# **Original Article**

# Doppler resistive index to reflect risk of acute kidney injury after major abdominal surgery: A prospective observational trial

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#### ABSTRACT

Background and Aims: Doppler renal resistive index (RI) has been studied to find its association with postoperative acute kidney injury (AKI). This study was conducted to evaluate the usefulness of preoperative RI, postoperative RI and RI variation before and after surgery expressed as a percentage (% RI) for early AKI detection in major abdominal surgery. Methods: This was a single-centre, prospective observational trial performed in the critical care unit of an academic hospital. Eligible patients posted for major abdominal surgery under general anaesthesia using intraperitoneal approach with at least two predefined risk factors for AKI were included in the study. Renal RI was measured preoperatively and on postoperative day zero. Statistical comparisons were performed for various parameters between the AKI and the non-AKI groups. Pre- and postoperative RI receiver operating characteristics (ROC) curves were drawn and areas under the curves computed. Positive and negative predictive values, sensitivity, specificity and positive and negative likelihood ratios were calculated. Results: A total of 69 subjects were enrolled, of which 14 developed AKI in the postoperative period. The mean resistive indices measured were  $0.65 \pm 0.09$  and  $0.74 \pm 0.09$  in the pre- and postoperative periods, respectively. The area under the ROC curve in the postoperative RI was 0.732 with 95% confidence intervals of 0.592-0.871. This most accurate cut-off value to detect postoperative AKI with sensitivity 57.1% and specificity of 85.5% was 0.77. Conclusion: Postoperative RI can detect early AKI after major abdominal surgery.

Key words: Acute kidney injury, abdominal surgery, Doppler, renal resistive index, risk factors

#### **INTRODUCTION**

Acute kidney injury (AKI) can progress from an early reversible condition to an established disease leading to potential renal damage,<sup>[1]</sup> prolonged hospitalisation, increased mortality rates and postoperative complications.<sup>[2-5]</sup> AKI in the hospital is mostly due to surgery.<sup>[6]</sup>

Fluid challenge and maintaining perfusion remain the optimal treatment options for this condition. It is accomplished by adequate fluid resuscitation and use of vasoconstrictor agents with monitoring of perfusion. Early recognition helps in preventing renal damage.

Doppler renal resistive index (RI) is a parameter that has generated substantial interest in recent years, for its ability to predict AKI during the perioperative period. It can be quantified expeditiously, with low intra- and interobserver variability. Small trials in cardiac<sup>[7]</sup> and orthopaedic surgery patients<sup>[8]</sup> have determined the utility of Doppler ultrasound-derived renal RI in detecting AKI. Its convenient utilisation against other clinical backdrops should now be

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defined. Therefore, we performed this single-centre, prospective, observational trial to test the hypothesis that the relationship between renal RI and AKI after major abdominal surgery allows early identification of such 'at-risk' patients among a group of subjects highly predisposed for the development of postoperative renal dysfunction. As primary objective, we evaluated whether preoperative RI, postoperative RI and RI variation pre- and postoperatively, expressed as a percentage (% RI) can predict AKI in major abdominal surgeries. Our secondary objectives were to study the effect of medical comorbidities, duration of surgical procedures, type of anaesthesia, blood loss and transfusion, amount and type of fluid replacement, number of hypotensive episodes and use of nonsteroidal anti-inflammatory drugs (NSAIDs) if any, on the incidence of AKI.

### **METHODS**

We conducted this single-centre, prospective observational trial with the approval of the Research Ethics Board of our hospital. Written and informed consent to participate in the study and consent to publish were obtained from all patients. Our institution is an academic and educational hospital with 2,100 beds, including 10 critical care unit (CCU) beds under the Department of Anesthesiology and Critical Care. This trial was performed in the CCU, and the subjects were patients admitted via various surgical specialities, for requirement of critical care treatment post-surgery. We did not accept any money from or speak on behalf of the manufacturer of the equipment used in our study.

The eligible subjects were adults (age  $\geq 50$  years) admitted to our CCU between June 2015 and June 2017, who were posted for major abdominal surgery under general anaesthesia, using intraperitoneal approach with a predicted length of stay in a given diagnosis-related group of more than 2 days, with at least two of the following risk factors for AKI: diabetes, hypertension, arteriopathy defined by severe lower limb arteriopathy or history of transient ischemic attack or history of stroke or carotid stenosis more than 50%, coronary artery disease, chronic renal dysfunction with estimated glomerular filtration rate (GFR) less than 60 mL/min/1.73 m<sup>2</sup>, chronic heart failure and patients receiving angiotensin converting enzyme (ACE) inhibitors or angiotensin receptor blockers (ARBs).<sup>[9]</sup> Patients who were having cardiac arrhythmias, poor echogenicity, haemodynamic instability, asymmetrical kidney disease, respiratory failure, pregnancy, end-stage renal disease, or chronic kidney disease with estimated GFR less than 30 mL/min/1.73 m<sup>2</sup>, nonsteroidal anti-inflammatory treatment, cirrhosis with hepatorenal syndrome, cardiogenic shock defined as a need for epinephrine or dobutamine or both, obstructive acute renal failure, renal artery stenosis assessed preoperatively by ultrasonography and those who refused to give written informed consent were excluded from the study. Poor echogenicity was defined as an inability to obtain a full envelope of Doppler signals from the vasculature of either of the kidneys after attempts by the anaesthesiologist and the radiologist.

A Sonosite S series ultrasound machine with a 4- to 5-MHz curved-array multifrequency transducer was used. The scans were performed by an anaesthesiologist under supervision by the radiologist. Point-of-care ultrasound scanning by the anaesthesiologists is a routinely performed procedure in our department and the CCU attached to it. Thus, all consultants and residents are used to performing such scans on a daily basis, which ensured that the learning curve for performing renal ultrasound to evaluate the Doppler RI under the guidance of the radiologist was not very steep. Intrarenal Doppler signals were obtained from two or three representative arcuate arteries at the corticomedullary junction. Three repeated measurements were taken on both kidneys, and the average was taken as the result.<sup>[10,11]</sup> The peak systolic velocity (Vmax) and the end diastolic velocity (Vmin) were determined by pulse wave Doppler and the RI was calculated as (Vmax - Vmin)/Vmax. % RI was calculated as (postoperative RI - preoperative RI)/ preoperative RI.

Each patient after inclusion had the following data recorded: age, presence of diabetes, hypertension, coronary artery disease, arteritis, cardiac failure, use of ACE inhibitors/ARBs and serum creatinine (sCr). GFR was estimated using Chronic Kidney Disease Epidemiology Collaboration equation,<sup>[12]</sup> taking into account sCr, sex and ethnicity. RI was assessed before arrival in the operating room. Owing to the observational nature of the study, the anaesthetic regimen was left to the discretion of the attending anaesthesiologists. Patients with documented chronic kidney disease had preoperative nephrology consultation obtained, and particular care was taken in this subgroup of patients to avoid dehydration with careful attention to fluid balance, and all known nephrotoxic drugs were avoided in these patients. The following data were recorded during surgery: length of surgery, type of anaesthesia, volume and type of fluid infused, blood transfusion required or not, blood loss, number of hypotensive episodes defined by mean arterial pressure under 80% of preoperative value for more than 5 min and use of perioperative NSAIDs. The decision to transfuse red cells was based on an institutional target haematocrit of 24%, as also on clinical factors, as perceived by the attending anaesthesiologist. Postoperative RI measurement was performed in the CCU on the first postoperative day, between 18 and 24 h after completion of surgery. The following criteria were needed before RI measurement: end of local bleeding defined by a blood loss of less than 100 mL for 30 min duration and absence of haemodynamic instability. Haemodynamic instability was defined by a mean arterial pressure of less than 65 mmHg or a heart rate more than 120 beats/min<sup>[13]</sup> or oxygen saturation less than 96%.<sup>[14]</sup> Oxygen therapy was introduced if the saturation objective was not attained.

Baseline sCr value was measured. Postoperative sCr value on day 1 or 2 was measured. Urine output was measured at 6-h interval over 48 h. AKI was defined by Acute Kidney Injury Network (AKIN) criteria as shown in Table 1.<sup>[15]</sup> The clinicians performing Doppler assessment of RI were blinded to the urine output recorded, sCr values obtained and AKIN class that the patient was put into. AKI was diagnosed only after achieving an adequate hydration and after excluding urinary obstruction. Adequate hydration was inferred from several parameters including the central venous pressure if such invasive line was inserted, the stroke volume variation if an arterial line was *in situ* and adequate capillary refill.

Table 1: Classification/staging system for acute kidney   injury by AKIN <sup>[15]</sup>				
Stage	Serum creatinine criteria	Urine output criteria		
1	Increase in serum creatinine of more than or equal to 0.3 mg/ dL (≥26.4 µmol/L) or increase to more than or equal to 150%-200% (1.5-2-fold) from baseline	<0.5 mL/kg/h for more than 6 h		
2	Increase in serum creatinine to more than 200%-300% (>2-3-fold) from baseline	<0.5 mL/kg/h for more than 12 h		
3	Increase in serum creatinine to more than 300% (>3-fold) from baseline [or serum creatinine of more than or equal to 4.0 mg/dL (≥354 µmol/l) with an acute increase of at least 0.5 mg/dL (44 µmol/L)]	<0.3 mL/kg/h for 24 h or anuria for 12 h		

AKIN – Acute Kidney Injury Network

Doppler RI was measured preoperatively and in the CCU, and % RI was calculated.

Demographic data, comorbidities and medication history were recorded at inclusion. sCr and estimated GFR (eGFR) were also recorded at inclusion. Intraoperative data were recorded real-time during surgery. Postoperatively, urine output was measured every 6 h and sCr was measured on postoperative days 1 and 2. Data have been represented as mean  $\pm$  standard deviation, median (range) and number (percentage) as appropriate. Comparisons were performed between the AKI and the non-AKI groups using t-test for pre- and postoperative RI and % RI, age, baseline GFR, length of surgery, volume of fluid infused, volume of blood infused, blood loss and the number of hypotensive episodes. Chi-square test was used for comparing presence of diabetes, hypertension, arteritis, cardiac failure, use of ACE inhibitors, type of surgery, anaesthesia and fluid used and use of perioperative NSAIDs. The most significant variables in the univariate analysis were included in a multivariate logistic regression analysis to investigate the influence of the variables on each other. Pre- and postoperative RI receiver operating characteristics (ROC) curves were drawn and area under the curve (AUC) computed. Positive and negative predictive values, sensitivity, specificity, positive and negative likelihood ratios were calculated. P < 0.05 has been considered statistically significant. Statistical analysis was done with SPSS 19.0 software (IBM Corp. Released 2010; IBM SPSS Statistics for Windows, Version 19.0; IBM Corp., Armonk, NY, USA).

#### RESULTS

The total number of patients evaluated in this study was 78. Six patients were excluded due to poor echogenicity and three due to haemodynamic instability. Sixty-nine patients were finally included in the study. Among them 14 patients developed AKI. There were no dropouts in the study. The patients were divided into AKI and non-AKI groups for purposes of analysis.

Among patients with AKI, 57.1% were male while 42.9% were females [Table 2]. In the non-AKI patients, males were 41.8% and 58.2% were females. The mean age in the total population studied was 59.94  $\pm$  9.05 years, while it is 59.6  $\pm$  8.36 in the non-AKI group and 61.2  $\pm$  11.64 in the AKI group.

The distribution of comorbidities in the AKI and non-AKI groups showed that diabetes had an incidence of 92.9% and 60%, hypertension 78.6% and 92.7%, congestive heart failure 7.1% and 14.5%, coronary artery disease 7.1% and 14.5% and chronic kidney disease 28.6% and 10.9%, respectively. The mean estimated GFR was  $86.50 \pm 21.103$  in patients with AKI and  $89.00 \pm 18.961$  in the non-AKI group. Only diabetes was significantly associated with development of AKI among the comorbidities studied. The incidence of use of ACE inhibitors was around 45.5% in the non-AKI patients and 21.4% in the AKI group, while none of the patients was on ARBs.

The mean duration of surgery in the non-AKI group was around 6.42 h, while it was around 6.86 h in the AKI group [Table 3]. The median number of hypotensive episodes in AKI group was around two. The mean volume of blood lost in the AKI group was 639.29  $\pm$  323.55 mL, while 50% of the patients required blood transfusion for the fluid lost. Colloid usage in the AKI group was 107.14  $\pm$  212.9 mL. About 78.6% of the patients with AKI received NSAIDs in the perioperative period. None of the intraoperative parameters was significantly associated with the development of AKI.

RI measured in the AKI group in the preoperative period was  $0.65 \pm 0.09$  and in the postoperative period  $0.74 \pm 0.09$ , while % RI was  $15 \pm 8$  [Table 4]. RI in the non-AKI group measured was  $0.61 \pm 0.09$  in the preoperative period,  $0.66 \pm 0.1$  in the postoperative period and  $14 \pm 10$  was % RI. Among these parameters, only the postoperative RI was significantly associated with AKI.

Univariate analysis showed that AKI correlated significantly with preoperative diabetes and postoperative RI [Tables 2 and 4]. The multivariate analysis of the two most significant variables, allowing the model to only retain the two variables with the greatest association level, shows that postoperative RI was the most significant diagnostic variable [Table 5].

Resistive indices assessed by ROC curves and the AUC to distinguish between non-AKI and AKI groups were 0.617 [95% confidence interval (95% CI 0.448–0.786)] for preoperative RI, 0.732 (95% CI 0.592–0.871) for

Patient characteristics	Total patients (69)	Non-AKI ( <i>n</i> =55)	AKI (n=14)	Р
Male, <i>n</i> (%)	31 (44.9%)	23 (41.8%)	8 (57.1%)	0.303
Female, n (%)	38 (55.1%)	32 (58.2%)	6 (42.9%)	
Age (years) (mean±SD)	59.94±9.05	59.62±8.36	61.21±11.64	0.559
Diabetes, n (%)	46 (66.7%)	33 (60%)	13 (92.9%)	0.025*
Hypertension, n (%)	62 (89.9%)	51 (92.7%)	11 (78.6%)	0.142
Congestive heart failure, n (%)	9 (13%)	8 (14.5%)	1 (7.1%)	0.674
Coronary artery disease, n (%)	9 (13%)	8 (14.5%)	1 (7.1%)	0.674
ACE inhibitors, n (%)	28 (40.6%)	25 (45.5%)	3 (21.4%)	0.102
Chronic kidney disease, n (%)	10 (14.5%)	6 (10.9%)	4 (28.6%)	0.109
Estimated glomerular filtration rate, mL/min/1.73 m <sup>2</sup> (mean±SD)	88.00±19.532	89.00±18.961	86.50±21.103	0.166

Table	3: Intraoperative data			
Intraoperative data	Total patients (69)	Non-AKI ( <i>n</i> =55)	AKI ( <i>n</i> =14)	Р
Duration of procedure (h) (mean±SD)	6.51+2.4	6.42±2.54	6.86±2.1	0.554
General anaesthesia (%)	66.7%	67.3%	64.3%	0.832
General+regional anaesthesia (%)	33.3%	32.7%	35.7%	
Blood loss, mL (mean±SD)	534.78±342.28	508.18±344.63	639.29±323.54	0.203
Fluid replacement, L (mean±SD)	3.62±1.38	3.54±1.4	3.92±1.14	0.359
Fluid replacement type (%)				
Crystalloids only	58.0%	61.8%	42.9%	0.486
Crystalloids + colloids	2.9%	1.8%	7.1%	
Crystalloids + colloids + blood	18.8%	18.2%	21.4%	
Crystalloids + blood	20.3%	18.2%	28.6%	
Requirement for blood transfusion (%)	42.0%	40.0%	50.0%	0.499
Colloid usage, mL (mean±SD)	97.83±206.58	95.45±206.88	107.14±212.90	0.852
Number of hypotensive episodes (median with percentiles)	1.00 (0-2)	1.00 (0-2)	2.00 (0-3)	0.053
Perioperative use of NSAIDs (%)	60.9%	56.4%	78.6%	0.128

AKI – Acute kidney injury; SD – Standard deviation; NSAIDs – Nonsteroidal anti-inflammatory drugs

postoperative RI and 0.561 (95% CI 0.397–0.725) for % RI [Figure 1]. The most accurate cut-off value to distinguish non-AKI and AKI groups was a postoperative RI of 0.77 at sensitivity of 57.1% and specificity of 85.5%. At this threshold, positive likelihood ratio was 3.93 and negative likelihood ratio was 0.501.

#### DISCUSSION

In our study, the incidence of AKI was 20.2%. No patient required dialysis. The incidence is higher than generally expected after abdominal surgery.<sup>[9]</sup>

This difference in incidence results probably from the different surgical procedures and risk factors chosen between the cited study and ours. We chose only open abdominal surgeries with a decision to select a population at risk based on certain risk factors, corresponding to the ones that would be of concern in our clinical practice. The authors in the study mentioned above included laparoscopic patients and laparotomies and all patients greater than 18 years of age. Our university hospital is a referral centre for major abdominal surgery, and this type of surgery

Table 4: Resistive indices						
Resistive index	Total	Non-AKI	AKI	Р		
Preoperative	0.62±0.09	0.61±0.09	0.65±0.09	0.149		
Postoperative	0.68±0.1	0.66±0.1	0.74±0.09	0.006**		
% Resistive index	14±9.6	14±10	15±8	0.868		
AKI – Acute kidney injury. **P≤0.05						

Table 5: Multivariate analysis					
Variable	Р	95% confidence interval		Odds	
		Lower	Upper	ratio	
Diabetes	0.052	0.013	1.015	0.113	
Postoperative RI	0.02	5.51	12881.59	8.1	
DI Desistiva indev					

RI - Resistive index

represents a source of increased risk of AKI. Another explanation for the difference might stem from the fact that we used AKIN classification for the diagnosis of AKI, while the authors in the study referred to used KDIGO to define AKI.

AKIN was used in our study because of its increased sensitivity in assessing postoperative mortality in patients.<sup>[15]</sup> Furthermore, AKIN criteria do not require a baseline value. The eGFR is also not required in estimating the occurrence of AKI.

Although we included patients with high-risk factors for AKI in our study, only diabetes was significantly associated with AKI in the postoperative period. Hypertension and chronic kidney disease were present in a higher percentage of patients with AKI, but did not reach statistical significance. In a study by Kim et al.<sup>[2]</sup> around 34% of the patients with AKI had hypertension and it was identified as an independent predictor of postoperative AKI. Similarly, in a study by Long *et al.*,<sup>[9]</sup> hypertension and chronic kidney disease were seen in a smaller percentage of patients, but these factors were found to be statistically significant and independent predictors of postoperative AKI. This difference in results between our study and others is probably because of our smaller study population. As shown in the results, none of the intraoperative parameters was associated with development of AKI. This is an important finding because AKI is a critical event associated with increased morbidity rates.<sup>[16]</sup> Identifying potential risk factors in the intraoperative period is essential as these factors could be potentially modified to prevent the development of AKI. Common intraoperative factors such as volumes of intravenous (IV) fluids used, the choice of IV fluids (crystalloids or colloids) and the decision to transfuse packed red cells were not found

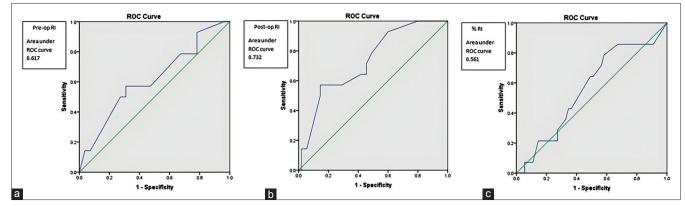


Figure 1: Receiver operating characteristic curves. (a) Preoperative RI. (b) Postoperative RI. (c) % RI. The cut-off value for postoperative RI was obtained at a sensitivity of 57.1% and specificity of 85.5%

to be statistically significant factors in our study, with respect to the incidence of AKI.

In our study, we also found that preoperative RI and % RI are not significant in predicting AKI, while postoperative RI is a significant predictor. Preoperative RI reflected the state of the renal vasculature at baseline in both the AKI and non-AKI groups. Since RI is a marker of renal vascular resistance,<sup>[17]</sup> perioperative changes could have influenced the postoperative RI. We are further presuming that patients who had statistically significant elevations of postoperative RI and developed AKI could have been patients who also had higher preoperative RIs than in the non-AKI population. However, the differences preoperatively did not achieve statistical significance. This could explain why the postoperative RIs could predict development of AKI, but the percentage change from baseline which was reflected by % RI (difference between pre- and postoperative RIs) was not predictive of subsequent development of AKI. However, the cut-off value obtained in our study for postoperative RI was 0.77, with a sensitivity of only 57.1% and specificity of 85.5%. Hence, postoperative RI cannot be used as a single tool in predicting postoperative AKI, but in combination with other markers could be helpful in predicting the risk. In this regard, it may be worth mentioning that while diverse biomarkers (NGAL, cystatin C) are being explored, in the background of postoperative AKI, their clinical gravity needs to be defined.

There were a few limitations in our study. This study was done on patients at high risk of developing AKI, so these results cannot be extrapolated to the normal population. Second, we included patients undergoing only abdominal surgery. Hence, the cut-off value obtained in this study cannot be used in other high-risk groups. Third, our sample size is small and our patients were not followed up, so long-term morbidity in these patients was not determined. Also, the small sample size could lead to Type 2 error, which implies whether RI could be a more sensitive or specific marker for AKI when compared to other modalities would not be answered by this study. Fourth, measurement of renal RI is operator-dependent. This study needs to be performed in different patient groups in different settings before using these results in the general population. Furthermore, one could also argue that certain parameters, such as the choice of inhalational agents, their minimal alveolar concentration values and the choice of antibiotics, were parameters which

could potentially have been studied, but which were not recorded in this trial.

#### CONCLUSION

Postoperative RI can detect early AKI after major abdominal surgery and could be performed early in the postoperative care unit in those at risk of AKI, so as to risk stratify patients and direct preemptive management.

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#### **Conflicts of interest**

There are no conflicts of interest.

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