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Incidence, Predictors, and Prognostic Value of Acute Kidney Injury Among Patients Undergoing Left Atrial Appendage Closure

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ABSTRACT

OBJECTIVES The aims of this registry were to determine the incidence, predictors, and prognostic value of periprocedural acute kidney injury (AKI) after left atrial appendage closure (LAAC).

BACKGROUND No data exist on the occurrence of AKI after LAAC.

METHODS A total of 355 patients undergoing LAAC were included in the study. AKI was defined as an absolute or a relative increase in serum creatinine of >0.3 mg/dl or ≥50%, respectively, after the procedure or the need for hemodialysis during index hospitalization.

RESULTS The incidence of AKI was 9%, and patients with worse baseline renal function were at higher risk for developing AKI (odds ratio: 1.32; 95% confidence interval [CI]: 1.09 to 1.61; p = 0.004 for each 10 ml/min decrease in glomerular filtration rate). In-hospital bleeding events occurred more frequently in the AKI group (5.3% vs. 15.6%; p = 0.037). After a median follow-up period of 18 months, patients in the AKI group had higher mortality (hazard ratio [HR]: 2.59; 95% CI: 1.36 to 4.92; p = 0.004), more embolic events (HR: 6.14; 95% CI: 2.23 to 16.92; p = 0.001) and major bleeding events (HR: 2.36; 95% CI: 0.89 to 6.24; p = 0.083). The occurrence of AKI was an independent predictor of midterm mortality (HR: 2.00; 95% CI: 1.02 to 3.91; p = 0.044).

CONCLUSIONS The occurrence of AKI was relatively frequent following LAAC, and patients with lower renal glomerular filtration rates were at high risk for developing this complication. AKI identified a group of patients with worse midterm outcomes, highlighting the importance of further preventive strategies in this population.
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Acute kidney injury (AKI) is a common complication after invasive cardiac procedures characterized by a sudden deterioration of renal function, frequently linked to contrast media administration. The association between AKI and percutaneous coronary intervention (PCI) has been extensively studied, affecting between 2% and 20% of the study population (1-3), depending on the definition of AKI and baseline characteristics. Despite small declines in kidney function, the occurrence of AKI is associated with short- and long-term adverse clinical outcomes, including in-hospital morbidity, longer hospitalizations, progression to chronic kidney disease (CKD), and increased mortality (3,4). In other percutaneous cardiac interventions, such as transcatheter aortic valve replacement (TAVR), cardiac resynchronization therapy, and mitral valve repair, the incidence and negative impact of AKI on outcomes have been also established (5-9).

SEE PAGE 1084

Left atrial appendage closure (LAAC) has emerged as an alternative percutaneous treatment for stroke prevention in patients with nonvalvular atrial fibrillation at high risk for bleeding (10,11). Patients undergoing LAAC are commonly old and have a high prevalence of diabetes and renal dysfunction (12), which are well-known factors associated with the occurrence of AKI (3,4). Thus, this population is at high risk for AKI and major adverse cardiovascular events, even if the procedure can be performed with a low volume of contrast administration. In addition, patients with end-stage CKD had lower overall survival after LAAC compared with those with better glomerular filtration rates (13). Thus, trying to avoid potential deterioration of renal function in patients with CKD may become an important strategy to improve clinical outcomes in these patients. However, no data exist on the occurrence, predictors, and prognostic value of AKI following LAAC. Therefore, the objective of this study was to determine the incidence, predictors, clinical course, and prognostic value of AKI following LAAC.

METHODS

STUDY POPULATION AND PROCEDURE. This multicenter study collected individual data from a total of 402 consecutive patients with atrial fibrillation, who underwent LAAC at 6 centers in Spain and Canada. Patients without baseline (within 7 days) or postprocedural (within 24 to 48 h) creatinine determination (n = 34) and those receiving regular dialysis (n = 11) were excluded from the analysis. In addition, 1 patient who died 6 h after the procedure because of intracranial bleeding without creatinine determination post-LAAC and 1 patient lost to follow-up were also excluded. The final study population was 355 patients. Demographics, baseline characteristics, indications for LAAC, CHA_2DS_2-VASc (congestive heart failure, hypertension, age ≥75 years, diabetes mellitus, prior stroke or transient ischemic attack, vascular disease, age 65 to 74 years, female) and HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition, Labile international normalized ratio, Elderly [>65 years], Drugs/alcohol concomitantly) scores, antithrombotic medications, procedural details, periprocedural adverse events, and clinical and echocardiographic follow-up results were prospectively collected in a dedicated database at each participating center, but data were retrospectively analyzed. All patients had contraindications to anticoagulation therapy or were at high risk for major bleeding and an estimated risk for annual stroke of ≥2% as determined by a $CHADS_2$ score ≥1 or a CHA_2DS_2-VASc score ≥2. LAAC was performed as previously reported (12,14), and the approach and device used were left at the discretion of the operators. All procedures but 1 were guided by transesophageal echocardiography and fluoroscopy. If LAAC was performed in combination with other percutaneous interventions, that was also reported. AKI prevention protocols were carried out according to local institutional policies. In summary, all patients with baseline CKD received intravenous hydration before and after the procedure. The use of other prophylactic treatment (*N*-acetylcysteine, intravenous bicarbonate) and the interruption of nephrotoxic drugs prior to the procedure were left at the discretion of the team performing the procedure. No patients received statins in addition to their current medications as a supplementary preventive strategy for AKI. Creatinine was measured at baseline and daily after the procedure until hospital discharge. Periprocedural complications as well as the need for hemodialysis were noted during the index hospitalization. Patients provided informed consent for the procedure and to have their clinical, procedural, and outcome data collected in a database in accordance with the ethics committee of each participating center. Standardized case report forms were used by all participating centers and after quality controls were sent to the coordinating center.

ABBREVIATIONS AND ACRONYMS

AKI = acute kidney injury
CI = confidence interval
CKD = chronic kidney disease
eGFR = estimated glomerular filtration rate
IQR = interquartile range
LAA = left atrial appendage
LAAC = left atrial appendage closure
PCI = percutaneous coronary intervention
TAVR = transcatheter aortic valve replacement

TABLE 1 Baseline Characteristics of the Study Population (N = 355) According to the Occurrence of Acute Kidney Injury

	All (N = 355)	Acute Kidney Injury		p Value
		No (n = 323)	Yes (n = 32)	
Baseline variables				
Age, yrs	76 (69-80)	76 (69-80)	73 (67-82)	0.396
Female	146 (41.1)	137 (42.4)	9 (28.1)	0.117
BMI, kg/m^2	27.7 ± 4.8	27.7 ± 4.8	27.5 ± 4.7	0.831
Diabetes	118 (33.2)	104 (32.2)	14 (43.8)	0.186
Hypertension	302 (85.1)	274 (84.8)	28 (87.5)	0.686
Atrial fibrillation type				0.498
Paroxysmal	112 (31.5)	100 (31.0)	12 (37.5)	
Persistent	32 (9.0)	28 (8.7)	4 (12.5)	
Permanent	211 (59.4)	195 (60.4)	16 (50.0)	
Prior stroke	104 (29.3)	94 (29.1)	10 (31.2)	0.799
Prior intracranial bleeding	114 (32.2)	108 (33.4)	6 (19.4)	0.109
Prior vascular disease	91 (25.6)	78 (24.1)	13 (40.6)	0.042
Coronary artery disease	120 (33.8)	105 (32.5)	15 (46.9)	0.101
Prior myocardial infarction	68 (21.9)	60 (21.1)	8 (29.6)	0.307
Prior major bleeding	265 (74.6)	243 (75.2)	22 (68.8)	0.421
eGFR, ml/min	65.2 (46.8-85.8)	66.3 (48.9-86.1)	50.7 (25.0-74.8)	0.012
Chronic kidney disease stage				0.001
1 and 2	199 (56.1)	185 (57.3)	14 (43.8)	
3a	76 (21.4)	72 (22.3)	4 (12.5)	
3b	51 (14.4)	4 (12.5)	47 (14.6)	
4 and 5	29 (8.2)	19 (5.9)	10 (31.2)	
$CHADS_2$ score	3 (2-4)	3 (2-4)	3 (2-4)	0.827
$CHADS_2$ score ≥2	305 (85.9)	278 (86.1)	27 (84.4)	0.793
CHA_2DS_2-VASc score	4 (3-5)	4 (3-5)	5 (3-5)	0.913
HAS-BLED score	4 (3-4)	4 (3-4)	3 (2-4)	0.337
Echocardiographic data				
LVEF ≤40%	29 (8.2)	24 (7.5)	5 (15.6)	0.106
LAA diameter by TEE	18 (16-21)	19 (16-21)	17 (16-22)	0.653
LAA length by TEE	26 (22-31)	27 (22-31)	26 (20-27)	0.134

Values are median (interquartile range), n (%), or mean ± SD.

BMI = body mass index; eGFR = estimated glomerular filtration rate; LAA = left atrial appendage; LVEF = left ventricular ejection fraction; TEE = transesophageal echocardiography.

DEFINITIONS. The estimated glomerular filtration rate (eGFR) was calculated on the basis of the Chronic Kidney Disease Epidemiology Collaboration equation before the procedure (15). AKI was defined according to the Acute Kidney Injury Network criteria as an absolute increase in serum creatinine of ≥0.3 mg/dl or a relative increase of ≥50% from baseline to 48 h after the procedure (16). The severity of AKI was further classified in 3 stages: stage 1, increase in serum creatinine of 1.50 to 1.99 times compared with baseline; stage 2, increase of 2.00 to 2.99 times compared with baseline; and stage 3, increase ≥3.00 times or serum creatinine >4.0 mg/dl with an acute increase of at least 0.5 mg/dl or need for renal replacement therapy. Embolic events were considered as either clinical ischemic stroke or systemic embolism. Bleeding events were classified according to the Bleeding Academic Research Consortium definition (17). Complete LAAC was defined as a stable position of the device in the left atrial appendage (LAA) and the absence of a significant (>3 mm) leak on last transesophageal echocardiography.

FOLLOW-UP. Clinical follow-up was carried out at 30 days, 12 months, and yearly afterward. Several sources of information were used to investigate outcomes: outpatient clinical visits; phone contacts with patients, families, or physicians; and review of medical records to determine the cause of death when necessary. Midterm outcomes included overall and cardiac mortality, bleeding events, cerebrovascular (including stroke or transient ischemic attack) events, systemic embolism, and any cause of unplanned hospital readmissions. Major adverse cardiac events were defined as the composite of all-cause mortality, embolic event (stroke or systemic embolism), or major bleeding event (type ≥3 of Bleeding Academic Research Consortium definition). Transesophageal echocardiography at follow-up was performed according to the center protocol to evaluate the presence of leak, device thrombosis, or dislodgment. Echocardiographic examinations and renal function were recorded at the last follow-up.

STATISTICAL ANALYSIS. Qualitative variables are expressed as percentages and quantitative variables as mean ± SD or median (interquartile range [IQR]). The normality distribution for continuous data was examined using the Shapiro-Wilk test. The Student's *t*-test or Wilcoxon rank sum test was used to compare numeric variables and the chi-square or Fisher exact tests for qualitative variables. Variables with p values <0.10 in the univariate analysis were entered into a logistic regression analysis to determine the predictive factors of AKI. Freedom from all-cause mortality, cardiac mortality, and major adverse cardiac event curves were calculated using the Kaplan-Meier method, and comparison between groups was performed using the log-rank test. Patients missing follow-up were considered at risk until the date of last contact follow-up, at which point they were censored. Predictors of cumulative death were analyzed using Cox regression analysis. The proportional hazard assumption was evaluated by means of log-minus-log survival plots. Absolute change in renal function was calculated as eGFR at last follow-up minus eGFR at baseline. Linear regression analysis was performed to assess changes in eGFR during follow-up adjusted by eGFR at baseline. Significant deterioration in renal function at follow-up was considered as a decrease of >25% in eGFR compared with baseline.

Differences were considered statistically significant at p values <0.05. All analyses were performed using SPSS for Windows version 24.0 (SPSS, Chicago, Illinois) and Stata version 13.0 (StataCorp, College Station, Texas).

RESULTS

Baseline clinical and echocardiographic characteristics of the study population are shown in Table 1. The median age was 76 years (IQR: 69 to 80 years), with high prevalence rates of hypertension (85%), diabetes (33%), prior stroke (29%), and vascular disease (26%), leading to median $CHADS_2$ and CHA_2DS_2-VASc scores of 3 (IQR: 2 to 4) and 4 (IQR: 3 to 5), respectively. Three-quarters of the patients had histories of major bleeding and one-third of intracranial bleeding. No patients underwent examinations with contrast administration 1 week before LAAC. The procedure was successful in 344 patients (97%), with complete occlusion of the appendage in 313 (91%). Procedural characteristics and in-hospital outcomes of the global population and according to the occurrence of AKI are depicted in Table 2. The Amplatzer cardiac plug and Amulet device (Abbott Vascular, Abbot Park, Illinois) were the most common devices used (78%), and 9% of the procedures were performed in combination with other interventions: atrial septal defect or patent foramen ovale closure (n = 20), TAVR (n = 4), PCI (n = 4), MitraClip placement (Abbott Vascular) (n = 3), and ventricular septal defect closure (n = 1).

INCIDENCE, PREDICTIVE FACTORS, AND IN-HOSPITAL IMPACT OF AKI. Post-procedural AKI occurred in 32 patients (9.0%): 7.0% stage 1, 1.1% stage 2, and 0.8% stage 3. Two patients (0.6%) needed renal replacement therapy after the procedure and 1 continued during follow-up. The changes in eGFR in the global population after the procedure are shown in Figure 1. Patients with AKI had a higher incidence of prior vascular disease (p = 0.042) and lower baseline eGFR (p = 0.012) and tended to have a lower left ventricular ejection fraction (p = 0.106) (Table 1). Median contrast volume administered during the procedure was numerically lower in patients with AKI (150 ml vs. 138 ml; p = 0.099), with similar ratio between contrast volume and eGFR (p = 0.473). Success rate and complete occlusion of the LAA were similar between groups. Patients with AKI had more bleeding events requiring blood transfusion during the index hospitalization (p = 0.056), with longer hospitalization length (Table 2). Otherwise, there were no differences between groups in terms of cerebrovascular events and in-hospital mortality, with a small number of events. In multivariate analysis, the only independent predictor of AKI following LAAC was a poorer baseline eGFR (odds ratio: 1.32; 95% confidence interval [CI]: 1.09 to 1.61; p = 0.004) (Table 3).

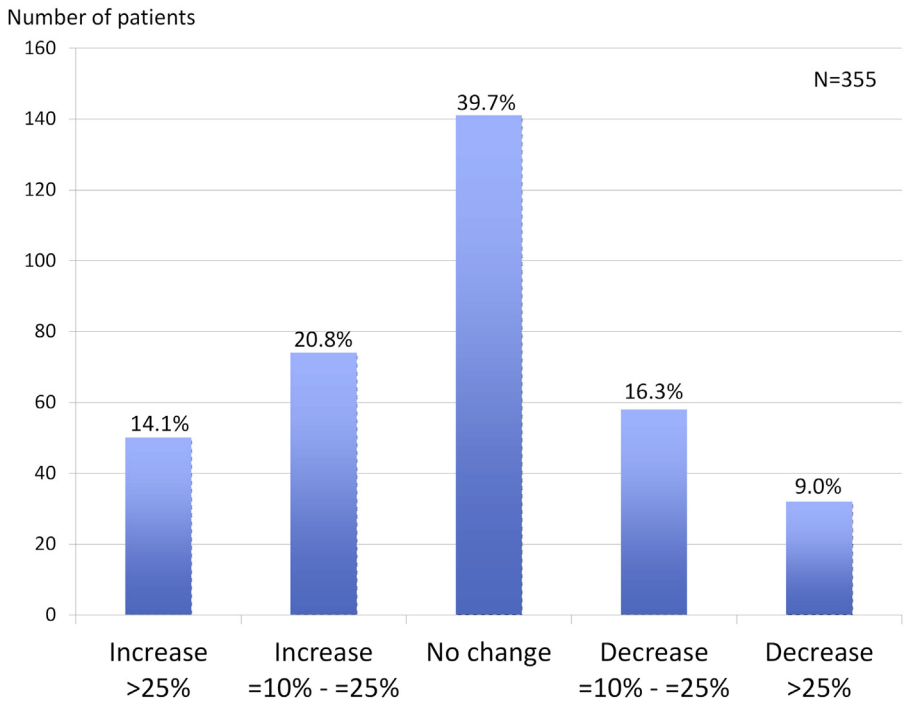
TABLE 2 Procedural Characteristics and In-Hospital Outcomes According to the Occurrence of Acute Kidney Injury

	All (N = 355)	Acute Kidney Injury		p Value
		No (n = 323)	Yes (n = 32)	
Procedural data				
Device				0.414
ACP/Amulet	273 (77.6)	246 (76.9)	27 (84.4)	
Watchman	65 (18.5)	60 (18.8)	5 (15.6)	
Other	14 (4.4)	14 (4.4)	0 (0)	
Device size, mm				0.865
≤18	29 (8.6)	26 (8.4)	3 (10.3)	
20–21	47 (13.9)	43 (13.9)	4 (13.8)	
22	69 (20.4)	62 (20.0)	7 (24.1)	
24	55 (16.2)	50 (16.1)	5 (17.2)	
25–26	55 (16.2)	53 (17.1)	2 (6.9)	
27–28	50 (14.7)	46 (14.8)	4 (13.8)	
≥30	34 (10.0)	30 (9.7)	4 (13.8)	
Fluoroscopy time, min	18 (13–36)	18 (13–36)	25 (14–36)	0.257
Contrast volume, ml	150 (102–228)	150 (104–230)	138 (80–185)	0.099
Ratio of contrast volume to eGFR	2.33 (1.49–3.66)	2.34 (1.49–3.61)	2.26 (1.43–5.24)	0.473
Combined procedure	32 (9.0)	29 (9.0)	3 (9.4)	0.940
Procedural success	344 (96.9)	313 (96.9)	31 (96.9)	0.652
Complete occlusion	313 (91.0)	284 (90.7)	29 (93.5)	0.454
In-hospital complications				
Procedural complication (any)	26 (7.3)	22 (6.8)	4 (12.5)	0.239
Pericardial effusion requiring treatment	7 (2.0)	5 (1.5)	2 (6.2)	0.124
Vascular complication	11 (3.1)	9 (2.8)	2 (6.5)	0.261
Embolic event (cerebrovascular and systemic)	6 (1.7)	5 (1.5)	1 (3.1)	0.435
Cerebrovascular event	5 (1.4)	4 (1.2)	1 (3.1)	0.378
Stroke	3 (0.8)	2 (0.6)	1 (3.1)	0.247
Systemic embolism	1 (0.3)	1 (0.3)	0	—
TIA	2 (0.6)	2 (0.6)	0	0.828
Any bleeding	22 (6.2)	17 (5.3)	5 (15.6)	0.037
Bleeding requiring red-cell transfusion	17 (4.8)	13 (4.0)	4 (12.5)	0.056
In-hospital mortality	2 (0.6)	1 (0.3)	1 (3.1)	0.172
30-day mortality	4 (1.1)	2 (0.6)	2 (6.2)	0.042
MACE	32 (9.0)	25 (7.7)	7 (21.9)	0.019
Treatment at hospital discharge				0.633
None	15 (4.2)	13 (4.0)	2 (6.5)	
Single antiplatelet therapy	60 (17.0)	53 (16.5)	7 (22.6)	
Dual antiplatelet therapy	242 (68.2)	222 (69.2)	20 (64.5)	
Warfarin	15 (4.2)	15 (4.7)	0 (0)	
NOAC	20 (5.6)	18 (5.6)	2 (6.5)	
Hospitalization length, days	1.5 (1.0–3.0)	1.5 (1.0–3.0)	4.2 (1.3–7.7)	0.001

Values are n (%) or median (interquartile range).

ACP = Amplatzer Cardiac Plug; eGFR = estimated glomerular filtration rate; MACE = major adverse cardiac event(s); NOAC = novel oral anticoagulant; TIA = transient ischemic attack.

FIGURE 1 Changes in Estimated Glomerular Filtration Rate After Left Atrial Appendage Closure



Percentages of patients with improvement, no change, or worsening estimated glomerular filtration rate following left atrial appendage closure.

MIDTERM OUTCOMES. At a median of 18 months (IQR: 6 to 30 months), clinical follow-up was available in 352 patients (99%), and a total of 54 patients had died, 9 (17%) from cardiovascular death. Causes of death in the global population are depicted in Figure 2. In the AKI group, all-cause mortality was 33% and 37%, compared with 8% and 14% in the non-AKI group (log-rank p = 0.003) at 1- and 2-year follow-up, respectively (Figure 3A, Table 4). The rate of cardiac mortality was similar between the groups (Figure 3B). Patients with post-procedural AKI were more likely to have embolic events (hazard ratio: 6.14; 95% CI: 2.23 to 16.92; p = 0.001) during follow-up and had a tendency toward more major bleeding events (HR: 2.36; 95% CI: 0.89 to 6.24; p = 0.083) compared with those without AKI. Consequently, the combined endpoint of major adverse cardiac events (death, embolic, or bleeding event) was higher in the AKI group (Figure 3C, Table 4). Unplanned readmission rates were also higher in the follow-up period (Figure 3D). The occurrence of post-procedural AKI was identified as an independent predictor of mortality at follow-up (HR: 2.00; 95% CI: 1.02 to 3.90; p = 0.044) (Table 5). Among patients with AKI stage 2 or 3 (n = 7), 4 patients had died within 1 year, and 3 were alive after 2-year follow-up.

Among patients (80%) with renal function assessment at follow-up, those with AKI exhibited a change in eGFR of −11.4 (IQR: −18.5 to 3.05) at follow-up compared with baseline, whereas patients with no AKI had no change in eGFR (+1.4; IQR: −8.0 to 13.1), independent of baseline eGFR (p = 0.005) (Figure 4A). More than 50% of patients in the AKI group had significant deterioration of renal function (decrease of eGFR >25%) at follow-up compared with 17% of patients without AKI (p = 0.001) (Figure 4B).

TABLE 3 Predictors of Acute Kidney Injury

	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	p Value	OR (95% CI)	p Value
Prior vascular disease	2.46 (1.03–5.89)	0.042	1.97 (0.78–4.95)	0.149
eGFR, ml/min*	1.15 (1.01–1.32)	0.046	1.32 (1.09–1.61)	0.004
LVEF <40%	2.31 (0.82–6.53)	0.106	1.07 (0.28–4.13)	0.924
Bleeding	3.33 (1.14–9.74)	0.037	2.44 (0.68–8.71)	0.169

*For each decrease of 10 ml/min.
CI = confidence interval; OR = odds ratio; other abbreviations as in Table 1.

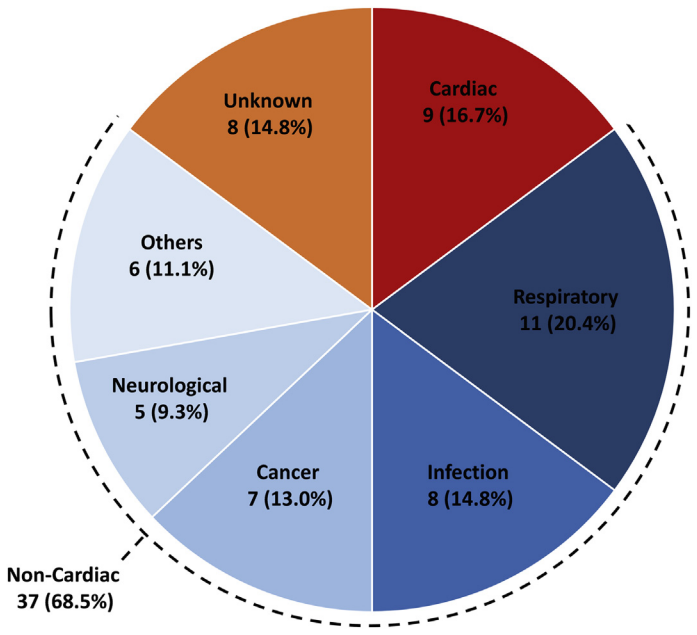
DISCUSSION

The main findings of the present study are as follows: 1) AKI occurred in 9% of the patients undergoing LAAC; 2) low baseline renal function was considered a major factor for development of this complication; and 3) patients who experienced AKI had worse clinical outcomes during follow-up, identifying a factor for poor prognosis in this population.

The global incidence of AKI, as defined according to the Acute Kidney Injury Network classification, was not infrequent (~10%) in our population undergoing LAAC, and severe renal deterioration (AKI stage 2 or 3) occurred in about 1%. Although AKI has not been previously reported after LAAC, this complication is a well-known adverse event after other percutaneous cardiac interventions, and its incidence is likely related to patient comorbidities and hemodynamic status as well as procedural characteristics (contrast media, preventive strategies, and so on). The incidence of AKI has been extensively evaluated after PCI, ranging from 3% in patients with low prevalence of risk factors to up to 20% in certain prone circumstances (1-3). This wide variability depending on clinical presentation and baseline characteristics reflected the multifactorial etiology of this complication. Also, different definitions of AKI may influence this wide range. Two recent studies, which adopted the Acute Kidney Injury Network definition, reported a similar incidence of AKI (~10%) in post-PCI patients (3,18). Our AKI incidence was also about 10%, suggesting that several factors may have influenced this relatively high incidence, such as patient comorbidities and contrast media used. However, patients undergoing TAVR had a higher incidence (~20%) of AKI, even with the same definition (7). TAVR populations are usually older and sicker, and the procedures may be associated with more hemodynamic instability. These differences could explain the higher incidence of AKI in TAVR compared with our study in patients undergoing LAAC. LAAC is usually performed in patients with a high prevalence of comorbidities but is typically considered a stable procedure. Furthermore, patients might have better tolerance to renal protection with fluids than TAVR patients. Thus, it is plausible that the incidence of AKI is between the lowest of the PCI and the highest of the TAVR procedures.

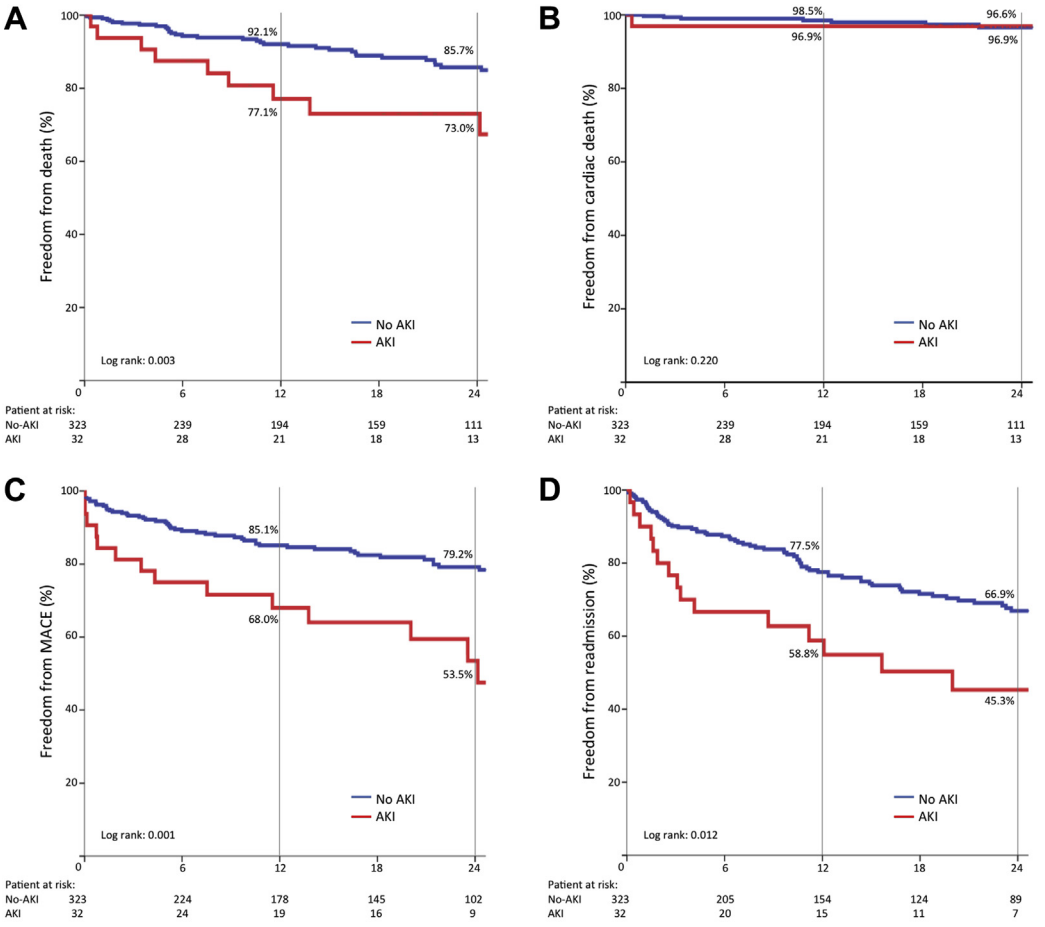
The factors associated with AKI in this population were consistent with previous studies in other percutaneous cardiac interventions. Prior vascular disease, CKD, left ventricular dysfunction, and bleeding requiring blood transfusion have been previously reported as predictors of AKI (19). After multivariate analysis, poorer baseline renal function was the only independent predictor of AKI in the present study. The association between renal dysfunction and AKI after invasive procedures is well known (4,7,20). Thus, baseline renal function should be previously analyzed and carefully monitored in patients undergoing LAAC, especially in those with CKD. In addition, intraoperative renal insults should be avoided. Mechanisms of AKI could not be established by the present study design, but this complication is likely to be multifactorial, including baseline characteristics predisposition, hemodynamic status, and procedural factors such as contrast media administration, microemboli associated with the device manipulation in the LAA, general anesthesia, procedural complications, or red blood cell transfusion. Most of these factors are general to percutaneous vascular procedures and not exclusive to LAAC, and as in other interventions, efforts should be made to avoid unstable situations, preventable blood transfusions, and catheter or device manipulations that prolong the procedure unnecessarily. Importantly, 9% of our procedures were performed in combination with other interventions, leading to longer procedures and more use of contrast media (especially if performed after TAVR or PCI). This

FIGURE 2 Causes of Death After Left Atrial Appendage Closure



Percentages of patients with cardiovascular and noncardiovascular death after left atrial appendage closure

FIGURE 3 Acute Kidney Injury Following Left Atrial Appendage Closure and Clinical Outcomes



Kaplan-Meier curves up to 2-year follow-up for **(A)** all-cause mortality, **(B)** cardiac mortality, **(C)** major adverse cardiac events (MACE), and **(D)** readmission, according to the occurrence of acute kidney injury (AKI).

TABLE 4 Midterm Outcomes According to the Occurrence of Acute Kidney Injury

	Acute Kidney Injury			
	No (n = 323)	Yes (n = 32)	HR (95% CI)	p Value
Mortality	43 (13.3)	12 (37.5)	2.59 (1.36–4.92)	0.004
Cardiac mortality	7 (2.2)	2 (6.3)	2.58 (0.54–12.45)	0.237
Any embolic event	10 (3.1)	6 (18.8)	6.14 (2.23–16.92)	0.001
Stroke	9 (2.8)	5 (15.6)	5.71 (1.91–17.06)	0.002
Systemic embolism	1 (0.3)	1 (3.1)	–	
Bleeding (BARC type ≥2)	50 (15.9)	7 (22.6)	1.43 (0.65–3.16)	0.372
Major bleeding (BARC type ≥3)	22 (7.0)	5 (16.1)	2.36 (0.89–6.24)	0.083
Unplanned readmission	94 (30.4)	17 (53.1)	1.95 (1.14–3.31)	0.014
MACE (death, stroke)	48 (14.9)	15 (46.9)	3.17 (1.78–5.67)	0.001
MACE (death, stroke/SE)	49 (15.2)	15 (46.9)	3.10 (1.74–5.53)	0.001
MACE (death, stroke/SE, major bleeding)	63 (19.5)	17 (53.1)	2.77 (1.62–4.73)	0.001

Values are n (%).

BARC = Bleeding Academic Research Consortium; CI = confidence interval; HR = hazard ratio; MACE = major adverse cardiac events; SE = systemic embolism.

factor may also have increased the incidence of AKI in our study, and the benefits of a combined procedure should be balanced with the potential risks in this ill population, especially if CKD is present previously. Although in our study the total volume of contrast and the ratio of volume to eGFR were similar between groups, and the impact of contrast media exposure on renal dysfunction after primary PCI is under debate (21), contrast administration may also play a role in the development of AKI. Future studies with echocardiographic guidance exclusively may determine the incidence and the impact of contrast media on developing AKI after LAAC.

The role of preventive strategies should be tested in future studies. Interestingly, a common practice during LAAC is to hydrate the patient

TABLE 5 Multivariate Predictors of Cumulative Mortality After Left Atrial Appendage Closure

	Multivariable Analysis	
	HR (95% CI)	p Value
Age*	1.39 (1.15–1.69)	0.001
Female	0.34 (0.18–0.64)	0.001
Baseline eGFR†	1.14 (1.05–1.25)	0.003
LVEF <40%	2.99 (1.30–6.87)	0.010
CHA_2DS_2-VASc score	1.18 (0.98–1.43)	0.083
Acute kidney injury	2.00 (1.02–3.91)	0.044

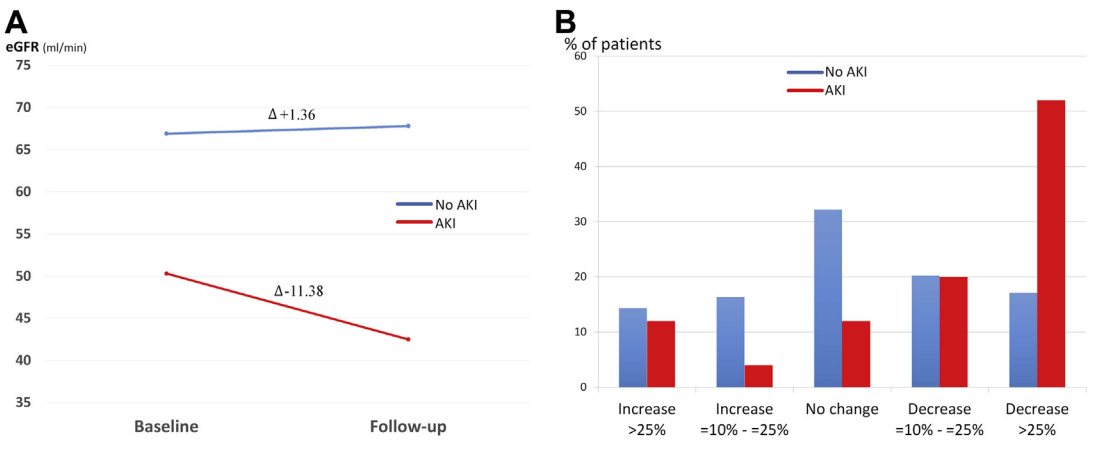
*For each increase of 5 years. †For each decrease of 10 ml/min.
Abbreviations as in Tables 1, 3, and 4.

periprocedurally to obtain relatively high left atrial pressure and a more expanded LAA (22). In fact, more than one-third of the patients experienced improvement in renal function post-procedurally, which could be related to this extra saline administration. Hydration before the procedure is an established preventive strategy and recommended in the guidelines in patients with CKD who undergo catheterization (23). This strategy should be implemented in patients with low eGFR undergoing LAAC. In addition, guided hydration with the RenalGuard System showed promising results, reducing the incidence of AKI during PCI (24,25) and TAVR (26). The role during LAAC, especially in patients with CKD, should be proved in the future. Reduction or even avoidance of contrast media administration and statins in patients without contraindications may be considered as an additional preventive measure (27).

AKI AND OUTCOMES. In accordance with previous PCI and TAVR studies (1–4), the occurrence of AKI had identified a group of patients with poorer midterm clinical outcomes following LAAC.

Patients with AKI had a higher prevalence of comorbidities such as peripheral vascular disease and renal and cardiac dysfunction, although the association between AKI and mortality remained after multivariate analysis. AKI may identify patients with clinical vulnerability who are at higher risk for subsequent short- and long-term major events and longer hospitalization. In addition, the most frequent causes of death during follow-up were from a respiratory and infectious origin. Noncardiovascular mortality and unplanned readmission rates were higher in patients who developed AKI, suggesting their susceptibility to future adverse events, probably related to their preexisting comorbidities rather than the procedure per se. In a previous LAAC registry, 1-year mortality was 9.8% (28), comparable with our study. However, patients who experienced AKI had a higher 1-year mortality rate (23%), which identified a subgroup of patients who may not benefit from LAAC, and a careful evaluation of patient life expectancy should be undertaken before the procedure to avoid a futile intervention. In addition, patients with AKI exhibited deterioration in their glomerular filtration rates during follow-up, while renal function remained stable in patients without AKI. This progression, in addition to more severe CKD, may also contribute to worse clinical outcomes. The present study is the first to demonstrate that the development of AKI could serve as a marker of poor prognosis following LAAC, and

FIGURE 4 Changes in Estimated Glomerular Filtration Rate in the Follow-Up According to the Occurrence of Acute Kidney Injury



Absolute change in estimated glomerular filtration rate (eGFR) **(A)** and percentage of patients with improvement, no change, or worsening in eGFR **(B)** during follow-up in the acute kidney injury (AKI) (n = 25) and no-AKI (n = 258) groups.

our findings further extend knowledge about the prognostic implications of AKI in a different scenario in interventional cardiology. Subsequently, these findings suggest the importance of assessing renal function following LAAC, as with other vascular procedures, to identify patients who develop AKI and require close monitoring during the post-procedural period. In patients with baseline CKD, combined procedures should be avoided to prolong the procedure and decrease the likelihood of developing AKI. Also, these findings could help improve clinical outcomes in patients undergoing LAAC, and future efforts in implementing preventive strategies should be made in those patients with higher risk for renal function deterioration.

STUDY LIMITATIONS. This study had the limitations inherent to an observational study without an external adjudication event committee. Although our results were obtained from prospectively gathered datasets, the retrospective nature of the analysis is exposed to potential (unmeasured) confounders even with multivariate analysis that could influence the results. We may have underdiagnosed and misclassified patients with AKI occurring after hospital discharge, because renal function values were not systematically recorded after discharge within 7 days after the procedure. Different definitions of AKI may change the results. Although there is no consensus on the best definition of AKI, we selected the most recent one adopted by the nephrology community. The numbers of events were relatively small precluding subanalyses for different stages of AKI.

CONCLUSIONS

The occurrence of AKI was a relatively frequent complication following LAAC and identified a group of patients with poorer midterm outcomes. Patients with lower renal glomerular filtration rates should be considered at high risk for development of this complication. The presence of AKI after LAAC could be used to identify high-risk patients for future clinical events and to guide further management. Further research focusing on interventions to prevent AKI after percutaneous vascular procedures, including LAAC, may assess the effect on clinical outcomes.

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PERSPECTIVES

WHAT IS KNOWN? AKI is a frequent complication after cardiac interventions and is associated with worse short- and long-term outcomes. LAAC has emerged as an alternative to oral anticoagulation for stroke prophylaxis in patients with nonvalvular atrial fibrillation and high bleeding risk. However, no data exist on the frequency, predictors, and impact of AKI following LAAC.

WHAT IS NEW? We found a rate of AKI of about 9% in patients undergoing LAAC, and special attention should be paid in patients with poor renal function. AKI identified a subgroup of patients with poorer outcomes.

WHAT IS NEXT? The higher mortality rate observed in patients with AKI after LAAC should be taken into account so that specific preventive measures and post-procedural management to reduce the occurrence of AKI and improve outcomes could be implemented.

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