RESEARCH LETTER

Estimated Urinary Flow Rate and Contrast-Associated Acute Kidney Injury Risk: The PRESERVE (Prevention of Serious Adverse Events Following Angiography) Trial

To the Editor:

Acute kidney injury (AKI) is a common clinical syndrome diagnosed in >20% of hospitalizations, and the administration of iodinated contrast is a common cause.[1,2] Contrast-associated AKI (CA-AKI) is marked by an abrupt decline in kidney function, typically occurring 2 to 5 days after administration of contrast, especially among those with risk factors for AKI such as older age, chronic kidney disease, cardiovascular disease, and diabetes mellitus. Identifying patients who are at increased risk for CA-AKI and instituting preventive measures is extremely important.

The mainstay of preventive strategies for CA-AKI is adequate intravascular volume expansion before radiocontrast exposure. The Prevention of Serious Adverse Events Following Angiography (PRESERVE) trial demonstrated that CA-AKI incidence was similar irrespective of the use of normal saline solution versus sodium bicarbonate solution for preprocedure volume expansion, and irrespective of the use of N-acetylcysteine or matched placebo.[3] Intravenous fluid protocols are often used in patients scheduled to undergo coronary angiography and other radiocontrast imaging studies. However, whether individual patients are sufficiently volume expanded at the time of radiocontrast exposure or whether measures of fluid administration predict risk for CA-AKI is untested.

An important correlate of fluid administration status is urinary flow rate. Its measurement before radiocontrast exposure is challenging because it typically requires collection of a timed urine specimen, and these are often impractical to obtain and frequently inaccurate.[4] We recently derived a formula to estimate urinary flow rate from urinary creatinine concentrations and demonstrated that the equation estimates were highly correlated (r=0.91) to measured urinary flow rates.[5] The formula to estimate urinary flow rate (eV) requires a single measurement of urinary creatinine concentration, as depicted next:

$$eV\left(\frac{mL}{\text{h}}\right)=9.5+\frac{[(140-age)\times wt(kg)\times(0.85 if female)\times 0.833]}{UCr\left(\frac{mg}{dL}\right)}$$

We hypothesized that a low eV obtained just before radiocontrast exposure would identify individuals at higher risk for CA-AKI. We evaluated a subgroup of 791 PRESERVE participants who gave a urine sample after intravenous crystalloid infusion and immediately before angiography.

We estimated urinary flow rate using the previously validated equation.[5] We categorized individuals into quartiles of eV and compared demographics and clinical parameters across quartiles (Table 1). CA-AKI was defined as an increase in serum creatinine level from the baseline preangiography value of either at least 25% or at least 0.5 mg/dL at 3 to 5 days after angiography. We used logistic regression models to evaluate the association of eV with CA-AKI.

Among the 791 study participants, mean age was 70 years, 97% were men, 82% had diabetes, and mean estimated glomerular filtration rate was 48 mL/min/1.73 m^2 at baseline. Participants within the highest quartile of eV were more likely to be younger, to be White, and to have greater albuminuria. Sixty-six (8.3%) participants developed CA-AKI during follow-up. The mean eV in those who ultimately developed CA-AKI was 78 mL/h, whereas the corresponding eV in those who did not develop CA-AKI was 74.8 mL/h (Fig S1). When evaluated across eV quartiles, unadjusted rates of CA-AKI increased, but not linearly (Fig 1). Results were similar in models that adjusted for age, sex, race, body weight, and precontrast estimated glomerular filtration rate (Table S1).

Thus, although the simple eV equation is highly correlated with urinary flow rate, we found no evidence that its measurement based on a spot urinary creatinine level just before radiocontrast exposure was associated with CA-AKI in PRESERVE. The reasons underlying these null findings are unclear, but several possibilities deserve consideration. First, all participants in PRESERVE received either intravenous sodium chloride or sodium bicarbonate solution on a weight-based standardized protocol, which may have led to little heterogeneity in the volume of preprocedural intravenous fluid administered when we measured eV and when participants were given radiocontrast. Thus, the protocolized fluid administration approach may have biased toward a null result. Second, relatively few (8.3%) participants developed CA-AKI. Most participants received relatively small volumes of contrast material and only ~25% had percutaneous interventions, which are associated with higher rates of CA-AKI. Finally, because providers performing the angiography among PRESERVE participants were able to augment the amount of intravenous fluid administered within certain boundaries, it is possible that participants deemed at higher risk for CA-AKI received higher volumes of intravenous crystalloid solution, which would have biased our results toward the null.

In conclusion, a low eV based on a spot urinary creatinine level after a preangiography intravenous fluid protocol was not associated with CA-AKI in participants undergoing radiocontrast studies in PRESERVE. However, we believe it remains plausible that a simple equation to estimate urinary flow rate may provide utility to identify AKI risk in other settings. These findings should be reevaluated in larger study samples in the future to determine whether a simple, practical, and actionable

Table 1. Select Demographic, Clinical, and Procedure Characteristics by eV in PRESERVE

	eV Quartile 1 (<42 mL/h)	eV Quartile 2 (42-<61 mL/h)	eV Quartile 3 (61-<92 mL/h)	eV Quartile 4 (>92 mL/h)
N	197	197	197	200
Age, y	73 (8)	70 (8)	69 (8)	68 (7)
Female sex	8 (4.1%)	5 (2.5%)	3 (1.5%)	8 (4%)
Race				
White	153 (77.7%)	144 (73.1%)	149 (75.6%)	167 (83.5%)
Black	33 (16.8%)	40 (20.3%)	34 (17.2%)	24 (12%)
Hispanic and other	11 (5.6%)	13 (6.6%)	14 (7.1%)	9 (4.5%)
Weight, kg	92 (18)	100 (20)	104 (24)	108.59 (22.60)
Baseline serum creatinine, mg/dL	1.55 (0.38)	1.54 (0.39)	1.62 (0.49)	1.59 (0.48)
UACR categories				
<30 mg/g	102 (51.8%)	78 (39.6%)	85 (43.1%)	63 (31.5%)
30-300 mg/g	70 (35.5%)	70 (35.5%)	51 (25.9%)	69 (34.5%)
>300 mg/g	22 (11.2%)	43 (21.8%)	56 (28.4%)	61 (30.5%)
Missing proteinuria	3 (1.5%)	6 (3%)	5 (2.5%)	7 (3.5%)
Baseline eGFR, mL/min/1.73 m^2	48 (12)	50 (14)	48 (14)	48 (14)
Diabetes	150 (76.1%)	159 (80.7%)	168 (85.2%)	171 (85.5%)
Procedure type				
Coronary	182 (92.4%)	171 (86.8%)	168 (85.2%)	176 (88%)
Noncoronary	15 (7.6%)	25 (12.7%)	28 (14.2%)	24 (12%)
Missing data	0 (0.0%)	1 (0.005%)	1 (0.005%)	0 (0.0)
Percutaneous intervention	44 (22.3%)	59 (29.9%)	55 (27.9%)	52 (26%)
Volume of contrast material, mL	75 [55-125]	102 [60.5-150]	80 [55-130]	85 [60-140]
LVEDP, mm Hg	18 (8)	20 (9)	21 (8)	19 (8)
Trial arm				
Saline solution + placebo	49 (24.9%)	45 (22.8%)	46 (23.4%)	39 (19.5%)
Saline solution + NAC	50 25.4%)	49 (24.9%)	54 (27.4%)	51 (25.5%)
Sodium bicarbonate solution + placebo	46 (23.4%)	53 (26.9%)	46 (23.4%)	62 (31%)
Sodium bicarbonate solution + NAC	52 (26.4%)	50 (25.4%)	51 (25.9%)	48 (24%)

Note: n = 791. Values expressed as mean (standard deviation), number (percent), or median [interquartile range].
Abbreviations: eGFR, estimated glomerular filtration rate; eV, estimated urinary flow rate; LVEDP, left ventricular end-diastolic pressure; NAC, *N*-acetylcysteine; PRESERVE, Prevention of Serious Adverse Events Following Angiography; UACR, urinary albumin-creatinine ratio.

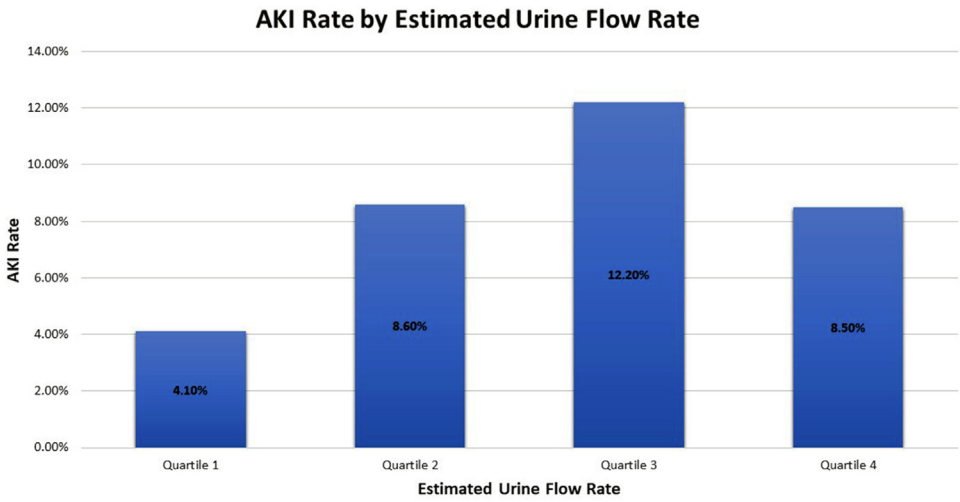

Figure 1. Acute kidney injury (AKI) rate by estimated urinary flow rate.

equation to assess urinary flow rate may identify those at higher risk for CA-AKI above and beyond traditional risk factors.

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SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1: Distribution of estimated urinary flow rate (eV) by CA-AKI

Table S1: Association of precontrast estimated urinary flow rate and CA-AKI

ARTICLE INFORMATION

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