

Introduction

- In recent years, the use of the renal angina index (RAI) to calculate and accurately predict risk for the development of acute kidney injury (AKI) has been heavily explored.
- AKI is traditionally diagnosed by an increase in serum creatinine (sCr) concentration or oliguria, both of which are neither specific or sensitive, especially among children.
- An RAI score may be calculated by combining objective signs of kidney dysfunction (such as sCr), and patient context, (such as risk factors for AKI), thus potentially serving as a more accurate biomarker for AKI.

Table 1: Calculating an RAI Score

Elevated Serum Creatinine (Injury Strata)	Associated Score	✖	Risk Factor	Associated Score	=	RAI Score
<0.1 mg/dl	1		ICU admission, concern for sepsis/shock	1 (moderate)		
≥0.1 mg/dl	2		Diabetes mellitus, oncologic disease, history of transplantation	3 (high)		
≥0.3 mg/dl	4		Vasopressor or Ventilator	5 (very high)		
≥0.4 mg/dl	8					

Adapted from Basu et al. [1] & Matsuura et al [2]; **RAI**, Renal angina index; ICU, intensive care unit

Objective

- Due to the propitious and novel nature of RAI, this systematic review aims to analyze how well RAI serves as a predictor of AKI outcomes.

Methods

- **Design:** Meta-analysis
- **Search Strategy:** A literature search was conducted in PubMed/Medline and Google Scholar. The search consists of the following medical subject heading (MeSH) terms, “Renal Angina Index”, “Acute kidney injury”, “Intensive Care units”, “Neonatal” in various combinations. All the articles were limited to the English language.

Table 2: A Systematic Review PICO Table

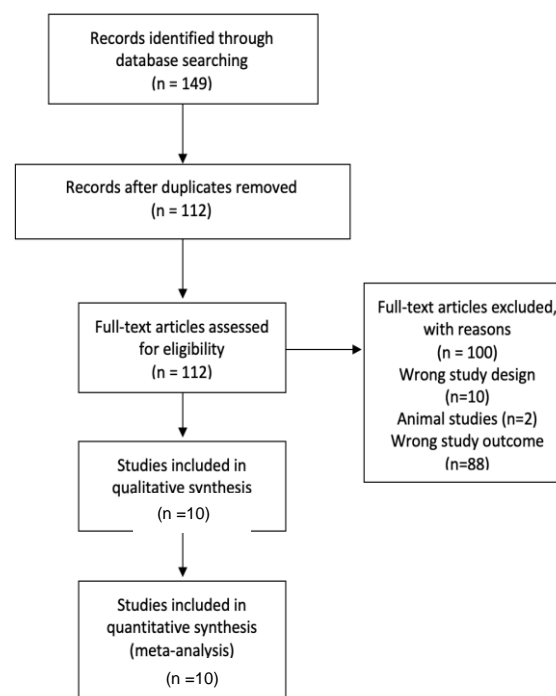
A systematic review PICO table		
Criteria	Inclusion	Exclusion
Population	Adult and pediatric patients with high-risk AKI	
Intervention	Patients with RAI measurement	Did not measure RAI
Comparison	No Controls	
Outcome	To see the prognostic aspect of early prediction of AKI in the pediatric and adult population via renal angina index versus serum creatinine.	
Study types	Case reports, Prospective and Retrospective studies	Systematic reviews, Literature reviews

AKI, acute kidney injury; RAI, Renal angina index

- **Data Analysis:** The outcomes included predictive ability of RAI [sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and area under the curve (AUC)] and mortality among RAI positive vs. RAI negative patients. These outcomes and its 95% confidence intervals (95% CI) were computed (calculated when not reported) for each study. A meta-analysis of these outcomes was conducted.

Results

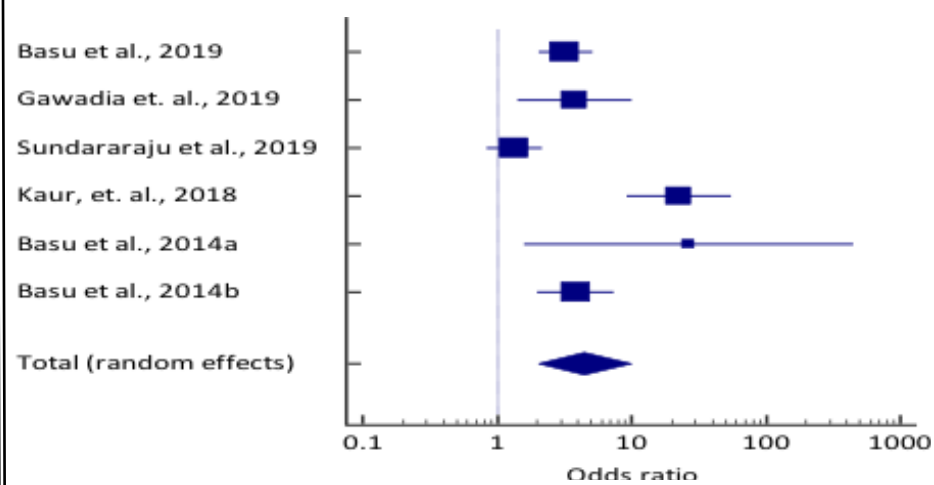
Figure 1. A PRISMA diagram



- The initial search yielded a total of 149 articles, and a total of 10 studies reporting the outcomes of interest were included.
- The overall sample size across these studies was 11,026 [RAI positive = 2,513 and RAI negative = 8,513].

Figure 2: Forest plot of the mortality among RAI positive vs. RAI negative across different studies.

The lower diamond in the graph represents the pooled estimate



- RAI positive patients (191/1,036) were observed to have a 4.5 times higher odds of mortality as compared to RAI negative patients (125/2,383) [pooled odds ratio: 4.51 (95% CI: 2.06 - 9.87) ($I^2 = 84.80\%$ (68.70% - 92.62%), $p < 0.0001$, random effects; 6 studies; $n = 3,419$)]

Table 3: Sensitivity Analysis for Different Outcomes

Parameter	Criteria	Event / Sample size	Pooled value (95% CI)	I^2 (95% CI)	N	p value
Sensitivity (95% CI)	Prospective	284/554	79.76% (51.75% - 97.29%)	96.95% (95.38% - 97.98%)	7	<0.0001
	Sample size >33	666/1,202	70.53% (45.50% - 90.27%)	98.39% (97.41% - 99.00%)	4	<0.0001
Specificity (95% CI)	Prospective	1,776/2,169	77.53% (66.89% - 86.61%)	95.62% (93.04% - 97.24%)	7	<0.0001
	Sample size >221	7,643/9,177	76.88% (66.95% - 85.49%)	98.38% (97.55% - 98.93%)	5	<0.0001
PPV (95% CI)	Prospective	284/677	45.88% (30.47% - 61.71%)	93.44% (88.94% - 96.11%)	7	<0.0001
	Sample size >114	655/2,263	26.69% (19.79% - 34.20%)	90.67% (81.16% - 95.38%)	5	<0.0001
NPV (95% CI)	Prospective	1,776/2,046	94.39% (86.64% - 98.92%)	95.87% (93.50% - 97.38%)	7	<0.0001
	Sample size >115	7,643/8,190	94.02% (87.08% - 98.41%)	98.44% (97.66% - 98.96%)	5	<0.0001
AUC (95% CI)	Prospective	978	0.88 (0.84 - 0.92)	51.35% (0.00% - 83.92%)	4	0.1038
	Sample size >250 ^A	1,282	0.81 (0.76 - 0.86)	0.00% (0.00% - 85.67%)	3	0.7913
Mortality [Odds ratio (95% CI)] [*]	Prospective	134/582 vs. 112/1,868	4.20 (1.50 - 11.53)	90.00% (77.33% - 95.59%)	4	<0.0001
	Sample size >350	88/607 vs. 69/1,980	6.13 (2.21 - 17.00)	86.11% (59.74% - 95.21%)	3	0.0007

^AFixed effect model, all else random effect model
^{*} Odds ratio for AKI mortality among RAI positive vs. RAI negative
N= number of studies
Sample size based on median values for sensitivity, specificity, PPV, and NPV across all the studies; and median values for the studies for AUC and mortality

Predictive ability of RAI:

- Sensitivity: 79.21% (95% CI: 64.28 % - 90.90%)
- Specificity: 73.22% (95% CI: 64.13% - 81.42%)
- PPV: 38.38% (95% CI: 29.37% - 47.81%)
- NPV: 94.83% (95% CI: 90.49% - 97.91%)

Discussion

- This systematic review evaluates the prognostic aspect of early prediction of AKI in the pediatric and adult population via RAI versus sCr.
- Improvement upon sCr with the use of RAI will serve to better detect and predict kidney injury.
- The change in sCr varies greatly with age and initial creatinine value. SCr, the main diagnostic measure of pediatric AKI, has been shown to lack precision in creatinine levels characteristic of young children [3].
- Small increases in sCr reflect significant kidney damage and are associated with poor patient outcomes. SCr has many limitations for a real-time accurate diagnosis of AKI, which is why RAI was originally proposed [1].
- **The use of RAI allows for providers to better risk stratify patients and predict mortality.**
 - RAI positive patients in our study had a 4.5 times higher odds of mortality as compared to RAI negative patients.
 - RAI has a high negative predictive value and sensitivity.
 - Awareness of AKI risk factors and clinician awareness of AKI susceptibilities will allow patients who are at risk of developing AKI to be closely monitored through the RAI scoring system.
 - The use of RAI is tailored more to the pediatric population than sCr. RAI has a higher sensitivity and specificity, especially for children, than sCr.

Conclusion

- Currently, without RAI, clinicians lack a way to risk stratify patients capable of developing AKI.
- RAI shows benefit in the prediction of AKI among pediatric populations.

References

1. Basu R.K., Zappitelli M., Brunner L. Derivation and validation of the renal angina index to improve the prediction of acute kidney injury in critically ill children. *Kidney Int.* 2014;85:659–667.
2. Matsuura R, Srisawat N, Claire-Del Granado R, et al. Use of the Renal Angina Index in Determining Acute Kidney Injury. *Kidney Int Rep.* 2018;3(3):677-683. Published 2018 Feb 3. doi:10.1016/j.ekir.2018.01.013
3. Xu X, Nie S, Zhang A, et al. A New Criterion for Pediatric AKI Based on the Reference Change Value of Serum Creatinine. *J Am Soc Nephrol.* 2018;29(9):2432-2442. doi:10.1681/ASN.2018010090