Acute kidney injury on normally functioning kidneys and long-term mortality after coronary bypass surgery

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Acute renal failure (ARF) can occur in up to 50% of patients after cardiac surgery, depending on the definition of ARF, which is based on changes in plasma creatinine. Dialysis-requiring ARF affects 1% of patients after cardiac surgery [1]. Therefore, most of the patients develop milder forms of ARF with a wide spectrum of severity. Acute kidney injury (AKI) is the new consensus term employed for ARF to highlight that the process is a continuum of kidney damage that starts well before any functional derangement in kidney excretory function is detectable by clinical standard methods, basically plasma creatinine [2]. Likewise, a consensus functional classification of AKI developed in 2004 (the RIFLE classification) categorizes patients in stages of severity that have been shown to be in stepwise direct association with morbidity and mortality [3]. It has been known for a long time that the short-term mortality of critically ill patients who develop dialysis-requiring AKI is very high and averages 60–70% [1]. AKI in the context of critical illness, surgery or any acute illness is clinically attributed to reversible acute tubular necrosis, either toxic or ischemic. However, even when most of the patients (around 85%) recover renal function, AKI has important consequences.

AKI has been demonstrated to be an independent determinant of mortality in cardiac surgery patients [1]. In recent years, it has become clear that less severe and reversible AKI is also associated with mortality in several contexts. Lassnigg et al. [4] demonstrated that the 30-day mortality in cardiac surgery patients who developed a 0- to 0.5-mg/dl and >0.5-mg/dl rise in serum creatinine was 2.77- and 18.64-fold higher, respectively, than in patients without a change in serum creatinine. AKI in the context of critical illness, surgery or any acute illness is clinically attributed to reversible acute tubular necrosis, either toxic or ischemic. However, even when most of the patients (around 85%) recover renal function, AKI has important consequences.

In this issue, Chalmers et al. [6] have evaluated the effects of AKI on long-term mortality in 4029 patients with normal preoperative plasma creatinine who underwent cardiac bypass surgery. The authors show that the development of AKI adversely affects mortality after a mean follow-up of 3.7 years. Although plasma creatinine is commonly used for evaluating renal function and estimating the risk of AKI in cardiothoracic surgery, it is known that this parameter is a poor estimate of kidney function. Dependence of this parameter on age, race and body mass index among others, has prompted the search for more accurate means of measuring renal function. In the past several years, the estimation of the glomerular filtration rate (GFR) by means of formulae based on serum creatinine that take into account confounding variables, the MDRD formula being the most used, has become widespread [7]. In the study by Chalmers et al., only about half of the patients had normal (>90 ml/min) estimated GFR by the MDRD formula, highlighting the limitation of using isolated plasma creatinine as a marker of GFR. AKI developed in 3.9% of the total sample and in 3% of the patients with normal estimated GFR, with a mean peak plasma creatinine of 222 μmol/l (2.5 mg/dl). This incidence is significantly lower than that observed in other recent studies, e.g. 6.9% in a study that included patients with chronic kidney disease (CKD) [8]. It is known that the presence of CKD is one of the major risk factors for developing AKI in cardiothoracic surgery. The higher incidence of AKI in the total sample unMASKS the higher risk in the patients with low GFR despite normal creatinine. The authors analyse the effects of AKI on mortality in the patients with normal preoperative estimated GFR, and observe that the adverse effects remain significant, with diabetes, female sex and EuroSCORE also influencing mortality in the Cox analysis.

This study highlights the important long-term consequences of AKI in a homogeneous sample of coronary bypass surgery patients with normal preoperative renal function. As the authors state, there is some limitation in this definition because proteinuria was not evaluated in these patients. With 36.7% patients with diabetes mellitus and 60% of the sample being hypertensive, it is reasonable to assume that a significant proportion of patients might have had some degree of proteinuria preoperatively. Thus, normal functioning kidneys, based on creatinine or estimated GFR does not mean ‘normal kidneys’, since it is well established that in hypertensive and diabetic patients, as well as in most renal disease, kidney damage appears well before a reduction of GFR is clinically detectable. The presence of microalbuminuria (i.e. albuminuria in the range of 30–300 mg/day, below the detection limits of traditional dipstick methods) is considered as a marker of both renal and cardiovascular risk, mostly in patients with diabetes and hypertension [7]. It has also been shown that the presence of microalbuminuria is a risk
factor for AKI, independent of the GFR [9]. Therefore, the presence of kidney damage could confer both an increased risk of AKI and also of long-term mortality. This may reflect the issue that acute illness affecting an increasing number of older patients with comorbid conditions, may include subclinical CKD, which all predispose to the long-term consequences of AKI. It would be important to distinguish total mortality from cardiovascular mortality, as well as to extensively characterize comorbidities and postoperative complications in these kinds of studies.

The effects of AKI in cardiothoracic surgery patients on long-term mortality has been evaluated previously in several studies [1, 8, 10], but mostly in patients with severe AKI requiring dialysis or in patients with previous evident CKD. More recent studies have evaluated this issue in patients who were considered not having CKD by history or by ICD-9-CM registered codes and show similar results, with even a reversible episode of AKI increasing the 10-year mortality, proportionally to the severity of AKI categorized by the RIFLE criteria, as compared with patients with no AKI [10]. However, in that study, though the patients were considered not to have CKD by history, the mean estimated GFR was <90 ml/min in all groups of patients, despite a normal serum creatinine (mean 0.9 mg/dl).

In summary, the study of Chalmers et al. clearly shows that in patients with normal preoperative renal function, as measured by creatinine or by estimated GFR, a single episode of AKI not requiring dialysis is associated with an increased mortality after a mean follow-up of 3.7 years. Therefore, AKI is not trivial in this kind of patient, and efforts at detecting the risk factors for developing AKI besides implementation of the clinical management of kidney protection are mandatory.

REFERENCES