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EDUCATIONAL REVIEW

# Pediatric acute kidney injury and the subsequent risk for chronic kidney disease: is there cause for alarm?

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## Abstract

Acute kidney injury (AKI) is characterized clinically as an abrupt decline in renal function marked by reduced excretion of waste products, disordered electrolytes, and disrupted fluid homeostasis. The recent development of a standardized AKI definition has transformed our understanding of AKI epidemiology and outcomes. We now know that in the short term, children with AKI experience greater morbidity and mortality; additionally, observational studies have established that chronic renal sequelae are far more common after AKI events than previously realized. Many of these studies suggest that patients who develop AKI are at greater risk for the subsequent development of chronic kidney disease (CKD). The goal of this review is to critically evaluate the data regarding the association between AKI and CKD in children. Additionally, we describe best practice approaches for future studies, including the use of consensus AKI criteria, the application of rigorous definitions for CKD and renal sequelae, and the inclusion of non-AKI comparator groups. Finally, based upon existing data, we suggest an archetypal approach to follow-up care for the AKI survivors who may be at greater CKD risk, including children with more severe AKI, those who endure repeated AKI episodes, patients who do not experience full recovery, and those with pre-existing CKD.

**Keywords** Acute kidney injury · AKI · Chronic kidney disease · CKD · Children · Pediatrics

## Introduction

Acute kidney injury (AKI), known previously as acute renal failure, is defined as an abrupt decline in renal function resulting in impaired elimination of waste products and dysregulation of electrolytes, acid–base status, and fluid balance [1]. AKI is a common complication among hospitalized children, and the incidence is rising, particularly in developed countries where AKI tends to be caused by systemic diseases or the treatments they necessitate [2–4]. Recent data suggest that AKI occurs in 27% of children receiving intensive care and in at least 5% of non-critically ill pediatric patients [5, 6].

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AKI has been associated with poorer short-term outcomes; children who develop AKI while hospitalized experience greater mortality, longer lengths of stay, and prolonged mechanical ventilation [1, 6–8]. More recently, investigators have established an association between AKI and long-term sequelae as well [9]. Previously thought to be a self-limited phenomenon, newer data have linked AKI with long-term renal morbidity, including proteinuria, hypertension, and chronic kidney disease (CKD) [10–15]. The potential ramifications of this association are profound since CKD is associated with neurodevelopmental impairment, anemia, bone disease, growth failure, and cardiovascular morbidity [16, 17]. Although not conclusive, emerging evidence of this connection is compelling. However, the association remains underrecognized, and pediatric AKI survivors rarely receive follow-up care or serial monitoring of renal function [18–20]. For example, a recent study examined a cohort of patients who developed AKI while in the intensive care unit (ICU) [21]. Of the children with AKI who survived to be transferred out of the ICU, only 66% had a follow-up creatinine measurement obtained between ICU transfer and hospital discharge. Similarly, Greenberg et al. demonstrated that fewer than 5% of children who experienced AKI after cardiac surgery saw a

nephrologist subsequent to discharge [18]. A more comprehensive understanding of the relationship between AKI and CKD, as well as a more definitive resolution to the causative question must be a high priority for the critical care and nephrology communities since it is possible to effectively treat CKD sequelae and slow progression if an accurate and early diagnosis can be made [16, 19, 22].

The goal of this educational review is to summarize the data describing the association between AKI events and the subsequent development of CKD in children and young adults. We emphasize the following: (1) the structural and parenchymal changes which occur in the kidney following AKI, (2) the best available data from adult studies, (3) the totality of the data available from pediatric studies, and (4) the gaps in the existing data and recommendations for further research studies. While a comprehensive review of the AKI/CKD relationship in neonates is beyond the scope of this manuscript, there have been several excellent manuscripts published recently which may serve as complementary references [23–26].

## Pathophysiology and structural changes following AKI

Regardless of underlying disease and cause of injury, the final common pathway for progressive renal dysfunction is fibrosis of the tubulointerstitial compartment [27, 28]. Experimental models have demonstrated that AKI is indeed associated with the development of tubular atrophy, reduced peritubular capillary density, and interstitial fibrosis; inflammation, ischemia and parenchymal hypoxia, endothelial damage, capillary rarefaction, and reperfusion injury all contribute to the profibrotic environment of AKI events [9, 27–32]. Interestingly, fibrosis is a self-limited process which is designed to confine the extent of an injury; it is not progressive in its own right [27]. Thus, while an episode of AKI creates a local environment which is conducive to fibrosis, additional factors are required for progressive injury and dysfunction to develop.

Although these mechanisms are not completely understood, animal models have provided some insight. One fundamental concept is that of renal mass reduction [27, 29]. Experimental models have demonstrated that in the setting of AKI, reduced renal mass enhances injury and is associated with progressive decline in function [27, 33]. Reduced renal mass has this effect whether it is due to pre-existing CKD, recurrent episodes of injury, or a single profoundly severe episode of AKI. In the setting of reduced nephron mass, tubular repair and regeneration becomes maladaptive [9, 27, 33]. Tubules fail to differentiate, do not regain normal function, and continue to produce proinflammatory and profibrotic signals [27]. Additionally, some models suggest that medullary injury may play a significant role in progressive dysfunction. The renal medulla, which is profoundly hypoxic, is particularly sensitive to ischemic injury [27, 34]. The ischemic and inflammatory environment of AKI further reduces oxygenation within the medulla and impairs tubular regeneration and repair. This hypoxic milieu may persist beyond the initial injury and has the potential to affect large swaths of cortex through hemodynamic and obstructive mechanisms [27, 31, 34]. As tubules and endothelial cells undergo maladaptive repair and atrophy, additional stress is placed upon the remaining, functional parenchyma. Tubules undergo hypertrophy and vascular autoregulation is impaired. Systemic and intrarenal hypertension is transmitted unabated to the glomeruli, causing progressive injury and hyperfiltration [27]. Although further work is needed to completely elucidate the mechanisms behind progressive dysfunction following AKI, it does seem clear that processes independent of the initial inciting event contribute to the decline.

## AKI and CKD studies in adult patients

While some controversy remains, an association between AKI and CKD has been endorsed in nearly all of the adult literature over the past decade [9]. The remaining debate centers on the causative aspect of the relationship; few authors debate that AKI and CKD are interconnected, but some remain unsure whether AKI actually causes CKD [9, 32, 35]. The association has been demonstrated in a number of observational studies. For example, in one study cohort comprising 233,803 elderly patients, the risk of end-stage renal disease (ESRD) was 13-fold higher following an episode of AKI [36]. A study involving more than 500,000 adults demonstrated that AKI severe enough to require renal replacement therapy is associated with a 28-fold higher risk of developing Stage 4/5 CKD [37]. Finally, a meta-analysis of 13 studies found that adults who survived AKI had an 8.8-fold higher risk of CKD and a 3.1-fold higher risk of ESRD [11].

While some concerns about confounding, ascertainment bias and definitional/classification issues (with both AKI and CKD) have been raised, there are a number of strong arguments which support the concept that AKI has a causative relationship with CKD [35]. The first is that while many published studies have been observational, these have found that the effect of AKI on the development of CKD remains after adjustment for demographics, potential confounders, and risk factors: these studies have found that AKI is independently associated with CKD [10, 11, 36, 37]. Secondly, there is a dose-dependent effect [10, 38, 39]. Ishani et al. examined AKI severity among nearly 30,000 adults who had undergone cardiac surgery [38]. They found that the magnitude of creatinine rise was directly related to the risk for incident CKD. Thakar et al. found that among more than 3600 diabetics, AKI was independently associated with an increased risk of Stage 4 CKD and that each subsequent AKI episode doubled that risk [39]. Thus, data support the concept that more severe AKI is associated with greater CKD risk and that subsequent AKI

events increase the cumulative risk. Finally, there is clear evidence that among patients with pre-existing CKD, AKI events accelerate CKD progression [38, 40, 41]. For example, the aforementioned Ishani et al. article found that AKI was associated with progression of CKD stage and that larger creatinine changes were correlated with greater risk [38]. Thus, while it is not possible to say unequivocally that AKI causes CKD, the best data currently available among adult patients support the claim that CKD can be a sequelae of AKI events.

## AKI and CKD studies in pediatric patients

The enduring effects of renal disease have been described in various circumstances. For example, post-streptococcal glomerulonephritis (PSGN) and hemolytic uremic syndrome (HUS), two of the more common acute renal disorders seen in children, have both been associated with long-term renal abnormalities [42–44]. Though they did not characterize the nature of the acute renal disease, Hoy et al. demonstrated that episodes of PSGN are a risk factor for albuminuria and CKD years later [42]. Similarly, Garg and colleagues demonstrated that 4 years after HUS, 25% of children experienced persistent renal sequelae [hypertension, proteinuria, and/or a reduced glomerular filtration rate (GFR)] and 3% developed ESRD [43]. This meta-analysis did not report AKI rates or describe the severity of renal involvement; however, they did find that CKD risk was higher in patients who required dialysis, echoing the dose-dependent effect described in adults.

Similarly, a number of studies have demonstrated that long-term renal sequelae are highly prevalent, specifically in the setting of AKI (Table 1). Askenazi et al. examined 29 children with AKI (based upon diagnostic coding) and found that both proteinuria and hypertension occurred in more than 20% of survivors; hyperfiltration (31%) and an estimated GFR (eGFR) of < 90 mL/min/1.73 $m^2$ (13.8%) were also common [14]. Buysse and colleagues studied 19 children who developed AKI (defined by a creatinine level of twofold the normal value) after septic shock events and found nearly identical rates of hypertension and proteinuria 10 years later [51]. Studies by Hingorani and Kist-van Holthe found that AKI is a risk factor for CKD among children receiving stem cell transplants [52, 56]. Specifically, Hingorani et al. found that AKI (doubling of serum creatinine level) increased the risk for CKD (eGFR < 60 mL/min/1.73 $m^2$) by 70% [52]. Mammen et al. reviewed 126 AKI survivors [Acute Kidney Injury Network (AKIN) Stage 1 or greater] 1–3 years after ICU discharge. They found only moderate rates of hypertension (3.2%) and proteinuria (9.5%); however, nearly 40% of these children had an eGFR of < 90 mL/min/1.73 $m^2$ [13]. While these data are compelling, a meta-analysis performed in 2014 underscored some of the issues plaguing available data [57], specifically noting that the studies they reviewed had widely variable follow-up timeframes, identified AKI in a variety of ways, and defined outcomes in dissimilar manners. The number of patients lost to follow-up was substantial, which raises concern for ascertainment bias. Additionally, nearly all of the studies available failed to include a non-AKI comparator group.

Since then, the majority of studies have used, at a minimum, one of the available consensus definitions for AKI. While they have continued to employ disparate definitions for long-term renal sequelae, many of these studies have compared outcomes between AKI and non-AKI cohorts. One such study examined hypertension rates among pediatric stem cell transplant survivors. The authors of this study found that while high blood pressure was common across the entire population, AKI [defined as doubling of serum creatinine level, equivalent to Kidney Disease: Improving Global Outcomes (KDIGO) Stage 2 or greater] was associated with a 2.5-fold increased risk for the development of hypertension. Menon et al. examined 100 children who developed nephrotoxic AKI (NTx-AKI) and found impressively high rates of proteinuria (68.5%), hypertension (37.6%), and an eGFR of < 90 mL/min/1.73 $m^2$ (23.4%) [15]. When compared with matched non-AKI controls, those who experienced NTx-AKI had a significantly lower eGFR, more proteinuria, and a higher incidence of hypertension [15]. One of the few studies to use a rigorous definition for both AKI and CKD (eGFR < 60 mL/min/1.73 $m^2$ for longer than 3 months) examined a pediatric heart transplant cohort. While the authors did not find an association between AKI and the subsequent development of CKD, they did find that patients with unrecovered AKI (a proxy for injury severity) were significantly more likely to have CKD (eGFR < 60 mL/min/1.73 $m^2$ for more than 3 months) [47].

Two recently published studies deserve special mention since they represent two of the few truly prospective reports on the subject. The first represents a 5-year follow-up of the Translational Research Investigating Biomarker Endpoints in AKI (TRIBE-AKI) study. This analysis found that hypertension (17%), proteinuria (8%), and an eGFR of < 90 mL/min/1.73 $m^2$ (13%) were common following cardiac surgery. However, these sequelae were not more common among the children who experienced perioperative AKI [18]. In the second study, entitled, "Follow-up Renal Assessment of Injury Long-term after AKI (FRAIL-AKI)", the authors compared renal findings in 51 children 7 years after they had undergone cardiopulmonary bypass. The 31 AKI and 18 non-AKI patients had similar rates of proteinuria and hypertension as well as comparable eGFRs [45]. However, those with AKI did have higher urinary biomarker levels of interleukin-18 and liver-type fatty acid binding protein (L-FABP) than either the non-AKI patients or healthy controls. This result certainly suggests that patients who experience AKI may have subtle evidence of chronic renal injury even in the absence of overt CKD. Interestingly, a subsequently published study did find that cardiac surgery-associated AKI was associated with a greater risk for CKD Stage 2 or greater [46]. In that study,

**Table 1** Pediatric studies examining chronic kidney disease and long-term renal sequelae after acute kidney injury

| Study (first author/ publication year) | Population | *n* | Follow-up (years) | AKI definition | Proteinuria* | Hypertension# | Hyperfiltration+ | eGFR < 90 mL/min/1.73 $m^2$ | eGFR < 60 mL/min/1.73 $m^2$ |
|---|---|---|---|---|---|---|---|---|---|
| Consensus AKI definition applied | | | | | | | | | |
| Cooper DS (2016) [45] | Cardiac surgery | 51 (33 AKI) | 7 | pRIFLE (≥ Stage 1) | 3.9% (a) | 21.2% (c | 0% | 14.3% | |
| Greenberg JH (2016) [18] | Cardiac surgery | 131 (57 AKI) | 5.4 | AKIN (≥ Stage 1) | 6% (a) | 11% (d) | | 0% | 0% |
| Madsen NL (2016) [46] | Cardiac surgery | 382 (127 AKI) | 4.9 | KDIGO (≥ Stage 1) | | | | 12% | |
| Hollander SA (2016) [47] | Cardiac transplant | 76 (54 AKI) | 1 | KDIGO (≥ Stage 1) | | | | | 6% |
| Menon S (2014) [15] | non-ICU | 77 | 0.5 | pRIFLE (≥ Stage 1) | 68.5% | 37.6% | 11.6% | 23.4% | 2.6% |
| Mammen (2012) [13] | PICU | 126 | 1–3 | AKIN (≥ Stage 1) | 9.5% (a) | 3.2% | 8.7% | 38.9% | 0.8% |
| Non-consensus AKI definition applied | | | | | | | | | |
| Mel E (2014) [48] | Cardiac surgery | 25 | 5.1 | Dialysis requirement | 0% | 0% | 36% | 4% | 0% |
| Viaud M (2012) [49] | General hospital | 13 | 16 | Dialysis requirement | | | | 61.5% | 23.1% |
| Hoffmeister PA (2010) [50] | Stem cell transplant | 227 | 16 | Creatinine 2× baseline | | 22% | | | |
| Buysse CM (2008) [51] | Septic shock | 19 | 9.8 | Creatinine > 2× normal | 27.3% | 23.1% | 6.7% | 6.7% | 0% |
| Hingorani S (2007) [52] | Stem cell transplant | 1319 (332 AKI) | NA | Creatinine > 2× baseline | | | | | 32% |
| Slack R (2005) [53] | Septic shock | 12 | 4.2 | Dialysis requirement | 18.2% | 25% | 0% | 25% | 8.3% |
| Askenazi DJ (2005) [14] | General hospital | 29 | 3–5 | Diagnostic code | 27.6% (a) | 20.7% (e) | 31.0% | 13.8% | 13.8% |
| Shaw NJ (1991) [54] | Cardiac surgery | 11 | 1–5 | Dialysis requirement | 18.2% (b) | 0% | | 18.2% | 0% |
| Georgaki HN (1989) [55] | General hospital | 10 | 7–12 | Dialysis requirement | | | | 20% | 0% |

AKI, Acute kidney injury; eGFR, estimated glomerular filtration rate; ICU, intensive care unit; PICU, pediatric intensive care unit; pRIFLE criteria, pediatric Risk, Injury, Failure, Loss of kidney function, End-stage kidney disease; AKIN, Acute Kidney Injury Network; KDIGO, Kidney Disease: Improving Global Outcomes guideline; NA, not available

# Hypertension is defined by a blood pressure (BP) of > 95th percentile, except when defined by taking an antihypertensive agent (c), by BP or self report (d), or by taking antihypertensive or chart documentation (e)

* Proteinuria is defined as a protein-to-creatinine ratio of > 0.2 mg/mg except when defined by an albumin-to-creatinine ratio of > 30 mg/g (a) or by tubular proteinuria identified on gel electrophoresis (b)

+ Hyperfiltration defined as an eGFR >150 mL/min/1.73 $m^2$

the 5-year cumulative incidence of CKD for patients with cardiac surgery-associated AKI was 12% [95% confidence interval (CI) 7–20%], which was significantly higher than the 3% (95% CI 1–5%) seen in those without AKI (adjusted hazard ratio 3.8; 95% CI: 1.4–10.4). While this study was retrospective in nature, it was large and used a consensus definition for AKI and a rigorous definition of CKD.

### Making sense of the data

Taken in total, the best available data in children, when combined with the existing adult findings, demonstrate that chronic renal sequelae are common following episodes of AKI and suggest that AKI may predispose patients to CKD. Many studies have found incident rates of hypertension, proteinuria, and reduced GFR that far exceed those in healthy populations. Additionally, most pediatric studies have found a dose-dependent association between AKI severity and CKD risk similar to that seen in adult studies. That said, several issues have limited our ability to definitively identify a causal relationship. While the vast majority of current studies are using a consensus AKI definition, few are using a rigorous definition of CKD. In many studies, proteinuria, hypertension, eGFR < 90 mL/min/1.73 $m^2$, eGFR < 60 mL/min/1.73 $m^2$, and hyperfiltration are grouped into a composite outcome of "renal dysfunction." Even in those where individual outcomes are evaluated separately, the manner in which they are assessed may differ (i.e., eGFR vs. measured GFR; spot urine sample vs. 24-h collection; casual blood pressure measurement vs. ambulatory blood pressure monitoring). This general lack of specificity and standardization makes interpretation of the available data challenging. Additionally, it is clear that the underlying disease has a tremendous impact on short-term AKI outcomes, and it would stand to reason that this would be true for CKD and other long-term sequelae. The severity of ICU-associated AKI is likely very different than that seen in non-ICU patients; more substantial injury is likely to have greater chronic ramifications for the physiologic reasons described above. This concept is related to that of the differential effect seen between AKI etiologies. It is likely that the direct tubular toxicity of profound nephrotoxic injury has a different impact than that of cardiopulmonary bypass. Given these issues and the limitations surrounding the currently available data, it is not surprising that a conclusive causative link between AKI and CKD has not been identified. What is clear, however, is that a very strong observational signal exists, and evidence suggests that certain factors confer a greater CKD risk than others (Fig. 1).

## Summary and future directions

Available observational data raise significant concerns for chronic kidney injury and disease among AKI survivors. Given the profound consequences associated with undiagnosed and untreated CKD, it is imperative that this relationship be studied more effectively. We suggest that future studies adopt rigorous definitions for AKI, CKD, and renal sequelae (Table 2). While it is reasonable to use any of the recently developed consensus definitions for AKI [pediatric Risk, Injury, Failure, Loss of kidney function, End-stage kidney disease (pRIFLE), AKIN, KDIGO], we recommend that studies use the KDIGO definition when possible [8, 58, 61]. This is the only definition which can be used in both adults and children, and it represents the harmonization of all previously available AKI criteria [58]. We believe it is important to describe individual chronic outcomes (i.e., proteinuria, hypertension, eGFR) separately when appropriate. Certainly, proteinuria or hypertension can be a component of a CKD diagnosis; however, even in the absence of a reduced GFR these outcomes have significance and should be reported if available. Additionally, we agree that the established, consensus definition of CKD should be utilized [62]. CKD may be defined at a GFR of < 60 mL/min/1.73 $m^2$ or at a higher GFR when there is evidence of kidney injury/damage, as long as either criteria is present at least 3 months after the AKI event (Table 2). We also advocate for an additional category which has been previously described as being "at risk" for CKD [13]. At risk for CKD is defined as a GFR which is between 60 and 90 mL/min/1.73 $m^2$ in the absence of signs of kidney damage/injury; this may be particularly useful when no data exist to assess signs of kidney damage or injury beyond eGFR. This is an important cohort to identify and monitor since there is evidence that even mild/moderate CKD is associated with reduced health-related quality of life, poorer neurocognitive function, and cardiovascular morbidity, including left ventricular hypertrophy and elevated carotid intima-media thickness [63–66]. Finally, we recommend avoiding the use of hyperfiltration as a CKD-related outcome because its inclusion may obscure the AKI–CKD relationship, mainly due to the inaccuracies associated with GFR estimating equations and the absence of a consensus definition for hyperfiltration.

While additional, more uniform studies are necessary, we feel that there is sufficient data supporting the association between AKI and CKD that clinical assessment may be warranted in many patients who experience AKI. Currently, no guidelines exist regarding the subset of patients that should be followed, the length and frequency of the follow-up, or the parameters which should be monitored. However, the KIDGO guidelines do suggest that AKI survivors should be re-evaluated 3 months after the event to assess for resolution of AKI, the development of new onset CKD, and (if applicable) progression of pre-existing CKD [58]. Patients who have CKD should be managed according to the appropriate clinical practice parameters; patients who do not yet have CKD may benefit from being considered at higher risk for CKD. This strategy would entail heightened awareness of nephrotoxins, avoidance of additional risk factors, and repeated periodic

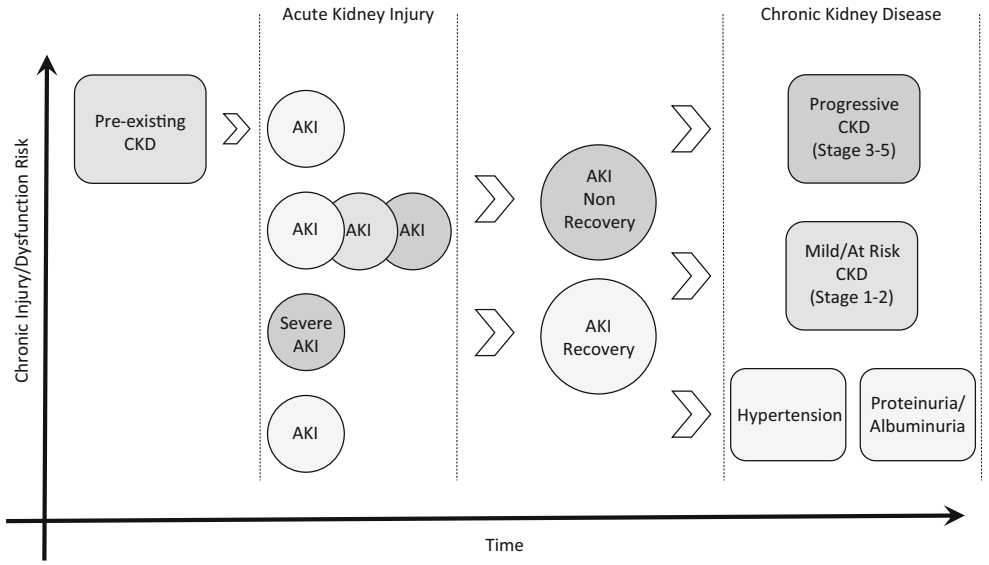


**Fig. 1** Risk for developing chronic kidney disease (CKD) across the spectrum of acute kidney injury (AKI). In the setting of AKI, observational evidence suggests that severe AKI events are more likely to be associated with chronic findings than mild events; so are repeated AKI events, independent of severity. Perhaps the greatest risk for chronic renal disease after AKI is pre-existing CKD. As the events which precipitated AKI abate, renal function begins to recover; non-recovery of AKI has been associated with greater CKD risk. Chronic renal injury has gradation as well. At its most mild form, chronic renal injury may manifest as proteinuria or hypertension. More severe injury may manifest with a mildly reduced glomerular filtration rate, and the most severe injuries may be associated with moderate/severe CKD

assessment [16]. Given the frequency with which we now see AKI in hospitalized children, it may prove challenging operationally to provide follow-up care for all such patients. We may find that it is necessary to risk stratifying the AKI cohort in order to identify a subgroup which is at higher CKD risk and which would benefit more greatly from monitoring. To date, causative risk factors are unknown; however, we may find that we can prioritize follow-up care based on a number

**Table 2** Recommended diagnostic criteria for acute kidney injury and chronic kidney disease-related outcomes

| Data element | Definition |
|---|---|
| AKI | Acute kidney injury according to KDIGO criteria (≥ Stage 1) [58]<br>N.B. Recent data suggest that use of the KDIGO serum creatinine criteria alone underdiagnoses AKI in children and young adults [6]. Clearly there are situations where UOP data are unavailable or uninterpretable; however, when possible, both the serum creatinine and UOP criteria should be applied. |
| Severe AKI | KDIGO AKI Stage ≥2 [58]<br>N.B. As above |
| Hypertension | 1) Receipt of anti-hypertensive medications<br>OR<br>2) Age 1–13 years: BP ≥ 95th percentile<br>Age ≥ 13 years: BP ≥ 130/80 [59, 60]<br>N.B. The strict diagnosis of hypertension requires BP measurement to be performed on three separate occasions. However, in many cases only one BP measurement may be available. These situations should not preclude analysis, and the above parameters should be applied. |
| Proteinuria | 1) Urinary protein/creatinine ratio > 0.2 mg/mg (20 mg/mmol)<br>OR<br>2) < 18 years; 24-h protein excretion >100 mg/m$^2$; ≥ 18 years: 24-h protein excretion >150 mg |
| Microalbuminuria | Urinary albumin/creatinine ratio > 30 mg/g (3 mg/mmol) |
| CKD | GFR < 60 mL/min/1.73 m$^e$ for ≥3 months<br>OR<br>GFR ≥ 60 mL/min/1.73 m$^2$ with evidence of kidney injury or damage (proteinuria, albuminuria, imaging abnormalities, abnormal urinary sediment, biopsy findings, history of renal transplantation) |
| At risk CKD | GFR ≥ 60 but < 90 mL/min/1.73 m$^2$ without additional evidence of renal injury or damage |

UOP, Urine output

of factors, including AKI severity, non-recovery of baseline function, location of event (ICU vs. acute care), urinary biomarker data, or recurrence.

In summary, the association between AKI and CKD is well established. To identify a causal relationship, however, it will be important to apply rigorous and standard definitions for AKI and CKD-related outcomes. It will be even more important to do so within large studies across a variety of pediatric populations which include comparative cohorts without AKI. Given the currently available data, many AKI survivors are likely to benefit from longitudinal follow-up and assessment of renal disease and dysfunction.

## Key summary points

1. Currently available data suggest that chronic renal disease (CKD, hypertension, proteinuria) is common among AKI survivors.
2. AKI survivors who are likely to be at higher risk for the development of CKD and long-term sequelae should receive appropriate investigations which may include nephrology follow-up care, assessment of renal function, urine studies, and blood pressure monitoring.
3. All future studies examining the relationship between AKI and CKD should use consensus definitions for AKI, CKD, and longitudinal renal sequelae.

## Review questions (answers are provided following the reference list)

1. True or false. Chronic renal findings are infrequently found in patients who experience AKI and survive to hospital discharge?
2. Following an episode of AKI, what is the most appropriate time to assess survivors for CKD?

a) 1 week
b) 1 month
c) 3 months
d) 3 years

3. Which of the following should be monitored in a patient who has experienced AKI and is thought to be at high risk for chronic renal disease?

a) Urine protein content
b) Serum creatinine
c) Blood pressure
d) All of the above

4. Which of the following are currently hampering our ability to assess the causal association between AKI and CKD?

a) A lack of studies containing a non-AKI comparator group
b) Inconsistent definitions of AKI
c) The absence of a consensus definition for CKD
d) The infrequency with which AKI is seen in hospitalized patients

5. CKD in children is defined as:

a) Serum creatinine of ≥ 3 mg/dL (265 umol/L)
b) GFR < 60 mL/min/1.73 $m^2$
c) GFR > 180 mL/min/1.73 $m^2$
d) GFR 60–90 mL/min/1.73 $m^2$ with evidence of kidney injury or damage
e) b and d

#### Compliance with ethical standards

**Conflict of interest** The authors do not have any conflicts of interest to declare.

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## Answers

1, False; 2, c; 3, d; 4, a; 5, e