Aprotinin, transfusions, and kidney injury in neonates and infants undergoing cardiac surgery

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Editor’s key points

- An association between the prophylactic use of aprotinin and acute kidney injury in cardiac surgery has been reported in adults but not in children.
- A single-centre, retrospective analysis of acute kidney injury in paediatric cardiac surgery was conducted to determine its association with aprotinin use and transfusions.
- Transfusion, but not aprotinin use, was associated with AKI in cardiac surgery in infants and neonates.

Background. A significantly increased risk of acute kidney injury (AKI) with the prophylactic use of aprotinin has been reported in adults undergoing cardiac surgery, but not in children. Blood product transfusions have also been shown to carry an independent risk of AKI. The present study assessed associations between AKI, aprotinin, and transfusions in neonates and infants undergoing cardiac surgery.

Methods. All neonates and infants undergoing surgery with cardiopulmonary bypass over a 42 month period, before and after the withdrawal of aprotinin, were included retrospectively. AKI was assessed by the Acute-Kidney-Injury-Network classifications. A propensity score was used to balance treated and untreated groups.

Results. Three hundred and ninety patients received aprotinin and 568 patients did not. Inverse probability of treatment weighting resulted in good balance between groups for baseline and surgical characteristics. Controls underwent surgery with smaller bypass circuits and fewer transfusions. After adjustment for the use of miniaturized circuits and for the year of surgery, no significant association between the incidence of AKI, dialysis, and aprotinin was noted. Red blood cell transfusions were associated with an increased risk of AKI and dialysis: odds ratios (ORs) 1.64 (1.12–2.41) and 2.07 (1.13–3.73), respectively; as were fresh frozen plasma transfusions, ORs 2.28 (1.68–3.09) and 3.11 (1.95–4.97), respectively. Platelet transfusions were associated with an increased risk of dialysis: OR 2.20 (1.21–4.01).

Conclusions. Blood product transfusions, but not the prophylactic use of aprotinin, are significantly associated with AKI after cardiac surgery in neonates and infants.

Keywords: acute kidney injury; aprotinin; blood transfusion; cardiac surgical procedures; heart defects, congenital

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Aprotinin, previously approved for prophylactic use to reduce perioperative blood loss in patients undergoing coronary artery surgery with cardiopulmonary bypass (CPB), was used for more than two decades. The younger and smaller the patient undergoing bypass, the greater the risk of postoperative bleeding,1 and the prophylactic use of aprotinin thus became commonplace in paediatric cardiac surgery.

Since 2006, several observational studies have reported an increased risk of renal dysfunction and death among adults who received aprotinin.2–5 In contrast, others6 demonstrated that aprotinin did not increase the risk of renal failure requiring renal replacement therapy independently of the number of transfusions and that the risk was solely attributable to the greater need for packed red blood cell (PRBC) transfusions in high-transfusion-risk patients. Since the results of the prospective randomized BART study in 2008,7 showing an increased risk of 30 day mortality with aprotinin compared with lysine analogues, the prophylactic use of aprotinin was abruptly discontinued. Even after the publication of the BART study, questions remained about whether adjustment for transfused PRBCs explained the association between aprotinin and renal dysfunction, and whether there were subgroups of patients undergoing complex high-transfusion-risk surgery in which the benefits of aprotinin outweighed the risks.

To date, there is no evidence relating renal dysfunction to the prophylactic use of aprotinin in children, but few studies analysed such a relationship.8–13 The aim of the present study was to analyse associations between the incidence of postoperative acute kidney injury (AKI), AKI requiring renal replacement therapy, the prophylactic use of aprotinin, and the number of blood product transfusions on the day of surgery (day 0) in neonates and infants with cardiac surgery.

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Methods

The study was reviewed and approved by the Ethics Committee of the French Society of Thoracic and Cardiovascular Surgery, Paris, France, who waived the need for parental consent for the use of de-identified records for this research. This retrospective analysis relied on a database that included the files of all consecutive patients who underwent congenital cardiac surgery between January 1, 2007 and June 30, 2010 at the Necker Enfants Malades Hospital, Paris, France. For all patients less than 1 yr old, data concerning pre-, intra-, and postoperative management were collected. Only the first procedure performed during the same hospitalization was analysed. Patient characteristics, cardiac diagnosis, surgical complexity assessed by the basic Aristotle Complexity score, the CPB characteristics, occurrence of early postoperative low cardiac output syndrome requiring the sternum be left open, all serum creatinine (SCr) measurements during the Intensive Care Unit stay, number of all blood product transfusions on day 0 (assessed as calendar day), including those used in the CPB prime, postoperative course, in-hospital mortality, and mortality during follow-up were noted.

Patients underwent surgery at normothermia or mild hypothermia with non-pulsatile CPB and warm blood cardioplegia, as described previously. Aortic arch repair was performed with deep hypothermic circulatory arrest (DHCA) and selective cerebral perfusion. The CPB circuits underwent modifications during the study period, with two circuits being used: conventional and miniaturized, as described previously. This affected the priming volume, and consequently the transfusion amounts and ultrafiltration rates.

Before August 1, 2008, all patients received high-dose aprotinin (TrasyloL, Bayer, Leverkusen, Germany): an i.v. loading dose of 30 000 kallikrein inhibitor units (KIU) kg⁻¹ after induction of anaesthesia, followed by 30 000 KIU kg⁻¹ in the prime and 8000 KIU kg⁻¹ h⁻¹ during bypass. After the withdrawal of aprotinin, tranexamic acid (Exacyl, Sanofi-Aventis, France) was administered to all patients: 20 mg kg⁻¹ after induction of anaesthesia, 20 mg kg⁻¹ in the bypass prime, and 10 mg kg⁻¹ h⁻¹ of bypass. The prophylactic use of tranexamic acid was suspended in December 2008, because of reported neurological complications.

Transfusion policy

The prime solution consisted of PRBCs, 8.4% sodium bicarbonate, and albumin 5%, in proportions that varied according to the estimated haemodilution, and 500 IU of heparin per 100 ml of prime solution. The intraoperative haemocrit target was 35% in cyanotic patients, 30% otherwise, kept constant throughout the bypass. All patients underwent conventional ultrafiltration to reach a haemocrit of ~40% by the end of the bypass. If haemocrit was lower, additional PRBCs were transfused during bypass. All neonates received one unit of fresh frozen plasma (FFP) during CPB and one unit of platelets afterwards. The FFP transfusion strategy in infants was governed by body weight, extent of priming-related haemodilution, length of CPB, and pre- and postoperative coagulation tests. All patients received 25–50 IU kg⁻¹ prothrombin complex concentrate after bypass. The average volume of PRBCs at our institution is 250–300 ml, the average volume of FFP units is 200 ml, and the average volume of platelet units is 35–40 ml. After bypass, residual blood in the CPB circuit was processed by cell salvage.

Postoperative transfusion was guided by measured blood loss, visual assessment of the surgical field, haematocrit, and laboratory coagulation tests (prothrombin time, activated partial thromboplastin time, platelet count, fibrinogen concentration, thrombin time, and the anti-factor X a assay). The lowest acceptable haematocrit ranged from 30% to 35%, depending on age, preoperative haematocrit, and the complexity of the surgical repair. Platelet transfusion (0.2 units kg⁻¹) was considered if the platelet count was either less than 50 × 10⁹ litre⁻¹ or less than 100 × 10⁹ litre⁻¹ with clinically significant bleeding (bloody drainage from chest tubes more than 3 ml kg⁻¹ h⁻¹). FFP transfusion was determined by blood loss and postoperative coagulation tests.

Assessment of postoperative AKI

SCr was measured with the Jaffe technique using a Hitachi 917 autoanalyzer (Roche, Meylan, France), calibrating for paediatric levels, and by the enzymatic method adapted on the Hitachi 917 for very low SCr concentrations (>20 μmol litre⁻¹). According to the Acute-Kidney-Injury-Network classification, AKI was defined as a >1.5-fold increase in SCr compared with baseline, occurring within 48 h of surgery. Baseline SCr was defined as the last measurement before surgery. SCr does not allow reliable estimates of glomerular filtration in neonates younger than 48 h of age. Measurements in patients younger than 48 h and missing measurements were imputed. Peritoneal dialysis (PD) was the only renal replacement therapy method used in the present cohort during the study period. Indications for PD were as follows: physical evidence of total fluid overload and positive fluid balance; oliguria or anuria (<1 ml kg⁻¹ h⁻¹) unresponsive to fluid challenge and i.v. furosemide for at least 4 h; concomitant low cardiac output syndrome; acid–base or electrolyte disturbances (pH<7.30, serum K⁺>5.5 mmol litre⁻¹). Indications for the withdrawal of PD were: resolution of clinical oedema with urine output sufficient for negative fluid balance for at least 12 h, and correction of electrolyte imbalance.

Statistical analysis

Data were summarized and compared between patients who received aprotinin (‘aprotinin group’) and those who did not (‘control’). The number of blood product transfusions and the priming volumes across the study period were compared by analysis of variance. The incidences of AKI and dialysis across the study period were compared using a χ² test.

A propensity score methodology was used to balance groups with regard to baseline and surgical characteristics.
using the inverse probability of treatment weighting (IPTW) method. This method has been shown to have good performance in estimation of odds in observational studies. Significant changes occurred in the peroperative management, the most important being the miniaturization of the bypass circuit in the late period of the study, which resulted in lower priming volumes and ultrafiltration rates and in fewer transfusions. Both miniaturized circuits and tranexamic acid were used exclusively in controls. Thus, the propensity score model included all preoperative and perioperative characteristics, except variables related to the use of miniaturized circuits, like priming volume and ultrafiltration rate, and except the use of tranexamic acid. Then, the contribution of each subject was weighted by 1/propensity score for ‘aprotinin group’ subjects and by 1/(1 – propensity score) for ‘control’ subjects. These weights ensured that for each combination of the covariates used in the propensity score model, the sum of the contributions of all subjects is equal. Balance on covariates between groups after the IPTW was assessed by computing their standardized differences, and groups were considered balanced if the standardized differences in all covariates were <0.10. Variables describing the postoperative course were compared using IPTW-weighted logistic regression models and mortality during follow-up using a IPTW-weighted Cox model. Finally, independent associations between AKI, aprotinin use, and PRBC transfusions were assessed by means of IPTW-weighted logistic regression models for AKI and AKI requiring PD, both adjusted for unbalanced covariates and for the year of surgery. Results were expressed as adjusted odds ratios (ORs) and 95% confidence intervals (CIs). Statistical significance was set to P<0.05. Analyses were performed with R software version 2.10.1 for Windows, using the ‘Design’ and ‘survey’ packages (www.r-project.org, last accessed 24 August 2011).

Results
Overall, 1478 neonates and infants underwent cardiac surgery during the study period. In 1176 patients, complete data on pre-, perioperative, and short-term outcome and transfusion and postoperative renal function data were available. A total of 975 patients underwent 54 different procedures with CPB; the most common ones are listed in Table 1. Another 17 patients required extracorporeal membrane oxygenation, 15 after operation and two as the primary indication for surgery, and were not analysed here, leaving 958 cases to be analysed: 390 received aprotinin and 568 did not. Overall, 139 patients received tranexamic acid and 115 patients underwent CPB with a miniaturized circuit, all in the control group. A flowchart is shown in Figure 1. No patient required renal replacement therapy before surgery. Overall, 244 (25.7%) patients developed AKI and 79 (8.3%) required PD.

Preoperative Scr was missing in 99 patients and measured within the first 48 h from birth in 150 neonates and imputed as described. Thus, patients with baseline measurements within 48 h from birth were attributed values between 51.3 and 52.5 mmol litre⁻¹. The duration of CPB and cross-clamping was missing in 14 (1.5%) and ultrafiltration rate...
in 22 (2.3%) patients (whereas all other CPB characteristics were available) and imputed by the median of the recorded values. Information concerning height was missing in 39 neonates and imputed by multiple imputation on age and weight.

Figure 2 shows that there was a significant decrease in all blood product transfusions and in priming volumes across the study period (all \( P \)-values <0.001). Table 2 shows patient baseline, surgical, and CPB characteristics. Overall, 388 patients (99.5%) in the aprotinin group and 566 (99.6%) in the control group received at least one blood product transfusion. Variables shown in Table 2 were included in the propensity score, except blood product transfusions, and variables related to the use of the miniaturized circuit and the use of tranexamic acid. The propensity score model (Appendix) had good discrimination ability (c-index 0.62) and there was a good overlap of the score between groups: mean 0.43, \( \pm 0.10 \) in the aprotinin group and 0.39, \( \pm 0.10 \) in the control group. The IPTW resulted in good balance between groups with regard to all variables included in the propensity score.

Figure 3 shows the incidence of AKI and dialysis across the study period: there was no linear trend for the overall AKI incidence, \( \chi^2 \) test (\( P \)=0.77), but the incidence of PD increased (\( P \)=0.02). The incidence of AKI and PD, as well as variables describing the postoperative course, in-hospital mortality, and mortality during follow-up, was similar between groups after IPTW, except the length of ICU stay, which was longer in the aprotinin group (the early period of the study), as shown in Table 3. Twenty-two patients in the aprotinin group required re-operation for surgical revision (\( n \)=3), mediastinitis (\( n \)=9), pericardial effusion (\( n \)=3), pacemaker implantation (\( n \)=1), and wound infection (\( n \)=4). Twenty-three controls required re-operation for bleeding (\( n \)=3), surgical revision (\( n \)=12), pericardial effusion (\( n \)=1), chylothorax (\( n \)=1), pacemaker implantation (\( n \)=3), and wound infection (\( n \)=3).

The results of the multivariable analysis are shown in Table 4. After IPTW and adjustment for the use of miniaturized circuits and for the year of surgery, aprotinin was not significantly associated with the occurrence of AKI or with the occurrence of AKI requiring dialysis. Each additional PRBC transfusion on day 0 was associated with a 1.6-fold increased probability of AKI and a two-fold increased probability of dialysis, and each additional FFP transfusion was associated with a more than two-fold increased probability of AKI and a more than three-fold increased probability of dialysis. Each additional platelet transfusion was associated with a more than two-fold increased probability of AKI requiring dialysis.

![Figure 2](https://example.com/figure2.png)

**Figure 2** Number of blood product transfusions and CPB priming volumes across the study period. Data are shown as means and \( \pm \). There was a significant decrease in all blood product transfusions and in priming volumes over time, as shown by the results of analysis of variance, all \( P \)-values <0.001. Day 0: the day of surgery.
Discussion

In a population of neonates and infants undergoing open heart surgery, with an incidence of AKI within the range reported over the past decade in paediatric cardiac surgery, this retrospective study found no significant association between the prophylactic use of aprotinin and the incidence and severity of AKI, but a significant association between the number of blood product transfusions on the day of surgery and the incidence and severity of AKI.
The overall evidence shows a 47% increased risk of renal dysfunction in adult patients receiving aprotinin for cardiac surgery, and aprotinin is no longer recommended for prophylactic use. However, Mangano and colleagues reported in 2006 that the renal composite outcome (renal dysfunction or failure requiring renal replacement therapy or in-hospital death with evidence at autopsy of acute renal failure) was related to intraoperative transfusions of PRBC, OR 1.71 (1.16–2.52), FFP, OR 2.40 (1.58–3.66), and surgical complexity. In 2007, Furnary and colleagues demonstrated that aprotinin did not increase the risk of dialysis-dependent renal failure independently of the number of transfusions administered and that the risk of renal failure was solely attributable to the greater need for PRBC transfusions in high-transfusion-risk patients. Recently, PRBC transfusions have been shown to increase the risk of AKI in anaemic patients undergoing cardiac surgery. Several authors hypothesized that there might be subgroups of patients undergoing complex and high-transfusion-risk surgery, in whom the number of transfusions would carry an independent risk of AKI and in which the beneficial blood-sparing effect of aprotinin could outweigh its risks. Therefore, when assessing the relationship between aprotinin, renal failure, and death, studies of adults have stratified high-transfusion-risk cardiac surgery. To date, studies of adults have failed to identify any patient subgroups spared from the adverse effects of aprotinin on renal function, and the majority of epidemiological evidence indicates risk in adults that cannot be fully explained by the need for blood product transfusions.

Neonates and infants undergoing cardiac surgery form a high-transfusion-risk surgery subgroup. No evidence relates kidney injury or kidney failure requiring dialysis to the use of aprotinin in children and neonates. Stratification according to the RACHS-1 surgical complexity score was attempted by Székely and colleagues, who found that aprotinin was associated with AKI in patients undergoing less complex surgery, although the difference

### Table 3

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before IPTW</th>
<th></th>
<th>After IPTW</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Aprotinin group</td>
<td>Controls</td>
<td>P-value</td>
<td>Weighted odds ratios, 95% CI</td>
</tr>
<tr>
<td>Acute kidney injury [no. (%)]</td>
<td>92 (23.6)</td>
<td>152 (26.8)</td>
<td>0.27</td>
<td>1.07 (0.79–1.46)</td>
</tr>
<tr>
<td>Acute kidney injury requiring peritoneal dialysis [no, (%)]</td>
<td>29 (7.4)</td>
<td>50 (8.8)</td>
<td>0.45</td>
<td>1.01 (0.62–1.65)</td>
</tr>
<tr>
<td>Duration of peritoneal dialysis (days) (median, IQR)</td>
<td>3.0, 2.0–5.0</td>
<td>2.0, 1.0–3.7</td>
<td>0.05</td>
<td>1.05 (0.95–1.16)</td>
</tr>
<tr>
<td>Peak plasma lactate within 48 h (mmol litre⁻¹)</td>
<td>3.4 (2.3)</td>
<td>3.3 (2.0)</td>
<td>0.59</td>
<td>1.00 (0.94–1.07)</td>
</tr>
<tr>
<td>Days with the sternum left open (median, IQR)</td>
<td>4.5 (3.4)</td>
<td>3.3 (2.8)</td>
<td>0.006</td>
<td>1.15 (1.00–1.33)</td>
</tr>
<tr>
<td>Requiring re-operation [no. (%)]</td>
<td>22 (5.6)</td>
<td>23 (4.0)</td>
<td>0.25</td>
<td>1.39 (0.74–2.59)</td>
</tr>
<tr>
<td>Length of mechanical ventilation (days)* (median, IQR)</td>
<td>1.0, 0.2–4.0</td>
<td>1.0, 0.3–5.0</td>
<td>0.66</td>
<td>1.01 (0.99–1.03)</td>
</tr>
<tr>
<td>Length of Intensive Care Unit stay (days)* (median, IQR)</td>
<td>4.0, 3.0–7.0</td>
<td>4.0, 2.0–7.0</td>
<td>0.06</td>
<td>1.02 (1.00–1.04)</td>
</tr>
<tr>
<td>Mortality during hospital stay [no. (%)]</td>
<td>22 (5.6)</td>
<td>20 (3.5)</td>
<td>0.11</td>
<td>1.01 (0.89–1.15)</td>
</tr>
<tr>
<td>Mortality during follow-up [no. (%)]</td>
<td>27 (6.9)</td>
<td>33 (5.8)</td>
<td>0.48</td>
<td>1.01 (0.89–1.14)</td>
</tr>
</tbody>
</table>

### Table 4

<table>
<thead>
<tr>
<th>Variable</th>
<th>AKIAdjusted OR (95% CI)</th>
<th>P-value</th>
<th>Severe AKI requiring dialysisAdjusted OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of aprotinin</td>
<td>0.62 (0.35–1.08)</td>
<td>0.09</td>
<td>1.40 (0.47–4.20)</td>
<td>0.54</td>
</tr>
<tr>
<td>Number of PRBC transfusions on day 0</td>
<td>1.64 (1.12–2.41)</td>
<td>0.01</td>
<td>2.07 (1.13–3.73)</td>
<td>0.02</td>
</tr>
<tr>
<td>Number of FFP transfusions on day 0</td>
<td>2.28 (1.68–3.09)</td>
<td>&lt;0.001</td>
<td>3.11 (1.95–4.97)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of platelet transfusions on day 0</td>
<td>1.33 (0.93–1.92)</td>
<td>0.12</td>
<td>2.20 (1.21–4.01)</td>
<td>0.01</td>
</tr>
<tr>
<td>Use of a miniaturized circuit</td>
<td>1.74 (0.82–3.66)</td>
<td>0.15</td>
<td>1.19 (0.41–3.50)</td>
<td>0.74</td>
</tr>
<tr>
<td>Priming volume (per 100 ml)</td>
<td>0.98 (0.66–1.43)</td>
<td>0.90</td>
<td>0.60 (0.32–1.14)</td>
<td>0.12</td>
</tr>
<tr>
<td>Ultrafiltration rate (per ml kg⁻¹ h⁻¹)</td>
<td>0.74 (0.59–1.03)</td>
<td>0.07</td>
<td>0.82 (0.57–1.16)</td>
<td>0.26</td>
</tr>
<tr>
<td>Use of tranexamic acid</td>
<td>0.92 (0.57–1.50)</td>
<td>0.74</td>
<td>0.86 (0.36–2.04)</td>
<td>0.73</td>
</tr>
<tr>
<td>Year of surgery</td>
<td>0.87 (0.65–1.16)</td>
<td>0.34</td>
<td>1.43 (0.87–2.36)</td>
<td>0.15</td>
</tr>
</tbody>
</table>
was not significant after adjustment. However, the intraoperative transfusion volume was associated with an overall higher incidence of renal dysfunction, and the risk increased by 1% for each 1 ml PRBCs kg\(^{-1}\) transfused.\(^2\)

To date, risk factors for AKI after cardiac surgery in patients less than 1 yr of age have not been identified, as most studies\(^{24,30,31}\) have investigated AKI requiring dialysis in heterogeneous populations. Besides, few studies have defined AKI according to creatinine criteria,\(^9,11,25\) which have not been validated in patients less than 1 yr old, and only two of them investigated a homogeneous population of neonates.\(^10,13\)

Young age, duration of CPB, surgical complexity, surgery requiring DHCA, and postoperative low cardiac output syndrome are risk factors reported by most authors.\(^{24,30,31}\) As a result of the IPTW carried out in the present study, groups were balanced for the variability related to these AKI risk factors, leaving two potential risk factors to be further analysed: aprotinin and transfusions. The prophylactic use of aprotinin was not significantly related to the occurrence of postoperative AKI. Consistent with previous findings in adults and children,\(^2,6,9,27\) the present study found significant associations between the number of PRBC and FFP transfusions on day 0, and the incidence of AKI and dialysis. The present study also suggests that the amount of platelet transfusions on day 0 is associated with the occurrence of severe AKI requiring dialysis. Thus, our findings suggest that multiple transfusions carry a significant risk of AKI and are not merely an indicator of a serious intraoperative, postoperative, or both conditions.

The high risk for bleeding and transfusions during cardiac surgery in neonates and infants is mainly due to haemodilution resulting from the disproportion between extracorporeal volume and patient size. Knowing that outcome in infants with cardiac surgery is related to the number and quantity of transfusions,\(^{32,33}\) efforts have been made to reduce priming volume and to reduce haemodilution and transfusions, and the miniaturized circuit used here has been shown previously to result in fewer PRBC and platelet transfusions.\(^{16}\) However, this study could not identify an association between the use of miniaturized circuits and a lower occurrence of AKI.

Limitations
The retrospective design of the present study requires that the validity of our findings be considered with caution. The present study was single-centre-based and had a small sample size. There is no reliable definition for AKI in patients less than 1 yr old, and the definition used here was not validated in paediatric populations. Despite adjustment for the year of surgery, bias related to improvements in the surgical and medical management of congenital cardiac diseases throughout the study period cannot be ruled out. Despite the transfusion policy in the unit, transfusion could have been influenced by the preheld belief in the usefulness of aprotinin. Only numbers, and not quantities, of blood product transfusions were available for analysis. Day of surgery could only be assessed as a calendar day, and this could have biased the assessment of the number of blood product transfusions on day 0. It is not certain whether all blood products were entirely infused. The propensity score strategy used here did not allow identification of other risk factors of AKI in this population. The use of miniaturized circuits and tranexamic acid exclusively in controls resulted in a large imbalance between groups, and residual bias cannot be excluded despite the propensity score methodology. The impact of the use of aprotinin and tranexamic acid on transfusions was not analysed.

Conclusions
The prophylactic use of aprotinin was not significantly associated with the incidence of AKI and the incidence of AKI requiring dialysis in neonates and infants undergoing cardiac surgery. However, blood product transfusions were associated with an increased risk of AKI and AKI requiring dialysis.

Declaration of interest
None declared.

Appendix
The propensity score regression model.

<table>
<thead>
<tr>
<th>Variables included in the propensity score</th>
<th>Regression coefficient</th>
<th>(SE)</th>
<th>(P)-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (days)</td>
<td>(-0.0005)</td>
<td>0.001</td>
<td>0.69</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>(-0.02)</td>
<td>0.08</td>
<td>0.276</td>
</tr>
<tr>
<td>Preoperative creatinine (mmol litre(^{-1}))</td>
<td>0.02</td>
<td>0.007</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Repeat sternotomy [no. (%)]</td>
<td>0.76</td>
<td>0.22</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>The basic Aristotle score</td>
<td>(-0.11)</td>
<td>0.05</td>
<td>0.03</td>
</tr>
<tr>
<td>Duration of CPB (min)</td>
<td>(-0.0009)</td>
<td>0.001</td>
<td>0.48</td>
</tr>
<tr>
<td>Duration of aortic cross-clamping (min)</td>
<td>0.008</td>
<td>0.004</td>
<td>0.07</td>
</tr>
<tr>
<td>Required deep hypothermic circulatory arrest</td>
<td>0.187</td>
<td>0.28</td>
<td>0.51</td>
</tr>
<tr>
<td>Required the sternum be left open [no. (%)]</td>
<td>(-0.61)</td>
<td>0.23</td>
<td>0.008</td>
</tr>
</tbody>
</table>

References