Levosimendan Improves Renal Outcome in Cardiac Surgery: A Randomized Trial

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Objective: The effect of levosimendan on renal function in patients with low ejection fraction undergoing mitral valve surgery was investigated.

Design: A prospective, double-blinded, randomized clinical trial.

Setting: Tertiary teaching and research hospital.

Participants: Of a total of 147 patients, 128 patients completed the study. In the levosimendan group (n = 64), levosimendan was administered in addition to standard inotropic support; whereas, in the control group (n = 64), only standard inotropic support was given.

Interventions: In the levosimendan group, a loading dose of levosimendan (6 μg/kg) was administered after removal of the aortic cross-clamp, followed by an infusion of 0.1 μg/kg/min in addition to standard inotropic therapy for 24 hours. In the control group, only standard inotropic therapy was administered. Preoperative characteristics, serum creatinine (sCr) levels, and estimated glomerular filtration rate (eGFR) were determined preoperatively, on postoperative days 1, 3, and 10. Independent risk factors for renal replacement therapy (RRT) requirement were investigated with stepwise multivariate logistic regression analysis.

Measurements and Main Results: The primary endpoint was the effect of levosimendan on postoperative renal clearance (sCr and eGFR). The secondary endpoint was the effect of levosimendan on clinical outcomes (length of intensive care unit and hospital stays, need for RRT). Preoperative characteristics and eGFR were similar between the groups (p > 0.05). On postoperative days 1 and 3, sCr values were lower and eGFR values were higher in the levosimendan group in comparison with the control group (p = 0.0001, p = 0.009, respectively). Six patients (9.4%) in the levosimendan group and 10 patients (15.6%) in the control group required RRT therapy (p = 0.284). Independent risk factors for need of RRT include preoperative sCr value between 1.2 to 2.09 mg/dL and ≥2.1 mg/dL (p < 0.05).

Conclusions: Perioperative treatment with levosimendan in addition to standard inotropic therapy in patients with a low ejection fraction undergoing mitral valve surgery improved immediate postoperative renal function and reduced need for RRT.

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Key Words: levosimendan, mitral valve surgery, cardiopulmonary bypass, serum creatinine, estimated glomerular filtration rate, ejection fraction

Material and Methods

Between the time period of July 1, 2009 and January 30, 2013, a prospective, randomized study was conducted on 140 patients undergoing mitral valve surgery (age range 31-79) with an ejection fraction ≤45% in a tertiary research and training hospital. Of 147 patients, 19 were excluded because 13 did not meet the inclusion criteria and 6 declined to participate. A total of 128 patients were randomized into two groups. The CONSORT 2010 Flow Diagram and CONSORT 2010 Checklist are presented in Figs 1 and 2. Ethical committee approval was obtained, and registration at ClinicalTrials.gov was completed and approved (No. NCT01969071). An informed consent was signed by the patient or first-degree relatives. Randomization into 2 groups was performed using sealed envelopes and the sequentially numbered assignments of the participant, which was concealed in an envelope and opened after anesthesia induction by health care personnel. The observers were blinded to the inotropic protocol. Caregivers were not

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blinded, but they did not participate in data collection or data interpretation.

Patients included in the study had a diagnosis of mitral valve insufficiency with or without coronary artery disease and an LVEF of ≤45%. Low LVEF and pulmonary hypertension (PH) are important risk factors for higher EuroSCORE and increased adverse outcomes.5,10 Exclusion criteria were unstable angina, diabetes mellitus treated with insulin, clinical findings of acute or chronic renal failure (sCr > 1.5 mg/dL), severe hepatic disease (alanine aminotransferase or aspartate aminotransferase > 100 U/L), severe chronic obstructive pulmonary disease (forced expired volume in 1 s < 50% of predicted or < 2.0 liter), a history of prior CABG surgery or myocardial infarction (MI) within the previous month, emergent operations, patients on inotropic support before surgery, aortic valvular disease, and infective endocarditis.

Patients in the levosimendan group (n = 64) received levosimendan in addition to standard inotropic support therapy. The control group (n = 64) was treated solely by standard inotropic agents (1 or more agent including; dobutamine, noradrenaline, adrenaline).

In the levosimendan group, all patients received a loading dose of levosimendan (Simdax, Orion Pharma, Espoo, Finland) at a dose of 6 μg/kg intravenously within 10 minutes after removal of the cross-clamp, followed by an infusion of 0.1 μg/kg/min, for a total of 24 hours.

The collected demographic data included age, weight, height, body mass index, and sex. The cardiovascular risk factors included diabetes mellitus, hypertension, hypercholesterolemia, obesity, history of smoking, and history of chronic obstructive pulmonary disease and peripheral vascular disease. Echocardiographic data were collected to evaluate the ejection fraction and valvular functions by the same cardiologist using a Vivid 3 echocardiography device (General Electric, Hamburg, Germany) preoperatively and on day 1 postoperatively. During surgery transesophageal echocardiography (TEE) was performed in selected cases. During this measurement, hemodynamic data, including heart rate (HR), mean arterial pressure (MAP), central venous pressure (CVP), mean pulmonary arterial pressure (MPAP), and cardiac index (CI), were collected. PH is defined by a mean pulmonary artery pressure (MPAP) > 25 mmHg at rest. The diagnosis of PH depends on direct measurement of the MPAP by right-heart catheterization. However, the authors used Doppler echocardiographic study to provide an estimate of the pulmonary artery systolic pressure (PASP), and MPAP was calculated with the formula: MPAP = 0.65 PASP + 0.55 mmHg.5 The risk of surgery was evaluated using the European System for the Cardiac Operation Risk Evaluation scale (EuroSCORE).18 AKI is defined as either an increase in serum creatinine by 0.3 mg/dL or an increase by 50% from baseline within 48 hours postoperatively.19

The need for early renal replacement therapy (RRT) was provided to all patients under the following criteria: (1) when urine output was less than 100 mL within the last 6 hours, (2) with no response to 50 mg intravenous dose of furosemide, (3) urine sodium concentration...
should be >40 mEq/L before administration of furosemide, (4) blood urea nitrogen level >50 mg/dL, (5) additional presence of 1 or more of the following factors: increase in serum creatinine level >0.3 mg/dL, from preoperative value, presence of metabolic acidosis, presence of hypervolemia, presence of hyperkalemia (potassium ion level >5 mEq/L).10,19,20 RRT included 1 form of hemodialysis: Venovenous hemofiltration, venovenous hemodialysis, or arteriovenous hemodialysis.

SCr levels were collected on preoperative and postoperative days 1, 3, and 10 and eGFR was calculated according to the abbreviated Modification of Diet in Renal Disease (MDRD) equation.14 Adverse outcome-related parameters were collected.20

Routine monitoring for cardiac anesthesia was established prior to induction of anesthesia, including five-lead ECG, radial and central venous catheters (CVP) with or without pulmonary artery catheters, pulse oximetry, and capnography. Hemodynamic data were recorded just before the start of surgery, at the end of CPB, on admission to the intensive care unit (ICU), and postoperatively at 6 hours and 24 hours later in the ICU. Cardiac output was measured by the use of 1 of the 3 different methods: (1) Aortic pulse-contour continuous cardiac output measurement using the PICCO system (PULSION Medical Systems, Munich, Germany), (2) pulmonary artery catheter by percutaneous cannulation of the right internal jugular vein (Super Arrow-Flex percutaneous Sheath Introducer Set, 8 French; Arrow International, Diegem, Belgium), or (3) TEE. Cardiac output was measured using the bolus thermodilution method by injecting 10 mL cold saline at end-expiration. Cardiac index was calculated by standard methods. Pulmonary artery and systemic arterial vascular resistance indices were calculated according to standard formulas: PVRI = (MPAP–PCWP)/CI and SVRI = (MAP–CVP)/CI, CI = CO/BSA, where PVRI = pulmonary vascular resistance index, SVRI = systemic vascular resistance index, MAP = mean arterial pressure, CVP = central venous pressure, MPAP = mean PAP, PCWP = pulmonary capillary wedge pressure, CI = cardiac index and BSA = body surface area. PVRI, MPAP, and PCWP cannot be obtained by PiCCO system and TEE. Hemodynamic targets were as follows: MAP ≥70 mmHg, CI ≥2.0 L/min/m² without signs of poor peripheral perfusion (oliguria, acidosis).

Anesthetic induction in all patients was with intravenous doses of midazolam (Roche, Basel, Switzerland), 0.2 mg/kg, fentanyl (Janssen-Cilag, Beerse, Belgium), 5 to 10 μg/kg, and rocuronium bromide (Organon, Oss, The Netherlands), 0.1 mg/kg. For maintenance, all patients received sevoflurane at an end-tidal concentration of 0.5% to 2% and intravenous maintenance doses of midazolam and fentanyl every half an hour.

Median sternotomy was performed on all patients. Before the beginning of the CPB, heparin at a dose of 300 IU/kg was administered intravenously to keep the ACT (Active Clotting Time) greater than 450 seconds. Mild hypothermia (28°C-32°C) was established during all cases. Antegrade and retrograde blood cardioplegia were supplied to each patient through appropriate cannulation. Before CPB, each patient received crystalloid solutions (Ringer’s lactate and isotonic sodium chloride (0.9%)) at a dose of 10 mL/kg. The bypass circuit was primed with Ringer’s lactate solution, 20 mL/kg; sodium bicarbonate 7.5%, 1 mEq/kg; and heparin, 100 IU/kg. Mannitol 20 % at a dose of 0.5 g/kg was added to the CPB prime solution. The use of 6 % hydroxyethyl starch 1300/4 (Voluven) (Fresenius Kabi, Bad Hamburg, Germany) was restricted at a dose of 10 mL/kg during CPB, and it was not used during other parts of the operative procedure. Central venous pressure was maintained between 8 and 14 mmHg by infusion of crystalloid solutions after CPB. Cardiopulmonary bypass circulation was provided by a roller Biomedicus pump (Biomedicus, Lindau, Germany) in all
patients. Systemic blood flow during CPB was maintained between 2 to 2.5 L/min/m², and systemic blood pressure was kept between 50 to 80 mmHg. Arterial blood gas values were observed every 60 minutes to keep the levels of PO2 greater than 250 mmHg, PCO2 between 35 to 45 mmHg, pH between 7.35 to 7.40, hematocrit between 22% and 28%, and blood glucose between 100 to 180 mg/dL. After rewarming the patient had an MAP of 60 to 90 mmHg and systemic vascular resistance (SVR) 1800 dyne/s/cm²/m². A norepinephrine infusion also was started, increased incrementally by 0.1 μg/kg/min until the mean arterial blood pressure was > 60 mmHg, (3) if cardiac index < 2.5 L/min/m² inotropic support was started initially with dobutamine, 5-10 μg/kg/min. When a patient had an MAP < 60 mmHg and systemic vascular resistance (SVR) > 600 dyne/s/cm²/m², a norepinephrine infusion also was started, followed (if necessary) with addition of epinephrine, 0.02-0.15 μg/kg/min, and/or norepinephrine, 0.2 to 1.3 μg/kg/min until MAP > 65 mmHg, depending on other clinical monitoring parameters, such as CVP > 14 mmHg or PCWP > 16 mmHg and heart rate < 70 beats/min. The treatment goal was to achieve an MAP > 60 mmHg, CI > 2.2 L/min/m², PCWP < 18 mmHg, and SVR < 1200 dyne/s/cm²/m². Dopamine at a dose of 2 to 3 μg/kg/min was provided at the end of CPB if the urine output was less than 2 mL/kg every hour during surgery. An intravenous bolus dose of furosemide at a dose of 0.2 mg/kg was added and repeated if necessary. Intraoperative ventricular tachyarrhythmias were treated with internal cardioversion or lidocaine (1 to 1.5 mg/kg). If the tachyarrhythmia was persistent, intravenous amiodarone, 300 mg bolus dose, was followed by an infusion of 8 mg/kg/h. An intra-aortic balloon pump (IABP) was applied when there was a pump insufficiency despite inotropic support, and it was continued until at least the first day after surgery. During the postoperative period, when hemodynamic stability was maintained, the inotropic agents were stopped, by reducing the dosage of each inotrope.

As a primary endpoint, the authors analyzed the effect of levosimendan on postoperative renal function measured by sCr and eGFR. The secondary endpoint was the effect of levosimendan on postoperative outcome-related parameters: (1) aortic cross-clamp time, (2) cardiopulmonary bypass time, (3) inotropic support, (4) intra-aortic balloon pump, (5) prolonged mechanical ventilation, (6) development of pneumonia, (7) perioperative myocardial infarction, (8) cerebrovascular event (stroke, transient ischemic attack), (9) atrial fibrillation and other rhythm disturbances, (10) need for early RRT (as described in the Parameters section), (11) reoperation secondary to bleeding, (12) ICU stay, and (13) hospital stay. Patients were weaned from mechanical ventilation when rewarmed and hemodynamically stable, including cardiac index ≥ 2, absence of frequent ventricular arrhythmias, fractioned inspired oxygen value (FiO2) < 50%, TV > 5 mL/kg, RR < 24 breaths per minute, vital capacity (VC) > 10-15 mL/kg, normal respiratory pressure (NIF) > 20 cm H2O, and with normal arterial blood gas values. Patients were discharged from the ICU when the following criteria were met: SpO2 ≥ 90% at FiO2 ≤ 0.5 by facemask, stable hemodynamics, chest tube drainage < 50 mL/h, urine output > 0.5 mL/kg/h, and no intravenous inotropic or vasopressor therapy.
All analyses were performed using SPSS Statistical Package 15.0 (SPSS Inc., Irvine, CA). For sample size analysis PASS 11 (NCSS Inc., Kaysville, UT) package program was used. The sample size was calculated based on the assumption that worsening of renal function was based on 2 criteria: an increase in sCr by at least 0.3 mg/dL in the absolute value and, additionally, by at least 25% with respect to the baseline value.11,20 We calculated that for a difference of 0.3 mg/dL in absolute value and, additionally, by at least 25% with respect to the baseline value, 52 patients in each group are sufficient to provide a power of 95% and 80% power.20 Data are presented as mean, standard deviation (SD), or median (range; minimum–maximum), as well as frequencies and percentages. Differences were assessed using χ² or Fisher’s exact test for categoric variables. Mann-Whitney U test was used for continuous or nonparametric data. After testing for normal distribution, data were compared using a two-way analysis of variance for repeated measurements. All p values <0.05 were considered statistically significant. Bonferroni correction was applied during evaluation of multiple comparisons. The main findings for the primary outcome renal function can be summarized as follows: (1) patients treated with levosimendan had lower sCr levels on postoperative day 1 and 3 in comparison with the control group (p<0.001 and p=0.0009, respectively); these significant differences disappeared on postoperative day 10 (p>0.05) (Table 3); (2)...
A comparison of the hemodynamic data is shown in Table 5, including heart rate, mean arterial pressure, cardiac index, central venous pressure, and systemic vascular resistance index. After the start of the infusion, in the levosimendan group, cardiac index improved at the end of surgery. Cardiac index increased from 1.8 ± 0.2 L/min/m² at baseline to 3.0 ± 0.3 L/min/m² (p = 0.02) at the end of surgery, increasing to 3.5 ± 0.3 L/min/m² (p < 0.001) at 6 hours after surgery. The increase in cardiac index was significantly less in the control group compared with the levosimendan group, which received only standard inotropes at the end of surgery, at 6 hours, and at 24 hours after surgery (p < 0.001, p < 0.001, and p < 0.001, respectively). In both groups, heart rate increased compared with baseline during and after surgery (p < 0.001); however, there was no significant change between time points during or after surgery (p > 0.05). In both groups, mean arterial pressure increased compared with baseline during and after surgery (p < 0.001); however, there was no significant change between time points during or after surgery (p > 0.05). In the levosimendan group, a comparison of systemic vascular resistance index values found a significant decrease compared with baseline values at all time points (p < 0.001); however, in the control group, although there was a decrease of systemic vascular resistance index values at 15 minutes after CPB, the values increased at other time points in comparison to the levosimendan group (p > 0.05, p < 0.001, p < 0.001, p < 0.001, respectively).

Use of other inotropic agents and vasopressors given in the OR and the first 24 hours in the ICU are presented in Table 4. There was no significant difference in both groups regarding administration of 1 or more standard inotropic agents, such as dobutamine, epinephrine, or norepinephrine (p > 0.05). The mean doses of dobutamine and adrenaline did not differ between groups; however, the 24-hour total dose of norepinephrine in the levosimendan group (0.12 ± 0.05 μg/kg/min) was lower than the control group (0.06 ± 0.03 μg/kg/min; p = 0.02).
The causes of deaths in both groups were related to postoperative complications. In the levosimendan group, 4 patients (6.3%) died, and all of them had renal failure requiring dialysis. One patient died secondary to stroke-related deterioration in neurologic functions, heart failure, and renal failure. Another patient died of heart and respiratory failure, and the last patient died of cardiopulmonary arrest secondary to renal and heart failure. In the control group, early RRT was necessary in 10 patients, and development of AKI was observed in all patients who died within 30 days in hospital. Reoperation and bleeding-related complications were present in 6 patients, and stroke causing hemiplegia, prolonged intubation, and deterioration in neurologic status were observed in 4 patients.

Multivariate logistic regression analysis found that (1) preoperative sCr value between 1.2 to 2.09 mg/dL increases the need for RRT 3.7-fold (% 95 CI 1.1-15.47), (2) preoperative sCr value ≥ 2.1 mg/dL increases the need for RRT 31.3-fold (% 95 GA 5.6-176.2), and (3) ICU stay greater than 3 days increases the need for RRT by 6.2-fold (% 95 CI, 1.5-26.2; Hosmer-Lemeshow \( \chi^2 \), 1.71; \( p = 0.931 \) (p < 0.05) (Table 6).

### Table 5. Comparison of Hemodynamic Data Between Groups

<table>
<thead>
<tr>
<th>Groups and Parameters</th>
<th>Baseline (T0)</th>
<th>15 min after CPB (T1)</th>
<th>End of Surgery (T2)</th>
<th>ICU 6 h (T3)</th>
<th>ICU 24 h (T4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (beats/min)(^\dag)</td>
<td>78.4 ± 4.2</td>
<td>94.1 ± 8.4(^*)</td>
<td>93.7 ± 6.1(^{*+})</td>
<td>94.5 ± 5.5(^{*+})</td>
<td>91 ± 4.4(^{+})</td>
</tr>
<tr>
<td>Control group</td>
<td>82.2 ± 5.1</td>
<td>93.4 ± 7.8(^*)</td>
<td>94.8 ± 5.3(^*)</td>
<td>89.3 ± 6.3(^*)</td>
<td>87.3 ± 3.2(^*)</td>
</tr>
<tr>
<td>Mean arterial pressure, mmHg(^*)</td>
<td>Levosimendan group</td>
<td>63.9 ± 3.5</td>
<td>74.8 ± 3.2(^*)</td>
<td>84.6 ± 4.3(^*)</td>
<td>82.4 ± 4.6(^*)</td>
</tr>
<tr>
<td>Control group</td>
<td>63.7 ± 3.8</td>
<td>75.9 ± 3.1(^*)</td>
<td>87.8 ± 3.8(^*)</td>
<td>83.6 ± 3(^*)</td>
<td>84.3 ± 3.9(^*)</td>
</tr>
<tr>
<td>Cardiac index, L/min/m(^2)(^\dag)</td>
<td>Levosimendan group</td>
<td>1.8 ± 0.2</td>
<td>3.0 ± 0.4(^*)</td>
<td>3.4 ± 0.3(^{+})</td>
<td>3.5 ± 0.3(^{+})</td>
</tr>
<tr>
<td>Control group</td>
<td>1.8 ± 0.3</td>
<td>2.7 ± 0.2(^*)</td>
<td>2.8 ± 0.2(^*)</td>
<td>2.7 ± 0.2(^*)</td>
<td>2.8 ± 0.2(^*)</td>
</tr>
<tr>
<td>Central venous pressure, mmHg(^\dag)</td>
<td>Levosimendan group</td>
<td>5 (3-15)</td>
<td>7 (5-18)</td>
<td>9 (7-15)</td>
<td>8.5 (7-14)</td>
</tr>
<tr>
<td>Control group</td>
<td>6.5 (4-14)</td>
<td>7 (4-16)</td>
<td>8 (6-16)</td>
<td>8 (6-15)</td>
<td>7.5 (5-16)</td>
</tr>
<tr>
<td>Systemic vascular resistance index, dyne/cm(^5)/m(^2)(^\dag)</td>
<td>Levosimendan group</td>
<td>2691.2 ± 136.4</td>
<td>1256.4 ± 87.8(^{+})</td>
<td>1169.5 ± 36.9(^{+})</td>
<td>1223.7 ± 24.8(^{+})</td>
</tr>
<tr>
<td>Control group</td>
<td>2753.6 ± 131.5</td>
<td>1284.7 ± 72.5(^*)</td>
<td>1311.8 ± 35.2(^*)</td>
<td>1459.6 ± 23.3(^*)</td>
<td>1638.2 ± 27.9(^*)</td>
</tr>
</tbody>
</table>

CPB, cardiopulmonary bypass; ICU, intensive care unit.
\(^*\): \( p < 0.05 \) indicates statistical significance between-group differences.
\(^\dag\): \( p < 0.05 \) indicates statistical significance within-group differences.
\(^\dag\): Student’s t test.
\(^\dag\): Mann Whitney U test.

### Table 6. Multivariate Logistic Regression Analysis of Risk Factors for Need for Renal Replacement Therapy

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Regression Coefficient</th>
<th>Standard Error</th>
<th>Wald</th>
<th>df</th>
<th>p</th>
<th>Odds Ratio 95% CI for EXP(B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative ejection fraction, (^\dag) (&lt;40%)</td>
<td>0.173</td>
<td>0.890</td>
<td>0.038</td>
<td>1</td>
<td>0.846</td>
<td>1.189 (0.208-6.809)</td>
</tr>
<tr>
<td>Preoperative sCr, 1.2-2.09 mg/dL</td>
<td>1.309</td>
<td>0.730</td>
<td>3.219</td>
<td>1</td>
<td>0.043</td>
<td>3.703 (1.086-15.473)</td>
</tr>
<tr>
<td>Preoperative sCr, ≥2.1 mg/dL</td>
<td>3.443</td>
<td>0.882</td>
<td>15.246</td>
<td>1</td>
<td>0.0001</td>
<td>31.288 (5.556-176.197)</td>
</tr>
<tr>
<td>Age</td>
<td>-0.025</td>
<td>0.029</td>
<td>0.732</td>
<td>1</td>
<td>0.392</td>
<td>0.975 (0.921-1.033)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>0.787</td>
<td>0.661</td>
<td>1.415</td>
<td>1</td>
<td>0.234</td>
<td>2.197 (0.601-8.031)</td>
</tr>
<tr>
<td>Intensive care unit stay ((&gt;3) d)</td>
<td>1.821</td>
<td>0.737</td>
<td>6.107</td>
<td>1</td>
<td>0.013</td>
<td>6.176 (1.457-26.165)</td>
</tr>
<tr>
<td>Constant</td>
<td>3.259</td>
<td>2.013</td>
<td>2.622</td>
<td>1</td>
<td>0.105</td>
<td>0.038</td>
</tr>
</tbody>
</table>

**DISCUSSION**

The present prospective randomized clinical trial, addressing the effect of levosimendan on renal function in patients with low ejection fraction undergoing mitral valve surgery with CPB, found that patients treated with levosimendan in addition to standard inotropic therapy showed an improvement in renal function on postoperative days 1 and 3 compared with the group of patients who received only standard inotropic therapy.

In previous animal studies, it has been shown that levosimendan significantly improved the ischemia reperfusion injury in the renal tubules. A study by Yilmaz et al. of a group of 88 patients with heart failure found that intravenous levosimendan infusion showed beneficial effects on GFR at the postoperative 24-hour and 72-hour measurement points compared with a group of patients who received only dobutamine as inotropic support therapy. A recent study of a relatively small group of 45 patients found that levosimendan provided a renal function-enhancing effect in patients with severe, acute decompensated systolic heart failure and worsening renal function.

Specific risk factors for the development of AKI were identified, including advanced age, diabetes mellitus, congestive heart failure, systolic blood pressure at admission, preoperative creatinine, and renal function on postoperative days 1 and 3 compared with the control group.
heart failure, low cardiac index, pre-existing renal dysfunction, and more complex cardiac surgery. Cardiopulmonary bypass time has not been shown as a risk factor for the development of AKI, and the role of age is still under debate as well.6

Recently, the Toronto and Cleveland clinical scoring systems for AKI were compared after cardiac surgeries, and it has been shown that there was underestimation of the risk of AKI. In the present study, preoperative and postoperative serum creatinine levels were used to evaluate outcome parameters, as described in the Cleveland scoring system.8,15 The independent risk factors for need for RRT included preoperative sCr value between 1.2 to 2.09 mg/dL and ≥2.1 mg/dL, ICU stay greater than 3 days (p < 0.05) In both groups, RRT was started as early as possible; however, these results showed that on postoperative days 1 and 3, sCr values were lower and eGFR values were higher in the levosimendan group in comparison with the control group (Table 3 and Fig 3). The need for RRT was observed in 6 patients (9.4 %) in the levosimendan group and 10 patients (15.6 %) in the control group (Table 4) (p = 0.284). In the present study, early RRT was recommended to all patients, and results are comparable to previous studies—that earlier RRT would lead to a better-than-predicted outcome in spite of significant differences in the timing of RRT using blood urea nitrogen, creatinine, or urine output.26–27 The overall mortality in this very high-risk study group of patients was 10.94%. In patients undergoing hemodialysis after cardiac surgery, a mortality of 50% to 80% is expected.28

One limitation of the present study was that dopamine at low doses was considered to increase renal blood flow and to inhibit proximal tubule sodium reabsorption; however, a clinical benefit of its use has not been shown.29 Comparison of outcome measures and consideration of cost-effectiveness require larger, placebo-controlled clinical trials. Another limitation of the study was that cardiac output was measured by the use of 1 of the 3 different methods.

CONCLUSION

In patients with low ejection fraction undergoing mitral valve surgery, a decrease in sCr and an increase in eGFR levels were observed in the early postoperative period in patients receiving levosimendan in addition to standard inotropic therapy, which included 1 or more of dobutamine, adrenaline, or noradrenaline. The independent risk factors for need for RRT in this patient group were preoperative sCr values between 1.2 to 2.09 mg/dL and sCr ≥2.1 mg/dL.

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