Preoperative antihypertensive medication intake and acute kidney injury after major vascular surgery

Emmanuelle Duceppe, MD,[a,b,c] Anne-Renee Lussier, MD,[a] Roxane Beaulieu-Dore, MD,[a] Yannick LeManach, MD, PhD,[c] Mikhael Laskine, MD, MSc,[a,b] Josee Fafard, MD,[a,d] *and* Madeleine Durand, MD, MSc,[a,b] *Montreal, Quebec, and Hamilton, Ontario, Canada*

ABSTRACT

Objective: Postoperative acute kidney injury (AKI) is frequent after major vascular surgery and is associated with significant morbidity and mortality. It remains unclear whether the administration of combined oral antihypertensive medications on the day of surgery can increase the risk of postoperative AKI.

Methods: We performed a retrospective cohort study of hypertensive patients undergoing elective major vascular surgery to determine the association between the number of antihypertensive medications continued on the morning of surgery and AKI at 48 hours postoperatively.

Results: A total of 406 patients who had undergone suprainguinal vascular surgery were included, and 10.3% suffered postoperative AKI. In multivariable analysis, the number of antihypertensive medications taken on the morning of surgery was independently associated with AKI ($P = .026$). Compared with patients who took no medication, taking one medication (adjusted odds ratio [aOR], 1.58; 95% confidence interval [CI], 0.68-3.75) and taking two or more medications (aOR, 2.70; 95% CI, 1.13-6.44) were associated with a 1.6-fold and 2.7-fold increased risk of postoperative AKI, respectively. Other predictors of AKI were suprarenal surgery (aOR, 3.37; 95% CI, 1.53-7.44), age (aOR, 2.29 per 10 years; 95% CI, 1.40-3.74), length of surgery (aOR, 1.40 per 1 hour; 95% CI, 1.10-1.76), hemoglobin drop (aOR, 1.37 per 10 g/L; 95% CI, 1.10-1.74), and history of coronary artery disease (aOR, 2.33; 95% CI, 1.08-5.00).

Conclusions: In patients undergoing major vascular surgery who are treated with chronic antihypertensive therapy, the administration of antihypertensive drugs on the morning of surgery is independently associated with an increased risk of postoperative AKI. Further prospective studies are needed to confirm this finding. (J Vasc Surg 2018;67:1872-80.)

Postoperative acute kidney injury (AKI) occurs in 10% of patients undergoing major noncardiac surgery and is associated with significant morbidity and mortality.[1,2] Patients undergoing major vascular surgery are at increased risk of AKI, which can be mediated through several mechanisms; renal arterial atherosclerotic disease, intravenous administration of contrast agent, and suprarenal aortic clamping are among the mechanisms that can increase the risk of perioperative AKI in this population.[3,4] Clinically significant hypotension is also associated with increased AKI risk after surgery.[1,5] More than 75% of vascular patients requiring surgical treatment (ie, the most advanced presentation of vascular diseases) are treated with chronic antihypertensive therapy.[6] In randomized placebo-controlled trials, the perioperative administration of oral antihypertensive agents, such as calcium channel blockers (CCBs), angiotensin-converting enzyme inhibitor (ACEIs), or other oral antihypertensive therapies, increased the frequency of intraoperative hypotension and the use of intraoperative vasopressors.[7-9] Studies have looked at postoperative renal outcomes associated with intake of antihypertensive medications, but the evidence remains scarce.[10] Most studies inform only on the perioperative impact of continuation of certain classes of antihypertensive agent (eg, ACEIs) without informing on the potential cumulative effect of antihypertensive agents in combination. There is a lack of evidence to guide clinicians in the management of patients taking more than one antihypertensive therapy.

We hypothesized that the administration of antihypertensive medications on the day of surgery has an impact on intraoperative hemodynamics and is associated with increased risk of postoperative AKI. The aim of this study was thus to determine whether continuing more than one antihypertensive agent on the morning of surgery is associated with a greater risk of postoperative AKI.

METHODS

We performed a retrospective cohort study by chart review of all patients who underwent suprainguinal vascular surgery at three Canadian teaching hospitals between January 2008 and December 2011. Patients were identified through the hospital administrative

From the Department of Medicine, Université de Montréal,[a] and the Centre de Recherche du Centre Hospitalier de l'Université de Montréal,[b] Montreal; the Department of Medicine and Anesthesia, McMaster University, Hamilton[c]; and the Division of General Internal Medicine, Hôpital Maisonneuve-Rosemont, Montreal.[d]

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Correspondence: Emmanuelle Duceppe, MD, Centre de Recherche du Centre Hospitalier de l'Université de Montréal, 900 Rue Saint-Denis, Tour St-Antoine S3.103, Montreal, QC H2X 0A9, Canada (e-mail: emmanuelleduceppe@gmail.com).

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database using major vascular surgery procedure codes. Suprainguinal surgery includes thoracic aortic repair, thoracoabdominal aortic repair, suprarenal open aortic repair, endovascular aortic repair, aortic-bifemoral graft, and iliofemoral graft. Patients were included if they were treated preoperatively for chronic hypertension with at least one antihypertensive medication. Patients were excluded if they were undergoing urgent or emergent surgery (ie, within 48 hours of acute symptoms), if they had an estimated glomerular filtration rate <30 mL/min, or if information on their medication intake on the morning of surgery was lacking. This study was approved by each hospital's Institutional Review Board; consent of individual patients was not required since data were collected retrospectively.

Data collection. Charts were reviewed by three clinicians who collected and entered data in case report forms. Data collectors were trained at study initiation, and a random sample of case report forms was reviewed by a study investigator to ensure data quality and completeness. Sequential random samples were reviewed until full agreement was met. Past medical history and baseline characteristics were collected in the surgical preoperative evaluation note, anesthesiology preoperative consultation, or any available perioperative medical consultation. Perioperative information was collected. This included type of surgery; length of surgery (from time of induction of anesthesia up to exit from the operating room); intraoperative intravenous fluid, vasopressor, and diuretic administration; intraoperative hypotension, defined as systolic blood pressure <100 mm Hg for ≥20 minutes; and intraoperative estimated blood loss. Hemoglobin values before and immediately after surgery were collected; perioperative hemoglobin drop was defined as the difference between these values. Preoperative creatinine concentration closest to surgery and highest within 48 hours after surgery was collected. Revised Cardiac Risk Index (RCRI) score was calculated for each patient, as follows (each worth 1 point): high-risk surgery (ie, suprainguinal vascular surgery); history of coronary artery disease (CAD), defined as previous evidence of ischemic heart disease, myocardial infarction, or coronary revascularization; history of congestive heart failure (CHF), defined as left ventricular ejection fraction <50%; history of cerebrovascular disease, defined as previous stroke or transient ischemic attack; preoperative insulin therapy; and preoperative creatinine concentration >177 μmol/L.[11]

The exposure of interest was the number of chronic antihypertensive medications taken on the morning of surgery. Types of antihypertensive agent included ACEIs, angiotensin II receptor blockers (ARBs), CCBs, thiazide diuretics, and beta blockers. For each type of medication, intake status was recorded in one of three ways for each patient: continued on the morning of surgery; taken chronically but withheld on the morning of surgery; or not taken chronically. Decisions on antihypertensive medication intake or withdrawal were at the discretion of the attending physician assessing the patient in the preoperative clinic. These were recorded in the preoperative orders and followed on the morning of surgery by the nurse, who ultimately recorded the patient's medication intake. If information on perioperative medication intake (ie, continuation or interruption) was unavailable after investigation and extensive chart review, patients were excluded. Nurse records were preferred to preoperative orders for data collection as patients may not have been compliant with preoperative orders (eg, patients may have taken their medications at home before coming to the hospital despite being instructed to withhold some medications).

The primary outcome was postoperative AKI at 48 hours after surgery. AKI was defined by the stage 1 criterion of the Acute Kidney Injury Network (AKIN), that is, an absolute increase in serum creatinine concentration ≥26 μmol/L or a ≥50% increase in baseline serum creatinine concentration.[12]

Statistical analysis. Descriptive statistics are reported in absolute number and percentage, mean and standard deviation (SD), or median and interquartile range (IQR), as appropriate. We performed multivariable logistic regression analysis to determine the association between preoperative antihypertensive medication intake and postoperative AKI, after adjusting for potential confounders. A semiparsimonious approach was used to select the potential predictors: number of antihypertensive medications taken on the morning of surgery, type of surgery, age, intraoperative variables, RCRI score, length of surgery, perioperative bleeding, administration of intravenous diuretics, and clinically significant intraoperative hypotension.

The final multivariable model performance was evaluated by assessing model discrimination by calculating the concordance statistic (C statistic) corrected for optimism. Correction for optimism accounts for both model

ARTICLE HIGHLIGHTS

- **Type of Research:** Retrospective, multicenter, cohort study
- **Take Home Message:** In 406 hypertensive patients, suprainguinal vascular surgical procedures resulted in acute kidney injury in 10.3%, directly associated with the number of antihypertensive agents taken the morning of surgery. Other factors included suprarenal surgery, age, length of surgery, history of coronary artery disease, and blood loss.
- **Recommendation:** This study suggests that antihypertensive agents should not be given on the morning of suprainguinal vascular surgery to decrease the risk of postoperative acute kidney injury.