KI REPORTS
KIReports.org

Use of the Renal Angina Index in Determining Acute Kidney Injury

Ryo Matsuura[1], Nattachai Srisawat[2], Rolando Claure-Del Granado[3], Kent Doi[4], Teruhiko Yoshida[1], Masaomi Nangaku[1] and Eisei Noiri[1]

[1]Department of Nephrology and Endocrinology, The University of Tokyo Hospital, Japan; [2]Division of Nephrology, Department of Medicine, Chulalongkorn University, Thailand; [3]Universidad Mayor de San Simon School of Medicine, Cochabamba, Bolivia; and [4]Department of Emergency and Critical Care Medicine, The University of Tokyo Hospital, Japan

Introduction: The renal angina index (RAI) is determined based on changes in the creatinine and condition scores of patients. The aim of this study is to evaluate the efficacy of the RAI in predicting persistent acute kidney injury (AKI) in Asian intensive care unit (ICU) patients.

Methods: This is a subanalysis of 3 prospective studies conducted in Japan and Thailand. The RAI was calculated for all enrolled patients using the method of Goldstein and colleagues, with a minor modification for adults on day 2. To determine the accuracy of RAI further, we evaluated a subgroup of patients for whom baseline serum creatinine values were available at ICU admission (i.e., those with hospital-acquired AKI). AKI biomarkers were evaluated for their efficacy in improving the performance of RAI. The outcome was defined as AKI stage 2 or 3 over 48 hours.

Results: Of the 263 patients analyzed, a total of 22 progressed to stage 2 or 3 AKI over 48 hours. The RAI was associated with an area under the curve (AUC) of 0.63 in receiver-operating characteristics analysis, with a cutoff of 10. In those admitted from general wards, the RAI had good performance, with an AUC of 0.73 and a cutoff of 6. A combination of L-type fatty acid–binding protein with the RAI improved the predictive performance for assessing persistent AKI with an AUC of 0.79.

Conclusion: The RAI may be effective in predicting persistent AKI in adult patients admitted from general wards. Incorporation of AKI biomarkers into the RAI may potentially improve prediction.

Kidney Int Rep (2018) ■, ■–■; https://doi.org/10.1016/j.ekir.2018.01.013
KEYWORDS: acute kidney injury; AKI biomarkers; prediction; renal angina

Acute kidney injury (AKI) is a common complication with miserable consequences in critically ill patients worldwide.[1,2] To prevent and reduce the incidence of severe AKI, risk stratification is deemed important for providing care to patients at high risk of AKI.

Although the Kidney Disease Improving Global Outcomes (KDIGO) guideline defines AKI according to serum creatinine and urine output, serum creatinine is an imperfect marker for detecting severe AKI, and novel AKI biomarkers are emerging. Thus, prediction of AKI or risk stratification of patients in danger of kidney damage is crucial for initiating preventive measures for AKI. AKI biomarkers, such as cell cycle arrest markers (tissue inhibitor of metalloproteinases 2 and insulin-like growth factor binding protein 7),[3–5] neutrophil gelatinase-associated lipocalin, and L-type fatty acid–binding protein (L-FABP)[6–8] were reported to predict AKI. However, it is necessary that these biomarkers be used in an appropriate setting, because they may be affected by comorbidities, and their performance may decrease in a different setting.[9,10] Thus, an appropriate risk assessment for AKI is required in every patient admitted to the intensive care unit (ICU).

Recently, the renal angina index (RAI), which is determined based on changes in renal function, was proposed to risk stratify critically ill children at high risk of AKI.[11,12] The concept of renal angina has come into use to highlight the characteristics of renal injury as an analogy to the concept of angina pectoris, which is used to increase the suspicion of acute coronary syndrome in cardiology. The RAI is assumed to serve as a potential biomarker for detecting early signs of persistent AKI. The RAI in adults was proposed, which involved a consistent, albeit more complicated, definition compared with that used in pediatric ICU patients.[13] Although the RAI appears to be an

Correspondence: Eisei Noiri, Department of Nephrology and Endocrinology, The University of Tokyo Hospital, 7-3-1 Hongo, Bunkyo, Tokyo 113-8655, Japan. E-mail: noiri-tky@umin.ac.jp

Received 26 September 2017; revised 12 January 2018; accepted 30 January 2018; published online 3 February 2018

attractive concept, it remains yet to be tested for its applicability and validated in non-Western populations, such as Asian populations.

Of all the multiple chronic comorbidities that represent risk factors for AKI, diabetes mellitus has been reported to be a high risk[14] and has been included in AKI prediction models.[15] Although multiple risk factors for AKI progression have been included in an earlier report,[13] we included factors that were thought likely to influence creatinine production, such as diabetes mellitus and severe illness that required vasopressor therapy or ventilation, to make the RAI simpler in this analysis.

The aim of this study was to evaluate the performance of RAI for predicting patients who were at higher risk of persistent severe AKI in the Asian population. Additional clinical parameters evaluated at ICU admission were also examined for their ability to predict severe AKI in this study.

METHODS

Study Population

This study was a subanalysis of 3 prospective observational studies conducted in a mixed medical and/or surgical ICU settings (i.e., 2 prospective observational studies in Japan[16–18] and the SEA-AKI study in Thailand, South East Asia-Acute Kidney Injury, https://www.theisn.org/programs/isn-programs/item/2645-clinical-research-the-epidemiology-and-prognostic-factors-for-mortality-in-intensive-care-unit-patients-with-acute-kidney-injury-in-south-east-asia[19]). As previously reported, serum creatinine was prospectively measured in all ICU patients in these studies every day for 1 week after ICU admission. In the first analysis, all patients were included, except for those who had already progressed to AKI stage 2 or 3 at ICU admission, those who stayed in ICU for <48 hours, and those whose serum creatinine values at ICU admission or on day 2 were not available. In the next analysis, patients were included if they met the following criteria: (i) those admitted from general wards with no AKI or in AKI stage 1; (ii) those who had their serum creatinine measured at 2 points (within 3 days before ICU admission and at ICU admission); and (iii) those who stayed in ICU for >48 hours. This study was approved by the institutional review committees of The University of Tokyo Hospital (Japan) and King Chulalongkorn Memorial Hospital (Thailand), and was conducted in accordance with the Declaration of Helsinki.

Renal Angina Index

The RAI in previous reports[13,20] was used with a minor modification (Figure 1 and Supplementary Figure S1).

Elevated Cr	score
<0.1 mg/dl	1
≥0.1 mg/dl	2
≥0.3 mg/dl	4
≥0.4 mg/dl	8

×

Condition	score
ICU admission	1
DM	3
Vasopressor or Ventilator	5

= RA index

Figure 1. Renal angina (RA) index. The scheme was derived from Basu *et al.*[20] for use with a minor modification for diabetes mellitus (DM) as an adult-specific disease. The RA index-based approach was originally reported by Claure-Del Granado *et al.*[21] Supplementary Figure S1 shows the influence of additional comorbidities. ICU, intensive care unit.

The condition of each patient was scored as follows: those with ventilation and/or vasopressor therapy, 5 points; those with ≥1 comorbidities (diabetes mellitus, advanced age [70 years or older], chronic kidney disease [CKD], or hypertension), 3 points; and those admitted to ICU, 1 point. The data on the history of cardiovascular diseases, including chronic heart failure, were not collected in these studies, and therefore, were not integrated into the RAI calculation. The creatinine score was determined by the difference in serum creatinine between that at ICU admission and that within 3 days before ICU admission at the latest, as follows: those with creatinine ≥0.4 mg/dl, 8 points; those with creatinine ≥0.3 mg/dl, 4 points; those with creatinine ≥0.1 mg/dl, 2 points; and those with creatinine <0.1 mg/dl, 1 point. The RAI score was defined as the worst condition score multiplied by the creatinine score and consisted of 1, 2, 3, 4, 6, 8, 10, 12, 24, and 40. All patients were evaluated for the RAI on the next day after ICU admission in the first analysis and at ICU admission in the second analysis (Figure 2).

Urinary L-FABP Measurement

Because urine output was measured hourly by an indwelling catheter, a fresh urine sample was obtained from all patients at ICU admission. The urinary L-FABP level was measured using *in vitro* diagnostic medical tests that formed part of enzyme-linked immunosorbent assay kits (Human L-FABP Assay Kit; CMIC Co. Ltd., Tokyo, Japan) in which the ability to detect AKI was proven in clinical and experimental settings in previous studies.[8,22–24]

Assessment of Kidney Function

The baseline serum creatinine value was defined as the last value measured in an outpatient setting within 6 months before ICU admission. For patients with an unavailable creatinine value before ICU admission, the baseline value was defined as the minimum among inpatient values obtained before ICU admission, the last value before hospital discharge, or the estimated value using the Modification of Diet in Renal Disease equation, which assumes a baseline estimated glomerular