



Comparison of Neutrophil Gelatinase-associated Lipocalin and Renal Resistive Index as Acute Kidney Injury Predictor in Critically Ill Patients at ICU H. Adam Malik Hospital Medan

Muhammad Aldi Rivai Ginting*, Achsanuddin Hanafie, Bastian Lubis

Department of Anesthesia and Intensive Care Medical, Sumatera Utara University, H. Adam Malik General Hospital Medan, North Sumatra, Indonesia

Abstract

Edited by: Mirko Spiroski
Citation: Ginting MAR, Hanafie A, Lubis B. Comparison of Neutrophil Gelatinase-associated Lipocalin and Renal Resistive Index as Acute Kidney Injury Predictor in Critically Ill Patients at ICU H. Adam Malik Hospital Medan. Open Access Maced J Med Sci. 2021 Dec 04; 9(B):1637-1639. <https://doi.org/10.3889/oamjms.2021.7014>
Keywords: Acute kidney injury; Neutrophil gelatinase-associated lipocalin; Renal resistive index
***Correspondence:** Muhammad Aldi Rivai Ginting, Department of Anesthesiology and Intensive Care, Faculty of Medicine, Sumatera Utara University, H. Adam Malik General Hospital Medan, North Sumatra, Indonesia. E-mail: aldi.oneal@yahoo.com
Received: 06-Aug-2021
Revised: 21-Nov-2021
Accepted: 24-Nov-2021
Copyright: © 2021 Muhammad Aldi Rivai Ginting, Achsanuddin Hanafie, Bastian Lubis
Funding: This research did not receive any financial support
Competing Interests: The authors have declared that no competing interests exist
Open Access: This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (CC BY-NC 4.0)

BACKGROUND: Acute kidney injury (AKI) is a complication found in critically ill patients. Current consensus explains that diagnosis of AKI based on increased serum creatinine and decreased urine output. Neutrophil gelatinase-associated lipocalin (NGAL) level is increased a few hours after tubular damage occurred and can predict AKI more significantly than serum creatinine. Renal resistive index (RRI) is also a good marker in predicting the early stage of AKI.

AIM: This study aimed to compare RRI and NGAL level as marker to predict incidence of AKI in critically ill patients treated in the Intensive Care Unit (ICU) at H. Adam Malik Hospital Medan.

METHODS: This was an observational prospective cohort study and conducted in ICU at H. Adam Malik Hospital Medan in April-May 2021. This study had been approved by the Ethics Committee of Faculty of Medicine, Sumatera Utara University and H. Adam Malik Hospital Medan. Inclusion criteria are critical patients aged 18–65 years with 1st and 2nd priority level. Consecutive sampling was used. Resistive Index (RI) measured using USG Doppler by researcher and the results confirmed by ICU supervisors, while urine NGAL level measured within 3 h after ICU admission. Plasma urea and creatinine level measured after 24 h after ICU admission.

RESULTS: A total of 40 samples were collected; percentage of men and women are 66–35%, respectively ($p = 0.001$). There was a significant difference RI between AKI-group and non-AKI group (0.719 ± 0.060 and 0.060 ± 0.077 , respectively) ($p = 0.001$). RI has a sensitivity of 71%, specificity of 84%, and accuracy of 87% in predicting occurrence of AKI with AUROC = 0.873. Meanwhile, NGAL has a sensitivity, specificity, and accuracy (66%, 89%, 78%, respectively) in early prediction of AKI incidence in critically ill patients.

CONCLUSION: RI value was higher in AKI group than non-AKI group. RRI has better sensitivity than NGAL in predicting incidence of AKI.

Introduction

Acute kidney injury (AKI) is a condition that describes as a broad spectrum from mild kidney function impairment to permanent kidney damage and complete loss of kidney function. AKI is a complication that is often found in critically ill patients treated in the Intensive Care Unit (ICU) [2], Neutrophil gelatinase-associated lipocalin (NGAL) is a glycoprotein that is stored in mature neutrophil granules and released by tubular kidney cells after an acute tubular damage.

Laboratory tests can detect an increase in NGAL several hours after tubular damage and are reported to predict AKI earlier than serum creatinine [1], [4], [8]. Apart from NGAL, Renal resistive index (RRI) also been reported to be a good early marker of AKI. In contrast to NGAL which is examined from blood, RRI is a sonographic index. Renal vasoconstriction is an early manifestation of AKI. Doppler ultrasound can measure RRI show changes in intrarenal or interlobar arcuate arteries blood flow profile [6].

Methods

This study is an observational analytic study with a prospective cohort design. Conducted at ICU of Haji Adam Malik Hospital Medan in April until May 2021 after obtaining approval from Health Research Ethics Commission and approved by the Ethics Committee of Medical Faculty, Sumatera Utara University and H. Adam Malik Hospital Medan. Sample in this study is 40 subjects. The sampling technique used non-probability sampling with consecutive sampling, where all subjects who came and met inclusion and exclusion criteria. Inclusion criteria in this study are patients aged 18–65 years and patients who met criteria for critically ill patients according to the Ministry of Health regulations with 1st and 2nd priority level, while exclusion criteria are patients with acute and chronic renal failure, patients receiving nephrotoxic drug therapy, and patients with malignancy. The study sample collection was in accordance with inclusion and exclusion criteria in critically ill and septic patients, who were admitted to the ICU at H. Adam Malik Hospital Medan.

Basic data collection such as gender, age, admission diagnosis, laboratory results, and urine output monitoring by volunteers. Renal Doppler ultrasound performed to assess RRI (performed by researcher and confirmed by ICU supervisor) and urine NGAL collected within 3 h of ICU admission. Then, urine output and creatinine clearance were monitored to assess whether AKI occurred according to the RIFLE criteria. Re-examination of urea and creatinine levels was carried out within 24 h of treatment.

Results

Characteristics of subjects, from 40 samples, number of male samples are 26 (66%) and female samples are 14 (35%), $p = 0.001$. Mean NGAL value sample are 80.35 ± 504.61 ng/dL with $p = 0.01$. Meanwhile, mean value of RRI are 0.68 ± 0.088 ($p = 0.038$), statistically not normally distributed. Mean value BMI in this study are 25.05 ± 2.214 , $p = 0.402$. Mean age are 48.35 ± 14.143 years, $p = 0.001$. And incidence of AKI in this study are 21 (52.5%) samples.

There is a statistically and clinically difference in mean value of RRI between AKI and non-AKI groups, 0.719 ± 0.060 compared to 0.060 ± 0.077 , with $p = 0.001$.

Table 1: Predictive value of RRI

(%)	TP	TN	FP	FN	Sensitivity	Specificity	Accuracy	PPV	NPV
RRI	6	3	16	15 (71.4)	71	84	87	78.9	27
	(28.6)	(15.8)	(84.2)						

TP: True positive, TN: True negative, FP: False positive, FN: False negative, PPV: Positive predictive value, NPV: Negative predictive value. RRI: Renal resistive index.

Table 1 describes predictive value of RRI on predicting AKI in ICU patients. In this study, value of True Positive was 28.6%, True Negative 15.8%, False Positive 84.2%, and False Negative 71.4%. RRI has a sensitivity of 71%, specificity of 84%, and accuracy of 87% in predicting AKI with AUROC = 0.873 (Figure 1). Meanwhile, Table 2 shows predictive value of NGAL on predicting AKI. Obtained a True Positive value of 66.7%, True Negative 89.5%, False Positive 10.5%, and False Negative 33.3%, with AUROC = 0.781 (Figure 2).

Table 2: Predictive value of NGAL

(%)	TP	TN	FP	FN	Sensitivity	Specificity	Accuracy	PPV	NPV
NGAL	14	17	2	7	66	89	78	87	29
	(66.7)	(89.5)	(10.5)	(33.3)					

TP: True positive, TN: True negative, FP: False positive, FN: False negative, PPV: Positive predictive value, NPV: Negative predictive value. NGAL: Neutrophil gelatinase-associated lipocalin.

Discussion

In our study, it found that RRI had a sensitivity of 71% and a specificity of 84% with an accuracy value of 87%. When compared with a study conducted by Muthukrishnan *et al.* (2019) where sensitivity is 57.1%,

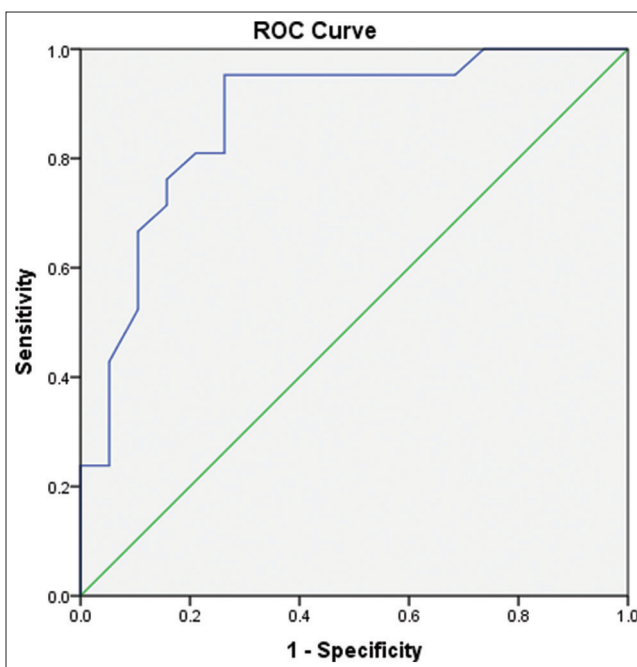


Figure 1: Renal resistive ROC curve

specificity 85.5%, accuracy 77%, and study conducted by Mulier *et al.* (2018) which sensitivity 53%, and specificity are 87% [7]. RRI value in our study was not much different. In addition, this study also found significant differences, where the RRI value was higher in AKI subjects. Therefore, Renal Doppler examination is a reliable examination and an easier assessment in assessing renal perfusion in critically ill patients.

NGAL has a 66% sensitivity and 89% specificity, with 78% accuracy. This is in accordance with research

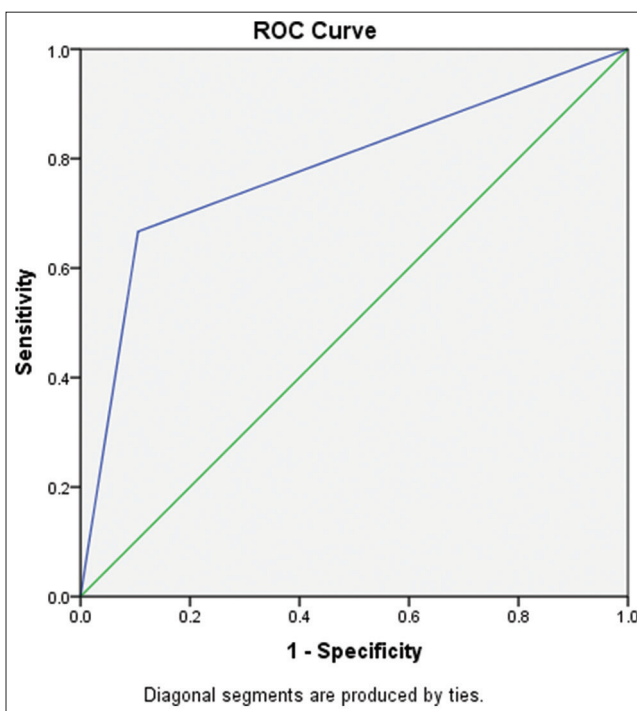


Figure 2: Neutrophil gelatinase-associated lipocalin ROC curve

conducted by Khawaja *et al.* (2019) which obtained a sensitivity of 78.5%, specificity of 88.8%, and study of Mahadevaiah *et al.* (2021) which obtained a 83.6% sensitivity and a 88.9% specificity. So, NGAL value in this study is not that much different. In addition, in this study, NGAL value was statistically significant and could predict incidence of AKI [3].

Based on the results of our study, it is known that RRI has better sensitivity than NGAL in predicting incidence of AKI in critically ill patients. However, a high NGAL value can also be a marker of AKI, because it has a high sensitivity. This is because NGAL is a glycoprotein that stored in mature neutrophil granules and found to be released by renal tubular cells after acute tubular damage. Laboratory examination can detect an increase in NGAL several hours after the occurrence of tubular damage [1], [3], [5].

Limitations in our study is RRI and NGAL cannot measure mortality rate because in this study there is no observations on outcome of specified samples.

Conclusion

RRI has better sensitivity than NGAL in predicting incidence of AKI. However, RRI and NGAL can be a good marker to predict incidence of AKI.

References

- Banai A, Rozenfeld K, Levit D, Merdler I, Loewenstein I, Banai S, *et al.* Neutrophil gelatinase-associated lipocalin (NGAL) for the prediction of acute kidney injury in chronic kidney disease patients treated with primary percutaneous coronary intervention. *IJC Heart Vasc.* 2021;32:1-5. <https://doi.org/10.1016/j.ijcha.2020.100695>
PMid:33364336
- Case J, Khan S, Khalid R, Khan A. Epidemiology of acute kidney injury in the intensive care unit. *Crit Care Res Pract.* 2013;2013:479730. <https://doi.org/10.1155/2013/479730>
PMid:23573420
- Khawaja S, Jafri L, Siddiqui I, Hashmi M, Ghani F. The utility of neutrophil gelatinase-associated Lipocalin (NGAL) as a marker of acute kidney injury (AKI) in critically ill patients. *Biomarker Res.* 2019;7:4. <https://doi.org/10.1186/s40364-019-0155-1>
PMid:30834123
- Li H, Yu Z, Gan L, Peng L, Zhou Q. Serum NGAL and FGF23 may have certain value in early diagnosis of CIN. *Renal Failure.* 2018;40(1):547-53. <https://doi.org/10.1080/0886022X.2018.1487860>
PMid:30278796
- Mahadevaiah M, Thimmaiah M, Yerramsetty V, Kumar J, Kumar R. Diagnostic relevance of neutrophil gelatinase associated lipocalin in early detection of acute kidney injury. *J Emerg Pract Trauma.* 2021;7(2):88-92.
- Mulier J, Rozemeijer S, Röttgering JG, Spoelstra-de Man AM, Elbers PW, Tuinman PR, *et al.* Renal resistive index as an early predictor and discriminator of acute kidney injury in critically ill patients; a prospective observational cohort study. *PLoS One.* 2018;13(6):1-18. <https://doi.org/10.1371/journal.pone.0197967>
PMid:29889830
- Muthukrishnan K, Parida S, Barathim S, Badhe A, Mishra S. Doppler resistive index to reflect risk of acute kidney injury after major abdominal surgery: A prospective observational trial. *Indian J Anaesth.* 2019;63(7):551-7. https://doi.org/10.4103/ija.IJA_189_19
PMid:31391618
- Shang W, Wang Z. The update of NGAL in acute kidney injury. *Curr Protein Peptide Sci.* 2017;17:1211-7. <https://doi.org/10.2174/1389203717666160909125004>
PMid:27634444