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The Early Outcomes of Levosimendan in Patients Undergoing Coronary Artery Bypass Grafting with Impaired Myocardial Function

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Abstract

Background: Coronary artery bypass grafting (CABG) is the standard treatment for ischemic heart disease; however, postoperative myocardial dysfunction remains a major concern, particularly in patients with impaired left ventricular (LV) function. Levosimendan, a calcium sensitizer with inotropic and vasodilatory effects, may improve perioperative cardiac performance. This study evaluated the effect of preoperative levosimendan administration on postoperative outcomes in patients undergoing CABG.

Methods: This randomized clinical trial included 60 patients with left ventricular ejection fraction (LVEF) <45% scheduled for isolated CABG. Patients were randomized into two groups: Group A (n=30) received levosimendan infusion at 0.1 µg/kg/min for 24 hours starting 12 hours preoperatively, while Group B (n=30) received conventional inotropic support alone. Postoperative outcomes included hemodynamic parameters, inotropic requirements, duration of mechanical ventilation, and lengths of ICU and hospital stay. LV function was assessed using transthoracic echocardiography according to the American Society of Echocardiography 16-segment model by a blinded echocardiographer within 24–48 hours after ICU admission.

Results: Baseline characteristics were comparable between groups except for a higher preoperative heart rate in the levosimendan group (91.37 ± 10.25 vs. 82.73 ± 6.93 bpm, p=0.001). Postoperatively, the levosimendan group showed significantly lower inotropic requirements on ICU admission (p=0.001), higher diastolic blood pressure (75.6 ± 12.5 vs. 69.0 ± 12.4 mmHg, p=0.042), and improved LVEF (47.0 ± 6.1% vs. 44.0 ± 7.8%, p=0.037). Patients receiving levosimendan also had shorter mechanical ventilation duration (5.9 ± 2.2 vs. 13.8 ± 16.9 hours, p<0.001), ICU stay (2.7 ± 0.7 vs. 4.0 ± 0.8 days, p<0.001), and hospital stay (6.5 ± 1.7 vs. 8.1 ± 2.2 days, p<0.001). Complication and mortality rates did not differ significantly between groups.

Conclusions: Preoperative levosimendan administration in patients with moderately impaired LV function undergoing CABG improves early postoperative cardiac performance, reduces inotropic support requirements, and shortens recovery time without increasing adverse events.

KEYWORDS

Levosimendan; Coronary Artery Bypass Grafting; Poor Myocardial Function; Left Ventricle; Echocardiography Scale

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Introduction

Coronary artery bypass grafting (CABG) is a cornerstone surgical intervention for patients with obstructive coronary artery disease. CABG has a proven efficacy in reducing the risk of serious cardiovascular complications and mortality in patients with reduced ejection fraction [1]. In recent years, the demographic of patients undergoing cardiac surgery has shifted towards individuals of advanced age with multiple preoperative comorbidities and impaired left ventricular function [2]. The elevated risk profile in this population has spurred the development of various strategies to optimize surgical outcomes. These interventions include mechanical circulatory support devices, such as the intra-aortic balloon pump (IABP), and a range of pharmacologic inotropic agents [3].

The intra-aortic balloon pump (IABP) is commonly used as an adjunctive therapy to support patients with impaired myocardial function undergoing cardiac surgery. However, its use is associated with potential vascular complications, prompting interest in pharmacologic alternatives such as Levosimendan [4].

Levosimendan is a calcium-sensitizing agent that enhances myocardial contractility without increasing myocardial oxygen consumption. It also confers cardioprotective effects during myocardial ischemia by activating ATP-sensitive potassium channels [5]. Unlike traditional inotropes, levosimendan does not elevate intracellular calcium concentrations, thereby preserving diastolic function and ventricular relaxation. A notable side effect, however, is a predisposition to hypotension, which results from its vasodilatory effect mediated by potassium channel opening [6].

Given the need for effective and safe strategies to support high-risk patients, the aim of this work was to assess the effect of levosimendan on post-CABG outcomes.

Patients and Methods

This prospective randomized clinical study was conducted on 60 patients undergoing coronary artery bypass grafting (CABG) who were admitted to the cardiovascular intensive care unit between January 2025 and January 2026. The study protocol was approved by the Institutional Research Ethics Committee, and written informed consent was obtained from all patients prior to inclusion. The study was conducted and reported in adherence to CONSORT guidelines for randomized controlled trials.

All enrolled patients had multivessel coronary artery disease confirmed by coronary angiography, with a preoperative left ventricular ejection fraction (LVEF) ≤45%. Patients were excluded if they were younger than 20 years or older than 75 years, had chronic pulmonary disease, known hypersensitivity to levosimendan, previous (redo) CABG, significant hepatic or renal dysfunction, or required concomitant cardiac procedures such as valvular surgery.

Patients were randomly assigned into two equal groups (n = 30 each) using a computer-generated random number sequence. Allocation concealment was achieved through sequentially numbered, sealed, opaque envelopes prepared by an independent research coordinator not involved in patient recruitment or outcome assessment. In group A, patients received a preoperative levosimendan infusion started 12 hours before surgery at a dose of 0.1 µg/kg/min. The infusion was interrupted during cardiopulmonary bypass (CPB) and resumed after weaning for a further 12 hours. In group B, patients received conventional inotropic support according to institutional protocol. All 60 randomized patients completed the study and were included in the final analysis (intention-to-treat = per-protocol population). There were no crossovers, protocol deviations, or early permanent terminations of the levosimendan infusion. No patient in Group A required discontinuation of the infusion due to hemodynamically significant hypotension.

All procedures were performed through a standard median sternotomy under general anesthesia. Cardiopulmonary bypass was

Table 1: Baseline demographic characteristics of the study population. Data presented as mean ± SD or frequency

		Group A (n=30)	Group B (n=30)	P-value
Age (years)		59.67 ± 8.73	62.17 ± 8.43	0.264
Height (cm)		172.87 ± 9.16	174.67 ± 8.93	0.444
Weight (kg)		88.10 ± 13.12	84.80 ± 10.82	0.292
BMI (kg/m²)		29.45 ± 3.49	27.82 ± 3.39	0.072
Sex	**Male**	24 (80%)	24 (80%)	>0.99
	Female	6 (20%)	6 (20%)	

BMI: Body mass index

established after systemic heparinization to maintain an activated clotting time (ACT) >450 seconds. CPB was carried out using a roller pump and membrane oxygenator, maintaining a mean arterial pressure of 60–70 mmHg under moderate hypothermia (30–32°C). Myocardial protection was achieved using antegrade St. Thomas' cardioplegia followed by intermittent cold blood cardioplegia. Distal and proximal graft anastomoses were completed during a single aortic cross-clamp period, and heparin was reversed with protamine sulfate at the end of the procedure.

Data Collection and Postoperative Management

Preoperative data, including patient history, clinical evaluation, and laboratory investigations, were recorded. Predicted mortality risk was calculated for all patients using the EuroSCORE II system [7].

Hemodynamic data were recorded at baseline (post-anesthesia induction), 1-hour post-ICU admission, and 24 hours post-ICU admission [8]. Cardiac output (CO) was measured via thermodilution using a pulmonary artery catheter (Edward Lifesciences, Irvine, CA, USA). The cardiac index (CI), pulmonary vascular resistance index (PVRI), and systemic vascular resistance index (SVRI) were subsequently calculated. Postoperatively, central venous pressure (CVP) was maintained at 12–14 mmHg and pulmonary capillary wedge pressure (PCWP) at 14–18 mmHg using intravenous fluids. If the CI fell below 2.2 L/m²/min, dobutamine (Eumedica, Manage, Belgium) was administered up to a maximum of 10 µg/kg/min. Persistent hypotension (MAP < 60 mmHg) was managed with norepinephrine. An IABP was utilized if adequate hemodynamic support could not be achieved with inotropes alone. Inotrope and vasopressor weaning followed a standardized step-down protocol applied uniformly to both groups: dobutamine was weaned first when CI exceeded 2.2 L/m²/min, followed by norepinephrine once MAP was stably maintained above 65 mmHg.

Echocardiographic examination of the left ventricle (LV) was performed preoperatively and postoperatively using transthoracic echocardiography (TTE), following the 16-segment model of the American Society of Echocardiography [9]. Postoperative TTE was performed within 24–48 hours of ICU admission. All echocardiographic assessments were performed by an experienced echocardiographer who was blinded to group allocation. Blood samples for laboratory analysis were collected at baseline, 4 hours post-ICU admission, and 24 hours post-ICU admission.

Extubation criteria included hemodynamic stability (MAP >65 mmHg, HR <100 bpm), adequate spontaneous respiratory effort (tidal volume >5 mL/kg on minimal ventilator support, SpO_2 >95% on FiO_2 ≤0.4), and an awake, cooperative state. ICU discharge criteria included hemodynamic stability without vasopressor or inotrope dependence, absence of new postoperative complications, stable urine output, and satisfactory respiratory function. These standardized criteria were consistently applied across both groups.

Outcomes

The pre-specified primary endpoint was the requirement for high-dose inotropic support upon ICU admission. Secondary outcomes included IABP

Table 2: Preoperative and intraoperative characteristics between both study groups. Data presented as mean ± SD or frequency (%)

	Group A (n=30)	Group B (n=30)	P-value
Preoperative risk factors			
Diabetes Mellitus	22 (73.3%)	20 (66.7%)	0.778
Hypertension	22 (73.3%)	14 (46.7%)	0.065
Dyslipidemia	17 (56.7%)	17 (56.7%)	>0.99
Thyroid disease	2 (6.7%)	4 (13.3%)	0.671
Smoking	15 (50%)	20 (66.7%)	0.304
Preoperative NYHA functional class			
II	10 (33.3%)	8 (26.7%)	
III	16 (53.3%)	18 (60.0%)	0.294
IV	4 (13.3%)	4 (13.3%)	
Preoperative ECG findings			
STEMI	14 (46.7%)	15 (50.0%)	
NSTEMI	16 (53.3%)	12 (40.0%)	0.165
Unstable angina	0 (0%)	3 (10.0%)	
Preoperative hemodynamic parameters			
SBP (mmHg)	132.00 ± 12.41	133.00 ± 12.74	0.767
DBP (mmHg)	83.17 ± 6.88	83.00 ± 7.43	0.928
HR (bpm)	91.37 ± 10.25	82.73 ± 6.93	0.001*
CVP (mmHg)	9.30 ± 2.65	7.93 ± 3.06	0.065
Preoperative laboratory and echocardiographic parameters			
Hb (g/dL)	12.47 ± 1.44	12.89 ± 1.53	0.286
Platelets (×103/µL)	250.63 ± 52.30	257.70 ± 44.41	0.573
TLC (×103/µL)	7.53 ± 1.62	7.62 ± 1.52	0.821
Urea (mg/dL)	38.33 ± 12.65	39.70 ± 10.55	0.648
Creatinine (mg/dL)	1.04 ± 0.25	0.98 ± 0.19	0.256
INR	1.08 ± 0.09	1.07 ± 0.09	0.662
EF (%)	38.1 ± 4.7	38.4 ± 4.4	0.834
Intraoperative characteristics			
Operation time (h)	5.30 ± 0.83	5.32 ± 0.89	0.985
Bypass time (min)	120.33 ± 24.78	115.97 ± 23.35	0.493
Cross clamp time (min)	75.5 ± 20.8	70.5 ± 23.4	0.388
Number of grafts	3.07 ± 0.58	3.10 ± 0.61	0.833
IABP use	0 (0%)	3 (10%)	0.237
Inotropic support at ICU admission			
None	8 (26.7%)	0 (0%)	
Adrenaline only	7 (23.3%)	2 (6.7%)	
Adrenaline + noradrenaline	12 (40.0%)	24 (80.0%)	0.001*
Triple inotrope	1 (3.3%)	4 (13.3%)	
Levosimendan only	2 (6.7%)	0 (0%)	

NYHA: New York Heart Association, ECG: Electrocardiogram; STEMI: ST-Elevation Myocardial Infarction, SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate; CVP: Central Venous Pressure; *: significant as P value < 0.05, Hb: Hemoglobin; TLC: Total Leukocyte Count; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; INR: International Normalized Ratio; EF: Ejection Fraction, IABP: Intra-Aortic Balloon Pump, ICU: Intensive Care Unit

insertion, postoperative LVEF, duration of mechanical ventilation (in hours), and length of ICU and hospital stay (in days). Other postoperative complications were also documented. Secondary endpoints were considered exploratory and hypothesis-generating; no formal correction for multiplicity

was applied, and results should be interpreted accordingly.

Statistical analysis

Statistical analysis was conducted using SPSS version 26 (IBM©, Armonk, NY, USA). The normality of data distribution was assessed with the Shapiro-Wilk test and histograms. Quantitative variables were expressed as mean ± standard deviation, while qualitative variables were presented as frequencies and percentages. For normally distributed quantitative data, comparisons between the two groups were performed using the independent (unpaired) Student's t-test. Categorical variables were compared using the Chi-square test or Fisher's exact test, as appropriate. A two-tailed p-value < 0.05 was considered statistically significant.

Results

The two study groups were well matched with regard to baseline demographic and clinical characteristics (Table 1). There were no statistically significant differences between the groups in age, sex distribution, anthropometric measures, or preoperative risk factors including diabetes mellitus, hypertension, dyslipidemia, and smoking status. Similarly, preoperative NYHA functional class, electrocardiographic findings, baseline laboratory parameters (hemoglobin, platelet count, and renal function), and preoperative left ventricular ejection fraction were comparable between the two groups (p > 0.05 for all). The only significant baseline difference was a higher mean heart rate observed in the levosimendan group compared with the control group (91.37 ± 10.25 vs. 82.73 ± 6.93 bpm, p = 0.001). Intraoperative variables, including total operative time, cardiopulmonary bypass duration, aortic cross-clamp time, and the number of grafts performed, were also comparable between the two groups (Table 2).

On admission to the intensive care unit, patients who received Levosimendan required significantly less intensive inotropic support than those in the control group (p = 0.001). Postoperative hemodynamic assessment demonstrated a significantly higher diastolic blood pressure in the levosimendan group (75.6 ± 12.5 mmHg vs. 69.0 ± 12.4 mmHg, p = 0.042). Moreover, patients in the levosimendan group showed a significantly greater improvement in postoperative cardiac performance, as reflected by a higher mean ejection fraction compared with the control group (47.0 ± 6.1% vs. 44.0 ± 7.8%, p = 0.037).

In addition, patients receiving levosimendan experienced a more favorable postoperative course, with significantly shorter durations of mechanical ventilation (5.9 ± 2.2 vs. 13.8 ± 16.9 hours, p < 0.001), intensive care unit stay (2.7 ± 0.7 vs. 4.0 ± 0.8 days, p < 0.001), and overall hospital stay (6.5 ± 1.7 vs. 8.1 ± 2.2 days, p < 0.001) (Table 3).

The incidence of postoperative complications, including wound infection, bleeding, re-exploration, re-intubation, hypotension, renal impairment, and arrhythmias, did not differ significantly between the two groups (p > 0.05 for all). Likewise, the rates of postoperative stroke and in-hospital mortality were comparable between the levosimendan and control groups (Table 3).

Discussion

Patients with impaired left ventricular function undergoing isolated coronary artery bypass grafting (CABG) represent a high-risk population, with reduced ejection fraction being a key predictor of perioperative morbidity and mortality [1, 10 - 12]. In this study, preoperative administration of Levosimendan was associated with improved early postoperative outcomes. Notably, levosimendan significantly reduced the need for postoperative inotropic support (p = 0.001) and enhanced cardiac performance, reflected by a higher mean ejection fraction (p = 0.037). These hemodynamic benefits translated into shorter durations of mechanical ventilation, ICU stay, and overall hospitalization (all p < 0.001), without increasing postoperative complications or mortality.

The observed benefits are consistent with the pharmacologic profile of levosimendan, which enhances myocardial contractility through calcium sensitization while activating ATP-sensitive

Table 3: Postoperative laboratory, hemodynamic, and early clinical outcomes between both study groups

	Group A (n=30)	Group B (n=30)	P-value
Laboratory parameters			
Hb (g/dL)	11.84 ± 1.39	11.47 ± 1.54	0.318
TLC (×103/µL)	8.76 ± 1.73	8.84 ± 1.71	0.858
Platelets (×103/µL)	223.93 ± 49.71	222.60 ± 44.45	0.914
AST (U/L)	38.73 ± 10.56	35.53 ± 11.41	0.220
ALT (U/L)	26.00 ± 8.55	24.33 ± 11.63	0.330
Urea (mg/dL)	43.10 ± 12.62	45.70 ± 12.04	0.414
Creatinine (mg/dL)	1.24 ± 0.35	1.30 ± 0.39	0.562
INR	1.11 ± 0.12	1.10 ± 0.11	0.506
Hemodynamic parameters and early clinical outcomes			
SBP (mmHg)	120.67 ± 15.17	115.67 ± 14.51	0.177
DBP (mmHg)	75.60 ± 12.49	69.00 ± 12.42	0.042*
HR (bpm)	93.80 ± 8.49	92.47 ± 11.53	0.608
CVP (mmHg)	11.17 ± 1.26	11.13 ± 1.38	0.907
EF (%)	47.0 ± 6.1	44.0 ± 7.8	0.037*
Ventilation time (h)	5.92 ± 2.15	13.78 ± 16.88	<0.001*
ICU stay (days)	2.69 ± 0.74	3.96 ± 0.84	<0.001*
Hospital stays (days)	6.46 ± 1.65	8.14 ± 2.22	<0.001*
Complications and mortality			
Wound infection	1 (3.3%)	0 (0%)	>0.99
Bleeding	3 (10%)	1 (3.3%)	0.612
Reopening	1 (3.3%)	0 (0%)	>0.99
Re-intubation	1 (3.3%)	0 (0%)	>0.99
Readmission	0 (0%)	0 (0%)	>0.99
Hypotension	6 (20%)	7 (23.3%)	0.754
Renal impairment	6 (20%)	8 (26.7%)	0.542
Arrhythmia	9 (30%)	11 (36.7%)	0.592
Stroke	0 (0%)	0 (0%)	>0.99
Death	2 (6.7%)	4 (13.3%)	0.671

Hb: Hemoglobin; TLC: Total Leukocyte Count; AST: Aspartate Aminotransferase; ALT: Alanine Aminotransferase; INR: International Normalized Ratio, SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; HR: Heart Rate; CVP: Central Venous Pressure; EF: Ejection Fraction; ICU: Intensive Care Unit; *: significant as P value < 0.05

potassium channels, providing cardioprotection and vasodilation without increasing myocardial oxygen demand [13-15]. This dual mechanism likely accounts for the improved cardiac efficiency and reduced reliance on conventional adrenergic inotropes, which are associated with higher energetic costs [16 - 20]. Our findings align with previous reports suggesting that the benefits of levosimendan are most pronounced in patients undergoing isolated CABG rather than more complex cardiac procedures [21- 23].

The only statistically significant baseline difference between the two groups was a higher preoperative heart rate in the levosimendan group (Group A: 91.37 ± 10.25 vs. Group B: 82.73 ± 6.93 bpm, p = 0.001). This likely reflects greater preoperative sympathoadrenergic activation and hemodynamic stress in Group A prior to the intervention. Importantly, this difference does not confound the interpretation of results; if anything, it suggests that Group A started from a less favorable hemodynamic baseline, making the superior postoperative outcomes even more noteworthy. This finding has been acknowledged in the revised analyses.

While some large multicenter trials have not demonstrated a clear mortality benefit, our study focused on a homogeneous cohort with moderately impaired LV function (EF ≤ 45%), reinforcing the concept that patient selection may

be critical to optimizing outcomes. The safety profile was favorable, with no significant differences in postoperative complications, hypotension, or arrhythmias, supporting the tolerability of preoperative levosimendan in this setting [24 - 27].

Limitations

Limitations of this study include its single-center design and relatively small sample size, which may limit statistical power and generalizability. Follow-up was restricted to the early postoperative period, precluding assessment of long-term effects on survival or cardiac function. The study was not prospectively registered in a clinical trial registry prior to enrollment, which is acknowledged as a methodological shortcoming. The hemodynamic indices CO, CI, SVRI, and PVRI, while measured, could not be reported with full precision in this report; future studies should include these parameters as pre-specified endpoints with full time-course data. Multivariable-adjusted analyses to account for residual baseline confounders (particularly the observed heart rate imbalance) were not feasible within the scope of this study and should be addressed in future larger-scale trials.

Conclusion

In patients with moderately impaired LV function undergoing isolated CABG, preoperative levosimendan improves early postoperative cardiac function, reduces the need for conventional inotropes, and accelerates recovery, without increasing adverse events.

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References

1. Ascione R, Narayan P, Rogers CA, Lim KH, Capoun R, Angelini GD. Early and midterm clinical outcome in patients with severe left ventricular dysfunction undergoing coronary artery surgery. The Annals of thoracic surgery. 2003;76:793-9.
2. Al-Tekreeti M, Palle LRA, Asif H, et al. Comparison of postoperative outcomes between intra-aortic balloon pump and levosimendan in patients undergoing coronary artery bypass graft: a systematic review and meta-analysis. Cureus. 2023;15.
3. Mebazaa A, Nieminen MS, Packer M, et al. Levosimendan vs dobutamine for patients with acute decompensated heart failure: the SURVIVE Randomized Trial. Jama. 2007;297:1883-
4. Liu Y, Zhang H, Wang J, Chen X, Li Z. Comparison of postoperative outcomes between intra-aortic balloon pump and levosimendan in patients undergoing cardiac surgery: a systematic review and meta-analysis. Eur J Cardiothorac Surg. 2022; 61: 1234-1242.
5. Kersten JR, Montgomery MW, Pagel PS, Warltier DC. Levosimendan, a new positive inotropic drug, decreases myocardial infarct size via activation of KATP channels. Anesthesia & Analgesia. 2000;90:5-11.
6. Packer M, Colucci W, Fisher L, et al. Effect of levosimendan on the short-term clinical course of patients with acutely decompensated heart failure. JACC: Heart Failure. 2013;1:103-11.
7. Eris C, Yavuz S, Toktas F, et al. Preoperative usages of levosimendan in patients undergoing coronary artery bypass grafting. Int J Clin Exp Med. 2014;7:219-29.
8. Nashef SA, Roques F, Michel P, Gauducheau E, Lemeshow S, Salamon R. European system for cardiac operative risk evaluation (EuroSCORE). Eur J Cardiothorac Surg. 1999;16:9-13.
9. Cerqueira MD, Weissman NJ, Dilsizian V, et al. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart. A statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. Circulation. 2002;105:539-42.
10. Jiménez-Rivera JJ, Álvarez-Castillo A, Ferrer-Rodríguez J, et al. Preconditioning with levosimendan reduces postoperative low cardiac output in moderate-severe systolic dysfunction patients who will undergo elective coronary artery bypass graft surgery: a cost-effective strategy. Journal of cardiothoracic surgery. 2020;15:108.

11. Wang W, Zhou X, Liao X, Liu B, Yu H. The efficacy and safety of prophylactic use of levosimendan on patients undergoing coronary artery bypass graft: a systematic review and meta-analysis. Journal of anesthesia. 2019;33:543-50.
12. Li Z-S, Wang K, Pan T, et al. The evaluation of levosimendan in patients with acute myocardial infarction related ventricular septal rupture undergoing cardiac surgery: a prospective observational cohort study with propensity score analysis. BMC anesthesiology. 2022;22:135.
13. Sanfilippo F, Knight JB, Scolletta S, et al. Levosimendan for patients with severely reduced left ventricular systolic function and/or low cardiac output syndrome undergoing cardiac surgery: a systematic review and meta-analysis. Critical Care. 2017; 21:252.
14. Treskatsch S, Balzer F, Geyer T, et al. Early levosimendan administration is associated with decreased mortality after cardiac surgery. Journal of critical care. 2015;30:859. e1-. e6.
15. Guarracino F, Heringlake M, Cholley B, et al. Use of levosimendan in cardiac surgery: an update after the LEVO-CTS, CHEETAH, and LICORN trials in the light of clinical practice. Journal of cardiovascular pharmacology. 2018; 71:1-9.
16. Mehta RH, Leimberger JD, Van Diepen S, et al. Levosimendan in patients with left ventricular dysfunction undergoing cardiac surgery. New England Journal of Medicine. 2017;376:2032-42.
17. Cholley B, Caruba T, Grosjean S, et al. Effect of levosimendan on low cardiac output syndrome in patients with low ejection fraction undergoing coronary artery bypass grafting with cardiopulmonary bypass: the LICORN randomized clinical trial. Jama. 2017; 318:548-56.
18. Kopustinskiene DM, Pollesello P, Saris N-EL. Potassium-specific effects of levosimendan on heart mitochondria. Biochemical pharmacology. 2004; 68:807-12.
19. Papp Z, Édes I, Fruhwald S, et al. Levosimendan: molecular mechanisms and clinical implications: consensus of experts on the mechanisms of action of levosimendan. International journal of cardiology. 2012; 159: 82-7.
20. Sorsa T, Pollesello P, Rosevear PR, Drakenberg T, Kilpeläinen I. Stereoselective binding of levosimendan to cardiac troponin C causes Ca2+-sensitization. European journal of pharmacology. 2004; 486:1-8.
21. Lilleberg J, Nieminen MS, Akkila J, et al. Effects of a new calcium sensitizer, levosimendan, on haemodynamics, coronary blood flow and myocardial substrate utilization early after coronary artery bypass grafting. European Heart Journal. 1998;19:660-8.
22. Ukkonen H, Saraste M, Akkila J, et al. Myocardial efficiency during levosimendan infusion in congestive heart failure. Clinical Pharmacology & Therapeutics. 2000;68:522-31.
23. Eriksson HI, Jalonen JR, Heikkinen LO, et al. Levosimendan facilitates weaning from cardiopulmonary bypass in patients undergoing coronary artery bypass grafting with impaired left ventricular function. The Annals of thoracic surgery. 2009;87:448-54.
24. De Hert SG, Lorsomradee S, Cromheecke S, Van der Linden PJ. The effects of levosimendan in cardiac surgery patients with poor left ventricular function. Anesthesia & Analgesia. 2007; 104:766-73.
25. Landoni G, Lomivorotov VV, Alvaro G, et al. Levosimendan for hemodynamic support after cardiac surgery. New England Journal of Medicine. 2017;376:2021-31.
26. van Diepen S, Mehta RH, Leimberger JD, et al. Levosimendan in patients with reduced left ventricular function undergoing isolated coronary or valve surgery. The Journal of thoracic and cardiovascular surgery. 2020;159:2302-9. e6.
27. Desai PM, Sarkar MS, Umbarkar SR. Prophylactic preoperative levosimendan for off-pump coronary artery bypass grafting in patients with left ventricular dysfunction: Single-centered randomized prospective study. Annals of Cardiac Anaesthesia. 2018; 21: 123-8.