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Does this patient have acute kidney injury? An AKI checklist

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Imagine receiving a call from a colleague asking for some help evaluating a patient in the emergency department. The patient is 66 years old and apart from some osteoarthritis is in excellent health. She has not seen a physician for several years. She now has fever, cough, and a right lower lobe infiltrate. The doctor has started antibiotics and given some IV fluid but he is concerned about a serum creatinine of 1.3 mg/dl and oliguria (voided only 20 ml in the last 2 h).

The serum creatinine gives her an estimated glomerular filtration rate (eGFR) of 44 ml/min [1]. Thus, although it may be unclear if she has acute kidney injury (AKI) or chronic kidney disease (CKD) or both, what is clear is that she has some form of kidney disease. Your colleague wants advice on how to determine whether this patient has developed or is developing AKI. How can you help?

The modified RIFLE criteria adopted by the Kidney Disease Improving Global Outcomes (KDIGO) workgroup [2] harmonize pediatric and adult criteria and include both relative and absolute changes in serum creatinine as well as criteria for urine output. However, as explained in the KDIGO guideline, AKI remains a clinical diagnosis. The purpose of the guideline is simply to standardize the objective criteria, but clinical judgment is still required to apply such criteria to a patient. For example, a patient with oliguria for 5 h and 59 min does not suddenly "develop AKI" 1 min later. Similarly, in a patient receiving high-volume fluid resuscitation, the serum creatinine will not reflect acute changes in GFR the same way it will in other patients. Clinicians are not just free to use their judgment in the diagnosis of AKI, they are required to. Large epidemiological studies of AKI may misclassify some patients in one direction or another but overall results will not change; conversely, misdiagnosing a single patient may have significant clinical implications for that patient. To help clinicians make the correct diagnosis, a checklist may be helpful.

AKI checklist

Table 1 provides a list of factors that should be considered when approaching the diagnosis of AKI. AKI is extremely common, especially among the critically ill [3]. Often, this list will be superfluous because it is obvious that a patient does or does not have AKI. On the other hand, in difficult cases such as the one posed here, this checklist may prove valuable. However, each user will need to decide how much weight to give to each factor, in

Table 1 The acute kidney injury checklist

	AKI More Likely	AKI Less Likely
Clinical Context		
Susceptible populations Volume depletion, Female, Black, CKD, Chronic diseases (heart, lung, liver), Diabetes mellitus, Cancer, Anemia, Over age 65	✓✓	
No susceptibilities		
Exposures *Sepsis, Critical illness, Circulatory shock, Burns,* *Trauma, Cardiac surgery (especially with CPB),* *Major noncardiac surgery, Nephrotoxic drugs,* *Radiocontrast agents, Poisonous plants and animals*	✓	
No exposures		
Alternative Diagnosis[a]		
For oliguria Dehydration, obstruction, retention		✓
For increased serum creatinine Endogenous chromogens (acetone, bilirubin) Medications (e.g., trimethoprim and cimetidine)		
AKI Criteria[b] [2]		
Serum creatinine increase ≥ 0.3mg /48h		
1.5x reference	✓	
Urine output < 0.5ml/kg/h for ≥ 6h		
Both serum creatinine and UO criteria		
Confirmatory Data		
Active urine sediment		
Serum creatinine changing (up or down)		
stable		
Biomarkers[c]		
[TIMP-2]•[IGFBP7] ≤ 0.3 $(ng/ml)^2/1000$		
>2.0 $(ng/ml)^2/1000$		
NGAL (serum or plasma) Low		
High		
Multiple markers Negative		
Positive		

Shading indicates the column that applies to each row. *Check marks* indicate conditions applicable to the case discussed

AKI acute kidney injury, *CKD* chronic kidney disease, *CPB* cardiopulmonary bypass. *NGAL* neutrophil gelatinase-associated lipocalin, *TIMP-2* tissue inhibitor of metalloproteinase 2, *IGFBP7* insulin-like growth factor binding protein 7

[a] Alternative diagnoses or explanations for oliguria or azotemia do not preclude AKI, indeed dehydration or obstruction may cause AKI if untreated

[b] Minimum criteria for AKI include an increase in SCr by ≥0.3 mg/dl (>26.5 μmol/l) observed within 48 h; or an increase in SCr to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or urine volume <0.5 ml/kg/h for 6 h

[c] Urinary [TIMP-2]·[IGFBP7] >0.3 $(ng/ml)^2/1000$ is associated with a risk for AKI of 27 % in the next 12 h in patients admitted to the ICU with either respiratory or circulatory failure, a relative risk of 7.2 compared to patients below this cutoff; this risk increases to 62 % or a relative risk of 16.8 when above 2.0 [16]. Cut offs for serum or plasma NGAL have not been standardized. While most studies have not found evidence that available biomarkers add much overall when used together, positive predictive value does increase when multiple markers are positive. Finally, for many of these factors (urine output, serum creatinine, [TIMP-2]·[IGFBP7]) the greater the abnormality the more likely AKI becomes

part depending on how much evidence exists for that factor. Nonetheless, the more factors in the "AKI more likely" column, the more likely AKI will be. We have added "check marks" to the table where they apply to this case.

Our patient is over 65 years of age and is female—both may increase the risk for AKI [4]. She has pneumonia and even non-severe pneumonia is commonly associated with AKI [5]. Might she have been taking over the counter NSAIDs for her arthritis as well? The serum creatinine elevation is extremely important here because either this is biochemical evidence of AKI or it represents CKD, which is an important risk factor for AKI. Similarly, while she has only been under medical observation for 2 h, the oliguria makes AKI more likely. These clinical variables are considered in the conceptual framework presented by Goldstein and Chawla [6, 7] to describe the clinical phenotype that is present before AKI can usually be diagnosed.

Conversely, this patient may be dehydrated and while dehydration may increase the risk for AKI, it may also result in oliguria without injury. Similarly partial urinary tract obstruction or simply urinary retention in a spontaneously voiding patient may lead to oliguria. When promptly corrected, these conditions may not lead to AKI. Careful physical examination is mandatory. Examination of the urine is also important as active sediment (e.g., cells, casts) can help clarify the diagnosis.

Serum creatinine must also be evaluated critically. Colorimetric assays like the Jaffe reaction can be affected by endogenous chromogens such as acetone or bilirubin. Some medications, e.g., trimethoprim and cimetidine, may also reduce creatinine secretion [8]. However, the most important alternate explanation for the abnormal serum creatinine is CKD. Workup for possible CKD should include assessment of risk factors, urinalysis for protein, red and white cells and, if necessary, imaging tests [9]. Reduced kidney size, for example, would provide strong evidence of CKD. However, the presence of CKD does not exclude AKI and, in fact, probably increases the risk. Furthermore, this level of CKD would not cause oliguria by itself. In ICU patients, the combination of mild oliguria and mild azotemia has been shown to be as strong a predictor of adverse outcomes or worse than more severe abnormalities in urine output or serum creatinine alone [10].

Baseline serum creatinine

The reference value for serum creatinine is the value used to judge acute changes. Ideally the reference creatinine is a stable premorbid "baseline" value. Unfortunately, patients rarely have their creatinine checked just before developing AKI. If a patient presents with a clinical history compatible with AKI and an abnormal creatinine with no evidence of CKD by history or examination, the best reference creatinine may be a derived one. Since a normal creatinine based on demographics (especially age, race and sex) may vary by more than twofold, it is not appropriate to use a single normal value for all patients. Instead, the patient's demographics can be fitted to the an estimated GFR equation such as the modification of diet in renal disease (MDRD) equation using a GFR of 75 mL/min/1.73 m^2 [11, 12]. This approach would have assigned our patient a reference creatinine of 0.8 mg/dL.

Renal biomarkers

Serum and urine renal biomarkers can help both in risk assessment for AKI and in prognostication [13]. For example, if our patient had very low or very high renal biomarker results, we could use these data to help guide our assessment. Note, biomarker tests do not have to be perfect to add value to our clinical evaluation [14]. Especially in challenging cases such as this, they may well prove very useful. Furthermore, there may be important outcome differences across biomarker positive and negative AKI phenotypes [15].

Conclusions

Weighing the various considerations presented in Table 1, we conclude that this patient likely has AKI. However, this is a provisional diagnosis and we as clinicians reserve the right to change our diagnosis as more information becomes available; we recommend that you do the same.

Compliance with ethical standards

Conflicts of interest JAK has received consulting fees and grant support from Alere, Astute Medical, Fresenius, and Baxter. RB has received consulting fees and grant support from Baxter and consulting fees from B Braun. CR has received consulting fees from Astute Medical and speaker honoraria from General Electric, Bioporto, and Asahi Medical.

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