Transfusion and risk of acute kidney injury in cardiac surgery

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Summary. Acute kidney injury (AKI) is a serious and common complication of major surgery. This narrative review focuses on the relationship between perioperative red blood cell transfusion and AKI after cardiac surgery with cardiopulmonary bypass (CPB). Numerous observational studies have shown that these two factors are independently associated with each other. Several lines of evidence suggest that the nature of this association is one of cause and effect. The pathophysiological mechanism by which transfusions might harm the kidney has not been fully elucidated, but it is known that erythrocytes undergo irreversible morphological and biochemical changes during storage. As a result, after transfusion, they can promote a pro-inflammatory state, impair tissue oxygen delivery, and exacerbate tissue oxidative stress. This in turn can cause AKI in susceptible patients undergoing cardiac surgery with CPB, such as those with pre-existing kidney dysfunction or anaemia. Interventions aimed at avoiding perioperative blood transfusion might, therefore, reduce the risk of AKI after cardiac and other types of surgery.

Keywords: blood, transfusion; kidney, failure; surgery, cardiovascular

Burden of acute kidney injury in cardiac surgery

Acute kidney injury (AKI) is a common and prognostically important complication of cardiac surgery with cardiopulmonary bypass (CPB). Up to 30% of patients undergoing cardiac surgery with CPB develop clinically significant AKI,1 defined as an abrupt reduction in kidney function characterized by a >50% increase in serum creatinine or >25% decrease in glomerular filtration rate.2–4 and about 3% of patients develop severe AKI that necessitates renal replacement therapy.1 There is a direct, independent relationship between the severity of AKI and short- and long-term morbidity and mortality.5–24 The morbidity and mortality risk is particularly high for those patients who develop severe AKI requiring renal replacement therapy, as their crude mortality rate can be as high as 50%5 and after controlling for comorbidities and other perioperative complications, their risk-adjusted mortality is increased by approximately eight-fold.8 Even relatively mild kidney injury has important negative prognostic implications, as a 50% increase in serum creatinine confers a two- to four-fold increase in the risk-adjusted mortality risk.11 14 17 25 In fact, recent observations suggest that any degree of kidney injury predisposes patients to increased risk.7 10 15 19 21 26

Transfusion as a risk factor for AKI in cardiac surgery with CPB

Identification of risk factors for AKI in cardiac surgery has been the focus of many observational studies,6 7 22–25 27–64 but most did not consider the risks of perioperative blood transfusion. Only in the last decade have such studies considered transfusion as a risk factor, using multivariable logistic regression or propensity score methods to determine if perioperative transfusions are independently related to AKI. After a systematic PubMed search (terms: renal or kidney and blood or erythrocyte or transfusion and cardiac or surgery or CPB; restrictions: English language, humans), 22 of such studies were identified, and all but four of them found an independent relationship between perioperative blood transfusion and AKI (Table 1).7 23–25 31 33 35 37 40–42 46 48 49 54 55 57 58 61–64 The four studies that did not find transfusions to be independently related to AKI were relatively small: Boyle and colleagues23 included only 44 patients with AKI, Palomba and colleagues24 included only 66 patients with AKI, de Somer and colleagues included only 53 cases with AKI. Moreover, Boyle and colleagues included only patients who underwent heart transplantation, Palomba and colleagues analysed transfusion and re-exploration as a single variable, and de Somer and colleagues might have missed the effect of transfusion by analysing oxygen delivery as a binomial variable (it is likely that a large number of transfused patients were in the low oxygen delivery category, but this number is not reported). In the 18 studies that did find perioperative transfusions to be an independent risk factor for AKI, the effect size varied, which is not surprising given that they used different definitions of AKI, controlled for different covariates, and categorized and analysed transfusions differently.
Table 1. Observational studies that assessed the relationship between perioperative red blood cell transfusion and AKI in cardiac surgery with CPB. OR, odds ratio; CI, 95% confidence interval

<table>
<thead>
<tr>
<th>Study</th>
<th>Definition(s) of AKI</th>
<th>Definition of transfusion</th>
<th>Relationship between transfusion and AKI</th>
<th>Influence of perioperative anaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ryckwaert and colleagues&lt;sup&gt;7&lt;/sup&gt;</td>
<td>≥ 20% increase in creatinine</td>
<td>Perioperative blood transfusion; binomial</td>
<td>Related to AKI in bivariate analysis; no multivariable analysis performed</td>
<td>Not analysed</td>
</tr>
<tr>
<td>Swaminathan and colleagues&lt;sup&gt;11&lt;/sup&gt;</td>
<td>Peak per cent change in creatinine</td>
<td>Perioperative blood transfusion; number of units</td>
<td>Independently related (linear regression); P=0.009</td>
<td>Preoperative and intraoperative anaemia also independently related</td>
</tr>
<tr>
<td>Bove and colleagues&lt;sup&gt;23&lt;/sup&gt;</td>
<td>≥ 100% increase in creatinine</td>
<td>Postoperative blood transfusion; binomial</td>
<td>Independently related (logistic regression); OR 7.1; CI 4.1–12.1; P&lt;0.0001</td>
<td>Preoperative anaemia related to AKI in bivariate analysis (P=0.007), but not independently related</td>
</tr>
<tr>
<td>Habib and colleagues&lt;sup&gt;37&lt;/sup&gt;</td>
<td>(1) ≥50% increase in creatinine (2) ≥100% increase in creatinine and ≥186 μmol litre&lt;sup&gt;−1&lt;/sup&gt; (2.1 mg dl&lt;sup&gt;−1&lt;/sup&gt;)</td>
<td>Intraperoperative blood transfusion; binomial</td>
<td>Independently related (propensity analysis) (1) AKI 26.0% in transfused vs 14.4% in non-transfused; P=0.003 (2) AKI 12.0% in transfused vs 3.4% in non-transfused; P=0.001</td>
<td>Intraoperative anaemia also independently related</td>
</tr>
<tr>
<td>Boyle and colleagues&lt;sup&gt;25&lt;/sup&gt;</td>
<td>Requirement for renal replacement therapy</td>
<td>Intraperoperative blood transfusion; number of units</td>
<td>Related to AKI in bivariate analysis (P&lt;0.001), but not independently related to AKI</td>
<td>Preoperative anaemia related to AKI in bivariate analysis (P=0.007), but not independently related</td>
</tr>
<tr>
<td>Koch and colleagues&lt;sup&gt;37&lt;/sup&gt;</td>
<td>Requirement for renal replacement therapy</td>
<td>Perioperative blood transfusion; number of units</td>
<td>Independently related (logistic regression); OR (per unit) 2.06; CI 1.87–2.27; P&lt;0.0001</td>
<td>Not analysed</td>
</tr>
<tr>
<td>Ranucci and colleagues&lt;sup&gt;36&lt;/sup&gt;</td>
<td>Requirement for renal replacement therapy</td>
<td>Perioperative blood transfusion ≥2 units; binomial</td>
<td>Not included in the multivariable analysis, but found to double the risk of AKI in patients with haematocrit &lt;23% during surgery</td>
<td>Intraoperative anaemia independently related</td>
</tr>
<tr>
<td>Landoni and colleagues&lt;sup&gt;41&lt;/sup&gt;</td>
<td>≥100% increase in creatinine</td>
<td>Postoperative blood transfusion; binomial</td>
<td>Independently related (logistic regression); OR 5.2; CI 2.6–10.3; P&lt;0.0001</td>
<td>Not analysed</td>
</tr>
<tr>
<td>Palomba and colleagues&lt;sup&gt;52&lt;/sup&gt;</td>
<td>&gt;50% increase in creatinine or &gt;177 μmol litre&lt;sup&gt;−1&lt;/sup&gt;</td>
<td>Re-exploration or ≥3 units of perioperative blood transfusion; binomial</td>
<td>Related to AKI in bivariate analysis (OR 3.4; CI 1.9–5.8; P=0.0001), but not independently related to AKI</td>
<td>Not analysed</td>
</tr>
<tr>
<td>De Santo and colleagues&lt;sup&gt;53&lt;/sup&gt;</td>
<td>&gt;50% increase in creatinine</td>
<td>Perioperative blood transfusion; number of units</td>
<td>Propensity for transfusion was independently related (logistic regression); OR 2.2; CI 1.8–2.8; P&lt;0.001</td>
<td>Preoperative anaemia independently related</td>
</tr>
<tr>
<td>Karkouti and colleagues&lt;sup&gt;75&lt;/sup&gt;</td>
<td>(1) &gt;25% decrease in estimated glomerular filtration rate (2) ≥50% decrease (3) ≥75% decrease</td>
<td>Perioperative blood transfusion; number of units</td>
<td>Independently related (logistic regression) (1) OR (per unit) 1.08; CI 1.05–1.12; P&lt;0.0001 (2) OR (per unit) 1.08; CI 1.04–1.13; P&lt;0.0001 (3) OR (per unit) 1.08; CI 1.03–1.13; P=0.001</td>
<td>Preoperative anaemia independently related</td>
</tr>
<tr>
<td>Argalious and colleagues&lt;sup&gt;56&lt;/sup&gt;</td>
<td>(1) ≥50% increase in creatinine (2) Renal replacement therapy</td>
<td>Perioperative blood transfusion; number of units</td>
<td>Independently related (logistic regression) (1) OR (per unit) 1.23; CI 1.20–1.26; P&lt;0.001 (2) OR (per unit) 1.21; CI 1.18–1.24; P&lt;0.001</td>
<td>Preoperative anaemia independently related</td>
</tr>
<tr>
<td>Hajjar and colleagues&lt;sup&gt;68&lt;/sup&gt;</td>
<td>Renal replacement therapy</td>
<td>Perioperative blood transfusion; number of units</td>
<td>Independently related (logistic regression); OR (per unit) 1.26; CI 1.08–1.46; P=0.004</td>
<td>Preoperative anaemia not independently related</td>
</tr>
<tr>
<td>Bossard and colleagues&lt;sup&gt;69&lt;/sup&gt;</td>
<td>&gt;30% increase in serum creatinine</td>
<td>Intraperoperative blood transfusion; binomial</td>
<td>Independently related (logistic regression); OR 9.0; CI 1.1–70.8; P=0.04</td>
<td>Not analysed</td>
</tr>
<tr>
<td>de Somer and colleagues&lt;sup&gt;74&lt;/sup&gt;</td>
<td>≥50% increase in serum creatinine</td>
<td>Perioperative blood transfusion; number of units</td>
<td>Related to AKI in bivariate analysis (P=0.002), but not independently related to AKI</td>
<td>Analysed as part of nadir oxygen delivery, which was independently related</td>
</tr>
</tbody>
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Continued
Nevertheless, taken together, these studies suggest that each unit of perioperative blood transfusion is independently associated with a 10–20% increase in the risk of AKI after cardiac surgery with CPB.

Whether this relationship is causal, however, cannot be determined solely on the basis of these studies. Because the decision to transfuse is influenced by numerous factors that are unmeasured in retrospective observational studies (such as the severity of pre-existing comorbidities and the extent of intraoperative bleeding) and hence cannot be accounted for by multivariable statistical testing,65 observational studies comparing transfused with non-transfused patients can over-estimate the risks of transfusion.66 Another important issue is that some important risk factors for AKI are likely to be interrelated with transfusion, making it difficult to account for their independent effects by multivariable statistical testing. One such factor is perioperative anaemia, but based on most of the studies listed in Table 1 that assessed the role of anaemia, and others that were not included in Table 1 because they reported AKI only as part of a composite outcome,67 68 it seems that both perioperative transfusion and anaemia are independently related to AKI. Two recent studies included only non-transfused patients to rule out the confounding effect of transfusion and found anaemia to be independently related to AKI.69 70 In another recent study, it was illustrated that the AKI risks of transfusion are more pronounced in anaemic than non-anaemic patients.71 Specifically, the study found that in 2113 propensity-score-matched pairs who received up to 3 units of red blood cells perioperatively, AKI rates in anaemic patients increased from 1.8% among those not transfused to 6.6% among those transfused three units, while in non-anaemic patients, the rates increased from 1.7% among those not transfused to 3.2% among those transfused three units.71 Thus, it seems that the independent effects of perioperative transfusion and perioperative anaemia on AKI may be synergistic.

Table 1 Continued

<table>
<thead>
<tr>
<th>Study</th>
<th>Definition(s) of AKI</th>
<th>Definition of transfusion</th>
<th>Relationship between transfusion and AKI</th>
<th>Influence of perioperative anaemia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Karkouti and colleagues71</td>
<td>&gt;50% reduction in estimated glomerular filtration rate</td>
<td>Perioperative blood transfusion; number of units</td>
<td>Independently related (propensity analysis), particularly in anaemic patients&lt;br&gt;Anaemic patients: AKI 1.9% in 0 units, 2.2% in 1 unit; 4.6% in 2 units, and 6% in 3 units&lt;br&gt;In non-anaemic patients: AKI 1.4% in 0 units; 2.8% in 1 unit; 2.2% in 2 units; 2.8% in 3 units</td>
<td>Preoperative anaemia independently related</td>
</tr>
<tr>
<td>Brown and colleagues55</td>
<td>≥50% increase in serum creatinine or ≥26.5 μmol litre⁻¹</td>
<td>Perioperative blood transfusion; number of units</td>
<td>Independently related (logistic regression); OR (per unit) 1.20; CI 1.16–1.24; P&lt;0.001</td>
<td>Intraoperative anaemia independently related</td>
</tr>
<tr>
<td>Demirjian and colleagues57</td>
<td>≥100% increase in serum creatinine or renal replacement therapy</td>
<td>Perioperative blood transfusion; number of units</td>
<td>Independently related (logistic regression)</td>
<td>Preoperative anaemia borderline independently related (P=0.08)</td>
</tr>
<tr>
<td>Haase and colleagues24</td>
<td>≥50% increase in serum creatinine</td>
<td>Intraoperative blood transfusion; volume</td>
<td>Independently related (logistic regression); OR (per ml) 1.001; CI 1.000–1.002; P=0.01</td>
<td>Intraoperative anaemia independently related</td>
</tr>
<tr>
<td>Heise and colleagues62</td>
<td>≥50% increase in serum creatinine</td>
<td>Perioperative blood transfusion; number of units</td>
<td>Independently related (logistic regression). Exact OR not reported</td>
<td>Preoperative anaemia not independently related</td>
</tr>
<tr>
<td>Ho and colleagues58</td>
<td>≥50% increase in serum creatinine or ≥26.5 μmol litre⁻¹</td>
<td>Intraoperative blood transfusion; binomial</td>
<td>Not related</td>
<td>Not analysed</td>
</tr>
<tr>
<td>Parolari and colleagues61</td>
<td>&gt;50% increase in serum creatinine</td>
<td>Perioperative blood transfusion; number of units</td>
<td>Independently related (logistic regression)&lt;br&gt;OR (per intraoperative units) 1.14; CI 1.04–1.24; P=0.003&lt;br&gt;OR (per postoperative units) 1.17; CI 1.10–1.24; P&lt;0.001</td>
<td>Intraoperative anaemia not independently related</td>
</tr>
</tbody>
</table>
Nevertheless, as noted above, the issue of selection bias due to unmeasured confounding cannot be fully excluded by observational studies. Selection bias is best addressed by random allocation of exposure, but randomizing patients to transfusion or no transfusion is hindered by the fact that in many patients, anaemia can become severe enough to necessitate transfusions. Recognizing this, several studies attempted to assess the risks of transfusion by randomizing patients to restrictive or liberal transfusion arms.72 While the transfusion triggers were variable in these studies, for the most part, the haemoglobin concentrations used in the restrictive arms were 70–90 g litre\(^{-1}\) and in the liberal arms, they were 90 g litre\(^{-1}\) or higher.72 The main finding of these studies was that the restrictive transfusion strategy significantly reduced the number of transfusions at the cost of a significant increase in the severity of anaemia.72 Only three of the studies reported renal outcomes and they did not find any between-group differences in the rate of AKI,72 suggesting that transfusions do not cause AKI. Assessing the effects of transfusion on AKI, however, was not a primary objective of these studies, and they were severely underpowered for this outcome (in total, there were only 38 reported cases of AKI in these studies).72 Even if these studies were adequately powered, since by design they have a diametrically different effect on transfusion rates and severity of anaemia, both of which are independent but interrelated risk factors for AKI, they cannot be used to ascertain the risks of transfusion on AKI. For example, while patients in the restrictive arm may benefit by receiving fewer transfusions than those in the liberal arm, they might also be harmed by becoming more anaemic, thereby masking the potential benefits of lower transfusion rates. It is also important to note that studies that randomize patients to different transfusion triggers have inherent methodological limitations that further reduce their interpretability.73

Outside of the observational studies noted above, there are other sources of evidence that link transfusions with AKI. One is the randomized trials of goal-directed fluid resuscitation in major surgery. A recent meta-analysis of these trials concluded that goal-directed therapy reduces AKI rates and attributed this beneficial effect to improved fluid management.74 Exploring the relationship between transfusion and AKI in these studies, however, suggests that the effects of the interventions on the amount of blood transfusion can provide an alternative explanation. In studies that reported the amount of blood transfusion, there was a direct relationship between amount of transfusion and risk of AKI (Fig. 1), suggesting that the observed benefit of goal-directed therapy can in part be explained by the effects of blood transfusion on the kidney. A similar relationship is observed in randomized trials of goal-directed coagulation management in cardiac surgery, where the goal-directed arms had lower transfusion rates and AKI rates.75 76

Thus, there are several lines of evidence suggesting that perioperative blood transfusion is an important risk factor for AKI, but the questions of causality and its interrelationship with severity of anaemia remain.

Possible pathophysiological mechanisms for transfusion-related AKI and the synergistic role of anaemia

Recent discoveries about the impact of CPB on the kidneys and also the important and interconnecting roles of inflammation, renal hypoxia, and oxidative stress in the pathogenesis of AKI have provided an explanation for why transfusions might harm the kidneys during cardiac surgery with CPB and why anaemic patients might be more susceptible to these deleterious effects.

Virtually, all patients subjected to cardiac surgery with CPB experience the ‘initiation phase’ of ischaemia–reperfusion kidney injury.77 This injury is characterized by renal artery vasoconstriction and increased tubular oxygen consumption, resulting in impaired renal oxygenation and proximal tubular dysfunction.78 Whether patients recover from this insult without sequelae or develop AKI by progressing into the ‘extension phase’ of kidney injury largely depends on the severity of the ensuing inflammatory response, renal hypoxia, and oxidative stress,77 all of which can be aggravated by transfusion and anaemia.

Currently, a unit of red blood cells can be stored for up to 42 days before it has to be transfused. During storage, erythrocytes undergo progressive, interrelated biochemical and morphological changes that are thought to contribute to any organ damage that might be caused by blood transfusion.79–82 These changes, which collectively are known as the storage defect, include depletion of adenosine
triphosphate and 2,3-diphosphoglycerate, alterations in nitric oxide-mediated functions, and increased lipid peroxidation.79–81 As a result, the erythrocyte membrane undergoes changes that are mostly irreversible and cause it to become less deformable and more fragile. This affects survival during storage, and leads to progressive haemolysis, formation of haemoglobin-laden microvesicles,83 and accumulation of pro-inflammatory molecules, free haemoglobin, and iron in the supernatant.79–81 83 Post-transfusion survival is also affected, such that within an hour of transfusion, up to 30% of the transfused erythrocytes are either haemolysed, potentially leading to the presence of free haemoglobin in the circulation, or removed from the circulation by macrophages.84 85 When macrophages are presented with small amounts of damaged erythrocytes, which occurs under normal circumstances, they are able to sequester the haemoglobin–iron contained in the erythrocytes and then slowly release the iron into the circulation safely bound to the iron-carrier protein transferrin.86 When there is an excessive amount of damaged erythrocytes due to transfusion, however, the amount of haemoglobin–iron released by macrophages can overwhelm the iron binding sites on transferrin, potentially resulting in the presence of free iron in the circulation.85 Thus, transfusion of several units of older blood can in particular lead to high concentrations of free haemoglobin and iron in the circulation, as has been shown in animal and human experiments.87–89 By some estimates, transfusion of 2 units of red blood cells could increase plasma free haemoglobin by ~10-fold above normal levels.90 Free haemoglobin and iron are highly toxic to the kidney and other organs: free haemoglobin can cause microcirculatory dysfunction through nitric oxide scavenging and free iron is a potent pro-oxidant.83 90 91 Cardiac surgery with CPB is itself an important instigator of the ‘extension phase’ of kidney injury. This risk explains, ‘none of these characteristics can bring indisputable evidence for or against the cause-and-effect hypothesis and none can be required as a sine qua non. What they can do, with greater or less strength, is to help us to make up our minds on the fundamental questions—is there any other way of explaining the set of facts before us, is there any other answer equally, or more, likely than cause and effect?’ As he explains, ‘none of these characteristics can bring indisputable evidence for or against the cause-and-effect hypothesis and none can be required as a sine qua non. What they can do, with greater or less strength, is to help us to make up our minds on the fundamental questions—is there any other way of explaining the set of facts before us, is there any other answer equally, or more, likely than cause and effect?’ As is outlined in Table 2, the observed association between transfusion and AKI has several, but not all, of these characteristics. Thus, while the evidence is not conclusive, it seems that the most likely explanation for the observed association between transfusion and AKI after cardiac surgery with CPB is one of cause and effect.

**Therapeutic implications**

To mitigate the burden of AKI after cardiac surgery with CPB, numerous therapies have been tested, but none has proven effective.1 106 107 Until we have identified safe and effective therapies, targeting modifiable risk factors, such as

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**Is the relationship between perioperative erythrocyte transfusion and AKI one of cause and effect?**

In his classic paper, Hill105 proposed nine characteristics of an association that would help in interpreting whether the nature of the association is one of cause and effect (Table 2). As he explains, ‘none of these characteristics can bring indisputable evidence for or against the cause-and-effect hypothesis and none can be required as a sine qua non. What they can do, with greater or less strength, is to help us to make up our minds on the fundamental questions—is there any other way of explaining the set of facts before us, is there any other answer equally, or more, likely than cause and effect?’ As is outlined in Table 2, the observed association between transfusion and AKI has several, but not all, of these characteristics. Thus, while the evidence is not conclusive, it seems that the most likely explanation for the observed association between transfusion and AKI after cardiac surgery with CPB is one of cause and effect.
perioperative transfusion, might offer the best means for reducing the burden of AKI after cardiac surgery with CPB.

There are several available or experimental therapeutic options that can help avoid or reduce the potential harms of perioperative red blood cell transfusions on the kidney in cardiac surgery with CPB. One option is to reduce the rate of perioperative transfusions, and several interventions are available that can help achieve this goal. Some interventions that can be readily applied to the majority of patients include reducing perioperative haemodilution by minimizing fluid administration and retrograde autologous priming of the cardiopulmonary circuit, salvage of shed blood, and tolerance of moderate haemodilution.108 One important caveat, however, is that severe haemodilution, such as can be caused by the use of acute normovolaemic haemodilution, might be harmful as it may predispose patients to the potential harms of anaemia outlined earlier. As to the level of anaemia that might increase the risk of AKI, current evidence is not conclusive but does indicate that haematocrit should be maintained at or >20% during CPB, and likely higher after CPB.109 It is important to note that since perioperative transfusion and anaemia likely have a synergistic effect on the risk of AKI, transfusing moderately anaemic patients to avoid the risks of anaemia are likely to further increase the risk of AKI.

Another option is to reduce the need for perioperative transfusions in anaemic patients by early identification and treatment with erythropoietin-stimulating agents and iron therapy.108 In cardiac surgery, however, this intervention has limited efficacy and major risk concerns (including increasing risk of thromboembolic events, cancer recurrence, and death).109 110 Another promising option to reduce perioperative transfusions is the use of transfusion-practice bundles that incorporate point-of-care coagulation testing. By allowing for rapid and directed therapy of bleeding patients, these bundles can help reduce perioperative blood loss and transfusions, and in that way reduce the risk of AKI.75 The effectiveness of these bundles in everyday clinical practice, however, needs to be verified.

Our group has proposed another experimental option that can reduce perioperative transfusions, which is to identify
and treat anaemic patients with prophylactic transfusions 1–2 days before surgery.\textsuperscript{111} Our hypothesis is that prophylactic transfusions can reduce the risk of AKI by reducing the severity of perioperative anaemia, reducing the need for perioperative transfusions, allowing time for the transfused blood to recover from the deleterious changes that they undergo during storage, and allowing time for the kidneys to recuperate from the harmful effects of transfused blood before they are exposed to other stressors that occur during cardiac surgery with CPB.\textsuperscript{110, 111} Clearly, however, this option will only apply to a minority of cardiac surgical patients, and its safety and efficacy needs to be assessed by adequately powered randomized clinical trials.\textsuperscript{111, 112}

Another strategy for reducing transfusion-related AKI is to improve the quality of the transfused blood or to blunt its harmful effects. One potentially promising option that might reduce the harms of transfusion is washing of haptoglobin to scavenge the free haemoglobin that could be responsible for transfusion-related AKI after cardiac surgery with CPB.\textsuperscript{87} The safety and efficacy of these interventions need to be assessed in future trials.

**Declaration of interest**

None declared.

**Funding**

The author’s research is funded in part by the Department of Anesthesia and Pain Management, Toronto General Hospital, University Health Network, University of Toronto, Toronto, Ontario, Canada; and a Merit Award from the Department of Anesthesia, University of Toronto, Toronto, Ontario, Canada.

**References**


4 Ricci Z, Cruz DN, Ronco C. Classification and staging of acute kidney injury: beyond the RIFLE and AKIN criteria. *Nat Rev Nephrol* 2011; 7: 201–8


Lombardi R, Ferreiro A. Risk factors profile for acute kidney injury after cardiac surgery is different according to the level of baseline renal function. *Ren Fail* 2008; 30: 155–60


Nielsen DV, Hjortdal V, Larsson H, Johnsen SP, Jakobsen CJ. Perioperative aminoglycoside treatment is associated with a higher incidence of postoperative dialysis in adult cardiac surgery patients. *J Thorac Cardiovasc Surg* 2011; 142: 656–61


104 Ozment CP, Turi JL. Iron overload following red blood cell transfusion and its impact on disease severity. Biochim Biophys Acta 2009; 1790: 694–701
115 Forget P, Lois F, De Kock M. Goal-directed fluid management based on the pulse oximeter-derived pleth variability index reduces lactate levels and improves fluid management. Anesth Analg 2010; 111: 910–4