Many published studies have demonstrated an association between perioperative acute kidney injury (AKI) and early and later morbidity and mortality.1,2 These studies have driven attempts to mitigate AKI incidence by using “goal-directed” intraoperative and postoperative strategies in adult cardiac surgery.3-5 One metric, investigated for more than a decade, is the global oxygen delivery (DO2i) during cardiopulmonary bypass (CPB), which, practically speaking, is proportional to the product of pump flow rate and hematocrit. Numerous studies have shown an association between AKI and such quantities as the nadir of DO2i, the area bounded by the DO2i-time curve (AUCDO2), and some “critical” threshold of DO2i, duration of DO2i below such a threshold (tDO2i), and similar measures that use the ratio of DO2i and the carbon dioxide production index. In this issue of the Journal, Mukaida and coworkers6 report a similar study of 112 patients, in which they found an association between stage 1 AKI and both AUCDO2 and tDO2i, but not nadir of DO2i, with a threshold of 300 mL/min/m². The incidence of AKI was 21%. AKI was predicted with a sensitivity of 87% and a specificity of 49% if tDO2i was greater than 15 minutes.

Although Mukaida and coworkers6 did not prove it, they suggest (and appropriately so) that frequent, even continuous measurements of DO2i are preferable to periodic measurements to optimize renal perfusion. In their study, the cut point—15 minutes—for predicting AKI is less than the typical interval (20-30 minutes) in which perfusionists conventionally measure hematocrit. The window of opportunity for intervening on low DO2i may thus be missed. The caveats of the study are as follows:

1. The threshold of 300 mL/min/m² used by Mukaida and coworkers6 was assigned on the basis of previous studies, rather than being determined from the data. The chosen value may not be the optimal one.

2. The patient cohort underwent CPB with near normothermia. The model results will change under conditions of hypothermia.

3. Many other operative and postoperative factors or events not appearing as covariates in the study of Mukaida and coworkers6 could influence the risk for AKI.

4. The study was not powered to detect the effects of the intervention on more severe stages (II and III) of AKI.

Finally, perioperative AKI may only be an epiphenomenon for stealthy underlying cardiovascular pathophysiology (CVPP), as suggested by (1) the observed association between mortality and “trivial” rises in creatinine (<0.3 mg/dL), (2) the observation that mortality is associated with transient rises in creatinine that normalize before hospital discharge, and (3) the absence of published comparisons of cause-specific mortality in patients with and without AKI.2,7 In statistical terminology, CVPP may be a confounder (or set of confounders), resulting in a spurious causal relationship between AKI and mortality. If so, then our efforts to reduce early and later mortality and morbidity after cardiac surgery solely by neutralizing the risk of perioperative AKI may be futile. The statistically rigorous way to work this out is by conducting a randomized study to estimate the following:

$$P(\text{mortality}|\text{do(AKI)}) = \sum P(\text{mortality}|\text{AKI}, \text{CVP})P(\text{CVP})$$

where do(AKI) is the directly observed incidence of AKI, P(a|b) denotes conditional probability of event a occurring,
given condition $b$, and the sum is over all values of CVPP. The challenge would be how to define and measure CVPP. A compromise is simply to conduct a clinical trial to determine whether an intervention that prevents perioperative AKI actually decreases short- and long-term mortality and morbidity. In any case, “goal-directed” strategies against AKI are still warranted, because no injury is better than injury.

References