

# Predictive Risk Factors for Acute Kidney Injury Following Cardiac Surgery

Acute kidney injury (AKI) is a common problem faced by patients undergoing cardiac surgery, either with or without cardiopulmonary bypass (CPB). Several widely accepted classification systems exist to define AKI in the adult population, including the AKIN (Acute Kidney Injury Network) criteria, RIFLE (risk, injury, failure, loss, end-stage renal disease) classification, and KDIGO (Kidney Disease: Improving global outcomes) stages.<sup>1</sup> Each of these classification systems agree on three commonalities of AKI: elevated serum creatinine (SCr), decreased glomerular filtration rate (GFR), and decreased urine output, or oliguria.<sup>1</sup> What are less agreed upon are the most predictive risk factors for cardiac surgery-associated AKI.

Research regarding cardiac surgery-associated AKI is ongoing, as new predictive factors and methods of kidney protection are studied and discovered. Several studies agree on some known risk factors of AKI, including female gender, old age, preoperative hypertension, diabetes, and redo operations.<sup>2,3</sup> Other studies suggest some risk factors of AKI that are not as widely studied or accepted, including lowest hematocrit (Hct) during CPB, lowest oxygen delivery (DO<sub>2</sub>) during CPB, prolonged CPB duration and cross-clamp time, blood product usage, high body mass-index (BMI), non-normal mean arterial pressure during CPB, and low CPB flow or cardiac index.

In a prospective study conducted by Gong et al., out of 198 patients that developed AKI, 52.38% were elderly, and the rate of mortality was also higher (42%) than the non-elderly patients (24%).<sup>7</sup> In a univariate analysis of risk factors for AKI, Palomba et al. concluded that several factors showed an increased risk of developing an AKI, including age > 65 (OR 2.32, 95% CI 1.35 - 3.98), female gender (OR 1.77, 95% CI 0.97 - 3.22), preoperative hypertension (OR 0.9, 95% CI 0.45 - 1.81), and diabetes (OR 1.43, 95% CI 0.81 - 2.52).<sup>2</sup> The same researchers also found that more complicated procedures, such as combined valve and bypass grafting surgeries, caused more frequent AKI than single surgeries (OR 3.19, 95% CI 1.62 - 6.25).<sup>2</sup>

In a 2019 retrospective study of 14,350 critically ill patients with AKI, Zhou et al. investigated the relationship between lowest Hct and mortality and found a significant inverse relationship between the incidence of 90-day mortality and Hct in both genders.<sup>8</sup> According to a 2019 randomized retrospective study by Newland et al., maintaining a DO<sub>2</sub> index above 270 ml/min/m<sup>2</sup> was associated with reducing the rate of AKI. This study also concluded that there was a 52% increased risk of AKI if the DO<sub>2</sub> was below this threshold (OR, 1.52; 95% CI, 1.29 - 1.77; P < .001).<sup>9</sup> The use of blood products, particularly red blood cells, typically attempt to solve the problems of low Hct and low DO<sub>2</sub>, but there is research showing that the transfusions themselves may also be an independent risk factor. When RBCs are stored there is a decrease in deformability, depletion of ATP, inability to generate nitric oxide, and increase in adhesiveness to vascular endothelium.<sup>10</sup> These factors can lead to an impairment in DO<sub>2</sub> and exacerbation of the inflammatory response that can cause kidney.<sup>10</sup>

In a retrospective observational study, Hiew et al. evaluated the outcomes of 1,228 patients that underwent CABG procedures. Using a stepwise multivariate analysis for AKI and AKI-D (patients that required renal replacement therapy), they found that for every one-minute increase in CPB time the odds of patients having AKI increased by 1.01.<sup>11</sup> Temperature and AKI is another studied topic, regarding both hypothermia and hyperthermia. Newland et al.

**Meghan Baker and  
Stephanie Canchola**

*Rush University Medical  
Center*

*Chicago, Illinois*



*Published in the Winter 2020 Issue  
of the AACP Newsletter.*

conducted an observational study relating arterial outlet temperature to AKI for a group of 193 consecutive patients. They found that for every 10 minutes that the arterial outlet read  $>37^{\circ}\text{C}$ , the risk for developing AKI also increased by 34 % (OR 1.03, 95% CI 1.01-1.05,  $p = 0.01$ ).<sup>12</sup>

Currently, there are no absolute predictive factors of perioperative AKI, though many studies have attempted to identify such factors. While results from many of the studies agree on the same predictors, other studies show differing results. For example, although several systematic reviews have concluded females have an increased risk for developing AKI<sup>1,3</sup>, two independent groups of researchers suggested no significant difference between genders and a protective effect from the female gender.<sup>4,5</sup> Similarly, while systematic reviews have concluded that diabetes is a known risk factor of AKI, a study conducted by Mukaida et al. found a p-value of 0.574 when comparing subjects with diabetes who did or did not experience AKI. In fact, the study showed that a higher percentage of the non-AKI group were diabetic, contradicting what much of the other literature had claimed about diabetes and AKI.<sup>6</sup>

Cardiopulmonary bypass can cause physiological changes in patients that can harm the patient's organs, especially the kidneys. Injury to the kidneys may occur in about 30% of all cardiac surgeries, some without recovery. Because of discrepancies in the literature regarding risk factors, it is important to continue researching AKI physiology to reduce the occurrence of AKI in the future, through evidence-based medicine and perfusion. It is clear that the patients who present for surgery with more disease states are the more vulnerable population, it is important to stay vigilant in minimizing any and all risk factors that can be avoided.

## References

1. Kramer, R.S., Herron, C.R., Groom, R.C., & Brown, J.R. (2015). Acute kidney injury subsequent to cardiac surgery. *J Extra Corpor Technol*, 47(1):16-28.
2. Palomba, H., de Castro, I., Neto, A.L.C., Lage, S., Yu, L. (2007). Acute kidney injury prediction following elective cardiac surgery: AKICS Score. *Kidney International* 72 (5), 624-631.
3. Kristovic, D., Horvatic, I., Husedzinovic, I., Sutlic, Z., Rudez, I., Baric, D., Unic, D., Blazekovic, rfro-MR., & Crnogorac, M. (2015). Cardiac surgery-associated acute kidney injury: risk factor analyses and comparison of prediction models. *Interactive CardioVascular and Thoracic Surgery*, 21; 366-373. <https://doi.org/10.1093/icvts/ivv162>
4. Yousif, N., Obeid, S., Binder, R., Denegri, A., Shahin, M., Templin, C., & Luscher, T. F. (2018). Impact of gender on outcomes after transcatheter aortic valve implantation. *Journal of Geriatric Cardiology*, 15, 394-400.
5. Neugarten J., Golestaneh L., & Kolhe N. V. (2018). Sex differences in acute kidney injury requiring dialysis. *BMC Nephrology*, 19 (5). <https://doi.org/10.1186/s12882-018-0937-y>
6. Mukaida, H., Matsushita, S., Kuwaki, K., et al. (2019). Time-dose response of oxygen delivery during cardiopulmonary bypass predicts acute kidney injury. *J Thorac Cardiovasc Surg*, 158(2):492-499. Doi: S0022-5223(18)32972-6
7. Gong, Y., Zhang, F., Ding, F., & Gu, Y. (2012). Elderly patients with acute kidney injury (AKI): Clinical features and risk factors for mortality. *Archives of Gerontology and Geriatrics*, 10(2), e47-e51. <https://doi.org/10.1016/j.archger.2011.05.011>
8. Zhou, Y., Zheng, M.-H., Chen, C.-S., Sun, D.-Q., Chen, X.-X., Sun, M., Zheng, C.-F. (2019). Prognostic value of hematocrit levels among critically ill patients with acute kidney injury. *European Journal of Inflammation*. <https://doi.org/10.1177/2058739219846820>
9. Newland, R.F., Baker, R.A., Woodman, R.J., Barnes, M.B., Willcox, T.W., Australian and New Zealand Collaborative Perfusion Registry. (2019). Predictive capacity of oxygen delivery during cardiopulmonary bypass on acute kidney injury. *Ann Thorac Surg*, 108 (6):1807-1814. [https://doi.org/S0003-4975\(19\)30881-1](https://doi.org/S0003-4975(19)30881-1).
10. Xie, X., Wan, X., Ji, X., Chen, X., Liu, J., Chen, W., & Cao, C. (2017). Reassessment of Acute Kidney Injury after Cardiac Surgery: A Retrospective Study. *Internal Medicine*, 56(3), 275-282. <https://doi.org/10.2169/internalmedicine.56.7638>
11. Hiew, K. C., Sachithanandan, A., Arif, M., Badmanaban, B., Muiz, A., Faisal, I., Evi Diana, O. (2016). Acute kidney injury following coronary artery bypass graft surgery in a tertiary public hospital in malaysia: An analysis of 1228 consecutive cases. *The Medical Journal of Malaysia*, 71(3), 126. <https://www.ncbi.nlm.nih.gov/pubmed/27495886>
12. Newland, R.F., Tully, P.J., & Baker, R.A. (2013). Hyperthermic perfusion during cardiopulmonary bypass and postoperative temperature are independent predictors of acute kidney injury following cardiac surgery. *Perfusion*, (3):223-31. <https://doi.org/10.1177/0267659112472385>