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ORIGINAL PAPER

Incidence, predictors, and relevance of acute kidney injury in patients undergoing left atrial appendage closure with Amplatzer occluders: a multicentre observational study

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Abstract

Aims Acute kidney injury (AKI) remains a frequent complication after cardiac interventions, such as left atrial appendage closure (LAAC), yet limited data are available on the incidence and clinical implication of AKI in this setting. We sought to assess incidence, predictors and relevance of AKI after LAAC.

Methods and results We retrospectively analyzed 95 LAAC patients in three European centers. AKI was defined according to the Acute Kidney Injury Network (AKIN) classification. The incidence of AKI was 13.7% with mild AKI in 92.3% and AKI stage > II in 7.7%. Total contrast volume was not linked to the occurrence of AKI (AKI: 127 ± 83 vs. no AKI: 109 ± 92 ml, $p = 0.41$), however increasing contrast volume (CV) to glomerular filtration rate (GFR) ratio (CV/GFR ratio) was associated with an increased risk of AKI (OR, per unit increase: 1.24, 95% CI 0.97–1.58, $p = 0.08$). ROC-analysis revealed a moderate predictive value of CV/GFR ratio for the prediction of AKI (AUC: 0.67, 95% CI 0.50–0.84, $p = 0.05$). Furthermore, AKI was associated with significantly increased mortality 6 months and 1 year after LAAC. No significant difference in the incidence of AKI was observed between patients with mere fluoroscopic and additional echocardiographic guidance (16.3% vs. 11.5%, $p = 0.56$).

Conclusion Whereas mild AKI is common in patients after LAAC, severe AKI is rare. AKI after LAAC is associated with poor baseline renal function, increased doses of contrast (CV/GFR ratio) and impaired outcome. Future studies will be needed to elaborate the benefit of reducing or avoiding contrast volume regarding this endpoint.

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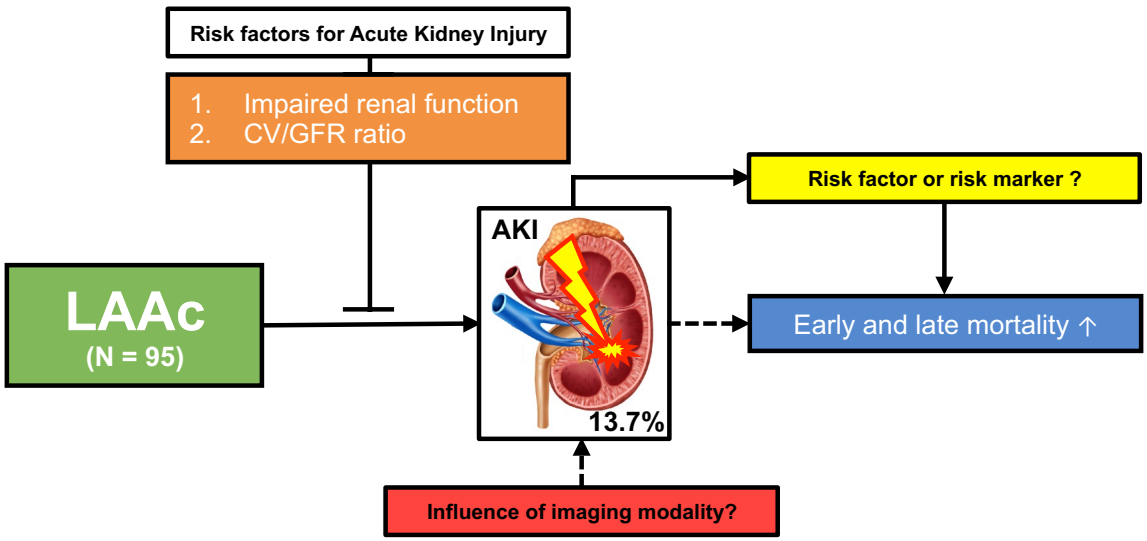
Graphic abstract



Keywords Left atrial appendage closure · Renal function · Acute kidney injury · Contrast dye volume

Abbreviations

ACP	Amplatzer Cardiac Plug
AF	Atrial fibrillation
AKI	Acute kidney injury
AKIN	Acute Kidney Injury Network
AUC	Area under the curve
CHA_2DS_2-VASC	CHA_2DS_2-VASC-Score
CI	Confidence interval
CV	Contrast volume
CV/GFR ratio	Contrast volume to glomerular filtration rate ratio
CKD	Chronic kidney disease
GFR	Glomerular filtration rate
HAS-BLED	HAS-BLED-score
KDIGO	Kidney disease improving global outcomes
LAAC	Left atrial appendage closure
LVEF	Left ventricular ejection fraction
OAC	Oral anticoagulation
OR	Odds ratio
PCI	Percutaneous coronary intervention
ROC	Receiver operating characteristic
SD	Standard deviation
TAVR	Transcatheter aortic valve replacement
TEE	Transesophageal echocardiography

Introduction

Left atrial appendage closure (LAAC) is a validated treatment option alternative in patients with non-valvular atrial fibrillation (AF) and absolute or relative contraindications for oral anticoagulation (OAC) [1–5]. As in all percutaneous cardiac interventions, postprocedural worsening of renal function, known as acute kidney injury (AKI), can occur after LAAC and may inflict a negative impact on clinical outcome [6–9]. The relevance of AKI during LAAC has recently been highlighted [10]. However, evidence on this topic remains limited. Given a high prevalence of chronic kidney disease (CKD), which is associated with an impaired clinical outcome after cardiac interventions [11] and has been reported to occur in > 1/3 of all patients undergoing LAAC (CKD stage III–V) [12], AKI is of special interest in this patient cohort. We sought to assess the incidence, predictors, and mid-term clinical impact of AKI in patients undergoing LAAC with Amplatzer occluders, namely the Amplatzer Cardiac Plug (ACP) and the Amplatzer Amulet (Abbott, St. Paul, MN, USA).

Methods

Study population

In this observational study, all patients who underwent left atrial appendage closure with an Amplatzer (ACP or

Amulet) device between December 2009 and September 2017 at three European centers (Bern, Bonn, and Zürich) were analyzed. Out of 415 patients, periprocedural creatinine values were available in 168 patients. For the purpose of the present analysis, only patients without concomitantly conducted procedures, e.g., coronary angiographies, coronary interventions or other structural interventions, and patients without end-stage renal failure requiring chronic dialysis were included, so that 95 patients constituted the final patient cohort. All patients presented with a defined indication for LAAC and were individually evaluated in local interdisciplinary teams prior to the procedure. LAAC was performed guided by periprocedural fluoroscopy and/or echocardiography depending on the preferences of the treating physicians and center. They provided written informed consent to be included in the respective registries, which have been approved by the local ethics committees. Prior to LAAC, all patients underwent transesophageal echocardiography (TEE) and laboratory testing in order to rule out contraindications for LAAC. Patient demographics and clinical baseline characteristics were determined including the assessment of individual stroke and bleeding risk by use of the CHA_2DS_2-VASC and HAS-BLED scores.

Study endpoints

The primary endpoint of this study was the occurrence of acute kidney injury, defined according to the Acute Kidney Injury Network (AKIN) classification [13]. Whereas this definition includes the assessment of urine output, the latter is commonly not measured after cardiac interventions. Therefore, classification of AKI was solely based on the change in serum creatinine levels. AKI stage I is defined as an increase in serum creatinine ≥0.3 mg/dl (≥ 27 µmol/l) or an increase to > 1.5- to 2-fold from baseline. AKI stage II is defined as an increase in serum creatinine to more than 2- to 3-fold, whereas AKI stage III is defined as an increase to more than threefold from baseline or serum creatinine of more than or equal to 4.0 mg/dl (354 µmol/l) with an acute increase of at least 0.5 mg/dl (44 µmol/l).

The peak creatinine level within 48 h after LAAC was taken as reference for the deviation from preprocedural baseline creatinine in order to determine the occurrence of AKI. For the present analysis, patients were categorized based on baseline glomerular filtration rate (GFR), in terms of defined KDIGO (Kidney Disease Improving Global Outcomes) stages [14]: no CKD/CKD stage I–II (GFR ≥ 60 ml/min/1.73 m^2), CKD stage III (GFR 30–60 ml/min/1.73 m^2), or CKD stage IV–V (GFR < 30 ml/min/1.73 m^2). In addition to total contrast volume (CV) used, the impact of the contrast volume to GFR ratio (CV/GFR ratio), a significant predictor for AKI in other cardiac interventions, was individually determined [15].

Device characteristics and procedural aspects were previously described in detail [16]. Further secondary outcomes were defined according to the Munich Consensus Document on LAAC. These included periprocedural and postprocedural complications (e.g., pericardial effusion or vascular complications), technical and procedural success, stroke or transient ischemic attack, as well as all-cause mortality after 1 year [17].

Statistical analysis

Continuous variables are presented as mean ± standard deviation (SD), if normally distributed and categorical variables as frequencies and percentages. Further descriptive analyses were performed by using Chi-square test for categorial variables. For comparing the central tendencies of two or more independent ordinal/interval scaled groups, Mann–Whitney *U* and Kruskal–Wallis analyses were performed. Receiver operator characteristics (ROC) analysis was performed to evaluate predictive value for the occurrence of AKI. Moreover, statistical analysis included Kaplan–Meier estimates to assess all-cause mortality. To evaluate independent predictors of all-cause 1-year mortality, multivariate analysis was performed. A binary logistic multivariate regression model was used, which included baseline parameters of clinical relevance (age, male sex, left ventricular ejection fraction (LVEF), serum creatinine) as well as parameters with $p < 0.1$ in univariate analysis. All statistical analyses were performed with SPSS software version 25.0.0.1 (IBM Corporation, Somers, NY). Statistical significance was assumed when the null hypothesis could be rejected at $p < 0.05$.

Results

Baseline characteristics

The study population constituted of 95 patients who underwent LAAC with AMPLATZER occluders. Hereof, 58.9% patients received the ACP and 41.1% were treated with the second-generation Amulet device. Patients were predominantly male (70.5%) with a mean age of 75.1 ± 8.0 years. In line with the recommendations for LAAC, they presented with both an increased thromboembolic as well as an increased bleeding risk (CHA_2DS_2-VASC 4.6 ± 1.4, HASBLED 3.3 ± 0.9). Mean LVEF was mildly impaired (52.6 ± 12.6%) with a prevalence of coronary artery disease in 64.2% patients. Concerning baseline renal function, no CKD/CKD stage I–II were observed in 47.4% (45/95) patients, CKD stage III–V was present in 52.6% (50/95) patients. Of these, stage III was seen in 39/95 (41.1%), whereas stage IV–V was present in 11/95 (11.6%) patients. Further baseline characteristics, including the

subcategorization by preprocedural renal function (no CKD/CKD stage I–II: GFR ≥ 60, CKD stage III: GFR 30–60 and CKD stage IV–V: GFR < 30 ml/min/1.73 m^2), are depicted in Table 1.

Decreased baseline GFR was associated with a trend to a higher age and a higher prevalence of non-paroxysmal AF. In the overall cohort, the mean volume of contrast used was 112 ± 90 ml. Mean CV differed significantly depending on renal function with 118 ± 94 ml in patients with no CKD/CKD stage I–II, 124 ± 88 ml with CKD stage III and 49 ± 55 ml in patients with CKD stage IV–V ($p = 0.02$). Of interest, CV/GFR ratio was significantly increased in patients with impaired renal function (overall: 2.2 ± 2.1; no CKD/CKD stage I–II: 1.5 ± 1.3; CKD stage III: 2.9 ± 2.5; CKD stage IV–V: 2.2 ± 2.7, $p = 0.02$).

Postprocedural outcome

Overall success of LAAC was high in all CKD groups. Device success was achieved in 97.9%, while technical success was achieved in 96.8%. Both rates did not differ in patients with or without AKI, although numerical differences were seen (92.3% vs. 98.8%, $p = 0.26$; 92.3% vs. 97.6% $p = 0.36$, respectively). Complications other than AKI occurred in 23.2% of all patients and occurred numerically more often in patients with AKI than in those without (30.8% vs. 22.0%, $p = 0.49$). Clinically relevant pericardial effusions tended to be more frequent in patients with AKI (15.4% vs. 2.4%, $p = 0.09$), whereas overall bleeding did not differ (23.1% vs. 15.9%, $p = 0.45$). Intraprocedural device resizing with an additional implantation attempt was necessary in 23.1% patients with AKI and only in 6.1% patients without AKI ($p = 0.08$). Length of hospitalization

Table 1 Clinical characteristics depending on baseline renal function

	All $N = 95$	No CKD/CKD I–II $N = 45$	CKD III $N = 39$	CKD IV–V $N = 11$	p value
Characteristics by GFR allocation					
Baseline characteristics					
Age (years)	75.1 ± 8.0	73.2 ± 8.2	77 ± 7.3	77 ± 8.5	0.09
Age ≥ 75 years	52 (54.7%)	21 (46.7%)	24 (61.5%)	7 (63.6%)	0.32
Male	67 (70.5%)	30 (66.7%)	30 (76.9%)	7 (63.6%)	0.51
Body mass index (kg/m^2)	27.6 ± 6.3	28.4 ± 7.8	26.6 ± 4.9	27.5 ± 3.8	0.54
Paroxysmal AF	38 (40.0%)	17 (37.8%)	20 (51.3%)	1 (9.1%)	0.04
Non-paroxysmal AF	57 (60.0%)	28 (62.2%)	19 (48.7%)	10 (90.9%)	0.04
Atrial hypertension	89 (93.7%)	43 (95.6%)	36 (92.3%)	10 (90.9%)	0.77
Ejection fraction (%)	52.6 ± 12.6	54.1 ± 11.7	50.6 ± 13.9	53.2 ± 11.3	0.63
Coronary artery disease	61 (64.2%)	31 (68.9%)	23 (59.0%)	7 (63.6%)	0.64
Myocardial infarction	33 (34.7%)	19 (42.2%)	13 (33.3%)	1 (9.1%)	0.11
Diabetes mellitus	33 (34.7%)	17 (37.8%)	15 (38.5%)	1 (9.1%)	0.16
Prior stroke/TIA	29 (30.5%)	17 (37.8%)	10 (25.6%)	2 (18.2%)	0.31
HAS-BLED-Score	3.3 ± 0.9	3.1 ± 1.0	3.4 ± 0.8	3.7 ± 1.0	0.19
CHA_2DS_2-VASC-Score	4.6 ± 1.4	4.7 ± 1.4	4.7 ± 1.3	4.2 ± 1.5	0.43
Creatinine (mg/dl)	1.36 ± 0.63	0.90 ± 0.20	1.53 ± 0.37	2.61 ± 0.55	< 0.01
GFR (ml/min/1.73 m^2)	59.6 ± 25.8	79.5 ± 21.7	46.8 ± 9.4	23.8 ± 3.7	< 0.01
Procedural characteristics					
Device size (mm)	24.3 ± 3.9	25.2 ± 4.2	23.4 ± 3.7	23.6 ± 2.5	0.09
Fluoroscopy time (min)	13 ± 8	12 ± 7	14 ± 9	13 ± 7	0.91
Contrast volume (ml)	112 ± 90	118 ± 94	124 ± 88	49 ± 55	0.03
CV/GFR ratio	2.2 ± 2.1	1.5 ± 1.3	2.9 ± 2.5	2.2 ± 2.7	0.02
Procedural outcome					
Periprocedural complications (excluding AKI)	22 (23.2%)	15 (33.3%)	7 (17.9%)	0 (0%)	0.04
Incidence of AKI	13 (13.7%)	5 (11.1%)	4 (10.3%)	4 (36.4%)	0.07
Device success	93(97.9%)	43 (95.6%)	39 (100%)	11 (100%)	0.32
Technical success	92 (96.8%)	42 (93.2%)	39 (100%)	11 (100%)	0.18

Data provided as number (%) or mean ± standard deviation

AF atrial fibrillation, *AKI* acute kidney injury, *CKD* chronic kidney disease, *CV* contrast volume, *GFR* glomerular filtration rate, *TIA* transient ischemic attack

did not differ in patients with or without AKI (7.9 ± 8.3 vs. 5.1 ± 5.9 days, $p = 0.47$).

Incidence of AKI after LAAC

In the overall cohort, acute kidney injury occurred in 13.7% (13/95) patients. Among these, 84.6% (11/13) presented with AKI stage I, whereas a total of two patients experienced AKI stage II (7.7%) and AKI stage III (7.7%).

After LAAC, a mean increase in serum creatinine of 0.09 ± 0.41 mg/dl (8 ± 36 µmol/l) compared to the values immediately prior to LAAC was observed. Patients with AKI showed a mean increase of 0.79 ± 0.73 mg/dl (70 ± 65 µmol/l, $p = 0.04$) while in patients without AKI no relevant change in renal function was seen (− 0.02 ± 0.15 mg/dl (− 2 ± 13 µmol/l), $p = 0.88$) (Table 2, Fig. 1). Similar results were seen in patients with or without echocardiographic guidance (0.06 ± 0.25 mg/dl (5 ± 22 µmol/l), $p = 0.61$ and 0.13 ± 0.55 mg/dl (12 ± 49 µmol/l), $p = 0.74$).

Patients experiencing AKI showed lower mean baseline GFR (48.9 ± 25.1 ml/min/1.73 m^2 vs. 61.3 ± 25.6, $p = 0.12$) and higher serum creatinine levels (1.62 ± 0.77 mg/dl (143 ± 68 µmol/l) vs. 1.31 ± 0.61 (116 ± 54 µmol/l), $p = 0.17$) without reaching statistical significance. The incidence of AKI was highest in patients with CKD stage IV–V (36.4%) in comparison to patients with less severe impairment of renal function (no CKD/CKD stage I–II: 11.1%; CKD stage III: 10.3%, $p = 0.07$).

Impact of procedural contrast volume on AKI

The amount of total contrast volume was similar in patients with and without AKI (127 ± 83 ml vs. 109 ± 92 ml, $p = 0.41$). However, a trend to an increased CV/GFR ratio was observed in patients experiencing AKI as compared to those without (3.2 ± 2.4 vs. 2.0 ± 2.0, $p = 0.05$). Hereby, a trend towards an increased risk of AKI was observed with increasing CV/GFR (OR per unit increase: 1.24, 95% CI 0.97–1.58, $p = 0.08$). A CV/GFR ratio of 3 was exceeded in 46.2% patients with AKI and in 20.3% patients without AKI ($p = 0.07$). ROC-analysis was performed, comparing the predictive value of the CV/GFR ratio and baseline serum creatinine levels for the incidence of AKI (Fig. 2). CV/GFR ratio revealed best predictive value with an area under the curve (AUC) of 0.67 (95% CI 0.50–0.84, $p = 0.05$), whereas serum creatinine showed an AUC of 0.61 (95% CI 0.42–0.81, $p = 0.19$).

Impact of imaging on AKI

To study the effects of imaging on the incidence of AKI, patients were divided into a group of LAAC treated with fluoroscopic guidance only and a group that had undergone either a hybrid approach featuring TEE and fluoroscopy or a merely TEE-guided procedure without any use of contrast medium. Overall, 45.3% (43/95) of patients underwent LAAC with fluoroscopic guidance only, whereas in 54.7% (52/95) additional TEE guidance was used. In the TEE group, no contrast volume was used in 23.1% (12/52) of patients. Despite the non-randomized character of this comparison, baseline characteristics were overall balanced between both groups. Patients with fluoroscopic guidance tended to be older (76.7 ± 7.4 vs. 73.7 ± 8.3 years, $p = 0.13$) and tended to have an increased thromboembolic risk (CHA_2DS_2-VASC-Score: 4.9 ± 1.5 vs. 4.4 ± 1.2, $p = 0.12$). Baseline renal function was numerically better in these patients compared to those undergoing echo-guided LAAC (serum creatinine: 1.32 ± 0.59 vs. 1.39 ± 0.67 mg/dl, $p = 0.89$) (Supplemental Table 3). Regarding procedural aspects, the use of contrast volume was significantly higher in patients treated under fluoroscopic guidance only (159 ± 80 vs. 72 ± 79 ml, $p < 0.01$), resulting in an increased CV/GFR ratio (3.2 ± 2.4 vs. 1.3 ± 1.4, $p < 0.01$). Of interest, no significant difference in AKI was observed between patients treated with fluoroscopic only and patients with echocardiographic guidance (16.3% vs. 11.5%, $p = 0.56$). In the 12 patients undergoing contrast-free purely TEE-guided LAAC, AKI occurred in 8.3% and was not statistically different compared to the other groups ($p = 0.56$). In this contrast-free purely echo-guided cohort, all of the patients presented with impaired baseline renal function with a mean serum creatinine of 1.62 ± 0.69 mg/dl.

AKI and long-term outcome

The impact of AKI is presented in the Kaplan–Meier estimate in Fig. 3. Follow-ups were available in 93.7% (89/95) patients after 6 months and in 91.6% (87/95) patients after 12 months. All-cause mortality at 6 months and 12 months after LAAC was significantly higher in patients with AKI than those without (25.0% vs. 3.8%, $p < 0.01$ and 34.4% vs. 9.0%, $p < 0.01$, respectively).

Multivariate analysis regarding the prediction of 1-year mortality was performed. For this purpose, baseline parameters of clinical relevance (age, male sex, LVEF, serum creatinine) and all parameters which tended to differ ($p < 0.1$) between patients who died within 1 year after LAAC and those who survived (contrast volume, CV/GFR ratio, CV/GFR ratio > 3 and incidence of AKI) were assessed for their independent predictive ability. As a result, a trend towards an increased mortality was only seen with increasing age ($p = 0.07$) and a CV/GFR ratio > 3 ($p = 0.06$). None of the variables showed significant independent predictive value (Supplemental Table 4).

Table 2 Baseline characteristics and periprocedural results of patients with and without AKI

	All $N=95$	AKI $N=13$	No AKI $N=82$	p value
Characteristics depending on incidence of AKI				
Baseline characteristics				
Age (years)	75.1 ± 8.0	76.3 ± 6.5	74.9 ± 8.2	0.64
Age ≥ 75 years	52 (54.7%)	8 (61.5%)	44 (53.7%)	0.76
Male	67 (70.5%)	9 (69.2%)	58 (70.7%)	1
Body mass index (kg/m^2)	27.6 ± 6.3	27.8 ± 5.8	27.5 ± 6.4	0.64
Paroxysmal AF	38 (40.0%)	4 (30.8%)	34 (41.5%)	0.55
Non-paroxysmal AF	57 (60.0%)	9 (69.2%)	48 (58.5%)	0.55
Arterial hypertension	89 (93.7%)	13 (100%)	76 (92.7%)	0.59
Ejection fraction (%)	52.6 ± 12.6	49.1 ± 14.8	53.1 ± 12.2	0.37
Coronary artery disease	61 (64.2%)	10 (76.9%)	51 (62.2%)	0.37
Myocardial infarction	33 (34.7%)	8 (61.5%)	25 (30.5%)	0.06
Diabetes mellitus	33 (34.7%)	4 (30.8%)	29 (35.4%)	1
Prior stroke/TIA	29 (30.5%)	3 (23.1%)	26 (31.7%)	0.75
HAS-BLED-Score	3.3 ± 0.9	3.4 ± 1.0	3.3 ± 1.0	0.95
CHA_2DS_2-VASC-Score	4.6 ± 1.4	4.8 ± 1.7	4.6 ± 1.3	0.87
Creatinine (mg/dl)	1.36 ± 0.63	1.62 ± 0.77	1.31 ± 0.61	0.17
GFR (ml/min/1.73 m^2)	59.6 ± 25.8	48.9 ± 25.1	61.3 ± 25.6	0.12
Procedural characteristics				
Fluoroscopic guidance only	43 (45.3%)	7 (53.8%)	36 (43.9%)	0.56
Echocardiographic guidance	52 (54.7%)	6 (46.2%)	46 (56.1%)	0.56
Device size (mm)	24.3 ± 3.9	23.5 ± 2.8	24.4 ± 4.0	0.41
Implantation attempts > 1	8 (8.4%)	3 (23.1%)	5 (6.1%)	0.08
Need for repositioning	5 (5.3%)	1 (7.7%)	4 (4.9%)	0.53
Fluoroscopy time (min)	13 ± 8	14 ± 10	12 ± 7	0.43
Contrast volume (ml)	112 ± 90	127 ± 83	109 ± 92	0.41
CV/GFR ratio	2.2 ± 2.1	3.2 ± 2.4	2.0 ± 2.0	0.05
Creatinine postprocedural (mg/dl)	1.45 ± 0.75	2.41 ± 1.02	1.29 ± 0.57	< 0.01
Procedural outcome				
Periprocedural complications (excluding AKI)	22 (23.2%)	4 (30.8%)	18 (22.0%)	0.49
Stroke or TIA	0 (0%)	0 (0%)	0 (0%)	
Air embolism	1 (1.1%)	0 (0%)	1 (1.2%)	1
Pericardial effusion	13 (13.7%)	2 (15.4%)	11 (13.4%)	1
Clinically relevant pericardial effusion	4 (4.2%)	2 (15.4%)	2 (2.4%)	0.09
Any bleeding	16 (16.8%)	3 (23.1%)	13 (15.9%)	0.45
VARC life threatening bleeding	2 (2.1%)	1 (7.7%)	1 (1.2%)	0.26
VARC major bleeding	3 (3.2%)	1 (7.7%)	2 (2.4%)	0.36
Any device embolization	2 (2.1%)	1 (7.7%)	1 (1.2%)	0.26
In hospital stay after procedure (days)	5.4 ± 6.3	7.9 ± 8.3	5.1 ± 5.9	0.47
Device success	93 (97.9%)	12 (92.3%)	81 (98.8%)	0.26
Technical success	92 (96.8%)	12(92.3%)	80 (97.6%)	0.36

Data provided as number (%) or mean ± standard deviation

AF atrial fibrillation, *AKI* acute kidney injury, *CV* contrast volume, *GFR* glomerular filtration rate, *TIA* transient ischemic attack, *VARC* valve academic research consortium

Discussion

The role of post-interventional acute kidney injury as both risk marker and risk factor of adverse outcome has been well established in several studies in the field of interventional cardiology. In this context, hemodynamic compromise, diabetes, CKD, and procedural characteristics, such as amount of contrast volume used or the access site [10, 15, 18–20] appear to be predictive factors for postprocedural worsening of renal function. In contrast to LAAC, the incidence and

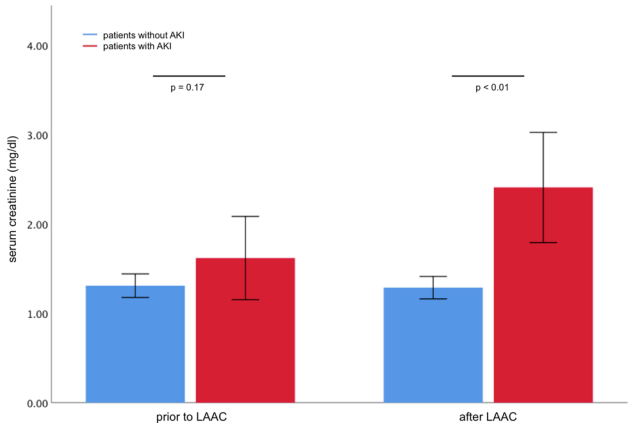


Fig. 1 Changes of serum creatinine (mg/dl) after LAAC in patients with and without AKI. *AKI* acute kidney injury, *LAAC* left atrial appendage closure

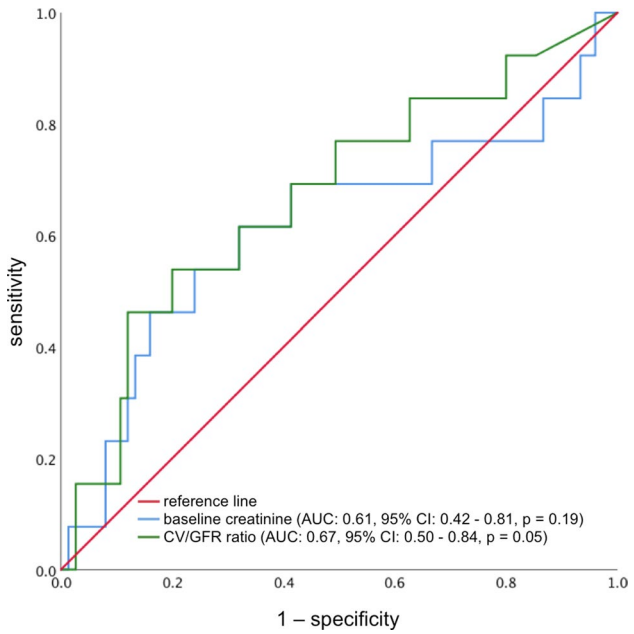


Fig. 2 ROC-analysis of CV/GFR ratio and baseline serum creatinine. *AUC* area under the curve, *CV* contrast volume, *GFR* glomerular filtration rate

clinical impact of AKI has been well evaluated in patients undergoing percutaneous coronary intervention (PCI) [21–23] or structural cardiac interventions such as transcatheter aortic valve replacement (TAVR) [24] or MitraClip [25]. Hereby, the incidence of AKI ranges between 7 and 13% among patients undergoing PCI [21–23], whereas more invasive procedures (such as TAVR and MitraClip) convey a higher risk of AKI (18–26%) [24, 25]. In contrast, only limited scientific data are available on the incidence and relevance of AKI after LAAC [10]. Although LAAC itself is not considered a highly invasive procedure, usually inflicting only minor hemodynamic compromise and contrast use, clinical data on AKI after LAAC are warranted. Especially given the increased prevalence of renal disease in patients with AF [12], patients undergoing LAAC appear to be exposed to an increased risk of postprocedural worsening of renal function.

In our study, the overall incidence of AKI was 13.7%. However, only two patients suffered from stage II and III. The latter was a polymorbid patient, who presented with an impaired renal function (GFR: 47 ml/min/1.73 m^2), congestive heart failure (LVEF: 25%) and received 212 ml of CV during LAAC, which resulted in an increased CV/GFR ratio of 4.5. Of note, no TEE guidance was used in this patient. The overall rates of AKI in our study are in line with the only data published thus far. The slightly higher incidence of AKI in our study is explained by a lower baseline GFR and a higher prevalence of CKD, both established risk factors for AKI [26]. Whereas Nombela-Franco et al. described a prevalence of 43.9% [10], in our study the prevalence of pre-existing CKD III–V was 52.6%. The latter is most likely the explanation for the overall higher incidence of AKI after LAAC in our cohort as compared to Nombela-Franco et al. who described an incidence of 9.0%.

In our analysis, AKI occurred among all groups of renal function with an incidence of approximately 10% in patients with CKD stage ≤ III and with a dramatic increase in patients with CKD stage IV–V (36.4%).

In addition to renal function, total contrast volume and the ratio of CV and GFR seem to play a significant role in AKI in LAAC patients. CV/GFR ratio, which has been identified as an independent risk factor and predictor for AKI in several studies mainly in patients undergoing PCI [15, 27, 28], was elevated in patients with AKI when compared to those without (3.2 ± 2.4 vs. 2.0 ± 2.0, $p = 0.05$). Furthermore, the percentage of patients with a CV/GFR ratio > 3, a proposed cut-off value for the prediction of AKI [15], was higher among patients with AKI (46.2% vs. 20.3%, $p = 0.07$). In the ROC-analysis, the ratio of CV/GFR provided the best predictive value for the incidence of AKI underlining its importance in this context. Comparable to patients undergoing other structural interventions such as TAVR [24] and in line with the results published by Nombela-Franco et al., AKI in our analysis was associated with impaired mid-term clinical outcome, highlighting the necessity to both minimize the incidence of AKI as well as the need for close clinical monitoring regarding the occurrence of AKI. Although both 6- and 12-month mortalities were significantly increased in patients experiencing AKI, multivariate analysis did not reveal an independent predictive value of AKI in this context. Especially given the overall limited cohort size in our study, it remains speculative to assume that AKI itself is causative for the increased mortality. More likely, patients experiencing AKI after LAAC

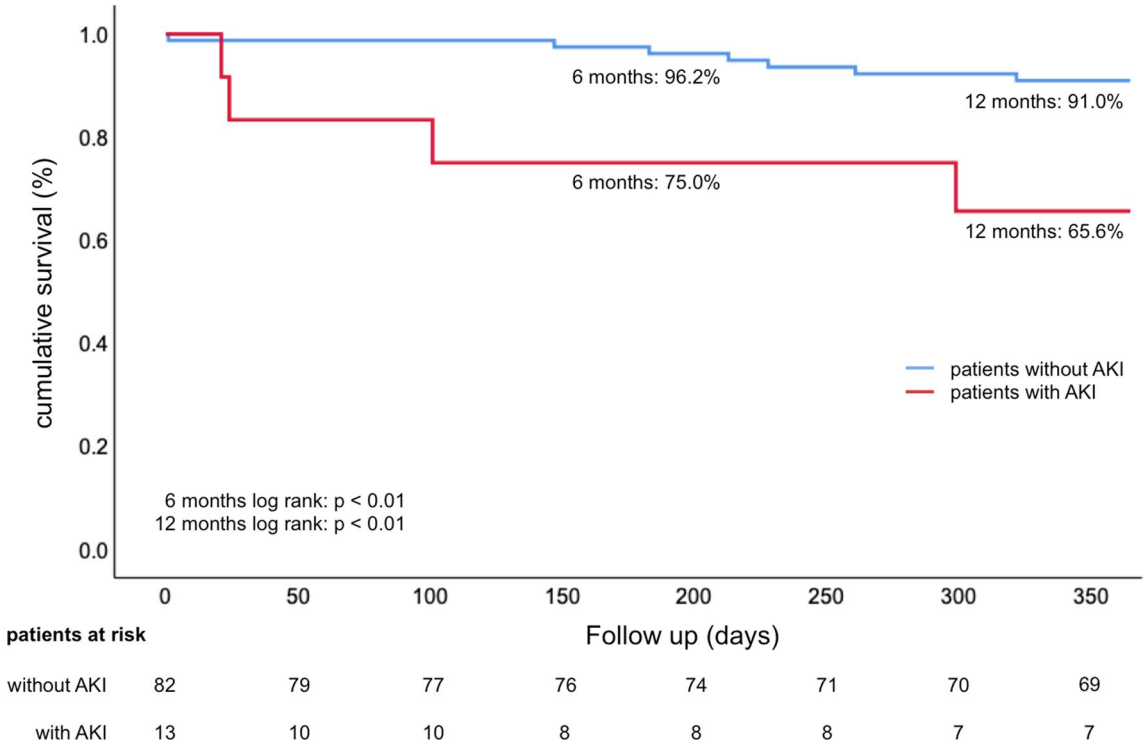


Fig. 3 Overall survival after LAAC up to 1-year follow-up. *AKI* acute kidney injury, *LAAC* left atrial appendage closure

constitute a group at a generally increased risk for mortality owing to an increased baseline morbidity. In this context, Nombela-Franco et al. even stated that indication for LAAC in these highly morbid patients should be critically evaluated [10]. Furthermore, periprocedural complications need to be taken to an account as both a risk factor for AKI as well as outcome. In fact, we observed a trend towards an increased incidence of clinically relevant pericardial in the AKI cohort of our analysis, suggesting a certain impact in this context. Of note, of these two patients, one deceased 24 days after LAAC.

In summary, similar to AKI in other fields of percutaneous cardiac interventions [10, 15, 18, 19], AKI after LAAC with Amplatzer devices is a frequent complication and is likely of multifactorial origin. Baseline renal function and contrast volume with regard to renal function appear to play a critical role. Although statistical significance was missed in the present study, a strong signal towards the impact of CV/GFR on AKI after LAAC was observed. In fact, statistical significance could have been achieved by excluding patients with CV/GFR ratio > 10, as suggested in previous studies on AKI [15]. However, only one patient with a ratio of 11.7, high CV (367 ml) and concomitantly impaired GFR (32 ml/min/1.73 m^2) was in our cohort.

Given the increased risk in the often polymorbid cohort of LAAC patients, aiming at a reduction of AKI is appealing and may lead to better clinical outcomes, particularly by limiting the amount of contrast volume. In our non-randomized study setting, the use of additional TEE guidance appeared not to be linked to a lower incidence of AKI. However, contrast volume and CV/GFR ratio were both significantly lower than in patients with fluoroscopic guidance only. A contrast-free, merely TEE-guided approach was performed in a small portion of 12 patients. Hereby, the decision to perform contrast-free LAAC was mainly based on renal function, which was severely impaired (mean serum creatinine: 1.62 ± 0.69 mg/dl). AKI was found in one of these patients (1/12, 8.3%). Overall, it is beyond the scope of this study to allow conclusions on the potential benefit of limited contrast use regarding AKI. Still, it is intuitive to assume that limiting the amount of contrast volume may be a key factor in preventing AKI. Minimal use of contrast volume or the implementation of contrast-free LAAC exclusively guided either by (3D) transesophageal/intracardiac echocardiography or fusion imaging technologies [29] may be helpful in this context. In fact, we have recently been able to demonstrate the safety and efficacy of contrast-free TEE-guided LAAC as an alternative approach to conventional LAAC. This approach may be especially useful in patients, in whom the avoidance of contrast volume is warranted, such as patients with chronic renal failure [30]. However, whether such an approach translates into favorable clinical outcomes, remains to be elucidated by future studies.

Limitations

The major limitation of this study was its retrospective character and the small sample size. Incidence rates may be biased due to varying incidences in excluded patient, i.e., it is likely that no testing was performed in patients who did well after LAAC. On the other hand, the rate of AKI could also be underestimated because of patients who were discharged early after the procedure. Finally, patients were treated at three centers. Therefore, study results may be influenced by different operator experiences, procedure techniques, and imaging preferences. Contrast-free LAAC was preferably used in patients with increasingly impaired renal function in Bonn.

Conclusions

The incidence of acute kidney injury in patients undergoing LAAC is linked to adverse clinical outcome with increased mortality. Patients with severely pre-existing impaired kidney function and increased CV/GFR ratio are more likely to suffer from AKI. Due to the high concomitant prevalence of AF and CKD, patients qualifying for LAAC are at an increased risk and hence, further preventive strategies are warranted.

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Compliance with ethical standards

Conflict of interest Alexander Sedaghat has received travel grants from Abbott, Boston Scientific, Medtronic and Edwards Lifesciences. Baravan Al-Kassou has received travel grants from Abbott. Jan Wilko Schrickel has participated in clinical trials conducted by Abbott. Fabian Nietlispach is a consultant to Abbott, Edwards Lifesciences, and Medtronic. Marco Valgimigli reports research grants, advisory board and lectures fees from Abbott; Stephan Windecker received grants to the institution from Abbott, Biotronik, Boston Scientific, Medtronic and Edwards Lifesciences; Bernhard Meier received speaker and proctor fees from Abbott. Georg Nickenig has received speaker honoraria from Abbott. Steffen Gloekler received institutional grants from Abbott and a grant from the Swiss Heart Foundation. The other authors have no conflicts of interest.

Ethical approval Declaration of Helsinki: The authors state that the study complies with the Declaration of Helsinki. The locally appointed ethics committee has approved the research protocol. Informed consent has been obtained from the subjects.

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