

Effect of AKI stage on clinical outcomes and residual renal function in adult patients undergoing on-pump cardiac surgery

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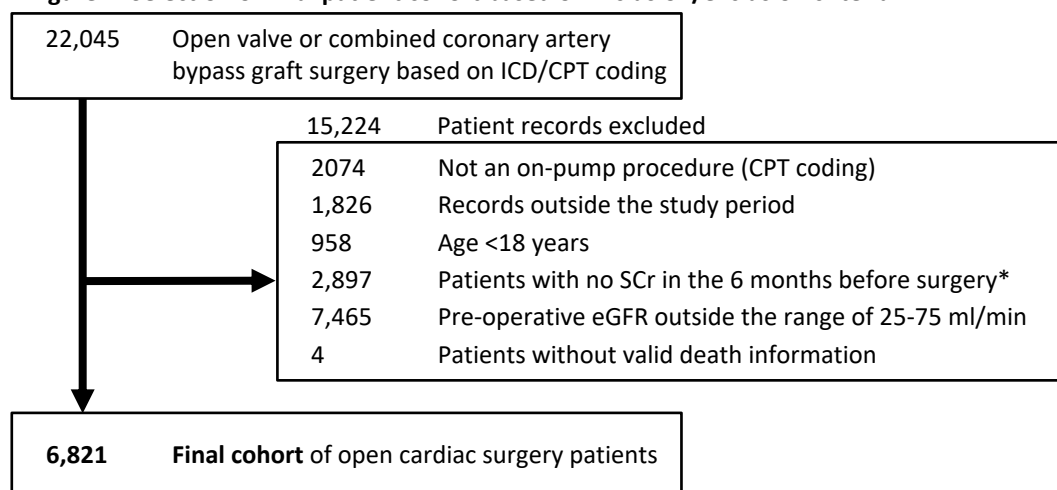
Introduction

- Cardiac surgery is performed for indications that are not primarily kidney-focused, but the resultant improvement in myocardial function may also lead to better kidney function
- However, Cardiac Surgery Associated Acute Kidney Injury (CSA-AKI) may affect up to 30% of cardiac surgery patients and can lead to reduced renal function and other adverse clinical outcomes¹
- Pre-operative factors such as elevated serum creatinine (SCr) / decreased estimated glomerular filtration rate (eGFR) have been shown to increase the risk of CSA-AKI, but the relationship between post-operative kidney function and CSA-AKI remains unexplored^{2,3}
- We hypothesized that in patients with impaired kidney function at baseline, the severity of CSA-AKI would correlate with residual kidney function and clinical outcomes**

Methods

- This retrospective study used electronic medical records from the Cerner® Real-World Data database of adult U.S. patients from January 1, 2016, to December 31, 2020
- Pre-operative eGFR was calculated using the CKD-EPI formula⁴

Figure 1. Selection of final patient cohort based on inclusion/exclusion criteria



*SCr closest to the surgery date (up to 6 months) was selected for calculating baseline eGFR
Abbreviations: ICD: International Classification of Diseases, CPT: Current Procedural Terminology, SCr: Serum Creatinine, eGFR: Estimated Glomerular Filtration Rate, CKD-EPI: Chronic Kidney Disease Epidemiology Collaboration

- The following outcome measures were reported for each patient:
 - Incidence and stage of AKI to post-operative Day 5** measured using Kidney Disease Improving Global Outcomes (KDIGO) via serum creatinine criteria (renal replacement therapy (RRT) at the index surgery encounter, increase in serum creatinine to ≥ 1.5 times baseline, or increase in serum creatinine by ≥ 0.3 mg/dl within 48 hours)
 - eGFR (mL/min)** between Day 6-90 (value closest to Day 90 utilized)
 - Incidence of Major Adverse Kidney Events** defined as death, RRT, or $\geq 25\%$ decline in eGFR relative to pre-surgery within 90 days (**MAKE90**)
- MAKE90 and patient characteristics (age/gender) were reported as descriptive statistics.
- eGFR values at baseline vs. within Day 90 in the same AKI group were compared using the Wilcoxon-Mann-Whitney test

Results

- Inclusion criteria were met by 6,821 out of 22,045 open cardiac surgery patients; mean (SD) age was 69.1 (10.5) years and 59.8% were male
- By post-operative Day 5, 49.9% patients developed AKI (78.1% stage 1; 21.9% stage 2/3)
- Results indicate that patients with AKI stages 2/3 experienced a decrease of ~ 7 mL/min in eGFR within 90 days ($p < 0.001$) while median baseline eGFR increased from 61.9 to 68.5 mL/min ($p < 0.001$) in patients who did not develop AKI (Table 1)
- Incidence of MAKE90 in the overall cohort was 18.2%
 - Rate of mortality and RRT for patients with AKI stages 2/3 was 28.2% and 46.5% respectively, and 3.7% and 0.4% for patients who did not develop AKI (Table 2)
 - A $\geq 25\%$ decline in eGFR within 90 days relative to the baseline was experienced by 41.6% of patients with AKI stages 2/3, in contrast to 4.6% of patients without AKI

Table 1. eGFR across AKI stages

	No AKI	AKI Stages 1-3	AKI Stages 2/3
Baseline			
N	2,843	3,111	671
eGFR (mL/min), Median [25th, 75th]	61.9 [53.2, 69.0]	55.3 [44.5, 64.9]	54.3 [42.3, 64.9]
Day 90			
N	2,777	3,109	669
eGFR (mL/min), Median [25th, 75th]	68.5 [56.3, 81.5]	55.5 [41.0, 70.5]	46.7 [28.1, 65.3]
P value: eGFR baseline vs within Day 90	<0.001	0.007	<0.001

Note: Ns at the two timepoints (baseline and Day 90) represent the number of patients with a valid eGFR at baseline (in the 6 months pre-surgery) and within 6-90 days, respectively. The N between baseline and within 90 days differs because patients may not have eGFR measurements in the EHR database within Day 6-90. Abbreviations: eGFR: Estimated Glomerular Filtration Rate, AKI: Acute Kidney Injury

Table 2. MAKE90: Overall incidence and breakdown by subcategories across AKI stages

	No AKI N=3,416	AKI Stages 1-3 N=3,405	AKI Stages 2/3 N=747
Overall MAKE90, N (%)	266 (7.8)	978 (28.7)	515 (68.9)
Dead	125 (3.7)	399 (11.7)	211 (28.2)
On RRT	15 (0.4)	379 (11.1)	347 (46.5)
$\geq 25\%$ decline in eGFR within Day 90 relative to pre-surgery reference level	157 (4.6)	679 (19.9)	311 (41.6)

Note: MAKE90 was investigated immediately following the index surgery to within 90 days (i.e., Day 1-90) in the final cohort of 6,821 patients. The Ns represent the number of patients that experienced MAKE90 stratified by AKI. Abbreviations: MAKE90: Major Adverse Kidney Events within 90 Days, AKI: Acute Kidney Injury, RRT: Renal Replacement Therapy, eGFR: Estimated Glomerular Filtration Rate

Discussion

- In this retrospective study of on-pump cardiac surgery patients with reduced baseline kidney function, we observed a statistically significant decrease in the eGFR from baseline up to 90 days in AKI stage 2/3 patients, while non-AKI patients exhibited improved eGFR in this timeframe
- This analysis is a multi-center database study of a large cohort of patients in a real-world setting. It is subject to the following limitations:
 - Due to the intrinsic characteristics of a retrospective study, not all patients had data available at Day 90. However, MAKE in the context of a database has been reliably calculated within a 90-day period⁵
 - SCr was utilized to evaluate AKI since the database does not provide urine volumes

Conclusion

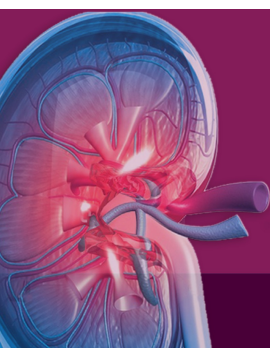
These data show a correlation between more severe AKI and sustained worsening of eGFR following cardiac surgery and point to eGFR as a robust clinical endpoint for AKI therapy trials

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Acknowledgements & Disclosures

Acknowledgements: Writing and editorial support were provided by Boston Strategic Partners Inc. (financed by AM-Pharma)
Disclosures: Candela-Toha A: nothing to disclose; Shaw A, Kellum J, Pickkers P, and Zarbock A report consultancy with AM-Pharma; Mehran R reports institutional research payments from AM-Pharma; Pardali K & Kraan M are AM-Pharma employees, from which they receive salaries and hold shares.



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