Procalcitonin as a biomarker of acute kidney injury in patients with suspected bacterial sepsis in the acute care setting

Austin Kantola, MS-4[1], Jose Navas Blanco, MD[2], Jacob Keeley, MS[1]

[1]Oakland University William Beaumont School of Medicine, Rochester, Michigan; [2]Corewell Health – Department of Anesthesiology, Royal Oak, Michigan

Background

Acute kidney injury (AKI) is a common, life-threatening complication in patients with sepsis and septic shock.

→ Approximately one-half of patients with sepsis experience an AKI.[4]
→ One-third of all acute kidney injuries are related to sepsis.[4]
→ Sepsis-associated AKI raises in-hospital mortality eightfold and the risk of chronic kidney disease development threefold.[1,2,3]

Early identification of AKI could save time and resources, lower costs, improve patient outcomes.
Therefore, a biomarker for earlier AKI detection in patients with sepsis would serve an outstanding role in health care.

In the setting of bacterial infection, an upregulation of innate immune system gene transcription and translation causes the surge in procalcitonin (PCT). This can be observed within 2-4 hours of an immune response, peaking within 12-24 hours.[5]

Procalcitonin is often used to monitor both the presence and resolution of bacterial infection.[6] PCT algorithms are also a biomarker for preventing antibiotic overconsumption, and allow reassurance during antibiotic cessation.[7]

Due to the utility of procalcitonin in monitoring bacterial sepsis incidence and resolution, the authors hypothesize that its concentration in serum could serve as a biomarker for AKI risk stratification in patients suspected of bacterial sepsis.

Methods

Population/cohort

We present a retrospective, multi-center, cohort study of patients admitted between 2015 and 2021. The patient population included patients admitted to any of three Corewell Health East hospitals (formerly Beaumont Health): Royal Oak, Grosse Pointe, or Troy. The inclusion and exclusion criteria reflect the data available in the acute care setting.

Inclusion Criteria: ≥ 18 years of age. SIRS score ≥ 2 recorded within 24 hours of admission. Serum procalcitonin drawn and a bacterial culture order must have been placed within 24 hours of admission, indicating physician concern for bacterial sepsis. A baseline serum creatinine must also have been drawn in the first 24 hours of admission. At least one additional serum creatinine value recorded between 24-48 hours after admission, as required in KDIGO criteria.

Exclusion Criteria: *Age < 18 years at admission, pregnancy at admission, history of chronic kidney disease (CKD), history of renal dialysis.

Results

→ In a univariable logistic regression model, lab PCT was found to have a significant effect on predicting AKI (OR 1.011, 95% CI 1.005 - 1.016).
→ E.g. for every 1 ng/mL increase, the odds of AKI were 1.01 greater. The median PCT of the population was 0.5, and the IQR was 0.1 to 2.1. Therefore, 75% of patients will not have a PCT recorded above 2.1 ng/mL. Consequently, a relatively significant increase in PCT (i.e. 2 ng/mL) is unlikely to represent a clinically significant increase in AKI risk for most patients suspected of bacterial sepsis.
→ Some patients had a serum PCT far above the mean or median PCT. In those cases, a rise in PCT from baseline to a concentration such as 60 ng/mL suggests a far more clinically meaningful PCT value in terms of elevated AKI risk.
→ Age and sex also independently predicted AKI in the presence of PCT. The odds of AKI in females are 0.791 that of males. Older age was more predictive of AKI, expectantly.
→ In a multivariable logistic regression model, PCT at admission still showed a statistically significant association with AKI in the presence of sex and age (OR = 1.011, 95% CI 1.006 - 1.016).

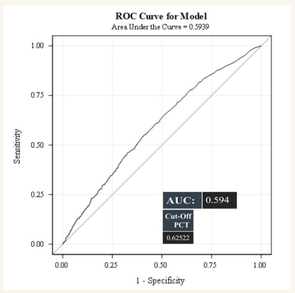

Figure 1 *(left)*: The AUC on the ROC was 0.5939, implying limited clinical applicability. The cutoff PCT for maximal sensitivity and specificity in predicting progression to AKI was 0.625.

Table 1: Procalcitonin Concentration (ng/mL) by KDIGO Stage

KDIGO	Total Observations	n	Missing Data	Minimum	Lower Quartile	Median	Upper Quartile	Max	Mean	SD
No AKI	3347	3225	122	0.02	0.13	0.40	1.87	192.12	3.94	12.21
1	602	575	27	0.02	0.23	0.84	4.06	155.21	6.71	16.87
2	94	91	3	0.03	0.23	0.59	2.44	99.13	4.46	12.81
3	93	86	7	0.03	0.30	0.76	2.80	38.70	4.13	7.79

Table 1 ***(above)***: Analysis of PCT parameters by KDIGO stage. The median serum PCT more than doubled from those with no AKI to those with KDIGO Stage 1 (0.40 ng/mL and 0.84 ng/mL, respectively). That trend did not persist with increasing AKI severity; median PCT even declined when AKI severity progressed from KDIGO Stage 1(0.84 ng/mL) to Stage 2 (0.59 ng/mL) or Stage 3 (0.76 ng/mL).

Discussion

The statistically significant association between PCT and the development of acute kidney injury is an important finding. However, the data suggests that the association between PCT and AKI occurrence or severity risk lacks clinical applicability.

PCT did not serve as a reliable biomarker for early AKI identification. The cut-off PCT value has limited applicability due to the low AUC, and also varies widely from the published threshold PCT values.[8,9]

More rigorous controls under a prospective setting and an intricate analysis of PCT by SIRS subcriteria (e.g., Is the AKI occurrence better predicted by specific SIRS criteria or the number of SIRS criteria met?) or patient subpopulation together may or may not demonstrate statistical significance.

The objective of this study was to mimic real-time patient triage, so patients were subject to relatively few exclusion criteria. Nonetheless, this study demonstrated the correlation between PCT and sepsis and the clinical applicability of such. A reliable, earlier indicator of acute kidney injury risk in patients suspected of bacterial sepsis would serve an outstanding role in medicine.

Clinical uses of procalcitonin and other biomarkers should be further investigated.

Citations

1. Kellum JA et al. The Effects of Alternative Resuscitation Strategies on Acute Kidney Injury in Patients with Septic Shock. American journal of respiratory and critical care medicine 193, 281–287, doi: 10.1164/rccm.201505-0995OC (2016).
2. Manrique-Caballero CL, Del Rio-Pertuz G, Gomez H. Sepsis-Associated Acute Kidney Injury. Crit Care Clin. 2021 Apr;37(2):279-301. doi: 10.1016/j.ccc.2020.11.010. Epub 2021 Feb 13. PMID: 33752856; PMCID: PMC7995616.
3. Coca SG, Yusuf B, Shlipak MG, Garg AX & Parikh CR Long-term risk of mortality and other adverse outcomes after acute kidney injury: a systematic review and meta-analysis. American journal of kidney diseases : the official journal of the National Kidney Foundation 53, 961–973, doi: 10.1053/j.ajkd.2008.11.034 (2009).
4. Bagshaw SM, George C, Bellomo R; ANZICS Database Management Committee. Early acute kidney injury and sepsis: a multicentre evaluation. Crit Care. 2008;12(2):R47. doi: 10.1186/cc6863. Epub 2008 Apr 10. PMID: 18402655; PMCID: PMC2447598.
5. Karzai W, Oberhoffer M, Meier-Hellmann A, Reinhart K (1997) Procalcitonin--a new indicator of the systemic response to severe infections. Infection 25: 329-334.
6. Assicot M, Gendrel D, Carsin H, Raymond J, Guilbaud J, et al. (1993) High serum procalcitonin concentrations in patients with sepsis and infection. Lancet 341: 515-518.
7. Schuetz P, Chiappa V, Briel M, Greenwald JL (2011) Procalcitonin algorithms for antibiotic therapy decisions: a systematic review of randomized controlled trials and recommendations for clinical algorithms. Arch Intern Med 171: 1322-1331.
8. Chávez-Iñiguez, Jonathan Samuel, Muñoz-Nevárez, Luis Arnoldo, Morraz-Mejía, Evelyn Fabiola, Moreno- Alvarado, Rodolfo Alejandro, López-Ceja, Marisol, Montalbán-Castellanos, José Manuel, & García-García, Guillermo. (2019). Procalcitonina como biomarcador de daño renal agudo en pacientes con sepsis y choque séptico. Revista Colombiana de Nefrología, 6(2), 130-137.
9. Fu G, Zhan HC, Li HL, Lu JF, Chen YH, Wu LF, Yang ZL, Huang JJ, Feng YW, Luan YY, Wu M. Association between Procalcitonin and Acute Kidney Injury in Patients with Bacterial Septic Shock. Blood Purif. 2021; 50(6):790-799. doi: 10.1159/000512351. Epub 2021 Mar 17. Erratum in: Blood Purif. 2021 Aug 27;:1. PMID: 33730732.