Acute Kidney Injury After Percutaneous Edge-to-Edge Mitral Repair

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ABSTRACT

BACKGROUND In catheter-based procedures, acute kidney injury (AKI) is a frequent, serious complication ranging from 10% to 30%. In MitraClip (Abbott Vascular, Santa Clara, California), a usually contrast-free procedure, there is scarce data about its real incidence and impact.

OBJECTIVES This study aimed to evaluate incidence, predictive factors, and midterm outcomes of AKI in patients with significant mitral regurgitation (MR) undergoing transcatheter valve repair with MitraClip.

METHODS A total of 721 patients undergoing MitraClip were included. AKI was defined as an absolute or a relative increase in serum creatinine of >0.3 mg/dl or ≥50%, respectively, or the need for hemodialysis during index hospitalization.

RESULTS The mean age of the patients was 72 ± 11 years (28.3% women). Median estimated glomerular filtration rate (eGFR) was 43.7 ml/min/1.73 m² (interquartile range: 30.9 to 60.1 ml/min/1.73 m²), and was <60 ml/min/1.73 m² in 74.9% of the patients. AKI after MitraClip occurred in 106 patients (14.7%). Baseline hemoglobin (<11 g/dl) (odds ratio [OR]: 1.97; p = 0.003), urgent procedure (OR: 3.44; p = 0.003), and absence of device success (OR: 3.37; p < 0.001) were independent predictors of AKI. Patients with AKI had worse outcomes compared to those without AKI, including a higher proportion of in-hospital bleeding events (3.8% vs. 0.8%; p = 0.011), 2-year all-cause mortality (40.5% vs. 18.7%; p < 0.001), and major adverse cardiac events (63.6% vs. 23.5%; p < 0.001). Combination of AKI with significant residual MR after the procedure conferred even worst outcomes (2-year all-cause mortality 50.0% vs. 19.6%; p = 0.001, and major adverse cardiac events 70.0% vs. 18.9%; p < 0.001).

CONCLUSIONS Despite being a “zero-contrast” procedure, one-sixth of patients undergoing transcatheter mitral valve repair had AKI, linked to device failure or other severe conditions. The occurrence of AKI was associated with worse outcomes, highlighting the importance to detect and reduce this complication in high-risk population.

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Acute kidney injury (AKI) is a serious and one of the most common major complications of cardiac surgery and catheter-based procedures, with an incidence ranging from 5% to 43%. It has been independently associated with 3 to 8-fold higher peri-operative mortality, prolonged length of stay, and increased cost of care (1-5). During many years, contrast-induced nephropathy (CIN) has been used to characterize AKI after iodinated contrast procedures. In addition, previous studies have identified the role of hemodynamic compromise and congestive heart failure to AKI, but it has been challenging to decipher their AKI contribution from that of dye (6). Nonetheless, doubts of dye-CIN causality have emerged, and the term contrast-associated AKI has been recently introduced (7). However, mitral regurgitation (MR) is the most common type of valve disease, and transcatheter mitral valve interventions have emerged over the last few years as a viable alternative to surgery to treat MR in inoperable or high surgical-risk patients. Among them, percutaneous mitral valve repair (PMVr) edge-to-edge with MitraClip (Abbott Vascular, Santa Clara, California) stands out because of its favorable results in functional MR (8). Approximately two-thirds of patients in clinical trials for MitraClip had some degree of renal impairment associated with other additional comorbidities that could increase the likelihood of AKI occurrence (8-10). In addition, changes in volumetric loading conditions when treating significant MR, including stroke volume, renal preload, and afterload, may affect kidney function in the peri-procedural phase and midterm follow-up (10). Despite being usually a zero-contrast procedure, previous studies, with a very limited number of patients, described an AKI rate of ~20% following MitraClip procedure, associated with higher in-hospital mortality (11,12). However, predictors of AKI occurrence, changes in renal function over time, and the impact of AKI in follow-up after MitraClip remain largely unknown. A contrast-less procedure such as MitraClip could help to characterize the procedural hemodynamic effect on AKI. Therefore, the objectives of the study are to determine: 1) the incidence and predictive factors of AKI; and 2) the impact of AKI for in-hospital and 2-year outcomes in patients undergoing MitraClip for significant MR.

Methods

Study Population and Procedure. This multicenter study collected individual data from a total of 775 consecutive patients at different stages of renal disease with organic, functional, or mixed grade 3+ or 4+ MR who underwent mitral edge-to-edge repair using the MitraClip device (Abbott Vascular, Santa Clara, California) at 16 centers from the Spanish MitraClip Registry. Patients requiring renal replacement therapy before the procedure (n = 8) and those in whom renal function was not available at baseline or post-procedural within 72 h were excluded from the analysis (n = 46). Thus, the final study population comprised 721 patients (Supplemental Figure 1). Eligibility for MitraClip was assessed at each center by the local heart team and the procedure was performed as previously described (13). Numbers of clips, selection of the device (NT, NTR, or XTR) and use of pre-operatively diuretic therapy were left to the operator’s discretion. All but 9 procedures were done under general anesthesia. Case report forms included whether or not MitraClip was performed in combination with other percutaneous interventions or if contrast agent was used for other purposes. Serum creatinine measurements were obtained at baseline, daily after the procedure until hospital discharge, within 1 to 6 months, and 12 months after the procedure. Peri-procedural complications and the need for renal replacement therapy during the index hospitalization were also noted. Clinical, procedural, and anatomic data were prospectively collected in a dedicated online database for the Spanish MitraClip Registry (14). The web site of the database is managed by an external statistician from the Autónoma University of Madrid, Spain, who also performed the statistical analysis, led by the coordinating center. The web site is supported

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by an unrestricted grant from Abbott. All patients signed informed consent for the procedure, and all studies were performed in accordance with the local ethics committee.

**DEFINITIONS.** The estimated glomerular filtration rate (eGFR) was calculated before the procedure on the basis of the Chronic Kidney Disease Epidemiology Collaboration equation (15). Baseline renal function was classified in 5 stages according to the value of eGFR (16), and chronic kidney disease (CKD) was defined as a stage ≥3 (eGFR < 60 ml/min/1.73 m²). 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 72 h after the procedure (17). The severity of AKI was further classified into 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. CIN risk was calculated using a previously described risk score based on clinical, analytical, and procedural characteristics (18). Surgical risk was calculated using the Society of Thoracic Surgeons predicted risk of mortality (STS-PROM) and the European system for cardiac operative risk evaluation (EuroSCORE II). Urgent procedure and poor mobility were classified according to the definitions of EuroSCORE II. Severity of MR was assessed by previous recommendations (19). Clinical outcomes were defined by Mitral Valve Academic Research Consortium criteria (20) and included device success and peri-procedural complications.

**OUTCOMES AND FOLLOW-UP.** Clinical and echocardiographic follow-up was carried out at 30 days, 12 months, and yearly afterward. Several sources of information were used to investigate outcomes in each participating center: outpatient clinical visits; phone contacts with patients, families, or physicians; and review of medical records to determine clinical outcomes and the cause of death when necessary. With a median follow-up time of 30.0 months (interquartile range [IQR]: 17.5 to 45.1 months), a complete follow-up at 2 years was achieved in 85.4% of patients. Midterm outcomes included overall and cardiac mortality, surgical or repeat percutaneous mitral valve intervention, and major cardiac adverse events (MACE) that included all-cause mortality, myocardial infarction, need for cardiac surgery, stroke, or major bleeding. The primary endpoint was 2-year mortality and MACE. Secondary endpoints were rate and predictive factors of AKI, impact of AKI on in-hospital outcomes, and changes in renal function at last follow-up.

**STATISTICAL ANALYSIS.** Categorical variables were expressed as numbers and percentages (%), and continuous variables as mean ± SD or median and IQR (25th to 75th percentile) according to their distribution. Assessment of normality for continuous data was performed using the Kolmogorov-Smirnov test. Qualitative variables were analyzed by the chi-square or the Fisher exact test, and differences in continuous variables by a 2-sided Student’s t-test or Wilcoxon rank test, when appropriate. Freedom from all-cause mortality, cardiac mortality, and MACE 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. Variables with p values <0.10 in the univariate analysis were entered into a logistic regression analysis to determine the predictive factors of AKI. Receiver-operating characteristic (ROC) curve was performed to assess the discriminatory power of the CIN risk score in this population (18). Predictors of cumulative death were analyzed using Cox regression analysis. The proportional hazard assumption was evaluated by means of log-minus-log survival plots. A subgroup analysis was done according to presence or absence of significant residual MR (+3/4) after the procedure and AKI. Absolute change in renal function during the index hospitalization and at follow-up was calculated as minimum eGFR during hospitalization and eGFR at follow-up, respectively, minus pre-procedural eGFR. Significant deterioration in renal function at 1-year follow-up was considered a decrease of >10% in eGFR compared with baseline, and was also grouped according to the presence or absence of significant residual MR and AKI. The results were considered significant at values of p < 0.05. All data were analyzed with SPSS Statistics version 21.0 (IBM, Armonk, New York) and Stata 14 (StataCorp, College Station, Texas).

**RESULTS**

The main baseline clinical and echocardiographic characteristics of the global study population are summarized in Table 1. The mean age was 72.4 ± 10.8 years, and 71.7% were men. Several comorbidities were present with an intermediate estimated surgical risk (STS-PROM score and EuroSCORE II of 4.02; IQR: 1.9 to 6.9; and 4.7; IQR 2.8 to 8.9, respectively). The vast majority of the patients had a functional or mixed MR etiology (~80%) with low left ventricular
ejection fraction (median 35% IQR: 29% to 51%). Baseline median eGFR was 43.7 ml/min/1.73 m² (IQR: 30.9 to 60.1 ml/min/1.73 m²), and 74.9% of the patients had some degree of CKD (stage ≥3), with a CIN risk score of 12.0 (IQR: 9.0 to 15.0) (Table 1). Regarding

the procedure, device success was achieved in 92.5% (n = 667) with a mean procedural time of 136 min (IQR: 109 to 181 min). A total of 45 (6.2%) patients required a concomitant intervention with a low amount of contrast (50 ml, IQR: 37.0 to 80.0 ml)
Procedural characteristics and in-hospital outcomes of the global population are summarized in Table 2. INCIDENCE, PREDICTIVE FACTORS, AND PERI-PROCEDURAL IMPACT OF AKI. Post-procedural AKI occurred in 106 patients (14.7%): 11.7% stage 1, 1.2% stage 2, and 1.8% stage 3 (Supplemental Figure 1). Six patients (0.8%) needed renal replacement therapy after the procedure. Patients with AKI had more prior vascular disease (p = 0.038), recent myocardial infarction (p = 0.024), baseline moderate to severe tricuspid regurgitation (p = 0.016), and higher surgical risk scores (p < 0.001 and p = 0.013 for EuroSCORE II and STS-PROM score, respectively) (Table 1). Regarding medical treatment, the AKI group had less use of beta-blockers (p = 0.027). Baseline hemoglobin and eGFR were lower in AKI patients (p = 0.001 and p = 0.049, respectively); however, the proportion of patients with CKD stage ≥3a was similar between groups (73.8% vs. 81.1%; p = 0.109). CIN risk score was higher in AKI patients (p < 0.001), with an area under curve by ROC analysis of 0.62 (95% confidence interval [CI]: 0.56 to 0.68; p < 0.001) (Table 1, Supplemental Figure 2). Procedural times (p = 0.576), use of general anesthesia (p = 0.999), concomitant interventions (p = 0.057), and contrast amount (p = 0.354) were similar between groups (Table 2, Supplemental Table 1). However, final residual MR ≤2 after the procedure was lower in the AKI group (87.3% vs. 95.2%; p = 0.005), leading to a lower device success in this group (82.1% vs. 94.3%; p < 0.001). In-hospital mortality tended to be higher in the AKI group (4.7% vs. 1.8%; p = 0.071).

Univariate and multivariate analysis for factors associated with AKI following MitraClip are depicted in Table 3. The presence of baseline anemia (odds ratio [OR]: 1.97; 95% CI: 1.81 to 3.09; p = 0.003), urgent procedure (OR: 3.44; 95% CI: 1.26 to 7.64; p = 0.003), and absence of device success (OR: 3.37; 95% CI: 1.81 to 6.26; p < 0.001) were independent predictors of AKI (Table 3).

MIDTERM CLINICAL OUTCOMES. At 2-year follow-up, 147 (20.8%) had died, 88 (12.4%) from cardiovascular causes. Cumulative rates of overall mortality

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

<table>
<thead>
<tr>
<th></th>
<th>All (N = 721)</th>
<th>No-AKI (n = 615)</th>
<th>AKI (n = 106)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Procedural data</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urgent procedure</td>
<td>31 (4.3)</td>
<td>20 (3.3)</td>
<td>11 (10.4)</td>
<td>0.002</td>
</tr>
<tr>
<td>Inotropic support</td>
<td>70 (9.7)</td>
<td>55 (8.9)</td>
<td>15 (14.2)</td>
<td>0.094</td>
</tr>
<tr>
<td>Residual MR ≤ grade 2</td>
<td>530 (94.0)</td>
<td>454 (95.2)</td>
<td>76 (87.3)</td>
<td>0.005</td>
</tr>
<tr>
<td>Device success</td>
<td>667 (92.5)</td>
<td>580 (94.3)</td>
<td>87 (82.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Post-procedural mitral gradient, mm Hg</td>
<td>3 (2-4)</td>
<td>3 (2-4)</td>
<td>3 (2-4)</td>
<td>0.561</td>
</tr>
<tr>
<td>Mitral gradient ≤5 mm Hg</td>
<td>70/498 (14.1)</td>
<td>61/431 (14.2)</td>
<td>9/67 (13.4)</td>
<td>0.875</td>
</tr>
<tr>
<td>Number of clips</td>
<td>1.45 ± 0.73</td>
<td>1.45 ± 0.73</td>
<td>1.46 ± 0.75</td>
<td>0.949</td>
</tr>
<tr>
<td>Catheter thrombosis</td>
<td>4 (0.6)</td>
<td>2 (0.3)</td>
<td>2 (1.9)</td>
<td>0.105</td>
</tr>
<tr>
<td>Cordal entrapment</td>
<td>5 (0.7)</td>
<td>4 (0.7)</td>
<td>1 (0.9)</td>
<td>0.550</td>
</tr>
<tr>
<td>Procedural time</td>
<td>136 (109-181)</td>
<td>138 (110-180)</td>
<td>120 (103-194)</td>
<td>0.576</td>
</tr>
<tr>
<td>General anesthesia</td>
<td>712 (98.8)</td>
<td>607 (98.7)</td>
<td>105 (99.1)</td>
<td>0.999</td>
</tr>
<tr>
<td>Concomitant intervention</td>
<td>45 (6.2)</td>
<td>34 (5.5)</td>
<td>11 (10.4)</td>
<td>0.057</td>
</tr>
<tr>
<td>Contrast amount, ml</td>
<td>40.0 (30.0-66.5)</td>
<td>45.0 (31.0-68.0)</td>
<td>33.0 (23.0-45.0)</td>
<td>0.154</td>
</tr>
</tbody>
</table>

**Peri-procedural complications and in-hospital outcomes**

<table>
<thead>
<tr>
<th></th>
<th>All (N = 721)</th>
<th>No-AKI (n = 615)</th>
<th>AKI (n = 106)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-hospital mortality</td>
<td>16 (2.2)</td>
<td>11 (1.8)</td>
<td>5 (4.7)</td>
<td>0.071</td>
</tr>
<tr>
<td>Clip detachment</td>
<td>10 (1.4)</td>
<td>7 (1.1)</td>
<td>3 (2.8)</td>
<td>0.171</td>
</tr>
<tr>
<td>Cordal rupture</td>
<td>8 (1.1)</td>
<td>7 (1.1)</td>
<td>1 (0.9)</td>
<td>0.999</td>
</tr>
<tr>
<td>Pericardial effusion</td>
<td>12 (1.7)</td>
<td>9 (1.5)</td>
<td>3 (2.8)</td>
<td>0.253</td>
</tr>
<tr>
<td>Hematoma</td>
<td>26 (3.6)</td>
<td>22 (3.6)</td>
<td>4 (3.8)</td>
<td>0.784</td>
</tr>
<tr>
<td>Pseudoaneurysm</td>
<td>9 (1.2)</td>
<td>6 (1.0)</td>
<td>3 (2.8)</td>
<td>0.333</td>
</tr>
<tr>
<td>Arteriovenous fistula</td>
<td>6 (0.8)</td>
<td>6 (1.0)</td>
<td>0 (0.0)</td>
<td>0.600</td>
</tr>
<tr>
<td>Major vascular complication</td>
<td>14 (1.9)</td>
<td>11 (1.8)</td>
<td>3 (2.8)</td>
<td>0.445</td>
</tr>
<tr>
<td>Red-cell transfusion</td>
<td>32 (4.4)</td>
<td>24 (3.9)</td>
<td>8 (7.5)</td>
<td>0.120</td>
</tr>
<tr>
<td>Bleeding (BARC type ≥ 3A)</td>
<td>9 (1.3)</td>
<td>5 (0.8)</td>
<td>4 (3.8)</td>
<td>0.011</td>
</tr>
<tr>
<td>Hospitalization length, days</td>
<td>4 (2-7)</td>
<td>4 (2-7)</td>
<td>5 (2-11)</td>
<td>0.576</td>
</tr>
</tbody>
</table>

Values are n (%), median (interquartile range), n/N (%), or mean ± SD. *Only patients that contrast media was used.
BARC = Bleeding Academic Research Consortium; MR = mitral regurgitation.
and cardiac mortality at 2-year follow-up were 21.8% (95% CI: 18.9% to 25.1%) and 13.5% (95% CI: 11.1% to 16.4%), respectively. The primary endpoint was significantly higher in patients who experienced AKI (mortality: 40.5% vs. 18.7%; \( p < 0.001 \); and MACE: 63.6% vs. 23.5%; \( p < 0.001 \)) (Central Illustration, Supplemental Figure 3, respectively). Patients in the AKI group also had a higher risk of myocardial infarction (hazard ratio [HR]: 4.79; \( p = 0.032 \)) and major bleeding (HR: 12.5; \( p < 0.001 \)) (Table 4, Central Illustration). The univariable and multivariable analyses evaluating the factors associated with 2-year all-cause mortality are shown in Table 5. In the multivariable analysis, chronic obstructive pulmonary disease (HR: 1.87; \( p = 0.001 \)), poor mobility (HR: 1.61; \( p = 0.032 \)), basal hemoglobin <11 g/dl (HR: 2.11; \( p < 0.001 \)), left ventricular (LV) ejection fraction below 30% (HR: 1.83; \( p = 0.002 \)), CKD stage ≥3 (HR: 1.75; \( p = 0.022 \)), and the occurrence of AKI (HR: 2.25; 95% CI: 1.52 to 3.33; \( p < 0.001 \)) determined a higher risk of cumulative death at 2-year follow-up. Kaplan-Meier survival curves and clinical outcomes according to the presence of significant residual MR and the occurrence of AKI were also evaluated, as shown in Figure 1 and Supplemental Table 2. The combination of these 2 factors determined a 2-year mortality and MACE rate of 50.0% and 70.0%, respectively, versus 19.6% and 18.9%, respectively, in the absence of these 2 factors (\( p < 0.001 \) for both comparisons).

Among patients with renal function assessment at 1-year follow-up (82.8%), those with AKI exhibited a decrease in eGFR of –20.1% (IQR: –40.7% to 1.9%) at follow-up compared with baseline, whereas non-AKI patients had a minimal increase of 2.7% (IQR: –20.9% to 26.7%) (\( p < 0.001 \)) (Figure 2A). In addition, the proportion of patients with >10% of deterioration in eGFR was higher in the AKI group (62.3% vs. 41.0%; \( p = 0.001 \)) (Figure 2B). These results correlated with the presence of concomitant significant residual MR, revealing the higher decline (–37.6%; IQR: –57.4% to 18.5%) in the AKI and significant residual MR group (Supplemental Figure 4).

**DISCUSSION**

The main findings of the present study are: 1) AKI occurred in ~15% of the patients undergoing MitraClip; 2) independent predictors of AKI were low baseline hemoglobin, urgent procedure, and suboptimal MR reduction with a lower rate of device success; and 3) patients who experienced AKI had worse clinical outcomes and greater renal function deterioration during follow-up, especially in the presence of significant residual MR.

AKI is a frequent and serious complication both in cardiac surgery and in catheter-based procedures, being associated with a worse prognosis even when slight deterioration of renal function occurs after the procedure (2,3,21–23). Furthermore, the link between renal function and heart disease is widely known, and it is well-established that patients with CKD will have worse cardiovascular outcomes (24). In patients with heart failure and severe MR, this becomes even more important, mostly due to changes in stroke volume, pre-load, and afterload, all of which are mechanisms that affect renal perfusion. Advanced CKD has also been identified as a predictor for poorer long-term outcomes in patients undergoing PMVr with MitraClip (9,25). However, interestingly, a successful repair may lead to an improvement in renal function (9,10), explainable by changes of strain and other loading conditions on the LV. MitraClip eliminates the low impedance regurgitant flow into the left atrium, leading to a reduction in the LV pre-load during diastole and an increment in the LV afterload during systole. However, acute LV failure after the surgical correction of MR, thought to be due to an acute afterload mismatch, is a well-known phenomenon that can lead to catastrophic outcomes (26). However, the interaction of LV strain and loading conditions with percutaneous rather than open surgical repair remains poorly understood (27), but has been described in up to one-third of patients with severe ventricular dysfunction undergoing MitraClip (28).

In this study, we demonstrate that AKI occurred in ~15% of the patients following MitraClip, and the
presence of anemia, urgent procedure, and absence of device success were independent risk factors for post-procedure AKI. Interestingly, and unlike other studies, neither basal eGFR nor low LV ejection fraction were predictors of AKI on multivariate analysis; however, they were found as independent predictors for 2-year mortality. Our incidence of AKI was slightly lower than previous smaller studies (ranging from 18% to 23.8%) (11,12). This could be explained by different definitions of AKI and some differences in baseline characteristics (younger patients, less hypertension, lower N-terminal pro-B-type natriuretic peptide level and STS score). However, the proportion having AKI after MitraClip was in the range of other percutaneous interventions (4,5,23,29) and, as demonstrated by others, lower than in surgical interventions (30). The fact that iodine contrast is almost never used during MitraClip, combined with the finding of a relatively high incidence of AKI (similar to other catheter-based procedures), leads one to believe that AKI in MitraClip is not an issue of contrast, but rather due to complex pathophysiology. A possible explanation is that long procedures with general anesthesia and transient hypotension, frequently needing vasopressors, in a comorbid population could lead to renal ischemia even in the
absence of contrast use. It is known that, normally, renal blood flow is maintained in a wide range of perfusion pressures (mean arterial pressure 60 to 100 mm Hg); nevertheless, many of these patients will have impaired autoregulation mechanisms due to their comorbidities, presence of a proinflammatory state, or use of drugs that impact kidney autoregulation (e.g., nonsteroidal anti-inflammatory drugs, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers) (31,32). The association between intraoperative hypotension and development of post-operative AKI is a clearly defined phenomenon, even suggesting that mild and transient hypotension will have negative outcomes on renal function (33). This is particularly relevant during MitraClip procedures, where profound hypotension may develop after the induction of anesthesia and at the moment while interacting with the mitral valve, when some patients may need vasopressor (34). Pre-procedural anemia has been described as a predictor of AKI in TAVR (35) and cardiac surgery (32), but their mechanisms have not been elucidated yet.

Some studies suggested that pre-operative anemia may harm the kidney directly or by increasing patients’ susceptibility to concomitant renal insults (inflammatory response, renal hypoxia, and oxidative stress) (36). Although red blood cell transfusion did not demonstrate any benefit before cardiac surgery (37), there is a paucity of data in percutaneous procedures. As the majority of these procedures are planned, baseline hemoglobin level should be assessed in all the patients to determine the necessity for anemia correction. A gradual improvement in hemoglobin levels with iron or stimulating agents weeks before the procedure will probably have a better outcome than acutely transfusing red blood cells immediately before the procedure, to avoid oxidative stress and other complications of transfusion. The impact of these potential preventive strategies could be the purpose of future trials.

Of note, 6% of the patients (10% in the AKI group) had a concomitant intervention with the MitraClip procedure. The procedures were combined to avoid a second intervention with general anesthesia and a transseptal puncture (i.e., left atrial appendage closure) (38) with their inherent risks. The risk versus benefit of a solo MitraClip procedure versus a combined intervention needs to be balanced in the heart team meetings and procedural planning.

Our study revealed that AKI patients had more than twice the risk of 2-year all-cause mortality or MACE compared with the non-AKI group, in accordance with previous findings from Taramasso et al. (11) and Spieker et al. (12). Thus, the occurrence of this complication identified a vulnerable group of poorer midterm clinical outcomes and a potential target for a close and careful follow-up. Significant residual MR after the procedure has been previously associated as a risk factor for future clinical events (39,40). The additive risk of significant residual MR after the procedure clearly identified a subgroup of patients at very high risk of poor outcomes.

Finally, the AKI group showed significant deterioration in their glomerular filtration rates during follow-up, whereas renal function improved or remained stable in the majority of patients without AKI. These findings were even more pronounced in case of a suboptimal result following PMVr. Interestingly, almost 40% of the patients without AKI (and higher in the group with no-AKI and residual MR ≤2), experienced a significant improvement of the eGFR in follow-up, highlighting the close interaction between cardiac and renal function. The deterioration or lack of change of renal function in the AKI group may also contribute to worsened clinical outcomes during follow-up.
STUDY LIMITATIONS. This study has several limitations inherent to its observational nature and retrospective analysis. Although prospective data collection was performed, some unmeasured confounders, even after multivariable adjustment, may influence the results. High doses of furosemide in bolus prior to the procedure for volume depletion and systematic assessment of invasive hemodynamics values during the procedure were not routinely recorded. This may have partially explained patient

![FIGURE 1 Impact of Significant Residual Mitral Regurgitation and Acute Kidney Injury Following MitraClip on Clinical Outcomes](image)

Kaplan-Meier curves up to 2-year follow-up for (A) all-cause mortality, and (B) major adverse cardiac events (MACE), according to the occurrence of acute kidney injury (AKI) and significant residual mitral regurgitation (MR) after MitraClip. Red and blue lines indicate acute kidney injury. Solid and dotted lines indicate significant residual MR.

![FIGURE 2 Changes in Renal Function in the Follow-Up According to the Occurrence of Acute Kidney Injury in Patients Undergoing MitraClip](image)

Absolute change in estimated glomerular filtration rate (A) and percentage of patients with improvement, no change, or worsening of estimated glomerular filtration rate (eGFR) (B) at last follow-up according to the occurrence of acute kidney injury (AKI).
hemodynamic status peri-procedurally that could influence the occurrence of AKI. There was no independent echocardiographic core laboratory to assess MR severity before and after the procedure and an external adjudication event committee for clinical outcomes, although this is a less essential fact when assessing overall mortality rate. Renal function assessment immediately after discharge (within 7 days) was not performed, with a potential under-diagnosis of the true incidence of AKI in those patients with a late AKI occurrence after hospital discharge. Changes in medical treatment after the procedure and follow-up was not routinely recorded and this could also influence clinical outcomes with a different impact between groups.

CONCLUSIONS

Percutaneous mitral valve edge-to-edge repair with the MitraClip device showed a 15% incidence of AKI after the procedure despite the lack of significant contrast use. Post-procedural AKI negatively affected survival and renal function at follow-up, with worse outcomes especially if mitral repair was suboptimal. A number of risk factors identified in the present report may help to optimize the management of these high-risk patients and to identify preventive preoperative measurements to be tested in the future.

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REFERENCES


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APPENDIX For supplemental figures and tables, please see the online version of this paper.