Saudi J Kidney Dis Transpl 2018;29(3):513-517

Saudi Journal of Kidney Diseases and Transplantation

Review Article

Prevention of Severe Acute Kidney Injury by Implementation of Care Bundles: Some Progress but Still a Lot of Work Ahead

Helmut Schiffl

Department of Internal Medicine IV, University Hospital Munich, LMU Munich, Munich, Germany

ABSTRACT. Routine health data, dating from 1990 to 2015, show a dramatic rise in the incidence of acute kidney injury (AKI) in the general population and an apparent increase in acute dialysis (AKI-D) prompting calls for improvement of care in AKI patients. Recent reports suggest flattening of population-based AKI occurrence rates or declining frequencies of AKI or AKI-D in subgroups of high-risk patients with known onset of AKI. These temporal changes in AKI occurrence relate at least in part to the widespread implementation of AKI prevention care bundles. Nevertheless, AKI frequencies and AKI morbidity and mortality remain high. Incorporation of real-time electronic alerts and the use of novel biomarkers in high-risk patients or patients with known onset of AKI may result in further reductions of AKI incidences by early recognition of AKI and by timely conservative management of AKI. There is an urgent need for further treatment options of established AKI.

Introduction

Hospital-acquired acute kidney injury (AKI) is a multifaceted syndrome defined as an abrupt (within 48 h) reduction of glomerular filtration rate. Current AKI diagnostic systems are based on the detection of elevated serum creatinine levels, a reduction in urine output, the need for renal replacement therapy (RRT), or a combination of these factors. Clinically, this renal syndrome has multiple etiologies and risk factors. AKI encompasses a broad spectrum of manifestations ranging from tubular stress (subclinical AKI) to oligoanuric renal failure (KDIGO or AKIN Stage 3; RIFLE class F) and infers a significant risk for short- and long-term mortality in those affected by it.

Hospital-acquired AKI occurs mostly in at-risk populations of patients secondary to a combination of hypovolemia/hypotension, sepsis, and nephrotoxins, particularly in elderly and critically ill patients. Using current diagnostic and grading criteria, AKI occurs in more than half of the patients treated in the Intensive Care Unit (ICU).[1] RRT is applied to 10%–15% of critically ill patients with AKI and its utilization is still on the rise.[2]

The prognosis remains poor for critically ill patients with severe forms of AKI. AKI adds significantly to the excess in-hospital mortality of ICU patients requiring RRT irrespective of

Correspondence to:

Prof. Dr. Helmut Schiffl,
Department of Internal Medicine IV,
University Hospital Munich,
LMU Munich, Munich, Germany.
E-mail: h-schiffl@t-online.de

its cause and duration[3] and increases the risk for *de novo* chronic CKD, progression of CKD to end-stage renal disease, and cardiovascular events. Patients surviving an episode of dialysis-requiring AKI retain diminished quality of life, and their long-term mortality is excessively high.[4]

At present, there is no proven pharmacologic therapy to reverse established AKI or to hasten recovery of renal function from AKI. Critical care is of paramount importance for the treatment of the underlying acute illness. Supportive care (prevention and management) of AKI encompasses the identification of high-risk individuals, the early recognition of AKI, preventive interventions (optimization of fluid and hemodynamic status and avoidance of further nephrotoxic insults), adequate renal replacement therapy (RRT), if necessary, and post discharge care of survivors.[5]

Whether or not advances in prevention and management of AKI have translated into temporal changes in the incidence of this renal syndrome remains unclear. I performed a systematic review for relevant articles that described the trends in AKI incidence over time within the past two decades. I used PubMed as database.

Temporal Changes in the Overall Incidence of Acute Kidney Injury in cCritically Ill Patients During the Past Two Decades

The inexorable rise of hospital-acquired acute kidney injury

AKI pervades health-care systems with an increasing use of RRT worldwide. Numerous database studies have exploited International Classification of Diseases (ICD) coding of hospital episodes or creatinine change criteria to quantify the incidence of AKI across a range of clinical settings. Over a combined period, spanning 25 years (up to 2014), they consistently reported a dramatic rise in rates of nondialysis requiring AKI and in parallel, of dialysis-requiring AKI (AKI-D).[6,7] Admittedly, temporal comparisons of AKI incidence may reflect changes in coding practice (code creeping), changing diagnostic criteria or increased awareness of AKI rather than a true change in disease incidence. However, it seems unlikely that an up to 10-fold increase in AKI incidence is attributable purely to changes in ICD coding. Furthermore, KDIGO-based AKI criteria provided a much higher estimated incidence of AKI than code-classified AKI.[7] Finally, the comparable rise of AKI-D (which is unlikely to be inflated by coding) across industrialized countries (America, Europe, and Australia) and health-care settings (internal medicine, surgery, obstetrics, and neurology) was striking and suggested that true increases in AKI occurred.[8] This growth of AKI over the past two decades may reflect changes in the characteristics of hospitalized patients (aging population and greater burden of comorbid diseases), changes in the severity of the precipitating illness (sepsis and cardiovascular diseases), and the expanding administration of contrast media or exposure to nephrotoxins.[6,9,10]

Bending the acute kidney injury growth curve: recent data

In contrast to previous data suggesting rapid growth in the population incidence of AKI, Kashani et al[11] found a relatively stable population-based incidence of AKI during their nine-year study.

The authors used a previously validated electronic AKI surveillance tool ("AKI Sniffer") to detect AKI in real-time utilizing both serum creatinine and urine output criteria. The unadjusted incidence rates were 186 (ICU) and 287 (general ward) per 100,000 person-years in 2006 and reached 179 and 317 per 100,000 person-years in 2014, respectively. Following adjustment for age and sex, there was no significant rise in the annual AKI incidence rates for both patient groups. Similar results were obtained when the ICD-9 codes or administrative data for AKI-D were utilized.

US Renal Data System 2016 Data report

Using representative administrative data sets (diagnostic codes) to identify hospitalized patients with AKI or AKI requiring dialysis, the actual annual US renal data report revealed: (a) that the percentage of patients experiencing

hospitalizations complicated by AKI increased from 2004 to 2010/11, and (b) that the reported rates of AKI for the following years seemed to have plateaued or even slightly decreased.[12] Within the well-known limitations of ICD-diagnosed AKI incidence trends, the actual data report suggested that the percentage of patients with severe AKI requiring RRT showed a continuous decline from 2004 to 2016 in spite of the increased or flattened overall incidence of hospital-acquired AKI.

Changes in the incidence of acute kidney injury due to renal insults at a known time

Patient subpopulations with myocardial infarction, postoperative AKI, or contrast media-induced nephropathy deserve special attention with regard to their trends in AKI incidence.

In a large US National study, the crude AKI incidence in 31,532 patients hospitalized with acute myocardial infarction (AMI) declined significantly from 26.6% in 2000 to 19.7% in 2008 despite an aging population and the rising prevalence of AKI risk factors. When adjusted for trends in potential confounders such as practice pattern changes over time, the trend of decreasing AKI rates persisted (4.4% decline per year). Using the AKIN criteria for the definition of AKI, the authors found a similar 5.2% decline in severe AKI per year.[13]

A large multicenter ICU adult database, the ANZICS study, corroborated the epidemic of AKI in critically ill patients. The authors noted that the overall AKI incidence in Australia/New Zealand increased almost 3% annually from 1996 to 2005. However, they found an apparent decline of AKI incidence in certain subgroups of ICU patients such as hematological malignancies, trauma, and cardiovascular surgery. Since the ANZICS definition of AKI remained constant over time, their results were less likely to be affected by changes in coding practices.[14] Possible explanations for this finding could be improved care in specialized trauma centers, advancement of prehospital care, and earlier identification of patients at high-risk for AKI.

To examine the temporal trends of AKI and AKI-D in patients over 75 years with AMI undergoing early percutaneous coronary intervention, Khera et al[15] analyzed the Nationwide Inpatient Sample Database from 2002 to 2010. From 2002 to 2010, the incidence of AKI increased from 5.6% to 14.2%, but there was a decrease in AKI-D. The authors concluded that this decrease in AKI requiring dialysis potentially reflects increased health-care provider awareness resulting in early recognition and implementation of renal-protective strategies.

A recent Mayo Clinic study examined the AKI occurrence in 452 octogenarians following open-heart valve replacement surgery in two periods (2002/03 vs. 2011/13) over the past 15 years. The postoperative occurrence of AKI in the contemporary cohort was lower than in the past cohort. The contemporary cohort had fewer modifiable perioperative AKI risk factors (such as surgical duration, cross-clamp time, blood transfusion, and large-volume intravenous fluids).[16]

The five R approach to prevention and management of AKI is critical for success. The onset of AKI is insidious and often goes unrecognized, allowing deterioration of excretory renal function that can result in life-threatening complications. Acutely ill patients, patients undergoing major surgery, and elderly people are particularly endangered, especially in the presence of additional comorbidities. Currently, identifying relevant risk factors and undertaking appropriate blood biochemistry and urine output monitoring are key factors to recognize those at risk and to prevent the onset of AKI or manage deterioration of renal function.

In the five R approach[17] – risk assessment, recognition, response, renal support, and rehabilitation – the first three Rs are useful for prevention.

Present diagnostic and therapeutic tools of AKI are suboptimal. Late recognition of AKI is likely to lead to delayed interventions and management with increased morbidity and mortality.

The AKI National Confidential Enquiry into Patient Outcomes and Deaths found that only 50% of AKI care was considered good. There

was poor assessment of risk factors for AKI, both in the assessment of established AKI and those who subsequently developed it. Failures of care included the noninstitution of basic measures such as administration of supplemental fluids or stopping nephrotoxic drugs and unacceptable delay in recognizing postadmission AKI in 43% of patients. A fifth of postadmission AKI was both predictable and avoidable in the view of the advisors. Complications of AKI were missed in 13% of cases, avoidable in 17%, and managed badly in 22% of cases.[18]

Electronic alerts and novel biomarkers for the early recognition of acute kidney injury

Identifying relevant risk factors and monitoring appropriate blood biochemistry and urine output in acutely ill patients are key factors to recognize those at risk of, or with AKI and to prevent onset or deterioration of renal injury. The use of electronic alerts, for example, when serum creatinine values rise, for the identification of patients at high risk and for drug dose adaptations may have the potential to improve AKI care and outcomes if these warning systems are coupled to a specific course of action and awareness campaign in the framework of a care bundle. A multifaceted quality improvement program utilizing an electronic alert system saw significant improvements in AKI care regarding the detection of AKI (improvement from 53% to 100%), fluid assessment (up to 90%), drug review (up to 95%), and reduced AKI incidence (from 9% to 6.5% of all hospitalizations), AKI days, and AKI-related deaths.[19]

New AKI biomarkers, along with clinical judgement, may be useful tools to assess the likelihood that a patient at high risk will develop AKI in the next 24 h. The PrevAKI randomized controlled trial found that the implementation of the KDIGO guidelines combined with standard care reduced both the frequency and severity of AKI after cardiac surgery in high-risk patients identified by elevated urinary cell cycle arrest biomarker levels (TIMP-2; IGFBP 7).[20]

Conclusions

Previous epidemiologic investigations have pointed to an alarming rise in the growth of AKI and AKI-D rates during the past two decades, prompting calls for improvements of its recognition and early intervention. However, recent data indicate slowing to stabilization of AKI and AKI-D incidence in the general population or declining AKI rates in subgroups of patients with known onset of AKI. More studies are needed to definitively confirm these trends. Regardless of the potential reasons for temporal changes of AKI incidence, one realistic hypothesis is that implementation of AKI prevention bundles may become more commonplace. The impact of e-alerts or AKI biomarkers on AKI care procedures/outcome in patients at high risk of AKI should be further examined. Finally, we must acknowledge that, although "best practice" prevention bundles may reduce AKI incidence somewhat, the incidence of AKI remains high in the most vulnerable patients. We must remind ourselves that only 20% of AKI cases are predictable and avoidable. There is still the unanswered dire need for proven pharmacologic therapeutics for established AKI.

Conflict of interest: None declared.

Date of manuscript receipt: *4 December 2017.*
Date of final acceptance: *8 January 2018.*

References

1. Hoste EA, Bagshaw SM, Bellomo R, et al. Epidemiology of acute kidney injury in critically ill patients: The multinational AKI-EPI study. Intensive Care Med 2015;41:1411-23.
2. Bellomo R, Ronco C, Mehta RL, et al. Acute kidney injury in the ICU: From injury to recovery: Reports from the 5th Paris International Conference. Ann Intensive Care 2017;7:49.
3. Metnitz PG, Krenn CG, Steltzer H, et al. Effect of acute renal failure requiring renal replacement therapy on outcome in critically ill patients. Crit Care Med 2002;30:2051-8.

4. Schiffl H, Lang SM, Fischer R. Long-term outcome of survivors of ICU acute kidney injury requiring renal replacement therapy: A ten year prospective cohort study. Clin Kidney J 2012;5:297-302.
5. Vanmassenhove J, Kielstein J, Jörres A, Biesen WV. Management of patients at risk of acute kidney injury. Lancet 2017;389:2139-51.
6. Siew ED, Davenport A. The growth of acute kidney injury: A rising tide or just closer attention to detail? Kidney Int 2015;87:46-61.
7. Sawhney S, Fraser SD. Epidemiology of AKI: Utilizing large databases to determine the burden of AKI. Adv Chronic Kidney Dis 2017;24:194-204.
8. Hsu RK, McCulloch CE, Dudley RA, Lo LJ, Hsu CY. Temporal changes in incidence of dialysis-requiring AKI. J Am Soc Nephrol 2013;24:37-42.
9. Brown JR, Rezaee ME, Marshall EJ, Matheny ME. Hospital mortality in the United States following acute kidney injury. Biomed Res Int 2016;2016:4278579.
10. Case J, Khan S, Khalid R, Khan A. Epidemiology of acute kidney injury in the Intensive Care Unit. Crit Care Res Pract 2013; 2013:479730.
11. Kashani K, Shao M, Li G, et al. No increase in the incidence of acute kidney injury in a population-based annual temporal trends epidemiology study. Kidney Int 2017;92:721-8.
12. Saran R, Robinson B, Abbott KC, et al. US renal data system 2016 annual data report: Epidemiology of kidney disease in the United States. Am J Kidney Dis 2017;69:A7-8.
13. Amin AP, Salisbury AC, McCullough PA, et al. Trends in the incidence of acute kidney injury in patients hospitalized with acute myocardial infarction. Arch Intern Med 2012;172:246-53.
14. Bagshaw SM, George C, Bellomo R; ANZICS Database Management Committee. Changes in the incidence and outcome for early acute kidney injury in a cohort of Australian Intensive Care Units. Crit Care 2007;11:R68.
15. Khera S, Kolte D, Aronow WS, et al. Trends in acute kidney injury and outcomes after early percutaneous coronary intervention in patients ≥75 years of age with acute myocardial infarction. Am J Cardiol 2013;112:1279-86.
16. Thongprayoon C, Cheungpasitporn W, Lin J, Mao MA, Qian Q. Acute kidney injury in octogenarians after heart valve replacement surgery: A study of two periods over the last decade. Clin Kidney J 2017;10:648-54.
17. Lewington AJ, Cerdá J, Mehta RL. Raising awareness of acute kidney injury: A global perspective of a silent killer. Kidney Int 2013;84:457-67.
18. Anathhanam S, Lewington AJ. Acute kidney injury. J R Coll Physicians Edinb 2013;43:323-8.
19. Ebah L, Hanumapura P, Waring D, et al. A multifaceted quality improvement programme to improve acute kidney injury care and outcomes in a large teaching hospital. BMJ Qual Improv Rep 2017;6. pii: u219176.w7476.
20. Meersch M, Schmidt C, Hoffmeier A, et al. Prevention of cardiac surgery-associated AKI by implementing the KDIGO guidelines in high risk patients identified by biomarkers: The PrevAKI randomized controlled trial. Intensive Care Med 2017;43:1551-61.