Acute Kidney Injury Risk Assessment and the Nephrology Rapid Response Team

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Key Words

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Abstract

Acute kidney Injury (AKI) is a serious medical condition affecting more than 10 million people around the world annually and resulting in poor outcomes. It has been suggested that late recognition of the syndrome may lead to delayed interventions with increased morbidity and mortality. Early diagnosis and timely therapeutic strategies may be the cornerstone of future improvement in outcomes. The purpose of this article is to provide a practical model to identify patients at high risk for AKI in different environments, with the goal to prevent AKI. We describe the AKI Risk Assessment (ARA) as a proposed algorithm that systematically evaluates the patient in high-risk situations of AKI in a simple way no matter where the patient is located, and allows different medical specialists to approach patients as a team with a nephrologist to improve outcomes. The goal of the nephrology rapid response team (NRRT) is to prevent AKI or start treatment if AKI is already diagnosed as a consequence of progressive events that can lead to progressive deterioration of kidney tissues and eventual decline in renal function and to ensure appropriate follow-up of patients at risk for progressive chronic kidney disease after the episode of AKI.

Prevention is the key to avoid mortality and morbidity associated with AKI. Integration of these assessment tools in a global methodology that includes a multi-disciplinary team (NRRT) is critical to success.

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Introduction

Acute kidney Injury (AKI) is a serious medical condition estimated to affect more than 10 million people around the world annually, resulting in a 1.7- to 6.9-fold increased risk of hospital mortality [1]. To put this in perspective, the incidence of AKI is now greater than that for myocardial infarction.

The etiologies of AKI vary by country and economic status. Some causes are preventable by interventions at the individual, community, regional and in-hospital levels [2]. The issue of preventability is critical as the costs associated with AKI are high, both in the short and long term [3].

Recent data suggests that AKI has consequences not only during the acute phase, but also in subsequent phases, leading to progressive chronic kidney disease (CKD) and end-stage kidney disease requiring dialysis or transplantation [1, 2, 4].

The majority of AKI cases in the developing world are likely to be community acquired [5]. A third of all AKI events are already present at admission or develop 24 h after hospital admission [6]. Therefore, early recognition is mandatory. Some causes of AKI are particularly prevalent in some geographical settings, for example, cases associated with hypovolemia secondary to diarrhea are frequent in developing countries, whereas procedures like open heart surgery are a common cause in advanced care environments [7].

Mortality and morbidity remain high in AKI, suggesting that current diagnostic and therapeutic methods are suboptimal [8]. A key aspect of this is that late recognition is likely to lead to delayed interventions and management with increased morbidity and mortality [4].

As pointed out by the International Society of Nephrology (ISN) '0 by 25' initiative, in parallel with advanced care and research for AKI, additional strategies are needed to raise awareness in community healthcare settings, especially in lower-income countries and the poorest part of the world [9–11].

The 0 by 25 snapshot, published by Lancet in May 2016, proposed a global strategy to address AKI involving all levels of healthcare systems including input from primary care providers and subspecialists [9]. The paper advocates attention to a global problem and urges community-wide efforts to increase the awareness of the devastating effects of AKI and provide guidance on preventive strategies, and early recognition and management. Efforts should be focused on preventing those causes of AKI which are amenable to this, increasing awareness of the importance of serial measurements of serum creatinine in high-risk patients, and documenting urine volume in critically ill patients to achieve early diagnosis [2, 12].

The purpose of this study is to provide a practical model to identify patients at high risk for AKI in different environments with a goal to prevent AKI. It is our opinion that the scientific and medical communities should appreciate that AKI is not only a problem for nephrologists but also a concern for every medical specialist.

Back to the Basics: The Fantastic 4

AKI is defined by an abrupt decrease in kidney function that includes, but is not limited to, acute renal failure [8]. AKI is a broad clinical syndrome encompassing various etiologies, with multiple conditions coexisting in the same patient. Epidemiological evidence supports the no-

tion that even mild, reversible AKI has important clinical consequences [5]. The damage induced by subclinical or manifest episodes of AKI may, in fact, produce an irreversible loss of a variable amount of renal mass with deleterious effects on the overall renal function. This may be the case even though baseline glomerular filtration rate (GFR) appears to return to normal. However, when measured in these patients, renal reserve is impaired [13].

In the 5-R approach proposed by The ISN '0 by 25' project: risk assessment, recognition, response, renal support and rehabilitation, the first 3 Rs concern the prevention area. We strongly believe that we must focus on simplifying every step to allow primary care providers to implement these measures independent of their care environment.

The first step must be the AKI Risk Assessment (ARA). Under most circumstances, AKI is diagnosed in high-risk situations such as intensive care units as a complication of sepsis or major surgery (especially open heart surgery). Other high-risk clinical scenarios can be identified such as hemorrhage, volume depletion and acute decompensated heart failure. However, AKI may develop not only in conjunction with a given exposure (insult), but also in the presence of specific patient and organ susceptibilities that vary widely from individual to individual. [5]. No matter when or how AKI develops, the mortality increases. As an example, AKI occurs in 40–50% of patients with sepsis and increases the mortality six- to eight-fold [14, 15]. Fluid overload is a major contributor to increased risk of death; 10–20% overload can be sufficient to cause adverse clinical consequences [1, 7].

Drugs and iatrogenic interventions are important causes of AKI, with nearly 25% of cases involving at least one nephrotoxic drug [1, 9]. Together, the many millions of people exposed to infectious diseases, nephrotoxic drugs and other exposures make AKI one of the most common medical disorders in the world [9, 16]. A common cause of adverse drug events is inappropriate prescription, especially in patients with subclinical or manifest kidney insufficiency. Since the majority of drugs are excreted by the kidney, it is imperative to adjust the dose and prescription depending on the patient's GFR [1]. Drug-induced AKI is important because the offending drug can often be identified and removed or substituted for one that is non-nephrotoxic or less nephrotoxic. The nephrotoxic drugs most commonly prescribed are aminoglycosides, amphotericin, vancomycin, non-steroidal anti-inflammatory drugs, β -lactam antibiotics, sulfonamides, acyclovir, methotrexate, cisplatin, cyclosporin, tacrolimus, angiotensin-converting-enzyme inhibitors and angiotensin receptor blockers [5, 7]. Other substanc-

es include nephrotoxic agents like herbal remedies or recreational drugs [5].

We should encourage every health professional to perform the ARA no matter where the patient is located. This assessment is ideally located in the electronic medical record and accessible to all team members. The proposed algorithm is based on 4 simple steps called the 'Fantastic 4' (AKI F4; fig. 1) that systematically evaluates the patient and allows for teamwork with a nephrologist to improve outcomes.

The approach to the patient should be the following—F1: consider the 'clinical scenario' where the patient's signs and symptoms and the surrounding circumstances and risks are reviewed and considered; F2: interview the patient or his/her relatives and review the 'past history' with a goal of identifying the level of susceptibility and intensity of exposures; F3: 'physical examination' aiming at characterizing hemodynamic instability, volume depletion or fluid overload and signs/source of infection, if any; F4: analyze 'laboratory results' including possible AKI biomarkers to complete the patient risk stratification (fig. 2). The AKI F4 should trigger activation of the nephrology rapid response team (NRRT).

The patient should be stratified as low, moderate and high risk. A patient in the low-risk category should be closely observed, but would not require an active intervention (fig. 3).

In the moderate-risk patient, we suggest follow-up over the next 24 and 48 h as follows: weight at arrival, daily weights, monitoring of daily intakes and output (if the patient has a urine catheter this must be measured hourly). Over the next day or so, frequent re-assessments including laboratory work (serum creatinine and possibly other urine or serum biomarkers) and physical examinations should be done. If the patient remains stable for 48 h after the exposure, then the patient is at low risk for subsequent AKI unless another risk exposure occurs.

High- and moderate-risk patients with a positive biomarker (such as urinary tissue inhibitor of metalloproteinases-2 (TIMP-2)*insulin-like growth factor-binding protein 7 (IGFBP7) should activate NRRT consultation. CKD stage 3 and higher patients are automatically considered at high risk for the possibility of developing acute on chronic kidney injury and should also trigger NRRT activation.

Of note, other factors that modify GFR should be considered including steroids, presence of gastrointestinal blood, muscle mass, muscle injury and nutritional status [7].

This AKI F4 model is best done as part of a collaborative team effort and would utilize available local resources

Fig. 1. The composition of ARA is based on the analysis of 4 following items: actual clinical scenario, past history, physical examination and laboratory analysis.

es such as the electronic medical record to alert caregivers to the risk assessment results.

Early Detection Biomarkers and the Alert System

Kidney Disease: Improving Global Outcomes (KDIGO) criteria for the diagnosis of AKI include specific changes in serum creatinine and urine output. However, serum creatinine changes can take up to 48 h to be manifested after an injury, and accurate urine output data is hard to obtain in certain circumstances. Recently, the discovery of several AKI biomarkers, neutrophil gelatinase-associated lipocalin, cystatin C, KIM 1, TIMP-2 and IGFBP7 has provided additional tools to detect patients at high risk of AKI with the hope that this knowledge would lead to improved outcomes [7, 17]. Biomarkers, along with clinical judgment, may be useful for determining the likelihood that a patient will develop AKI in the next 24 h. However, more data is needed on the integration of biomarkers into clinical practice and how they may alter outcomes [9].

Fig. 2. The algorithm is based on 4 simple steps that systematically evaluates if patients have AKI risk. Patient with a positive item is at moderate risk, 2 or more items is at high risk.

Groups of special interest are those patients with ‘sub-clinical AKI’ where injury biomarkers are positive but there is no detectable change in serum creatinine or estimated GFR [10]. The management of these patients requires special study as the hypothesis is that these are patients at high risk for subsequent falls in GFR and should be monitored closely and that they should avoid further nephrotoxin exposure.

AKI biomarkers might be integrated into emergency room protocols much like troponin utilized for chest pain. The goal would be to identify patients at risk or with early signs of injury. The rapid and early identification of these patients would lead to avoidance of nephrotoxic exposure and involvement of the NRRT. While the integration of biomarkers may increase ‘upfront’ costs, the goal is that the avoidance of clinically evident AKI will lead to greater cost savings. However, studies must be performed to substantiate this hypothesis [9, 18].

At San Bortolo Hospital in Vicenza, we have been working on the use of biomarkers for early identification of AKI in critically ill patients and introduced them into

clinical practice as part of a protocol [18]. A positive biomarker result leads to an automated electronic alert that calls the nephrologist on duty when a patient at high risk of AKI is discovered in the emergency room using the AKI F4 algorithm. The most important feature of this alert system is that the nephrologist must compile a checklist in which all preventive-protective measures suggested by KDIGO AKI guidelines are considered and implemented, if necessary. The goal is to detect patients as early as possible to avoid complications like fluid overload and renal replacement therapy [11, 19–21].

Time for Teamwork: The NRRT

As previously proposed, we need to work in collaboration to improve outcomes. Our patients have complex medical problems, and their care spans many disciplines. We recommend a rapid response checklist when a positive biomarker-driven alarm is issued (fig. 3). We propose a NRRT that would manage these at-risk patients (fig. 4).

Fig. 3. Flowchart representing the activation of NRRT.

In some clinical scenarios, it is difficult to discern which patients will progress to clinically manifest AKI following a nephrotoxic exposure. The care of patients with AKI is very time sensitive, and the ability of NRRT to gain more time to treat these patients may allow significant improvement of the process of AKI care.

It is vital to educate clinicians about the necessity to establish risk mitigation strategies for the patient at high risk of AKI as Kellum and Murugan [1] have pointed out.

It is important to screen patients who have undergone any exposure and to continue monitoring highly susceptible, high-risk patients until the risk has subsided. Exact intervals for checking serum creatinine and for which individuals' urine output should be monitored remain matters of clinical judgment; however, as a general rule, high-risk in-patients should have urine output monitoring and serum creatinine measured at least daily if not more frequently after an exposure [5].

Lower risk patients may still be at risk for AKI, and although they are less likely to receive recommendations to

avoid unnecessary nephrotoxic drugs and contrast media [1, 22], they should be carefully monitored if an alarm has triggered the NRRT activation [23].

In case of a high-risk patient, the nephrologist must be called immediately to make all necessary suggestions in an aggressive preventive management approach. For practical reasons, we created a checklist with controls and interventions suggested by KDIGO for these patients. In all cases, the nephrology consultation ensures a precise and professional evaluation of the patient's clinical condition and a thorough analysis of the balance between kidney susceptibility and intensity of exposures [23].

Acute kidney insults should not be considered as isolated episodes but rather a consequence of progressive events that lead to progressive deterioration of kidney tissues and eventual decline in renal function [13]. Finally, the care team can ensure appropriate follow-up of patients at risk for progressive CKD after their episode of AKI.

Fig. 4. Flowchart representing the NRRT actions faced with a high-risk patient and the follow-up at discharge even if the patient presented AKI.

Conclusion

AKI has been identified as a commonly occurring independent risk factor for morbidity and mortality. Given that we have no effective therapies to treat AKI, prevention is critical to improve outcomes.

AKI biomarkers are being studied as a first-line risk assessment tool together with clinical assessment to detect patients at risk for AKI as fast as possible and to prevent further damage. Prevention is the key to avoid the heavy burden of mortality and morbidity associat-

ed with AKI [24–29]. Integration of these assessment tools in a global methodology that includes a multidisciplinary team (NRRT) is critical to success.

Disclosure Statement

Rosner M.H. and Rizo-Topete L.M. have nothing to declare.
Ronco C. Speaker honoraria from ASahi, Toray, Astute Medical, FMC, B. Braun, GE, Bellco.

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