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Original Article

Optimizing Haemodynamics in Off Pump Coronary Artery Bypass Grafting: The Impact of Prophylactic Vasopressin Administration

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ABSTRACT

Objective: To evaluate the haemodynamic effects of prophylactic low-dose vasopressin in patients undergoing off-pump coronary artery bypass grafting (OPCAB).

Study Design: Quasi-experimental study.

Place and Duration of Study: Department of Cardiac Anaesthesia, Armed Forces Institute of Cardiology/National Institute of Heart Diseases (AFIC/NIHD) Rawalpindi, Pakistan from Oct 2024 to Mar 2025.

Methodology: Seventy-six male and female patients, aged between 30 and 70 years, who were scheduled for elective OPCAB were included. Patients were divided into two groups of 38 patients. Group-A received Vasopressin (0.03 IU/min) and Group-B (control group) received Normal Saline, initiated during left internal mammary artery (LIMA) harvesting and continued until the end of surgery. Haemodynamic parameters i.e. mean arterial pressure (MAP), heart rate (HR), and central venous pressure (CVP) were recorded at key surgical stages. Lactate, creatinine, and CK-MB levels were measured at baseline, and 6 hours and 24 hours postoperatively.

Results: The overall cohort comprised 59.2% males with a mean age of 55.6±8.1 years. During grafting, the Group-A maintained a higher MAP compared with Group-B ($p \leq 0.05$) and a lower mean HR ($p \leq 0.05$). No significant differences were observed in CVP or postoperative biochemical markers. Postoperative complications occurred in 21.05% of the Group-A and 28.95% of Group-B, a difference that was not statistically significant ($p > 0.05$).

Conclusion: Low-dose vasopressin improves intraoperative haemodynamic stability in OPCAB without adverse effects.

Keywords: Anaesthesia, Coronary Artery Bypass, Off-Pump, Intraoperative Care, Vasoconstrictor Agents, Vasopressin.

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INTRODUCTION

Coronary artery bypass grafting (CABG) is one of the most frequently performed cardiac surgeries worldwide, estimating to 1 to 1.5 million cardiac operations done annually. Data from 35 high-income countries shows an average annual CABG rate of 36.7 procedures per 100,000 population.[1] CABG procedural data in Pakistan is sparse. Estimates indicate that Pakistan performs more than 20,000 CABGs across more than 40 centres which suggests approximately 10 CABG procedures per 100,000 population per year.[2]

Off-pump coronary artery bypass grafting (OPCAB) over on-pump surgery causes less inflammation and fewer neurological complications. However, it may still cause significant haemodynamic instability, mainly from heart manipulation causing transiently reduce cardiac output (CO) and mean arterial pressure (MAP).[3] Additional factors include myocardial ischemia, surgical stress, use of mechanical devices and increased blood transfusions.[4]

Noradrenaline and phenylephrine are used to treat hypotension and stabilise haemodynamics during OPCAB but may cause arrhythmias and increase myocardial oxygen demand.[5] Vasoplegic syndrome is a particularly challenging complication that can occur during and after OPCAB.[6] Vasopressin, an endogenous non-catecholamine vasoconstrictor, has emerged as a promising solution for the management of haemodynamic disturbances. Vasopressin acts on V1 receptors in the vascular smooth muscles thus maintaining vascular tone and blood pressure. It also increases coronary perfusion pressure and improves left ventricular function without significantly elevating pulmonary vascular resistance. Its prolonged vasoconstrictor effects, lasts up to two hours.[7] At prophylactic doses of 0.03-0.1U/min, Vasopressin is safe, and has shown potential in limiting the haemodynamic instability during OPCAB.[8] This study aimed to evaluate the effect of low dose Vasopressin on maintaining haemodynamic stability during OPCAB. Limited

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studies have been done before in our general population. By providing detailed data of its benefits and safety, this study seeks to refine the approach to improve surgical outcomes and enhance the overall safety of OPCAB procedures.

METHODOLOGY

This quasi-experimental study was conducted at the Department of Cardiac Anaesthesia, Armed Forces Institute of Cardiology/National Institute of Heart Diseases (AFIC/NIHD), Rawalpindi, Pakistan from Oct 2024 to Mar 2025, following approval from the institutional ethics committee (Letter No. 9/2/R&D/2024/326 dated 12-Sep-2024). The study population comprised of patients scheduled for elective OPCAB during the specified period. Non-probability, consecutive sampling technique was employed for participant selection. The sample size was calculated using data from a reference study,[9] which reported a mean difference of 5.96 mmHg in MAP during left anterior descending artery (LAD) grafting in patients undergoing OPCAB, with a standard deviation of 9.5 mmHg. With these parameters, 38 patients per group were required to achieve 80% power at a 5% significance level, resulting in a total sample size of 76 patients using sample size calculator.[10]

Inclusion Criteria: Men and women aged 30 to 70 years, classified as American Society of Anaesthesiologists (ASA) physical status III & IV, and diagnosed with triple-vessel coronary artery disease scheduled for elective OPCAB were included.

Exclusion Criteria: Subjects with left ventricular ejection fraction (LVEF) of less than 40%, documented hepatic or renal dysfunction, a known allergy to vasopressin, valvular surgery or requirement for emergent or on-pump surgical intervention were excluded.

Patients meeting the inclusion criteria were consecutively enrolled. Baseline demographic variables, including age, sex, height, and weight were recorded. Written informed consent was obtained from all subjects. Subjects were assigned to either the Vasopressin group (Group-A) or the Saline group (Group-B). In the Group-A, an infusion of Vasopressin at 0.03 IU/min was commenced during LIMA harvesting and continued until the conclusion of the surgery. In the Group-B, an equivalent volume of Normal Saline was infused during the same period using identical protocols, as shown in Figure.

Anaesthetic management was standardised per institutional protocols. All patients had peripheral IV and radial artery lines placed. Preoxygenation with 100% oxygen for five minutes preceded induction with Midazolam (0.15 mg/kg), Fentanyl (5 µg/kg), Propofol (1–1.5 mg/kg), and Rocuronium (0.6–0.9 mg/kg) IV. Tracheal intubation followed after 1.5–2 minutes. Internal jugular cannulation and Foley catheterisation were performed post-induction. Anaesthesia was maintained with Isoflurane in oxygen–air and Dexmedetomidine infusion; Cisatracurium maintained muscle relaxation. Patients were positioned supine, and median sternotomy performed. LIMA was harvested from the chest wall, with saphenous veins taken from the legs. In the Group-A, Vasopressin (0.03 IU/min) was infused via pump throughout; in the Group-B, saline was infused identically, both starting during LIMA harvest. Systemic Heparin was given to achieve ACT >300 s. After pericardiotomy, stabilisers and positioners provided access to target coronaries. LIMA was grafted to the LAD, and vein grafts to LCX/OM and PDA. Haemostasis, graft patency assessment, and de-airing followed. Protamine reversed Heparin, drains were placed, and the sternum closed. Patients were transferred intubated to ICU for postoperative care.

Haemodynamic parameters (HR, MAP, and CVP) were measured in both groups at multiple time points: at baseline (immediately before induction), after sternotomy (prior to heart manipulation), during LIMA harvesting, during LAD grafting, during LCX/OM grafting, during PDA grafting, and at the end of surgery. Creatinine, urea, lactate, and creatine kinase–MB fraction (CK-MB) was measured at baseline, 6 hours, and 24 hours postoperatively.

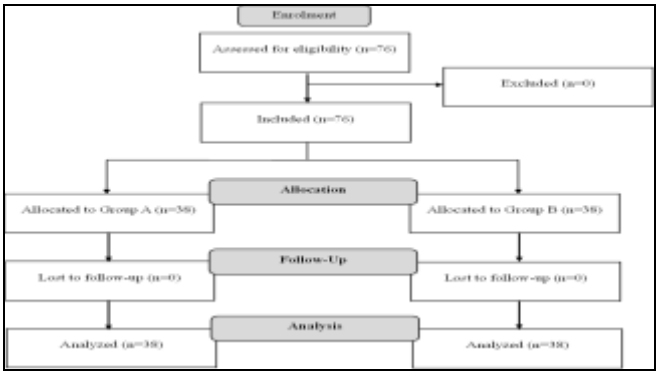

Figure : Patient Flow Diagram (n=76)

Data analysis was performed using Statistical Package for Social Sciences (SPSS) (version 23.00).

Shapiro Wilk test was performed to assess the normality of continuous variables (age, gender, LVEF, blood pressure, heart rate, creatinine etc) while medians and interquartile ranges (IQR) were calculated for continuous variables that did not meet the criteria for normality (height and weight). Categorical variables (e.g., gender) were reported as frequencies and percentages. Categorical variables were compared using the Chi-square test, while non-normally distributed continuous data were analysed with Man Whitney U tests. The independent samples t-test was used to compare the means of normally distributed continuous variables between the two groups. A *p*-value of ≤0.05 was considered statistically significant.

RESULTS

A total of 76 patients were enrolled, with 38 patients each in groups A and B. The overall cohort (n=76) comprised 59.2% males, with median height 168.55 cm (IQR 166.03 – 170.38 cm), median weight 69.00 kg (IQR 66.00 – 80.00 cm), mean age 55.57 ± 8.13 years, and mean LVEF 50.66 ± 7.40%. No significant baseline differences existed between groups A and B: gender (*p*=0.82), height (*p*=0.41), weight (*p*=0.36), age (*p*=0.65), and LVEF (*p*=0.65). The baseline characteristics of the study population are presented in Table-I.

Although baseline MAP, HR, and CVP were similar between groups, patients of Group-A maintained significantly higher MAP during LIMA harvesting (*p*<0.001), and during LAD (*p*<0.001), LCX/OM (*p*=0.001), and PDA grafting (*p*=0.01). Additionally, the Group-A demonstrated a more controlled HR response, with significantly lower HR during LAD (*p*<0.001), LCX/OM (*p*<0.001), and PDA grafting (*p*=0.03) compared to the Group-B. CVP values remained comparable across all time points (*p*≥0.05). These intraoperative haemodynamic observations are summarised in Table-II.

Biochemical parameters at baseline, 6 hours, and 24 hours postoperatively are summarised in Table-III. Creatinine, urea, lactate, and CK-MB levels remained comparable between the and B groups at all measured time points, with no statistically significant differences observed (*p* ≥ 0.05).

A total of 19 postoperative complications occurred among the 76 patients (25.0%), with 8 events (21.05%) in the Group-A and 11 events (28.95%) in the

Table - I: Baseline Characteristics of the Study Population (n=76)

			Study Group				*p*-value
Baseline Characteristics	**Overall**		**Group-A (n=38)**		**Group-B (n=38)**		
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	
Gender	Male	Female	Male	Female	Male	Female	
	45(59.2%)	31(40.8%)	23 (60.5%)	15(39.5%)	22(57.9%)	16(42.1%)	0.82*
	Median (IQR)		Median (IQR)		Median (IQR)		
Height (cm)	168.17 (166.03 – 170.38)		168.20 (166.15 – 169.95)		169.10 (165.98 – 170.70)		0.41**
Weight (kg)	69.00 (66.00 – 80.00)		70.00 (66.00 – 82.00)		69.00 (65.00 – 77.25)		0.36**
	Mean ± SD		Mean ± SD		Mean ± SD		
Age (Years)	55.57 ± 8.13		55.13 ± 7.82		56.00 ± 8.51		0.65***
LVEF (%)	51.46 ± 6.06		51.84 ± 5.93		51.08 ± 6.24		0.65***

Analyzed using Chi-square test ; Analyzed using Man Whitney U test; *** Analyzed using independent t-test LVEF:left Ventricular Ejection Fraction*

Table-II: Intraoperative Haemodynamics Parameters at Key Surgical Stages (n = 76)

	Mean Arterial Pressure (mmHg)			Heart Rate (bpm)			Central Venous Pressure (mmHg)		
Study Group	**A**	**B**	***p*-value**	**A**	**B**	***p*-value**	**A**	**B**	***p*-value***
	Mean ± SD			Mean ± SD			Mean ± SD		
Baseline	80.95± 5.28	77.42±11.63	0.26	71.58± 13.19	71.76± 10.56	0.95	9.56± 0.89	9.49± 0.97	0.77
Sternotomy	77.26± 9.10	84.34± 12.61	0.01	80.05± 13.17	86.24± 10.94	0.03	9.47± 0.95	9.49± 0.97	0.91
LIMA Harvesting	84.13±11.77	74.89± 10.05	< 0.001	72.66± 10.44	78.97± 14.26	0.03	9.51± 1.02	9.34± 0.92	0.48
LAD Grafting	83.21± 12.48	67.05± 9.32	< 0.001	66.61± 9.47	77.55± 9.55	< 0.001	9.52± 1.02	9.19± 0.99	0.15
LCX/OM Grafting	83.68± 12.77	73.34± 14.37	< 0.001	69.76± 17.28	83.50± 15.18	0.01	9.72± 0.94	9.38± 0.96	0.12
PDA Grafting	77.29± 10.80	70.39± 12.18	0.01	75.89± 20.58	85.84± 19.39	0.03	9.58± 1.06	9.39± 1.10	0.45
End of Surgery	80.11± 10.59	76.55± 11.34	0.16	68.79± 23.08	79.89± 22.93	0.04	9.60± 1.10	9.29± 1.09	0.22

LIMA=Left Internal Mammary Artery; LAD=Left Anterior Descending Artery; LCX/OM= Left Circumflex/Obtuse Marginal Artery; PDA=Posterior Descending Artery
** Analyzed using independent t-test*

Table-III: Perioperative Trends in Renal, Metabolic and Myocardial Injury Biomarkers (n = 76)

	Baseline			6 hours Post-op			24 hours Post-op		
Study Group	**A**	**B**	***p*-value**	**A**	**B**	***p*-value**	**A**	**B**	***p*-value***
	Mean ± SD			Mean ± SD			Mean ± SD		
Creatinine (mg/dL)	0.76± 0.23	0.77± 0.19	0.79	0.92± 0.23	0.94± 0.25	0.67	0.80± 0.17	0.80± 0.21	0.95
Urea (mg/dL)	30.66± 9.66	32.26± 9.49	0.47	39.07± 8.70	37.60± 8.19	0.45	30.28± 8.06	32.64± 0.80	0.28
Lactate (mmol/L)	1.43± 0.43	1.31± 0.45	0.23	1.68± 0.46	1.60± 0.48	0.47	1.53± 0.43	1.45± 0.44	0.42
CK-MB (ng/mL)	3.40± 1.14	3.40± 1.26	0.99	3.35± 1.14	3.51± 1.37	0.58	3.38± 1.18	3.59± 1.53	0.52

** Analyzed using independent t-test*

Group-B (p=0.43). The most frequent complication overall was bleeding, observed in 6 patients (7.89%), occurring equally in both groups (3 patients each, 7.89%). These findings are summarised in Table-IV.

Table - IIV: Post-operative Complications (n=76)

		Study Group		*p*-value
Complication	Overall	A (n=38)	B (n=38)	
	n (%)	n (%)	n (%)	
Bleeding	6 (7.89%)	3 (7.89%)	3 (7.89%)	
Re-opening	5 (6.58%)	2 (5.26%)	3 (7.89%)	0.43
Arrhythmia	5 (6.58%)	2 (5.26%)	3 (7.89%)	
Other	3 (3.95%)	1 (2.63%)	2 (5.26%)	
Total	19 (25.00%)	8 (21.05%)	11 (28.95%)	

** Analyzed using Chi-square test*

DISCUSSION

Efficacy of Vasopressin in correcting haemodynamic instability during and after cardiac surgery is well established.[11] In the present study, prophylactic low-dose Vasopressin administration during OPCAB was associated with improved intraoperative haemodynamic stability, characterized by higher MAP and attenuated HR responses during critical grafting phases, without significant differences in CVP or postoperative biochemical markers. The incidence of postoperative complications was lower in the Vasopressin group, although this difference did not reach statistical significance. These findings support the potential role of Vasopressin as a useful adjunct in maintaining stability during OPCAB.

OPCAB, by avoiding CPB, requires cardiac manipulation to access target vessels, often causing haemodynamic instability, particularly hypotension during grafting. While usually reversible, this may lead to adverse outcomes and, in severe cases, emergency conversion to on-pump surgery with markedly increased morbidity and mortality. Optimal haemodynamic management is essential.[12] Haemodynamic instability during OPCAB is most pronounced during grafting of the LCX/OM as well as PDA, due to the anatomical challenges posed by these vessels.[13]

Our findings align with and extend existing evidence on prophylactic Vasopressin use during OPCAB, as highlighted in prior key clinical studies. A randomised, double-blind trial evaluated the haemodynamic effects of low-dose Vasopressin in 60 patients undergoing elective OPCAB for triple-vessel CAD.[9] The methodology was comparable to ours regarding Vasopressin administration, though with different primary endpoints (HR vs MAP). Anaesthetic techniques were similar, differing in induction agents. Both studies standardised intraoperative care and measurement timing. Intraoperative results in both showed significantly higher MAP and lower HR with Vasopressin during critical grafting. While we found no biochemical differences, the reference study reported significantly lower postoperative lactate, creatinine, and CK-MB, suggesting improved perfusion and possible cardio protection. They also noted reduced inotropic requirements, not assessed in our study. Overall, both support the haemodynamic benefits of prophylactic Vasopressin in OPCAB.

The effects of vasopressin during CABG have also been investigated in a small randomized trial comparing it with norepinephrine.[14] In this study comprising 20 patients, vasopressin was more effective in maintaining haemodynamics stability, with lower pulmonary vascular resistance (PVR) and reduced beta-blocker use. In contrast, our study demonstrated similar improvements in MAP and HR control with vasopressin, without effects on CVP or biochemical markers, and additionally evaluated postoperative outcomes, thereby reinforcing its efficacy and safety in the off-pump setting.

The comparative haemodynamic effects of Vasopressin and Norepinephrine in OPCAB have also been evaluated by Jeon *et al*., who specifically investigated their use in the management of Milrinone-induced hypotension.[15] In their double-blind randomised trial involving 50 patients, both agents effectively restored systemic vascular resistance (SVR) and MAP. Our study did not involve milrinone use but similarly demonstrated that low-dose Vasopressin significantly improved MAP and attenuated HR increase during grafting phases without changes in CVP or biochemical markers. While the reference study used pulmonary artery catheterisation and advanced haemodynamic indices, our study assessed more commonly available parameters. Together, these findings reinforce the favourable systemic haemodynamic effects of low-dose Vasopressin during CABG.

A randomised, double-blind trial assessed the prophylactic use of 0.03 IU/min Vasopressin in

patients on chronic Ramipril therapy undergoing CPB during CABG.[16] They found that continuation of ACE inhibitors led to intraoperative and post-CPB hypotension, which was mitigated by Vasopressin infusion initiated during rewarming. In contrast, our study evaluated the same Vasopressin dose in patients undergoing OPCAB, without ACE inhibitor exposure, and assessed its effect throughout the intraoperative period. While Hasija et al. focused on post-CPB haemodynamic recovery, our measurements were focused on haemodynamic trends during cardiac displacement and grafting. Both studies support the haemodynamic stabilising effect of low-dose Vasopressin administered during CABG, though in differing clinical situations.

Pandit *et al*. conducted a prospective, randomised, double-blind study comparing Vasopressin and Noradrenaline in 60 patients undergoing OPCAB.[17] Patients received either Vasopressin (0.01–0.06 IU/min) or Noradrenaline (0.02–0.12 µg/kg/min) as intraoperative support. The study assessed MAP, SVR, PVR, and the PVR/SVR ratio, as well as postoperative renal function markers. Both agents were found to be effective in maintaining MAP, however, vasopressin was associated with a more favourable haemodynamic profile, including a reduced PVR/SVR ratio, and better preservation of postoperative renal function. In comparison, our study used a fixed-dose Vasopressin infusion (0.03 IU/min) and neither included Noradrenaline as a comparator nor the PVR-related indices. The findings from both studies support the haemodynamic stability and renal safety of low-dose Vasopressin during OPCAB.

A prospective, randomised study evaluated the prophylactic use of low-dose Vasopressin (0.03 IU/min) in patients on ACE inhibitors who had reduced LVEF (30–40%) and underwent CABG.[18] Vasopressin was infused intraoperatively and continued for four hours postoperatively. Compared to placebo, Vasopressin significantly reduced catecholamine requirements and 24-hour mortality. It was also associated with improved MAP, CVP, SVR, LVEF, and greater diuresis. In contrast, our study involved a broader OPCAB population without mandatory ACE inhibitor use. Although we did not exclude patients with LVEF of 30–40%, most of our patients had higher LVEF. We focused on intraoperative haemodynamic trends, using the same Vasopressin dose but without extended postoperative infusion. We did not assess mortality or Catecholamine requirements. Nonetheless, both studies support the stabilising haemodynamic effects of low-dose Vasopressin in high-risk cardiac surgical populations, albeit in different perioperative contexts.

A retrospective observational study from Japan evaluating OPCAB practices identified 40 patients who received intraoperative Vasopressin and matched them to 40 controls. Postoperative AF incidence was lower with Vasopressin (27.5% vs 45%), although not statistically significant (p=0.16).[19] In our prospective study, overall complications were also lower in the Group-A (21.05%) than in the Group-B (28.95%), with arrhythmias occurring in 5.26% and 7.89% of patients, respectively. The Japanese study assessed AF over four days, while our 24-hour follow-up may have underestimated complications, particularly arrhythmias. Both studies suggest a trend toward fewer arrhythmias and complications with Vasopressin, underscoring the need for larger, longer trials.

In summary, our prospective quasi-experimental study demonstrates that prophylactic low-dose Vasopressin during OPCAB confers significant intraoperative haemodynamic benefits, with consistently higher MAP and attenuated HR responses during grafting phases, without adverse effects on CVP or postoperative biochemical markers. Although the reduction in postoperative complications did not reach statistical significance, the observed trend, coupled with the absence of harmful effects, supports the potential role of low-dose Vasopressin as a safe and effective adjunct for haemodynamic optimisation in OPCAB. This will in turn decrease the duration of stay in post-op facility, limiting the financial burden on the patients and health care system.

LIMITATIONS OF STUDY

Our study has some limitations. The sample size was relatively small, and the study was conducted at a single centre, which may limit how well the findings apply to other settings. We did not measure advanced heart and blood vessel function and used a fixed dose of Vasopressin without adjusting for individual needs. High-risk patients were excluded, so the results may not apply to all OPCAB patients.

CONCLUSION

Our study shows that low-dose Vasopressin enhances intraoperative haemodynamic stability in patients undergoing OPCAB, with a trend toward fewer complications.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

TAK & MAA: Data acquisition, data analysis, critical review, approval of the final version to be published.

SAH & UK: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

KA & SJR: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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