

# Association between Urinary Potassium Excretion and Acute Kidney Injury in Critically Ill Patients

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## ABSTRACT

**Introduction:** Acute kidney injury (AKI) is defined in terms of serum creatinine (SrCr) and urine output (UO). AKI occurs in 25% of critically ill patients, which increases the risk of morbidity and mortality. Early diagnosis of AKI is challenging, as utility of biomarkers is limited. This study is the first of its kind to estimate urinary potassium (UrK) excretion and its association with AKI in an Indian intensive care unit (ICU).

**Aims and objectives:** To study the association between UrK excretion and its ability to predict AKI in ICU patients.

**Material and methods:** During this prospective observational study, the patient's urinary indices and renal function tests were measured on day 1 of the ICU admission. UrK excretion and creatinine clearance (CrCl) were calculated from a 2-hour morning urine sample. Association between 2-hour UrK excretion and calculated CrCl and their ability to predict AKI in the subsequent 7 days was evaluated by Kidney Disease Improving Global Outcome (KDIGO)-AKI grading.

**Results:** Hundred patients admitted to ICU with a mean age of  $53.59 \pm 15.8$  years were studied. The mean UrK excretion of  $4.39 \pm 2.52$  was correlated linearly with CrCl and has a better prediction to AKI with the area under the receiver-operating characteristic curve value of 0.809 (CI 0.719–0.899), with a significant  $p$ -value ( $p < 0.05$ ). UrK excretion value of 3.49 on day 1 of ICU admission had 87% sensitivity and 74% specificity in predicting AKI. Thirty-one (31%) developed AKI, of which seven (22.58%) required renal replacement therapy (RRT), with 19% of all-cause mortality.

**Conclusion:** Diagnosis of AKI with traditional methods is not promising. UrK excretion correlates well with CrCl, which can be considered as the simplest accessible marker for predicting AKI in ICUs.

**Keywords:** Acute kidney injury, Creatinine clearance, Intensive Care Unit, Urinary potassium.

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## INTRODUCTION

Acute kidney injury (AKI) is one among the majority of admissions toward hospitals and ICUs; the incidence of AKI is around 25% among critically ill patients, which increases the risk of morbidity and mortality.<sup>1</sup> Early diagnosis and monitoring of AKI is challenging, as utility of biomarkers as bedside tools is limited.<sup>2-4</sup> Infections, chemicals, animal and plant toxins, and obstetric complications are the leading causes of AKI in tropical countries.<sup>5</sup>

AKI is defined in terms of a rise in serum creatinine (SrCr) by 0.3 mg/dL within 48 hours; or a rise in SrCr by 1.5 times from baseline, which is known or presumed to have occurred within the prior 7 days; or drop in urine volume up to 0.5 mL/kg/hour for 6 hours.<sup>6</sup>

Diagnosis of AKI is dependent on changes in urine output (UO) and SrCr.<sup>6</sup> To detect AKI with UO as a criterion at ICU admission, took a median of 13 hours [interquartile range (IQR) 7–22 hours; using Risk, Injury, Failure, Loss of kidney function and End stage kidney disease (RIFLE) definition] after admission compared to a median of 24 hours using SrCr as a criterion (IQR 24–48 hours).<sup>7</sup> Both these criteria have their own limitations.<sup>8</sup>

The incidence of AKI among critically ill patients is associated with higher morbidity and mortality, especially in patients receiving renal replacement therapy (RRT).<sup>9,10</sup> AKI prolongs hospital stay, increases costs, and worsens long-term renal function.<sup>11</sup> Approximately 5 to 20% of patients, who survive a hospitalization with RRT, will continue receiving RRT at discharge, and the risk of end-stage renal disease and chronic kidney disease (CKD) rises by three and eight folds, respectively.<sup>12</sup>

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SrCr levels are influenced by many other factors apart from glomerular filtration rate (GFR), like age, gender, muscle mass, muscle metabolism, hydration, and drugs.<sup>13</sup> In patients who are critically ill, there is a surge in volume of distribution leading to a decrease in SrCr levels and delayed AKI diagnosis.<sup>14</sup> In sepsis, there is decreased production or decreased release of creatinine from muscles.<sup>15</sup> Acute changes in GFR do not project onto SrCr, as the equilibrium between production and elimination takes few days duration to occur, thus SrCr underestimates the degree of renal functional loss, especially in the initial 48 hours of an insult.<sup>16</sup>

The quantification of UO may be erroneous without a urinary catheter, which is preferred only in critically ill patients.<sup>17</sup> On average, 33% of patients with diagnosed AKI are nonoliguric.<sup>18</sup>

Nonoliguric states may be seen in almost all types of AKI, including hypotensive, traumatic, postoperative, rhabdomyolysis, and nephrotoxic. In critically ill patients, volume expansion, aggressive fluid resuscitation, high-dose diuretics, and renal vasodilators lead to nonoliguric AKI.<sup>2</sup>

Owing to the reasons quoted above, measurements of SrCr<sub>t</sub> and UO as markers to predict AKI are not reliable in ICUs. Similarly, biomarkers have their own limitations in predicting AKI as they are costly, and no single marker is specific and has slow turnaround time, making the diagnosis of AKI challenging in ICUs.<sup>19</sup>

Urinary indices are another domains being used in the diagnosis of AKI. Urinary biochemistries are being studied extensively in recent times. As these are simple to perform, noninvasive, cost-effective, and available in daily clinical practice, and they have been even studied in sepsis patients for diagnosing AKIs.<sup>2,20</sup>

The human body is *per se* a potassium manufacturer unit. The kidney has an ability to reabsorb potassium from the glomerular filtrate and can secrete actively potassium primarily from H/K-ATPase in the intercalated cells and Na/K-ATPase cells located in the distal convoluted tubule (controlled by aldosterone) and collecting duct to maintain potassium homeostasis. Due to a combination of reduction in GFR and tubular function, a surge in plasma potassium (PIK) concentration is not rare in patients with severe chronic renal failure. Evidence suggests that CKD patients who maintain a reasonable amount of daily urinary potassium (UrK) excretion have a better long-term prognosis than patients with a lower UrK excretion.<sup>21</sup> It is still uncertain whether UrK excretion would be a useful tool in identifying patients who are at risk of AKI in the acute care setting.<sup>19</sup>

This study is the first of its kind done in an Indian ICU to estimate UrK excretion and its association with AKI. The present study was aimed to identify the association between 2-hour UrK excretion and simultaneously calculated creatinine clearance (CrCl) and its role in diagnosing AKI.

## MATERIALS AND METHODS

### Overview

This prospective, observational study was performed under the supervision of the institutional ethical committee in an ICU of South India from August 2019 to February 2020. After explaining the study, an informed, written consent was taken from all the ICU patients or their near ones, who fulfilled the inclusion criteria, for measuring urinary indices and renal function tests to conduct the study.

Patients were categorized as eligible for inclusion into the study if they were of age group between 16 and 85 years and were enrolled in the first 24 hours of the ICU admission with urinary catheter *in situ*.

The patients were excluded from the study, if they received any diuretic in the first 24 hours of ICU admission, had preexisting renal failure, or any form of RRT prior to admission, and those who are anuric on admission.

### Procedure

All patients fulfilling the inclusion criteria were subjected to testing of the urinary indices along with renal function tests on day 1 of ICU admission. The patient's demographic data, baseline acute physiology and chronic health evaluation (APACHE II), and sequential organ failure assessment (SOFA) were also measured. The patient's urine volume was measured between 4 a.m. and 6 a.m. (fixed time daily for uniformity), on the day of ICU admission, and these 2-hour samples were sent for

measuring urinary indices like urinary sodium (UrNa), Urk, and urinary creatinine. The blood was sent for serum electrolytes and renal function tests measured on day 1 during the same time. UrK excretion and CrCl were calculated from this 2-hour urine sample.

UrK excretion was calculated by multiplying the amount of UrK excreted in the 2-hour urinary sample (mmol/L) with the measured 2-hour urinary volume in liters to give mmol of potassium excreted in the 2 hours. CrCl is calculated by formula [Urine creatinine/plasma creatinine (PlCr<sub>t</sub>)] × (Urine volume/Time).

The patients were followed up for the subsequent 7 days for measuring the peak SrCr<sub>t</sub> values and UO, KDIGO-AKI grading, the need for RRT, the vasopressor requirement, the ventilator support, ICU, hospital stay, and the mortality in the enrolled patients were recorded.

### Statistical Analysis

The association between 2-hour UrK excretion and simultaneously calculated CrCl of critically ill patients and their ability to predict AKI in the subsequent 7 days was evaluated by KDIGO-AKI grading (≥ stage 1) were assessed using Microsoft Excel, SPSS.

Discrete variables were expressed as counts and continuous variables as mean ± standard deviation. Pearson's correlation coefficient was used to assess the degree of linear relationship between UrK excretion and the calculated 2-hour CrCl. The area under the receiver-operating characteristic (AUROC) curve was used to assess the ability of UrK excretion (in 2 hours) and calculated 2-hour CrCl and was used to predict the risk of KDIGO-AKI grading (≥ stage 1). A *p*-value of < 0.05 was taken as statistically significant.

## RESULTS

Hundred patients who fulfilled the inclusion criteria were studied; mean age among the study population was 53.59 ± 15.8 years, of which 63 were males and 37 were females with a mean APACHE II and SOFA scores of 11 and 3, respectively. Mean ICU stay of these patients was 5.7 ± 3.5 days.

Mean UrK excretion of 4.39 ± 2.52 was linearly correlated with CrCl and found to have a better prediction for AKI with an AUROC value of 0.809 [95% confidence interval (CI) 0.719–0.899] and with a significant *p*-value (*p* < 0.05). A UrK excretion value of 3.49 had a sensitivity of 87% and specificity of 74% in predicting the risk of AKI in ICU patients (Figs 1 and 2).

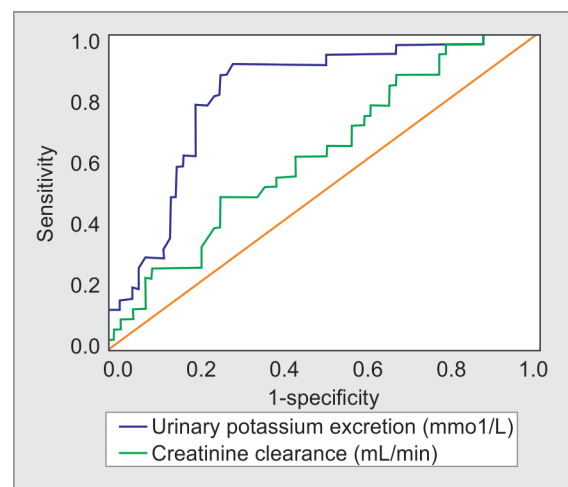
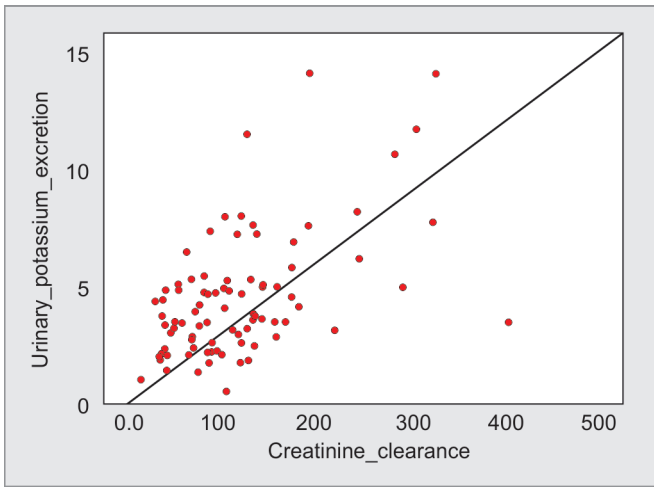
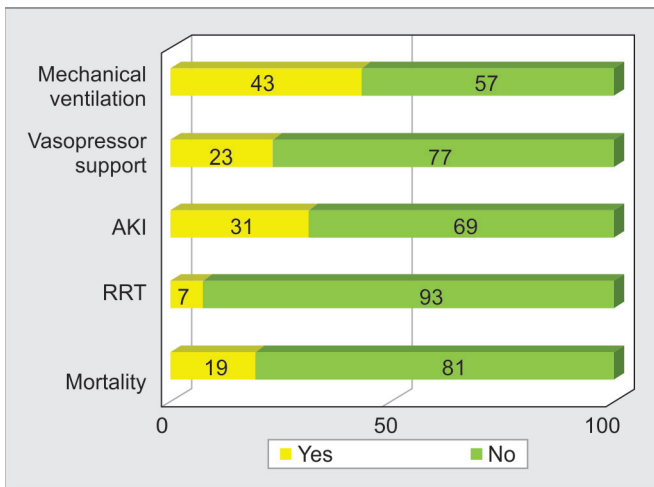


Fig. 1: ROC curve of urinary potassium excretion and creatinine clearance



**Fig. 2:** Scatter plot and Pearson's correlation coefficient between urinary potassium excretion and creatinine clearance



**Fig. 3:** Study parameters distribution among the study population

Thirty-one (31%) out of the total study population developed AKI, of which only seven (22.58%) required RRT support. Forty-three (43%) required ventilator support, and 23 (23%) required vasopressor support, out of the total study population. Nineteen patients (19%) out of the total 100 population expired; among them, 11 (57.89%) died out of 31 who were diagnosed to be having AKI and five (26.32%) died out of seven who required RRT support (Fig. 3).

## DISCUSSION

In hospital, the development of AKI is a common complication of many different disease states, including sepsis, toxic exogenous, endogenous substances, dehydration, acute chronic liver failure, heart failure, and shock due to various causes.<sup>22</sup> In tropical countries, causes can be broadly divided into those caused by infection, chemicals or obstetrics complications, and animal or plant toxins.<sup>5</sup>

Long-term outcomes of AKI secondary to acute tubular necrosis (ATN) have shown increased chances of chronic renal failure as a long-term complication, particularly in the elderly, and an increased mortality in such cases during the acute hospitalization phase.<sup>22</sup>

AKI is characterized by a sudden decline in kidney function and manifested by an increase in SrCr level with or without decreased UO. SrCr value is used as a surrogate marker for estimation of the GFR and aid for the diagnosis of AKI. Drawbacks associated with SrCr as the measure for diagnosis of AKI are that the value of SrCr is influenced by various factors like age, gender, muscle mass, muscle metabolism, hydration status, and medications. Acute changes in the GFR are not often followed by a simultaneous increase in SrCr concentrations. Thus, SrCr underestimates the degree of drop in renal function, especially in the first 48 hours of post-insult period. SrCr is a late biomarker of drop in GFR in diagnosis of AKI. There is a need for some easily assessed blood and urine parameters that are potentially useful in AKI diagnosis and monitoring in low-resource settings.<sup>13,19</sup>

Measuring UO to estimate AKI also has its own limitations. The reasons are being as it is not always feasible to quantify urine in all the patients and over that, 33% of patients at AKI diagnosis are nonoliguric. Researchers have identified that changes in the SrCr and UO do not alarm early changes in intrinsic kidney injury, which may be the most opportune time for pharmacological interventions and management.<sup>23</sup>

Many biomarkers were developed for an early diagnosis of AKI. An ideal biomarker has not been developed, and no single biomarker is self-sufficient in diagnosing AKI.<sup>24</sup> This necessitates sending a battery of biomarkers to diagnose AKI and act on it, which makes the role of biomarkers limited at the bedside, as they are expensive, not widely available, and slow turnaround time, making AKI diagnosis is challenging process.<sup>19</sup>

Numerous studies have tried to look into blood and urinary indices to try to establish their roles in identifying early AKI, prior to a rise in blood urea and SrCr concentration. Increase in SrCr is usually observed in the next 2 days after ICU admission, but low UrNa, and lower fractional excretion of urea (FEUr) and higher fractional excretion of potassium (FEK) values may signal toward a drop in GFR, even at ICU admission.<sup>19</sup> More recently, fractional excretion of sodium (FENa) also has been shown to be a poor indicator in diagnosing AKI in critically ill patients, as it has been extensively used to differentiate the type of AKI.<sup>25,26</sup> Though FENa and FEUr were used in diagnosis of AKI, they gave rise to many controversies and had no diagnostic accuracy. No significant differences were found in FENa and FEUr among patients with and without AKI.<sup>25</sup>

Potassium handling is different from sodium and urea handling in the renal tubules. Potassium ion is exchanged for Na-ion in the distal renal tubules. Hence, potassium secretion is enhanced by sodium reabsorption, which is stimulated by aldosterone, and this is a part of the mechanism for the development of AKI. Potassium is secreted distally in renal tubules that lead to greater and more obvious variations in FEK, compared to FENa and FEUr. Median FEK increases in 2 days preceding the AKI diagnosis, and patients without AKI had stable low FEK values; moreover, patterns of FEK were also not significantly altered by the use of a diuretic.<sup>27</sup>

Hyperkalemia usually occurs in the presence of a very significant fall in GFR, a phenomenon explained by the exponential increase in FEK with a decrease in GFR, until it reaches very low levels (15–20 mL/minutes); hence, results regarding FEK may be in part of an epiphenomenon of impaired GFR.<sup>27</sup>

Theoretically, increased potassium intake and use of diuretics may interfere in the analysis, which is a limitation of our study, but diuretic use did not seem to interfere much in the interpretation of results.<sup>27</sup>

FEK is also related to the severity and duration of AKI. It increases as AKI progress and is possibly a result of drop in GFR and associated aldosterone activation (an attempt to maintain potassium homeostasis). This seems to be more promising than classically measured FENa and FEUr.<sup>27</sup> Preliminary data on FEK indicate that increase in its value may signal to drop in GFR and act as a surrogate marker of a decrease in GFR even before a rise in SrCr.<sup>19,27</sup>

A high FEK [FEK = (UrK × PICr) × 100/(PIK × UrCr)] was used to diagnose AKI, but FEK is mathematically inversely related to the calculated CrCl and thus acting as confounder in the relationship between reduced CrCl and poor renal outcomes.<sup>27</sup>

FEK values were significantly high in patients with AKI from day 1 to 3. FEK was found to have a characteristic pattern and to be more clinically relevant than the other FENa and FEUr. Patients with increased creatinine usually had increased FEK. FEK has high specificity and predictive value.<sup>19</sup> So FEK has been recently described as more valuable tool for AKI diagnosis and monitoring.<sup>27</sup> Most of the patients were diagnosed on day 1, and the majority of the patients with AKI had only a mild increase in SrCr during the observational period.<sup>19</sup>

Single spot urinary biochemistry assessment once daily, usually at the same hour (during the routine blood examination), is useful and more practical than in a 24-hour urine sample. Based on this data, we planned and executed a 2-hour urinary biochemistry study of UrK excretion for predicting AKI.<sup>19</sup>

Spot urine samples provide random information due to the variation in urinary electrolyte concentration over the course of the day; however, in clinical practice, a daily sequential evaluation of these parameters in spot urine samples together with routinely collected blood parameters seems quite useful.<sup>25,28,29</sup>

An ideal test should have less patient discomfort, aid in the management, need to be cost-effective, and should be of major interest; there has always been avidity toward an ideal test.<sup>22</sup>

We initially conducted a pilot study with 35 ICU-admitted patients and found that their UrK excretion (median 4.34, range 2.19–14.06) correlated linearly with CrCl and found to have a better predictor of AKI with AUROC value of 0.765 (95% CI 0.609–0.921), with a significant *p*-value (*p* = 0.032). UrK excretion value of 3.54 had a sensitivity of 85% and specificity of 72% in predicting the risk of AKI. We extended this study to include a total of 100 ICU patients and found that there is a well correlation and linear relationship between the 2-hour UrK excretion and the simultaneously calculated CrCl in diagnosing AKI.

Mean UrK excretion of  $4.39 \pm 2.52$  for 100 patients was linearly correlated with CrCl and found to have a better prediction to AKI with AUROC value of 0.809 (95% CI 0.719–0.899), with a significant *p*-value (*p* < 0.05). UrK excretion value of 3.49 had a sensitivity of 87% and specificity of 74% in predicting the risk of AKI in ICU patients. Thirty-one (31%) out of the total 100 population developed AKI, of which only seven (22.58%) required RRT support.

Similar study was done by Burns and Ho in 2018, where they concluded that UrK excretion correlates linearly with CrCl and using a cutoff point of UrK excretion  $\leq 3.8$  mmol in 2 hours would have a specificity of 85% and sensitivity of 77% in predicting subsequent AKI (KDIGO stage  $\geq 1$ ) within 7 days of testing in critically ill patients without recent diuretic exposure. The major limitation of Burns and Ho study was that it was conducted in a trauma center with younger population and the number of patients included was less. Thus, it lacked the diversified population generally found in an

ICU and also modest cases of sepsis patients, which was the major strength of our study.<sup>30</sup>

This study was conducted in diversified ICU population without a diuretic exposure. UrK excretion as a marker of renal function deserves further large studies, and further studies are also required to assess whether diuretic exposure will affect the UrK excretion, calculated CrCl, and their prediction in AKI in critically ill. This is an alluring line of research that deserves prompt additional studies on larger platforms.

## CONCLUSION

Prediction of AKI has become underdiagnosed and challenging with the use of traditional methods like SrCr and UO. Urinary biomarkers have their own limitations in AKI diagnosis. Urinary biochemistry is gaining new importance in AKI prediction, as they are easy, noninvasive, and cost-effective to perform. UrK excretion is one such kind of test, which correlates well with CrCl and predicts AKI in ICU patients. This 2-hour UrK excretion can be used as the simplest and accessible marker for AKI prediction. Many such newer studies on larger platform are needed in this area to conclude these findings.

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## REFERENCES

- Bouchard J, Acharya A, Cerda J, Maccariello ER, Madarasu RC, Tolwani AJ, et al. A prospective international multicenter study of AKI in the intensive care unit. *Clin J Am Soc Nephrol* 2015;10(8):1324–1331. DOI: 10.2215/CJN.04360514.
- Lima C, Macedo E. Urinary biochemistry in the diagnosis of acute kidney injury. *Dis Markers* 2018;2018:4907024. DOI: 10.1155/2018/4907024.
- Vaidya VS, Ferguson MA, Bonventre JV. Biomarkers of acute kidney injury. *Annu Rev Pharmacol Toxicol* 2008;48:463–493. DOI: 10.1146/annurev.pharmtox.48.113006.094615.
- Hoste E, Kellum J, Katz N, Rosner M, Haase M, Ronco C. Epidemiology of acute kidney injury. *Contrib Nephrol* 2010;1(165):1–8. DOI: 10.1159/000313737.
- Jha V, Parameswaran S. Community-acquired acute kidney injury in tropical countries. *Nat Rev Nephrol* 2013;9(5):278–290. DOI: 10.1038/nrneph.2013.36.
- Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract* 2012;120(4):c179–c184. DOI: 10.1159/000339789.
- Koeze J, Keus F, Dieperink W, van der Horst ICC, Zijlstra JG, van Meurs M. Incidence, timing and outcome of AKI in critically ill patients varies with the definition used and the addition of urine output criteria. *BMC Nephrol* 2017;18(1):70. DOI: 10.1186/s12882-017-0487-8.
- Palevsky PM, Liu KD, Brophy PD, Chawla LS, Parikh CR, Thakar CV, et al. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for acute kidney injury. *Am J Kidney Dis* 2013;61:649–672. DOI: 10.1053/j.ajkd.2013.02.349.
- Brivet FG, Kleinknecht DJ, Loirat P, Landais PJ. Acute renal failure in intensive care units—causes, outcome, and prognostic factors of hospital mortality; a prospective, multicenter study. *French Study Group on Acute Renal Failure. Crit Care Med* 1996;24(2):192–198. DOI: 10.1097/00003246-199602000-00003.



10. Uchino S, Kellum JA, Bellomo R, Doig GS, Morimatsu H, Morgera S, et al. Acute renal failure in critically ill patients: a multinational, multicenter study. *JAMA* 2005;294(7):813–818. DOI: 10.1001/jama.294.7.813.
11. Brandt M-M, Falvo AJ, Rubinfeld IS, Blyden D, Durrani NK, Horst HM. Renal dysfunction in trauma: even a little costs a lot. *J Trauma* 2007;62(6):1362–1364. DOI: 10.1097/TA.0b013e318047983d.
12. Wald R, Quinn RR, Luo J, Li P, Scales DC, Mamdani MM, et al. Chronic dialysis and death among survivors of acute kidney injury requiring dialysis. *JAMA* 2009;302(11):1179–1185. DOI: 10.1001/jama.2009.1322.
13. Brown RS Jr, Lombardero M, Lake JR. Outcome of patients with renal insufficiency undergoing liver or liver-kidney transplantation. *Transplantation* 1996;62(12):1788–1793. DOI: 10.1097/00007890-199612270-00018.
14. Macedo E, Bouchard J, Soroko SH, Chertow GM, Himmelfarb J, Ikizler TA, et al. Fluid accumulation, recognition and staging of acute kidney injury in critically-ill patients. *Crit Care* 2010;14(3):R82. DOI: 10.1186/cc9004.
15. Doi K, Yuen PST, Eisner C, Hu X, Leelahavanichkul A, Schnermann J, et al. Reduced production of creatinine limits its use as marker of kidney injury in sepsis. *J Am Soc Nephrol* 2009;20(6):1217–1221. DOI: 10.1681/ASN.2008060617.
16. Yong K, Dogra G, Boudville N, Pinder M, Lim W. Acute kidney injury: controversies revisited. *Int J Nephrol* 2011;2011:762634. DOI: 10.4061/2011/762634.
17. Fernández-Ruiz M, Calvo B, Vara R, Villar RN, Aguado JM. Inappropriate use of urinary catheters in patients admitted to medical wards in a university hospital. *Enferm Infecc Microbiol Clin* 2013;31(8):523–525. DOI: 10.1016/j.eimc.2013.02.013.
18. Macedo E, Malhotra R, Bouchard J, Wynn SK, Mehta RL. Oliguria is an early predictor of higher mortality in critically ill patients. *Kidney Int* 2011;80(7):760–767. DOI: 10.1038/ki.2011.150.
19. Maciel AT, Salles LD, Vitorio D, on behalf of the Imed Research Group of Investigators. Simple blood and urinary parameters measured at ICU admission may sign for AKI development in the early postoperative period: a retrospective, exploratory study. *Ren Fail* 2016;38(10):1607–1615. DOI: 10.3109/0886022X.2016.1144162.
20. Saha H, Mustonen J, Helin H, Pasternack A. Limited value of the fractional excretion of sodium test in the diagnosis of acute renal failure. *Nephrol Dial Transplant* 1987;2(2):79–82. DOI: 10.1093/oxfordjournals.ndt.a091519.
21. Smyth A, Dunkler D, Gao P, Teo KK, Yusuf S, O'Donnell MJ, et al. The relationship between estimated sodium and potassium excretion and subsequent renal outcomes. *Kidney Int* 2014;86(6):1205–1212. DOI: 10.1038/ki.2014.214.
22. Shankel T, Shankel S. Urinary sodium/potassium ratio in acute kidney injury accurately differentiates prerenal azotemia from acute tubular necrosis. *Acta Med Marisiensis* 2019;65(3):103–110. DOI: 10.2478/amma-2019-0011.
23. Murray PT, Devarajan P, Levey AS, Eckardt KU, Bonventre JV, Lombardi R, et al. A framework and key research questions in AKI diagnosis and staging in different environments. *Clin J Am Soc Nephrol* 2008;3(3):864–868. DOI: 10.2215/CJN.04851107.
24. McIlroy DR, Wagener G, Lee HT, Riou B. Biomarkers of acute kidney injury: an evolving domain. *Anesthesiology* 2010;112(4):998–1004. DOI: 10.1097/ALN.0b013e3181cded3f.
25. Maciel AT, Park M, Macedo E. Physicochemical analysis of blood and urine in the course of acute kidney injury in critically ill patients: a prospective, observational study. *BMC Anesthesiol* 2013;13(1):31. DOI: 10.1186/1471-2253-13-31.
26. Prowle J, Bagshaw SM, Bellomo R. Renal blood flow, fractional excretion of sodium and acute kidney injury: time for a new paradigm? *Curr Opin Crit Care* 2012;18(6):585–592. DOI: 10.1097/MCC.0b013e328358d480.
27. Maciel AT, Park M, Macedo E. Fractional excretion of potassium in the course of acute kidney injury in critically ill patients: potential monitoring tool? *Rev Bras Ter intensiva* 2014;26(2):143–147. DOI: 10.5935/0103-507X.20140021.
28. Toledo Maciel A, Vitorio D, Delphino Salles L. Urine sodium profile in the course of septic acute kidney injury: insights relevant for kidney function monitoring. *Minerva Anesthesiol* 2014;80(4):506–507 PMID: 24226498
29. Maciel AT, Park M, Macedo E. Urinary electrolyte monitoring in critically ill patients: a preliminary observational study. *Rev Bras Ter intensiva* 2012;24(3):236–245 PMID: 23917824.
30. Burns AR, Ho KM. Urinary potassium excretion and its association with acute kidney injury in the intensive care unit. *J Crit Care* 2018;46:58–62. DOI: 10.1016/j.jcrc.2018.04.009.