	46.83 ± 34.4	n.s.	48.64 ± 41.8	46.44 ± 35.5	n.s.
	Group 5 63/492 (12.8%)	**Group 6 314/492 (63.8%)**	**p**	**Group 7 378/492 (76.8%)**	**Group 8 114/492 (23.2%)**	**p**
Creatinine	1.15 ± 0.8	1.13 ± 0.4	n.s.	1.13 ± 0.7	1.48 ± 0.9	n.s.
GFR	54.56 ± 31.8	62.36 ± 44.3	n.s.	63.56 ± 35.7	42.60 ± 29.4	n.s.
Urea	48.64 ± 20.7	43.88 ± 19	n.s.	42.62 ± 32.7	58.82 ± 21.8	n.s.

GFR = glomerular filtration rate, n.s. = not significant

For each combination of groups and the examined parameter we performed a chi square test according to Pearson.

RESULTS

During the study period 492 consecutive transfused patients, aged of 68 ± 12.8 years, 169/492 (34%) females, fulfilled the inclusion criteria and were involved in the analysis. Altogether, 2,133 RBC units were transfused with a mean storage time of 21.87 days. The mean age of RBCs according to the different groups is shown in *Table 1*. The percentage of patients receiving 1, 2, 3, 4, 5 RBC units or more than 5 RBC units is shown in *Figure 1.* Two RBC units were transfused in 128/492 (26%) patients while 114/492 (23.2%) patients received more than 5 RBC units and 29/492 patients (5.9%) received more than 10 RBC units. Groups were well matched with regard to pre and intraoperative data (*Table 2*). Preoperative serum creatinine, GFR, and urea values according to the different groups are shown in *Table 3*. On the second postoperative day, the mean valve of creatinine, GFR, and urea was 1.45 mg/dl, 58.96 ml/min, and 48.74 mg/dl respectively. There was a significant correlation of postoperative pathological serum creatinine ($p < 0.01$), GFR ($p < 0.01$), and urea ($p < 0.01$) with the amount of transfused RBCs (group 7 vs 8) but not with the storage time (comparing groups 1-6) (*Table 4*). Of 492 patients, 141 (29%) developed acute kidney insufficiency and 47 (9.6%) acute kidney failure. Concerning acute kidney insufficiency, there was a significant difference between group 1 and group 2 ($p = 0.042$), group 5 and group 6 ($p = 0.028$), and between group 7 and group 8 ($p < 0.01$). Acute kidney failure (need for dialysis) was performed in 47/492 patients (9.6%). Concerning acute kidney failure, there was a significant difference only between group 7 and 8 ($p < 0.01$) (*Table 5*).

DISCUSSION

The most important finding of this study is to confirm that worsening of renal function after cardiac surgery is associated with storage time and amount of transfused red

Table 4 - *Postoperative pathological serum creatinine, glomerular filtration rate, and urea according to the different groups.*

	Creatinine	GFR	Urea
Group 1	56/86 (65.1%)	35/85 (41.2%)	36/85 (42.4%)
Group 2	245/400 (61.3%)	181/398 (45.5%)	144/390 (36.9%)
p	n.s.	n.s.	n.s.
Group 3	40/61 (65.6%)	23/60 (38.3%)	25/60 (41.7%)
Group 4	261/425 (61.4%)	193/423 (45.6%)	155/415 (37.3%)
p	n.s.	n.s.	n.s.
Group 5	40/61 (65.6%)	23/60 (38.3%)	25/60 (41.7%)
Group 6	178/312 (57.1%)	159/311 (51.1%)	100/302 (33.1%)
p	n.s.	n.s.	n.s.
Group 7	210/375 (56%)	195/372 (52.4%)	109/364 (29.9%)
Group 8	91/111 (82%)	21/111 (18.9%)	71/111 (64.0%)
p	< 0.01	< 0.01	< 0.01

GFR = glomerular filtration rate, n.s. = not significant

Table 5 - *Acute renal insufficiency and acute renal failure according to the different groups.*

	acute renal insufficiency	acute renal failure
Group 1	33/86 (38.4%)	9/88 (10.2%)
Group 2	108/395 (27.3%)	38/404 (9.4%)
p	0.042	n.s.
Group 3	22/61 (36.1%)	4/63 (6.3%)
Group 4	119/420 (28.3%)	43/429 (10%)
p	n.s.	n.s.
Group 5	22/61 (36.1%)	4/63 (6.3%)
Group 6	70/308 (22.7%)	19/314 (6.1%)
p	0.028	n.s.
Group 7	84/371 (22.6%)	18/378 (4.8%)
Group 8	57/110 (51.8%)	29/114 (25.4%)
p	< 0.01	< 0.01
n.s. = not significant.		

blood cell units. Numerous surveys have investigated the influence of RBC transfusions on human organs (1-22,24,26). Complications like increased hospital stay, prolonged intubation (period) or an increase in mortality and morbidity rates are the dominating end-points in these trials. In this retrospective observational cohort study, 492 consecutive transfused cardiac surgery patients were analysed with regard to postoperative renal function. The pathophysiology of renal injury is multifactorial and is related to perioperative renal hypoperfusion and the presence of endogenous and exogenous nephrotoxins (e.g. RBCs) and microembolism (16). Some previous studies support the hypothesis that the duration of storage and the amount of transfused RBC units is associated with morbidity and mortality (1, 4, 9-15).

Studies showing an association between RBC transfusion and morbidity and mortality. Koch et al. examined 6,002 standard cardiac surgical patients (2,872 patients received 8,802 RBCs that had been stored for 14 days or less, and 3,130 patients received 10,782 RBC units that had been stored for more than 14 days). Patients who were given older RBCs had higher rates of in-hospital mortality (2.8% vs 1.7%, $p = 0.004$), intubation beyond 72 hours (9.7% vs 5.6%, $p < 0.001$), renal failure (2.7% vs 1.6%, $p = 0.003$), and sepsis or septicemia (4.0% vs 2.8%, $p = 0.01$). Even 1 year mortality was significantly lower in patients given newer blood (7.4% vs 11.0%, $p < 0.001$) (10). Furthermore, Koch et al. published three other studies showing the negative effect of RBC transfusion (4, 9, 11). Summarizing these studies, data showed that transfusion of RBCs was associated with a risk-adjusted reduction in survival for "early" (defined as until 6 months postoperatively, $p < 0.0001$) and "late" (defined as about 10 years, $p < 0.0001$) phases (9). Clinical parameters, like renal failure ($p < 0.001$), prolonged ventilatory support ($p < 0.0001$), serious infection ($p < 0.0001$), cardiac complications ($p < 0.0001$), and neurologic events ($p < 0.0001$) were increased if RBCs were transfused (4). Van Straten et al. focused on the impact of the amount of RBC transfusions on mortality in a retrospective study with 10,626 CABG patients. The authors concluded that transfusion of RBC is an independent and dose-dependent risk factor for early mortality after revascularisation ($p < 0.001$).

Even secondary end-points like renal failure ($p < 0.001$), mediastinitis ($p < 0.001$) and perioperative myocardial infarction ($p < 0.001$) were significant dose-dependent risk factors (15). In our retrospective observational study we showed that postoperative pathological laboratory findings of serum creatinine ($p < 0.01$), glomerular filtration rate ($p < 0.01$), and urea ($p < 0.01$) had a significant correlation with the amount of transfused RBCs, but not with storage time. The onset of acute kidney insufficiency and acute kidney failure was correlated to storage time ($p = 0.042$, $p = 0.028$), and to the amount of transfused RBC units ($p < 0.01$ for both). In order to calculate the adjusted hazard ratio Surgenor et al. investigated 9,079 consecutive patients undergoing CABG surgery, valve surgery, or a combination of both at eight centres in northern New England. Survival was significantly decreased for all patients exposed to 1 or 2 RBC units during hospitalisation for cardiac surgery compared with those who received none ($p < 0.001$).

After adjustment for patient and disease characteristics, patients exposed to 1 or 2 RBC units had a 16% higher long-term mortality risk (adjusted hazard ratio = 1.16, 95% CI: 1.01-1.34, $p = 0.035$) (14). Chelemer et al. highlighted the association of bacterial infection with RBC transfusion in a prospective cohort study with 533 CABG patients. After adjusting for patient and disease characteristics, invasive treatments, surgical time, and the transfusion of other substances, the (adjusted) rates of bacterial infection were 4.8% with no RBC transfusion, 15.2% with one or two units, 22.1% with three to five units, and 29% with ≥ to six units ($p < 0.001$) (12). Even Murphy et al. showed that RBC transfusion was strongly associated with infection, and a strong dose-response relationship was present (odds ratio 3.38; 95% confidence interval, 2.60 to 4.40) (13).

Postoperative infections after allogenic blood transfusions have been attributed to transfused white blood cells in red blood cell components. In a prospective observational study with 1,553 elective and emergency cardiac surgery patients Vymazal et al. described the relationship between sternal dehiscence (following cardiac surgery) and the total number of packed red blood cells. On average, 7.6 transfusion units of allogenic blood were administered to patients with sternal dehiscence versus 1.6 (transfused units of allogenic blood) to patients without sternal dehiscence ($p < 0.00005$) (25). Capraro et al. investigated the effect of leukocyte reduction of transfused red blood cells in patients undergoing cardiac surgery (782 patients received buffy-coat-depleted RBCs before leukocyte reduction versus 632 patients with leukocyte-reduced RBCs after leukocyte reduction).

The authors could not find a beneficial effect of the universal leukocyte reduction on infection ($p = 0.19$), 90-day mortality ($p = 0.28$), and the length of intensive care unit stay ($p = 0.34$) (21). These results are even demonstrated by Murphy et al. (13) and Bilgin et al. (18) who investigated, in a double-blinded randomized controlled trial, the effect of leukocyte-depleted RBC transfusion in cardiac valve surgery.

Studies denying an association between RBC transfusion and morbidity and mortality. In contrast to these data, other studies did not corroborate the previously reported association between transfusion of old RBCs and morbidity and mortality (3, 8, 17-22, 26). In a retrospective analysis of 6,994 *noncardiac surgical patients* receiving transfusions during of general surgery Saager et al. reported no association between increasing median storage duration time and postoperative mortality (hazard ratio, 0.99 [0.94-1.04]; $p = 0.64$) (26). Van de Watering et al. compared 950 cardiac surgical patients who had received only

RBCs older than a median storage time of 18 days (median, 24 days) with 945 patients who had received the same number of RBCs all fresher than 18 days (median, 13 days). In the multivariate analyses no significant correlation of storage time variables with 30-day survival, hospital stay, and intensive care unit (ICU) stay was seen. However, the number of transfusions were independently correlated with mortality and ICU stay ($p < 0.001$) (19). Even Vamvakas et al. has related, in 268 consecutive CABG patients, the postoperative length of hospitalization ($p > 0.50$), the postoperative length of stay in the ICU ($p > 0.50$), and the length of endotracheal intubation ($p = 0.61$) with the length of storage of the oldest transfused RBC units, the mean length of storage of the oldest and second oldest RBC units, and the mean length of storage of all RBC units transfused to each patient. All clinical parameters were without a significant association after adjustment for the effects of confounding factors (17). Furthermore, Leal-Noval et al. evaluated 795 cardiac surgical patients. The authors could not find any correlation between the duration of storage of RBC and a prolonged stay in the ICU, mechanical ventilation time, increased rates of perioperative infarction, mediastinitis, or sepsis (3). Despite missing significance, the multivariate analyses figured out that each day of storage of the oldest unit was associated with an increment of 6% of the risk of pneumonia (95% confidence interval, 1-11; $p = 0.018$). The cut-off point of maximum sensitivity and specificity (54.8 and 66.9%) associated with a greater risk for pneumonia corresponded to 28 days of storage for the oldest unit (odds ratio, 2.74; 95% confidence interval, 1.18-6.36, $p = 0.019$) (3). Similar results were achieved by Yap et al. who studied 670 consecutive non-emergency cardiac surgery patients in a retrospective observational cohort study. The authors reported that the storage age of RBCs was not independently associated with postoperative early mortality ($p = 0.89$), renal failure ($p = 0.16$), pneumonia ($p = 0.47$), ICU stay ($p = 0.79$), and ventilation hours ($p = 0.09$) (8). Hébert et al. defined "fresh" RBCs as stored for < 8 days (median of 4 days) and compared them to standard RBCs (median of 19 days) in 66 critically-ill cardiac surgery patients. Patients receiving "fresh" RBCs tended to be older on average (68 ± 8.54 years vs. 63 ± 15.30 years, $p = 0.13$) and to have more comorbidities (85% vs 65%, $p = 0.09$). In total, 27% of patients in the "fresh" RBCs group died or had a life-threatening complication as compared to 13% in the standard group ($p = 0.31$). There were no differences in prolonged respiratory, cardiovascular, or renal support after randomization ($p > 0.05$) (22). Van de Watering performed a Meta-analysis evaluating (publications of) clinical studies comparing storage time of transfused RBCs with physiological or clinical outcomes. The authors found sixteen observational studies comparing clinical outcome that yielded contradictory results regarding the effect of RBCs on mortality, length of intensive care unit and hospital stay, infections, organ failure, and composite adverse effects. Summarizing the results of the selected studies, Van de Watering et al. concluded that available studies provide no evidence that longer stored RBCs are more harmful than younger RBCs (20). The differences between the published results may be explainable by the different study designs (retrospective vs prospective and observational vs randomized), different study populations [critically-ill patients vs less severely-ill patients, only CABG patients vs all cardiac surgery patients, patients excluded due to being expired during the first few days after surgery (3)], different definitions of "old" and "fresh" RBCs [14 days (10) vs 8 days (22)], and

different transfusion triggers. Hardy et al. summarized this sophisticated issue of RBC transfusion and its clinical consequences as follows "some patients are helped, for others it has no impact and for some it is harmful" (24).

Limitations

The most important limitation of the present study is the retrospective observational design, which may have led to bias in confounding parameters among the different groups in contrast to a randomized design. A study using a rare resource such as blood transfusion has difficulties in being blinded and randomized. In an ongoing observational study we are analyzing patient data from 500 consecutive transfused cardiac surgery patients versus a cohort of 500 consecutive not-transfused (matched pair) patients.

CONCLUSION

Transfusion of RBCs was associated with postoperative increased serum creatinine and urea, decreased glomerular filtration rate, acute kidney insufficiency, and acute kidney failure. The storage time was associated with acute kidney insufficiency, but not with acute kidney failure. Based on these findings, on recent international literature, and on the increasing problem of distributing the rare resource of human blood, it is mandatory to develop an evidence-based transfusion trigger for cardiac surgery patients.

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