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Editorial

Perioperative Dialysis: What is "Just Right"?

MUCH LIKE Goldilocks, we seem to prefer that patients be dialyzed prior but not immediately prior, the patient be euvolemic but not intravascularly depleted, and the potassium be low but not too low prior to the induction of anesthesia. However, when we examine this neither "too hot nor too cold" approach to perioperative dialysis, it is difficult if not impossible to provide specific, evidence-based recommendations for the high-risk procedures that concern us. Although the retrospective cohort study recently published in the *Journal of the American Medical Association* by Fielding-Singh et al. added much needed data to the perioperative dialysis discussion, it unfortunately did not define what is "just right."[1]

Much like the not "too hot nor too cold" approach mentioned above, in 1968, Hampers et al. recommended that dialysis be performed the day prior to major surgery, hypertension be controlled by either medication or ultrafiltration, and the serum potassium be <5.5 milliequivalent/L on the day of surgery.[2] This general approach has persisted to present day and is consistent with the quoted benefits of appropriately-timed dialysis. For example, the goal of obtaining a patient at their "dry weight" at the time of surgery potentially avoids the risks of pulmonary edema, hypertension, and poor wound healing associated with hypervolemia. However, excessive ultrafiltration that results in hypovolemia can contribute to hypotension that is exacerbated by anesthesia and perioperative blood loss.[3] Therefore, an equilibrated, euvolemic patient at their dry weight is preferable. Unfortunately, dry weight, much like the optimal timing of perioperative dialysis, remains a nebulous target and is often defined as the lowest postdialysis weight tolerated without signs of hypo- or hypervolemia.[4]

Given that chronic renal failure patients do not display a significant hyperkalemic response to succinylcholine if the serum potassium level is within normal, the 1968 recommendation of a serum potassium <5.5 milliequivalent/L again seems reasonable.[3] Dialysis 24 hours before surgery, which on retrospective review by Renew et al. was associated with a lower potassium level on the day of surgery, seems to accomplish this goal.[5] In addition to lower serum potassium levels, dialysis has other beneficial effects for the perioperative environment such as reduced uremia, which improves platelet function.[3] On the contrary, longer dialysis-free periods that result in underdialysis are associated with anorexia and changes in taste. This side effect could contribute to poor perioperative nutrition and, thus, have a negative effect on infection and wound healing.[3] All of these findings reinforce the recommendations made in 1968 that dialysis should be performed the day before or even within 24 hours of surgery.

If hemodialysis within 24 hours of surgery is beneficial, some have postulated that more dialysis and more recent dialysis must be even better! This is also unclear. According to Trainor et al., dialysis above the normal target levels has not been shown to improve surgical outcomes.[3] Furthermore, dialysis immediately prior to surgery could contribute to hypotension, bleeding from residual anticoagulation, and electrolyte imbalances. For example, blood sampled immediately after dialysis may reveal below normal serum potassium levels, which could result in inappropriate repletion or transient arrhythmias.[3] Therefore, some authors recommend a period of at least 6 hours after the completion of dialysis prior to elective surgery.[4] However, to the authors' knowledge, the justification for this recommendation is largely expert opinion or predicated upon anticoagulation being used during dialysis. A retrospective study of 194 patients by Deng et al. attempted to correlate postoperative complications (eg, arrhythmia, hypotension, hypertension, delirium, electrolyte abnormality, reintubation, advanced cardiac life support, and death) and the time interval between dialysis and induction of anesthesia. The authors concluded that a time interval of <7 hours between completion of dialysis and the induction of anesthesia posed a higher risk of postoperative hypotension in high-risk procedures. On the other hand, lower-risk procedures and a short time interval between dialysis and the induction of anesthesia (eg, <7 hours) was not a risk for postoperative hypotension.[6]

Despite the lack of evidence regarding optimal timing of dialysis prior to elective surgery, the practice of performing it the day prior has persisted since at least the 1960s. In the November issue of the *Journal of the American Medical Association*, Fielding-Singh et al. published a retrospective cohort

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study focused on dialysis-to-elective surgery time intervals and 90-day postoperative mortality. This retrospective study of 1,147,846 surgical procedures in 346,828 Medicare beneficiaries compared 1-, 2-, and 3-day intervals between dialysis and elective procedures, with the primary outcome being 90-day postoperative mortality. The authors concluded that longer intervals between dialysis and elective surgery were associated with a higher risk of 90-day postoperative mortality. Patients who underwent dialysis the day before surgery (ie, maintained their dialysis schedule) had better outcomes as compared to patients in the 2- or 3-day interval who did not receive day-of-procedure dialysis (2 days *v* 1 day: absolute risk, 4.7% *v* 4.2%, absolute risk difference, 0.6% [95% CI, 0.4% to 0.8%], adjusted hazard ratio [HR], 1.14 [95% CI, 1.10 to 1.18]; 3 days *v* 1 day: absolute risk, 5.2% *v* 4.2%, absolute risk difference, 1.0% [95% CI, 0.8% to 1.2%], adjusted HR, 1.25 [95% CI, 1.19 to 1.31]). In addition, the authors found that patients who had a 2- or 3-day interval had unadjusted 90-day mortality rates that were similar to the 1-day interval group if they underwent day-of-procedure dialysis.[1] Therefore, the conclusions of this retrospective cohort study would seem to support the historic (dialysis the day before surgery) or same- day dialysis approach.

However, what the publication by Fielding-Singh et al. failed to clarify for the anesthesiologist is the management of patients who do not maintain their dialysis schedule (ie, receive dialysis the day before). Should day-of-procedure dialysis be completed before or after the procedure? And for same-day dialysis, how much time should be allowed between dialysis and the surgical procedure to optimize outcome? Furthermore, do these results apply to higher-risk elective procedures?

Of the 1,147,846 surgical procedures included in this retrospective study, almost half were completed at an ambulatory surgery center, physician's office, or home. Approximately 30% of the procedures involved intraocular drug injection and fluid removal or lens and cataract procedures. Furthermore, inpatients (ie, patients who had an emergency department visit or hospital admission within 1 week of the procedure) and emergent procedures were excluded from analysis. Finally, Fielding-Singh et al. could not determine if patients who underwent day-of=surgery dialysis completed dialysis prior to or after the procedure or how much time elapsed between surgery and the day-of-dialysis session. This final point is particularly important as some authors previously have advocated for a delay of at least 6-to-7 hours after the completion of dialysis to begin a surgical procedure.[4,6] Others suggest that postoperative dialysis be delayed at least 24 hours to minimize the risks posed by fluid shifts and bleeding.[3,7]

As elaborated on by Dr. Bleyer in their editorial, maintenance and consistency of the dialysis schedule are paramount to the dialysis dependent patient. Performing elective procedures the day after dialysis does not interrupt this schedule and, thus, may be associated with better outcomes.[8] However, it is not clear from this retrospective study whether it is the interval between dialysis and the surgical procedure that affects patient outcomes or merely the disruption of the dialysis schedule alone. Comparing mortality in patients who have various dialysis-free time periods to patients who experience dialysis interruptions due to elective surgical procedures could provide some clarification.

For their time-to-event analysis (the primary outcome), Fielding-Singh et al. applied a log-rank test to determine if there was a significant difference between the cohorts. Then, to both estimate the effect size and test the effect of multiple independent variables (covariates) on survival, the authors computed the HR for each cohort pair using a Cox proportional hazards model. The HR is the ratio of the probability of death at any given instant in one cohort divided by the same probability in another cohort.[9] The Cox regression assumes that patients in both cohorts survived up to the time of interest and these probabilities are called "hazard rates". The HR is the ratio of the 2 rates. The validity of the HR rests on several assumptions. First, it assumes that all patients have a common baseline hazard of dying that depends only on time, and that the baseline hazard does not change for the period of the study. Second, the model assumes that each subject enrolled in the study has a hazard function that is a multiple of the common baseline hazard and is a time-independent constant determined only by any patient's covariate values. Simply put, the effect of a covariate on any patients's hazard rate is assumed to be the same at all time points during the study. This is called the "proportional hazard (PH) assumption". In addition to the PH assumption, the model assumes that the relationship among covariates (eg, age, sex, race) is fixed at baseline and that the effect of any covariate is fixed throughout the duration of the study. If this assumption is true, then the ratio between the 2 hazard rates is attributable only to the designation of the cohorts—in this case the interval between dialysis and surgery.

In this study, the authors appropriately tested the validity of these assumptions, but unidentified covariates that violate the proportional hazard assumption cannot be identified easily and stratified from retrospective data sets. Mining large data sets assembled for a purpose other than the study narrows the choice of covariates only to those that are recorded in the data set. The authors credibly validated the covariates to justify their use in the model, but it is not hard to imagine that the data set might be missing important covariates whose relationship to a cohort might not be fixed and time-independent. For example, for some patients, a 3-day interval between dialysis and surgery might represent a surrogate marker for intolerance to dialysis from an underlying infection or worsening cardiac function. In this case, an unidentified covariate might not be an immutable time-independent linear multiplier in every patient in the cohort; but for some patients in the cohort, just a surrogate that affects the hazard rate in a way that varies in both intensity and time. The investigators, who did not collect the data, have no way of identifying these covariates. Instead, a 3-day interval between surgery and dialysis is lumped into one cohort and treated as single fixed category. This points directly to the dilemma for anesthesiologists in practice. To decide if any study should modify practice, clinicians first need to believe that the

results are true and then, if true, that these results apply to their patients. Large data mining enterprises frequently can generate hypotheses or, as in this case, lend evidence to existing practice patterns (eg, the widespread practice of scheduling surgery on the day after dialysis), but they may not provide enough evidence to change clinical practice. Prospective trials can be much more cumbersome and labor-intensive, but investigators can control the collected data and, thus, they have the potential to provide practice modifying evidence.

Overall, the information provided by Fielding-Singh et al. added evidence to the current practice of scheduling patients for elective procedures the day after dialysis. In addition, it suggested that day-of- procedure dialysis may improve outcomes for those patients in whom elective surgery would disrupt the typical dialysis schedule. However, it failed to clarify whether the disruption of a patient's dialysis schedule or the disruption and elective surgery affect outcomes, if the difference in outcomes is present in a higher-risk population, when day of dialysis should be performed, the best same day dialysis prescription (eg, ultrafiltration, potassium, and bicarbonate goals), and the optimal time interval between dialysis and elective surgery. Unfortunately, there is much more research needed to determine what is "just right."

Conflict of Interest

None.

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