

# Prediction of acute kidney injury: the ratio of renal resistive index to semiquantitative power Doppler ultrasound score—a better predictor?

## A prospective observational study

Hai Jun Zhi, MD<sup>a</sup>, Jing Zhao, MBBS<sup>b</sup>, Shen Nie, MD<sup>a</sup>, Yun Jie Ma, MBBS<sup>a</sup>, Xiao Ya Cui, MD<sup>a</sup>, Meng Zhang, MD<sup>a</sup>, Yong Li, MD<sup>a,\*</sup>

### Abstract

This study aimed to explore the diagnostic performance of the ratio of renal resistive index (RRI) to semiquantitative power Doppler ultrasound (PDU) score in predicting acute kidney injury (AKI) 3 in critically ill patients.

This study was a prospective, observational study that included 101 critically ill patients. RRI and semiquantitative PDU score were measured within 6 hours following admission to the intensive care unit (ICU). The ratio of RRI to PDU (RRI/PDU) was calculated as follows: RRI / PDU. If PDU score was 0, the RRI/PDU was 1. Meanwhile, AKI was defined according to the Kidney Disease Improving Global Outcomes criteria.

Median RRI/PDU was 0.234 (0.190, 0.335) in patients with AKI 0–2 and 0.636 (0.411, 0.738) in patients with AKI 3 ( $P < .001$ ). As assessed by the area under the receiver operator characteristic curves (AUC), RRI/PDU performed best in diagnosing AKI 3 [AUC = 0.935 (95% CI: 0.868–0.974)]. Optimal cut-off for RRI/PDU was  $> 0.37$ , and the sensitivity and specificity were 90.5% and 90.0%, respectively. In 93 patients, except for 8 patients with a PDU score of 0, the AUC of RRI/PDU [0.938 (95% CI: 0.868–0.977)] was superior to the PDU score (0.905 [95% CI: 0.826–0.956],  $P = .133$ ), RRI [0.782 (95% CI: 0.684–0.861),  $P = .016$ ], serum creatinine [0.801 (95% CI: 0.705–0.877),  $P = .017$ ], or 6 hours AKI stage (0.876 [95% CI: 0.791–0.935],  $P = .110$ ) in predicting AKI 3 on D5.

In our study, RRI, PDU score, RRI/PDU, and 6 hours AKI stage were useful in predicting AKI 3. Furthermore, RRI/PDU may be a better predictor of AKI 3.

**Abbreviations:** AKI = acute kidney injury, ICU = intensive care unit, PDU = power Doppler ultrasound, RRI = renal resistive index, RRT = renal replacement therapy.

**Keywords:** acute kidney injury, renal resistive index, semiquantitative power Doppler ultrasound score

## 1. Introduction

Acute kidney injury (AKI) is common in patients confined in intensive care units (ICU) and remains to be associated with poor outcomes.<sup>[1]</sup> According to the current diagnostic criteria, serum creatinine (SCr) and urine volume are used as diagnostic and staging criteria for AKI.<sup>[2]</sup> However, oliguria is not specific to renal dysfunction, and SCr elevation is usually delayed for several hours after the renal insult and occurs only when the glomerular filtration rate is severely diminished.<sup>[3]</sup> Moreover, Zarbock

et al<sup>[4]</sup> found that early renal replacement therapy (RRT) (RRT within 8 hours of diagnosis of KDIGO stage 2) reduced mortality over the first 90 days compared with the delayed initiation of RRT (RRT within 12 hours of KDIGO stage 3 or no RRT). Additionally, patients with KDIGO stage 3 always need RRT. However, the diagnosis of KDIGO stage 3 would usually take 12 to 24 hours. Hence, if an indicator is available for predicting KDIGO stage 3 within 6 hours of admission, the patients may receive early RRT and obtain improved outcomes.

Many biomarkers such as serum cystatin C,<sup>[5]</sup> neutrophil gelatinase-associated lipocalin,<sup>[6]</sup> urinary kidney injury molecule<sup>[7]</sup> and so on are potentially useful to predict AKI in critical care. However, most of these biomarkers have not been widely used in clinical practice, and the detection is time-consuming and cannot be performed at any time. Doppler-based renal resistive index (RRI) calculation and semiquantitative power Doppler ultrasound (PDU) score provide rapid, noninvasive, and repeatable investigations, possibly granting early AKI detection in patients confined in the ICU,<sup>[8,9]</sup> but its diagnostic performance remains insufficiently evaluated. Acute tubular necrosis is the main mechanism of AKI in intensive care settings and persists even when the hemodynamic status has been restored. Three preliminary human studies have shown that RRI is useful in distinguishing the condition from prerenal azotemia.<sup>[10–12]</sup> Meanwhile, semiquantitative PDU assesses renal perfusion; prolonged renal hypoperfusion may lead to kidney injury. Thus, we combined these 2 indicators to RRI/PDU, which may have a

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<sup>a</sup>Emergency Department, <sup>b</sup>Ultrasonic Department, Cangzhou Central Hospital, Yunhe Qu, Cangzhou, China.

\*Correspondence: Yong Li, Cangzhou Central Hospital, Cangzhou, Hebei 061000, China (e-mail: ly13333367871@hotmail.com).

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better performance than RRI or PDU score in predicting KDIGO stage 3 in critically ill patients.

## 2. Materials and methods

### 2.1. Patients

The study was approved by the ethics committee of the Cangzhou Central Hospital in Cangzhou City, Hebei Province, China (ethical approval number: 2017-078-01), and every patient or next of kin was informed that the collected data could be used for research purposes. We studied critically ill patients admitted in the Emergency ICU of Cangzhou Central Hospital from January 2018 to July 2018 but only those who met the following criteria: admission for sepsis (as defined by the sepsis-3 criteria<sup>[13]</sup>), polytrauma (as defined by an Injury Scaling Severity score  $\geq 25$ <sup>[14]</sup>), cardiac failure (as defined by Killip classification grade IV in patients with acute myocardial infarction or by New York Heart Association functional class IV in patients with acute heart failure), and critical conditions due to other causes. Noninclusion criteria included the age younger than 18 years, survival time of less than 24 hours, pregnancy, intraperitoneal pressure of more than 15 mm Hg, suspected or confirmed obstructive renal failure, arrhythmia, and known renal artery stenosis. Additionally, we did not include patients recovering from previously diagnosed AKI at the time of inclusion and those with severe chronic renal failure with a basal creatinine clearance value of lower than 30 mL/min. AKI was defined according to KDIGO criteria (Table 1). Baseline creatinine was estimated by the Modification of Diet in Renal Disease equation, assuming a low normal value for baseline GFR (75 mL/min /1.73 m<sup>2</sup>).<sup>[15]</sup> The equation is as follows (Creatinine is in mg/dL).

$$\begin{aligned} \text{GFR}(\text{mL}/\text{min}/1.73\text{m}^2) &= 186 \times \text{Scr}^{-1.154} \times (\text{Age})^{-0.203} \\ &\times (\text{Female} \times 0.742) \times (\text{Chinese} \\ &\times 1.233) \end{aligned}$$

### 2.2. Study protocol and data collection

In addition to the demographic data, height, weight, type of admission (sepsis, cardiac failure, polytrauma, or other causes), and accompanying diseases, the following data were collected within 6 hours from admission: SCr level, 6 hours urine output, arterial lactate concentration, use of mechanical ventilation, use of vasoactive drugs, and 6 hours KDIGO stage. APACHE II score and SOFA score were evaluated 24 hours after admission. Renal function was assessed on D5 according to the KDIGO criteria. The mortality and use of continuous renal replacement therapy (CRRT) were collected on day 28.

**Table 1**  
Staging of AKI.

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline OR $\geq 0.3$ mg/dL ( $\geq 26.5 \mu\text{mol/L}$ ) increase	$<0.5$ mL/kg/h for 6–12 h
2	2.0–2.9 times baseline	$<0.5$ mL/kg/h for $\geq 12$ h
3	3.0 times baseline OR Increase in serum creatinine to $\geq 4$ mg/dL ( $\geq 353.6 \mu\text{mol/L}$ )	$<0.3$ mL/kg/h for $\geq 24$ h OR Anuria for $\geq 12$ h

AKI = acute kidney injury.

**Table 2**

Semiquantitative PDU score for evaluating intrarenal perfusion.

Grade	Renal perfusion
0	Unidentifiable vessels
1	Few vessels visible in the vicinity of the hilum
2	Hilar and interlobar vessels visible in most of the renal parenchyma
3	Renal vessels identifiable until the arcuate arteries in the entire field of view

PDU = power Doppler ultrasound.

### 2.3. RRI and semiquantitative PDU score measurements

Renal echography was performed by an intensivist with sufficient experience in this technique within the first 6 hours of admission and after mean arterial pressure (MAP)  $\geq 65$  mm Hg. The operators were aware of the results of the other tests and other available clinical information. RRI was calculated from the right kidney in most patients. The ultrasound machines used were CX30 (Philips) and HD15 (Philips). Renal Doppler was performed on the interlobar arteries by using a convex array probe. The Doppler gain was set to obtain a clear outline of flow waves with minimal background noise. The Doppler spectrum was considered optimal when at least 3 similar consecutive waveforms were visualized. The RRI was calculated as follows: (peak systolic velocity – end diastolic velocity)/peak systolic velocity. The RRI value is independent of the angle between the ultrasound beam and blood flow. Three measurements were performed and averaged to obtain the mean RRI value. Renal perfusion was assessed by semiquantitative PDU score (Table 2).<sup>[16]</sup> The ratio of RRI to PDU (RRI/PDU) was calculated as follows: RRI/PDU. If the PDU score was 0, the RRI/PDU was 1. MAP, heart rate (HR), type and dose of catecholamine infusion, and oxygenation index were recorded during the renal ultrasound examination.

### 2.4. Statistical analysis

Results were described as median and interquartile ranges, mean, and standard deviation, or numbers and percentages (%), as appropriate. Kolmogorov–Smirnov test was used to examine the normality of all numeric continuous variables. Nonparametric tests (Mann–Whitney *U* test) were used to examine the difference in variables without a normal distribution, whereas independent sample *t* tests were used if with a normal distribution. Categorical data including gender accompanying diseases, use of mechanical ventilation, use of vasoactive drugs, mortality, and use of CRRT were compared between AKI 3 group and AKI 0 to 2 groups by  $\chi^2$  test. When there was only less than 5 observations in a group–outcome combination, the Fisher test was used.<sup>[17]</sup> Receiver operator characteristic (ROC) curves were plotted to examine the RRI, PDU score, RRI/PDU, and 6 hours AKI stage in predicting AKI 3. A binary logistic regression was performed to identify the independent predictors of AKI 3. First, univariable analysis was used to explore the unadjusted association between variables and outcome. Continuous variables were checked for their linearity in relation to the logit of the outcome by examining the smoothed scatter plot.<sup>[18]</sup> Correlations between RRI/PDU and some parameters were evaluated using Pearson correlation coefficient. Statistical tests were performed using SPSS 19. ROC curves were performed using MedCalc. Delong test was used to compare AUROCs between each predictor. All tests were 2-sided, and *P* values  $< .05$  were considered statistically significant.

**Table 3****Main patient characteristics according to KDIGO stage assessed on D5.**

	All patients (n=101)	AKI 0-2 (n=80)	AKI 3 (n=21)	P value
Male, n (%)	64 (63.4%)	51 (63.8%)	13 (61.9%)	.876
Age, y	68 (52, 73)	68 (49, 73)	68 (62, 77)	.313
BMI, kg/m <sup>2</sup>	24.2 (22.5, 26.1)	24.2 (22.5, 26.5)	24.0 (22.5, 25.9)	.586
APACHE-II score	21 (11, 27)	18 (11, 25)	29 (18, 34)	.002
SOFA score	7 (4, 11)	6 (3, 9)	10 (8, 14)	.001
History of hypertension, n, %	40 (39.6%)	31 (38.8%)	9 (42.9%)	.732
History of diabetes, n, %	24 (23.8%)	19 (23.8%)	5 (23.8%)	.995
History of CHD, n, %	41 (40.6%)	28 (35.0%)	13 (61.9%)	.025
HR (beats per minute)	101 ± 24	101 ± 24	104 ± 22	.516
MAP, mm Hg	85 (75, 99)	87 (75, 100)	81 (74, 89)	.309
Pulse pressure difference, mm Hg	48 (38, 58)	48 (38, 59)	49 (38, 53)	.459
Catecholamine dose, µg/kg/min	0 (0, 0.30)	0 (0, 0.19)	0.38 (0.09, 1.20)	<.001
PaO <sub>2</sub> /FiO <sub>2</sub> , mm Hg	201 (133, 272)	209 (137, 274)	170 (79, 248)	.082
Arterial lactate, mmol/L	3.0 (1.7, 5.3)	3.0 (1.7, 4.8)	2.7 (1.7, 11.5)	.414
Serum K, mmol/L	4.0 (3.7, 4.7)	4.0 (3.6, 4.6)	4.2 (3.9, 4.9)	.023
Serum Na, mmol/L	138 (135, 142)	138 (135, 142)	139 (134, 142)	.672
SCr, µmol/L	114 (78, 149)	103 (68, 139)	143 (115, 219)	<.001
Urine output, mL/h	50 (20, 100)	50 (30, 100)	0 (0, 20)	<.001
RRI	0.631 ± 0.085	0.618 ± 0.081	0.701 ± 0.073	<.001
PDU score	2 (2, 3)	3 (2, 3)	1 (0, 1)	<.001
RRI/PDU	0.302 (0.198, 0.413)	0.234 (0.190, 0.335)	0.636 (0.411, 0.738)	<.001
6 h AKI stage	0 (0, 1)	0 (0, 1)	1 (1, 2)	<.001
Vasoactive drugs, n, %	55 (54.5%)	38 (47.5%)	17 (81.0%)	.007
Mechanical ventilation, n, %	69 (68.3%)	51 (63.8%)	18 (85.7%)	.067
CRRT, n, %	21 (20.8%)	6 (7.5%)	15 (71.4%)	<.001
Mortality on day 28, n, %	19 (18.8%)	8 (10.0%)	11 (52.4%)	<.001

BMI=body mass index (weight/height<sup>2</sup>), CHD=coronary heart disease, AKI = acute kidney injury, PDU = power Doppler ultrasound, RRI = renal resistive index, SCr = serum creatinine.

**3. Results****3.1. General characteristics of patients**

During the study period, 124 patients were included. Among these patients, 10 died within 24 hours, 5 abandoned treatment during hospitalization, 3 unsuitable for RRI due to arrhythmia or abdominal hypertension, and 5 patients progressed to AKI 3 stage within 6 hours from admission. Therefore, 101 patients (31 with sepsis, 40 with cardiac failure, 6 with polytrauma, and 24 with other causes) were included in the study. According to KDIGO stage assessed on D5, 48 patients (48/101, 47.5%) had no AKI. Of the 53 patients with AKI, 15 (15/101, 14.9%) had AKI 1, 17 (17/101, 16.8%) had AKI 2, and 21 (21/101, 20.8%) had AKI 3. The patients' characteristics are shown in Table 3. APACHE II score, SOFA score, complicated coronary heart disease (CHD), serum K, SCr, RRI, PDU score, RRI/PDU, 6 hours AKI stage, urine output, use of vasoactive drugs, use of CRRT, mortality on day 28, were significantly different in the AKI 3 group compared with those in AKI 0 to 2 groups ( $P < .05$ ).

**3.2. Comparison of predictive value for AKI 3**

ROC curves were plotted to examine the values of SCr, RRI, PDU score, RRI/PDU, and 6 hours AKI stage in predicting AKI 3. The ROC curves of these indicators are shown in Tables 4 and 5. The area under the ROC curves (AUC) of SCr, RRI, PDU score, RRI/PDU, and 6 hours AKI stage were 0.756, 0.782, 0.912, 0.935, and 0.850, respectively. As assessed by the AUC, RRI/PDU performed best in diagnosing AKI 3 [AUC=0.935 (95% CI: 0.868–0.974)]. Optimal cutoff for RRI/PDU was  $> 0.37$ , and the sensitivity and specificity were 90.5% and 90.0%, respectively.

We compared the AUC of SCr, RRI, PDU score, RRI/PDU, and 6 hours AKI stage in predicting AKI 3 in 93 patients, except for 8 patients with a PDU score of 0 (Fig. 1). The AUC of RRI/PDU [0.938 (95% CI: 0.868–0.977)] was superior to the PDU score (0.905 [95% CI: 0.826–0.956],  $P = .133$ ), RRI [0.782 (95% CI: 0.684–0.861),  $P = .016$ ], SCr [0.801 (95% CI: 0.705–0.877),  $P = .017$ ], or 6 hours AKI stage (0.876 [95% CI: 0.791–0.935],  $P = .110$ ) in predicting AKI 3 on D5.

**Table 4****The best cutoff value analysis for the prediction of AKI 3.**

Indicator	Cutoff value	Sensitivity	Specificity	Youden index
SCr	$>90$	100.0	42.5	0.425
RRI	$>0.692$	73.3	78.2	0.515
PDU	$\leq 1$	81.0	91.2	0.722
RRI/PDU	$>0.37$	90.5	90.0	0.805
6 h AKI stage	$\geq 1$	100	68.7	0.688

AKI = acute kidney injury, PDU = power Doppler ultrasound, RRI = renal resistive index, SCr = serum creatinine.

**Table 5**  
**AUC for SCr, RRI, PDU, RRI/PDU, and 6 h AKI stage as predictors of AKI 3 on D5.**

Indicator	AUC	Standard deviation	P value	95% CI	
				Minimum	Maximum
SCr	0.756	0.051	<.001	0.660	0.836
RRI	0.782	0.066	<.001	0.684	0.861
PDU	0.912	0.029	<.001	0.839	0.959
RRI/PDU	0.935	0.024	<.001	0.868	0.974
6 h AKI stage	0.850	0.032	<.001	0.765	0.913

AKI = acute kidney injury, PDU = power Doppler ultrasound, RRI = renal resistive index, SCr = serum creatinine.

### 3.3. Correlation analysis of RRI/PDU

We analyzed the correlations between RRI/PDU and age, HR, MAP, pulse pressure difference, oxygenation index, catecholamine dose, arterial lactate concentration, complicated CHD, hypertension, or diabetes. Positive correlations were found between RRI/PDU and age ( $r=0.276$ ,  $P=.005$ ), between RRI/PDU and catecholamine dose ( $r=0.420$ ,  $P<.001$ ), and between RRI/PDU and complicated CHD ( $r=0.283$ ,  $P=.004$ ). Conversely, a negative correlation was found between RRI/PDU and oxygenation index ( $r=-0.223$ ,  $P=.025$ ).

We also analyzed the correlations between RRI and age, HR, MAP, pulse pressure difference, oxygenation index, catecholamine drug dosage, arterial lactate concentration, complicated CHD, hypertension, or diabetes, and PDU score. Positive correlations were found between RRI and age ( $r=0.374$ ,  $P<.001$ ), between RRI and catecholamine dose ( $r=0.290$ ,  $P=.005$ ), between RRI and pulse pressure difference ( $r=0.206$ ,  $P=.047$ ), and between RRI and complicated CHD ( $r=0.217$ ,  $P=.037$ ). Conversely, a negative correlation was found between RRI and MAP ( $r=-0.301$ ,  $P=.003$ ), and between RRI and PDU score ( $r=-0.508$ ,  $P<.001$ ).

### 4. Discussion

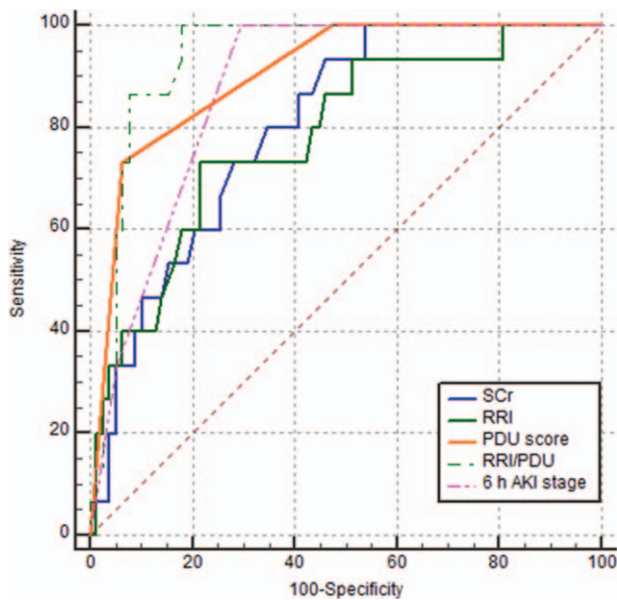
RRI and semiquantitative PDU score are easy to perform, rapid, noninvasive, and repeatable. The normal range for the RRI is 0.50 to 0.70.<sup>[8]</sup> In a population of patients with septic shock, a high RRI is predictive of AKI.<sup>[8,9,19]</sup> Meanwhile, arterial RRI correlated not only with intrarenal arterial resistance but also with arterial compliance (i.e., renal interstitial and intra-abdominal pressures), age, and central hemodynamic parameters.<sup>[20,21]</sup> In our study, a positive correlation was found among RRI and age, catecholamine dose, pulse pressure difference, and complicated CHD, and a negative correlation was found between RRI and MAP.

Semiquantitative PDU assesses renal perfusion. PDU is easier to perform than Doppler-based RRI. Furthermore, power Doppler evaluation of renal perfusion using a semiquantitative scale has been advocated. However, bloated abdomen, intestinal distension, and difficulty in changing body position in patients confined in the ICU are common. These circumstances influence the operation and results of PDU score to some extent. Thus, we combined these 2 indicators to RRI/PDU and compared the diagnostic performance of RRI, PDU score, or RRI/PDU in predicting AKI 3 in critically ill patients.

In our study, RRI/PDU performed best in diagnosing AKI 3 as assessed by the AUC, and a statistically significant difference was observed between RRI/PDU and RRI, and between RRI/PDU and Scr. The AUC of RRI/PDU was superior to PDU score and 6 hours AKI stage, although the differences are not statistically significant.

In conclusion, in our population of critically ill patients, the RRI, PDU score, and RRI/PDU, which were measured within 6 hours from admission to the ICU, and 6 hours AKI stage, were useful in predicting AKI 3. RRI/PDU may be a better predictor of AKI stage 3.

However, this present study has some limitations that must be discussed. Chronic renal lesions may impair the renal vasculature and cause an elevated RRI. We tried to limit this effect by systematically excluding patients with chronic renal dysfunction. However, we cannot exclude the role of early asymptomatic chronic renal lesions in this elevation. Furthermore, hemodynamic conditions could influence the RRI and PDU score. We tried to limit this effect by measuring the RRI and PDU score after the interventions that aimed at restoring hemodynamic status. Moreover, some patients may not survive for day 5 which actually creates a problem called competing risk that mortality is a competing risk for AKI.<sup>[22]</sup> This was also a limitation of our study. Given these limitations, additional studies are needed in larger populations and in critically ill patients with different diseases, such as sepsis, polytrauma, and cardiac shock.



**Figure 1.** ROC curves for SCr, RRI, PDU score, RRI/PDU, and 6 hours AKI stage as predictors of AKI 3. AKI = acute kidney injury, PDU = power Doppler ultrasound, RRI = renal resistive index, ROC = receiver operator characteristic, SCr = serum creatinine.

## Author contributions

**Data curation:** Yong Li.

**Formal analysis:** Hai Jun Zhi.

**Investigation:** Hai Jun Zhi, Jing Zhao, Shen Nie, Yun Jie Ma, Xiao Ya Cui, Meng Zhang.

**Writing – original draft:** Hai Jun Zhi.

**Writing – review & editing:** Yong Li.

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