The effect of acute kidney injury after revascularization on the development of chronic kidney disease and mortality in patients with chronic limb ischemia

Pradeep Arora, MBBS,[a] **Sina Davari-Farid, MD,**[b] **Leili Pourafkari, MD,**[b,d] **Anu Gupta, MBBS,**[a] **Hasan H. Dosluoglu, MD,**[c] and **Nader D. Nader, MD, PhD,**[b] *Buffalo, NY; and Tabriz, Iran*

Objective: **This study examined the effect of perioperative acute kidney injury (AKI) on long-term kidney dysfunction and death after lower extremity revascularization. Perioperative AKI is commonly seen in the form of mild rises of serum creatinine after major cardiovascular surgeries. Its effect on long-term survival and development of chronic kidney disease (CKD) is well established in cardiac surgery patients. However, there are no data on the effect of AKI on long-term outcomes after revascularization for lower limb ischemia.**

Methods: **We retrospectively reviewed the patients with peripheral arterial occlusive diseases who underwent endovascular or surgical revascularization of the lower extremities from 2001 through 2010. All demographic and clinical information have been maintained prospectively by the surgeon and followed up by the research team. Perioperative AKI was defined as rises of ≥0.3 mg/dL in serum creatinine from the values measured preoperatively. The primary end points were development of CKD (estimated glomerular filtration rate <60 mL/min) and all-cause mortality. Univariate and multivariate analyses were performed to examine relevant associations.**

Results: **Within the study period, 717 patients underwent 875 procedures. Mean follow-up was 42 ± 14 months. AKI developed in 86 patients after the index procedure. Overall prevalence of CKD diagnosed postoperatively was 14.9%. Overall mortality reported within the follow-up period was 55.9%. Perioperative AKI was a significant predictor of CKD (area under the curve, 0.84 ± 0.13) and all cause mortality (area under the curve, 0.82 ± 0.12).**

Conclusions: **Perioperative AKI is associated with an increased occurrence of CKD and a higher mortality rate after revascularization procedures of the lower extremities. (J Vasc Surg 2015;61:720-7.)**

Acute kidney injury (AKI) has been reported in 5% to 7% of hospitalized patients, and its prevalence is mounting.[1-3] The outcome for postoperative AKI varies depending on several risk factors, including advanced age, male gender, presence of other organ failure, cause of AKI, and the presence of overt renal failure. A prolonged hospital stay and associated higher cost of patient care, along with increased postoperative morbidity and mortality, are among the adverse outcomes reported by several investigators.[1-3] Several studies have shown that AKI is associated with higher occurrence of long-term morbidity such as progression to chronic kidney disease (CKD) and development of end-stage renal disease (ESRD).[4,5] In addition, long-term survival in patients with AKI is significantly decreased.[6,7]

From the Departments of Medicine,[a] Anesthesiology,[b] and Surgery,[c] University at Buffalo, The State University of New York, Buffalo; and the Cardiovascular Research Center, Tabriz University of Medical Sciences, Tabriz.[d]

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Reprint requests: Nader D. Nader, MD, PhD, VA Western NY Healthcare System, 3495 Bailey Ave, Buffalo, NY 14215 (e-mail: nnader@buffalo.edu).

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Predictors of poor long-term renal outcome include advanced age, lower serum albumin levels, presence of diabetes, and severe AKI during hospitalization.[8] These predictors have been successfully used to identify those patients at highest risk for progression to advanced CKD. Furthermore, these patients may benefit from continuous long-term surveillance and preventive measures to avoid additional insult to the kidneys and minimize the rate of progression of CKD or ESRD, or both.

Perioperative AKI is a frequent and serious complication of major surgery, specifically after cardiac surgery, carrying an inherent higher rate of postoperative complications and death.[9] Even a mild decrement in renal function, represented by small and reversible changes in serum creatinine levels, is increasingly recognized as a marker of poor outcomes in patients undergoing cardiac surgery.[10,11] Although there is considerable evidence about the occurrence of AKI and poor outcome in cardiac surgery patients, the clinical significance of AKI episodes after lower extremity revascularization with respect to clinically relevant long-term outcomes has not been studied.

We previously showed that prevalence of AKI after a vascular intervention (surgery or endovascular repair) was 12%.[12] In this study, we examined the effect of perioperative AKI after vascular surgery for lower extremities and the incidence and progression to CKD and death. We hypothesized that presence of kidney injury shortly after revascularization of the lower extremities is associated with a poor long-term survival and development of CKD.

METHODS

The study population included all patients who presented with disabling claudication, acute ischemic nonhealing ulcer, rest pain, or tissue loss and underwent endovascular or open surgical revascularization of the lower extremities between January 1, 2001, and December 31, 2009. The Veterans Affairs (VA) Western New York Healthcare System has maintained a prospective database of patients undergoing revascularization procedure for peripheral arterial diseases of lower extremities since 2000. The VA Western New York Healthcare System Institutional Review Board has evaluated and approved the use of this database. In view of the descriptive nature of the study and the absence of any intervention that carries more than a minimal risk to the patients, the study was exempted from obtaining informed consent.

Patient population. The laboratory information and follow-up data were extracted from the VISTA-based Computerized Patient Record and entered into the Excel database (Microsoft Corp, Redmond, Wash). Initially, 875 patients were identified. After exclusions were made for repeat surgery and ESRD, the final analysis included 717 patients (Fig 1). Data collected for each patient included age at the time of surgery, gender, race (Caucasian or others), body mass index, coronary artery disease (CAD), hypertension, diabetes mellitus, chronic obstructive pulmonary disease, congestive heart failure, cerebrovascular accident, preoperative serum creatinine, and preoperative use of niacin, statins, angiotensin-converting enzyme inhibitors/angiotensin receptor blockers, and β-blockers. Polynomial ordinal variables included the Kidney Disease Outcomes Quality Initiative (K-DOQI) stages and the American Society of Anesthesiologists (ASA) Physical Status Classification of the patient at the time of the primary surgical procedure. Missing data variables were treated to limit the introduction of bias by their exclusion. Outcome data included death, estimated glomerular filtration rate (eGFR), and development of CKD.

Definitions. AKI was defined using the Acute Kidney Injury Network (AKIN) criteria[13] as stage 1, increase in serum creatinine ≥0.3 mg/dL (25 μmol/L) or an increase of 50% to 200% from baseline; stage 2, serum creatinine increase of more than twofold from baseline; and stage 3, serum creatinine ≥354 μmol/L (≥4.0 mg/dL) with an acute increase of at least 44 μmol/L (0.5 mg/dL) or need for renal replacement therapy. A urine output criterion for defining AKI was not used.

Race was categorized as Caucasian or others according to patient self-report in the medical record. Dates of death were obtained from the VA death files, which have a sensitivity of 98.3% and a specificity of 99.3% compared against the national death index.[14] CKD was defined as eGFR <60 ml/min/1.73 m^2 based on National Kidney Foundation K-DOQI guideline criteria.[12]

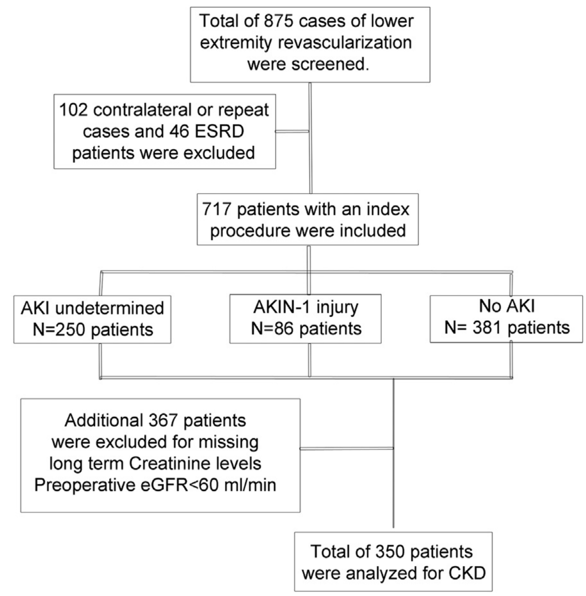

Fig 1. Flow diagram of the patients at different stages of exclusion and statistical analyses. *AKI,* Acute kidney injury; *AKIN,* Acute Kidney Injury Network; *CKD,* chronic kidney disease; *eGFR,* estimated glomerular filtration rate; *ESRD,* end-stage renal disease.

The ASA class was determined from preoperative anesthesia records and stratified into five categories: ASA 1—a healthy individual; ASA 2—a patient with mild systemic disease; ASA 3—a patient with severe systemic disease; ASA 4—a patient with severe systemic disease with a constant threat to life; and ASA 5—moribund patient who is not expected to survive without surgery.[15]

Statistical analysis. Statistical analyses were performed with NCSS-2007 1.12 software (NCSS LLC, Kaysville, Utah). All vascular surgical patients were grouped by the outcome variable of postoperative CKD and all-cause mortality. The comparison of continuous variables for outcomes used the Wilcoxon rank sum test, and the comparison of proportions was done using the χ^2 test or the Fisher exact test. Time-to-event analysis for survival was computed with log-rank Kaplan-Meier test. After univariate analyses for the confounding factors, the following variables were selected to construct a multivariate logistic regression model ($P < .1$): age, ASA class, smoking status, serum albumin levels <3.0 g/dL, high-density lipoprotein (HDL) <40 mg/dL, diabetes mellitus, CAD, hypertension, critical limb ischemia, and preoperative use of clopidogrel.

The predictive value of multivariate risk models was tested with receiver operating characteristic curves and the calculation of the area under the curve. We constructed a Cox regression model with the above-mentioned variables to examine their association with all-cause mortality. Several sensitivity analyses were performed using diabetes treatment modality as oral hypoglycemic agents or insulin in the model and then constructed a model using preoperative eGFR for mortality analysis. All tests were two-tailed,