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ORIGINAL RESEARCH / *ÖZGÜN ARAŞTIRMA*

Funda Atar,
Helin Şahintürk,
Aycan Özdemirkan,
Özgür Ersoy,
Pınar Zeyneloğlu

The Incidence and Risk Factors of Acute Kidney Injury After Left Ventricular Assist Device Implantation

Sol Ventrikül Destek Cihazı Sonrası Akut Böbrek Hasarının İnsidansı ve Risk Faktörleri

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ABSTRACT *Objective:* Left ventricular assist device surgery (LVAD) associated acute kidney injury (AKI) is a severe complication of cardiac surgery with 15-45% incidence. The study evaluated AKI in the early postoperative period after LVAD surgery using the Kidney Disease: Improving Global Outcomes (KDIGO) criteria and compare patients with and without AKI to determine the incidence, risk factors, and clinical outcomes.
Materials and Methods: In this retrospective cohort study, the medical records of all patients aged between 18 and 75 years who underwent LVAD implantation from January 2011 to December 2016 were reviewed. Patients were divided into two groups based on the development of AKI to analyze demographic features and perioperative variables. AKI was defined according to the KDIGO criteria.
Results: Out of 57 patients, 10 (18%) were female, and the cohort's mean age was 44.6±16.1 years. Thirty-six patients (63%) developed AKI following LVAD implantation. Logistic regression analysis revealed the duration of cardiopulmonary bypass (CPB), mean arterial pressure, and cumulative fluid balance on the first postoperative day as independent risk factors for AKI [odds ratio (OR): 1.013, confidence interval (CI) 95% 1.000-1.025, p=0.05; OR: 0.929, CI 95% 0.873-0.989, p=0.02; OR: 1.001, CI 95% 1.000-1.001, p=0.04 respectively]. Hospital mortality (58% vs. 24%, p=0.01) and 30-day mortality (39% vs. 5%, p=0.01) were significantly higher in patients who had AKI.
Conclusion: Risk factors for the occurrence of AKI include a longer duration of CPB, lower mean arterial pressures, and higher cumulative fluid balance on the first postoperative day. Therefore, AKI is one of the most important causes of morbidity and mortality after LVAD.
Keywords: Acute kidney injury, intensive care, left ventricle assist device

ÖZ *Amaç:* Sol ventrikül destek cihazı cerrahisi (LVAD) ile ilişkili akut böbrek hasarı (ABH), %15-45 insidans ile kalp cerrahisinin ciddi bir komplikasyonudur. Çalışma, LVAD cerrahisi sonrası erken dönemde ABH'yi Böbrek Hastalığı: Küresel Sonuçların İyileştirilmesi (KDIGO) kriterlerini kullanarak değerlendirmeyi ve ABH olan ve olmayan hastaları insidans, risk faktörleri ve klinik sonuçları belirlemek için karşılaştırmayı amaçladı.
Gereç ve Yöntem: Bu retrospektif kohort çalışmada, Ocak 2011 ile Aralık 2016 arasında LVAD implantasyonu uygulanan 18-75 yaş arasındaki tüm hastaların tıbbi kayıtları gözden geçirildi. Hastalar, demografik özellikleri ve perioperatif değişkenleri analiz etmek için ABH gelişimine göre iki gruba ayrıldı. ABH, KDIGO kriterlerine göre tanımlandı.
Bulgular: Elli yedi hastanın 10'u (%18) kadındı ve ortalama yaş 44,6±16,1 yıldı. Otuz altı hastada (%63) LVAD implantasyonunu takiben ABH gelişti. Lojistik regresyon analizi, ABH için bağımsız risk faktörleri olarak postoperatif birinci günde kardiyopulmoner bypass süresi, ortalama kan basıncı ve kümülatif sıvı dengesini ortaya koydu [olasılık oranı (OR): 1.013, güven aralığı (GA) %95 1,000-1,025, p=0,05; OR: 0,929, GA %95 %0,873-0,989, p=0,02; OR: 1,001, GA %95 1,000-1,001, p=0,04]. ABH'li hastalarda hastane mortalitesi (%58'e karşı %24, p=0,01) ve 30 günlük mortalite (%39'a karşı %5, p=0,01) anlamlı olarak daha yüksekti.
Sonuç: Sonuçlarımız, LVAD cerrahisi sonrası hastaların %63'ünde ABH geliştiğini göstermektedir. ABH oluşumu için risk faktörleri, uzun kardiyopulmoner bypass süresini, daha düşük ortalama kan basınçlarını ve postoperatif ilk gün daha yüksek kümülatif sıvı dengesini içerir. Bu nedenle ABH, LVAD'den sonra en önemli morbidite ve mortalite nedenlerindendir.
Anahtar Kelimeler: Akut böbrek hasarı, yoğun bakım, sol ventrikül destek cihazı

Funda Atar
University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Anesthesiology and Reanimation, Ankara, Turkey

Helin Şahintürk, Pınar Zeyneloğlu
Başkent University Faculty of Medicine, Department of Anesthesiology and Reanimation, Ankara, Turkey

Aycan Özdemirkan
Gazi University Faculty of Medicine, Department of Anesthesiology and Reanimation, Ankara, Turkey

Özgür Ersoy
University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Cardiovascular Surgery, Ankara, Turkey

Funda Atar MD (✉),
University of Health Sciences Turkey, Dışkapı Yıldırım Beyazıt Training and Research Hospital, Clinic of Anesthesiology and Reanimation, Ankara, Turkey

E-mail : fundaatar81@gmail.com
Phone : +90 506 492 74 32
ORCID ID : orcid.org/0000-0002-3534-2233

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Introduction

Left ventricular assist devices (LVAD) is used as a safe treatment for end-stage heart failure patients. Acute kidney injury (AKI) that can occur following LVAD surgeries is one of the life-threatening complications. A wide range of AKI incidence among patients undergoing LVAD has been reported in previous studies (15-45%) (1). This study aimed to determine the incidence and perioperative risk factors for AKI and postoperative outcomes associated with AKI following LVAD implantation in our cohort.

Materials and Methods

This study was approved by the Institutional Review Board of the Başkent University (no: KA 17/75, date: 02.06.2017). We retrospectively analyzed the records of patients who underwent LVAD implantation between January 2011 to December 2016. Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) classification is a classification system that assists physicians in deciding on mechanical assist devices or heart transplant treatment for patients with advanced heart failure. This registry system, which aims to support the choice of mechanical assist devices in which patients, the regulations for the devices developed, and the treatments for heart failure, has determined 7 patient profiles that can classify advanced heart failure patients more appropriately (2). LVAD is planned with the INTERMACS system in our hospital.

Patients between 18-75 years of age were included in the study. Patients with chronic renal failure, preoperative acute renal failure and those requiring renal replacement therapy (RRT) before surgery were excluded from the study. Preexisting renal failure is defined as abnormalities of kidney structure or function, present for >3 months, with implications for health, and requires one of two criteria documented or inferred for >3 months: either glomerular filtration rate (GFR) <60 mL/min/1.73 m^2 or markers of kidney damage, including albuminuria (3). AKI was determined according to Kidney Disease: Improving Global Outcomes (KDIGO) 2012 criteria. According to KDIGO criteria, AKI is defined as an increase in serum creatinine by 0.3 mg/dL in 48 hours or an increase of serum creatinine of 1.5 times or more versus baseline or urine output within 0.5 mL/kg/h in the first 6 hours (4). Incidence and stages of early postoperative AKI among the included patients were evaluated. Patients were then divided into two groups according to the presence of AKI to define risk factors and clinical outcomes.

Anesthesia was induced with intravenous midazolam 0.02-0.05 mg/kg, fentanyl 500 µg, and rocuronium bromide 0.6-1 mg/kg. Desflurane was used for maintenance anesthesia at a 4-6% concentration and 10 µg/kg/h fentanyl. Routine monitoring included electrocardiography, pulse oximetry, capnography, nasopharyngeal temperature, invasive arterial blood pressure (radial pressure), and central venous pressure via the subclavian or internal jugular vein. Transesophageal echocardiography (TEE) was performed in all cases. And a pulmonary artery catheter was placed in all patients intraoperatively.

LVAD (HeartWare®, Medtronic, MN, USA) type was continuous flow and implantations were performed through a standard median sternotomy on the beating heart, utilizing cardiopulmonary bypass (CPB) through aortic and right atrial cannulation. The driveline was tunneled subcutaneously before systemic heparinization and existed in the patients' abdominal wall in the subcostal region. The velocity of circulation (in rate/min) was optimized to ensure proper cardiac output to the patients and to decompress the left ventricle. We changed the device's velocity to left atrial pressure at 15 to 20 mmHg and maintained central venous pressure at 10 to 15 mmHg, with interventricular septum in the midline position for TEE. Deairing was done under TEE guidance. Weaning from CPB was accomplished by gradual increases in assist device pump speed under TEE guidance.

After surgery, all patients were admitted to intensive care unit (ICU) with vasoactive drug support and mechanical ventilatory support [S1 (Hamilton Medical, Switzerland)]. Transthoracic echocardiographic studies were done for hemodynamic management and flow settings of LVADs on the following postoperative days. Blood pressure in the postoperative period was measured continuously with invasive artery cannulation and the mean arterial pressure (MAP) was followed. Weaning from vasoactive drug support and mechanical ventilatory support was performed according to hemodynamic and blood gas parameters. The same surgical, anesthesia, and intensivist teams were assigned during the perioperative period for all patients.

Statistical Analysis

SPPS 25 (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0, Armonk, NY: IBM Corp.) statistical package program is used for the analysis. Variables' mean, standard deviation, percentage, and frequency values are used. Variables are considered after accounting for normality and homogeneity of variances (Shapiro-Wilk and Levene test). For data analysis, the independent 2-group t-test (Student's t-test) is used to compare the two groups, and Mann-Whitney U test is used when the prerequisites are not met. Categorical data are analyzed by Fisher's Exact test and chi-square test. In cases where the expected frequencies are less than 20%, Monte Carlo Simulation Method is used to include these frequencies in the analysis. For the significance level of the tests, p<0.05 and p<0.01 are considered.

Results

Out of 57 patients, 10 (17.5%) were female, and the mean age was 44.6±16.1 years. Dilated cardiomyopathy was the main diagnosis for most cases [n=55 (96.5%)], and destination therapy was the leading indication for LVAD implantation. The demographic characteristics and main diagnosis of the patients included in the study are shown in Table 1.

The patients were divided into two groups based on the development of postoperative AKI. Thirty-six patients (63.2%) developed AKI following LVAD implantation. Out of 36 patients 13 (36.1%) had stage 1, 5 (13.9%) had stage 2, 18 (50%) had stage 3 AKI. The two groups were similar in demographic characteristics, preoperative circulatory support devices, intraoperative anesthetic and surgical management, and postoperative LVAD flow rates. Redo cases included in the study. There was no significant difference in terms of redo cases in the 2 group comparisons. Preoperative laboratory values, INTERMACS score and vital signs were similar between the two groups (p>0.05) (Table 2, 3). Intraoperative duration of CPB was longer in the patients who developed AKI (p=0.04), (Table 4). Intraoperative and postoperative lactate levels were higher in patients who developed AKI during this period when compared to those without AKI (p=0.03, and p=0.04, respectively), (Table 4, 5). Postoperative mechanical ventilation times were longer in the group with AKI when compared to those without AKI (p=0.02), (Table 5).

Fluid balance (FB) was higher in the first two days in patients who developed AKI in the postoperative period compared to patients who did not develop AKI (p=0.04, and p=0.03, respectively). Creatine levels were found to be significantly higher only on the 2nd day in patients who developed AKI (p=0.01). Patients who developed AKI had lower MAP (p=0.01), (Table 5). Patients who developed AKI required more frequent RRT (p=0.01). Prolonged mechanical ventilation (PMV) was defined as the inability to wean from the ventilator for more than 24 hours after surgery and/or a total duration on mechanical ventilation more than 24 hours following admission to ICU. The frequency of PMV among patients with AKI was higher when compared to those without AKI (p=0.01). Patients who developed AKI had higher incidences of postoperative infection, and higher frequency of norepinephrine (NE) usage on the postoperative first day (p<0.01, p=0.02, respectively). Hospital mortality (p=0.01) and 30-day mortality (p=0.01) were significantly higher in patients who developed AKI (Table 6). Logistic regression analysis revealed the duration of CPB, MAP, and cumulative FB on the postoperative first day as independent risk factors for AKI [Odds ratio (OR): 1.013, confidence interval (CI) 95% 1.000-1.025, p=0.05; OR: 0.929, CI 95% 0.873-0.989, p=0.02; OR: 1.001, CI 95% 1.000-1.001, p=0.04, respectively) (Table 7).

Table 1. Demographic characteristics and main diagnosis of the study population [median (minimum-maximum), mean ± SD or n (%)]

	n=57 (%)
Age (years)	44.6±16.1
Female	10 (17.5)
Diagnosis	
Dilated cardiomyopathy	55 (96.5)
Restrictive cardiomyopathy	2 (3.5)
Indications for LVAD	
Destination	28 (49.1)
Bridge to transplantation	22 (38.6)
Bridge to recovery	7 (12.3)

LVAD: Left ventricular assist device, SD: standard deviation

Table 2. Comparison of two groups in terms of demographics and preoperative features [median (minimum-maximum), mean ± SD or n (%)]			
	AKI (-) (n=21)	**AKI (+) (n=36)**	**p-value**
Age (years)	44.7±16.5	44.5±16.0	0.97
Female (n, %)	1 (5)	9 (25)	0.05
Body weight index (kg)	67.7±16.9	72.4±17.8	0.33
Height (cm)	169±12.9	167.3±10.5	0.71
Redo patients	8 (38.1%)	19 (52.8%)	0.41
Ejection fraction (%)	17.7±4	22.4±13.2	0.06
TAPSE (mm)	14.8±4.3	13.8±3.4	0.34
Systolic pulmonary artery pressure (mmHg)	52.5±14.2	54.7±14.2	0.63
Urine output* (mL)	2056.4±1454.2	1519.3±1115.4	0.36
Requriment for renal replacement therapy	3 (14.3%)	7 (19.4%)	
Continuous renal replacement therapy	0	6	0.70
Intermittent hemodialysis	2	0	
Slow continuous ultrafiltration	1	1	
Use of bronchodilators (n, %)	0 (0)	1 (2.8)	0.46
INTERMACS score			
1	3 (14.3%)	7 (19.4%)	0.95
2	6 (28.6%)	9 (25%)	
3	4 (19%)	6 (16.7%)	
4	8 (38.1%)	14 (38.9%)	
Comorbidities (n, %)	14 (66.7)	23 (63.9)	0.83
Diabetes	8 (38.1)	8 (22.2)	0.20
Hypertension	6 (28.6)	13 (36.1)	0.56
COPD	1 (4.8)	4 (11.1)	0.41
Coronary artery disease	3 (14.3)	3 (8.3)	0.48
History of cardiac arrest	1 (4.8)	4 (11.1)	0.44
Use of inotropic agent			
Use of dobutamine (µg/kg/min)	11 (52.4)	15 (41.6)	0.43
Use of dopamine (µg/kg/min)	4 (19)	7 (19.4)	0.97
Intraaortic balloon pump (n, %)	0 (0)	1 (2.8)	0.44
Extracorporeal membrane oxygenation (n, %)	3 (14.3)	4 (11.1)	0.73

INTERMACS: Interagency Registry for Mechanically Assisted Circulatory Support, AKI: acute kidney injury, COPD: chronic obstructive pulmonary disease, TAPSE: tricuspid annular plane systolic excursion, SD: standard deviation

*The day before surgery

Table 3. Comparison of two groups in terms of preoperative laboratory values and vital signs [median (minimum-maximum) mean ± SD or n (%)]

Preoperative laboratory values	AKI (-) (n=21)	AKI (+) (n=36)	p-value
Hemoglobin (g/dL)	12.2±2.5	11.9±2.1	0.64
White blood cells (1000/mm^3)	9.8±4.6	9±2.7	0.44
AST (U/L)	25.8±15.4	29.7±16.9	0.45
ALT (U/L)	61.9±81.2	36.9±69.5	0.22
Total bilirubin (g/dL)	1.5±0.9	2.2±1.4	0.20
Direct bilirubin (g/dL)	0.7±0.6	0.6±0.3	0.90
BUN (mg/dL)	26±14.3	26.7±13.7	0.85
Creatinine (mg/dL)	1.1±0.8	1.1±0.4	0.70
Albumin (g/dL)	3.7±0.4	3.4±0.6	0.06
Sodium (mmol/L)	192.4±251.1	134.5±4.5	0.33
Potassium (mmol/L)	4.1±0.4	7.9±23	0.46
Magnesium (mg/dL)	2.2±0.3	2±0.4	0.45
INR	1.3±0.3	1.4±0.3	0.61

AKI: Acute kidney injury, ALT: alanine aminotransferase, AST: aspartate aminotransferase, BUN: blood urea nitrogen, INR: international normalized ratio, SD: standard deviation

Table 4. Comparison of two groups in terms of intraoperative features [median (minimum-maximum) mean ± SD or n (%)]

	AKI (-) (n=21)	AKI (+) (n=36)	p-value
Duration of surgery (hrs)	5.8±1.4	6±2	0.72
Duration of CPB (min)	128.7±48.6	162.5±58.2	0.04
Blood products			
Packed red blood cells	21 (100%)	30 (90.9%)	0.38
Fresh frozen plasma	18 (85.7%)	32 (88.9%)	0.10
Platelets	0	3 (8.3%)	0.29
Urine output (mL)	669.5±433.7	699.7±634.6	0.85
Highest lactate level (mmol/L)	3.7±1.7	5.2±3.5	0.03
Lowest systolic blood pressure (mmHg)	77.9±13	74.6±14.1	0.39
Use of inotropic agents			
Highest dose of dobutamine (μg/kg/min)	8.6±1.6	9.4±3.4	0.34
Highest dose of dopamine (μg/kg/min)	7.6±2	9±4.5	0.19
Highest dose of adrenaline (μg/kg/min)	0.3±0.2	0.6±1.1	0.13
Highest dose of norepinephrine (μg/kg/min)	0.1±0.1	0.1±0.3	0.77
Highest dose of milrinone (μg/kg/min)	0.7±0	1.1±1.5	0.51

AKI: Acute kidney injury, CPB: cardiopulmonary bypass, SD: standard deviation

Table 5. Comparison of two groups in terms of postoperative features [median (minimum-maximum) mean ± SD or n (%)]			
	AKI (-) (n=21)	AKI (+) (n=36)	p-value
LVAD flow rate (L/min)	4.1±1	3.9±1.4	0.50
Ejection fraction (%)	22±7.5	23.1±11.6	0.81
TAPSE (mm)	11±2.9	11.3±3.1	0.82
Systolic pulmonary artery pressure (mmHg)	40±7.1	45±8.3	0.45
Postoperative first day mean arterial pressure (mmHg)	62.8±6.9	54.9±13.1	0.01
Hemoglobin (g/dL)	10.2±1.2	10±1.4	0.51
Hematocrit (%)	32±6.7	30±4.3	0.17
White blood cells (1000/mm^3)	13±3	15±7	0.14
Platelets (1000/mm^3)	7993.3±35974.8	133.8±51.8	0.33
AST (U/L)	53.4±16.7	121.1±123.6	0.05
ALT (U/L)	29.2±21.8	53.4±87.7	0.12
BUN (mg/dL)	24.2±11.3	30.7±12.6	0.06
Creatine (mg/dL)	1.1±1	1.7±0.6	0.01
Total bilirubin (g/dL)	2.3±2	2.3±1.7	0.91
Direct bilirubin (g/dL)	0.5±0.3	1.7±1.6	0.03
Albumin (g/dL)	3.3±0.4	3.1±0.4	0.06
INR	1.4±0.3	1.5±0.5	0.18
Sodium (mmol/L)	138.8±3.7	138.4±4.4	0.73
Potassium (mmol/L)	4±0.6	4.1±0.6	0.76
Magnesium (mg/dL)	7.9±23.5	2.5±0.5	0.35
Highest lactate level (mmol/L)	4.5±2.1	6.3±4.3	0.04
Duration of mechanical ventilation (hrs)	32.3±28.3	87.4±134.9	0.02
Fluid balance			
POD1 (mL)	1240.8±1160.4	2316.7±2109.9	0.04
POD2 (mL)	541.9±897	1457.8±1934.2	0.03
POD3 (mL)	-162.7±1393	-121.3±1627.9	0.93

AKI: Acute kidney injury, LVAD: left ventricular assist device, ALT: alanine aminotransferase, AST: aspartate aminotransferase, BUN: blood urea nitrogen, INR: international normalized ratio, POD: postoperative day, TAPSE: tricuspid annular plane systolic excursion, SD: standard deviation

Discussion

In this retrospective review of 57 LVAD implanted patients, the incidence of AKI was 63%. Out of 36 patients with AKI, 22.8% had mild, 8.7% had moderate, 31.5% had severe AKI. Almost 1/4 of patients (26%) with severe AKI required RRT. Postoperative hypotension and NE usage was significantly higher in patients with AKI when compared to patients without AKI. Longer CPB time, lower MAP and higher cumulative FB on the first postoperative day were determined as risk factors for AKI development among LVAD implanted patients. Besides, AKI after LVAD implantation was associated with an increased incidence of PMV, hospital mortality and 30-day mortality.

It has been reported that AKI incidence is as high as 70% after LVAD surgery, there are also publications reporting lower incidences like 28% (5). The incidence of AKI after LVAD surgery was 63% in our cohort, similar to the study by Muslem et al. (5), who reported AKI incidence as 70% after LVAD surgery. In our study, we defined AKI according to the KDIGO criteria. We calculated the incidence by evaluating stages 1 to 3 and including them in the results. In their study where Harmon et al. (6) reported AKI incidence as 28% after LVAD surgery, they obtained this incidence by

Table 6. Comparison of groups in terms of postoperative follow-up and outcomes [median (minimum-maximum) mean ± SD or n (%)]			
	AKI (-) (n=21)	AKI (+) (n=36)	p-value
Requriment for renal replacement therapy	2 (10%)	15 (41.7%)	
Continuous renal replacement therapy	0	14	0.01
Intermittant hemodialysis	2	1	
Prolonged mechanical ventilation (day)	5 (23.8%)	21 (58.3%)	0.01
Need for ECMO	2 (9.5%)	8 (22.2%)	0.22
Revision surgery	3 (14.3%)	12 (33.3%)	0.16
Infections	6 (28.6%)	21 (58.3%)	0.03
Catheter-related blood circulation Infection	2 (9.5%)	9 (25%)	0.50
Wound occupied infection	2 (9.5%)	4 (11.1%)	0.70
Pnomonia	1 (4.8%)	4 (11.1%)	0.67
Urinary tract infection	1 (4.8%)	4 (11.1%)	0.64
Cardiac arrest	1 (4.8%)	13 (36.1%)	0.01
Use of inotropic agent			
Norepinephrine	3 (14.3%)	16 (44.4%)	0.02
Dobutamine	20 (95.2%)	33 (91.7%)	0.61
Adrenaline	17 (81%)	31 (86.1%)	0.61
Dopamine	17 (81%)	22 (61.1%)	0.12
Length of ICU stay (days)	16.6±12.7	24.1±23.6	0.12
Length of hospital stay (days)	34.1±17.4	44.4±36.9	0.16
30 day mortality	1 (4.8%)	14 (38.9%)	0.01
Hospital mortality	5 (23.8%)	21 (58.3%)	0.01

AKI: Acute kidney injury, ECMO: extracorporeal membrane oxygenation, ICU: intensive care unit, RRT: renal replacement therapy, SD: standard deviation

Table 7. Results of logistic regression analysis to find risk factors associated with postoperative acute kidney injury			
	Odds ratio	95% CI	p-value
Duration of CPB (min)	1.013	1.000-1.025	0.05
Postoperative first day mean arterial pressure (mmHg)	0.929	0.873-0.989	0.02
Cumulative fluid balance (L)	1.001	1.000-1.001	0.04

CI: Confidence interval, CPB: cardiopulmonary bypass

including moderate and severe AKI. However, they did not include mild/stage 1 AKI (6). Consistent with the publications reporting that the incidence of RRT after LVAD surgery is between 10-35%, we also found the incidence of RRT to be 26% in our study (5).

Our study found that the duration of CPB is a risk factor for AKI development. It has been reported in many studies that the prolongation of the CPB time during cardiac surgery is a risk factor for the development of renal failure (7). For similar reasons, prolonged CPB after LVAD surgery is a risk factor for AKI development (5).

We observed in our study that lactate concentrations increased significantly during and after LVAD surgery and were substantially higher in patients with LVAD-AKI. Significant elevations in serum lactate may originate from renal tissues under circumstances of hypoperfusion during cardiac revascularization procedures (8). Previous studies have examined postoperative serum lactate levels and have shown a correlation between these levels and patients with cardiac surgery-associated AKI (8). Pölönen et al. (9) showed that normalizing lactate concentrations as a therapeutic goal reduce morbidity and hospital stay among patients with cardiac surgery. Our results indicate that hyperlactatemia and long-term lactate clearance were consistent with AKI, similar to other reports (8).

The effect of optimum blood pressure in preventing AKI development, especially in vasopressor-dependent patients, cannot be ignored. Although our data show the relationship between hypotension and AKI, the optimal treatment of hypotension remains controversial. In a randomized study of 292 high-risk, elderly patients, most of whom had undergone abdominal surgery, Futier et al. (10) developed an individualized management strategy systolic blood pressure (SBP) was targeted to remain within ±10% of the reference value (i.e., patient's resting SBP) using a continuous infusion of NE. Ultimately, they showed that the risk of postoperative organ dysfunction, including AKI, was reduced from 63% to 46% with individualized management aimed at SBP compared to standard therapy. We think that in addition to vasopressor therapy, anesthesiologists can treat the hypotensive patient with fluid resuscitation, inotropic support, or reducing dosage of cardiovascular depressant sedative, analgesic, or anesthetic agents. Previous studies have shown that changes in renal blood flow are associated with AKI (11). Lehman et al. (12) reported that the severity and duration of hypotension were risk factors for AKI development. Large observational studies have suggested that even brief exposure to a 10 mmHg reduction in SBP below 80 mmHg or a 5 mmHg reduction in MAP below 70 mmHg is associated with adverse outcomes (13). Our results show that hypotension, especially on the postoperatıve fırst day, is a risk factor for the development of AKI, similar to other studies. Accordingly, a requirement for NE was higher among those who developed AKI.

Several studies have found that positive FB is associated with adverse outcomes after cardiac surgery (14). In adult patients who have undergone cardiovascular surgery, a positive FB of >849 mL on the first postoperative day has been shown to be at high risk for AKI (15). Patients with hemodynamic instability may take in excess fluid. This paves the way for the development of AKI. In addition, patients who develop AKI may remain in a positive FB because they have low urine output. Whatever the cause, fluid overload can cause impaired tissue oxygenation in the kidneys (16). Similar to studies published, we determined that after LVAD surgery, postoperative first day high cumulative FB (2317 mL) is a risk factor for AKI development (17).

Previous studies have examined right ventricular (RV) function as associated with the development of AKI and described that preoperative RV function was associated with an increased risk and severity of AKI in heart transplant patients (18,19). This may be explained by that long-standing venous congestion makes the kidneys more vulnerable to the development of AKI after heart transplantation or LVAD (20). Wiersema et al. (21) found that lower tricuspid annular plane systolic excursion (TAPSE) was independently significantly associated with the development of AKI in critically ill patients. However, in our study, TAPSE was low in all groups, and our results showed no difference in AKI development. In addition, it has been reported that the evaluation of isolated TAPSE can be potentially misleading (22). Other indices of RV function, such as inferior vena cava measurements, may also reflect venous congestion and be associated with AKI (23). FB may influence RV function and thus interact with the association with AKI (24). In conclusion, we think that the combination of RV failure variables may indicate a higher predictive value for venous congestion and AKI in critically ill patients compared to TAPSE alone.

Many publications suggest that acute renal failure developing after LVAD surgery increases 30-day, 180-day, and 1-year mortality and total hospital mortality (5). However, these studies defined AKI according to the creatinine-based RIFLE "Risk" criteria. Studies defining AKI as an RRT requirement reported 40-70% high mortality rates in AKI patients and emphasized that patients requiring RRT were at the highest risk of mortality after LVAD implantation (25). Consistent with this, we also found that postoperative AKI increased 30-day mortality and hospital mortality. However, we classified the mortality risk of the patients according to the KDIGO criteria and found the hospital mortality to be 58% and the 30-day mortality to 39% in patients who developed AKI. Multiple preoperative risk stratification systems have been developed to predict the development of AKI and mortality in conventional cardiac surgery (26). However, such a classification system has not been developed after LVAD implantation yet. With further prospective studies on this, a risk classification can be established. In addition, our analysis determined that postoperative AKI is associated with postoperative PMV development. We think that this may be due to fluid overload and deterioration of lung mechanics as a result. We found that the need for RRT and the incidence of postoperative infection was statistically higher in patients who developed PMV.

Limitations of this study include those related to any retrospective analyses. Renal function was assessed using calculated estimates of GFR; other renal variables such as renal histology or ultrasonography were not routinely available. In addition, conditions such as sarcopenia and cachexia cause lower creatinine levels. The diagnosis of AKI was made according to the increase in serum creatinine. Therefore, the use of muscle-independent biomarkers (NGAL, cystatin C) may be appropriate for prospective studies. It may be useful to support this study with the results of prospective studies.

Conclusion

AKI is a common and severe complication after LVAD implantation, usually seen in advanced stages and associated with high morbidity and mortality. Risk factors for the occurrence of AKI included longer CPB time, hypotension and higher cumulative FB on the postoperative first day after LVAD surgery. A peroperative AKI risk classification system for patients undergoing LVAD surgery may help to indentify patients at risk and hereby reduce AKI occurrence after LVAD surgery.

Ethics

Ethics Committee Approval: This study was approved by the Institutional Review Board of the Başkent University (no: KA 17/75, date: 02.06.2017).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Ö.E., Concept: H.Ş., Design: A.Ö., Data Collection and Process: F.A., Analysis or Interpretation: P.Z., Literature Search: F.A., Writing: F.A.

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