



AKI: long-term impact on mortality and renal function



Acute kidney injury (AKI) is defined as an abrupt loss in renal function and may be caused by a wide variety of clinical conditions. AKI is a frequent complication of hospitalisation and is associated with an increased risk of chronic kidney disease (CKD), end-stage renal disease (ESRD), and mortality.

Based on more recent studies, AKI is also known to be a risk factor for other adverse outcomes, including stroke, cardiovascular disease (CVD), sepsis, malignancy, bone fracture, and upper gastrointestinal haemorrhage. The results of these studies suggest that the risk of mortality and renal dysfunction extends far beyond hospital discharge.

This review article notes, however, that it is difficult to determine whether there is indeed a causal relationship between AKI and long-term adverse outcomes or whether AKI is simply an indicator of poor clinical condition. This is because most of the published literature consists of retrospective cohort studies that were not designed to demonstrate a causal relationship and therefore carry a substantial risk for selection bias, information bias, and residual confounding.

AKI and long-term mortality

Although most evidence has been obtained through retrospective research, the results of the numerous well-designed large studies indicate that a causal relationship between AKI and a worsened long-term prognosis is highly likely. The largest study, by Lafrance et al., demonstrated in a retrospective analysis among U.S. veterans ($n = 864,933$) that patients with an episode of AKI not requiring renal replacement therapy (RRT) had an adjusted hazard ratio (HR) of 1.41 for long-term mortality (95% CI = 1.39-1.43).

Meanwhile, similar results were shown for subgroup analyses restricted to patients who survived at least 3 or 6 months after discharge; even more interestingly, the negative effect of AKI persisted in patients who showed only short-term impairment in renal function during hospitalisation. These results demonstrate that even a short transient deterioration in renal function is associated with a poorer outcome.

In addition to the severity of AKI, the risk of long-term mortality is strongly determined by other clinical and demographic patient characteristics, including age, baseline renal function, malignancy, severe sepsis and septic shock, recurrent episodes of AKI, and particularly, renal recovery.

AKI and long-term risk for CKD and ESRD

While the association between AKI and long-term mortality seems to be based on a complex interplay between AKI and many other patient-specific factors, this interplay is even more complex for the association between AKI and long-term deterioration in renal function. Many recent studies have described the association between AKI and progression to CKD or even ESRD.

In 2012, Coca et al. demonstrated, in a meta-analysis including 13 studies with a maximum follow-up of 75 months, a strong association between AKI and the development of CKD as well as ESRD, with adjusted HRs of 8.82 (95% CI = 3.05–25.48) and 3.10 (95% CI = 1.91–5.03), respectively. Moreover, a large study by Lo et al. that included more than 500,000 patients with a baseline estimated glomerular filtration rate (eGFR) of > 45 ml/min/1.73 m² showed that AKI requiring RRT was strongly associated with the development of stage 4 or 5 CKD, with an adjusted HR of 28.1 (95% CI = 21.1–37.6).

Conclusions

In summary, those with the highest risk of progression towards CKD or ESRD after an episode of AKI are those who already have an increased risk for CKD progression independent of an episode of AKI. However, the magnitude of this risk depends on the presence of premorbid conditions and the susceptibility to accelerated injury with impaired renal recovery.

While these findings are undoubtedly of great importance, they still have limited significance for clinical practice, as effective therapeutic interventions are not yet available, according to the review article. Future research therefore should focus on the prevention of AKI, the identification of therapeutic targets, and the provision of adequate follow-up and treatment to preserve the renal function of patients who survive an episode of AKI.

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Published on : Wed, 30 Jan 2019