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MEETING REPORT

Strategies to Enhance Rehabilitation After Acute Kidney Injury in the Developing World

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Acute kidney injury (AKI) is independently associated with new-onset chronic kidney disease (CKD), end-stage kidney disease, cardiovascular disease, and all-cause mortality. However, only a minority of patients receive follow-up care after an episode of AKI in the developing world, and the optimal strategies to promote rehabilitation after AKI are ill-defined. On this background, a working group of the 18th Acute Dialysis Quality Initiative applied the consensus-building process informed by a PubMed review of English-language articles to address questions related to rehabilitation after AKI. The consensus statements propose that all patients should be offered follow-up within 3 months of an AKI episode, with more intense follow-up (e.g., <1 month) considered based on patient risk factors, characteristics of the AKI event, and the degree of kidney recovery. Patients should be monitored for renal and nonrenal events post-AKI, and we suggest that the minimum level of monitoring consist of an assessment of kidney function and proteinuria within 3 months of the AKI episode. Care should be individualized for higher risk patients, particularly patients who are still dialysis dependent, to promote renal recovery. Although evidence-based treatments for survivors of AKI are lacking and some outcomes may not be modifiable, we recommend simple interventions such as lifestyle changes, medication reconciliation, blood pressure control, and education, including the documentation of AKI in the patient's medical record. In conclusion, survivors of AKI represent a high-risk population, and these consensus statements should provide clinicians with guidance on the care of patients after an episode of AKI.

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Acute kidney injury (AKI) is a common complication that affects as many as 20% of hospitalized patients in both high- and lower middle–income countries.[1,2] Most of our current efforts for patients with AKI are concentrated on the period when kidney function is worsening. If the patient survives and experiences what appears to be full or partial recovery of kidney function, the physician typically "signs off," and no routine follow-up care is arranged.

However, it has become increasingly clear that individuals who survive an episode of AKI are at persistent risk of adverse outcomes. Such complications include *de novo* or accelerated chronic kidney disease (CKD),[3,4] end-stage renal disease (ESRD),[5] hypertension,[6] and cardiovascular disease.[7,8] Although the nature of the relation (causal vs. correlative) between AKI and long-term outcomes remains a topic of debate,[9,10] there is no doubt that, for many patients, an episode of AKI heralds an ominous prognosis. AKI and CKD may best be viewed as interrelated syndromes, with AKI leading to CKD and CKD strongly predisposing to the development of AKI (Figure 1).[11] No matter the relationship, patients who survive an episode of AKI constitute a high-risk population who may benefit from more intensive post-AKI follow-up care.[12]

Despite their high-risk status, in the United States, only 2 in 5 patients will have their serum creatinine

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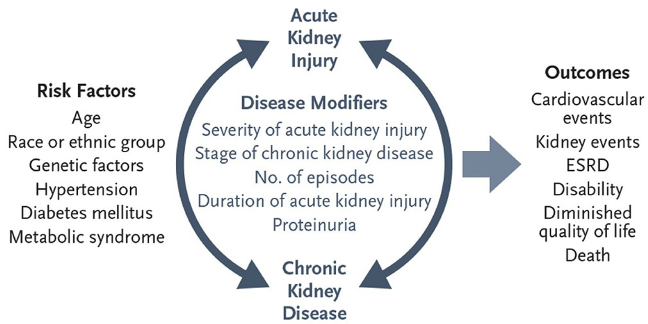

Figure 1. Acute kidney injury (AKI) and chronic kidney disease (CKD) as interrelated syndromes. AKI and CKD often form a continuum of disease as opposed to separate entities. They share common risk factors, with both AKI and CKD associated with adverse outcomes. ESRD, end-stage renal disease

checked within 30 days of an AKI episode, and fewer than 1 in 6 patients will see a nephrologist within 90 days of an AKI episode.[13,14] Even among patients hospitalized for dialysis-requiring AKI who recover sufficient kidney function to no longer require dialysis, <50% see a nephrologist within 1 year of hospital discharge.[15] Although observational studies from high-income countries suggest that patients who receive follow-up by a nephrologist after an episode of AKI have improved outcomes compared with patients who do not receive follow-up,[15,16] little is known about specific strategies to increase follow-up, monitor, and promote recovery after an AKI episode. Even less is known about how to tailor AKI follow-up programs to the sociocultural, policy, financial, and medical circumstances in lower middle–income countries.

On this background, the steering committee of the 18th Acute Dialysis Quality Initiative (ADQI) conference dedicated a work group with the task of considering elements of rehabilitation after an episode of AKI in the developing world. More specifically, the work group addressed 5 questions:

1. Which patients should be followed after an AKI episode?
2. What are the outcomes for which patients should be monitored after an AKI episode?
3. What are the components of patient-centered monitoring after an AKI episode?
4. What management strategies are recommended after an AKI episode?
5. What educational strategies are recommended after an AKI episode?

Methods

This consensus meeting followed the established ADQI process, as previously described.[17] The broad objective of ADQI is to provide expert-based statements and interpretation of current knowledge for use by clinicians according to professional judgment as well as identify evidence care gaps to establish research priorities. The 18th ADQI Consensus Conference focused on "Management of AKI in the Developing World," convening a diverse panel for a 2.5-day meeting in Hyderabad, India, from September 27 to 30, 2016. The consensus-building process was informed by pre-conference, conference, and post-conference activities. Before the conference, the work group searched PubMed for English-language articles on rehabilitation strategies after an episode of AKI. This search included both monitoring and management strategies to enhance recovery after AKI as well as the epidemiology of AKI survivors. A pre-conference series of e-mails involving work group members was used to identify the current state of knowledge and enable the formulation of key questions. At the in-person meeting, the work group developed consensus statements through a series of alternating breakout and plenary sessions. In each breakout session, the work group refined the key questions, identified the supporting evidence, and generated consensus statements. Work group members presented the results for feedback to all ADQI participants during the plenary sessions and then revised the drafts based on the plenary comments until a final version was accepted. After the conference, this summary report was generated, revised, and approved by all members of the work group.

Results

Overview of Existing Literature on Rehabilitation After AKI in the Developing World

We identified only 4 published reports of AKI follow-up programs,[12,18–21] 2 of which were from lower middle–income countries.[20,21] However, these latter experiences did not describe their patient selection strategy, follow-up care models, or patterns of care delivered to patients. Most studies on the epidemiology of AKI in the developing world also end patient follow-up within 30-days of the AKI episode.[2,22–25] Therefore, the work group based most of its recommendations on long-term AKI follow-up data from the developed world. Care was taken to adapt these consensus statements to the sociocultural, policy, financial, and medical circumstances in lower middle–income countries.

Question 1: Which patients should be followed after an AKI episode?

Consensus Statement

- *Consensus Statement 1A:* All patients should be considered for follow-up after an episode of AKI because multiple studies in the literature have demonstrated that all stages of AKI are associated with adverse outcomes.

- *Consensus Statement 1B:* The intensity of patient follow-up should be individualized based on patient risk factors, characteristics of the AKI episode, and the degree of kidney recovery (Figure 2).
- *Consensus Statement 1C:* Patients with preexisting CKD are at high risk of adverse events after an episode of AKI and therefore should be prioritized for follow-up regardless of the degree of renal recovery.

The unanswered question is what threshold of AKI warrants follow-up. A meta-analysis showed that the risk of CKD increased in a graded manner with mild AKI (adjusted hazard ratio [HR] 2.0, 95% confidence interval [CI] 1.4–2.8), moderate AKI (adjusted HR 3.3, 95% CI 1.7–6.2), and severe AKI (adjusted HR 28.2, 95% CI 21.1–37.5).[26] Moreover, the association with adverse events seems to be present even among patients with mild and rapidly reversible AKI who recover with normal or nearly normal kidney function.[4,27] These results reinforce that it is challenging for clinicians to determine who remains at risk after an episode of AKI.

Accordingly, we recommend that all patients with AKI receive some level of follow-up care. The intensity of follow-up care should be based on established risk factors for adverse events, which can be divided into 3 groups (Figure 2):

- Patient-specific risk factors
- Characteristics of the AKI episode
- Degree of kidney recovery

Patient-Specific Risk Factors

Several studies have reported patient-specific predictors for adverse events after an episode of AKI, which should inform the intensity of follow-up required. Although there are notable differences in methodology, case mix, and outcome ascertainment, many of these studies identified similar risk factors. These include older age,[4,20,21,28–30] higher comorbidity score,[4,31] preexisting hypertension or cardiovascular disease,[4,20,31–33] diabetes,[29,32,33] low serum albumin,[28,33] and recurrent AKI.[34] One study combined several risk factors into a prognostic score for stage 4 CKD, but its feasibility is limited by the inclusion of serum albumin, a laboratory parameter that may not be routinely measured in lower middle–income countries.[28]

One risk factor that should prioritize patients for follow-up is preexisting CKD. Proteinuria is a risk factor for adverse outcomes after AKI, which is not surprising given its strong association with CKD progression.[35] However, preexisting proteinuria is absent from many AKI studies, and post-AKI proteinuria has been reported as an outcome rather than incorporated into multivariable models of adverse post-AKI outcomes. Thakar *et al.*[34] found that preexisting proteinuria was associated with a 3-fold increase in stage 4 CKD in patients with diabetes after AKI, and James *et al.*[36] reported increased rates of death, ESRD, and doubling of serum creatinine across increasing levels of proteinuria in their population-based study. Most studies found that lower baseline kidney function increased the risk of ESRD and death after an episode of AKI.[20,21,31,37] Pannu *et al.*[37] found that the impact of

	Patient-Specific Risk Factors	Characteristics of the AKI Episode	Degree of Kidney Recovery
	Preexisting CKD (low eGFR or proteinuria)	Dialysis-requiring AKI	Dialysis dependent
	Diabetes mellitus	KDIGO stage 3 AKI	
High-Risk/High-Intensity Follow-up	Hypertension	Primary kidney disease associated with kidney recovery	AKD with persistently elevated serum Cr
	Cardiovascular disease	Acute tubular necrosis	
	History of AKI episodes	AKI duration ≥7 days	Serum Cr ≥25% of preexisting baseline
Moderate-Risk/Medium-Intensity Follow-up	↑ Comorbidities	KDIGO stage 2 AKI	Serum Cr <25% of preexisting baseline
	↑ Age	AKI duration 3–6 days	
	Few comorbidities	KDIGO stage 1 AKI	
Low-Risk/Low-Intensity Follow-up		AKI duration 1–2 days	Serum Cr at baseline with no other evidence of kidney damage
	First AKI episode	Prerenal injury	

Figure 2. Determinants of adverse outcomes and higher intensity follow-up after an AKI episode. Patient follow-up should be individualized based on 3 categories: patient risk factors, characteristics of the AKI episode, and the degree of kidney recovery. One high-risk or high-intensity feature within any of these 3 categories is sufficient to designate the patient for closer monitoring. Red, high risk/high intensity; yellow, moderate risk/medium intensity; and green, low risk/low intensity. Despite different shading, we make no distinction between the importance of factors within and between categories. AKD, acute kidney disease; AKI, acute kidney injury; CKD, chronic kidney disease; Cr, creatinine; eGFR, estimated glomerular filtration rate; KDIGO, Kidney Disease Improving Global Outcomes.

AKI on ESRD and death increased as the estimated glomerular filtration rate (eGFR) decreased, and in patients with a baseline eGFR <30 ml/min per 1.73 m^2, ESRD was most likely to develop after AKI (16.6% with AKI vs. 7.9% without AKI).[37] A lower eGFR is also a risk factor for recurrent AKI.[33] A few studies have observed that patients with normal GFR before AKI have a higher relative risk for the development of ESRD compared with AKI patients who have a decreased baseline GFR.[3,5,36,38] However, there is an extremely low probability of ESRD in patients without AKI or a decreased baseline GFR, which leads to higher relative risks even though the absolute risk of ESRD after AKI is much higher in patients with preexisting CKD. This observation was reinforced by Sawhney *et al.*,[39] who found that baseline kidney function was the strongest predictor of long-term outcomes, with the effect of AKI diminishing after 1 year.[39] Regardless of the role that AKI plays in CKD progression, an episode of AKI provides clinicians with an opportunity to identify patients with preexisting CKD and arrange follow-up for this high-risk population.[40]

Characteristics of the AKI Episode

Patients may have *de novo* AKI, acute-on-chronic kidney injury, or AKI with unknown previous kidney history. In 2012, the Kidney Disease Improving Global Outcomes (KDIGO) AKI work group proposed the term *acute kidney disease* to help unify the established concepts of AKI and CKD.[41] ADQI 16 further defined acute kidney disease as the acute to subacute loss of kidney function and/or damage from initiation or recognition to patient and kidney outcomes up to 90 days including recovery, recurrence, and/or progression (Figure 3). An AKI event will usually be observed, but this is not required to diagnose acute kidney disease. For example, community-acquired AKI is particularly common in the developing world, responsible for 50% to 80% of AKI episodes with high accompanying mortality.[2,3] These episodes may not be observed, but rather inferred by the persistence of kidney disease

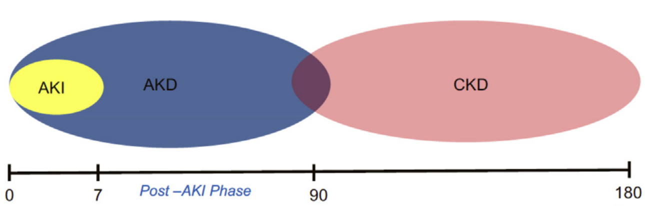

Figure 3. Acute kidney disease–chronic kidney disease continuum. For those patients with preexisting kidney disease, AKI and AKD are superimposed on the CKD state, and the new level of renal function represents the updated degree of CKD. The *x*-axis depicts time in days, with time 0 representing the onset of AKI/AKD. AKD, acute kidney disease; AKI, acute kidney injury; CKD, chronic kidney disease.

beyond 7 days, especially when a baseline creatinine value is unavailable. Such data reinforce that the intensity of patient follow-up should be individualized and need not meet strict definitions for AKI or CKD.

Beyond the severity of the AKI episode according to KDIGO AKI staging, patients with AKI who require dialysis and then recover to become dialysis independent are at especially high risk for adverse events.[3,5] In 1 study, the need for dialysis increased the likelihood of progression to stage 4 CKD by 500-fold (>5000%).[28] The duration of the AKI episode is also important. Persistent AKI (defined by KDIGO criteria) is characterized by the continuance of AKI creatinine or urine output criteria beyond 48 hours from onset. Two studies in postoperative patients demonstrated that the duration of persistent AKI is directly proportional to long-term mortality. Relative to patients without AKI, an episode of AKI lasting ≥7days increased the risk of long-term mortality by a magnitude of 2 to 3 times.[42,43] The etiology of the AKI episode may also influence the intensity of follow-up. Acute tubular necrosis relative to acute renal failure (as defined using ICD-9 diagnosis codes) is associated with 60% higher odds for progression to stage 4 CKD,[28,44] and hypotension, shock, and sepsis are common causes of AKI in lower middle–income countries.[2] Paradoxically, diagnoses associated with kidney recovery may also warrant closer follow-up to administer disease-specific therapies and to protect the kidney from further insults. Such etiologies that are more common in the developing world relative to the developed world include acute interstitial nephritis, glomerulonephritis, nephrotoxin-induced AKI, and postpartum AKI.[2,23,24]

Degree of Kidney Recovery

There is currently no standardized definition of recovery, but ADQI 16 recently aligned a framework for kidney recovery with the KDIGO categories for AKI. One of the main messages is that it is difficult to know whether kidney recovery is complete. For example, diminished serum creatinine generation, loss of muscle mass, changes in volume of distribution, and hyperfiltration may confound the assessment of functional recovery.[45–50] A recent study by Stoumpos *et al.*[51] demonstrated that in patients with AKI-requiring dialysis, CKD will develop in very few who recover to an eGFR >60 ml/min per 1.73 m^2 at 12 months.[51] Conversely, an episode of AKI that does not return to its preexisting baseline constitutes a high-risk event. A retrospective study of 1500 cardiac surgery patients found that for each 88 μmol/l increase in creatinine at discharge, the HR for death was 1.9 (95% CI 1.5–2.3).[29] Pannu *et al.*[32] also found in their population-based study that survivors of AKI who did not recover kidney function had a higher risk of mortality and adverse kidney outcomes than individuals who recovered to within 25% of their baseline serum creatinine (adjusted HR for mortality 1.3, 95% CI 1.1–1.4; adjusted HR for kidney outcomes 4.1, 95% CI 3.4–5.0). The degree of kidney recovery may be an even more important factor in the developing world, as 1 study in critical care patients found that only 52% of lower middle–income country patients recovered kidney function compared with 72% of patients in developed countries.[24] Therefore, patients whose creatinine does not return to baseline (including patients who still require dialysis) should be prioritized for follow-up. Baseline creatinine values may not be available in all patients due to limited resources,[23] and when available, differences in laboratory assays and standardization may threaten their accuracy and interpretation.[25] When in doubt, a persistently elevated creatinine level with no clear baseline should be recognized as AKD and managed as a high-risk event.

Special Considerations

Pediatric studies usually contain <100 patients,[52] so it is difficult to generate models that identify determinants of adverse events after AKI. For example, Mammen *et al*.[53] found an association between AKI severity and CKD in their 126-patient study, but this relationship did not reach statistical significance. A systematic review from Sub-Saharan Africa identified 22 studies in pediatric AKI patients, but only 5 reported rates of long-term CKD that could not be further analyzed due to inconsistent reporting.[25] While we await publication of the multicenter Assessment of Worldwide AKI, Renal Angina, and Epidemiology (AWARE) study, we recommend applying our consensus statements to the pediatric population until further evidence becomes available.

In resource-limited settings, it may be challenging to provide follow-up care to all patients after an AKI episode. One approach is to stratify barriers to care by sociocultural, policy, financial, and medical factors.[54] Sociocultural barriers include health beliefs and customs of patients (e.g., use of traditional medicine), and providers that may limit AKI follow-up care, such as the practice of treating male patients at the expense of female patients.[25] Policy and financial factors include financial constraints (patients and hospitals), health insurance coverage, and physician availability (both primary care and nephrologists) that may limit access to care.[25] Such issues are particularly relevant to community-acquired AKI, which may occur in remote settings. Medical factors include inconsistent clinical practice guidelines and health care provider education/awareness of AKI and its long-term consequences.[23,55]

However, several of these barriers also apply to high-income countries. Certainly, there are opportunity costs to targeting all survivors of AKI for follow-up care. Ideally, a simple and practical risk score would identify patients at high risk of CKD progression and mortality post-AKI. These patients could then be triaged for follow-up care based on local resources and practices, accounting for the aforementioned barriers that affect the developing world. Until such a score is available and validated in both high- and low-resource settings, we recommend prioritizing patients for follow-up similarly in both high-income and lower middle–income countries.

Question 2: What are the outcomes for which patients should be monitored after an AKI episode?

Consensus Statement

- *Consensus Statement 2A:* Because AKI is associated with adverse kidney events, patients should be monitored for *de novo* CKD, CKD progression, ESRD, and further AKI episodes.
- *Consensus Statement 2B:* Patients should be monitored for several nonrenal sequelae after an AKI episode, including new-onset hypertension, cardiovascular disease, all-cause hospital readmission, functional status, quality of life, and death.

It is recognized that an episode of AKI is associated with a high incidence of poor outcomes, some of which may occur in the rehabilitation phase following recovery from the acute illness. There are limited data published on the longer term outcomes of AKI survivors in the developed world and even less information on those in the developing world. It is therefore proposed that more data should be collected on patient outcomes following AKI to enable the identification of specific risk factors for this patient population. This in turn may allow the development new therapeutic interventions.

Based on our current understanding, patients in the developing world are at risk of both renal and nonrenal sequelae. The renal sequelae include *de novo* CKD, CKD progression, ESRD, and further episodes of AKI.[11] A recent meta-analysis demonstrated that AKI survivors have a 10-fold higher risk of CKD, 3-fold increased risk of ESRD, and double the risk of death.[26] A retrospective study in India reported that 15% of AKI survivors were discharged on renal replacement therapy, 12.5% remained dialysis dependent, and 19% to 31% had CKD at long-term follow up (1–10 years).[22] A systematic review of outcomes of AKI in 186 adults and 676 children in Sub-Saharan Africa demonstrated that 13% of adults and 10% of children had persistence of renal dysfunction (not requiring dialysis) at the time of discharge.[25] Most of these adverse events occur in the first few months after the AKI episode.[3] Survivors of AKI therefore represent a vulnerable population that needs to be reviewed early in an effort to improve outcomes.

There are many nonrenal sequelae that have been identified in patients in the developed world.[56] It is proposed that the nonrenal sequelae to monitor include hypertension,[6] cardiovascular disease,[57] all-cause readmission,[58] functional status,[59] quality of life,[59] and death.[26]

Special Considerations

There is very little published literature on the longer term outcomes after AKI in pediatric patients. Many of these patients will be lost to follow-up, either through failure to refer after an episode of AKI or at the time of transition from childhood to adulthood. The outcome measures should be the same as in adults, but perhaps modified to include developmental parameters.

In developing countries, it must be recognized that a substantial proportion of patients with AKI do not receive dialysis due to restrictions on health care provision. Poor outcomes in these countries will reflect the severity of patient illness and delayed presentation to a nonuniform health care infrastructure.[25] Currently in most countries in Sub-Saharan Africa, access to specialist nephrology care is dependent on out-of-pocket payments by patients. There is increasing pressure across both the developing and developed worlds to justify where to spend scarce financial resources on health care. The collection of more data describing the vulnerable nature of these patients and their adverse outcomes will be key. Medical managers and politicians must be informed of the consequences of failing to prevent avoidable readmission and progression of CKD with its cost to society. In many countries, resources are scarce or restricted with multiple health care priorities competing for the same pot of money. It is important to emphasize the nature of AKI in identifying vulnerable patients with a variety of health care needs, many of which are not nephrology centered.

Question 3: What are the components of patient-centered monitoring after an AKI episode?

Consensus Statement

- *Consensus Statement 3A:* All patients with AKI should have continued access to the health care system.
- *Consensus Statement 3B:* Low-risk patients (Figures 2 and 4) should have their kidney function and proteinuria checked within 3 months of the AKI episode (per the KDIGO guidelines). Monitoring can be done by any health care provider or a nephrologist in an outpatient setting.
- *Consensus Statement 3C:* High-risk patients (Figures 2 and 4) should preferably be assessed by a nephrologist within 1 month of the AKI episode. Earlier follow-up may be necessary to reduce recurrent AKI and hospital readmission.
- *Consensus Statement 3D:* Patients who remain dialysis dependent should be closely monitored by a nephrologist for renal recovery because renal function may recover several months after an episode of AKI.

Patient monitoring after an episode of AKI should begin as soon as possible. In 2 single-center studies, less than half of physician discharge summaries documented the presence of AKI.[60,61] A recent United States Renal Data System report showed that 75% of patients will see a primary care physician within 3 months of an AKI episode compared with 13% of patients who will see a nephrologist.[13] However, the proportion of patients who have their serum creatinine measured within 3 months of an AKI episode only ranges between 55% and 70%.[13,62,63]

In the developing world, 1 study found that scheduled follow-up for AKI is similar to that in the developed world.[2] However, another study from China reported a 74% AKI nonrecognition rate.[23] This observation suggests patient follow-up in the developing world may be much lower than anticipated. Reasons for a lower follow-up rate in survivors of AKI may include the policy and financial barriers listed earlier (financial constraints, health insurance coverage, physician availability). These factors limit access to care, which may be magnified by the cost of diagnosing and monitoring AKI with expensive serum creatinine testing.[23] Medical barriers may include the silent and asymptomatic nature of kidney disease and competing health demands of higher priority (e.g., postsurgical care), so patients and health care providers may not emphasize follow-up care after AKI. Therefore, communication is critical between health care providers who care for patients during the AKI episode and health care providers responsible for longitudinal post-AKI care. Simple quality-improvement initiatives may help to track patients and facilitate follow-up care,[12,19] but, at the very least, patients with AKI should be offered continued access to the health care system.

Currently, there is a lack of evidence to guide the timing, frequency, and method of evaluation after an episode of AKI, including what type of health care provider (e.g., community provider or nephrologist) should assume primary responsibility for patient follow-up. Multiple observational studies have

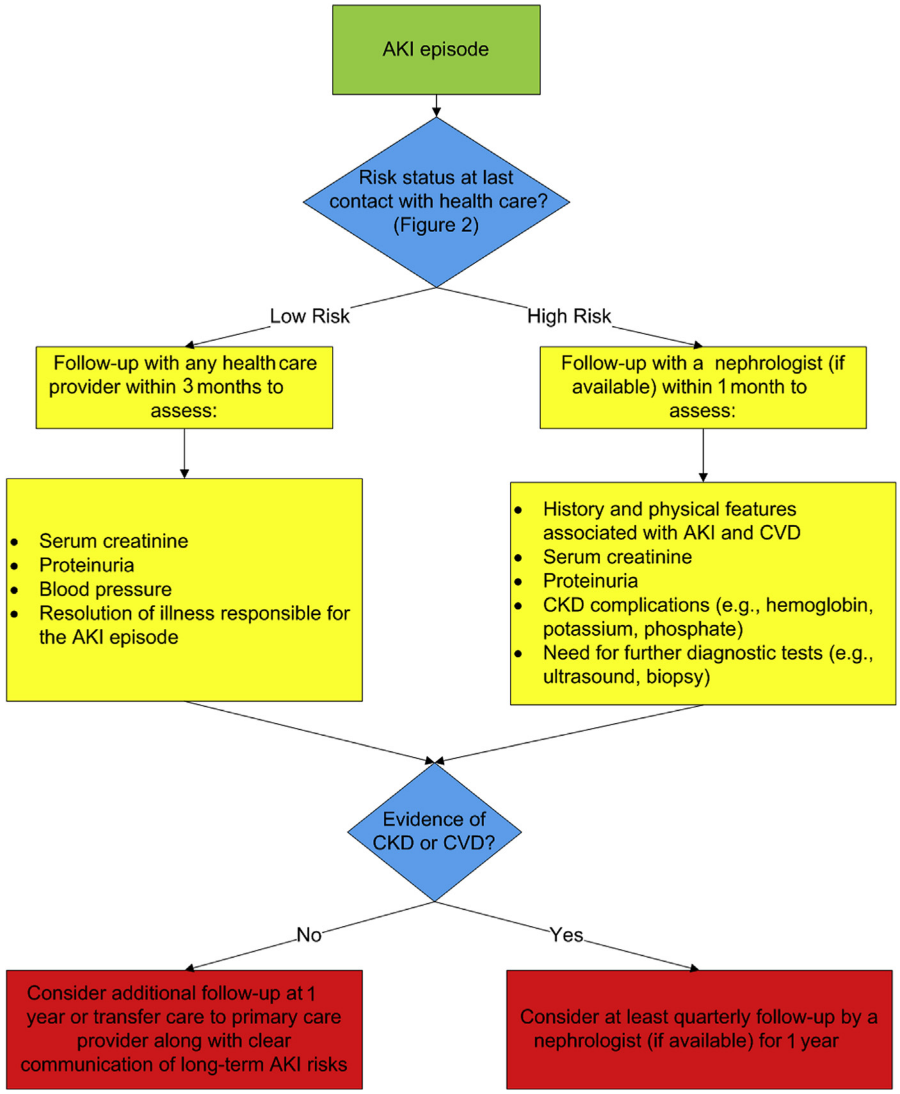

Figure 4. A potential follow-up pathway for patients after an AKI episode. This pathway shows different recommended strategies for patient monitoring after an AKI episode. The intensity of monitoring depends on the patient's risk of adverse events (Figure 2, to be assessed at the patient's last point of contact with the health care system) and the results of the initial follow-up visit. Follow-up should also be individualized (e.g., moderate-risk patients could be treated as low risk or high risk) and dynamic. For example, patients thought to be low risk may require more frequent, nephrologist-led monitoring if they are found to have evidence of CKD or CVD at their initial post-AKI visit. AKI, acute kidney injury; CKD, chronic kidney disease; CVD, cardiovascular disease.

demonstrated that new-onset and progressive CKD tends to occur soon after an episode of AKI, with a median time to CKD of ∼30 days.[3,4] The timing of microalbuminuria after AKI has not been extensively studied, but between 40% and 50% of patients had evidence of microalbuminuria within 3 months in 2 studies[19,64]; these results are consistent with long-term follow-up from the Randomized Evaluation of Normal versus Augmented Levels of Renal Replacement Therapy (RENAL) trial.[65] The 90-day time point also appears to be important for recurrent episodes of AKI. Among 11,683 AKI hospitalizations, Siew *et al.*[33] found that the median time to recurrent AKI was 64 days. Of the 2954 patients (25%) with recurrent AKI, close to 60% of the episodes occurred within the first 90 days after hospital discharge. For nonrenal outcomes, less is known about the timing of events after AKI to guide monitoring strategies. Hsu *et al.*[6] demonstrated that new-onset hypertension was present within 180 days of hospital discharge, affecting 31% of patients after an AKI episode. Patients who survive an episode of AKI are also at higher risk of hospital readmission at 30 days compared with patients without AKI, primarily due to heart failure and pulmonary edema.[58,66,67] Rates of all-cause 30-day readmission range between 15% and 25%, with a median time to readmission of 11 days.[66–70]

Given this limited evidence on the timing of adverse outcomes after AKI, we agree with the KDIGO AKI guidelines that patients should be evaluated within 3 months of the AKI episode.[41] This 3-month window should begin at the last point of contact with the health care system, whether that be a community provider in an outpatient clinic or a nephrologist during an inpatient hospitalization. We would only delay the first follow-up visit until 3 months for low-risk patients (Figure 2), given that CKD and recurrent AKI events tend to occur before 3 months. Follow-up visits for low-risk patients should consist of at least a serum creatinine check and proteinuria assessment. Other considerations for low-risk patients include a brief history to ensure resolution of the illness responsible for the AKI episode and a blood pressure check. Such monitoring can be done by a local health care provider or a nephrologist in an outpatient setting, including remotely via telemedicine as local resources permit (Figure 4).

For higher risk patients (Figure 2), we recommend an assessment by a nephrologist within 1 month of the AKI episode. This shorter follow-up period precedes the onset of CKD and recurrent AKI for most patients, but may be too delayed to prevent hospital readmissions. A visit with a nephrologist has been associated with enhanced survival; Harel *et al*.[15] demonstrated lower mortality in survivors of dialysis-requiring AKI who saw a nephrologist relative to propensity score–matched AKI patients without such follow-up (HR 0.8, 95% CI 0.6–0.9). Although the processes of care responsible for these improved outcomes remain to be determined, with prospective studies under way (ClinicalTrials.gov NCT 02483039),[12,71] previous research has demonstrated that nephrologists are more skilled at recognizing and managing CKD complications according to evidence-based guidelines compared with primary care providers.[72,73] Although our preference is for nephrologist-led follow-up, there is a shortage of nephrologists throughout much of the developed world.[74] In such cases, it is reasonable for a nonnephrologist physician or local health care provider to direct the follow-up plan, with nephrology support via telemedicine, if available.

We cannot be sure that any monitoring strategy will be effective in mitigating adverse outcomes in the post-AKI setting. Nonetheless, it seems reasonable to provide interventions designed to prevent recurrent AKI and acute illness and recognize CKD. Such monitoring should include a complete history and physical examination that targets risk factors for AKI and cardiovascular disease (e.g., an assessment of intravascular volume status). We recommend that kidney function and proteinuria be assessed, with other laboratory studies (hemoglobin, electrolytes, cholesterol, mineral metabolism) ordered based on the clinical context. More invasive investigations such as imaging tests (e.g., abdominal ultrasound) or a kidney biopsy should not be overlooked, depending on the etiology of the patient's AKI and current level of kidney function (Figure 4).

Patients cannot be followed for an indefinite period of time after an episode of AKI. We recommend that the frequency of visits be individualized based on patient risk for adverse events and results from the initial visit (Figures 2 and 4). Most reported post-AKI clinics assess patients every 3 months, but there is no evidence that this approach modifies outcomes.[12,19–21] One year after the AKI episode, kidney function appears to stabilize.[21,75] Therefore, patients could be assessed for specialized CKD care at this time point. One approach currently being evaluated is to use the KDIGO CKD guidelines to triage patients at 1 year[35]; patients without CKD or with low-risk CKD are transitioned to their primary care provider along with an educational pamphlet on post-AKI care, whereas patients with moderate- to high-risk CKD are referred for ongoing specialized nephrology care.[12] This approach may help to ensure adequate resources to schedule follow-up visits for patients with new-onset AKI within the recommended time intervals.

One patient population that warrants additional discussion is patients who still require dialysis for AKI. Rates of renal recovery among outpatient hemodialysis patients who started dialysis for AKI are not as uncommon as previously reported.[76,77] Despite a high prevalence of comorbid conditions, Hickson *et al*.[78] found a recovery rate to dialysis independence of 21% at 6 months. Median time to recovery was 8 months, with 94% of recoveries occurring within 6 months. No patients recovered to dialysis independence after spending >12 months on dialysis. These results are consistent with Centers for Medicare and Medicaid Services data, where recoveries are most common within 3 months and rare after 12 months.[79] In many lower middle–income countries, dialysis for AKI is limited to a specific period of time. If there is no renal recovery and no plan for kidney transplantation, dialysis may be stopped unless patients can afford continued treatment.[80] This practice emphasizes the importance of rehabilitation strategies in AKI patients on dialysis, especially during the first few months of dialysis when most renal recovery may occur.

Currently, no guidelines exist regarding monitoring of renal recovery in dialysis patients, and research in this area is urgently needed. To further complicate matters, there is no single symptom, sign, or investigation that identifies renal recovery (Table 1). We agree with the American Society of Nephrology AKI Advisory Group that monitoring for recovery in dialysis-dependent patients after AKI requires careful observation and an individualized approach.[81] Symptoms suggestive of recovery include muscle cramps,

Table 1. Indicators of renal recovery in patients with acute kidney injury requiring dialysis

Symptoms	Signs	Laboratory and drug changes
Muscle cramps	Intradialytic hypotension	Decrease in predialysis serum creatinine
Light-headedness	Decreased interdialytic weight gain	Normalization of potassium, phosphate, or parathyroid hormone
Decreased ultrafiltration on hemodialysis	Increased urine output	Decreased need for phosphate binders
Decreased need for hypertonic peritoneal fluid		Decreased need for erythropoietin
		Estimated GFR >15 ml/min per 1.73 m^2 (using a 24-hour urine for urea and creatinine clearance)

GFR, glomerular filtration rate.

lightheadedness, and lower requirements for ultrafiltration or hypertonic peritoneal fluid. Although some patients may develop an improved sense of well-being, other patients may feel worse because of unnecessary fluid removal.[82] Signs to monitor for include intradialytic hypotension, increasing urine output, and decreasing interdialytic weight gain.[81] Falling serum creatinine is a well-recognized investigation that indicates renal recovery; however, decreasing serum creatinine values could also reflect catabolism, decreased muscle mass, or malnutrition. Other laboratory changes that may indicate renal recovery include normalization of serum electrolytes, mineral metabolism (e.g., elimination of phosphate binders), and hemoglobin (e.g., elimination of erythropoietin therapy). These changes are likely to occur gradually and may not be apparent without carefully monitoring patient trends, underscoring the individualized approach needed to monitor dialysis patients for recovery after AKI.[81,82]

When renal recovery is suspected, the next step is a 24-hour urine for urea and creatinine clearance measurement starting 24 hours before the next dialysis session during the longest interdialytic interval. Both creatinine and urea clearance are inaccurate in dialysis patients, but the direction and magnitude of the different clearances produce a reasonable estimate of inulin clearance.[83] It has been suggested that a mean clearance above >15 ml/min per 1.73 m^2 warrants a reduction in dialysis treatment, but this approach has yet to be validated.[82]

Until additional data are available, we reinforce the importance of an individualized approach to monitoring patients who are still on dialysis after an episode of AKI. There are several nuances to caring for these patients, so a nephrologist may be best equipped for this role. The entire dialysis unit should also be aware of the potential for renal recovery in this population to decrease the health and economic costs from inadvertent prolongation of dialysis.

Special Considerations

Because the pathogenesis of cardiovascular disease begins early in children with CKD, prompt identification of CKD in the pediatric population is arguably of greater importance than in adults.[84] Earlier follow-up must be balanced against caregiver stress and competing specialist appointments because pediatric AKI is most often a sequelae of other serious illnesses or their treatment. In terms of patient monitoring, the most common renal sequela in the largest pediatric cohort study was the presence of persistent microalbuminuria in 10% of patients.[53] An additional consideration is cystatin C as a marker of kidney function because decreased muscle mass in children older than 2 years of age renders serum creatinine a less sensitive measure of kidney function when used in isolation.[85]

In our experience, some patients in resource-limited settings face sociocultural pressures to return to work soon after their acute illness has resolved. In addition to the policy, financial, and medical factors described previously, follow-up care pathways in the developing world need to be individualized, given the high rates of community-acquired AKI. Follow-up care should be flexible to both work needs and remote settings, including telemedicine and point-of-care monitoring options to ensure that some assessment of kidney function is performed. Similar to high-income countries, particular attention is required in lower middle–income countries to improve the process of care for patients who still require dialysis after AKI. A sizable portion of these patients recover kidney function up to 1 year after the AKI episode, so they should not arbitrarily be labeled and treated as ESRD patients.

Question 4: What management strategies are recommended after an AKI episode?

Consensus Statement

- *Consensus Statement 4A:* Patients should continue to receive treatment tailored to the etiology of their AKI to promote renal recovery.
- *Consensus Statement 4B:* After an AKI episode, all patients should receive counseling on lifestyle changes and dietary modification.
- *Consensus Statement 4C:* Patients should receive comprehensive medication reconciliation and cardiovascular risk reduction appropriate to their clinical circumstances.

- *Consensus Statement 4D:* Patients who remain dialysis dependent should have their dialysis regimens individualized.

Patients recovering from AKI often have underlying diseases that require ongoing drug therapy. These conditions may be primarily renal (e.g., acute interstitial nephritis, Goodpasture syndrome) or nonrenal (e.g., lupus, myeloma). These diseases may still be treated with steroids and immunosuppressant/cytotoxic drugs based on the clinical context to promote renal recovery. The dosage of immunosuppressant/cytotoxic drugs may need to be adjusted for renal function.

To maintain renal and cardiovascular health, patients should receive basic counseling on lifestyle and dietary modifications. Key areas include maintaining adequate hydration and increasing fluid intake during episodes of diarrhea/vomiting, which are common in tropical countries. Additional fluid balance assessments and diuretic adjustments may also be needed for patients with heart failure.

In terms of pharmacologic management, patients may have underlying conditions such as heart failure that require specific treatment with medications (e.g., angiotensin-converting enzyme inhibitors [ACEIs] or angiotensin receptor blockers [ARBs]). The well-recognized increase in serum creatinine with ACEIs/ARBs means that these drugs are usually discontinued in patients with AKI. However, there is compelling evidence that these drugs are associated with renoprotection in patients with proteinuria and diabetic and nondiabetic CKD and patients with systolic dysfunction.[35] The safety of these drugs in the immediate post-AKI period is not known. In 1 study using administrative databases, patients with an acute coronary syndrome in whom post-contrast AKI developed were significantly less likely to be started on ACEIs/ARBs, and patients with KDIGO stages 2 and 3 AKI were less likely to be started on beta-blockers and statins compared with non-AKI patients. On follow-up, the use of each of these cardioprotective medications was associated with a lower risk of cardiovascular mortality.[86] These benefits were found across all categories of patients, including those with preexisting CKD, diabetes, heart failure, and proteinuria. In another study, 142 of 1463 subjects with AKI (9.7%) were treated with an ACEI. There was no associated reduction in mortality after full adjustment for covariates.[87]

Beta-blockers are not associated with an increased risk of the development of AKI, and there is no *a priori* reason not to restart them post-AKI if needed. The potential for statins to increase the risk of AKI due to rhabdomyolysis is well recognized.[88] In subjects who experience AKI due to another cause, however, there seems to be no reason to discontinue statins during or after an episode of AKI. More studies are required to establish the optimal timing of reintroduction of ACEIs/ARBs post-AKI. However, there is no reason to stop these and other cardiovascular medications indefinitely in all patients after an episode of AKI. Decisions should be individualized, especially because the risk of AKI due to cardiovascular medication appears to be small compared with the risk of AKI due to preexisting patient characteristics.[89,90]

Other medication classes should be avoided if possible, which emphasizes the importance of medication reconciliation after AKI. In 1 study, 19% of survivors of AKI used nonsteroidal anti-inflammatory drugs, which are potentially nephrotoxic.[91] The use of other nephrotoxic agents, such as aminoglycosides and radiocontrast media, should also be restricted in patients after AKI unless there is a compelling need.

The management of patients still requiring dialysis after AKI is particularly challenging without evidence-based guidelines. Important issues include prevention of intradialytic hypotension, determination of fluid removal targets, and medication adjustments for renal function. In addition, patients recovering from AKI are likely to be anemic. Although erythropoietin treatment does not prevent further injury or reduce the risk of recurrent AKI, such treatment is safe and should be offered to anemic patients (dialysis dependent or independent) in the recovery phase of AKI based on established targets for patients with CKD.[92,93] Similar to monitoring strategies for dialysis patients post-AKI, we agree with the American Society of Nephrology AKI Advisory Group that the management of dialysis-dependent patients after AKI requires an individualized approach.[81,94]

Special Considerations

We are unaware of any studies on post-AKI management in children. It seems reasonable to apply many of these principles in adults to the pediatric population, including treatment of the cause of AKI (e.g., hemolytic-uremic syndrome), counseling to avoid dehydration, and medication reconciliation.

In developing countries, important considerations involve medication adjustments and reconciliation. Patients may be taking indigenous or allopathic therapies, which will need to be carefully reviewed for nephrotoxicity. Specialized pharmacist expertise is also not always available, so health care providers may need to rely on published resources to assist with drug dosing and therapeutic drug monitoring.[95]

Question 5: What educational strategies are recommended after an AKI episode?

Consensus Statement

- *Consensus Statement 5A:* After an episode of AKI, patients, their caregivers, and their health care providers should be made aware of the AKI diagnosis. AKI should also be documented in the patient's medical record to increase its recognition as a health issue.
- *Consensus Statement 5B:* All patients, their caregivers, and their health care providers should receive information on the etiology of the AKI episode, patient risk profile, and the importance of follow-up, including steps to monitor, manage, and prevent future AKI episodes.
- *Consensus Statement 5C:* We recommend standardized strategies to communicate and educate patients, caregivers, and health care providers. Education should begin early on after AKI diagnosis and continue throughout follow-up.

It is recommended that education should be focused on a patient-centered approach, which is often not the case.[14] The importance of kidney health should be emphasized throughout developed and developing countries to allow providers to deliver the appropriate follow-up care in a more systematic manner. Patients should be encouraged to become active partners in their own health management. It would be expected that patient follow-up rates may improve by empowering them with knowledge concerning their own health and future risks. Currently, very few patients are aware that they have had an episode of AKI, let alone that they are at an increased risk of long-term adverse outcomes.[96] Going forward, this is a situation that must change.

There have been no formal studies on when to educate patients after an episode of AKI. It would therefore seem prudent to provide information to the patient shortly after the diagnosis of AKI and provide an opportunity for the patient and other family members to discuss immediate management as well as longer term care.

There is also very little published literature describing what information is routinely given to patients after an episode of AKI. Patient education should include information on maintaining good hydration and avoiding nephrotoxins. There have been some reports of patients provided with "sick day" guidance, which promotes self-care with respect to holding medications at the time of illness (e.g., during episodes of dehydration).[12] However, tailoring such initiatives for patients with multiple conditions can be complex.[97]

Lunyera *et al.*[98] administered an 18-item Web-based questionnaire to physicians actively engaged in providing nephrology care in developing countries. This identified a lack of meaningful and targeted approaches to education with a reliance on international guidelines rather than local guidelines tailored for particular patient populations. Evans *et al.*[99] identified the deficiencies in the management of AKI among Malawian health care workers. One hundred delegates attended a course on AKI in Malawi. At this workshop, 32% of all health care workers had never received training in any aspect of renal disease, and 50% had never received training in AKI, even though 69% had managed patients with AKI. This lack of awareness is multifactorial with a high turnover of staff making this task an ongoing challenge. A lack of knowledge on the current definitions of AKI and when to refer were reported in the United Kingdom recently.[100] Evidence that an education package could improve patient outcomes as part of a quality improvement program was provided by Xu *et al.*[101] in 2 large teaching hospitals in the UK. The "Think Kidneys" program (www.thinkkidneys.nhs.uk)[102] in the United Kingdom has developed a range of educational resources for both primary and secondary care that are freely available.

Special Considerations

It has been reported that parents/guardians of children who have recovered from an episode of AKI are especially interested in the recovery process and preservation of their child's kidney function. Initiatives include the use of information distributed on laminated wallet cards; this provides a handy reference on nephrotoxic medications and contact information for additional questions.[12]

The delivery of education on AKI to health care workers from developed countries must be tailored to meet the needs of the learners. Local, regional, or national events supported by experts in the field provide an opportunity to raise awareness among a large number of health care professionals but can prove difficult to attend. The development of electronic AKI learning modules as part of a coordinated program of education with credits attached should be explored as a way to reach a larger audience. Such modules should include all phases of AKI care and propose improvements in the rehabilitation phase of AKI.[103]

Research Questions

- When is further recovery of kidney function unlikely after an episode of AKI? How do patient, kidney disease, and process of care factors affect the likelihood of kidney recovery?
- Can a simple and practical risk equation be developed to predict adverse events after an AKI episode?
- In what proportion of patients who survive an AKI episode do adverse events develop over the short

term and long term, including renal and nonrenal events?
- Does follow-up with a health care provider after an episode of AKI improve outcomes in lower middle–income countries? What is the economic impact of different models of care after an AKI episode?
- What monitoring strategies and interventions are critical for improving outcomes after an episode of AKI in lower middle–income countries?
  - —What are the best methods to assess for functional and structural kidney recovery?
  - —Are eGFR equations accurate after an episode of AKI?
  - —What is the role of conventional and novel biomarkers?
  - —What is the optimal management of cardioprotective medications (e.g., ACEIs, ARBs, and statins) in patients who survive an episode of AKI?
- How do the sociocultural, policy, financial, and medical factors specific to lower middle–income countries affect long-term patient outcomes, monitoring strategies, and treatment options after AKI?

Conclusions

Survivors of AKI represent a high-risk group, and we have summarized several opportunities to improve their long-term outcomes in the developing world. While the evidence base matures, an episode of AKI should be viewed as a serious health event with downstream consequences that have renal and nonrenal sequelae. Our recommendations urge health care providers to consider intensive follow-up for every patient who survives an episode of AKI, especially patients with preexisting CKD and patients who remain dialysis dependent at hospital discharge. Simple interventions such as lifestyle changes, medication reconciliation, blood pressure control, and education could have significant population-level effects, and promoting renal recovery in a small number of patients with dialysis-dependent AKI could have significant cost savings. More research is clearly needed to identify the highest risk patients with AKI and to determine the components of evidence-based rehabilitation after AKI. However, AKI is a global public health problem that affects 13.3 million people per year,[2] continuing the status quo, and hoping for different results no longer seems like a reasonable option. We hope that the consensus statements developed in this review help to provide clinicians with guidance on the care of patients after an episode of AKI and serve as a road map for future research efforts.

DISCLOSURE

All the authors declared no competing interests.

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AUTHOR CONTRIBUTIONS

All authors formulated and finalized questions, prepared consensus statements, drafted the manuscript, and approved the final manuscript for publication. SAS and AL had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. We certify that this manuscript nor one with substantially similar content has been published or is being considered for publication elsewhere.

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