

Impact of vasopressin use for postoperative atrial fibrillation in off-pump coronary artery bypass grafting

Kochi Yamane^{1,2}, Tasuku Fujii¹, Tadashi Aoyama²,
Mikio Nonogaki² and Kimitoshi Nishiwaki¹

¹Department of Anesthesiology, Nagoya University Graduate School of Medicine, Nagoya, Japan

²Department of Anesthesiology, Yokkaichi Municipal Hospital, Yokkaichi, Japan

ABSTRACT

Postoperative atrial fibrillation complicates 15–40% of cardiac surgery cases and is associated with various adverse health outcomes including high mortality. Although vasopressin administration decreases postoperative atrial fibrillation in on-pump coronary artery bypass grafting, its use in off-pump coronary artery bypass grafting has not been investigated. Therefore, we evaluated the effect of vasopressin use in off-pump coronary artery bypass grafting. For this retrospective, observational study at a single-center community hospital in Yokkaichi, Japan, 298 patients who had undergone elective or emergency off-pump coronary artery bypass grafting between April 2015 and March 2021 were enrolled. Participants were divided into two groups: vasopressin and non-vasopressin groups. The outcomes in both groups were analyzed after propensity score matching, which revealed 40 patients in each matched group. Patients with chronic atrial fibrillation and those who were converted from off-pump to on-pump surgery were excluded. The primary outcome was postoperative atrial fibrillation occurrence within 4 days post-surgery. Secondary outcomes were 30-day mortality, intensive care unit and hospital stays, and postoperative complications (acute kidney injury, stroke, acute myocardial infarction, and respiratory complications). Although 11 patients (27.5%) in the vasopressin group were affected by postoperative atrial fibrillation when compared to 18 (45%) patients in the non-vasopressin groups, the difference was not significant ($P=0.163$). Similarly, no significant differences were observed in the secondary outcomes between groups. In off-pump coronary artery bypass grafting, vasopressin use may contribute to reduced postoperative atrial fibrillation; however, a large prospective study needs to be conducted for confirmation.

Keywords: off-pump coronary artery bypass, grafting, atrial fibrillation, vasopressin, norepinephrine

Abbreviations:

POAF: postoperative atrial fibrillation

CABG: coronary artery bypass grafting

OPCAB: off-pump coronary artery bypass grafting

ICU: intensive care unit

AKI: acute kidney injury

V: with vasopressin

Non-V: without vasopressin

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Corresponding Author: Kochi Yamane, MD

Department of Anesthesiology, Nagoya University Graduate School of Medicine, 65 Tsurumai-cho, Showa-ku, Nagoya 466-8550, Japan

Tel: +81-52-744-2340, E-mail: yama-anesth@med.nagoya-u.ac.jp

INTRODUCTION

Postoperative atrial fibrillation (POAF) is a serious complication of cardiac surgery associated with high mortality, hemodynamic instability, increased risk of stroke, prolonged hospital and intensive care unit (ICU) stays, and greater costs.^{1,2} The incidence of POAF after coronary artery bypass grafting (CABG) is 15–40%.^{3–5} A previous study demonstrated that the risk of atrial fibrillation (AF) in conventional on-pump CABG was higher than that in off-pump CABG (OPCAB).⁶ A wide variety of mechanisms, that combine to trigger AF development have been implicated, such as inflammation, sympathetic stimulation, and oxidative stress.^{2,7} Sympathetic stimulation induces calcium gradients, which lead to arrhythmia after depolarization.⁸

Recent studies have encouraged the use of a non-catecholamine vasopressor, such as vasopressin, in combination with catecholamines for treatment of postoperative vasoplegic syndrome or sepsis.^{9,10} Hajjar et al⁹ conducted a prospective randomized, controlled study involving two agents, vasopressin and norepinephrine, for the treatment of vasodilatory shock that occurred after cardiac surgery. Patients who had been administered vasopressin exhibited a lower incidence of perioperative AF than those administered norepinephrine. An earlier meta-analysis reported that patients who underwent cardiac surgery and received vasopressin had a lower rate of new-onset AF likely due to the absent beta-adrenergic and relevant catecholamine-sparing effects of vasopressin.¹¹ Because of sympathetic stimulation, the occurrence of tachyarrhythmias in response to vasopressin use is lower than that observed in patients treated with norepinephrine.¹² However, the efficacy of vasopressin in OPCAB is not well studied, and the association of OPCAB with POAF remains unclear.

In OPCAB, hypotension occurs due to surgical procedures such as heart positioning and stabilizing, which are aimed at facilitating bypass grafting. Many studies have reported that the conversion from OPCAB to on-pump CABG results in poor treatment outcomes.^{13,14} To maintain hemodynamics in OPCAB, many anesthesiologists use catecholamine or vasopressin, or a combined infusion of both the drugs.

We hypothesized that the administration of vasopressin during OPCAB would reduce the incidence of POAF and other post-surgical complications. We conducted this study to evaluate the occurrence of POAF in patients who underwent OPCAB with or without intraoperative vasopressin use.

MATERIALS AND METHODS

Study design and patients

This retrospective, observational study was approved by the institutional review board of Yokkaichi Municipal Hospital (chairman of the board: Dr Yano Motoyoshi; date of approval: June 23, 2021; approval no. 2021-3f) and conducted in accordance with the principles set forth in the Helsinki declaration. The need for a written informed consent was waived owing to the retrospective nature of the study.

The inclusion criteria were as follows: patients who had undergone elective or emergency OPCAB between April 2015 and March 2021, and those whose characteristics and outcomes could be extracted from the electronic medical records. The exclusion criteria were as follows: cases of conversion from OPCAB to on-pump surgery and/or patients with chronic AF. A total of 298 patients were enrolled, and divided into two groups based on intraoperative vasopressin use: with vasopressin (V) and without vasopressin (non-V) groups.

Our institute has a unified revascularization technique. First, we revascularize the region

governed by the left anterior descending artery. We then revascularize diagonal artery's governed region. Next, we revascularize the governed region of the left circumflex artery, then the governed region of the right coronary artery. Finally, we anastomose the aorta to the graft. Vasopressin is administered if catecholamines failed to maintain hemodynamics. If we anticipate difficulty in maintaining hemodynamics during anastomosis based on pre-anesthesia evaluation (for example, left ventricular dysfunction), we normally initiate with vasopressin (0.5–1 unit/h) and titrate before anastomosing graft to left anterior descending artery, or circumflex artery. We rarely use vasopressin over 3 units/h.

The preoperative respiratory complications in patients included for analyses were chronic obstructive pulmonary disease and bronchial asthma. Similarly, the preoperative cardiac complications included left ventricular dysfunction (ejection fraction <40%), and previous incidences of myocardial ischemia and acute heart failure. Preoperative β -blocker use was divided into continuously medicated and discontinued until the day of surgery.

Perioperative medications included amiodarone and β -blocker. Perioperative risk analyses were performed based on the European System for Cardiac Operative Risk Evaluation II (euroSCORE II).¹⁵

Outcome measurements

The primary outcome was an event of POAF occurring within 4 days of surgery. Consequently, patients who underwent cardiovascular surgery in our hospital were continuously monitored for 4 days postoperatively. POAF was defined as the acute onset of AF diagnosed by electrocardiography. Secondary outcomes were 30-day mortality, ICU and hospital stay, days of POAF events, and postoperative complications. Postoperative complications included stage 3 acute kidney injury (AKI), stroke, myocardial infarction, and respiratory complications. Postoperative stage 3 AKI was defined based on the criteria of the Kidney Disease Improving Global Outcomes.¹⁶ Stroke was defined as sustained neurological deficit and confirmed by imaging modality or clinical course. Myocardial infarction was defined based on elevated biomarkers and respiratory complications including postoperative intubation time >48 h, reintubation, and tracheostomy.

Statistical analyses

Patients' characteristics were analyzed using the Mann–Whitney U and chi-squared tests for continuous and categorical variables, respectively. Continuous variables are expressed as medians (inter-quartile range). Patients' characteristics were adjusted to two groups at a 1:1 ratio based on the correspondence of propensity score. For the propensity score calculation, logistic regression analysis was used, for which the covariates included age, sex, height, weight, body mass index, preoperative cardiac complications, preoperative amiodarone and β -blocker use, euroSCORE II, anesthesia time, operation time, fluid balance, intraoperative fentanyl dose, and red blood cell transfusion.

The vasoactive inotropic score (VIS) was used to quantify the degree of hemodynamic support and calculated as follows: dopamine [$\mu\text{g}/\text{kg}/\text{min}$] + dobutamine [$\mu\text{g}/\text{kg}/\text{min}$] + 100 \times (epinephrine [$\mu\text{g}/\text{kg}/\text{min}$] + 100 \times (norepinephrine [$\mu\text{g}/\text{kg}/\text{min}$] + 10 \times (milrinone [$\mu\text{g}/\text{kg}/\text{min}$])). The total inotropic exposure score is another index for quantification of prolonged inotropic support and is calculated as follows: {dopamine [$\mu\text{g}/\text{kg}/\text{min}$] + dobutamine [$\mu\text{g}/\text{kg}/\text{min}$] + 100 \times (epinephrine [$\mu\text{g}/\text{kg}/\text{min}$] + 100 \times (norepinephrine [$\mu\text{g}/\text{kg}/\text{min}$] + 10 \times (milrinone [$\mu\text{g}/\text{kg}/\text{min}$]))} \times length of administration [in days].¹⁷ We also focused on the amount of intraoperative vasoactive and inotropic drugs used. Intraoperative total vasopressor and inotropes dose were calculated by modifying the total inotrope exposure score as follows: dopamine [$\mu\text{g}/\text{kg}$] + dobutamine [$\mu\text{g}/\text{kg}$] + 100 \times epinephrine [$\mu\text{g}/\text{kg}$] + 100 \times norepinephrine [$\mu\text{g}/\text{kg}$] + 10 \times milrinone [$\mu\text{g}/\text{kg}$].

We defined a caliper width at 0.25 of the standard deviation of the logit score. After matching, we compared the primary and secondary outcomes between the two groups. All analyses were performed using EZR statistical software, version 1.55 (Jichi Medical University Saitama Medical Centre, Tokyo, Japan).¹⁸ *P*-value<0.05 was considered statistically significant.

RESULTS

Patients' characteristics

Two hundred and ninety-eight patients were included in this study, with 237 and 61 in the non-V group and V groups, respectively. After propensity score matching, 40 patients in each group were assessed. Patient characteristics before and after propensity score matching analysis are listed in Table 1.

Table 1 Patient characteristics

	All patients			Propensity-matched patients		
	Non-V group (n=237)	V group (n=61)	<i>P</i> -value	Non-V group (n=40)	V group (n=40)	<i>P</i> -value
Age (y)	71 [64, 76]	74 [69, 78]	0.007	72 [65, 78]	72 [64, 76]	0.762
Sex (male)	187 (78.9%)	51 (83.6%)	0.523	34 (85%)	32 (80%)	0.769
Height (cm)	164.0 [160.0, 169.0]	162.0 [158.0, 168.0]	0.307	165.0 [160.0, 169.0]	165.0 [160.0, 170.0]	0.965
Weight (kg)	60.0 [53.7, 67.2]	59.0 [50.5, 67.0]	0.325	60.0 [53.7, 66.1]	60.0 [50.5, 71.3]	0.92
Body mass index (kg/m ²)	22.2 [20.3, 24.5]	21.7 [18.5, 24.6]	0.101	22.2 [20.1, 25.4]	21.9 [18.5, 26.2]	0.74
Preoperative complication						
DM	130 (54.9%)	38 (62.3%)	0.368	24 (60.0%)	28 (70.0%)	0.482
HL	197 (83.1%)	43 (70.5%)	0.041	29 (72.5%)	30 (75.0%)	1.000
HT	211 (89.0%)	52 (85.2%)	0.551	34 (85.0%)	35 (87.5%)	1.000
OSAS	2 (0.8%)	3 (4.9%)	0.099	2 (5%)	3 (7.5%)	1.000
Respiratory complication	17 (7.2%)	6 (9.8%)	0.631	5 (12.5%)	3 (7.5%)	0.709
COPD	16 (6.8%)	6 (9.8%)		5 (12.5%)	3 (7.5%)	
Bronchial asthma	1 (0.4%)	0 (0%)		0 (0%)	0 (0%)	
Renal dysfunction	18 (7.6%)	7 (11.5%)	0.474	4 (10.0%)	5 (12.5%)	1.000
Cardiac complication	57 (24.1%)	27 (44.3%)	0.003	21 (52.5%)	16 (40.0%)	0.37
LV dysfunction	29 (12.2%)	16 (26.2%)	0.012	9 (22.5%)	10 (25.0%)	1.000
OMI	37 (15.6%)	19 (31.1%)	0.01	17 (42.5%)	13 (32.5%)	0.488
Acute heart failure	4 (1.7%)	3 (4.9%)	0.312	1 (2.5%)	1 (2.5%)	1.000
Mitral regurgitation	175 (73.9%)	51 (83.7%)	0.001	32 (80%)	33 (82.5%)	0.161
Trivial	131 (55.3%)	45 (73.8%)		23 (57.5%)	28 (70.0%)	
Mild	41 (17.3%)	2 (3.3%)		8 (20.0%)	2 (5.0%)	
Moderate	3 (1.3%)	4 (6.6%)		1 (2.5%)	3 (7.5%)	
Severe	0 (0%)	0 (0%)		0 (0%)	0 (0%)	
Ejection fraction	59 [49.0, 64.0]	50 [40.0, 60.0]	<0.001	58 [45.0, 63.0]	50 [41.0, 60.0]	0.14
End-diastolic diameter	46 [41.0, 51.0]	47 [42.0, 52.0]	0.211	48 [42.0, 51.0]	46 [40.7, 52.5]	0.889
End-systolic diameter	31 [27.0, 37.0]	34 [29.0, 41.0]	0.021	32 [29.0, 37.5]	34 [28.8, 42.3]	0.525
LMT lesion	88 (37.1%)	24 (39.3%)	0.865	14 (35.0%)	18 (45.0%)	0.494

Intraoperative vasopressin use in OPCAB

Acute myocardial infarction	10 (4.2%)	5 (8.2%)	0.348	1 (2.5%)	3 (7.5%)	0.608
Unstable angina	25 (10.5%)	7 (11.5%)	1.000	5 (12.5%)	4 (10.0%)	1.000
Elective surgery	198 (83.5%)	50 (82.0%)	0.919	33 (82.5%)	32 (80.0%)	1.000
Perioperative IABP use	32 (13.5%)	15 (24.6%)	0.055	6 (15.0%)	11 (27.5%)	0.274
Number of bypass	3 [3.0, 3.0]	3 [3.0, 4.0]	0.029	3 [3.0, 4.0]	3 [3.0, 4.0]	0.429
Perioperative medications						
Perioperative amiodarone use	48 (20.3%)	19 (31.1%)	0.100	10 (25.0%)	12 (30.0%)	0.802
Preoperative amiodarone use	6 (2.5%)	3 (4.9%)	0.581	2 (5.0%)	2 (5.0%)	1.000
Postoperative amiodarone use	47 (19.8%)	19 (31.1%)	0.084	10 (25%)	12 (30.0%)	0.802
Perioperative β -blocker use	138 (58.2%)	50 (82.0%)	0.001	27 (67.5%)	32 (80.0%)	0.309
Preoperative β -blocker use	92 (38.8%)	22 (36.1%)	0.805	22 (55.0%)	13 (32.5%)	0.071
Continued	34 (14.3%)	17 (27.9%)	0.021	12 (30%)	11 (27.5%)	1.000
Postoperative β -blocker use	114 (48.1%)	46 (75.4%)	<0.001	24 (60.0%)	29 (72.5%)	0.344
LA diameter (cm)	37.0 [33.0, 41.0]	37.0 [33.0, 43.0]	0.581	38.5 [34.0, 42.3]	38.0 [33.0, 43.5]	0.78
euroSCORE II	1.8 [1.0, 3.4]	2.75 [1.8, 5.0]	0.001	2.43 [1.1, 3.9]	2.09 [1.6, 4.7]	0.715
Anesthesia time (min)	369 [329, 410]	416 [367, 483]	<0.001	390 [363, 449]	403 [356, 453]	0.784
Operation time (min)	284 [251, 323]	338 [295, 397]	<0.001	308 [265, 368]	323 [274, 379]	0.462
Fluid balance (mL)	2167 [1657, 2750]	2827 [1882, 3634]	<0.001	2612 [1748, 3093]	2574 [1679, 3381]	0.996
Fentanyl dose (μ g)	500 [500, 700]	500 [500, 700]	0.042	600 [500, 800]	550 [500, 700]	0.561
Transfusion of RBC (mL)	0 [0, 560]	840 [560, 1120]	<0.001	560.0 [0, 1120]	560.0 [0, 1120]	0.509
Total vasopressor and inotrope dose (μ g/kg)	2050 [1219, 3110]	4368 [3198, 7120]	<0.001	2203 [1694, 3663]	3867 [3054, 5619]	<0.001
Intraoperative vasopressin dose (units)	0 [0, 0]	3.5 [2.2, 5.3]	<0.001	0 [0, 0]	3.1 [2.0, 4.1]	<0.001
Postoperative vasopressin dose (units)	0 [0, 0]	8.2 [0, 15.8]	<0.001	0 [0, 0]	4.3 [0, 15.8]	<0.001
Postoperative maximum VIS	8.8 [5.6, 12.6]	11.9 [8.5, 15.9]	<0.001	8.8 [5.6, 12.3]	11.7 [8.5, 16.0]	0.063

Values are expressed as medians [25 percentiles, 75 percentiles]. Number of patients, n (%). *P*-value < 0.05 was considered significant.

Non-V: without vasopressin

V: with vasopressin

DM: diabetes mellitus

HL: hyperlipidemia

HT: hypertension

OSAS: obstructive sleep apnea syndrome

COPD: chronic obstructive pulmonary disease

LV: left ventricle

OMI: old myocardial infarction

LMT: left main trunk

IABP: intra-aortic balloon pumping

LA: left atrial

euroSCORE II: The European System for Cardiac Operative Risk Evaluation II

RBC: red blood cell

Total vasopressor and inotrope dose: dopamine dose [μ g/kg] + dobutamine dose [μ g/kg] + 100 \times epinephrine dose [μ g/kg] + 100 \times norepinephrine dose [μ g/kg] + 10 \times milrinone dose [μ g/kg].

Vasoactive and inotropic score (VIS): dopamine dose [μ g/kg/min] + dobutamine dose [μ g/kg/min] + 100 \times epinephrine dose [μ g/kg/min] + 100 \times norepinephrine dose [μ g/kg/min] + 10 \times milrinone dose [μ g/kg/min].

Regarding the continuous variables, a significant difference was observed before matching with respect to age, ejection fraction, end-systolic diameter, number of bypasses, euroSCORE II, anesthesia time, operation time, fluid balance, intraoperative fentanyl dose, transfusion of red blood cell, intraoperative total vasopressor and inotrope dose, intraoperative and postoperative vasopressin dose (within 4 days), and postoperative maximum VIS. Regarding the categorical variables, a significant difference was observed with respect to the presence of hyperlipidemia, cardiac complication, mitral regurgitation, perioperative β -blocker use, continuous preoperative β -blocker use, and postoperative β -blocker use.

Outcome measurements

The primary and secondary outcomes are listed in Table 2. Regarding the primary outcome, after propensity score matching, 18 and 11 patients were affected by POAF in the non-V group and V group, respectively. POAF was observed in 45.0% of patients in the non-vasopressin use group and in 27.5% of patients in the vasopressin use group, but the difference was not significant ($P = 0.163$). The secondary outcomes listed in the Table 2 indicate that there was no significant difference between the non-V and V groups with respect to 30-day mortality, ICU stay, hospital stay, event days of POAF, and postoperative complications, such as AKI at stage 3, stroke, myocardial infarction, and respiratory complications.

Table 2 Outcomes

	All patients			Propensity-matched patients		
	Non-V group (n=237)	V group (n=61)	P-value	Non-V group (n=40)	V group (n=40)	P-value
POAF	78 (32.9%)	18 (29.5%)	0.724	18 (45.0%)	11 (27.5%)	0.163
30-day mortality	1 (0.4%)	3 (4.9%)	0.036	0 (0%)	1 (2.5%)	1.000
ICU stay (days)	3 [3, 3]	3 [3, 4]	0.013	3 [3, 4]	3 [3, 3]	0.787
Hospital stay (days)	19 [16, 22]	21 [17, 36]	0.007	21 [17, 29]	21 [17, 35]	0.900
Event day of POAF (day)	0 [0, 1]	0 [0, 1]	0.880	0 [0, 2]	0 [0, 1]	0.124
Postoperative complications	15 (6.3%)	7 (11.5%)	0.273	5 (12.5%)	3 (7.5%)	0.709
AKI at stage.3	5 (2.1%)	2 (3.3%)	0.949	1 (2.5%)	1 (2.5%)	1.000
Stroke	4 (1.7%)	2 (3.3%)	0.781	1 (2.5%)	1 (2.5%)	1.000
Myocardial infarction	0 (0%)	0 (0%)	NA	0 (0%)	0 (0%)	NA
Respiratory complications	10 (4.2%)	6 (9.8%)	0.055	3 (7.5%)	3 (7.5%)	0.549
—Intubation time over 48 hours	6 (2.5%)	6 (9.8%)		2 (5.0%)	3 (7.5%)	
—Reintubation	1 (0.4%)	0 (0%)		0 (0%)	0 (0%)	
—Tracheostomy	3 (1.3%)	0 (0%)		1 (2.5%)	0 (0%)	

Values are expressed as median [25 percentiles, 75 percentiles]. Number of patients, n (%). P -value < 0.05 was considered significant.

Non-V: without vasopressin

V: with vasopressin

POAF: postoperative atrial fibrillation

ICU: intensive care unit

AKI: acute kidney injury

DISCUSSION

To the best of our knowledge, this is one of the first studies to investigate the outcomes of vasopressin use on the occurrence of POAF in OPCAB. Although there was a decrease in the number of patients with POAF in the V group after propensity-matching when compared to that in the non-V group, it was unclear whether intraoperative vasopressin use might contribute to reduction of POAF in OPCAB as the difference was not significant. In this study, severely affected patients were included in V group, and less number of patients were affected by POAF; there is a possibility that vasopressin use was associated with reduction in POAF. The mechanism of POAF was multifactorial, and myocardial ischemia was also crucial mechanism in the pathogenesis of POAF.^{7,8} Vasopressin has two effects, vasoconstriction and vasodilatation, on the coronary artery vasculature.¹⁹ Vasopressin induced vasoconstriction on the coronary vasculature mediated by the V1 receptor.²⁰ In animal experimental model, a very high dose of vasopressin use induced vasoconstriction and increased vascular resistance.²¹ Small artery led to ischemia owing to high vascular resistance, resulting in coronary artery resistance. However, vasopressin is considered to have an effect of NO-mediated vasodilatation mechanism on the coronary artery. A previous report showed that vasopressin induced coronary artery vasodilatation, and NO synthase inhibitor blocks the vasodilatation.²² Martin et al conducted a prospective, randomized controlled study comparing combination infusion of vasopressin and norepinephrine or norepinephrine alone for vasodilatory shock including cardiac surgery or systemic inflammatory response syndrome.¹² There was a significant difference in new-onset tachycardiac AF, with 8.3% of the vasopressin group patients affected by POAF and 54.3% of the norepinephrine group patients affected by POAF. They concluded that vasopressin increased myocardial blood flow owing to increasing systemic blood pressure and effect of vasodilatation, which contributed to reducing new-onset POAF. In general, on-pump surgery is considered to pose a higher risk for the occurrence of POAF than off-pump surgery. Zacharias et al conducted a retrospective observational study to investigate risk factors of POAF occurrence and reported that cardiopulmonary bypass was associated with the occurrence of POAF²³ (OR=0.65, 95% CI [0.47-0.91]). Ascione et al conducted randomized controlled trial and reported that on-pump surgery was seven times higher than off-pump surgery for the incidence of POAF.⁶ The mechanism of occurrence of POAF associated with cardiopulmonary bypass included long duration of myocardial ischemia, requirement of atrial cannulations, the systemic inflammatory response for cardiopulmonary bypass, and adverse effect of cardioplegia.^{3,6}

Intraoperative vasopressin has been shown to be associated with an increase in postoperative AKI in CABG.²⁴ Furthermore, in cardiac surgery, vasopressin use decreases postoperative complications such as vasodilatory shock, AKI, new-onset AF, myocardial infarction, acute mesenteric ischemia, digital ischemia, and stroke.¹¹ Our study showed no significant differences in postoperative complications between the two groups of OPCAB. POAF increases the duration of hospital stays and postoperative costs.^{25,26} Almashrafi et al²⁷ reported that, as postoperative complications increase, there is a gradual increase in the probability of a prolonged hospital stay. In our study, we did not find a significant difference in the length of ICU and hospital stays between the two groups, and postoperative complications were also not associated with vasopressin use. Thus, the impact of intraoperative vasopressin use in OPCAB was unclear. In cardiac surgery, catecholamines constitute the first line of therapy for maintaining hemodynamics. However, there is no large cohort study indicating the superiority of catecholamines to non-catecholamines in hemodynamics instability.²⁸ Moreover, in vasoplegic shock, vasopressin deficiency is associated with hypotension. From these concerns, vasopressin therapy seems to be the first alternative choice to maintain blood pressure. Nonetheless, several recent recommendations are that norepi-

nephrine is the first line of therapy in hemodynamics instability.²⁹ Nevertheless, if a high dose of catecholamine is needed to maintain hemodynamics, then initiating vasopressin use early may be useful for avoiding cardiac instability.

In OPCAB, occasionally there may arise a need for emergent conversion to on-pump surgery. Ntinopoulos et al³⁰ performed a retrospective analysis of the data of 2742 patients who underwent planned OPCAB and reported that non-elective conversion to on-pump was required for 3.4% of patients. In addition, they revealed that risk factors for non-elective conversions were female sex, left ventricular dysfunction and limited experience of anesthesiologist. In a clinical trial conducted with 4718 patients, Stevens et al¹⁴ found that the incidence of emergent conversion during OPCAB was 3.2%, and reported that the most frequent timing of conversion was prior to cardiac manipulation. They additionally found that during anastomosing, the majority of conversions 18.3% (34/186) occurred during revascularization of the region governed by the left anterior descending artery, followed by 9.7% (18/186) during the revascularization of the circumflex artery-governed region, 3.8% (7/186) during the revascularization of the right coronary artery-governed region, and 0.5% (1/186) during the proximal anastomosis.

Additionally, they showed that the frequent reasons for conversion except for anatomical factors, were hypotension (32.3%), myocardial ischemia (17.7%), and arrhythmias (11.3%). From these perspectives, we think the experience of an anesthesiologist can contribute to avoiding emergent conversion from OPCAB to on-pump surgery. In our institute, based on pre-anesthesia evaluation and intraoperative clinical situation, we normally initiate vasopressin (0.5–1 unit/h) and adjusted the dose for maintaining hemodynamics, before anastomosing a graft to the left anterior descending artery, or circumflex artery. We believe that the use of vasopressin to maintain hemodynamics and reduce the dosage of catecholamines has a beneficial effect on the completion of OPCAB.

Despite this study being novel in incorporating the outcomes of vasopressin use in OPCAB, there were some limitations. First, this was a retrospective, single-center, observational study, and we adjusted patients' characteristics using propensity score matching. Only a few number of patients in the center used vasopressin, and sample size was small after propensity score matching. Therefore, a prospective study with a larger cohort needs to be undertaken to study the outcomes of intraoperative use of vasopressin in OPCAB. Second, our revascularization process is basically the same, however the commencement of vasopressin use, the amount of vasopressin, and the timing of the initiation were based on the anesthesiologist discretion. Thus, a prospective study with a standardized protocol is necessary. Under stable infusion of vasopressin and by setting a target blood pressure, comparison between the event of POAF and catecholamine dose between the non-V and V groups is warranted.

CONCLUSIONS

This study demonstrated that the incidence of POAF was reduced by approximately 18% in the vasopressin group, but the difference was not significant. The association of intraoperative vasopressin use with postoperative complications and ICU and hospital stays remain unclear. A prospective study with an approved protocol is warranted for comparing the incidence of POAF under the stable infusion of vasopressin.

ARTICLE INFORMATION

Author contributions

All authors have substantially contributed to the conception or the design of the manuscript. KY contributed to data collection, analyzed, and wrote the manuscript. TF, TA, MN, and KN reviewed and edited the manuscript. All authors read and approved the final version of the manuscript.

Conflict of interest

The authors declare that they have no conflicts of interest.

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Data availability

The data used for this observational study are available from the corresponding author upon reasonable request.

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REFERENCES

- 1 Elahi M, Hadjinikolaou L, Galiñanes M. Incidence and clinical consequences of atrial fibrillation within 1 year of first-time isolated coronary bypass surgery. *Circulation*. 2003;108(Suppl 1):II207–II212. doi:10.1161/01.cir.0000089188.45285.fd.
- 2 Maesen B, Nijs J, Maessen J, Allessie M, Schotten U. Post-operative atrial fibrillation: a maze of mechanisms. *Europace*. 2012;14(2):159–174. doi:10.1093/europace/eur208.
- 3 Peretto G, Durante A, Limite LR, Cianflone D. Postoperative arrhythmias after cardiac surgery: incidence, risk factors, and therapeutic management. *Cardiol Res Pract*. 2014;2014:615987. doi:10.1155/2014/615987.
- 4 Siebert J, Anisimowicz L, Lango R, et al. Atrial fibrillation after coronary artery bypass grafting: does the type of procedure influence the early postoperative incidence? *Eur J Cardiothorac Surg*. 2001;19(4):455–459. doi:10.1016/s1010-7940(01)00621-2.
- 5 Kaw R, Hernandez AV, Masood I, Gillinov AM, Saliba W, Blackstone EH. Short- and long-term mortality associated with new-onset atrial fibrillation after coronary artery bypass grafting: a systematic review and meta-analysis. *J Thorac Cardiovasc Surg*. 2011;141(5):1305–1312. doi:10.1016/j.jtcvs.2010.10.040.
- 6 Ascione R, Caputo M, Calori G, Lloyd CT, Underwood MJ, Angelini GD. Predictors of atrial fibrillation after conventional and beating heart coronary surgery: A prospective, randomized study. *Circulation*. 2000;102(13):1530–1535. doi:10.1161/01.cir.102.13.1530.
- 7 Boons J, Van Biesen S, Fizev T, de Velde MV, Al Tmimi L. Mechanisms, prevention, and treatment of atrial fibrillation after cardiac surgery: A narrative review. *J Cardiothorac Vasc Anesth*. 2021;35(11):3394–3403. doi:10.1053/j.jvca.2020.11.030.
- 8 Gaudino M, Di Franco A, Rong LQ, Piccini J, Mack M. Postoperative atrial fibrillation: from mechanisms to treatment. *Eur Heart J*. 2023;44(12):1020–1039. doi:10.1093/eurheartj/ehad019.
- 9 Hajjar LA, Vincent JL, Barbosa Gomes Galas FR, et al. Vasopressin versus norepinephrine in patients with vasoplegic shock after cardiac surgery: the VANCS randomized controlled trial. *Anesthesiology*. 2017;126(1):85–93. doi:10.1097/ALN.0000000000001434.
- 10 Russell JA, Walley KR, Singer J, et al. Vasopressin versus norepinephrine infusion in patients with septic shock. *N Engl J Med*. 2008;358(9):877–887. doi:10.1056/NEJMoa067373.
- 11 Dünser MW, Bouvet O, Knotzer H, et al. Vasopressin in cardiac surgery: A meta-analysis of randomized

- controlled trials. *J Cardiothorac Vasc Anesth*. 2018;32(5):2225–2232. doi:10.1053/j.jvca.2018.04.006.
- 12 Dünser MW, Mayr AJ, Ulmer H, et al. Arginine vasopressin in advanced vasodilatory shock: a prospective, randomized, controlled study. *Circulation*. 2003;107(18):2313–2319. doi:10.1161/01.CIR.0000066692.71008.BB.
 - 13 Chakravarthy M, Prabhakumar D, Patil TA, George A, Jawali V. Conversion during off-pump coronary artery bypass graft surgery: A case-control study. *Ann Card Anaesth*. 2019;22(1):18–23. doi:10.4103/aca.ACA_227_17.
 - 14 Stevens LM, Noiseux N, Avezum A, et al. Conversion after off-pump coronary artery bypass grafting: the CORONARY trial experience. *Eur J Cardiothorac Surg*. 2017;51(3):539–546. doi:10.1093/ejcts/ezw361.
 - 15 Nashef SA, Roques F, Sharples LD, et al. EuroSCORE II. *Eur J Cardiothorac Surg*. 2012;41(4):734–744; discussion 744–745. doi:10.1093/ejcts/ezs043.
 - 16 Khwaja A. KDIGO clinical practice guidelines for acute kidney injury. *Nephron Clin Pract*. 2012;120(4):c179–c184. doi:10.1159/000339789.
 - 17 Zangrillo A, Alvaro G, Pisano A, et al. A randomized controlled trial of levosimendan to reduce mortality in high-risk cardiac surgery patients (CHEETAH): rationale and design. *Am Heart J*. 2016;177:66–73. doi:10.1016/j.ahj.2016.03.021.
 - 18 Kanda Y. Investigation of the freely available easy-to-use software ‘EZR’ for medical statistics. *Bone Marrow Transplant*. 2013;48(3):452–458. doi:10.1038/bmt.2012.244.
 - 19 Pelletier JS, Dicken B, Bigam D, Cheung PY. Cardiac effects of vasopressin. *J Cardiovasc Pharmacol*. 2014;64(1):100–107. doi:10.1097/FJC.0000000000000092.
 - 20 Fernández N, García JL, García-Villalón AL, Monge L, Gómez B, Diéguez G. Coronary vasoconstriction produced by vasopressin in anesthetized goats. Role of vasopressin V1 and V2 receptors and nitric oxide. *Eur J Pharmacol*. 1998;342(2–3):225–233. doi:10.1016/s0014-2999(97)01504-5.
 - 21 Maturi MF, Martin SE, Markle D, et al. Coronary vasoconstriction induced by vasopressin. Production of myocardial ischemia in dogs by constriction of nondiseased small vessels. *Circulation*. 1991;83(6):2111–2121. doi:10.1161/01.cir.83.6.2111.
 - 22 Okamura T, Ayajiki K, Fujioka H, Toda N. Mechanisms underlying arginine vasopressin-induced relaxation in monkey isolated coronary arteries. *J Hypertens*. 1999;17(5):673–678. doi:10.1097/00004872-199917050-00011.
 - 23 Zacharias A, Schwann TA, Riordan CJ, Durham SJ, Shah AS, Habib RH. Obesity and risk of new-onset atrial fibrillation after cardiac surgery. *Circulation*. 2005;112(21):3247–3255. doi:10.1161/CIRCULATIONAHA.105.553743.
 - 24 Porhomayon J, Davari-Farid S, Li CM, Arora P, Pourafkari L, Nader ND. Intraoperative administration of vasopressin during coronary artery bypass surgery is associated with acute postoperative kidney injury. *J Crit Care*. 2015;30(5):963–968. doi:10.1016/j.jcrc.2015.06.013.
 - 25 Echahidi N, Pibarot P, O’Hara G, Mathieu P. Mechanisms, prevention, and treatment of atrial fibrillation after cardiac surgery. *J Am Coll Cardiol*. 2008;51(8):793–801. doi:10.1016/j.jacc.2007.10.043.
 - 26 Gillinov AM, Bagiella E, Moskowitz AJ, et al. Rate control versus rhythm control for atrial fibrillation after cardiac surgery. *N Engl J Med*. 2016;374(20):1911–1921. doi:10.1056/NEJMoa1602002.
 - 27 Almashrafi A, Alsabti H, Mukaddirov M, Balan B, Aylin P. Factors associated with prolonged length of stay following cardiac surgery in a major referral hospital in Oman: a retrospective observational study. *BMJ Open*. 2016;6(6):e010764. doi:10.1136/bmjopen-2015-010764.
 - 28 Guarracino F, Habicher M, Treskatsch S, et al. Vasopressor Therapy in Cardiac Surgery—An Experts’ Consensus Statement. *J Cardiothorac Vasc Anesth*. 2021;35(4):1018–1029. doi:10.1053/j.jvca.2020.11.032.
 - 29 Sponholz C, Schelenz C, Reinhart K, Schirmer U, Stehr SN. Catecholamine and volume therapy for cardiac surgery in Germany—results from a postal survey. *PLoS One*. 2014;9(8):e103996. doi:10.1371/journal.pone.0103996.
 - 30 Ntinopoulos V, Haeussler A, Odavic D, et al. Conversion from off-pump to on-pump coronary artery bypass grafting: impact of surgeon and anaesthetist experience. *Interdiscip Cardiovasc Thorac Surg*. 2023;37(6):ivad205. doi:10.1093/icvts/ivad205.