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Intraoperative administration of vasopressin during coronary artery bypass surgery is associated with acute postoperative kidney injury☆

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ABSTRACT

Background: Severe vasodilatation is commonly seen upon weaning from cardiopulmonary bypass (CPB). We examined the effects of vasopressin (arginine vasopressin [AVP]) on acute kidney injury (AKI) in postoperative period.
Methods: The records of 483 patients undergoing coronary bypass surgery on CPB from 2004 to 2008 were retrospectively reviewed. Demographic, anthropometric, comorbid condition, and perioperative clinical/laboratory data were collected along with postoperative complications. Patients were grouped based on the perioperative use of AVP, and AKI was used as the primary end point. Univariate and multivariate logistic regression analyses were used, followed by propensity score matching for AKI. Null hypothesis was rejected at $P < .05$.
Results: Postoperative AKI occurred in 14.5% of patients. Arginine vasopressin was administered to 280 patients during the perioperative period. The prevalence of AKI in AVP was 20%, whereas it was 6.1% in controls ($P < .0001$). Arginine vasopressin was an independent factor that predicted the occurrence of AKI (odds ratio, 3.60; 95% confidence interval, 1.22-10.62; $P = .02$). However, after propensity score matching, the association between AKI and AVP was lost ($P = .073$).
Conclusion: Acute kidney injury is a common complication after cardiac surgery, and vasopressin use increases its incidence; however, this effect may rely on several clinical factors, and its true effect should be examined by large randomized trials.

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1. Introduction

Profound hypotension is a common occurrence after cardiac surgery, and providing the proper treatment is crucial because of the negative impact of hypotension on postoperative complications [1]. Hypotension could be the result of low preload state, decreased cardiac contractility, and systemic vasodilatation after cardiopulmonary bypass (CPB), concurrent use of vasodilators such as dobutamine or milrinone, or any combination of these factors. Vasodilatory shock after cardiac surgery is occasionally refractory to conventional inotropes and adrenergic vasopressors such as epinephrine, dopamine, phenylephrine, and norepinephrine. This clinical picture is particularly common in adult with complex cardiac physiology, with long duration of CPB, and after deep hypothermic cardiac arrest [2]. Similar to septic shock [3], low levels of serum arginine vasopressin (AVP) have been suggested as the possible cause of the vasodilatory shock in these patients [4,5].

Arginine vasopressin is synthesized in the hypothalamus. It is released by increased plasma osmolality, decreased arterial pressure, and reductions in cardiac volume. Three subtypes of vasopressin receptors, V1, V2, and V3, have been identified, mediating vasoconstriction, water reabsorption, and central nervous system effects, respectively [6]. Direct measurement of plasma levels of AVP is inaccurate because it avidly binds platelets. Recently, copeptin [7], a novel biomarker and surrogate of AVP, has been used to assess its pleiotropic role in kidney function [8].

Although the beneficial effects of AVP on hemodynamics have been widely recognized in cardiac surgery, concerns have been raised about its potential adverse effects on other vital organs. Several reports have indicated that liver dysfunction, thrombocytopenia, elevated blood urea nitrogen and creatinine levels, and a decreased urine output may occur after AVP administration [9-11]. In general, AVP decreases renal medullary blood flow and maintains cortical blood flow, but its overall intrarenal hemodynamics are currently debated [12-16]. Therefore, the exact impact of AVP on kidney function is unknown. Several investigators such as Guarido et al [17] have demonstrated in a rat model that arterial pressure is maintained in refractory shock with AVP. They primarily contributed that the increase in blood pressure is caused by vasoconstriction of renal blood vessels and not by increase in cardiac output or vasoconstriction of large blood vessels. Presumably, the decrease in

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renal vascular pressure could contribute to kidney injury. At the same time, we know from Vasopressin and Septic Shock Trial (VASST) trial in septic shock patients that there were no differences between AVP and non-AVP groups in terms of acute kidney injury (AKI). However, it should be noted that, in this trial, AVP was used primarily for its pressor-sparing effects. Therefore, conflicting data exist concerning AVP and its impact on kidney injury. The current use of AVP during cardiac surgery is nonstandardized with some centers favoring the use of AVP and others relying on other vasopressors for treating hypotension.

The development of AKI in cardiac surgery is probably multifactorial [18,19], and its frequency varies from 3.0% to 30.0% after cardiac surgery as reported in previous studies [18,20]. Although Acute Kidney Injury Network (AKIN) classification 1 is defined by only modest levels of creatinine postoperatively (≥0.3 mg/dL), its occurrence increased the rates of subsequent chronic kidney disease and mortality [21].

The primary objective of this study was to assess the clinical impact of perioperative use of AVP on postoperative AKIN [22]. We hypothesized that AVP administration during cardiac surgery was not associated with any increase in renal injury during the postoperative period.

2. Methods

This study was a retrospective case-control study of 483 consecutive patients who underwent surgical revascularization of coronary arteries (coronary artery bypass graft) in Veterans Affairs Western New York health care system from April 2004 to March 2008. The study protocol was reviewed and approved by the institutional review board for its merit and ethics. The study was exempted from obtaining informed consent due to its noninvasive approach; however, extreme care was taken to maintain patient privacy.

The list of the patients was extracted from the cardiac database that is prospectively maintained for every patient undergoing open heart surgery. We screened 900 medical records, and after excluding a total of 417 patients, the records from 483 patients were comprehensively reviewed (Fig. 1). In total, 301 patients with valve surgery, combined valve/coronary artery bypass graft, aortic surgery, and off-pump procedures were excluded. In addition, 116 patients with baseline serum creatinine greater than 1.5 mg/dL or stage III chronic kidney disease (estimated glomerular filtration rate <60 mL/min) were also excluded.

This database includes demographic and anthropometric perioperative laboratory data and medical history with clinical information of comorbid diseases as well as intraoperative information related to CPB. New York Heart Association classification score, Canadian Cardiovascular Society angina classification score (as a binary variable for Canadian Cardiovascular Society 4), and the urgency of intervention were recorded. Additional information regarding transfusion of blood products and intraoperative use of vasoactive drugs such as AVP and/or epinephrine was obtained from the review of the computerized patients' anesthesia records.

Postoperative survival was followed for 8-year period. The frequency of perioperative complication within 30 days of surgery was recorded for death, reinfarction, cerebrovascular accidents, pneumonia, sepsis, surgical bleeding, and postoperative need for hemodialysis. Postoperative laboratory information included hematocrit, creatinine, cardiac enzymes, white blood cell count, and platelets. The length of stay in the intensive care unit and hospital was also recorded and used as secondary end points.

Postoperative occurrence of AKI was extracted by an absolute increase of greater than or equal to 0.3 mg/dL or 50% of the baseline creatinine in 48-hour AKIN-1. Although AKIN-2 level was also collected, AKIN-1 was used as the primary end point in this study. This parameter by definition included all AKIN-2 level kidney injuries. Perioperative kidney injury can be the result of multiple factors besides the perioperative vasopressor administration; intraoperative arterial and venous

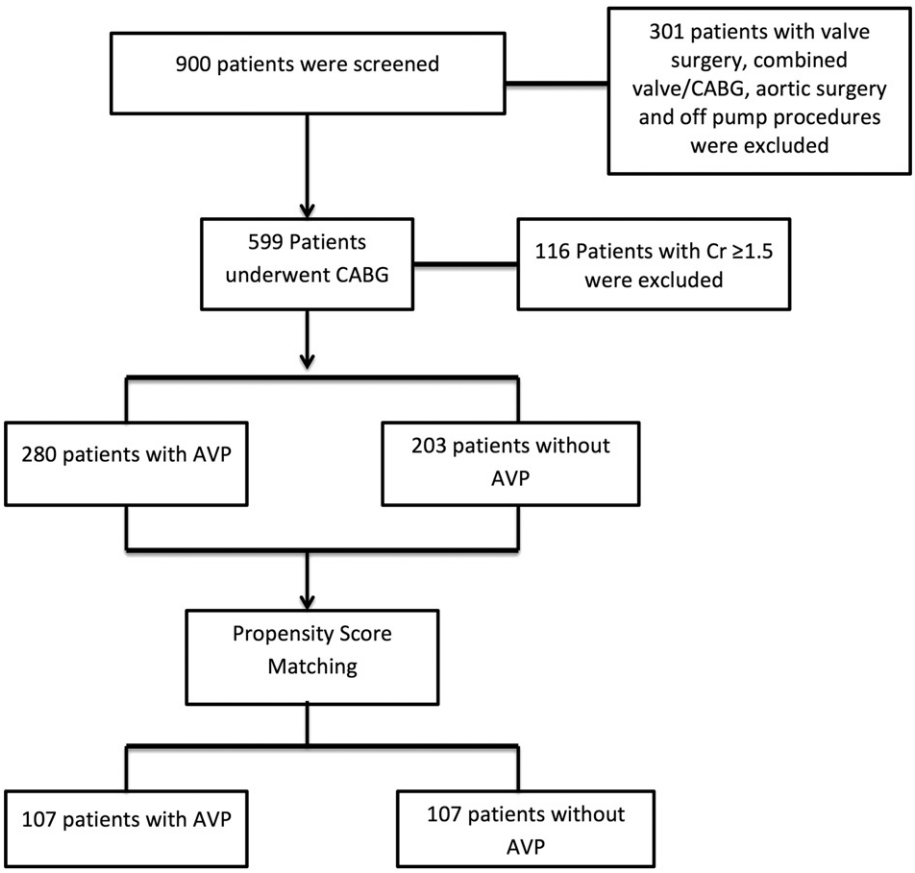

Fig. 1. The flow diagram depicts the screening and enrollment process of the patients.