Original Article

Assessing the effectiveness of levosimendan use and intra-aortic balloon pump use in controlling postoperative complications in patients undergoing coronary artery bypass graft surgery with low ejection fraction: A comparative study

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ABSTRACT

Introduction: Coronary artery bypass grafting (CABG) is done for prognostic as well as symptomatic purposes. Even though it has been demonstrated that decreased myocardial function can recover following CABG, left ventricular contractile dysfunction is still a risk factor for poor postoperative outcome. Positive inotropy, vasodilation, and cardiac cytoprotection are the three main modes of action of the inotropic medication levosimendan. Levosimendan and/or its active metabolite has also been shown to provide cardioprotection during acute and chronic heart failure by reducing myocardial remodeling, inflammation, ischemia-reperfusion damage, and myocyte death. The purpose of this study was to assess the effectiveness of levosimendan against an intra-aortic balloon pump (IABP) in controlling complications and lowering death rates in patients after CABG surgery with low ejection fraction 60 days after surgery.

Patients and Methods: The study was conducted at Cardiothoracic Surgery Department; Suez Canal University, it was a comparative prospective randomized study and the sample included 50 patients undergoing CABG operation with poor left ventricle function (less than 40%) divided into two groups, group A including patients administered levosimendan i.v. infusion and group B included patients having IABP insertion.

Results: The current results showed that there was no statistically significant difference between both studied groups concerning demographic data, as regards preoperative hemodynamic parameters, there was also no statistically significant difference between both studied groups. As for postoperative complications, there was no statistically significant difference between both studied groups. Regarding 60-day survival, there was no statistically significant difference between both groups.

Conclusion: Prophylactic levosimendan can be considered an alternative to prophylactic IABP in patients with low ejection fraction in whom IABP is contraindicated. The use of prophylactic levosimendan is comparable to the use of prophylactic IABP when risk and rate of complications are estimated in both approaches.

Key Words: Bypass time, coronary artery bypass grafting, coronary endarterectomy, intra-aortic balloon pump, levosimendan.

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INTRODUCTION

Coronary artery disease is defined as the narrowing or blockage of the vessel lumen as a result of atheroma subintimal deposition thickening the arterial wall and the arterial wall's decreased flexibility. The proximal coronary arteries are affected by atherosclerosis, particularly at the branching points[1]. Percutaneous intervention, coronary artery bypass graft surgery, and medication care are the three approaches used to treat coronary artery disease[2,3].

A surgical method of coronary revascularization is coronary artery bypass grafting (CABG). Using an interposed saphenous vein graft, Dr Rene Favaloro conducted his first coronary bypass operation in May 1967. Shortly after, he employed aortocoronary bypasses sutured proximally to the ascending aorta. The practical use of coronary bypass surgery was first made possible by Dr Denton Cooley. It has been demonstrated to be quite successful in relieving severe angina, and in certain cases, it can significantly extend usable life. Numerous studies have demonstrated the superiority of surgical revascularization over percutaneous interventional therapy and medication in the treatment of multivessel CAD. Before bringing a patient in for surgery, a thorough workup should be performed[4].

CABG is done for prognostic as well as symptomatic purposes. The American Heart Association and the American College of Cardiology have categorized CABG indications based on the degree of evidence demonstrating the procedure's utility and effectiveness[5,6].

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(1) Class I: conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective.

(2) Class II: conditions for which there is conflicting evidence and/or a divergence of opinion about the usefulness or efficacy of a procedure or treatment.

(3) Class IIa: weight of evidence or opinion is in favor of usefulness or efficacy.

(4) Class IIb: usefulness or efficacy is less well established by evidence or opinion.

(5) Class III: conditions for which there is evidence and/or general agreement that the procedure/treatment is not useful or effective, and in some cases it may be harmful indications for CABG as detailed by the American College of Cardiology and the American Heart Association are listed in Table 1 below.

When an ST-segment elevation MI occurs, CABG may be carried out as an emergency procedure if percutaneous coronary intervention (PCI) has failed or if PCI has not been successful and there is ongoing pain and ischemia endangering a sizable portion of the myocardium despite treatment[6].

Contractile dysfunction of the left ventricle (LV) is still a negative predictor of postoperative prognosis even after CABG, despite evidence of recovery of impaired myocardial function. Recent research has identified a subgroup of patients with a higher likelihood of improving left ventricular function and a more favorable postoperative survival following revascularization: those with an akinetic yet viable myocardium, or hibernating myocardium[7].

Heart failure is a long-term medical condition that can arise from issues with the heart valves, myocardial, endocardium, pericardium, or certain metabolic irregularities. It is typically linked to a range of structural and functional LV abnormalities. These abnormalities can include patients with reduced ejection fraction (classically reported as <40%), a significantly dilated LV cavity, and a decline in ventricular filling. Patients with normal LV dimensions and preserved ejection fraction (classically reported as ≥50%) can also be affected. According to Yancy *et al*.[8] and Ponikowski *et al*.[9], patients frequently exhibit limits in their ability to tolerate exercise, fluid retention, pulmonary and/or splanchnic congestion, and dependent edema.

There is a little association between LV function and symptom severity, despite the clear link between survival and symptom intensity[10]. Consequently, even individuals with little symptoms may have deteriorating clinical state that necessitates repeated hospital stays or possibly result in mortality[11,12].

According to Metra *et al*.[13], individuals who exhibit significant symptoms, recurring decompensation, and markedly severe cardiac dysfunction are classified as having "advanced heart failure." Goal-directed medical therapy, such as ivabradine, β-adrenergic blockers, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, angiotensin receptor–neprilysin inhibitors, mineralocorticoid receptor antagonists, and diuretics, becomes intolerable for patients with advanced heart failure[9].

Although the administration of catecholaminergic inotropes has been shown to improve hemodynamics and NYHA functional class in clinically low-output patients, it has not been shown to have an effect on mortality[14]. The maintenance of health-related quality of life and hemodynamic stability are the main objectives of receiving an intervention. Preventing hospitalizations for heart failure, maintaining patient comfort, and reducing worsening mortality are crucial objectives for palliative care[15–17]. Levosimendan may have a role in the treatment of acute and advanced heart failure; excerpts from evidence-based recommendations offer a framework for this[18].

According to De Hert and colleagues (190) and Jia *et al*.[19], these beneficial changes in patients' hemodynamic profiles may help to alleviate the symptoms of acute decompensated heart failure and lower the risk of hospitalization. To further distinguish this drug from other inotropic drugs, it has been reported to be the sole inotrope linked to enhanced survival[20,21].

According to De Hert *et al*. (2011)[22], levosimendan is an inotropic medication with three main modes of action: positive inotropy, vasodilation, and cardiac cytoprotection. Levosimendan's first main mode of action is its Ca2+-sensitizing mechanism, which is based on its interaction with cardiac troponin C[23]. According to Sorsa *et al*.[24], the drug's binding to troponin C enhances the fibers' sensitivity to ionic free calcium. This, in turn, helps prolong the molecular interaction between troponin C and troponin I, resulting in an increase in cardiac contractility without an increase in ionic free calcium.

Compared to all other inotropic drugs, which raise the concentration of ionic free calcium in cardiomyocytes and expose them to deadly amounts of ionic calcium, levosimendan has this unique quality. Heart remodeling, arrhythmia, and increased oxygen consumption have all been linked to elevated intracellular ionic calcium[25]. Levosimendan does not influence LV relaxation, despite its direct effects of boosting fast ventricular filling and myocardial contractility[26,27]. Levosimendan's vasodilatory qualities are its second mode of action[28]. According to Erdei *et al*.[20] and Hansen *et al*.[29], the medication has the ability to open ATP-dependent potassium channels in vascular smooth muscles, which dilates the coronary, peripheral, and pulmonary circulation arteries and venodilates the

portal and saphenous systems, lowering the preload and afterload of the right ventricle. The drug's cytoprotective qualities are its third mode of action. According to experimental research, levosimendan can lower the amount of free radicals produced by cells by opening cardiac mitochondrial ATP-sensitive K+ channels[22].

As a result, the cell is protected from stressful situations, cell death is decreased, and the generation of inflammatory response markers is stimulated[30]. Levosimendan and/or its active metabolite OR1896 have also been shown to provide cardioprotection during acute and chronic heart failure by reducing myocardial remodeling, inflammation, ischemia-reperfusion damage, and myocyte apoptosis[31]. Onichimowski *et al*.[32] reported that this impact was also seen in brain cells in addition to cardiac cells.

One form of mechanical hemodynamic support that has become the most popular circulatory assist device is intra-aortic balloon pump counterpulsation (IABP)[33]. The overall coronary blood flow is affected by the IABP in a varied way. While some studies have shown a large increase in coronary blood flow, others have observed little to no change in this area[34]. When coronary vascular beds are maximum dilated by ischemia, autoregulation is at its peak and flow becomes pressure-dependent, which is when increased blood flow is most likely to happen. By raising the perfusion pressure, counterpulsation can improve blood flow to these regions[34].

According to recommendations on myocardial revascularization published by the European Society of Cardiology and the European Association of Cardiothoracic Surgery, routine use of IABP is not advised in patients experiencing cardiogenic shock brought on by acute coronary syndrome (ACS). The patient's age, comorbidities, neurological function, chances for long-term survival, and quality of life should all be taken into account when deciding whether to provide short-term mechanical circulatory support for patients with refractory cardiogenic shock complicating ACS[35].

The ESC/EACTS 2014 guidelines' Class IIa recommendation states that IABP implantation should be promptly followed by defect correction in patients who have hemodynamic instability or cardiogenic shock as a result of mechanical problems. Additionally, in ACS patients experiencing cardiogenic shock, the Class IIb prescription for brief mechanical circulatory support may be taken into account[36].

When an ACS patient is admitted to the hospital, cardiogenic shock is the main cause of death within the hospital (ACS). In case of cardiogenic shock (SHOCK), should we revascularize occluded coronaries immediately? According to the Trial Registry, the most prevalent cause of cardiogenic shock in patients with ACS is mostly LV failure (78.5%); however, mechanical problems, such as ventricular septal defect, mitral regurgitation, or cardiac tamponade, accounted for 12% of cardiogenic shock cases[37]. Early revascularization with PCI or CABG has been shown to have a substantial survival advantage in patients with ACS accompanied with cardiogenic shock, according to the SHOCK Trial and SHOCK Registry[38].

There are two types of IABP complications: vascular and nonvascular. The incidence of any complication was 7.6% in the aforementioned review of nearly 17 000 patients who had an IABP inserted between 2010 and 2011, whereas major complications – major acute limb ischemia, severe bleeding, balloon leak, death directly related to the IABP insertion, or IABP failure – occurred in 2.6% of cases. Of the 21 percent in-hospital deaths, half happened during the IABP's implementation. Merely 0.5% of deaths were linked to IABP[39].

The purpose of this study was to assess the effectiveness of levosimendan against an IABP in controlling complications and lowering death rates in patients after CABG surgery with low ejection fraction 60 days after surgery.

PATIENTS AND METHODS:

This study is a comparative prospective randomized study, conducted at the Department of cardiothoracic surgery at Suez Canal University Hospital that started in 2018 and the duration was 3 years. The sample size had been calculated using the following equation:

$$n = \left[\frac{Z\alpha_{/2} + Z_{\beta}}{P1 - P2}\right](P_1 - q_2 q_2) = 43.276$$

Where

n=sample size.

$Z\alpha/2$=1.96 (The critical value that divides the central 95% of the Z distribution from the 5% in the tail).

$Z\beta$=0.84 (The critical value that separates the lower 20% of the Z distribution from the upper 80%)

$P1$=incidence of usage of IABP = 0.24 (2).

$P2$=incidence of usage of levosimendan= 0.04 (2).

q=1-P.

The sample size=43.276≈43+(10% drop out). The final sample size was 25 participants per each group[40].

This study included 50 patients undergoing CABG operation. Half are patients that were administered levosimendan infusion; and the other half are patients having IABP insertion.

The inclusion criteria included patients aged more than or equal to 40 years; patients with scheduled CABG; patients undergoing CABG with aortic valve, patients undergoing CABG with mitral valve; surgery using cardiopulmonary bypass pump; or patients with left ventricular ejection fraction (LVEF) less than or equal to 40% measured by echo at any time within 30 days before surgery.

Patients excluded were patients with several condition such as restrictive or obstructive cardiomyopathy constrictive pericarditis; restrictive pericarditis; pericardial tamponade; chronic dialysis; estimated glomerular filtration rate 30 ml/min/1.73 m^2 before CABG surgery; weight more than or equal to 150 kg; uncontrolled systolic blood pressure heart rate more than or equal to 120 beats/min, unresponsive to treatment; hemoglobin 8 g/dl within 4 h before baseline; serum potassium less than 3.5 or more than 5.5 mmol/l at baseline; liver dysfunction; compromised immune function; allergic reaction to levosimendan; administered commercial levosimendan within 30 days before the start experiment; or used an experimental medical device within 30 days before the planned start of experiment.

All the patients for both groups undergoing CABG surgery had been given a number, odd number were given drug group while even numbers were given to of IABP insertion group, this encoding was done by the principal investigator of the study.

Group A is allocated to levosimendan infusion as it was started after insertion of an arterial line and before skin incision at a dose of 0.2 μg kg/min for the first hour and then reduced to 0.1 μg kg/min to be continued for another 23 h (total infusion time of 24 h).

Group B was patient with IABP, the IABP catheter is inserted percutaneously into the femoral artery through an introducer sheath using the modified Seldinger technique. Once vascular access is obtained, the balloon catheter was inserted and advanced, under fluoroscopic guidance, into the descending thoracic aorta, with its tip 2–3 cm distal to the origin of the left subclavian artery (at the level of the carina). Intraoperatively, balloon placement was ascertained using transesophageal echocardiography. Balloon inflation causes augmentation of diastolic pressure and a second peak was observed. IABP was started before weaning from bypass.

Data collection

Preoperative assessment

Patients from both groups were subjected to written consent, full history taking including HTN, DM, renal, liver as well as cardiac diseases, complete drug history including levosimendan 30 days before going to surgery and any record of sensitivity; general and cardiac examinations, laboratory investigations including CBC, liver and kidney functions, coagulation profile, cardiac enzymes, serum lactate, as well as electrolytes; radiology including CXR was done for all patients of both groups, as well as CT chest for redo patients, and patient with chest surgery; cardiac examination including ECG for arrhythmias or any abnormalities, echo for dimensions: LVED, LVES, cardiac function: LVEF, LVFS, pulmonary artery pressure, valve morphology, and coronary angiography for detecting coronary arteries lesions.

Intraoperative assessment

(1) Total cardiopulmonary bypass time and cross-clamp time.

(2) The resumption to normal rhythm after declamping (spontaneous or with DC shock.)

(3) Recirculation time.

(4) The need for inotropic support (type, dose, and duration).

(5) ECG changes in the form of ischemia or arrhythmia.

Sixty-day assessment of complications and survival

Patient was reassessed after 60 days regarding history taking; clinical examination for evaluation of the improvement of preoperative symptoms; and echocardiography for comparison between current and preoperative echo findings. Survival rate was assessed regarding the two groups.

Ethical approval

An ethical approval of the study (IRB) was obtained from Suez Canal University Research and ethical committee. All patients signed an informed written consent for acceptance of the operation with all details explained thoroughly.

Data management and statistical analysis

Data entry, coding and statistical analysis was performed using MedCalc, ver. 18.2.1 (MedCalc, Ostend, Belgium). Tests of significance (Wilcoxon's and χ^2) were used. Data were analyzed and presented according to the type of data (parametric and nonparametric) obtained for each variable. Student t test and χ^2 test were used to assess the statistical significance of the difference. *P values* less than 0.05 (5%) was considered statistically significant. *P value*: level of significance were *P value* more than 0.05: nonsignificant; *P value* less than 0.05: significant; and *P value* less than 0.01: highly significant. Mean, SD as well as range for parametric numerical data, while median and interquartile range for nonparametric numerical data. Frequency and percentage of nonnumerical data.

RESULTS:

A comparative prospective randomized study included 50 patients undergoing CABG surgery with poor LV function (<40%), the sample was 50 patients divided into two groups, 25 patients in each group: the first group

"group A" included patient administered levosimendan i.v. infusion, while the second group "group B" included patient having IABP insertion.

Demographic and clinical data of groups of research

Our study results revealed that there was no statistically significant difference between group A and group B regarding age, sex, BMI (group A: 27.9±3.7, group B: 29.5±2.3, *P=0.462*), NYHA classification, comorbidities, ejection fraction (group A: 29.2±3.5, group B: 31.8±4.1, *P=0.517*), and EuroSCORE (group A: 5.3±1.3, group B: 6.1±1.7, P=0.426) (Table 1).

Preoperative assessment

Concerning preoperative hemodynamic parameters, our results revealed that there was no statistically significant difference between both studied groups regarding mean arterial blood pressure (group A: 82.5±11.3, group B: 76.1±10.1, *P=0.241*) and central venous pressure (group A:10.4±3.6, group B: 9.2±3.2, *P=0.667*).

As for the heart rate measures, it was found that there was also no statistically significant difference (group A: 68.2±5.4, group B: 73.2±4.6, *P=0.318*), the same findings are noted in cardiac index results (group A: 1.5±0.3, group B: 1.7±0.5, *P=0.271*) (Table 2).

Intraoperative assessment

As regard intraoperative data, our results revealed there was no statistically significant difference between both studied groups as regard bypass time (group A: 75.2±9.3, group B: 82.1±11.5, *P=0.652*) and cross-clamp time (group A: 46.7±7.6, group B: 54.7±8.2, *P=0.426*). Comparing between both groups in number of grafts, we observed no statistically significant difference between both studied groups (group A: 2.2±1.4, group B: 2.6±1.1, *P=0.293*) the same results observed regarding comparing blood loss in 1st 24 h (group A: 235.7±152.4 ml, group B: 316.4±164.9 ml, *P=0.428*). As for the coronary endarterectomy there was also no statistically significant difference (group A: 8%, group B: 4%, *P=0.082*), the same findings is noted in LV reconstruction results (group A: 40%, group B: 30%, *P=0.153*) and LV thrombectomy (group A: 3%, group B: 2%, *P=0.126*) (Table 3).

Postoperative assessment

Early postoperative assessment

As regard postoperative hemodynamic variables during 1st 24 h after surgery, our results revealed there was a statistically significant difference between both studied groups as regard serum lactate (group A: 4.5±2.1, group B: 7.3±3.5, *P=0.036*). However, there was no statistically significant difference between both studied groups considering heart rate (group A: 95±14.3, group B: 103±15.1, *P=0.251*) and mean arterial pressure (group A: 75.4±11.7, group B: 63.6±9.5, *P=0.167*). Comparing between both groups in central venous pressure, we observed no statistically significant difference between both studied groups (group A: 12.4±5.2, group B: 13.2±5.6, *P=0.615*) the same results observed regarding comparing cardiac index (group A: 2.4±1.1, group B: 2.6±1.3, *P=0.249*) and urine output (group A: 1683±422.5 ml/24 h, group B: 1526.3±253.5 ml/24 h, *P=0.182*) (Table 4).

Early postoperative complications

Considering postoperative complications, by comparing both groups regarding arrhythmia, we observed no statistically significant difference between both studied groups (group A: 12%, group B: 8%, *P=0.135*) the same results detected as for postoperative dialysis (group A: 4%, group B: 8%, *P=0.226*) and incidence of mediastinitis (group A: 8%, group B: 12%, *P=0.165*).

As for hospital stay by days there was also no statistically significant difference between both groups regarding (group A: 10.2±5.2, group B: 12.6±3.8, *P=0.264*) (Table 5).

Sixty-day assessment

Regarding 60-day survival, our study results found that IABP group have higher nonsignificant survival rate (88%) than levosimendan group (84%) with *P value* of 0.428 (Table 6).

Table 1: Demographic and clinical data of studied groups

	Levosimendan group (*N*=25)	IABP group (*N*=25)	*P* value
Age (years), $_{\text{mean (SD)}}$	54.7 (3.5)	57.3 (3.9)	0.217
BMI (kg/m^2), $_{\text{mean (SD)}}$	27.9 (3.7)	29.5 (2.3)	0.462
Sex [$_{n\ (\%)}$]			0.251
Male	14 (56)	12 (48)	
Female	11 (44)	13 (52)	
NYHA functional class [$_{n\ (\%)}$]			
Class II	2 (8)	1 (4)	

Class III	22 (88)	23 (92)	0.614
Class IV	1 (4)	1 (4)	
Comorbidity [$_{n\ (\%)}$]			0.194
Diabetes mellitus	9 (36)	11 (44)	
Triple-vessel disease	13 (52)	12 (48)	
Peripheral vascular disease	1 (4)	1 (4)	
Unstable angina	2 (8)	1 (4)	
Ejection fraction (%), $_{\text{mean (SD)}}$	29.2 (3.5)	31.8 (4.1)	0.517
EuroSCORE, $_{\text{mean (SD)}}$	5.3 (1.3)	6.1 (1.7)	0.426

Table 2: Preoperative hemodynamic parameters in both groups

	Levosimendan group (*N*=25)	IABP group (*N*=25)	
	Mean (SD)	Mean (SD)	*P* value
Mean arterial pressure (mmHg)	82.5 (11.3)	76.1 (10.1)	0.241
Central venous pressure (mmHg)	10.4 (3.6)	9.2 (3.2)	0.667
Heart rate (beat/min)	68.2 (5.4)	73.2 (4.6)	0.318
Cardiac index (l/min/m^2)	1.5 (0.3)	1.7 (0.5)	0.271

Table 3: Comparison between both groups regarding intraoperative data

	Levosimendan group (*N*=25)	IABP group (*N*=25)	*P* value
Bypass time (min), $_{\text{mean (SD)}}$	75.2 (9.3)	82.1 (11.5)	0.652
Cross-clamp time (min$_{\text{), mean (}}$SD)	46.7 (7.6)	54.7 (8.2)	0.426
Number of grafts, $_{\text{mean (SD)}}$	2.2 (1.4)	2.6 (1.1)	0.293
Blood loss in 1st 24 h (ml), $_{\text{mean (SD)}}$	235.7 (152.4)	316.4 (164.9)	0.428
Coronary endarterectomy [$_{n\ (\%)}$]	2 (8)	1 (4)	0.082
LV reconstruction [$_{n\ (\%)}$]	10 (40)	6 (30)	0.153
LV thrombectomy [$_{n\ (\%)}$]	3 (12)	2 (8)	0.126

Table 4: Average hemodynamic variables during first 24 h after surgery in both study groups

	Levosimendan group (*N*=25)	IABP group (*N*=25)	*P* value
Heart rate (beat/min), $_{\text{mean (SD)}}$	95.0 (14.3)	103.0 (15.1)	0.251
Mean arterial pressure (mmHg), $_{\text{mean (SD)}}$	75.4 (11.7)	63.6 (9.5)	0.167
Central venous pressure (mmHg), $_{\text{mean (SD)}}$	12.4 (5.2)	13.2 (5.6)	0.615
Serum lactate (mmol/l), $_{\text{mean (SD)}}$	4.5 (2.1)	7.3 (3.5)	0.036*
SvO_2 (%), $_{\text{mean (SD)}}$	58.2 (6.2)	50.8 (5.4)	0.283
CO2 gap (mmHg) $_{\text{mean (SD)}}$	5.3 (2.4)	5.6 (1.8)	0.548
SV (ml/beat), $_{\text{mean (SD)}}$	64.5 (7.5)	55.2 (5.3)	0.136
Cardiac index (l/min/m^2), $_{\text{mean (SD)}}$	2.4 (1.1)	2.6 (1.3)	0.249
Urine output (ml/24 h), $_{\text{mean (SD)}}$	1683.0 (422.5)	1526.3 (253.5)	0.182
Serum creatinine (mg/dl), $_{\text{mean (SD)}}$	1.6 (0.3)	1.7 (0.5)	0.427
CK (IU/l), $_{\text{mean (SD)}}$	3194.5 (923.8)	3148.4 (816.7)	0.518
CKMB (IU/l), $_{\text{mean (SD)}}$	163.0 (84.4)	185.3 (140.9)	0.119

SV, stroke volume; SvO_2, mixed venous oxygen saturation.
Unpaired t test.

Table 5: Comparison between both groups regarding early postoperative complications

	Levosimendan group (*N*=25) [$_{n\ (\%)}$]	IABP group (*N*=25) [$_{n\ (\%)}$]	*P* value
Arrhythmia	3 (12)	2 (8)	0.135
Postoperative dialysis	1 (4)	2 (8)	0.226
Stroke	2 (8)	1 (4)	
Hospital stay (days), $_{\text{mean (SD)}}$	10.2 (5.2)	12.6 (3.8)	0.264
Mediastinitis	2 (8)	3 (12)	0.165

Table 6: Sixty-day survival in both study groups

60-day survival	Levosimendan group (*N*=25)	IABP group (*N*=25)	*P* value
Survived	21 (84)	22 (88)	0.428
Died	4 (16)	3 (12)	0.291

DISCUSSION

Three to 14% of individuals receiving isolated CABG experience preoperative acute cardiovascular impairment. The ensuing low cardiac output syndrome is linked to end-organ failure, which causes significant morbidity and death rates to increase by 10-17 times, respectively (16.9 vs. 0.9%). Preoperative decreased LVEF was found by Maganti *et al*.[41] to be the primary risk factor for the emergence of low cardiac output syndrome. Mebazaa *et al*.[42] conducted an intriguing research on 700 000 coronary cases from the Society of Thoracic Surgeons National Adult Cardiac Surgery Database. The analysis suggested that a 19% increase in the probability of mortality was related with every 10-unit fall in preoperative LVEF.

Maintaining optimal hemodynamics is the major goal in preventing problems. Historically, this has been accomplished by the use of mechanical support, namely the IABP. A novel inotropic medication called levosimendan has been used to treat acute decompensated heart failure. By binding to cardiac troponin C, it improves myofilament responsiveness to calcium and lengthens actin-myosin overlap, which in turn increases myocardial contractility. This process occurs without raising intracellular calcium concentration or myocardial oxygen consumption[43].

This study's primary goal was to assess the effectiveness of levosimendan against an IABP in controlling complications and lowering death rates in patients after CABG surgery with low ejection fraction 60 days after surgery.

The study, which was carried out at Suez Canal University's Cardiothoracic Surgery Department, was a comparative prospective randomized study with a sample of 50 patients undergoing CABG operation with poor left ventricular function (<40%). The patients were split into two groups, group A consisting of patients receiving levosimendan intravenous infusion and group B consisting of patients undergoing IABP insertion.

The findings of our investigation revealed that there was no statistically significant difference in terms of age, sex, BMI (group A: 27.9±3.7, group B: 29.5±2.3, *P=0.462*), comorbidities, NYHA classification, ejection fraction (group A: 29.2±3.5, group B: 31.8±4.1, *P=0.517*), EuroSCORE (group A: 5.3±1.3, group B: 6.1±1.7, *P=0.426*), NYHA classification, and comorbidities.

Our findings align with the research conducted by Mate *et al*.[44], which contrasted levosimendan infusion (group L) with IABP implantation (group B). The authors reported that no statistically significant differences were seen between the two groups with respect to age, sex, BMI, and ejection percentage.

According to the current study, there was no statistically significant difference in mean arterial blood pressure (group A: 82.5±11.3, group B: 76.1±10.1, *P=0.241*) or central venous pressure (group A: 10.4±3.6, group B: 9.2±3.2, *P=0.667*) between the two groups when it came to preoperative hemodynamic parameters. The results of the cardiac index (group A: 1.5±0.3, group B: 1.7±0.5, *P=0.271*) and heart rate measurements (group A: 68.2±5.4, group B: 73.2±4.6, *P=0.318*) similarly indicated no statistically significant difference.

In the Anastasiadis *et al*.[45] trial, 32 CABG patients with poor LVEF less than 40% were randomly assigned to receive a placebo or a continuous infusion of levosimendan for 24 h without a loading dose at a dosage of 0.1 μg/kg/min. Prophylactic levosimendan administration resulted in a relatively stable PCWP trend, reflecting the inotropic and vasodilatory properties of the drug. In contrast, the control group experienced higher values after 24 h of infusion (6.3±2.8 vs. 8.9±3.4 mmHg, *P=0.02*) and at 24 h postoperatively (9.3±3.1 vs. 13.5±4.2 mmHg,

P=0.006), respectively. However, following surgery, the mean pulmonary artery pressure rose in both groups, with no discernible variation in the recorded values.

The current study showed as regard to intraoperative, there was no statistically significant difference between both studied groups in bypass time (group A: 75.2±9.3, group B: 82.1±11.5, *P=0.652*) and cross-clamp time (group A: 46.7±7.6, group B: 54.7±8.2, *P=0.426*). Comparing between both groups in number of grafts, we observed no statistically significant difference between both studied groups (group A: 2.2±1.4, group B: 2.6±1.1, *P=0.293*). As for the coronary endarterectomy there was also no statistically significant difference (group A: 8%, group B: 4%, *P=0.082*), the same findings is noted in LV reconstruction results (group A: 40%, group B: 30%, *P=0.153*) and LV thrombectomy (group A: 3%, group B: 2%, *P=0.126*).

Our results were supported by study of Omar *et al*.[46], as they reported that the mean bypass time in group A ranging between 60 and 135 min with a mean 85.4±20.99 min. In group B, it ranged between 67 and 133 min with a mean 90.7±20.4 min. The number of grafts ranged from two to four with a mean of 3.2±0.48 in group A, while group B had a number of grafts ranging from three to four with a mean of 3.3±0.47. There was no statistical significance between the two groups in both bypass time and number of grafts.

As regard postoperative hemodynamic variables during first 24 h after surgery, our results revealed there was a statistically significant difference between both studied groups as regard serum lactate (group A: 4.5±2.1, group B: 7.3±3.5, *P=0.036*). However, there was no statistically significant difference between both studied groups considering blood loss (group A: 235.7±152.4 ml, group B: 316.4±164.9 ml, *P=0.428*), heart rate (group A: 95±14.3, group B: 103±15.1, *P=0.251*) and mean arterial pressure (group A: 75.4±11.7, group B: 63.6±9.5, *P=0.167*). Comparing between both groups in central venous pressure, we observed no statistically significant difference between both studied groups (group A: 12.4±5.2, group B: 13.2±5.6, *P=0.615*) the same results observed regarding comparing cardiac index (group A: 2.4±1.1, group B: 2.6±1.3, *P=0.249*) and urine output (group A: 1683±422.5 ml/24 h, group B: 1526.3±253.5 ml/24 h, *P=0.182*).

In the study of Mate *et al*.[44], early postoperative hemodynamic data recorded at baseline were comparable in both groups. This study results agree with our results as difference was not statistically significant regarding heart rate, mean arterial pressure, vasoactive inotropic score. Also, progressive increase in the cardiac index was observed in both groups, the increase was observed to be statistically significant on within the group in both groups. However, the differences in the cardiac index at different time points between the two groups were not statistically significant. Furthermore, the mentioned study was consistent with our study as revealed that there was no statistically significant difference between their studied groups as regard blood loss in first 24 h and ventilation time. However, this study was found to be inconsistent with the current study regarding serum lactate concentration as it was consistently lower in group B compared to group L at all-time points.

After accounting for postoperative complications, our study's findings showed that by group A and group B comparing the two groups' incidence of mediastinitis (group A: 8%, group B: 12%, *P=0.165*) and postoperative dialysis (group A: 4%, group B: 8%, *P=0.226*), we found no statistically significant difference between the two groups (group A: 2%, group B: 8%, *P=0.135*). Regarding the number of days spent in the hospital, there was no statistically significant difference between the two groups group A and group B by days (group B: 12.6±3.8, *P=0.264*, group A: 10.2±5.2).

Omar *et al*.'s[46] study, which found no statistically significant difference between the two groups with respect to postoperative mechanical breathing time, arrhythmias, reopening, hemodialysis requirement, mediastinitis, or length of hospital stay, corroborated our findings.

Mate *et al*.[44] revealed a statistically significant difference (*P<0.001*) between group L's (4.4+0.2 days) and group B's (6.5+0.1 days) for the mean ICU stay. Group B patients were discharged from the hospital after a delay of 13.4 days, whereas group L patients were discharged after 10.2 days. This difference was statistically significant (*P<0.001*). Two patients in group B developed acute thrombosis, necessitating femoral artery embolectomy. Group B and group L patients did not have any acute renal damage. Group L had a lower incidence of postoperative atrial fibrillation than group B, which showed a statistically significant difference (*P=0.01*). The need for noradrenaline was comparable in the two groups. Sepsis and various organ failure ultimately claimed the lives of two individuals, one from each group. The length of ICU and hospital stay were higher in group B, compared to group L, indicating a statistically significant difference (*P=0.001*).

Additionally, Lomivorotov *et al*.[47] revealed that the study groups' hospital stays, which ranged from 19 to 22 days for group A, 20 to 27 days for group B, and 18 to 32 days for group C, were also comparable

in length. One patient from group B experienced preoperative myocardial infarction; individuals from groups A or C did not experience this. The other postoperative problems did not significantly differ between the groups. Of the patients, four (4.4%) patients died. Fifteen days following surgery, one patient in group A passed away due to multiple organ failure brought on by abrupt heart failure. One patient in group B passed away 26 days following surgery due to multiple organ failure brought on by acute heart failure and preoperative myocardial infarction, while the other patient died 5 days following surgery as a result of an unexpected death on the ward. Nine days following surgery, a patient in group C passed away due to multiple organ failure resulting from a preoperative stroke. There was no discernible variation in the death rates between the groups. Three groups were randomly assigned to patients. A prophylactic IABP was given to group A the day before surgery. Group B underwent a levosimendan infusion at a rate of 0.1 mg/kg/min with an initial bolus of 12 mg/kg for 10 min following the induction of anesthesia, as well as a prophylactic IABP 1 day before to surgery. After inducing anesthesia, group C was given a levosimendan infusion at a rate of 0.1 g/kg/min, starting with an initial bolus of 12 mg/kg for 10 min.

Desai *et al*. (2018)[48] found that while two patients in the control group required hemodialysis, none of the patients in the levosimendan group did. The majority of patients in the control group experienced acute renal damage, which was indicated by an increase in blood creatinine concentration and was treated with fluids and diuretics. The control group had a greater incidence of postoperative atrial fibrillation. Hemodynamic instability necessitated the transfer of three patients in the control group to cardiopulmonary bypass and IABP in order to complete the surgery; in contrast, only one patient in the levosimendan group required IABP support. Both groups' ICU and hospital stays were comparable. Compared to none in the research group, two individuals in the control group passed away from sepsis and cardiogenic shock. Levosimendan (group L) and the control group (group C) were the two randomly assigned groups (n=30 each) of 60 patients receiving elective OPCAB.

Landoni *et al*.[49] highlighted in a meta-analysis that levosimendan treatment significantly decreased mortality in heart patients who had positive results. Alvarez *et al*.[50] found that in order to prevent hypotensive episodes in patients with decompensated heart failure, a loading dose of levosimendan needed to be skipped.

CONCLUSION

As a result, prophylactic levosimendan can be considered an alternative to prophylactic IABP in patients with low ejection fractions for whom IABP is contraindicated. The use of prophylactic levosimendan is comparable to the use of prophylactic IABP when risk and rate of complications are estimated in both approaches.

CONFLICT OF INTEREST

There are no conflicts of interest.

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