Published in final edited form as:

J Crit Care. 2013 August ; 28(4): 371–378. doi:10.1016/j.jcrc.2012.10.007.

Urine biochemistry in septic and non-septic acute kidney injury: a prospective observational study^{☆,☆☆}

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Abstract

Purpose—Determine whether there are unique patterns to the urine biochemistry profile in septic compared with non-septic acute kidney injury (AKI) and whether urinary biochemistry predicts worsening AKI, need for renal replacement therapy and mortality.

Materials and Methods—Prospective cohort study of critically ill patients with septic and non-septic AKI, defined by the RIFLE (Risk, Injury, Failure, Loss, End-Stage) criteria. Urine biochemistry parameters were compared between septic and non-septic AKI and were correlated with neutrophil gelatinase-associated lipocalin (NGAL), worsening AKI, renal replacement therapy (RRT), and mortality.

Results—Eighty-three patients were enrolled, 43 (51.8%) with sepsis. RIFLE class was not different between groups ($P = .43$). Urine sodium (UNa) < 20 mmol/L, fractional excretion of sodium (FeNa) $< 1\%$, and fractional excretion of urea (FeU) $< 35\%$ were observed in 25.3%, 57.8%, and 33.7%, respectively. Septic AKI had lower UNa compared with non-septic AKI ($P = .04$). There were no differences in FeNa or FeU between groups. Urine NGAL was higher for FeNa $\geq 1\%$ compared to FeNa $< 1\%$ (177.4 ng/mL [31.9–956.5] vs 48.0 ng/mL [21.1–232.4], $P = .04$). FeNa showed low correlation with urine NGAL ($P = .05$) and plasma NGAL ($P = .14$). There

[☆]**Conflicts of Interest:** Drs Bagshaw, Devarajan and Bellomo have received consulting/speaking fees from Alere Inc. Dr Bellomo has received consulting fees from Abbot Diagnostics Inc.

^{☆☆}**Author contributions:** SMB conceived the study, participated in its design and coordination, performed statistical analysis and drafted the manuscript. MB participated in the data collection and helped draft the manuscript. PD participated in the data collection and helped draft the manuscript. RB conceived the study, participated in its design, data interpretation, and helped to draft the manuscript. All authors read and approved the final manuscript.

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Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.jcrc.2012.10.007>.

was poor correlation between FeU and urine NGAL ($P = .70$) or plasma NGAL ($P = .41$). UNa, FeNa, and FeU showed poor discrimination for worsening AKI, RRT and mortality.

Conclusion—Urine biochemical profiles do not discriminate septic and non-septic AKI. UNa, FeNa, and FeU do not reliably predict biomarker release, worsening AKI, RRT or mortality. These data imply limited utility for these measures in clinical practice in critically ill patients with AKI.

Keywords

Acute kidney injury; Fractional excretion of sodium; Fractional excretion of urea; Neutrophil gelatinase-associated lipocalin; Sepsis; Renal replacement therapy

1. Background

Acute kidney injury (AKI) is a common complication amongst critically ill patients and has an important modifying effect on mortality, kidney recovery, and resource utilization [1–3]. Sepsis is the most common predisposing factor for the development of AKI [2]. Septic AKI patients generally have a poorer prognosis when compared to AKI of non-septic origin [4–6]. Experimental data have suggested there may be important pathophysiologic differences between septic and conventional ischemic/toxic-induced AKI [7–9]. Considering these differences, discriminating septic and non-septic AKI may have clinical relevance and prognostic importance.

The diagnosis of AKI had traditionally relied on absolute or relative changes to conventional laboratory values (ie, serum creatinine) and urine output. These parameters, at selected thresholds, have been integrated into consensus definitions and classification schemes for AKI and were recently applied to the KDIGO Clinical Practice Guideline for AKI [10,11].

In addition, the diagnosis of AKI often integrates an assessment of urine biochemistry and derived indices (ie, urinary sodium [UNa], fractional excretion of sodium [FeNa], fractional secretion of urea [FeU]) as complementary data to further aid in the diagnostic evaluation and discrimination of the etiology of AKI. These urine biochemical tests have traditionally been used as a method to categorize AKI into states of “pre-renal azotemia”, whereby AKI may be milder and reversible (UNa <20 mmol/L; FeNa < 1%; FeU <35%), and “acute tubular necrosis” (ATN), whereby AKI is more severe and established (UNa >40 mmol/L; FeNa >2%; FeU >35%). In addition, no studies have utilized novel biomarkers of kidney “damage” such as neutrophil gelatinase-associated lipocalin (NGAL) to evaluate the diagnostic and prognostic value of urine biochemistry in AKI [12].

Few studies have evaluated and compared the diagnostic and prognostic value of urine biochemistry and derived indices in septic compared with non-septic AKI [13,14]. In fact, two systematic reviews have recently challenged the validity of routine urine biochemistry in septic AKI [15,16]. In addition, no studies have correlated novel biomarkers of kidney “damage”, such as neutrophil gelatinase-associated lipocalin (NGAL), into an evaluation of the diagnostic and prognostic value of urine biochemistry in AKI.

We hypothesized there would be marked variation in the urine biochemical profile and derived indices among critically ill patients with septic compared with non-septic AKI that would preclude diagnostic and prognostic utility. Accordingly, our objectives were to describe: (1) the differences in the urine biochemical profile and derived indices between septic and non-septic AKI; (2) the association between urine biochemical profile and derived indices and the kidney damage biomarker neutrophil gelatinase-associated lipocalin (NGAL); (3) the association between urine biochemical profile and derived indices and worsening AKI; (4) the association between urine biochemical profile and derived indices and need for renal replacement therapy (RRT) and hospital mortality.

2. Methods

2.1. Study design

This was a prospective observational cohort study. The reporting of this study follows the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guideline [17]. The Human Research Ethics Committee at the Austin Hospital in Melbourne, Australia, approved this study prior to commencement.

2.2. Setting and participants

We studied critically ill patients with early AKI and an expected duration of stay in intensive care (ICU) of ≥ 24 hours. A total of 83 eligible patients (43 with septic AKI and 40 with non-septic AKI) were recruited from 2 participating centers in Australia (1 academic tertiary—Austin Hospital; 1 private—Warringal Private Hospital) between December 1, 2005, to November 30, 2006.

Eligible participants fulfilled all the following inclusion criteria: (1) adult (age ≥ 18 years); (2) evidence of early AKI, defined as fulfilling the RIFLE (Risk, Injury, Failure, Loss, End-Stage) category—RISK or higher [10]; and (3) evidence of sepsis (cases) or no sepsis (controls).

Participants were excluded if they had any one or more of the following: (1) prior kidney transplant; (2) end-stage kidney disease, defined as estimated glomerular filtration rate (eGFR) $< 15 \text{ mL min}^{-1} \text{ m}^{-2}$ or chronic dialysis therapy; (3) prior renal replacement therapy (RRT) during index hospitalization; (4) confirmed and/or suspected acute glomerulonephritis, acute interstitial nephritis, renal vasculitis or post-renal etiology for AKI.

2.3. Study definitions

Acute kidney injury (AKI) was defined according to the RIFLE classification scheme based on changes from baseline serum creatinine and/or changes in urine output [10]. We defined early onset AKI as occurring at the time of or within the first 48 hours of admission to ICU. Baseline serum creatinine was defined by the lowest outpatient serum creatinine in the 6 months preceding index hospitalization and eGFR was calculated by the Modification of Diet in Renal Disease equation [18]. Sepsis syndrome was defined according to consensus guidelines [19]. Illness severity was captured by the Acute Physiology and Chronic Health

Evaluation (APACHE) II score [20]. Organ dysfunction/ failure was assessed by the Sequential Organ Failure Assessment (SOFA) score [21]. Vasoactive therapy was defined by the use any vasopressor or inotropic agent at the time of enrollment. Shock was defined as a mean arterial pressure < 60 mmHg and/or a need for vasoactive support plus a blood lactate ≥ 4 mmol/L. Oliguria was defined as a urine output < 400 mL/24 hours. Renal replacement therapy (RRT) encompassed any of form of intermittent hemodialysis or continuous renal replacement; however, all patients started on RRT initially received continuous renal replacement. Worsening AKI was defined as an increase in RIFLE category (ie, from RISK to INJURY, RISK to FAILURE, or INJURY to FAILURE) in the 48 hours after enrollment or RRT initiation, as previously defined [22].

2.4. Study protocol and data sources

Participants were identified by daily surveillance of the two participating sites. Patients were evaluated for the first 2 days after admission for eligibility and if eligible, they were enrolled. Those enrolled were followed daily until ICU discharge for evidence of the outcomes of interest. Consecutive eligible participants underwent a medical record review and documentation of baseline clinical, physiologic and laboratory data. Data was extracted on standardized data forms. Clinical data extracted included: demographics (ie, age, sex, race); comorbid illness (ie, Charlson comorbidity index [23]); and any exposure to diuretics and/or nephrotoxins (ie, radiocontrast media, aminoglycosides; cardiopulmonary bypass, rhabdomyolysis [serum creatine kinase > 1500 U/L]; amphotericin). Data were further extracted on acute physiology and laboratory parameters (ie, hemodynamics; use of mechanical ventilation; use of vasoactive drugs; illness severity score [APACHE II]; organ failure scores [SOFA]) and premorbid and enrollment kidney function. All patients had indwelling urine catheters to continuously monitor hourly urine output. Each patient had blood and urine samples collected at the time of enrollment.

2.5. Urine biochemistry profile and derived indices

Urinary biochemistry included urinary sodium (UNa), potassium, chloride, creatinine (UCr) and urea (UU). Calculated indices included fractional excretion of sodium (FeNa) and fractional excretion of urea (FeU). The FeNa was calculated as $[(\text{UNa}/\text{plasma Na}) / (\text{UCr}/\text{SCr}) \times 100]$. The FeU was calculated as $[(\text{UU}/\text{plasma Urea}) / (\text{UCr}/\text{SCr}) \times 100]$.

2.6. Serum and urine neutrophil gelatinase-associated lipocalin (NGAL)

Blood samples for plasma NGAL were collected in EDTA anticoagulated tubes, centrifuged at 5000 rpm × 5 min, and plasma stored at – 70 °C for batched analysis. We used the Triage NGAL Test (Biosite Inc, San Diego, CA), a point-of-care, fluorescence immunoassay for quantitative measurement of plasma NGAL, as previously described [24]. Urine samples for urine NGAL (uNGAL) testing were centrifuged at 1,500 rpm × 10 min and supernatant stored at – 70°C for batched analysis. uNGAL was measured by a chemiluminescent microparticle assay using the ARCHITECT platform (Abbott Diagnostics Inc, Abbott Park, IL), as previously described [24]. uNGAL was expressed as ng/mg creatinine to standardize and correct for changes in urine concentration. All blood and urine samples were processed directly after collection. All samples were stored and transported frozen until immediately prior to plasma and uNGAL testing.

2.7. Study outcomes

The primary outcome was a comparison of the urine biochemical profile and derived indices between septic and non-septic patients. Secondary outcomes evaluated the association of septic status and urine profiles with: (1) plasma and uNGAL; (2) worsening AKI; and (3) initiation of RRT and hospital mortality.

2.8. Statistical analysis

Normally or near normally distributed variables are reported as means with SDs and compared using the Student's *t* test or one-way repeated measures analysis of variance where appropriate. Non-normally distributed continuous data are reported as medians with either inter-quartile (IQR) or total range and compared using the Mann-Whitney *U* test, Kruskal-Wallis test, or Friedman test where appropriate. Categorical data are reported as proportions and compared using χ^2 or Fisher exact test. Spearman correlation was used to assess the relationship between urine biochemistry and NGAL. Multivariable linear regression was used to adjust for sepsis, age, APACHE II score, loop diuretic exposure, and baseline kidney function. The association of urine biochemistry values and indices and worsening AKI, RRT and mortality were assessed by univariate and multi-variable logistic regression. Covariates initially considered for these analyses included age, baseline kidney function, comorbidity score, APACHE II, sepsis, and surgical status. Model fit was assessed by the Hosmer-Lemeshow goodness-of-fit test, and discrimination was assessed by the area under the receiver operator characteristic curve. $P < .05$ was considered significant. All statistical analysis was performed with STATA version 11.2 (Stata-Corp, College Station, TX).

3. Results

Eighty-three patients were enrolled. The mean (SD) age was 64.3 (16.6) years, 60.2% ($n = 50$) were male, and median (IQR) Charlson comorbidity score was 3 (1-5) points. The mean (SD) APACHE II score was 21.4 (7.6), and 71.1 % ($n = 59$) received both mechanical ventilation and vasoactive support. The median (IQR) duration from ICU admission to enrollment was 1 (0-1) day. Tables 1 and 2 summarize the baseline clinical and kidney-specific characteristics of patients with septic and non-septic AKI.

3.1. Urine biochemistry and derived indices

Table 3 shows the differences in strata of urine biochemical profile and derived indices between septic and non-septic AKI at enrolment. Overall, a $UNa < 20$ mmol/L, $FeNa < 1\%$, and $FeU < 35\%$ were observed in 25.3%, 57.8%, and 33.7%, respectively. Septic AKI was associated with a lower UNa compared with non-septic AKI; however, there was no between group difference across strata of UNa . There were no additional differences in urine biochemistry or derived indices between septic and non-septic patients. Both urine and plasma NGAL were higher in septic compared with non-septic patients ($P = .004$; $P = .02$).

There remained no association between sepsis and UNa ($P = .20$), $FeNa$ ($P = .33$) or FeU ($P = .96$) after adjustment for age, APACHE II score, loop diuretic exposure, and baseline kidney function. Urine NGAL was higher in those with a $FeNa \geq 1\%$ when compared to a $FeNa < 1\%$ (177.4 ng/mL [31.9-956.5] vs 48.0 ng/mL [21.1-232.4], $P = .04$); however, there

was no significant difference when stratified by FeNa 1% to 2% compared to FeNa $\geq 2\%$ (338.1 ng/mL [31.9-1948.8] vs 97.0 ng/mL [33.8-838.0], $P = .67$) (Table 3). However, FeNa showed low correlation with uNGAL (Spearman's $\rho = 0.21$; $P = .05$) and plasma NGAL (Spearman's $\rho = 0.22$; $P = .14$), respectively. There was no significant correlation between FeU and uNGAL (Spearman's $\rho = 0.04$; $P = .70$) or plasma NGAL (Spearman's $\rho = -0.12$; $P = .41$) (Supplementary Figures).

3.2. Clinical outcomes

Worsening AKI occurred in 20 patients (24.1%). Of patients with worsening AKI, 7 (8.4%) transitioned from RISK to INJURY, 3 (3.6%) from RISK to FAILURE, and 5 (6.0%) from INJURY to FAILURE, respectively.

There was no significant association between strata of UNa ($P = .82$), FeNa ($P = .45$), and FeU ($P = .58$) and worsening AKI. (Table 4) The discrimination of worsening AKI was poor for all strata of UNa, FeNa, and FeU (Table 5).

Overall, 13 patients received RRT (15.7%) and there was similarly no association with UNa ($P = .47$); FeNa ($P = .44$) or the FeU ($P = .80$). In-hospital death occurred in 25 patients (30.1%). There was no association with UNa ($P = .34$), FeNa ($P = .29$) or the FeU ($P = .51$).

4. Discussion

4.1. Statement of key findings

We conducted a prospective cohort study comparing the urine biochemistry profile and derived indices in critically ill patients with septic and non-septic AKI and their association with kidney-injury specific biomarkers, worsening AKI, need for RRT initiation, and in-hospital death. We found that UNa, FeNa, and FeU at the time of presentation did not reliably predict whether AKI would worsen or RRT or in-hospital death would occur. In addition, despite one third of patients have more advanced AKI at presentation (RIFLE category INJURY or FAILURE), a significant proportion had a UNa < 20 mmol/L; close to half had a FeNa $< 1\%$ and a third had a FeU $< 35\%$. These data imply little diagnostic and predictive value for conventional urine biochemistry and derived indices in critically ill patients with AKI. Finally, biochemical urine tests, specifically FeNa, had relatively poor correlation with urine or plasma NGAL.

4.2. Strengths and limitations

Our study has several strengths. It provides prospective information on routinely performed urine biochemistry for patients with septic AKI compared with other forms of AKI. It also reports novel information on the correlation between an established biomarker (NGAL) of kidney damage and urine biochemical tests in septic and non-septic patients with AKI. Finally, it provides information on the diagnostic and prognostic value of such tests. However, our study also carries several limitations. First, the sample size was relatively small. Second, it had relatively limited statistical power. This greatly limited the statistical capacity for more comprehensive multi-variable adjustment of potential confounding variables. However, the limitations of urine biochemistry were apparent and strong. Third,

we did not capture detailed data on all types and amounts of fluid administered to patients prior to or during enrollment in the study. However, it is within the context of fluid resuscitation, vasopressor therapy, and the use of diuretics, where there may be large variation in the filtered load of sodium, that urine biochemical indices have yet to show their utility. Finally, we included relatively few patients with chronic kidney disease to perform a more detailed stratified analysis. Nonetheless, we recognize our findings are preliminary and require additional confirmatory investigation.

4.3. Comparison with prior literature

Systematic reviews challenge the relevance of urine biochemistry/derived indices, especially in ICU patients [15,16]. In addition, clinical studies have been inconsistent [25–28]. Recent data have shown FeNa and FeU to be of limited usefulness in the diagnosis of early AKI and for the prediction worsening AKI [29,30]. We previously showed that urine biochemical indices (ie, FeNa, FeU) correlated poorly with urine microscopy in AKI [22], where urine microscopy was a predictor of worsening AKI and kidney outcomes and appeared to be a relevant surrogate of kidney damage. In this study, we found that approximately 50% of patients with significant microscopic evidence of renal tubular damage had a FeNa < 1%, a value considered indicative of preserved renal tubular function in the setting of possible pre-renal azotemia. The simultaneous presence of structural kidney injury, as shown by urine microscopy, challenges the notion that a FeNa of < 1% can be used to separate functional pre-renal azotemia from structural kidney injury. This would suggest a significant proportion of patients with microscopic evidence of tubular injury may be incorrectly diagnosed with functional “pre-renal azotemia”. These findings may relate to the heterogeneous nature of tubular injury associated with AKI in critical illness or the use of vasopressors and/or diuretics [10,31,32]. Irrespective of the mechanism, urine biochemical indices do not appear to be robust tests for identifying the risk of worsening AKI, need for RRT or mortality, NGAL-defined tubular injury, pre-renal functional azotemia or urine microscopy-defined kidney injury [33].

4.4. Interpretation and clinical relevance

Our data imply that the routine use of urine biochemistry/ derived indices in critically ill patients with AKI may be unreliable and does not assist with diagnosis, risk identification, or risk stratification. On the basis of the findings of this study and of other investigations, their use for primary diagnostic purposes or prognostication in AKI cannot be recommended. Given these diagnostic and prognostic shortcomings, these tests are unlikely to have any therapeutic implications in the critical care setting.

5. Conclusion

Urine biochemical tests and derived indices do not discriminate septic and non-septic AKI in critically ill patients. Moreover, UNa, FeNa, and FeU fail to reliably predict worsening AKI, need for RRT and mortality, and show relatively poor association with kidney damage biomarkers, such as urine and plasma NGAL. These findings imply low utility for these tests in the clinical evaluation of critically ill patients with AKI.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

This study was funded by a grant from the Austin Anaesthesia and Intensive Care Trust. Dr Bagshaw is supported by a Canada Research Chair in Critical Care Nephrology and Clinical Investigator Award from Alberta Innovates–Health Solutions.

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Table 1
Summary of baseline characteristics

Characteristic	Septic (n = 43)	Non-septic (n = 40)	P
Age (y) (mean [SD])	67.9 (16.3)	60.6 (16.3)	.04
Male sex (n, %)	23 (53.5)	27 (67.5)	.26
Weight (kg) [mean (SD)]	71.2 (15.4)	81.1 (17.8)	.01
Charlson Comorbidity Score (mean [SD])	4.1 (3.0)	2.4 (2.2)	.005
Cardiac disease (%)	41.9	55	.28
COPD (%)	27.9	12.5	.11
Diabetes mellitus (%)	20.9	25.0	.80
Liver Disease (%)	11.6	17.5	.54
Surgical admission (n, %)	22 (51.2)	26 (65.0)	.27
Cardiac surgery (n, %)	2 (9.1)	18 (69.2)	< .001
Emergency surgery (n, %)	19 (86.4)	4 (15.4)	< .001
APACHE II Score (mean [SD])	23.5 (5.4)	19.2 (8.9)	.008
SOFA Score (mean [SD])	8.2 (3.1)	6.3 (3.4)	.008
Mechanical ventilation (n, %)	26 (60.5)	33 (82.5)	.03
Vasoactive therapy (n, %)	34 (79.1)	25 (62.5)	.15
Shock (n, %)	38 (88.4)	30 (75.0)	.16

Table 2
Details of kidney function and outcomes

Parameter	Septic (n = 43)	Non-septic (n = 40)	P
Baseline kidney function:			
Serum creatinine ($\mu\text{mol/L}$) [med (IQR)]	75 (65-85)	76 (68-90)	.73
Serum urea (mmol/L) [mean (SD)]	5.6 (2.8)	5.8 (2.3)	.75
eGFR ($\text{mL/min per } 1.73\text{m}^2$) [mean (SD)]	87.9 (27.0)	92.5 (34.4)	.50
eGFR $<60 \text{ mL/min per } 1.73\text{m}^2$ (n, %)	3 (7.0)	6 (15.0)	.30
Enrolment kidney function:			
Serum creatinine ($\mu\text{mol/L}$) [mean (SD)]	155 (94)	146 (146)	.71
Serum urea (mmol/L) [mean (SD)]	12.2 (7.1)	10.1 (8.5)	.25
RIFLE category at enrolment:			
Risk (n)	26 (60.5)	30 (75.0)	.43
Injury (n)	10 (23.3)	6 (15.0)	
Failure (n)	7 (16.3)	4 (10.0)	
Urine Output (mL/h) (median [IQR]) [¶]	63 (46–132)	69 (44–145)	.74
Oliguria/anuria (n, %) [§]	5 (12.2)	7 (19.4)	.53
Nephrotoxin (n, %) [*]	24 (55.8)	29 (72.5)	.17
Radiocontrast media (n, %)	12 (27.9)	11 (27.5)	1.0
Aminoglycosides (n, %)	16 (37.2)	4 (10.0)	.005
Cardiopulmonary bypass (n, %)	2 (9.1)	18 (69.2)	< .001
Rhabdomyolysis (n, %)	1 (2.3)	7 (17.5)	.03
Amphotericin (n, %)	1 (2.3)	1 (2.5)	1.0
Other drugs (n, %)	0 (0)	2 (2.5)	.34
Loop diuretics (n, %)	29 (67.4)	21 (52.5)	.19
Worsened AKI (n, %)	11 (25.6)	9 (22.5)	.80
Renal replacement therapy (n, %) ^φ	5 (12.5)	8 (18.6)	.55
ICU Length of stay (median [IQR])	6 (2–11)	2 (2–4.5)	< .001
ICU Death (n, %)	14 (32.6)	4 (10.0)	.02
Hospital length of stay (median [IQR])	17 (10–30)	9 (7–18)	.003
Hospital death (n, %)	19 (44.2)	6 (15.0)	.004

FeNa = fractional excretion of sodium; FeU = fractional excretion of urea.

[¶]Urine output average over 6 hours prior to study enrollment.

[§]Oliguria defined as $<400 \text{ mL}$ urine output in 24 hrs prior to enrollment.

^φContinuous RRT was the initial modality received by all patients.

^{*}Nephrotoxin exposure: rhabdomyolysis was defined as a serum creatine kinase $>1500 \text{ U/L}$; other drugs included tacrolimus and acyclovir.

Table 3
Summary of enrolment urine biochemistry and derived indices

Parameter	Septic (n = 43)	Non-septic (n = 40)	P
UNa (mmol/L) (median [IQR])	43 (15-85)	57 (25-112)	.04
UNa <20 mmol/L (n, %)	13 (30.2)	8 (20.0)	.32
UNa 20-40 mmol/L (n, %)	6 (13.9)	6 (15.0)	1.0
UNa >40 mmol/L (n, %)	24 (55.8)	26 (65.0)	.50
FeNa (%) (median [IQR])	0.93 (0.13-2.20)	0.72 (0.28-2.89)	.85
FeNa <0.5% (n, %)	17 (39.5)	17 (42.5)	.83
FeNa 0.5%-1% (n, %)	7 (16.3)	6 (15.0)	1.0
FeNa 1%-2% (n, %)	8 (18.6)	4 (10.0)	.35
FeNa >2% (n, %)	11 (25.6)	13 (32.5)	.63
FeU (%) (median [IQR])	38.7 (27.2-49.3)	42.0 (31.1-51.3)	.44
FeU <35% (n, %)	16 (37.2)	12 (30.0)	.64
FeU 35%-50% (n, %)	17 (39.5)	18 (45.0)	.66
FeU >50% (n, %)	10 (23.3)	10 (25.0)	1.0
Urine specific gravity (mean [SD])	1.015 (0.01)	1.014 (0.01)	.48
Urine pH (mean [SD])	5.16 (0.6)	5.58 (0.9)	.02
Urine NGAL (ng/mg) (median [IQR])	203.6 (33.3-719.6)	39.0 (13.9-201.9)	.004
Plasma NGAL (ng/mL) (median [IQR])	292.8 (154.0-557.6)	166.2 (91.8-252.3)	.02

Table 4
Summary of outcomes stratified by enrolment urine derived indices, FeNa and FeU

Variable	FeNa		P		FeU		P	
	<1%(n = 48)	1%-2%(n= 11)	2%(n = 24)		<35% (n = 28)	35%-50% (n = 35)	50% (n = 20)	
RIFLE category (n, %)								
Risk	33 (68.8)	7 (63.6)	14 (58.3)	.82	17 (60.7)	24 (68.6)	13 (65.0)	.73
Injury	9 (18.8)	3 (27.3)	5 (20.8)		5 (17.8)	8 (22.9)	4 (20.0)	
Failure	6 (12.5)	1 (9.1)	5 (20.8)		6 (21.4)	3 (8.6)	3 (15.0)	
Loop diuretics (n, %)	28 (58.3)	6 (54.6)	16 (66.7)	.77	18 (64.3)	23 (65.7)	9 (45.0)	.28
uNGAL (ng/mL) *	48.0 (21.1-232.4)	338.1 (31.9-1948.8)	96.9 (33.7-838.0)	.11	167.5 (24.2-401.2)	57.7 (25.0-202.0)	83.1 (27.2-821.3)	.50
Worsening AKI (n, %)	10 (20.8)	2 (18.2)	8 (33.3)	.45	8 (28.6)	9 (25.7)	3 (15.0)	.58
RRT (n, %)	5 (10.4)	2 (18.2)	6 (25.0)	.24	5 (17.9)	6 (17.1)	2 (10.0)	.80
Death (n, %)	16 (33.3)	3 (27.3)	6 (25.0)	.84	10 (35.7)	11 (31.4)	4 (20.0)	.51

* Expressed as median [IQR].

Table 5
Summary of receiver operating characteristic (ROC) analysis for urine derived indices and worsening AKI

Worsening AKI	n (%)	AUC (95% CI)	Sensitivity (%)	Specificity (%)
UNa <20 mmol/L	21 (25.3)	0.53 (0.42-0.64)	30.0	76.2
UNa <40 mmol/L	50 (60.2)	0.46 (0.34-0.59)	55.0	38.1
FeNa <0.5%	34 (40.9)	0.43 (0.31-0.55)	30.0	55.6
FeNa <1.0%	47 (56.6)	0.54 (0.42-0.67)	50.0	58.7
FeNa <2.0%	24 (28.9)	0.54 (0.42-0.66)	35.0	73.0
FeU <35%	28 (33.7)	0.54 (0.42-0.67)	40.0	68.3
FeU <50%	20 (24.1)	0.44 (0.34-0.54)	15.0	73.0