Acute kidney injury after cardiac surgery: a preventable event?

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Received: 6 June 2017 / Accepted: 6 July 2017 / Published online: 19 July 2017
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Cardiovascular surgery (CVS) is one of the major causes of acute kidney injury (AKI). A recently published single-center retrospective study conducted in 767 adult critically ill patients, mainly cardiac and postoperative patients, showed that the incidence of AKI was high in this cohort (51.9%) and that the mortality rate increased with progression of the AKI stage [1]. A similar high incidence of AKI and its association with poor outcomes have also been reported in post-CVS patients in several studies [2–5].

In the past decade, many studies have been carried out with the aim to identify a sensitive biomarker for the early diagnosis of AKI in patients who had undergone CVS. To date, several useful biomarkers have been reported, including urine neutrophil gelatinase-associated lipocalin (NGAL), kidney injury marker 1, *N*-acetyl- β -D-glucosaminidase (NAG), cystatin C, liver-type fatty acid-binding protein (L-FABP) and interleukin-18 [6, 7]. Among these biomarkers, NGAL, NAG, cystatin C and L-FABP are covered by Japan's National Health Insurance system. Early identification of AKI using such biomarkers may improve the outcome by widening the therapeutic time window in post-CVS patients. Thus, it is time to ask whether the development of AKI in patients who have undergone CVS is a preventable event or not.

Multiple pathophysiologies are considered to be involved in the development of AKI in patients post-CVS. Numerous risk factors have been reported, including advanced age, anemia, diabetes, chronic lung disease, chronic heart failure, chronic renal dysfunction, administration

of nephrotoxic agents, hypoperfusion, embolization and increased aortic clamp time [8]. Some of the risk factors can be treated or avoided. For example, it may be crucial to avoid ischemic damage during renal hypoperfusion due to perioperative low cardiac output syndrome and cardiogenic shock [8, 9]. A systematic review by Brienza et al. showed that postoperative AKI was significantly reduced using perioperative hemodynamic optimization [10]. However, it is not easy to achieve perioperative hemodynamic optimization in CVS patients, especially in those with low output syndrome. In this context, recent studies have provided useful information for determining the optimal inotrope in CVS patients [11–13]. Levosimendan is a calcium sensitizer that binds to troponin-C, thereby sensitizing the myocardial filaments to calcium. Although several meta-analyses of small trials have suggested that levosimendan improves the survival rates among patients undergoing cardiac surgery [11, 13, 14], a recently published randomized controlled trial has shown that levosimendan does not reduce the incidence of AKI and other clinical outcomes, including 30-day mortality and duration of mechanical ventilation and hospital stay, respectively [15]. In this regard, the optimal inotrope to improve outcomes, including the prevention of AKI, remains unidentified.

Pharmacologic renal protection is another important issue in patients undergoing CVS. Various agents, including dopamine, fenoldopam, statins, sodium bicarbonate, mannitol, *N*-acetylcysteine, atrial natriuretic peptide and free hemoglobin scavengers, have been proposed as agents providing pharmacologic renal protection [16–19]. However, the results of studies in which the impact of such pharmacologic renal protection was assessed have not been consistent.

Studies have been carried out recently to assess the risks and benefits of various interventions to prevent AKI in

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patients who have undergone CVS [16–19], but as yet no definitive strategy to prevent AKI has been identified. Considering the multiple pathophysiologies of AKI post-CVS, it is possible that the prevention of AKI in this context can not be achieved through a single intervention [20]. It may therefore be better to consider combination interventions in future trials.

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