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LETTER

# The AKI care bundle: all bundle components are created equal—are they?

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Dear Editor,

Acute kidney injury (AKI) remains a common and significant complication in critically ill patients. As no curative treatment exists, prevention of AKI is paramount, especially in high-risk patients. Several randomized controlled trials suggest that a biomarker-guided implementation of the Kidney Disease Improving Global Outcomes (KDIGO) care bundle reduces the incidence of AKI postoperatively [1–3]. Implementation of this care bundle is recommended in high-risk patients after cardiac surgery [4]. This comprises regular monitoring of kidney function, hemodynamic optimization, and consideration of advanced hemodynamic monitoring, as well as avoidance of hyperglycemia, nephrotoxic drugs, and radiocontrast agents, if possible.

So far, the impact of each individual component of the bundle is unclear. Better understanding would enable prioritization, resource-allocation and clinical management of those at high risk of AKI. To investigate the treatment effects of individual bundle components, we combined data of the two PrevAKI-trials including 554 cardiac surgery patients at high risk for AKI, as defined by elevated urinary biomarkers TIMP2*IGFBP7 [1, 2]. Patients were randomized to standard care versus implementation of the care bundle (Supplementary S1).

Univariate logistic regression of the bundle's components was performed as a risk factor analysis of the whole cohort. Following this, individual treatment effects were analyzed, using the same method for the intervention group only (Fig. 1a). Hypotension, low cardiac index (CI), and use of radiocontrast agents significantly increased the risk for AKI. Optimizing the hemodynamic situation (avoiding hypotension and a low cardiac output state) and avoidance of nephrotoxic drugs were the most important measures to prevent AKI (Fig. 1a). Based on these results, we investigated the role of hemodynamic optimization. AKI occurred significantly less frequently, when hypotension and low CI were prevented (Fig. 1b), particularly for severe stages of AKI.

Testing the effect of hemodynamic optimization, further analyses demonstrated the effect of hemodynamic optimization between the first and the consecutive hemodynamic measurement (Fig. 1c). Patients with hypotension at presentation had statistically lower rates of AKI when successfully optimized until the next measurement, compared to patients in which median arterial pressure optimization could not be achieved. AKI rates were lowest in patients in which hypotension was avoided entirely. Differences of AKI rates in patients with successful optimization of cardiac index were not statistically significant.

In conclusion, our findings demonstrate the importance of maintaining adequate systemic blood pressure and cardiac output. If hypotension or low cardiac output occurs, timely hemodynamic optimization should be performed to prevent AKI. Whilst our analyses suggested a possible role for radiocontrast agents and nephrotoxic drugs, these factors had wide confidence intervals, indicating low certainty of these findings. Besides hemodynamic optimization, other bundle components had little or no impact on the bundle's overall effectiveness.

For patients at risk for AKI, we recommend avoiding even short periods of hypotension [5]. Finally, we suggest that improvement of cardiac index using inotropes,

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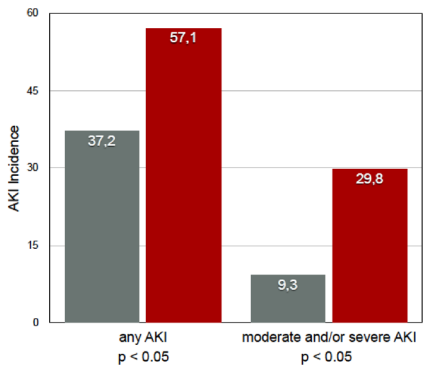
**a**

| Analysis: | Risk factor (intervention + control arms; n=554) | | Individual treatment effect (intervention arm; n=274) | |
|---|---|---|---|---|
| | OR (95%CI) | p-value | OR (95%CI) | p-value |
| Hypotension | 2.30 (1.61 - 3.27) | < 0.05 | 2.37 (1.41 – 3.98) | < 0.05 |
| cardiac index < 3.0 | 1.93 (1.10 - 3.38) | < 0.05 | 1.97 (1.11 – 3.52) | < 0.05 |
| cardiac index < 3.0 and/or hypotension | 2.25 (1.15 - 4.39) | < 0.05 | 2.10 (1.06 – 4.17) | < 0.05 |
| hyperglycemia | 1.44 (0.99 - 2.10) | 0.056 | 1.07 (0.64 – 1.77) | 0.8 |
| Use of ACEi or ARBs | 1.19 (0.75 - 1.90) | 0.456 | 0.85 (0.41 – 1.76) | 0.85 |
| Use of contrast agents | 3.57 (1.55 - 8.24) | < 0.05 | 2.57 (0.81 – 8.18) | 0.11 |
| nephrotoxic drugs | 1.58 (0.91 - 2.73) | 0.107 | 8.19 (1.86 – 36.02) | < 0.05 |

**b**




**c**

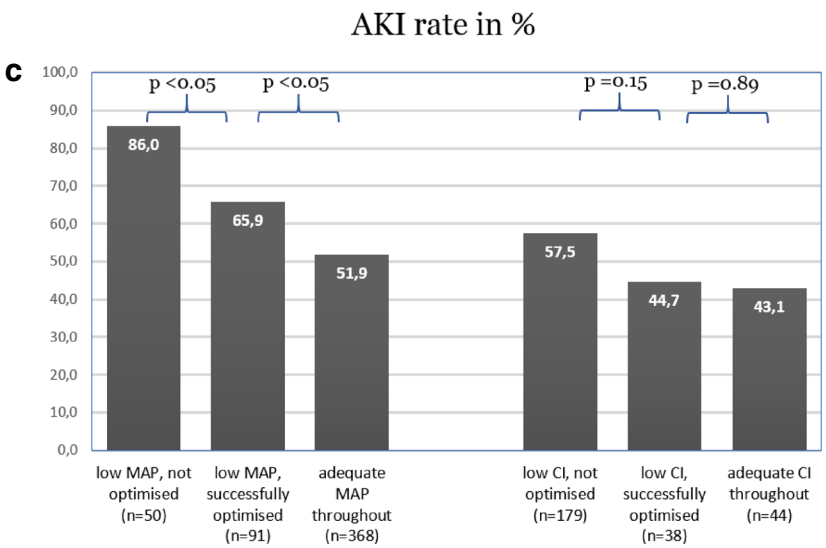



**Fig. 1** **a** Univariate, binary logistic regression analysis for development of any AKI. *ACEi* angiotensin-converting enzyme inhibitors, *ARBs* angiotensin receptor blockers, *OR* odds ratio, *MAP* median arterial pressure, *CI* cardiac index. Hypotension: MAP < 60 mmHg on one reading or MAP < 65 mmHg on two readings during the intervention period. Hyperglycemia defined as: blood glucose levels ≥ 150 mg/dl longer than three hours during intervention period. **b** Hemodynamic status and AKI incidence. (gray = high MAP and/or CI; red = low MAP and/or CI). **c** Treatment effects of hemodynamic optimization for AKI prevention

may be a key, yet all too often ignored, aspect of AKI prevention.

**Supplementary Information**
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**Author contributions**
TCVG, MMD and AZ conceived and designed the study and drafted the manuscript. TVCG performed the data retrieval. TVCG, MMD and AZ performed the statistical analysis. TVCG, MMD, MO, LGF and AZ were involved in the interpretation of the data, and made critical revisions to the manuscript. All authors read and approved the final version of the manuscript to be published.

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**Declarations**

**Conflict of interest**
TCVG and MO declared no conflict of interest. AZ reported receiving research grants from Baxter, Fresenius, Astute Medical, and Astellas and receiving personal fees from Fresenius, AM Pharma and Biomerieux. MM reported receiving personal fees from Astute Medical, FMC, and Baxter. LGF declared research support and personal fees from Astute Medical, La Jolla Pharmaceuticals, Medibeacon, Baxter, and Fresenius.

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Not required.



## Publisher's Note



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