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Levosimendan Use Increases Cardiac Performance after Coronary Artery Bypass Grafting in End-Stage Renal Disease Patients

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ABSTRACT

Background: The effect of levosimendan on myocardial performance has not been studied in dialysis-dependent end-stage renal disease patients who have undergone coronary artery bypass grafting (CABG) surgery. Our aim was to investigate the effect of levosimendan on postoperative hemodynamic effects in end-stage renal disease patients undergoing CABG operation.

Methods: We performed 58 elective isolated CABG operations in end-stage renal disease patients. The study group received levosimendan at a slow bolus dose of 3 µg/kg, followed by a 24-hour infusion of 0.03-0.05 µg/kg/kg/min. (study group [SG]: n = 25). The remaining patients received a placebo (control group [CG]: n = 33). The mean left ventricular ejection fraction of both groups was similar (44.6 ± 55.4% versus 42.8 ± 53.9%). Hemodynamic data were collected at the end, at 1 hour after CPB, and thereafter at 6, 12, and 24 hours in the ICU. Preoperatively, at the end of the operation, at 1 hour after CPB, and thereafter at 6, 12, and 24 hours in the ICU, blood samples from the peripheral vein were collected for cardiac troponin-I (c-TnI) and lactate levels. Norepinephrine if needed started during the rewarming period in both groups.

Results: One patient in SG (4%) and 4 patients (12.1%) in CG died postoperatively ($P < .01$). Cardiac output and cardiac index values did not change early after weaning from extracorporeal circulation, and they were nearly similar during the next 6 hours in both groups. In SG, cardiac output and cardiac index significantly improved at 6 hours, and were stable at the end of 24 hours ($P < .001$). Hemodynamic parameters were nearly similar after the operation, and did not change significantly at the end of 24 hours in CG. Hemodynamic improvement caused a significant reduction in systemic and pulmonary artery vascular resistance index in SG ($P < .002$). Pulmonary capillary wedge pressure decreased significantly in SG ($P < .034$). Cumulative inotrope dose requirement and intraaortic balloon pump use were significantly lower in SG. In addition, blood lactate and cTnI levels were significanly lower in SG ($P < .044$).

Conclusion: No important adverse effect was detected during levosimendan infusion. Because levosimendan at a dose of 0.03-0.05 µg/kg/min increased myocardial performance significantly in the postoperative period, it can be used safely in end-stage renal disease patients undergoing isolated CABG. The requirement of vasopressors were lower in SG.

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INTRODUCTION

Levosimendan, as a calcium sensitizer, exerts positive inotropic effect without increasing intracellular cAMP. Levosimendan causes venous, arterial, and coronary vasodilation, probably by opening ATP-sensitive potassium channels in smooth muscle by opening K+ channels on vascular smooth muscles [Follat 2002; Lehtonen 2004]. Levosimendan is also beneficial in the setting of pulmonary vasoconstriction, right ventricular dysfunction, and reduces pulmonary vascular resistance. Because levosimendan does not increase myocardial oxygen demand it is provided myocardial anti-stunning effect [Kivikko 2005]. Some previous reports including the LIDO trial [Follat 2002] demonstrated that levosimendan stabilized the troponin molecule in the cardiac muscle. Prolonging its effect on contractile proteins with concomitant vasodilating properties showed that levosimendan increases cardiac output (CO) and reduced pulmonary vascular resistance index (PVRI) in heart failure patients who have normal renal function [Kivikko 2005; Ahmed 2009]. Levosimendan also enhanced functional myocardial tissue mass and ensured positive hemodynamic effect in the early postoperative period in patients with low ejection fraction undergoing CABG [Sahin 2014]. According to previous publications, 30-75% of end-stage renal disease patients (ESRDPs) required inotropic(s). Mortality rate was 8.4-13.2% due to low output syndrome (LOS) after elective CABG in end-stage renal disease patients (ESRDPs) [Lim 2015; Deutsch 2013; Vohra 2014; Papadopoulos 2010].

As we know, levosimendan infusion is contraindicated in patients with severe renal impairement. There is a limited number of reports about the use of levosimendan in dialysis-dependent ESRDPs who undergo elective CABG [Papadopoulos 2010; Lobo Martínez 2011]. Lobo et al

reported a succesful myocardial effect with the use of levosimedan in ESDRPs with severe myocardial dysfunction resistant to inotropic support [Lobo Martínez 2011]. Marked clinical and echocardiographic improvement without any side effect has been reported previously. Papadopoulos et al showed perioperative levosimendan and norepinephrine use in 25 chronic kidney disease patients with impaired myocardial contractility [Lobo Martínez 2011]. Papadopoulos et al showed successful use of levosimendan-norepinephrine combination in 13 chronic kidney disease patients with impaired myocardial contractility [Papadopoulos 2010; Lobo Martínez 2011].

According to a limited number of previous publications, we hypothesized that low-dose levosimendan administration preoperatively (during 24 hours) may inhibit postoperative LOS and mortality in ESRDPs undergoing elective CABG using extracorporeal circulation.

PATIENTS AND METHODS

This study was performed between January 2006 and July 2013 in two centers. Fifty-eight consecutive ESRDPs were included in this study. Twenty-five patients were enrolled as a study group. Demographic data of both groups, for age, sex, left ventricular ejection fraction (LVEF), creatinine level, medication, and the number of bypassed coronary arteries were similar. Intraoperative properties such as duration of extracorporeal circulation (ECC) and aortic cross-clamp time were similar. Preoperative and perioperative patient data have been summarized in Tables 1 and 2, respectively.

The mean LVEF was 44.6 ± 55.4, and 42.8 ± 53.9 % in SG and CG, respectively (P = .89). Left ventricular hypertrophy was indicated by a wall thickness of 12 mm by the use transthoracic echocardiography. The exclusion criteria was a known allergy to levosimendan; previous cardiovascular operation; severe chronic obstructive lung disease; liver disease; and cardiac valve disaease requiring replacement or repair.

The ethics committee of the hospital approved the study protocol. Written informed consent was obtained from all patients before enrolling. Experienced nurses prepared and diluted the study drugs (levosimendan and 5% of dextrose solution), thereby ensuring that the operation and ICU teams were blinded to the group assignment. Preoperative lactate, creatine kinase-myocardial band (CK-MB), and cardiac troponine-I (cTnI) levels were measured. Because levosimendan elimination half-life time was reported longer in ESRDPs who underwent hemodialysis (1.5 ± 0.09 h), we administered levosimendan at a slow bolus dose of 3µg/kg/min 6 hours prior to surgery. 0.03-0.05 µg/kg/min dose of levosimendan started after the release of aortic cross-clamp and it continued during 24 hours in SG. CG received a placebo that was made to look identical to levosimendan with water-soluble vitamin concentrate (10 mL diluted in 500 mL of glucose 5%).

Prior to anesthesic management, the blood samples were taken from the peripheral vein for measurements of cardiac enzymes and lactate level (T0). Enzyme analyses were collected at the end (T1), at 1 hour after CPB (T2), and thereafter at 6 (T3), 12 (T4), and 24 hours (T5) in the ICU.

A pulmonary artery catheter (Criticath; Becton-Dickinson) was inserted for monitoring in the operating room. At admission to the operating theater and thereafter, the goals and means of hemodynamic support were to keep the pulmonary capillary wedge pressure (PCWP) at the level of 12-18 mmHg with fluid administration, and the mean arterial pressure between 60 and 90 mmHg. We paid careful attention to ensure the cardiac index (CI) above 1.8 L/min/m² in both groups. Epinephrine (0.10-0.15 µg/kg/min) was administered to patients if CI was lower than 1.8L/min/m².

Surgery

After midline sternotomy, an aortic and single venous cannulation was performed. Patients were heparinized with 1 mg/kg intravenously to achieve activated clotting time > 450 seconds. The central temperature, which was measured by a pulmonary artery catheter, was maintained above 32°C. Extracorporeal circulation was instituted according to clinical practice. The saphenous vein and right internal thoracic or left internal thoracic artery were harvested for bypass conduits. All operations were completed using aortic cross clamp. Cardiac arrest was provided by the use of antegrade cold blood cardioplegia. Retrograde cardioplegia was given every 15-20 minutes. After the completion of distal coronary artery anastomosis, the cross-clamp was released. Proxymal anastomosis was performed using an aortic side clamp.

Hemodynamic measurements including the mean arterial pressure (MAP), central venous pressure (CVP), CO, CI, PVRI, and systemic vascular resistance index (SVRI) were recorded after induction of anesthesia (T0), at the end (T1), at 1 hour after ECC (T2), and thereafter at 6 (T3), 12 (T4), and 24 hours (T5) in the ICU. Cardiac enzymes and lactate levels were calculated at the same time. Levosimendan administration started again during the rewarming period, and continued until the end of first day in the ICU. Transthoracic echocardiography was performed at baseline and prior to discharge from the hospital.

Statistical Analysis

All statistical analyses were performed using the SPSS statistical software (SPSS for Windows 17.0, Chicago, IL, USA). Normally distributed continuous variables were expressed as mean values ± standard deviation (SD). Categorical variables were expressed as numbers and percentages. Demographic characteristics, perioperative variables, and calculated values were compared using independent-sample t test for continuous variables and the Pearson chi-square test or Fisher exact test for categorical variables. Within-group differences were evaluated with the paired-samples t test. A P value < .05 was considered statistically significant. Time point comparisons were done with the t-test. Cumulative doses of steradine and additional vasopessor use were compared between groups using the Mann-Whitney U test.

RESULTS

Demographic data of patients in the study and control group are shown in Table 1. There was no difference between

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Table 1. Preoperative Patient Characteristics*

	SG (n = 25)	CG (n = 33)	*P*
Sex, M/F	15/10	19/14	NS
Age, y (median)	66.5 (61.8-69.8)	69.5 (64-71.5)	NS
Previous myocardial infarction, n	9	6	NS
Diabetes, n	13	18	NS
EF (mean, %)	44.6 ± 15.4	42.8±13.9	NS
Medication			
ACE inhibitors, n	23	26	NS
ß-blockers, n	13	19	NS
Calcium channel inhibitors, n	15	19	NS
Platelet aggregation inhibitors, n	17	23	NS
Nitrates, n	13	18	NS

*Data are presented as the mean ± SD where indicated.

Table 2. Intraoperative and Postoperative Data

	SG	CG	*P*
Cardiopulmonary bypass time, min	88 ± 12.9	78 ± 14.4	NS
Cross-clamp time, min	43 ± 17.9	44 ± 11	NS
Operation time, min	119.5 ± 83.2	134.0 ± 49.4	NS
No. of bypasses, mean	2.90 (1-4)	3.1 (1-5)	NS
Need for inotropic drug	12	20	.012
Need for IABP	2	6	.021
Mortality, n (%)	1 (2.1)	4 (12.1)	.01
Low cardiac output, n (%)	6 (12.5)	5 (37.5)	.001
Length of stay in ICU, d	8.3 ± 3.6	4.1 ± 0.9	.14
Length of stay at hospital, d	26.3 ± 7.2	4.1 ± 5.0	.12
Atrial or ventricular arrhythmia, n (%)	11 (22.9)	8 (45)	.010

IABP indicates intraaortic balloon pump.

Table 3. Cumulative Doses of Propofol, Sufentanil, and Norepinephrine*

	Cumulative doses	*P*
Propofol, mg		
Control	1799 (132)	.89
Levosimendan	1818 (126)	
Sufentanil, mg		
Control	237 (29)	.91
Levosimendan	240 (26)	
Epinephrine, mg		
Control	38 ± 10.7	.01
Levosimendan	23 ± 8.5	
Dobutamine, mg		
Control	3486 ± 245	.001
Levosimendan	2170 ± 309	

*Data are presented as the mean ± SD where indicated.

the two groups in regard to patients' age, female-male ratio, LVEF, preoperative cardiac enzyme levels, EuroSCORE, intraoperative and postoperative data including aortic cross clamp, and ECC, and operation times were similar in both groups (Table 2). No significant difference was found when comparing intraoperative properties of the groups (Table 2). Cumulative dose of inotropic drugs, IABP use, mortality rate, postoperative LOS, length of stay in ICU and at hospital were statistically significant (Table 2). Cumulative doses of propofol and sufentanil were similar when comparing the groups. 12 patients in SG and 20 patients in CG required dobutamine as an additional inotropic drug (*P* = .012). Cumulative doses of epinephrine and dobutamine was higher in CG (*P* = .001). Data are presented as mean (SD) (Table 3).

Patients who developed LOS following surgery demonstrated higher rates of respiratory failure (12% [2 patients in SG]; 30.3% [10 patients in CG]). New onset of atrial fibrillation was detected in 4% in SG, and 18.1% in CG (*P* = .001). In addition, patients who developed LOS following CABG surgery had longer duration of ICU and postoperative hospital stays (8.3 ± 3.6 versus 4.1 ± 0.9 days; 26.3 ± 7.2 days versus 14.1 ± 5.0 days, respectively) compared with those without this complication.

A statistically significant difference in favor of the SG was recorded regarding the statistical values of CO and CI between the two groups. Pre- and postoperative hemodynamic data are summarized in Table 4. There were no significant differences when compared to preoperative mean arterial pressure (MAP), CI, CO, and heart rate (HR).

The LVEFs of the two groups were not statistically significant at baseline. At discharge period, the LVEF decreased minimally in CG, and increased significantly in SG. The mean LFEV was 52.3 ± 14.4%, and 44.2 ± 11.4% in SG and CG, respectively (*P* = .030). Fluid input was greater in CG compared with SG during drug infusion from baseline to the morning of surgery. From the morning of surgery to the first postoperative morning, there was no difference in total fluid balance in the SG versus CG. A statistical difference was found when compared to the requirement of inotropic drugs, and the need of intraaortic balloon pump (IABP) insertion. The length of ICU stay and entubation time was longer in CG (*P* = .01; *P* = .026).

A statistically significant difference in favor of the SG plus CG was recorded regarding the statistical values of CO and CI between the two groups. Considering all measurements, 6 hours after surgery, CO(2) and CI(2) values in SG were higher than those of the CG (*P* = .001). The mean value of

CO(2) was 5.3 ± 0.4 L/min/m² and 4.1 ± 0.9 L/min/m² in SG and CG, respectively. The second CI value was 3.1 ± 0.7 L/min and 2.3 ± 0.6 L/min in SG and CG, respectively (P = .001). CO showed a significant increase with time compared to baseline values (CO(3): 5.3 ± 0.90 L/min; CO(4): 5.6 ± 0.75 L/min) (P = .018) (Figure 1).

SVRI significantly decreased immediately after surgery in SG and was stable postoperatively (P = .024). Increases in CI were about 22-25% with levosimendan over placebo, and decreases of SVRI were about 23-30%. PCWP decreased significantly after surgery in SG (from 14.0 to 9.20) (P = .004) at the end of 24 hours. PCWP increased after surgery and decrased to preoprative levels in CG within 24 h. Decrease in SVRI with time was significant in SG [SVRI(1): 2016 (1803-2096) dyne/s/cm^5 versus SVRI(5): 1710 (1482-1990) dyne/s/cm^5] (P = .014). No significant difference was found when compared to SVRI(1) and SVRI(5) in CG (P > .05) (Figure 2).

At the end of 24 hours, PCWP was 13.0 (11.0-14.0) in CG, and 9.20 (8.6-13.7) in CG (P < .001). The decrease in PVR over time was marked in SG [(PVR(1): 332.4 ± 163.4 dyne/s/cm^5 versus PVR(5): 218.7 ± 178.2 dyne/s/cm^5] (P = .001). This decrease was not significantly different with time in the CG group [(PVR(1): 411.2 ± 255 dyne/s/cm^5 versus PVR(5): 346.1 ± 149.6 dyne/s/cm^5].

The specificity of cTnI has been confirmed in various situations, myocardial infarction and myocarditis. Blood lactate and cardiac enzymes were measured in different times. In SG and CG, basal levels of cardiac enzymes were similar [respectively for SG and CG; cTnI(0): 0.033 ng/mL (0.01-0.11) versus 0.035 ng/mL (0.01-0.14)] (P = .84). At 6 hours after surgery, cTnI levels were significantly higher in CG than in SG [3.15 (2.10-3.50) versus 4.90 (3.50-6.00)] (P = .001). At the end of 24 hours, cTnI levels of SG and CG were measured as 2.20 (2.0-3.75) and 3.90 (3.50-6.00), respectively (P = .004). At T(3) and T(4), the same difference was noted between the groups (P = .001) (P = .003). cTnI values in all patients with a Q-wave infarction were ≥0.04 ng/mL (Table 5).

DISCUSSION

Our study demonstrated that levosimendan improved cardiac hemodynamics significantly and provided a significant reduction in systemic and pulmonary artery vascular resistance index in hemodialysis-dependent ESRDPs. Pulmonary capillary wedge pressure decreased significantly with the use of low-dose levosimendan infusion. Postoperative inotrope use and intraaortic balloon pump requirement were significantly lower after levosimendan use. Therefore, according to our study results, a half dose of levosimendan administration significantly increased myocardial performance after CABG in ESRDPs.

Previous publications including the LIDO trial [Follath 2002] showed that levosimendan increased cardiac output and reduced systemic and PWRI in heart failure patients with normal renal function [Lehtonen 2004; Kivikko 2005]. In patients with normal creatinine clearance, levosimendan itself has a short elimination half life but has been shown to have active metabolites with elimination half lives up to 80 hours [Puttonen 2007].

As we know, mortality and morbidity is high in ESRDPs after elective CABG. Poor clinical results depend on some risk factors such as patients' age, ischemic or hypertrophic

Table 4. Perioperative and Postoperative Hemodynamic Data in Both Groups

	Baseline	End of surgery	Postop 1	Postop 6	Postop 24
Mean arterial pressure, mmHg					
Control	70.0 (65.8-76.5)	68.0 (65.0-71.5)	69.0 (65.0-75.0)	70.0 (68.0-77.0)	74.5 (70.0-80.0)
Levo.	72.5 (65.2-77.7)	69.0 (65.0-76.7)	77.0* (70.7-79.5)	77.5 (72.2-79.7)	78.5 (73.2-84.5)
Pulmonary capillary wedge pressure, mmHg					
Control	12.5 (11.2-15.7)	16.1† (12.2-18.0)	14.0 (13.0-16.0)	14.0 (11.2-15.0)	13.0 (11.0-14.0)
Levo.	14.0 (12.0-15.7)	10.5* (8.2-15.5)	9.4* (11.0-14.0)	9.8* (10.5-15.0)	9.20† (8.6-13.7)
Central venous pressure, mmHg					
Control	10.5 (9.2-12.0)	12.0† (11.0-13.7)	12.0† (11.5-14.5)	12.5 (9.5-12.0)	11.5 (9.0-12.0)
Levo.	11.5 (9.0-12.5)	10.5† (8.2-13.0)	9.0 (8.5-11.7)	8.5 (8.0-11.7)	8.5 (8.2-11.0)
Cardiac index, L/min/m²					
Control	2.4 (2.1-2.7)	2.1 (1.9-2.3)	2.29 ± 0.63	2.40 ± 0.30	2.5 (2.1-2.9)
Levo.	2.3 (2.0-2.6)	2.2 (2.2-2.5)	3.14 ± 0.57	3.10 ± 0.7	3.20*,† (2.7-3.4)
Systemic vascular resistance index, dynes/cm^5/m²					
Control 2126 (1824-2285)	2127 (1834-2315)	2016 (1789-2190)	2007 (1785-2223)	2008 (1724-2285)	
Levo.	2137 (1922-2270)	2016†(1803-2096)	1931† (1730-2138)	1754† (1561-2081)	1710† (1482-1990)

Data are presented as median (IQR). Levo indicates levosimendan. *Different from the control group. †Different compared with baseline (P < .05).

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cardiomyopathy, electrolite disturbances peroperatively, and myocardial resistance to inotropic agents. Therefore, in this research, we hypothesised that inodilator and anti-stunning properties of levosimendan can be effective on ventricular performance after CABG in ESRDPs who are resistant to inotropic agents or have myocardial impairement postoperatively.

There are case reports [Papadopoulos 2010; Lobo Martínez 2011] and one clinical article about the effects of levosimendan in hemodialysis patients in the English literature [Puttonen 2007]. However, the hemodynamic effects of levosimendan after CABG operation in ESRDPs have not been studied to date. The results of our study showed that preoperative levosimendan administration in ESRDPs could decrease postoperative hemodynamic impairement, low output, and mortality. Cardiac intropic agents and IABP use decreased significantly. Levosimendan significantly increased cardiac output by 20-40% and reduced SVRI and PVRI by 20-35% in ESRDPs.

Because one of the contraindications of levosimendan is described in patients with renal impairement, a number of surgeons have not studied it in dialysis-dependent patients who underwent CABG. Previously published reports show that perioperative levosimendan/norepinephrine combination could be used in select ESRDPs with impaired myocardial contractility [Papadopoulos 2010; Lobo Martínez 2011]. Lobo et al reported a successful myocardial effect with the use of levosimendan in ESRDPs with severe myocardial dysfunction resistant to inotropic support [Lobo Martínez 2011]. Marked clinical and echocardiographic improvement without any side effects has been detected by the authors. Papadopoulos et al showed that perioperative levosimendan and norepinephrine use in 25 patients with chronic kidney disease improved impaired myocardial contractility due to myocardial failure [Papadopoulos 2010].

Pharmacodynamic study showed that levosimendan was eliminated rapidly from the plasma after discontinuation of its infusion, with an elimination half-life of 1.5 ± 0.09 hours in ESRDPs undergoing hemodialysis, 1.0 ± 0.2 hours in patients with severe chronic renal failure, and 0.91 ± 0.03 hours in healthy subjects [Puttonen 2007]. According to this research, elemination time of levosimendan was longer in ESRDPs than in healthy subjects. Therefore, the dose of levosimendan should be set carefully for the treatment of congestive heart failure in patients with severe renal insufficiency. Thus, we used a half dose of levosimendan including bolus and infusion rate in our patient population preoperatively and during 24 hours.

Pharmacokinetics and pharmacodynamics of levosimendan are very important for managing patients with renal impairement. Renal failure affects glomerular blood flow and filtration rates, and tubular secretion and reabsorption of drugs may also be altered. Therefore, dosing regimens must be adjusted accordingly [Lam 1997]. The most common reason for dose reduction in patients with renal impairment is decreased excretion of the drug, which can lead to increased plasma concentrations and toxicity [Lam 1997; Dimmitt 1998; Johnson 1998; Martin 1998; Karara 1996]. The clearance rate for eliminated drugs is proportional to creatinine clearance, a commonly used clinical measure of renal function and an estimate of the glomerular filtration rate [Puttonen 2007; Dimmitt 1998]. Changes in drug distribution are usually caused by alterations in the binding of acidic drugs to plasma proteins [Martin 1998; Karara 1996]. In ESRDPs, the concentration of total plasma proteins can be reduced, resulting in reduced protein binding. Thus, the pharmacodynamics of levosimendan may be altered due to severe renal diseases.

Because perioperative myocardial infarctus is a main reason of LOS and mortality, we measured myocardial enzymes and lactate levels in both groups. According to our research, the rate of perioperative myocardial ischemia was significantly lower in SG. These results in SG may be related to arteriolar and venous dilation by opening K+ channels on vascular smooth muscles, and anti-stunning effect of levosimendan. Our results supported that levosimendan stabilized the cardiac troponin molecule perioperatively [Smith 1997; Cummins 1987; Etienvent 1995; Pagel 1994; Abacilar 2013].

Rajek et al demonstrated a dramatic increase in CO after 1 hour of levosimendan administration and it stayed higher during the first postoperative day in patients who underwent cardiac surgery [Rajek 2003]. Rajek's study exhibited that the heart rate, MAP, and pulmonary arterial pressure did not change during levosimendan infusion [Rajek 2003]. Sahin et al showed significantly better hemodynamic and

Table 5. Preoperative and Postoperative Blood c-TnI (ng/mL) and Lactate Levels

	Baseline (T0)	T(1)	T(2)	T(2).	T(4)
c-TnI (ng/mL)					
SG	0.033 (0.01-0.11)	2.0 (1.60-2.90)*	3.15 (2.10-3.50)*	3.15 (2.20-4.05)*	2.20 (2.0-3.75)*
CG	0.035 (0.01-0.14)	3.15 (2.10-4.10)*	4.86 (3.50-6.00)*	4.20 (3.50-6.00)*	3.90 (3.50-6.00)*
Lactate (mmol/L)					
SG	1.10 (1.1-2.1)	2.0 (1.2-3.6)**	1.25 (0.9-2.1)§	1.0 (0.8-2.0)¥	1.15(0.9-2.1) €
CG	1.15 (1.0-1.9)	2.80 (1.8-4.2)**	2.85 (1.0-2.0) §	2.65 (1.0-2.7)¥	1.90(1.70-3.6) €

*Statistically significant. P values between groups: T(1): $P = .001$; T(2): $P = .003$; T(3): $P = .004$; T(4): $P = .004$.

**, §, €, ¥ Statistically significant. P values between groups: **$P = .002$; ¥$P = .005$; §$P < .05$; €$P = .004$.

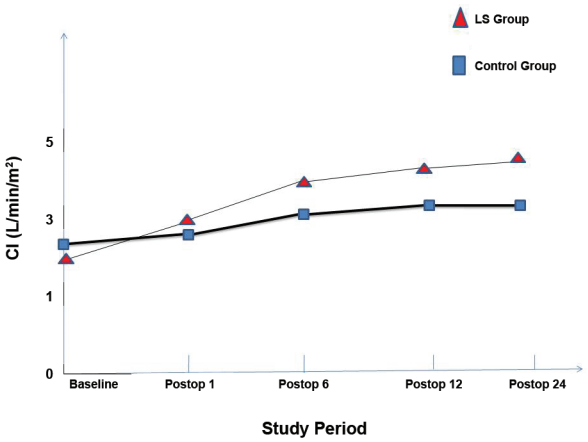

Figure 1. The change of cardiac index in the levosimendan and control group.

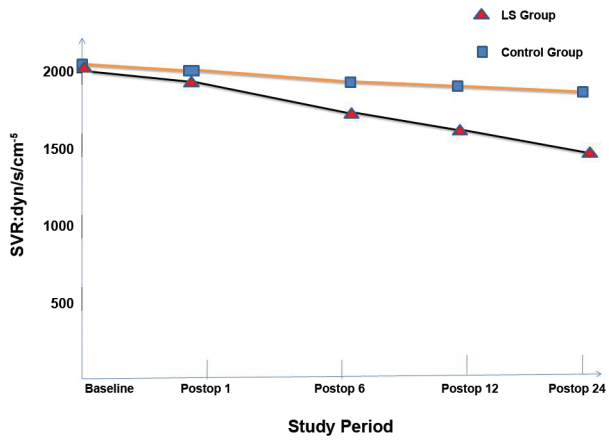

Figure 2. Changes in systemic vascular resistance in both groups pre- and postoperatively.

echocardiographic parameters after CABG in patients who received levosimendan [Eris 2014]. We determined that a low dose of levosimendan is more effective 6 hours after the operation. Shortening of the duration of ICU and hospital stay provides better evidence for early administration of levosimendan.

Conclusion

A half dose of levosimendan may be used pre- and perioperatively in hemodialysis-dependent ESRDPs undergoing elective coronary artery bypass graft operation. Perioperative low output and mortality can be decreased with levosimendan administration. A half dose of levosimendan also decreases blood cTnI, CK-MB, and lactate levels, as a marker of perioperative myocardial infarction. Additional inotropic and intraaortic balloon pump use may be decreased using levosimendan. Because our patient group included a small number of ESRDPs, additional research on the myocardial protective effect of levosimendan in ESRDPs is needed in the future.

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