EDITORIAL COMMENT

Anaemia and acute kidney injury: the tip of the iceberg?

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ABSTRACT

Acute kidney injury (AKI) is a common disorder that complicates the hospital course of many patients. AKI is linked with an independent risk of death, hospital length of stay and chronic kidney disease (CKD). Several preoperative predictors are found to be associated with AKI after surgery independent of its origin (cardiac versus non-cardiac). Among these, anaemia has been widely recognized and studied. Anaemia is more common within the surgical population for various reasons (iron deficiency, blood loss, anaemia of chronic disease such as inflammatory state, malignancy or CKD). Both pre- and postoperative anaemia have a deleterious impact on different clinical outcomes including AKI. In this issue, Nishimoto et al. investigated whether AKI could be a risk factor for anaemia (and not the opposite) and whether anaemia could be an independent mediator of mortality after AKI.

Keywords: AKI, anaemia, CKD, epidemiology, survival analysis

INTRODUCTION

Acute kidney injury (AKI) is a critical condition in modern medicine that complicates the hospital course of many patients [1]. Postoperative AKI is a leading cause of morbidity and mortality in patients undergoing surgery [2, 3]. It is also linked with the duration of hospital stay and healthcare costs. The incidence varies between 1 and 36% depending on the type of surgery and the definition of renal failure, but tends to be lower (10%) according to the Risk, Injury, Failure, Loss, End-stage renal disease criteria [3].

Several studies have highlighted the importance of early recognition of AKI by a nephrologist for at least two reasons. First, the delayed nephrology consultation can be associated with increased intensive care unit (ICU) mortality [4]. Second, multiple cohort studies have revealed AKI is an independent risk factor for chronic kidney disease (CKD) progression [5, 6].

AKI: PREDICTING FACTORS AND LONG-TERM OUTCOME

AKI is consistently associated with increased short- and long-term mortality [1]. The association between AKI and mortality can also be partly explained by confounding factors, as many factors are associated with both AKI and mortality [e.g. CKD, diabetes, heart failure (HF), etc.] [1]. In this context, AKI can be viewed as both a risk factor for mortality and a surrogate marker for global frailty.
AKI following major surgery is also associated with increased short- and long-term mortality. [2]. Importantly, most studies have focused on cardiac surgery, where AKI occurs frequently—up to 42% [7–9]. Factors associated with AKI occurrence in this context are age, pre-existing CKD, diabetes or HF, combined surgeries, high cardiopulmonary bypass time, low cardiac output and central venous pressure [10]. Factors underlying this increase in mortality associated with AKI are unclear, but in most severe cases of AKI, fluid overload, cardiorenal syndrome and increased length of ICU stay may play a role. Whether early initiation of renal replacement therapy could improve clinical outcomes is still controversial [11, 12]. Early detection of AKI (i.e. before serum creatinine increases) using new biomarkers may be a promising approach, but their use in clinical practice is currently limited, mainly because no therapeutic strategy to prevent AKI occurrence based on biomarkers has been validated [9].

In the context of major non-cardiac surgery, data are lacking, but the same association between AKI and mortality as in cardiac surgery has been described [13]. Interestingly, serum creatinine decreased after surgery, which could reflect significant protein–energy malnutrition, leading to an underestimation of AKI severity and an overestimation of AKI recovery.

ANAEMIA AND AKI: A STRANGE RELATIONSHIP

Anaemia is more common within the surgical population for various reasons (iron deficiency, blood loss, anaemia of chronic disease such as inflammatory state, malignancy or CKD). Most studies have focused on the impact of preoperative anaemia and clinical outcomes, but with inconsistent results [14–16]. It has been questioned whether anaemia was more an independent marker of the severity of comorbid disease or a risk factor for prognosis?

A recent meta-analysis by Fowler et al. [14] showed that perioperative anaemia was associated with increased AKI, stroke, infection and 30-day mortality. Most of the studies included (14 of 24) were non-cardiac surgery. However, these results should be interpreted with caution due to the high levels of heterogeneity between the studies.

Postoperative anaemia and a decrease in haemoglobin levels (pre-haemoglobin level and post-haemoglobin level) have also been reported as predictive factors for AKI and in-hospital mortality in cardiac surgery by other groups [15, 16].

Data regarding the association between anaemia and long-term outcomes such as renal recovery or mortality after AKI are limited and the results are disparate [17, 18].

Collectively these studies emphasize the deleterious impact of anaemia after surgery in different clinical outcomes including AKI. Anaemia has recently been integrated into a simple prediction tool [Simple Postoperative AKI Risk (SPARK)] to estimate the risk of AKI [19].

HOW DO THE FINDINGS BY NISHIMOTO ET AL. CHANGE OUR CURRENT UNDERSTANDING/PRACTICE?

In this issue of Clinical Kidney Journal, Nishimoto et al. [20] investigated whether AKI and its interstitial damage could predict anaemia (and not the opposite) and whether anaemia could be an independent mediator of mortality after AKI. They tested their hypothesis using the NARA-AKI study cohort, a single-centre retrospective study that included in the final analysis 6692 patients who underwent non-cardiac surgery.

They showed that AKI was an independent predictor of anaemia during the first year (at 3, 6 and 12 months) following surgery. The slopes of haematocrit levels from baseline to 3, 6 and 12 months postoperatively were also greater among patients with AKI [−0.26 %/month (−0.49 to −0.04), −0.23 (−0.35 to −0.10) and −0.08 (−0.13 to −0.02), respectively].

The rate of death events was 3.97/100 years during the follow-up after a median follow-up of 4.2 years. They confirmed that AKI was a strong predictor of all-cause mortality [hazard ratio 1.54 (95% confidence interval 1.12–2.1)], but more importantly they showed that the haematocrit level at 3 months after surgery was also an independent predictor of mortality. This association between haematocrit at 3 months and mortality was similar even after further adjustment for potential confounders such as C-reactive protein, albumin or surgery for malignancy, which represented the main cause of death in the cohort.

Unfortunately the specific cause of anaemia could not be investigated because information regarding iron levels, medications (chemotherapy, angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers) and anaemia management (blood transfusion) were not available. The authors suggested that AKI-induced damage to the renal interstitium might lead to impaired erythropoietin production and subsequent anaemia, but this hypothesis (not tested here) is probably the tip of the iceberg.

Finally, because cancer was frequent in this population, we might also wonder if anaemia reflected current guidelines in order to avoid adverse events of specific treatments (e.g. erythropoietin-stimulating agents) [21]. Whether the correction of anaemia after AKI improves clinical outcomes remains elusive.

CONCLUSIONS

Nishimoto et al. highlight for the first time in a large cohort the negative impact of anaemia during long-term follow-up and address new perspectives on the management of anaemia following AKI. Their results emphasize the importance of detecting and correcting anaemia in this cohort. It is mandatory to first focus on the causes of anaemia and second to define specific groups at risk. Future studies should determine whether correction of anaemia following AKI improves mortality.

CONFLICT OF INTEREST STATEMENT

None declared.

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