

HYPOTENSION



and Adverse Perioperative Outcomes

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We read with interest the May 2017 ASA Monitor article written by Ken Pauker, M.D., and colleagues regarding the association of increased postoperative troponin with non-cardiac surgery, myocardial injury (MINS) and increased 30-day mortality.¹ While the authors describe Type I

myocardial injury as being caused by coronary occlusion secondary to a thrombosis or plaque rupture, and Type II myocardial injury caused by a mismatch of myocardial oxygen supply and demand,² they don't offer much guidance on how we can reduce the incidence of MINS.

Over the last few decades, several seemingly minor clinical strategies have been shown to decrease perioperative complications. Examples include the use of beta-blockers in patients at high risk of coronary disease to decrease the incidence of perioperative cardiac ischemia (e.g., ST-segment depression) and cardiac mortality rate.³⁻⁵ In patients who are mechanically ventilated, decreasing tidal volume and peak inspiratory pressure is associated with a decrease in ventilator-associated lung injury (VALI) and appears to improve longitudinal pulmonary function.⁶⁻⁸

Anesthesiologists may be able to decrease the incidence of perioperative MINS and acute kidney injury (AKI) by improving the care we deliver during the perioperative



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period. Recent studies have demonstrated a significant association between the degree and length of intraoperative hypotension and both MINS and AKI.

In 2017, Salmasi and colleagues reported in a retrospective study of 57,315 noncardiac surgery patients that exposure to mean arterial blood pressure (MAP) of <65 mmHg for 13-28 minutes was associated with increased risk of both MINS, odds ratio (OR) 1.34 (95 percent confidence interval [CI] 1.06 to 1.68) $P = 0.0015$, and AKI, OR 1.20 (CI 1.02 to 1.40) $P = 0.0049$.⁹ The study also showed that the risk of both MINS and AKI increased with lower MAP and/or increased length of exposure to low MAP. Exposure to MAP <50 mmHg for >4 minutes was associated with increased risk of MINS (OR 2.12 [CI 1.45-3.09] $P < 0.001$) and AKI (OR 1.43 [CI 1.15-1.78] $P < 0.0001$). The study also reported that absolute MAP values were just as predictive as percent decrease of baseline MAP.

In a 2015 multicenter retrospective cohort study of 18,756 noncardiac surgery patients, Monk and colleagues reported that exposure to MAP <49 mmHg for ≥ 5 minutes was associated with increased 30-day mortality rates (OR 2.4; CI 1.3 to 4.6) $P < 0.0001$.¹⁰ While Monk did not associate hypotension with either MINS or AKI, it would appear reasonable that since other investigations have shown a clear association with MINS/AKI and 30-day mortality that a portion of Monk's reported mortality was associated with MINS/AKI.

In a 2013 retrospective observational study of 33,330 noncardiac surgeries, Walsh and colleagues reported an association between exposure to MAP <55 mmHg and MINS and AKI.¹¹ There was an independent graded relationship between the length of time spent with a MAP <55 mmHg and MINS, AKI and cardiac complications. Those with the longest periods of a MAP <55 mmHg had about a 1.5-fold increased risk of MINS or AKI and an almost two-fold increase in cardiac complications ($p < 0.001$). As time increased with MAP <55 mmHg, there was a trend to a higher 30-day mortality that reached statistical significance at $t > 20$ minutes.

In a 2015 retrospective study of 5,127 patients undergoing noncardiac surgery, Sun and colleagues reported an increased risk of AKI when patients were exposed to MAP <60 mmHg for >20 minutes and MAP < 55 mmHg for >10 minutes.¹² The risk of AKI for MAP <55 mmHg was an OR 2.34 (CI 1.35-4.05) for 11-20 minutes exposure and an OR 3.53 (CI 1.51-8.25) for >20 minutes. For MAP <60 mmHg, the risk of AKI was OR 1.84 (CI 1.11-3.06) for 11-20 minutes of exposure. The authors did not present data regarding MINS or postoperative mortality.

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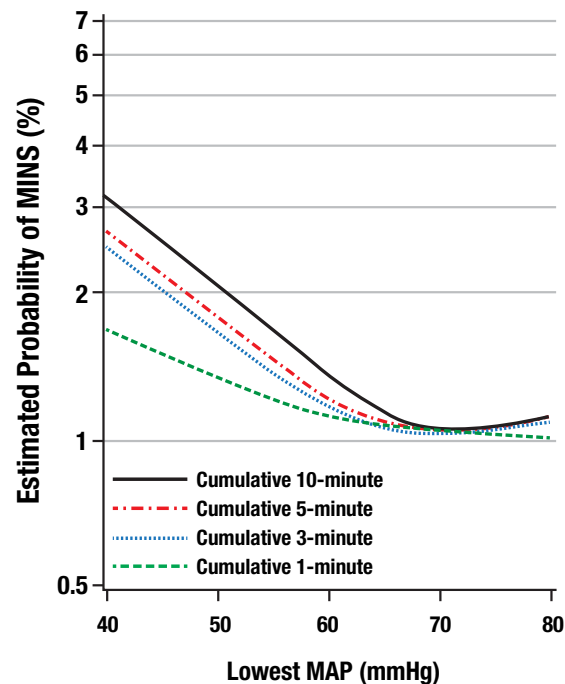


Figure 1: Lowest mean arterial pressure (MAP) thresholds for myocardial injury after noncardiac surgery (MINS). Multivariable relationship between MINS and absolute lowest MAP thresholds. From multivariable logistic regression smoothed by restricted cubic spline with three degrees and knots at 10th, 50th and 90th percentiles of given exposure variable.⁹

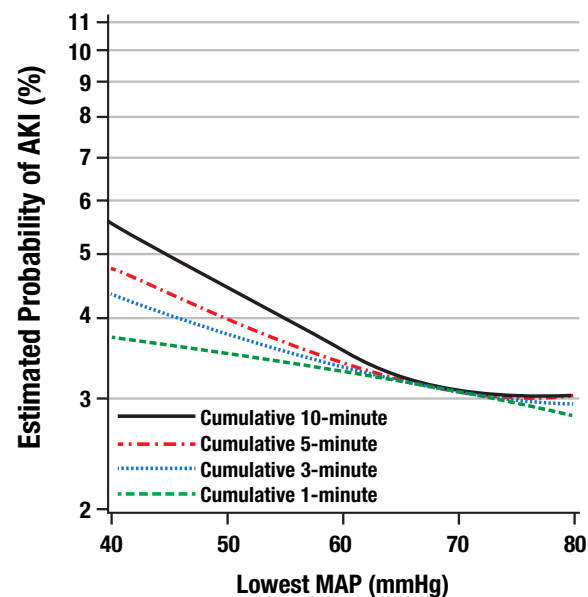


Figure 2: Lowest mean arterial pressure (MAP) thresholds for acute kidney injury after noncardiac surgery (AKI). Multivariable relationship between AKI and absolute lowest MAP thresholds. From multivariable logistic regression smoothed by restricted cubic spline with three degrees and knots at 10th, 50th and 90th percentiles of given exposure variable.⁹

Figures modified with permission, from Salmasi V, Maheshwari K, Yang D, et al. Relationship between intraoperative hypotension, defined by either reduction from baseline or absolute thresholds, and acute kidney and myocardial injury after noncardiac surgery: a retrospective cohort analysis. *Anesthesiology*. 2017;126(1):47-65.

The consistent message from these studies is that a prolonged MAP <55-65 mmHg is dangerous. The deeper and longer the patient's exposure to hypotension, the risk of MINS and AKI increases exponentially (Figures 1-2, note: Y-axis is logarithmic). Even short periods of MAP <55 mmHg are unsafe. MINS and AKI are associated with morbidity and mortality and are costly. While we can certainly optimize our patient's comorbidities prior to delivering anesthesia care, we cannot cure their underlying disease(s). However, perioperative MAP can be managed.

The question then comes down to, what can we do about this? As a general rule, the greater the dose of anesthetic drugs, the lower the blood pressure due to decreases in myocardial contractility (MC) and systemic vascular resistance (SVR). We all have the goal of delivering the appropriate level of anesthesia. Many anesthesiologists are hesitant to lighten the anesthetic as a means to increase MAP secondary to concerns with movement (e.g., causing patient harm during delicate surgery), intraoperative awareness and other consequences. There are various technologies available that claim to measure depth of anesthesia (or sedation or analgesia), and there is some evidence showing the use of processed EEG reduces the incidence of postoperative delirium that is associated with exposure to low MAP.¹⁵⁻¹⁹ Studies of the role of processed EEG to reduce hypotension and associate perioperative MINS, AKI, cardiac complications or mortality are desperately needed. In our opinion, utilization of a depth of anesthesia monitor is a useful way to decrease exposure to overly deep anesthetics and may decrease the incidence of low MAP in the context of appropriate fluid management.

We all have had patients who seem to be particularly sensitive to our anesthetic, although it's difficult to know if this is just a patient-specific response or an expression of the underlying disease state. The usual treatments for low MAP during the intraoperative period are to increase preload (i.e., fluids), lighten the anesthetic, or increase MC and/or SVR (i.e., give inotropes or vasopressors). Unfortunately, the scientific literature is essentially silent regarding the consequences of treating intraoperative hypotension with inotropes or vasopressors. Unless the patient has a central venous access, we are generally limited to using ephedrine, phenylephrine or vasopressin. These medications have significant cardiovascular effects. Ephedrine increases MC, SVR and heart rate (HR), which increases myocardial oxygen consumption (MVO₂). Phenylephrine increases SVR and decreases HR and renal perfusion. Vasopressin increases SVR and decreases mesenteric perfusion. Although there is some evidence of improved outcomes of septic patients in the ICU whose hypotension is treated

with vasopressors,¹³ there is no evidence showing that the treatment of perioperative hypotension with vasopressors "improves patient outcomes. In fact, there is evidence that intraoperative total vasopressor dose and use of vasopressor infusions are associated with AKI and increased postoperative mortality.¹⁴ Nevertheless, considering the clear danger of perioperative hypotension, in our opinion, patients should be treated with a vasopressor(s) if conservative treatment of hypotension is unsuccessful.

In conclusion, perioperative exposure to low MAP is dangerous and is associated with increased incidence of MINS and AKI. As Dr. Pauker and colleagues discussed, MINS is associated with cardiac complications and increased postoperative mortality. Hypotension is a condition that we can treat. Conservative measures should be employed first (e.g., optimize fluid status and anesthetic depth). Depth of anesthesia monitoring may assist in optimizing the anesthetic dose. If unsuccessful, the use of vasopressors is likely better than continued exposure to low MAP.

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A complete list of references can be found in the online version of this article at monitor.pubs.asahq.org.