VIEWPOINT

Optimizing Postoperative Acute Kidney Injury Monitoring Using a Urine Biochemical Approach—Time to Bring More Dynamism to Serum Creatinine Evaluation!

Alexandre T Maciel

Abstract

Glomerular filtration rate (GFR) impairment is common both intraoperatively and in the early postoperative period of major surgeries, even elective ones. In some patients, such impairment is subtle and short-lasting, not even detected by increases in serum creatinine (sCr) and, consequently, not of sufficient magnitude to fulfill acute kidney injury (AKI) sCr-based criteria. In patients with a GFR decrease of greater magnitude, significant increases in sCr will occur but, unfortunately, usually at a late time in its progression. Both urinary and serum biomarkers have been proposed to be capable of anticipating AKI development but they are not widely available nor cost-effective in most centers. In this context, a urine biochemical approach using urinary sodium concentration (NaU) and the fractional excretion of potassium (FeK) has been proposed, anticipating the level of renal microcirculatory stress and decreases in GFR. An educational postoperative case example is presented highlighting the relevance that this approach can have in the correct interpretation of sCr values, bringing more dynamism to renal function monitoring.

Keywords: Elective surgery, Fractional excretion of potassium, Monitoring, Postoperative acute kidney injury, Urine biochemistry, Urinary sodium concentration.

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Highlights

The current approach to acute kidney injury (AKI) monitoring is far from adequate for situations of rapid changes in glomerular filtration rate (GFR). Our group proposes a different viewpoint and an alternative approach (the urine biochemical approach) that can be more dynamic and on-time in comparison to serum creatinine (sCr) and urine output (UO) assessment.

Introduction

Serum creatinine has long been used as a marker of renal function. It is practical, widely available, and usually not as expensive as other more promising biomarkers of AKI.[1] However, it is common sense that there is a delay between changes in GFR and its repercussions in sCr. Yet, significant initial decreases in GFR may occur that are "blinded" to sCr.

Elective major surgical procedures are a frequent situation in which abrupt changes in GFR may occur and, consequently, an interesting scenario to study potential, more dynamic markers of acute GFR variations and AKI. The urinary creatinine concentration has been proposed to be a relevant component of creatinine excretion (excCr) and a missing link between sCr and UO.[2] Using a very simple rationale, sCr is used as a surrogate of excCr, inferring that increases in sCr represent a jeopardized excCr (considering a stable creatinine production, an even harder variable to be clinically monitored). Instead of a surrogate, increases in sCr might actually be seen as a consequence of a decreasing urinary excCr. And if it is a consequence, it occurs posteriorly to the phenomenon itself, and the phenomenon should be the focus of an early monitoring, not its consequence (Fig. 1). This is also true for the opposite process: decreases in sCr are delayed in comparison to an improving excCr and AKI resolution. Therefore, the question is: Is it better to monitor sCr (consequence) or urinary excCr (cause) while trying to detect early changes in GFR (Fig. 1)?

It has been previously demonstrated that urinary electrolyte composition begins to change 1–2 days before sCr-based AKI diagnosis.[3,4] It has been similarly described that these early urinary changes also occur in cases of very transient AKI, in which very brief, short-lasting (less than 24 hours) elevations in sCr occur postoperatively in cardiac surgical patients.[5] The hypothesis was that urinary biochemical changes were a reflection of early decreases in GFR starting in the "blinded" zone of sCr monitoring.

Both the urinary sodium concentration (NaU) as well as the fractional excretion of potassium (FeK) were considered to be relevant parameters to be monitored and the magnitude of their changes was important in terms of both AKI severity and duration.[4,6] The fractional excretion of potassium is indeed the "future index of sCr,"[7] indicating in which direction sCr is expected to move in the subsequent hours. Similarly to the financial market, being a "future index" is not a

Imed Group Research Department, Adult ICU, Hospital São Camilo Pompéia Unit, São Paulo, Brazil

Corresponding Author: Alexandre T Maciel, Head, Imed Group Research Department, Adult ICU, Hospital São Camilo Pompéia Unit, São Paulo, Brazil, Phone: +55 11993430960, e-mail: alexandre.toledo@imedgroup.com.br

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Table 1: Sequential values of relevant blood and urinary parameters in the first 48 postoperative hours

Postoperative values	*ICU admission*	*6 hours*	*24 hours*	*30 hours*	*48 hours*
Serum urea (mg/dL)	19	23	–	38	29
sCr (mg/dL)	0.7	0.8	–	1.2	0.9
sK^+ (mEq/L)	4.1	4.7	–	4.4	4.2
NaU (mEq/L)	93	60	19	21	53
KU (mEq/L)	42	154	180	84	8
CrU (mg/dL)	37	153	190	206	23
KU/CrU	1.13	1.01	0.95	0.41	0.35
FeK (%)	19.4	17.1	–	11.1	7.5
CRP (mg/L)	13.8	28.0	–	53.6	79.5

CRP, C-reactive protein; CrU, urinary creatinine concentration; FeK, fractional excretion of potassium; KU, urinary potassium concentration; KU/CrU, ratio between urinary potassium and creatinine concentrations; NaU, urinary sodium concentration; sCr, serum creatinine; sK^+, serum potassium

certainty of the future behavior but it points out the direction in case the current scenario is not actively modified. In other words, FeK keeps a tight inverse correlation with creatinine clearance.[8] This implies that decreases in FeK are also expected to precede decreases in sCr in AKI resolution, at least in less severe AKI cases.

Since most intensivists are not familiar with urine biochemistry monitoring and its relevance for a more dynamic and on-time evaluation of renal function, we decided to describe a postoperative case in which this "extra" monitoring tool was able to change the way sCr values were interpreted.

Case Description and Discussion

In order to describe a typical case in which urine electrolytes assessment was useful in clinical practice, we report the postoperative evolution of a 71-year-old, 60 kg, 162 cm height female patient with only hypertension and dyslipidemia as comorbidities, admitted to our ICU after an elective video-laparoscopic rectosigmoidectomy (the patient has previously given her written informed consent).

The procedure had no complications. She received 750 mL of crystalloids and was admitted to the ICU extubated and hemodynamically stable. Shortly after her arrival, both blood and urine samples were collected. In our service, to prevent excessive manipulation of the indwelling urinary catheter for sequential spot urine sample collection (10–20 mL), urine was removed from the bottom of the collecting bag as usual for quantification and disposal. All urine volume in the bag coming from the operating room was previously discarded (~300 mL) so that we ensure that the sample represented the present moment. All relevant lab results are shown in Table 1.

Taking into account only intraoperative UO and serum urea and creatinine, the patient was considered to have normal renal function at ICU admission (Table 1). However, as previously stated, these classic parameters for AKI monitoring are late in detecting subtle decreases in GFR (Fig. 1). The first additional monitoring tool that seems promising is FeK, which is around 10–12% in normal conditions.[9] Albeit the sCr value of 0.7 mg/dL, this patient had an initial FeK value of 19.4%, indicating a decreased excCr (Fig. 2) and, consequently, a significant potential for a sCr increase soon. It is important to highlight that sCr and serum K^+ are part of the FeK formula. Since they were both normal (Table 1), the other element of the formula (KU/CrU) is actually responsible for the increased value of FeK. This ratio is usually around 0.40–0.50 (mEq/L for KU and mg/dL for CrU).[10] Nonetheless, in our experience, a KU/CrU value close

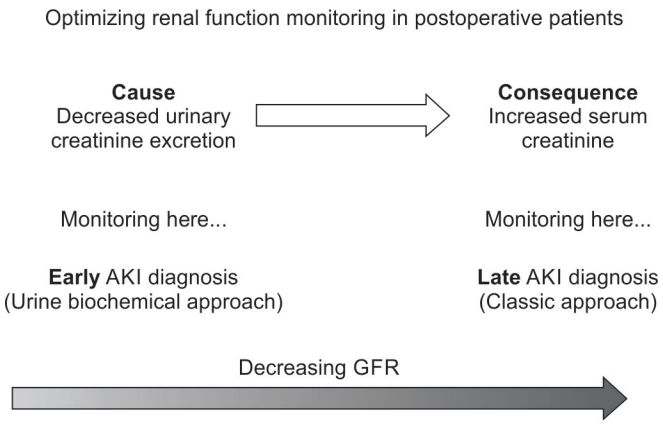
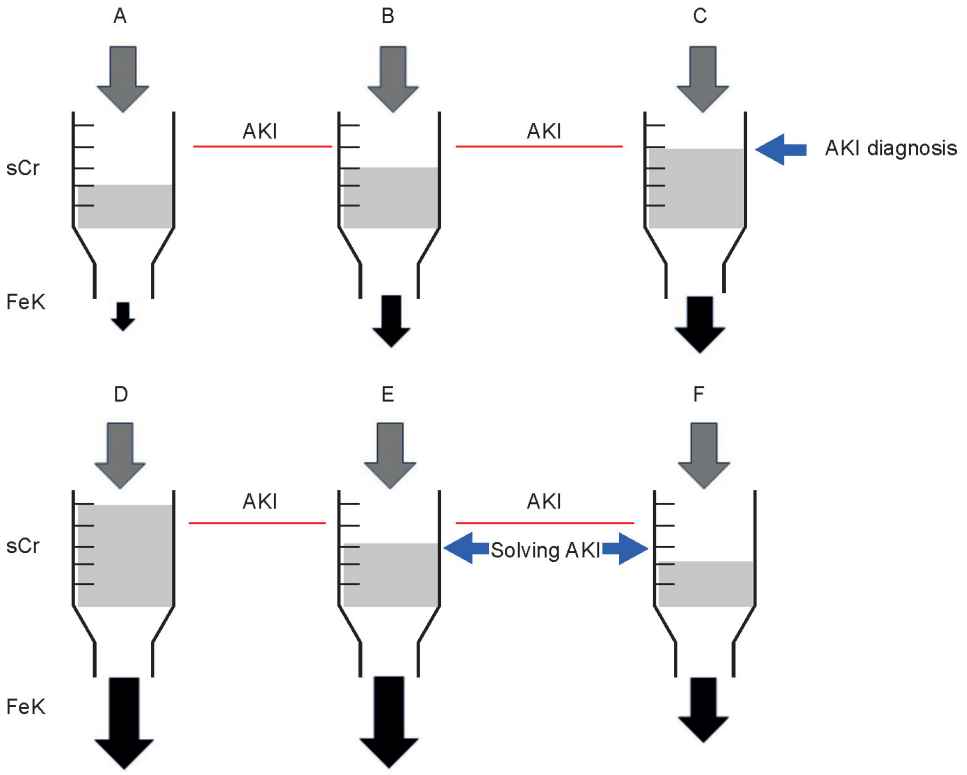


Fig. 1: An alternative approach for acute kidney injury monitoring considering urinary biochemical changes preceding increases in serum creatinine
AKI, acute kidney injury; GFR, glomerular filtration rate

to 1.0 is not infrequent at ICU admission in postoperative patients and may suggest some degree of renal microcirculatory stress (RMS) and GFR impairment. The KU/CrU ratio can be seen as the proportion between urinary flow and creatinine concentration.[10] A high value means an imbalance between these two variables, which means an inadequate excCr (low creatinine concentration in proportion to urinary flow). This is why a high FeK points toward a subsequent increase in sCr, as has progressively occurred with this patient (Table 1).

The subsequent measurements also brought relevant information. The patient remained clinically stable. Six hours after ICU admission, the increase in sCr was subtle and FeK remained at high levels but already decreasing (Table 1 and Fig. 2). Again, the KU/CrU ratio was primarily responsible for changes in FeK. A possible interpretation for this data is that excCr was already increasing but it was not able to prevent additional increases in sCr, although it has possibly attenuated such increase and the maximum value reached by sCr (unfortunately a 24 hours sCr value was not collected so we considered the 30 hours sCr value as the peak value). In our point of view, gradual decreases in FeK are a hallmark of renal recovery. From an alternative perspective, this patient had a jeopardized renal function at ICU admission which gradually recovered in the subsequent hours but not fast enough to prevent increases in sCr (Fig. 2). The classic interpretation would be a normal renal function



Figs 2A to F: Schematic representation of postoperative KDIGO grade I AKI development of the described patient. Systemic creatinine production (dark gray arrows) was considered constant and stable during the observation period. (A) At ICU admission, a low sCr level was considered to be a synonym of preserved renal function; However, a simultaneous high FeK level (see Table 1 for values) alerted for the fact that urinary creatinine excretion (black arrow) was decreased. (B to D) As a result of this decrease, sCr began to increase in the subsequent measurements. In parallel with increasing sCr, FeK was already decreasing, suggesting a progressive recovery of urinary creatinine excretion (increasing black arrow sizes); At (E) and (F), a decreased FeK (increased urinary creatinine excretion) reestablished equilibrium between creatinine production and excretion, leading to a decreasing sCr and solving AKI. It is noteworthy that an improving creatinine excretion might not be fast enough to prevent significant increases in sCr but it has probably attenuated the magnitude of the increase and, consequently, AKI severity and duration
AKI, acute kidney injury; FeK, fractional excretion of potassium; KDIGO, Kidney Disease: Improving Global Outcomes; sCr, serum creatinine

at ICU admission which gradually worsened leading to a subsequent sCr increase and AKI diagnosis. Interestingly, the FeK approach to renal function monitoring changes the way and the moment that AKI is actually diagnosed or at least suspected, allowing in some occasions an anticipated intervention by the intensivist to revert the ongoing renal dysfunction. If FeK rapidly decreases, this usually prevents or at least mitigates increases in sCr. This is a common finding for patients that have stable and normal sCr values postoperatively: urine biochemistry is able to diagnose a RMS, that usually reverts without increases in sCr.[11] Patients with FeK below 10–12% in all measurements are actually those that GFR was not even threatened by the surgical procedure.

Abrupt decreases in NaU were not surprising in the present case, being a common and early characteristic of systemic inflammation-induced AKI[12] as well as increases in serum C-reactive protein (Table 1). As previously demonstrated in cases of transient AKI,[3,5] NaU value has decreased to very low levels and then raised very rapidly in this patient. The magnitude of the fall in NaU value has probably a correlation with the chance of AKI development. It is important to emphasize that decreases in NaU to very low levels must not be viewed mandatorily as a "pre-renal" AKI and unequivocal hypovolemia or low renal perfusion.[13,14] Decreasing NaU values may occur even in the presence of high renal blood flow[15] as a marker of RMS and activated sodium-retaining mechanisms. In the present case, there were no signs of hypovolemia and no fluid challenge was made, with spontaneous return of NaU values to higher levels along the time.

Predicting postoperative AKI diagnosis based solely on decreased intraoperative UO is a matter of controversy.[16] Some authors believe that some degree of decreased UO is physiological and suggested that a cutoff value of 0.3 mL/kg/h is more appropriate than the classic 0.5 mL/kg/h.[17] In fact, many postoperative patients with oliguria do not progress to increased sCr values ("permissive oliguria"). The present patient had an informed intraoperative UO greater than 1 mL/kg/h, decreasing to 0.4 mL/kg/h in her first postoperative day and increasing again to 0.8 mL/kg/h in her second postoperative day (we do not have the values separated by each interval presented in Table 1). We believe that urinary biochemical composition may distinguish the patients with "permissive oliguria." When oliguria is present but FeK value is normal, there is no impairment in urinary excCr. This is because urinary creatinine concentration has proportionally increased in a lower urine volume, keeping stable the mass of excreted creatinine per unit of time. The KU value is inversely correlated with UO,[10] so its value usually increases in the presence of oliguria. This has actually happened with the described patient (Table 1). Normal KU value is usually around 40 to 50 mEq/L, but it has progressively increased until reaches 180 mEq/L after 24 hours, reflecting the decreased UO of our patient. In order

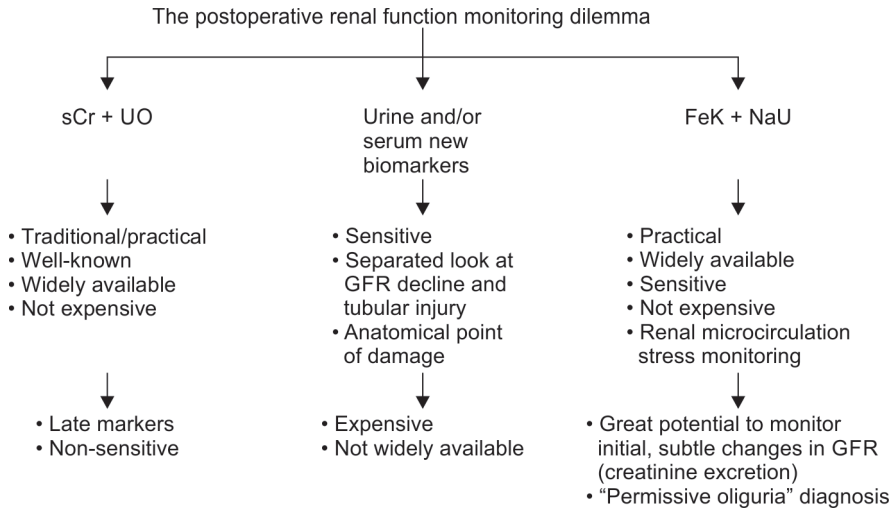


Fig. 3: Different approaches to postoperative renal function monitoring. The urine biochemical approach seems to bring relevant advantages over the classic approach and the expensive and usually unavailable biomarkers approach
FeK, fractional excretion of potassium; GFR, glomerular filtration rate; NaU, urinary sodium concentration; sCr, serum creatinine; UO, urine output

to be considered a case of postoperative "permissive oliguria" our patient would have to have a urinary creatinine concentration that kept the KU/CrU ratio around 0.5, i.e., around 360 mg/dL, which is a very high urinary creatinine concentration value, hard to be achieved. In this case, increases in sCr would not be expected to occur even with oliguria.

Inevitably, there are also some limitations and drawbacks while interpreting urinary biochemical parameters. First, diuretic use will certainly interfere with the values, making them to some extent "artificial" for some hours after its administration,[12] even though the magnitude of urinary biochemical changes after diuretic administration has been demonstrated to have prognostic implications in some cases.[18,19] Other medications such as angiotensin-receptor blockers, angiotensin-converting enzyme inhibitors, and anti-inflammatory drugs may also theoretically interfere with urinary biochemical composition and interpretation, although, in our experience, to a lesser extent. None of these medications were given to our patient during the monitoring time. Another important variable to be considered is the volume and composition of the fluids administered, especially in surgeries in which large volumes are infused. As a general rule, surgical patients receive a very high sodium load and this is the reason why, in the absence of RMS, NaU concentration values higher than their equivalent in the blood are frequently observed.[20] Spontaneous high natriuresis can be viewed as a good prognostic marker in critically ill patients and postoperative patients.[20]

Conclusion

The present case is an interesting example of the dynamism that urine biochemistry evaluation can bring to postoperative renal function monitoring, confirming the sCr delay for both AKI diagnosis and recovery. As a very accessible tool in most centers, we believe that it is time to incorporate the NaU + FeK approach and its usefulness in daily ICU practice (Fig. 3).

Orcid

Alexandre T Maciel https://orcid.org/0000-0001-6043-0967

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