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Acute kidney injury early after left ventricular assist device implantation: incidence, risk factors and clinical consequences

E. GÜNDÜZ

Department of Anesthesiology and Reanimation, Faculty of Medicine, Akdeniz University, Antalya, Turkey

Abstract. – OBJECTIVE: Renal dysfunction or renal failure is a common complication in patients undergoing a left ventricular assist device (LVAD). Measurement of serum creatinine and estimated glomerular filtration rate (eGFR) is the most commonly used inexpensive and easy method for the evaluation of kidney function. In studies, the development of acute kidney injury (AKI) after LVAD has generally been studied at 1, 3 months and 1 year, but there are almost no studies with 1-week data.

PATIENTS AND METHODS: We retrospectively analyzed the incidence of AKI, risk factors, length of stay in hospital and intensive care unit (ICU), and postoperative complications of 138 patients who underwent LVAD implantation in our center between 2012 and 2021, according to Kidney Disease Improving Global Outcomes (KDIGO) criteria. We evaluated the preoperative, postoperative 1st day, 2nd day, 1st week, 1st month, 3rd month and 1st year serum creatinine, eGFR and blood urea nitrogen (BUN) values.

RESULTS: The mean age of 138 patients who underwent LVAD implantation and evaluated the development of AKI was 50.4 (±10.86) and 119 (86.2%) were males.

The incidence of AKI, the need for renal replacement therapy (RRT) and dialysis after LVAD implant were respectively 25.4%, 25.3% and 12.3%.

According to the KDIGO criteria, in the AKI (+) patient group, 21 (15.2%) cases were identified as stage 1, 9 (6.5%) as stage 2 and 5 (3.6%) as stage 3.

The incidence of AKI was found to be high in cases with diabetes mellitus (DM), age, preoperative creatinine level ≥1.2, and eGFR ≤60 ml/min/m^2.

There is a statistically significant relationship between having AKI and right ventricular (RV) failure (p=0.0033). Right ventricular failure developed in 10 (28.6%) of 35 patients who developed AKI.

CONCLUSIONS: If perioperative AKI is recognized early, the development of advanced stages of AKI and mortality can be reduced with nephroprotective measures.

Key Words:
Left ventricular assist device, Akut kidney injury, Heart failure.

Introduction

Left ventricular assist devices (LVAD) are of great importance in salvage, bridging to transplantation or permanent destination treatment of patients with acute or chronic end-stage heart failure. It is known that cardiac output increases with LVAD implantation, and kidney and liver functions are impaired secondary to hypoperfusion[1,2].

However, LVAD implantation remains a life-threatening high-risk surgical procedure. Acute kidney injury (AKI) is a complication associated with high mortality and morbidity, seen in 15-45% after LVAD implantation. In addition, AKI has also been associated[3] with right heart failure, arrhythmia, and shortened life expectancy. In these cases, impaired renal perfusion may lead to a decrease in estimated glomerular filtration rate (eGFR) and failure. Despite scholars[4] reporting an increase in eGFR in the early period 1 month after LVAD, there are studies[5] showing the opposite in the literature. It has been emphasized[6] that the high creatinine and low eGFR in the preoperative period may impair postoperative renal function in these cases, tissue perfusion reduction due to possible hypotension in the perioperative period.

In studies[4], the development of AKI after LVAD was generally studied at 1, 3 months, and 1 year, but there are almost no studies with week 1 data. Therefore, our study retrospectively analyzed the rate of AKI development after LVAD, risk factors, complications, relationship between renal replacement therapy (RRT) and dialysis, and mortality in a single center.

Patients and Methods

This single center, retrospective database analysis included 264 consecutive patients with end-stage heart failure and LVAD implantation as

Corresponding Author: Emel Gündüz, MD; e-mail: dregunduz@hotmail.com

a bridge to transplantation or destination therapy between January 2012 and 2021.

Exclusion criteria were age <18 years, heart transplantation, patients whose data could not be reached. Data were obtained from a computerized database and electronic patient records, which were systematically collected during follow-up.

Gender, age, body mass index (BMI), EuroSCORE, Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) profile and other comorbidities were evaluated from preoperative characteristics, cardiopulmonary bypass (CPB) duration from perioperative data, and hospital and intensive care stay durations and complications were examined as postoperative data.

Preoperative, postoperative 1st day, 2nd day, 1st week, 1st month, 3rd month and 1st year serum creatinine, eGFR and blood urea nitrogen (BUN) values were evaluated according to Kidney Disease Improving Global Outcomes (KDIGO) criteria. In addition, the presence of renal replacement therapy and the need for dialysis were investigated from the records.

The study protocol was approved by the Akdeniz University Faculty of Medicine Clinical Research Ethics Committee (approval number: KAEK-396). Written informed consent forms were obtained from each patient. The study was conducted in accordance with the Helsinki Declaration principles.

Statistical Analysis

We summarized baseline characteristics of the study participants using descriptive statistics. We expressed normally distributed continuous variables as mean (standard deviation) and categorical variables as frequencies and proportions. We used Wilcoxon rank-sum and χ^2 tests to assess differences in demographics between those who developed AKI and those who did not. A Kaplan-Meier plot for cumulative survival was constructed to display mortality during LVAD support by different stages of AKI, with log-rank testing for significance, censored on LVAD implantation and end of follow-up. The changes in eGFR, BUN and serum creatinin over 12 months from preoperative to 365 days of LVAD support stratified by AKI and no AKI groups was displayed as a line graph. All tests were two-tailed, and differences were considered statistically significant at p-values < 0.05. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

The mean age of 138 patients who underwent LVAD implantation between January 2012 and January 2021 and whose AKI development was evaluated was 50.4 (±10.86). 119 (86.2%) were males and 19 (13.8%) females. The demographic data of patients with AKI (+) and AKI (-) are shown in Table I. All patients were evaluated according to the KDIGO criteria, and 35 (25.4%) cases were found to have AKI. In the AKI (+) patient group, 21 (15.2%) cases were stage 1, 9 (6.5%) cases were stage 2 and 5 (3.6%) cases were stage 3 KDIGO. After the operation, RRT was required in 35 cases, and dialysis was required in 17 (12.3%) cases. Hypervolemia was observed in 11 (31.4%), anuria in 18 (51%), and acidosis in 15 (42.9%) patients who developed AKI and required dialysis (Table I).

In our study, AKI developed in 16 (45.7%) of 60 patients with INTERMACS 1, in 15 (42.9%) of 59 patients with INTERMACS 2, and in 4 (11.4%) of 19 patients with INTERMACS 3-4 (p>0.005).

A significant correlation was found between AKI status and age, preoperative serum creatine level, eGFR, and diabetes mellitus (DM) value (p=0.002, 0.0024, 0.0070, 0.0360, respectively). Statistically, the incidence of AKI development was found to be higher in patients with age, DM, creatinine level ≥1.2, and eGFR ≤60 ml/min/m^2.

In our study, 21 of 32 (31%) patients with preoperative creatinine above 1.2 mg/dl developed postoperative AKI. Fourteen patients (66.7%) were stage 1, 4 patients (44.4%) were stage 2, and 3 patients (60%) were stage 3 KDIGO.

When the patients included in the study were examined in terms of postoperative complications, it was found that the number of complications was significantly higher in AKI (+) patients (p=0.0365) (Figure 1). There was no significant incidence difference between stroke, gastrointestinal bleeding, thrombosis, and driveline site infection in those who developed AKI. However, a significant correlation was found between AKI status and right ventricular (RV) failure (p=0.0033), and RV failure developed in 10 (28.6%) of 35 patients who developed AKI.

After surgery, the duration of the patients' stay in the intensive care unit (ICU) and hospital (p=0.0072 and 0.0046, respectively) showed a significant difference in the AKI (+) and AKI (-) groups. The length of stay in the ICU was 12.3±10.5 days in the AKI (+) patient group, 25.9±9.9 days in the hospital, 7.7±2.88 days between the AKI (-) patient group, and 21.0±6.59 days in the hospital (Table I).

Table I. Patient characterics (n=138).

Characteristics	No AKI (n=103)	AKI (n=35)	*p*-value
Age (mean, SD), year	48.8±10.99	55.1±9.09	0.006
Sex, n (%)			
Male	88 (85.4%)	31 (88.6%)	0.630
Female	15 (14.6%)	4 (11.4%)	
Body mass index [kg/m²] SD	27.9±4.41	28.1±4.67	
Comorbidities, n (%)			
Hypertension	44 (42.7%)	16 (45.7%)	0.757
DM	38 (36.9%)	20 (57.1%)	**0.036**
INTERMACS 1 [n, %]	44 (42.7%)	16 (45.7%)	0.968
INTERMACS 2 [n, %]	44 (42.7%)	15 (42.9%)	
INTERMACS 3, 4 [n, %]	15 (14.6%)	4 (11.4%)	
Device type			
HeartMate 2 (Abbott,	12 (11.6%)	7 (20%9)	0.075
Inc., Pleasanton, CA, USA)	15 (14.5%)	6 (17.1%)	
HeartMate 3 (Thoratec Corp.	76 (73.8%)	22 (62.9)	
Pleasanton, CA, USA) HeartWare			
(Medtronic, Inc., Framingham,			
MA, USA)			
LOS ICU (d) SD	7.7±2.88)	12.3±10.51	**0.007**
LOS hospital (d) SD	21.0±6.59	25.9±9.92	**0.004**
RRT n (%)	1 (1%)	35 (100%)	**<.0001**

DM: Diabetes mellitus; INTERMACS: Interagency Registry for Mechanically Assisted Circulatory Support; ICU: Intensive care unit; LOS: Length of stay; RRT: Renal replacement therapy.

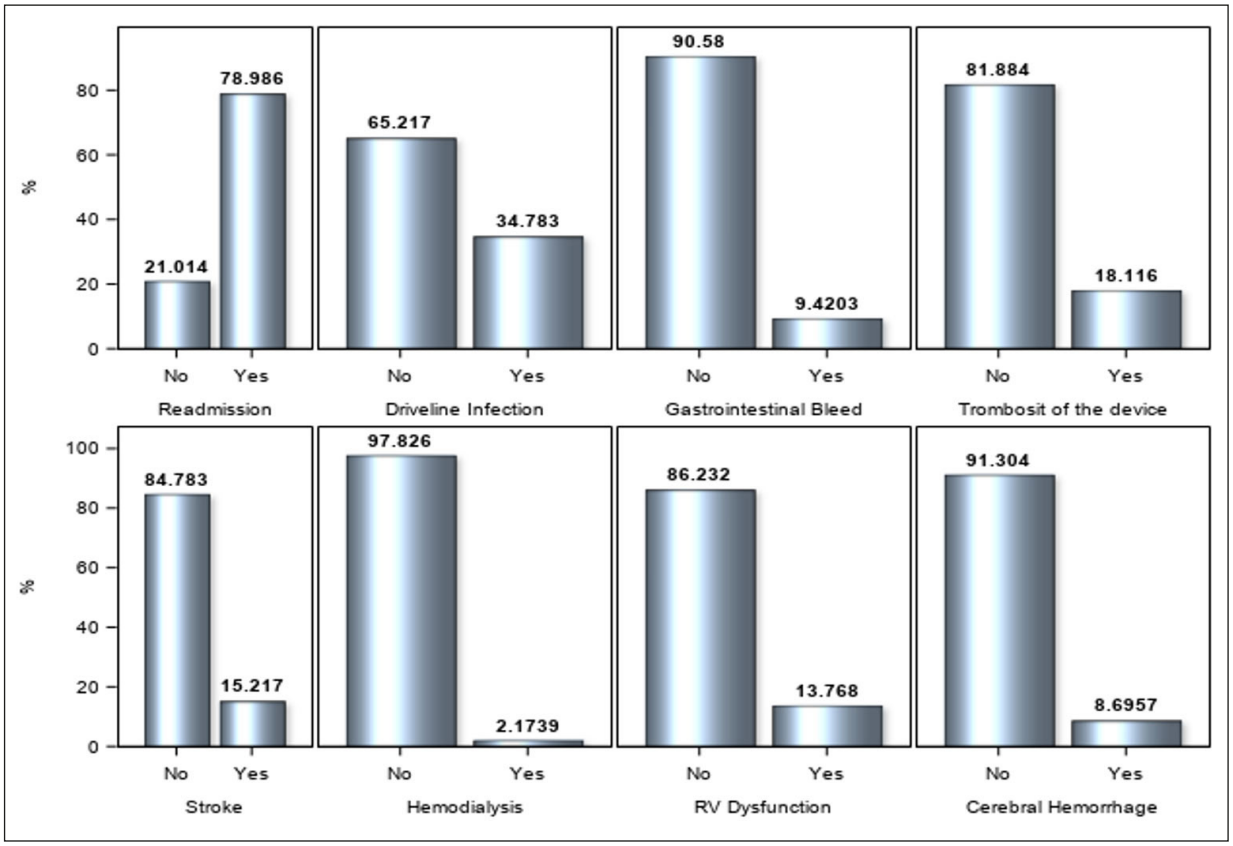

Figure 1. Complication After LVAD implantation.

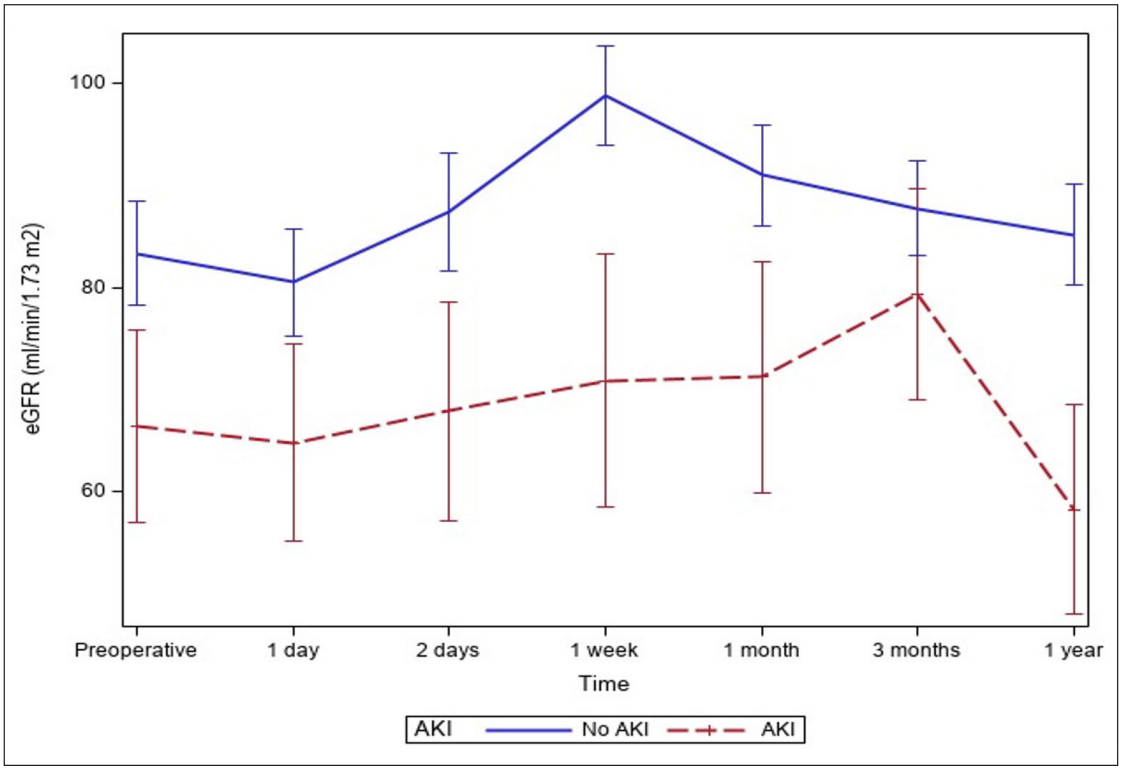

Figure 2. Average estimated glomerular filtration rate (eGFR) from before left ventricular assist device (LVAD) implantation to 12 months after implantation.

CPB duration was compared in AKI (+) and AKI (-) cases, and it was found that the pump duration was longer in the AKI (+) patient group than in the AKI (-) patient group, but there was no significant difference (p=0.06). While the mean duration was 90.3±33.5 minutes in the AKI (+) patient group, this time was 79.9±33.5 minutes in the AKI (-) patient group.

Preoperative, postoperative 1st day, 2nd day, 1st week, 1st month, and 1st year eGFR averages were found to show statistically significant differences between AKI (+) and AKI (-) patient groups (p=0.0004, 0.0030, 0.0025, 0.0001, 0.0030, 0.0001, respectively). eGFR values were significantly lower in patients with AKI (+) than in patients with AKI (-). The eGFR values of the AKI (+) patients were 66.3±27.64, 64.7±28.09, 67.9±31.35, 70.8±36.21, 71.2±31.05, and 58.2±25.00, respectively (Figure 2).

When the preoperative, postoperative 1st day, 2nd day, 1st week, 1st month, and 1st year BUN values of the patients with and without AKI were compared, the BUN values of the AKI (+) group were found to be significantly higher (p=0.0008, 0.0001, 0.0001, 0.0001, 0.0001, 0.0001, 0.0001) (Figure 3).

Preoperative, postoperative, 1st day, 2nd day, 1st week, 1st month, and 1st year creatinine levels of patients with and without AKI were compared. Those who had AKI (+) had significantly higher creatinine values (p=0.0012, 0.006, 0.0027, 0.001, 0.0001) (Figure 4).

The mortality rate showed significant differences between the AKI (+) and AKI (-) patient groups (p=0.0001). The 1st month and 1st year survival rates were 94.9% (131 of 138) and 82.6% (114 of 138), respectively. Among the patients who developed AKI, 13 (61%) were in KDIGO stage 1, 6 (66.7%) were in stage 2, and in stage 3, the mortality rate was 100%. Figure 5 illustrates the impact of AKI on LVAD implantation.

Discussion

In this study, we found that AKI developed in approximately one-quarter of the 138 patients. All patients who developed AKI needed RRT, while half of them required dialysis during their hospitalization. After discharge, dialysis was required in 3 (8.6%) patients. In previous studies[7,8], the incidence of AKI after LVAD was reported to be 11-45%.

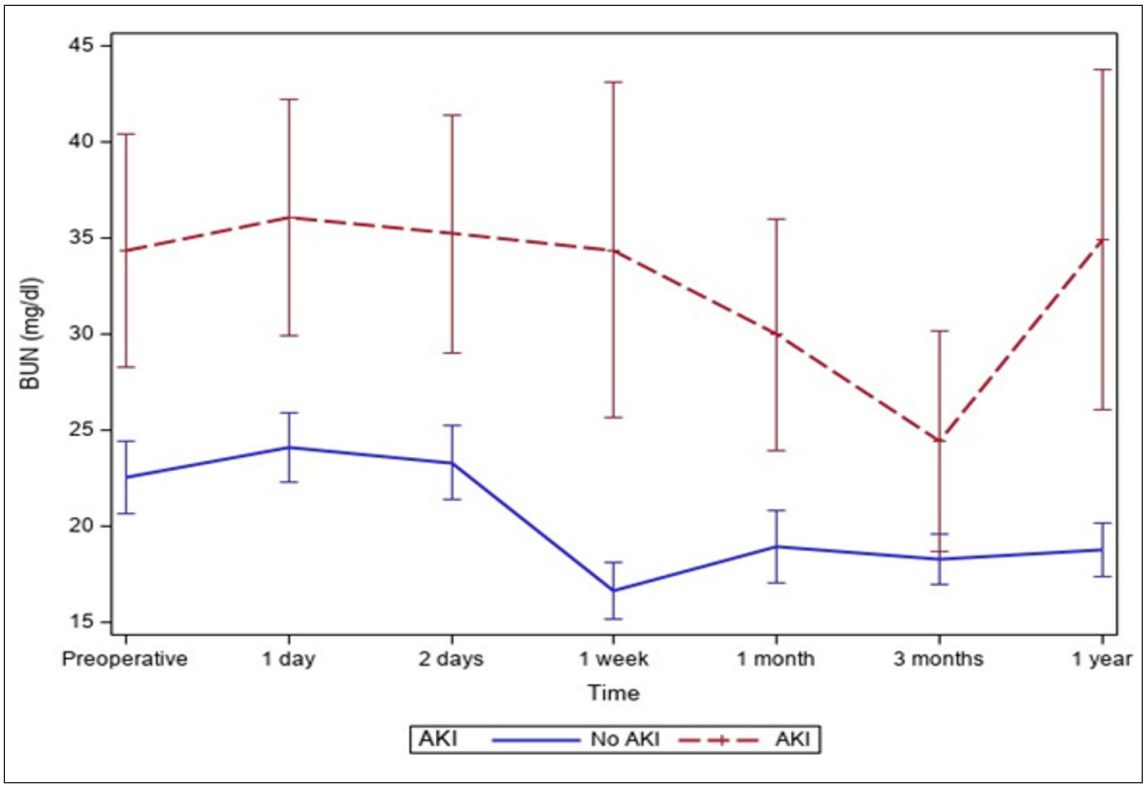

Figure 3. Average BUN from before left ventricular assist device (LVAD) implantation to 12 months after implantation.

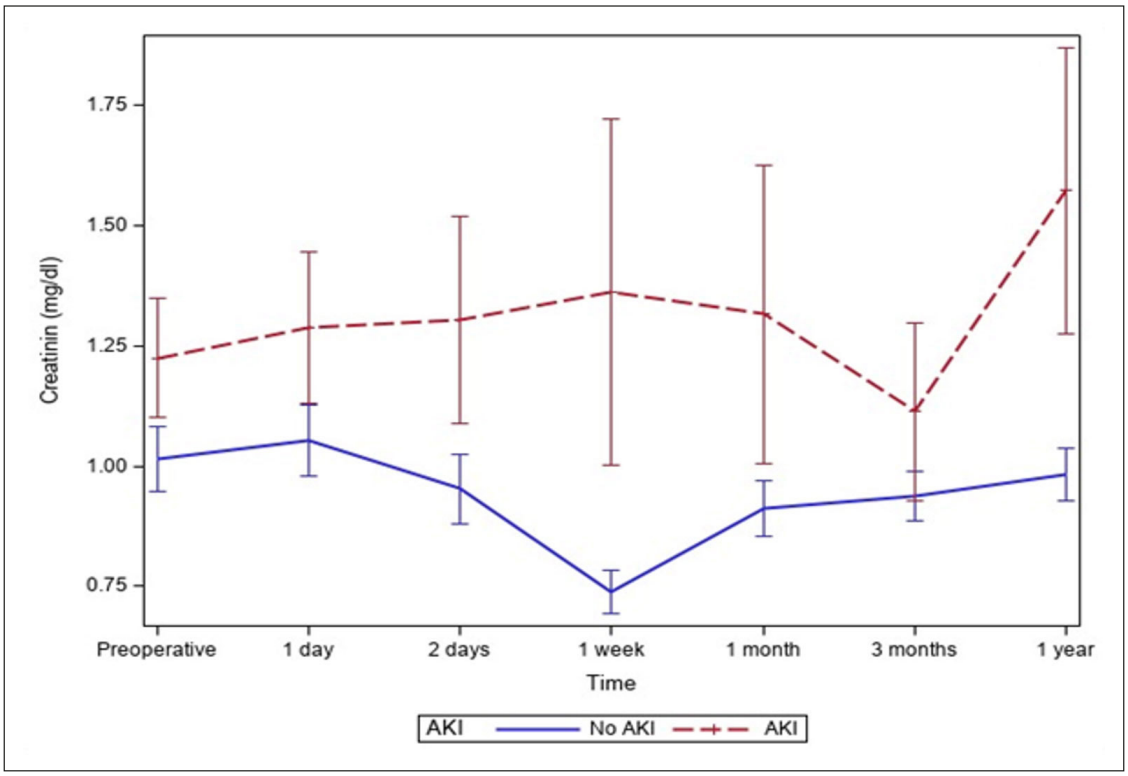

Figure 4. Average BUN from before left ventricular assist device (LVAD) implantation to 12 months after implantation.

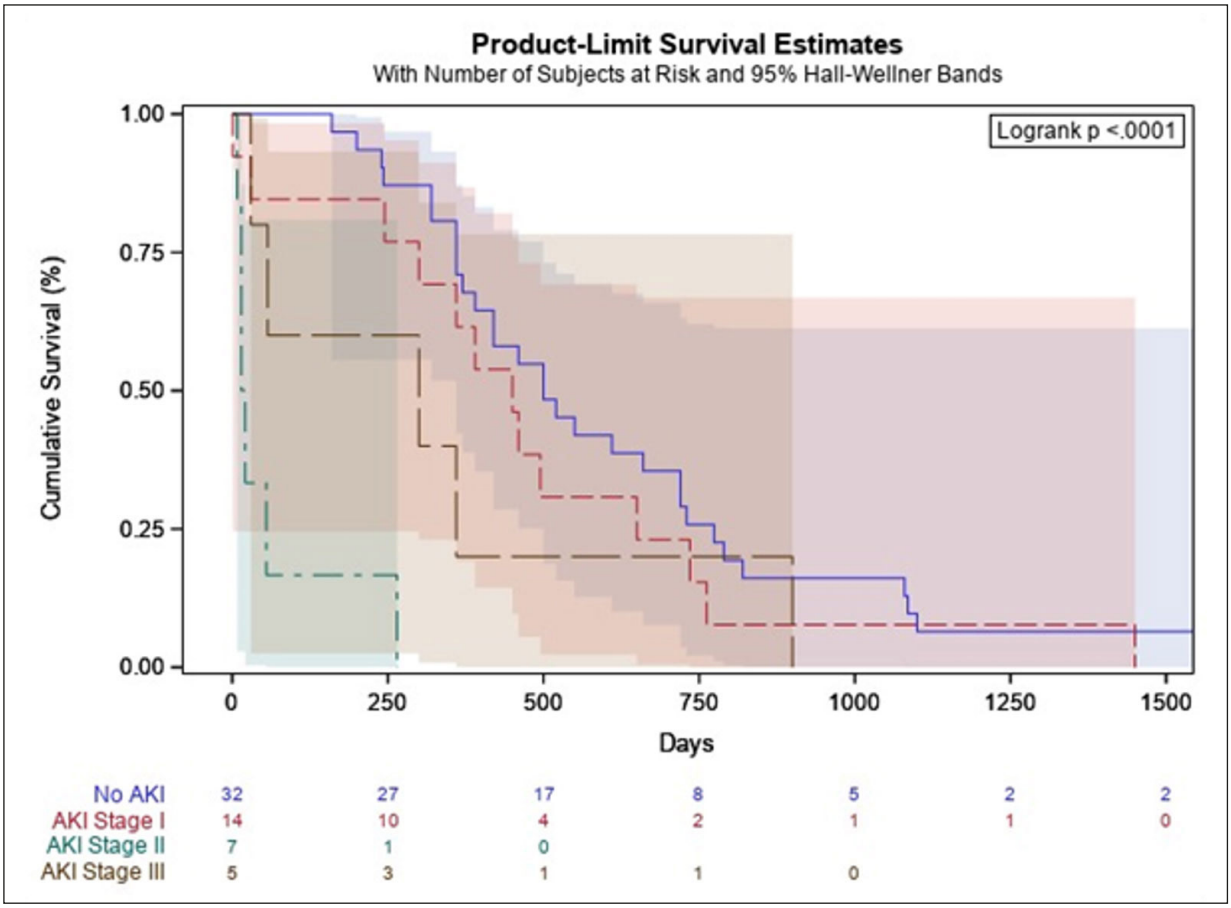

Figure 5. Kaplan-Meier curves for cumulative survival during after LVAD implantation.

The incidence of RRT intervals in patients with acute kidney injury after LVAD ranges from 11% to 33%.

In a meta-analysis[9] of 63,663 patients, the rate of development of severe AKI requiring RRT after LVAD was 37% and 13%, respectively.

Renal dysfunction due to decreased forward flow or high back pressure is an expected outcome with progressive heart failure. Because LVAD implantation improves cardiac output and tissue perfusion by increasing forward flow, improvement in renal function after LVAD implantation is an expected outcome. Moreover, neurohormonal activation has been shown[10] to decrease particularly atrial natriuretic peptide, aldosterone, renin arginine, and vasopressin. However, Brisco et al[7] showed that eGFR levels initially improved after LVAD implantation in approximately half of the patients. This improvement lasted for only 1 month, after which eGFR values decreased again. Generally, these studies[7] show that renal functions that improve immediately after LVAD implantation cannot maintain this function over a longer period.

One of the mechanisms involved in the worsening of renal function 1 month after LVAD implantation is associated with RV dysfunction. RV dysfunction has been attributed[11] to increased RV preload and decreased contractility to cope with the increased cardiac output after LVAD. In addition, previous studies[12] have shown that as a result of an increase in RV filling pressures that is not proportional to the left ventricular filling pressure, AKI may develop due to hypotension and to increased central venous pressure, decreased left ventricular filling, low device flow, and worsening of systemic perfusion. In our AKI (+) patients, the rate of development of complications was higher, especially right ventricular failure (28.6%), compared with those who did not develop complications. In the group with KDIGO stage 3, right ventricular failure developed in 4 (80%) patients. When RV insufficiency develops, treatments to correct hemodynamics to reduce RV afterload may prevent worsening renal function[13].

In a study[7] conducted on 3,363 patients, it was concluded that pre-implant INTERMACS, an eGFR of 60±35 ml/min/1.73 m^2, and a mean serum creatinine level of 1.4 mg/dl were important indicators of renal function. It has been reported[5,14] that each 1 mg/dl increase in serum creatinine concentration doubles the risk of death.

In the study by Yoshioka et al[15] it was reported that cases with INTERMACS scores of 1 and 2 had a higher risk of acute kidney injury. This finding is confirmed by our study. The incidence of developing AKI was increased approximately 4-fold in our patients with INTERMACS scores of 1 and 2 compared with those with INTERMACS scores of 3 and 4.

In our study, the incidence of AKI development was found to be higher in patients with DM, age, preoperative creatinine level ≥1.2 and eGFR ≤60 ml/min/m^2 as important risk factors for AKI development following LVAD placement.

In a study[4] that analyzed 48 parameters and analyzed a single-center multivariate in an observational cohort of 131 subjects, there was an improvement in eGFR at 1 month after LVAD in young, non-DM, and subjects with low eGFR.

In our study, there was an increase in creatinine values on the 1st and 2nd day, especially in the 1st-week creatinine (p<0.0001), compared with preoperative creatinine values in patients with AKI (p<0.0001).

Iwashima et al[16] reported that the 2-week eGFR after implantation was a strong predictor of mortality and morbidity. Preoperative eGFR values are consistent with 1st-week and 1st-month values in patients with AKI. When the eGFR values on 1st and 2nd day, and 1st week immediately after LVAD implantation are examined, there were no or very few studies in the literature, which included cases with low eGFR. In the light of the data we obtained, we think that postoperative 2nd-day and 1st-week eGFR values after LVAD are early predictors of AKI development.

More complications were detected in AKI (+) cases, and in these cases, the duration of ICU (12.3±10.5) and hospital stay (25.9±9.9) were significantly longer than those who did not develop AKI. This is consistent with the studies in the literature[17].

Limitations

Limitations of our study include the fact that it was a retrospective study at a single center and that the number of patients decreased because they were unable to meet the criteria we sought in all patients. If the research is conducted in larger series, the results we obtained can be confirmed.

Conclusions

The development of AKI after LVAD is an important complication with high mortality requiring RRT treatment or even dialysis. In the early stages of a procedure, it is important to take into account the factors that contribute to the development and severity of AKI, such as DM, age, preoperative creatinine level 1.22, and eGFR 60 ml/min/m^2, and to develop a good preoperative approach.

The inclusion of biomarkers for earlier identification of renal dysfunction, along with eGFR, BUN, and creatinine values, will allow the early detection of renal dysfunction and reduce mortality and morbidity.

ORCID ID
Emel Gündüz: 0000-0002-0306-9770

Conflict of Interest
The authors declare that they have no conflict of interests.

Ethics Approval
This study was approved by the Akdeniz University Non-interventional Ethical Board.

Informed Consent
All patients provided written informed consent.

Funding
No funding was obtained for this study.

Availability of Data and Materials
Data are available upon request to the corresponding author.

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