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UNDERSTANDING THE DISEASE

Understanding renal recovery

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The traditional view of recovery following acute kidney injury (AKI) was that patients who successfully overcame the severe illness underlying their AKI would experience a full restoration of their premorbid kidney function. Recent work has suggested that patients who survived an episode of AKI are at ongoing risk of adverse outcomes. These include de novo chronic kidney disease (CKD), progression of pre-existing CKD, end-stage kidney disease (ESRD), and death [1–4]. With a greater appreciation of the fact that AKI survivors often have a challenging clinical course, healthcare providers and researchers must establish practical definitions to cover the full spectrum of post-AKI kidney outcomes.

While ESRD reflects the extreme end of the CKD spectrum and fortunately affects a minority of AKI survivors, progressive non-dialysis requiring CKD is a far more frequent outcome following an episode of AKI. The incidence of progressive CKD in AKI survivors may be underestimated partly because kidney function is not routinely monitored in structured follow-up programs [5]. This is further limited by the existence of variable definitions for kidney recovery. Finally, even when serial assessments of kidney function are available, reliance on creatinine as a marker of glomerular filtration rate (GFR) risks overestimating renal function shortly after an acute illness during which muscle wasting might have occurred. Prowle and co-workers demonstrated that a potential 135% increase in CKD diagnoses when adjusting for the confounding effect of prolonged major illness on the serum creatinine concentration [6].

Data from large registries have shed some light on the risk of CKD following critical illness that was complicated by AKI. In a cohort of 130,134 critically ill patients from the Swedish Intensive Care Register from 2005 to 2011, followed for 1–7 years, the relative risks of de novo CKD and ESRD after an episode of AKI (patients with pre-admission CKD excluded) were 7- and 22-fold higher as compared to patients who did not experience AKI [7]. The incidence of CKD was 6.0% (95% CI 5.1–7.0) at 1 year and 10.5% (95% CI 8.5–13.0) at 5 years, with ESRD occurring in 0.44% (95% CI 0.18–0.24) and 1.8% (95% CI 1.6–1.9) at corresponding time points. This confirms data from prior studies that have demonstrated an association between AKI and subsequent CKD, whereby CKD develops in 20–40% of AKI survivors [8–10].

Numerous factors impact the trajectory of kidney function after an episode of AKI. Prompt recovery of AKI anticipates a lower likelihood of CKD as compared to a slower recovery [11]. In a cohort of 17,000 patients, the authors observed five patterns of recovery following an initial episode of AKI: early reversal, with kidney function sustained to discharge (26.6%); no reversal at all (26.5%); late reversal after day 7 (9.7%); early reversal with relapse/relapses but ultimate recovery (22.5%); and relapse without recovery (14.7%) [11]. Schiffl and Fischer demonstrated that 26% of AKI survivors with non-recovery of kidney function at discharge improved renal function and 10.7% returned to a normalized estimated GFR; all changes took place within the first year [12]. A study of hospitalized patients described a return to baseline creatinine in 92.5%, partial recovery in 7%, and no recovery in 0.6% of patients 3 months after AKI. Patients with RIFLE F had significantly lower rates of recovery ($p < 0.001$) [13].

The Acute Disease Quality Initiative (ADQI) group has developed consensus definitions for renal recovery after AKI (Fig. 1). The new proposed definitions differentiate rapid recovery from delayed recovery and provide a framework for staging the post-AKI/pre-CKD period. Once validated, this proposed scheme could help

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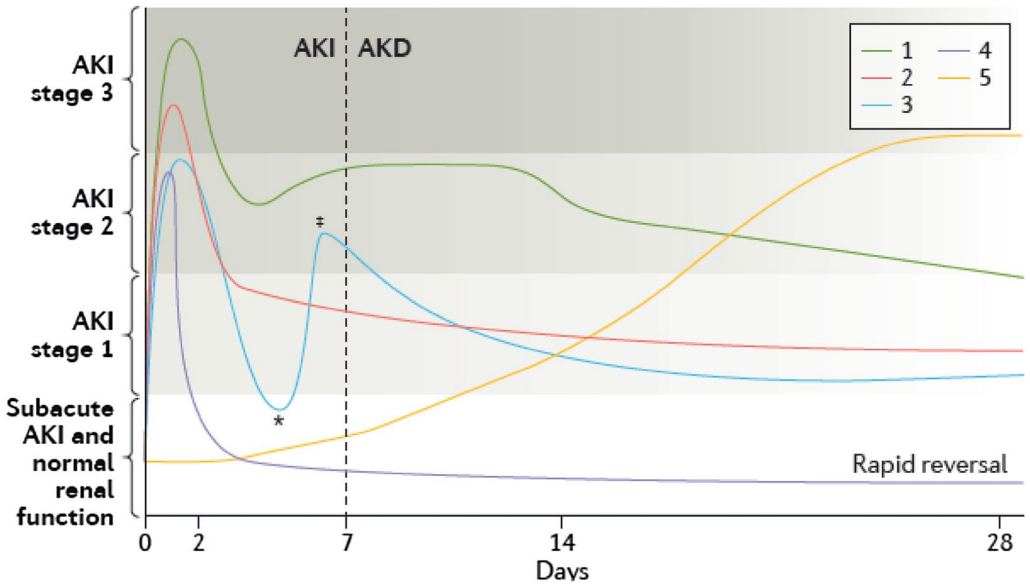

Fig. 1 Hypothetical trajectories of acute kidney disease (AKD). AKD follows on from acute kidney injury (AKI) in those patients who do not fully recover within 7 days. The trajectory of AKD can take many forms largely depending on the severity of the initial AKI episode. Here, a series of hypothetical scenarios representing typical trajectories of the AKI–AKD continuum are depicted. Stage 3 AKI might slowly improve to stage 2 AKI and then progress to AKD (*1*). Stage 1 AKI might progress to stage 3, then improve rapidly to stage 1 AKI before progressing to stage 1 AKD (*2*). An episode of persistent AKI (>48 h) might be followed by a period of sustained reversal (*asterisks*), then a second episode of AKI (*double dagger*) leading to AKD (*3*). Stage 2 AKI might rapidly reverse (*4*). Subacute AKD might occur wherein the first 7 days are marked with slowly worsening renal function that does not technically meet the criteria for AKI, and progress to Stage 3 AKD (*5*). This trajectory can be seen in patients treated with chronic nephrotoxic medications (e.g., with aminoglycosides) Modified from Acute Dialysis Quality Initiative 16; www.adqi.org

standardize the nomenclature of kidney recovery and enable the design of robust trials that examine kidney recovery as an outcome in trials testing various candidate interventions [14].

The optimal follow-up of AKI survivors remains controversial. In a cohort of patients discharged from hospital after an episode of dialysis-requiring AKI, Harel et al. showed that only a minority of patients visited a nephrologist in the weeks following their hospitalization; however, there was an association between visiting a nephrologist and improved survival [15]. Though it might seem intuitive to extend early nephrology follow-up to all survivors of non-dialysis requiring AKI, the high incidence of hospital-associated AKI would make this impracticable. Moreover, many AKI survivors will have a benign clinical course suggesting that more targeted selection of high-risk patients is required. At present, there is limited information to predict adverse outcomes in AKI survivors and a biomarker that could reliably predict such outcomes would be of high value to clinicians. Dedicated clinics for the follow-up of AKI survivors have been established at some centers [16]. An ongoing multicenter pilot trial in Canada is randomizing survivors of AKI (KDIGO stage 2 or higher) to follow-up in a dedicated post-AKI clinic for 1 year as compared to usual care [Clinicaltrials.gov NCT02483039]. As we await the findings of this trial more research is needed to clarify the most impactful components of care delivery in such clinics.

In the meantime we suggest that patients with severe AKI, KDIGO stage 3 and certainly those who received renal replacement therapy, receive targeted follow-up with a nephrologist within 30 days of hospital discharge with further follow-up individualized to the patient's needs. Such follow-up should comprise a reassessment of kidney function/kidney damage, attention to blood pressure control and cardiovascular risk factors, medication reconciliation, and patient education regarding the implications of a prior AKI episode.

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Compliance with ethical standards

Conflicts of interest
None.

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