JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 76, NO. 21, 2020
© 2020 BY THE AMERICAN COLLEGE OF CARDIOLOGY FOUNDATION
PUBLISHED BY ELSEVIER

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

Germán Armijo, MD,[a] Rodrigo Estevez-Loureiro, MD,[b] Fernando Carrasco-Chinchilla, MD,[c] Dabit Arzamendi, MD,[d] Felipe Fernández-Vázquez, MD,[e] Pilar Jimenez-Quevedo, MD,[a] Xavier Freixa, MD,[f,g,h] Isaac Pascual, MD,[i] Ana María Serrador, MD,[j] Dolores Mesa, MD,[k] Juan H. Alonso-Briales, MD,[c] Javier Goicolea, MD,[l] Rosana Hernández-Antolin, MD,[m] Estefania Fernández-Peregrina, MD,[d] Ana Belen Cid Alvarez, MD,[n] Leire Andraka, MD,[o] Ignacio Cruz-Gonzalez, MD,[p] Alberto Berenguer, MD,[q] Juan Sanchis, MD,[r] Jose Luis Diez Gil, MD,[s] Jose M. Hernández-García, MD,[c] Chi-Hion Li, MD,[d] Tomas Benito-González, MD,[e] Jose A. de Agustin, MD,[a] Pablo Avanzas, MD,[i] Ander Regueiro, MD,[f,g,h] Ignacio Amat-Santos, MD,[j] Manuel Pan, MD,[k] Luis Nombela-Franco, MD[a]

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 m^2 (interquartile range: 30.9 to 60.1 ml/min/1.73 m^2), and was <60 ml/min/1.73 m^2 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.
(J Am Coll Cardiol 2020;76:2463–73) © 2020 by the American College of Cardiology Foundation.

Listen to this manuscript's audio summary by Editor-in-Chief Dr. Valentin Fuster on JACC.org.

From the [a]Cardiovascular Institute, Hospital Clínico San Carlos, IdISSC, Madrid, Spain; [b]Interventional Cardiology Unit, Hospital Álvaro Cunqueiro, Vigo, Spain; [c]Hospital Clínico Universitario Virgen de la Victoria, Málaga, CIBERCV, Málaga, Spain; [d]Division of Interventional Cardiology, Hospital de la Santa Creu i Sant Pau, Universitat Autónoma de Barcelona, Barcelona, Spain; [e]Department of Cardiology, University Hospital of León, León, Spain; [f]Cardiology Department Cardiovascular Institute, Hospital Clínic, Barcelona, Spain; [g]Universitat de Barcelona, Barcelona, Spain; [h]Institut d'Investigacions Biomèdiques August Pi i Sunyer, Barcelona, Spain; [i]Heart Area, Hospital Universitario Central de Asturias, Instituto de Investigación Sanitaria del Principado de Asturias, University of Oviedo, Asturias, Spain; [j]Cardiology Department, Hospital Clínico Universitario de Valladolid, CIVERCV, Valladolid, Spain; [k]Cardiology Department, Hospital Reina Sofía, Universidad de Córdoba, Instituto Maimónides de Investigación Biomédica de Córdoba (IMIBIC), Córdoba, Spain; [l]Cardiology Department, Hospital Universitario Puerta de Hierro, Majadahonda, Spain; [m]Cardiology Department, Hospital Universitario Ramón y Cajal, Madrid, Spain; [n]Hospital Clínico Universitario de Santiago, CIBERCV, Santiago, Spain; [o]Cardiology Department, Hospital de Basurto, Bilbao, Spain; [p]Cardiology Department, Hospital Clínico Universitario de Salamanca-Instituto de Investigación Biomédica de Salamanca, Centro de Investigación Biomédica en Red de

ISSN 0735-1097/$36.00 https://doi.org/10.1016/j.jacc.2020.09.582

ABBREVIATIONS AND ACRONYMS

AKI = acute kidney injury

CIN = contrast-induced nephropathy

CKD = chronic kidney disease

eGFR = estimated glomerular filtration rate

LV = left ventricle

MACE = major adverse cardiac events

MR = mitral regurgitation

PMVr = percutaneous mitral valve repair

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.

SEE PAGE 2474

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 operatoŕs 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

Enfermedades Cardiovasculares, Salamanca, Spain; [q]Cardiology Department, Hospital General Universitario de Valencia, Valencia, Spain; [r]Cardiology Department, Hospital Clínico Universitario, Universitat de Valencia, INCLIVA, Valencia, CIBERCV, Spain; and the [s]Cardiology Department, Hospital Universitario y Politécnico, La Fe, Valencia, Spain.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC* author instructions page.

Manuscript received August 10, 2020; accepted September 18, 2020.

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 m^2). 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

TABLE 1 Baseline Characteristics of the Study Population According to the Occurrence of AKI

	All (N = 721)	No-AKI (n = 615)	AKI (n = 106)	p Value
Baseline clinical characteristics				
Age, yrs	72.4 ± 10.8	73.0 ± 10.9	73.1 ± 10.2	0.465
Female	204 (28.3)	180 (29.3)	24 (22.6)	0.162
BMI, kg/m^2	27.2 ± 4.7	27.1 ± 4.5	27.9 ± 5.5	0.149
Hypertension	481 (66.7)	411 (6.8)	70 (66.0)	0.873
Diabetes mellitus	226 (31.3)	186 (30.2)	40 (37.7)	0.125
Atrial fibrillation	385 (53.4)	332 (54.0)	53 (50.0)	0.448
Coronary artery disease	355 (49.2)	299 (48.6)	56 (52.8)	0.423
Recent MI (<90 days)	41 (5.7)	30 (4.9)	11 (10.4)	0.024
Previous CABG	112 (15.5)	93 (15.1)	19 (17.9)	0.462
Previous PCI	244 (33.8)	208 (33.8)	36 (34.0)	0.977
COPD	144 (20.0)	122 (19.8)	22 (20.8)	0.827
Peripheral vascular disease	97 (13.5)	76 (12.4)	21 (19.8)	0.038
Cerebrovascular disease	60 (8.3)	51 (8.3)	9 (8.5)	0.946
Baseline NYHA functional class III to IV	580/649 (89.4)	492/553 (89.0)	88/96 (91.7)	0.429
At least 1 HF admission within 1 yr	432 (59.9)	365 (59.3)	67 (63.2)	0.454
EuroSCORE II	4.7 (2.8-8.9)	4.4 (2.7-8.1)	7.9 (3.7-12.3)	<0.001
STS-PROM score	4.02 (1.9-6.9)	3.86 (1.78-6.62)	5.19 (2.94-8.71)	0.013
Medical treatment				
ACE inhibitors	291 (40.4)	248 (40.3)	43 (40.6)	0.963
Angiotensin-II receptor blockers	155 (21.5)	137 (22.3)	18 (17.0)	0.220
Beta-blockers	463 (64.2)	405 (65.9)	58 (54.7)	0.027
Aldosterone antagonists	317 (44.0)	274 (44.6)	43 (40.6)	0.445
Echocardiographic data				
LVEDV, ml	152.5 (109-199)	152 (109-199)	158 (102.5-203)	0.905
LVESV, ml	89 (55-187)	91 (55.5-146)	85 (51.5-139)	0.467
LVEF, %	35 (29-51)	35 (29-51)	36 (30-55)	0.589
LVEF <35%	278 (42.5)	240 (42.9)	38 (40.0)	0.593
Moderate or severe TR	140 (26.0)	112 (24.1)	28 (37.3)	0.016
TAPSE	17 (12-20)	17 (12-20)	17 (12-20)	0.840
MR mechanism				0.556
Degenerative	128 (20.2)	108 (20.0)	20 (21.5)	
Functional	414 (65.4)	351 (65.0)	63 (67.7)	
Mixed	91 (14.4)	81 (15.0)	10 (10.8)	
Laboratory assessment				
eGFR, ml/min/1.73 m^2	43.7 (30.9-60.1)	44.1 (31.1-61.0)	41.8 (28.0-56.1)	0.049
Chronic kidney disease stage				0.011
1 and 2	181 (25.1)	161 (26.2)	20 (18.9)	
3a	155 (21.5)	135 (22.0)	20 (18.9)	
3b	219 (30.4)	183 (29.8)	36 (34.0)	
4 and 5	166 (23.0)	136 (22.1)	30 (28.3)	
eGFR <60 ml/min/1.73 m^2, %	540 (74.9)	454 (73.8)	86 (81.1)	0.109
CIN risk score*	12.0 (9.0-15.0)	12.0 (9.0-15.0)	14.0 (11.5-17.0)	<0.001
Hemoglobin, g/dl	12.4 ± 1.9	12.5 ± 1.9	11.8 ± 2.0	0.001
NT pro-BNP	2,479 (1,154-5,495)	2,532 (1,151-5,666)	2,180 (1,712-3,845)	0.825

Values are mean ± SD, n (%), n/N (%), or median (interquartile range). *Refers to Mehran et al. (18).

ACE = angiotensin-converting enzyme; BMI = body mass index; CABG = coronary artery bypass grafting; CIN = contrast-induced nephropathy; COPD = chronic obstructive pulmonary disease; NYHA = New York Heart Association; eGFR = estimated glomerular filtration rate; HF = heart failure; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; MI = myocardial infarction; MR = mitral regurgitation; PCI = percutaneous coronary intervention; STS-PROM = Society of Thoracic Surgeons predicted risk of mortality; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation.

ejection fraction (median 35% IQR: 29% to 51%). Baseline median eGFR was 43.7 ml/min/1.73 m^2 (IQR: 30.9 to 60.1 ml/min/1.73 m^2), 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)

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

	All (N = 721)	No-AKI (n = 615)	AKI (n = 106)	p Value
Procedural data				
Urgent procedure	31 (4.3)	20 (3.3)	11 (10.4)	0.002
Inotropic support	70 (9.7)	55 (8.9)	15 (14.2)	0.094
Residual MR ≤ grade 2	530 (94.0)	454 (95.2)	76 (87.3)	0.005
Device success	667 (92.5)	580 (94.3)	87 (82.1)	<0.001
Post-procedural mitral gradient, mm Hg	3 (2-4)	3 (2-4)	3 (2-4)	0.561
Mitral gradient ≥5 mm Hg	70/498 (14.1)	61/431 (14.2)	9/67 (13.4)	0.875
Number of clips	1.45 ± 0.73	1.45 ± 0.73	1.46 ± 0.75	0.949
Catheter thrombosis	4 (0.6)	2 (0.3)	2 (1.9)	0.105
Cordal entrapment	5 (0.7)	4 (0.7)	1 (0.9)	0.550
Procedural time	136 (109-181)	138 (110-180)	120 (103-194)	0.576
General anesthesia	712 (98.8)	607 (98.7)	105 (99.1)	0.999
Concomitant intervention	45 (6.2)	34 (5.5)	11 (10.4)	0.057
Contrast amount, ml (overall population)	0 (0-0)	0 (0-0)	0 (0-0)	0.273
Contrast amount, ml*	40.0 (30.0-66.5)	45.0 (31.0-68.0)	33.0 (23.0-45.0)	0.154
Peri-procedural complications and in-hospital outcomes				
In-hospital mortality	16 (2.2)	11 (1.8)	5 (4.7)	0.071
Clip detachment	10 (1.4)	7 (1.1)	3 (2.8)	0.171
Cordal rupture	8 (1.1)	7 (1.1)	1 (0.9)	0.999
Pericardial effusion	12 (1.7)	9 (1.5)	3 (2.8)	0.253
Hematoma	26 (3.6)	22 (3.6)	4 (3.8)	0.784
Pseudoaneurysm	9 (1.2)	6 (1.0)	3 (2.8)	0.133
Arteriovenous fistula	6 (0.8)	6 (1.0)	0 (0.0)	0.600
Major vascular complication	14 (1.9)	11 (1.8)	3 (2.8)	0.445
Red-cell transfusion	32 (4.4)	24 (3.9)	8 (7.5)	0.120
Bleeding (BARC type ≥ type 3A)	9 (1.3)	5 (0.8)	4 (3.8)	0.011
Hospitalization length, days	4 (2-7)	4 (2-7)	5 (2-11)	0.576

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.

(Supplemental Table 1). 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 3 Predictors of Acute Kidney Injury

	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	p Value	OR (95% CI)	p Value
Recent myocardial infarction (<90 days)	2.26 (1.10–4.66)	0.027	–	0.722
Peripheral vascular disease	1.75 (1.03–2.99)	0.040	–	0.368
Stages of eGFR, ml/min/1.73 m^2		0.024		0.563
Stage 1, ≥90	1.00	–	–	
Stage 2, 60–89	1.60 (0.55–4.63)	0.386	–	
Stage 3A, 45–59	1.66 (0.59–4.64)	0.334	–	
Stage 3B, 30–44	2.20 (0.83–5.88)	0.115	–	
Stage 4, 16–29	1.97 (0.71–5.47)	0.193	–	
Stage 5, ≤15	8.15 (2.24–29.62)	0.001	–	
Basal hemoglobin <11 g/dl	2.05 (1.32–3.16)	0.001	1.97 (1.81–3.09)	0.003
Moderate or severe baseline TR	1.88 (1.12–3.13)	0.017	–	0.158
Urgent procedure	3.45 (1.60–7.42)	0.002	3.44 (1.26–7.64)	0.003
Device success, no/yes	3.62 (1.98–6.61)	<0.001	3.37 (1.81–6.26)	<0.001

CI = confidence interval; OR = odds ratio; other abbreviations as in Table 1.

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).

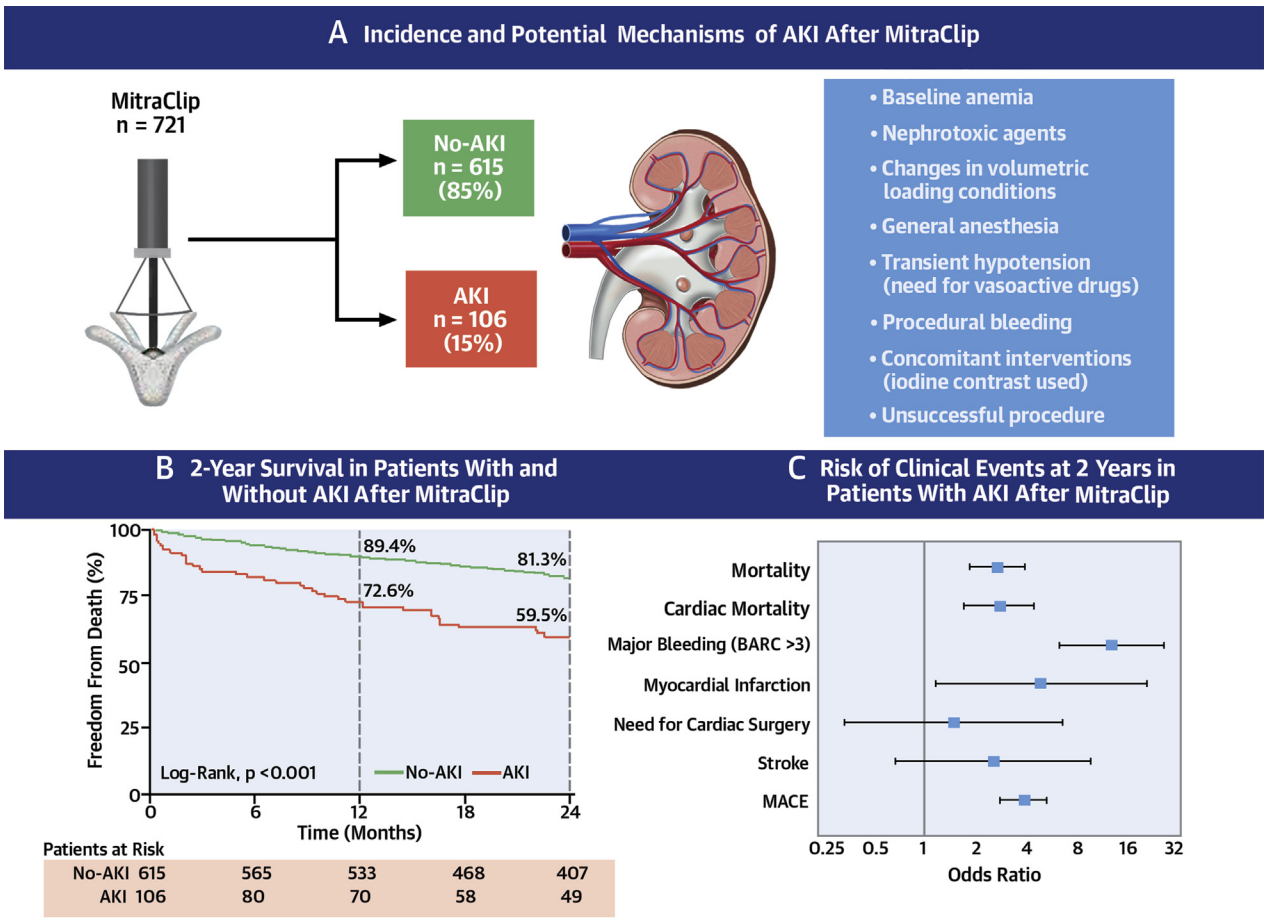
DISCUSSION

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

CENTRAL ILLUSTRATION **Incidence, Mechanisms, and 2-Year Clinical Outcomes of Acute Kidney Injury in Patients Undergoing MitraClip**



Armijo, G. et al. J Am Coll Cardiol. 2020;76(21):2463–73.

Possible mechanisms involved and its incidence **(A)**; Kaplan-Meier curve and relative risks up to 2-year follow-up for all-cause mortality and serious clinical events (**B and C**, respectively).

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 led to renal ischemia even in the

TABLE 4 2-Year Clinical Outcomes According to the Occurrence of Acute Kidney Injury

	No-AKI (n = 615)	AKI (n = 106)	HR (95% CI)	p Value
Mortality	108 (17.8)	39 (38.6)	2.65 (1.84–3.83)	<0.001
Cardiac mortality	64 (10.5)	24 (23.8)	2.73 (1.70–4.36)	<0.001
Major bleeding (BARC ≥3)	13 (2.2)	19 (19.4)	12.50 (6.16–25.37)	<0.001
Myocardial infarction	5 (0.8)	3 (3.1)	4.79 (1.14–20.05)	0.032
Need for cardiac surgery	17 (2.8)	2 (2.0)	1.46 (0.33–6.43)	0.619
Stroke	9 (1.5)	3 (3.1)	2.51 (0.68–9.29)	0.168
MACE	137 (22.3)	62 (58.5)	3.74 (2.77–5.06)	<0.001

Values are n (%).
HR = hazard ratio; MACE = major adverse cardiac events (defined as a composite of death, myocardial infarction, need for cardiac surgery, stroke, or major bleeding); other abbreviations as in Tables 2 and 3.

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.

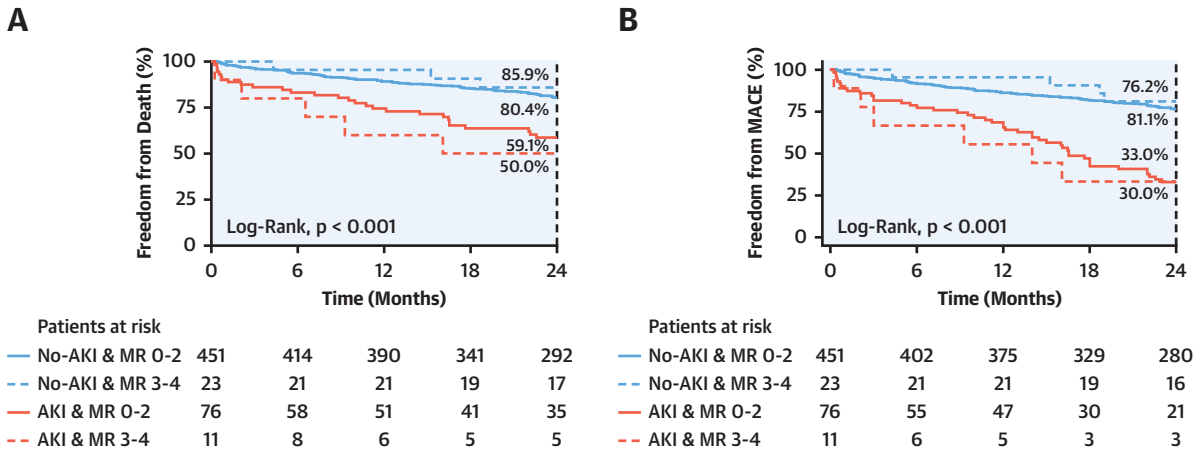
Finally, the AKI group showed significant deterioration in their glomerular filtration rates during follow-up, whereas renal function improved or remained stable in the majority of patients without AKI. These findings were even more pronounced in case of a suboptimal result following PMVr. Interestingly, 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.

TABLE 5 2-Year All-Cause Mortality Predictors

	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	p Value	OR (95% CI)	p Value
Age (≥60 yrs)	2.94 (1.38–6.29)	0.005	–	0.072
Recent MI (<90 days)	1.93 (1.07–3.48)	0.030	–	0.136
Diabetes mellitus	1.62 (1.17–2.25)	0.004	–	0.102
COPD	1.74 (1.22–2.48)	0.002	1.87 (1.29–2.71)	0.001
Peripheral vascular disease	1.88 (1.26–2.79)	0.002	–	0.146
Poor mobility	1.62 (1.05–2.49)	0.028	1.61 (1.04–2.50)	0.032
Basal hemoglobin <11 g/dl	2.17 (1.56–3.02)	<0.001	2.11 (1.47–3.02)	<0.001
LVEF <30%	1.47 (1.03–2.12)	0.036	1.83 (1.26–2.66)	0.002
Baseline eGFR <60 ml/min/1.73 m^2	1.67 (1.09–2.55)	0.017	1.75 (1.08–2.84)	0.022
Acute kidney injury	2.65 (1.84–3.83)	<0.001	2.25 (1.52–3.33)	<0.001

COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; LVEF = left ventricular ejection fraction; MI = myocardial infarction.

FIGURE 1 **Impact of Significant Residual Mitral Regurgitation and Acute Kidney Injury Following MitraClip on Clinical Outcomes**



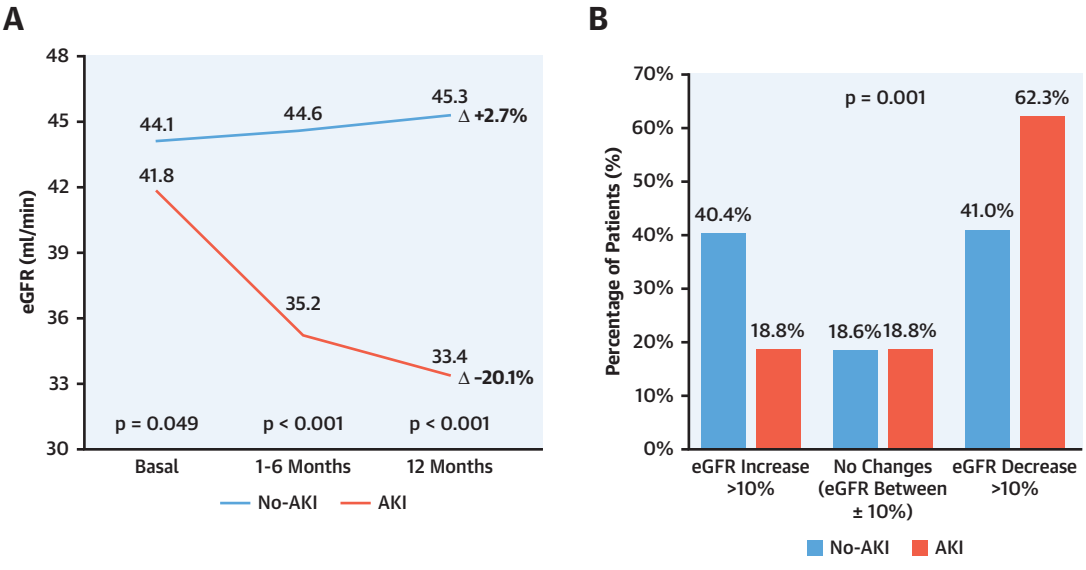
Patients at risk					
No-AKI & MR 0-2	451	414	390	341	292
No-AKI & MR 3-4	23	21	21	19	17
AKI & MR 0-2	76	58	51	41	35
AKI & MR 3-4	11	8	6	5	5

Patients at risk					
No-AKI & MR 0-2	451	402	375	329	280
No-AKI & MR 3-4	23	21	21	19	16
AKI & MR 0-2	76	55	47	30	21
AKI & MR 3-4	11	6	5	3	3

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.

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 patients

FIGURE 2 **Changes in Renal Function in the Follow-Up According to the Occurrence of Acute Kidney Injury in Patients Undergoing MitraClip**



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 underdiagnosis 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.

ACKNOWLEDGMENTS The authors thank Juan José de la Cruz Troca from the Autónoma University of Madrid for his help in the statistical analyses, and W. Aaron Kay, MD (Kay Cardiology Consulting, Zionsville, Indiana), for assistance with manuscript revision.

AUTHOR RELATIONSHIP WITH INDUSTRY

The electronic database for the Spanish MitraClip registry is maintained by an unrestricted grant from Abbott. This study was supported by Fundación Interhospitalaria para la Investigación Cardiovascular (FIC Foundation) via an unrestricted grant from Abbott. Drs. Estevez-Loureiro, Arzamendi, Freixa, Cruz-Gonzalez, de Agustin, and Nombela-Franco have served as proctors for Abbott. Dr. Pan has received lecture fees from Abbott. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr. Luis Nombela-Franco, Instituto Cardiovascular, Hospital Universitario Clínico San Carlos, IdISSC, C/ Prof. Martin Lagos s/n, 28040 Madrid, Spain. E-mail: luisnombela@yahoo.com. Twitter: @luisnombela, @RodrigoEstvez1, @structuralheartbcn, @ignamatsant, @german_armijo.

PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: AKI occurs in ~15% of patients undergoing PMVr with the MitraClip, and the risk is higher in patients with baseline anemia, when the procedure is performed urgently, and when and the device is unsuccessful. Post-procedural renal injury, when coupled with suboptimal valve repair, identifies a subgroup prone to further deterioration of renal function and adverse outcomes.

TRANSLATIONAL OUTLOOK: Randomized trials are needed to evaluate strategies to avoid kidney injury in patients undergoing percutaneous mitral valve interventions.

REFERENCES

1. Wang Y, Bellomo R. Cardiac surgery-associated acute kidney injury: risk factors, pathophysiology and treatment. Nat Rev Nephrol 2017;13:697–711.

2. Hobson CE, Yavas S, Segal MS, et al. Acute kidney injury is associated with increased long-term mortality after cardiothoracic surgery. Circulation 2009;119:2444–53.

3. Ortega-Loubon C, Fernández-Molina M, Carrascal-Hinojal Y, Fulquet-Carreras E. Cardiac surgery-associated acute kidney injury. Ann Card Anaesth 2016;19:687–98.

4. McCullough PA, Choi JP, Feghali GA, et al. Contrast-induced acute kidney injury. J Am Coll Cardiol 2016;68:1465–73.

5. Liao Y-B, Deng X-X, Meng Y, et al. Predictors and outcome of acute kidney injury after transcatheter aortic valve implantation: a systematic review and meta-analysis. EuroIntervention J Eur Collab Work Group Interv Cardiol Eur Soc Cardiol 2017;12:2067–74.

6. Dangas G, Iakovou I, Nikolsky E, et al. Contrast-Induced nephropathy after percutaneous coronary interventions in relation to chronic kidney disease and hemodynamic variables. Am J Cardiol 2005;95:13–9.

7. Mehran R, Dangas GD, Weisbord SD. Contrast-associated acute kidney injury. N Engl J Med 2019;380:2146–55.

8. Stone GW, Lindenfeld J, Abraham WT, et al. Transcatheter mitral-valve repair in patients with heart failure. N Engl J Med 2018;379:2307–18.

9. Kaneko H, Neuss M, Schau T, Weissenborn J, Butter C. Interaction between renal function and percutaneous edge-to-edge mitral valve repair using MitraClip. J Cardiol 2017;69:476–82.

10. Wang A, Sangli C, Lim S, et al. Evaluation of renal function before and after percutaneous mitral valve repair. Circ Cardiovasc Interv 2015;8:e001349.

11. Taramasso M, Latib A, Denti P, et al. Acute kidney injury following MitraClip implantation in high risk patients: incidence, predictive factors and prognostic value. Int J Cardiol 2013;169:e24–5.

12. Spieker M, Hellhammer K, Katsianos S, et al. Effect of acute kidney injury after percutaneous mitral valve repair on outcome. Am J Cardiol 2018;122:316–22.

13. Feldman T, Foster E, Glower DD, et al. Percutaneous repair or surgery for mitral regurgitation. N Engl J Med 2011;364:1395–406.

14. Pascual I, Arzamendi D, Carrasco-Chinchilla F, et al. Transcatheter mitral repair according to the cause of mitral regurgitation: real-life data from the Spanish MitraClip registry. Rev Esp Cardiol (Engl Ed) 2020;73:643–51.

15. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. Ann Intern Med 2009;150:604–12.

16. Levey AS, Eckardt K-U, Tsukamoto Y, et al. Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney Int 2005;67:2089–100.

17. Mehta RL, Kellum JA, Shah SV, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Crit Care Lond Engl 2007;11:R31.

18. Mehran R, Aymong ED, Nikolsky E, et al. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: development and initial validation. J Am Coll Cardiol 2004;44:1393–9.

19. Zoghbi WA, Enriquez-Sarano M, Foster E, et al. Recommendations for evaluation of the severity of native valvular regurgitation with two-dimensional and Doppler echocardiography. J Am Soc Echocardiogr 2003;16:777–802.

20. Stone GW, Adams DH, Abraham WT, et al. Clinical trial design principles and endpoint definitions for transcatheter mitral valve repair and replacement: part 2: endpoint definitions: a consensus document from the mitral valve academic research consortium. J Am Coll Cardiol 2015;66:308–21.

21. Chertow GM, Levy EM, Hammermeister KE, Grover F, Daley J. Independent association between acute renal failure and mortality following cardiac surgery. Am J Med 1998;104:343–8.

22. Lassnigg A, Schmidlin D, Mouhieddine M, et al. Minimal changes of serum creatinine predict prognosis in patients after cardiothoracic surgery: a prospective cohort study. J Am Soc Nephrol JASN 2004;15:1597–605.

23. Nombela-Franco L, Rodés-Cabau J, Cruz-Gonzalez I, et al. Incidence, predictors, and prognostic value of acute kidney injury among patients undergoing left atrial appendage closure. J Am Coll Cardiol Intv 2018;11:1074–83.

24. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu C. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med 2004;351:1296–305.

25. Ross J. Afterload mismatch in aortic and mitral valve disease: implications for surgical therapy. J Am Coll Cardiol 1985;5:811–26.

26. Estévez-Loureiro R, Settergren M, Pighi M, et al. Effect of advanced chronic kidney disease in clinical and echocardiographic outcomes of patients treated with MitraClip system. Int J Cardiol 2015;198:75–80.

27. Essandoh MK. Afterload mismatch after MitraClip implantation: the potential impact of pharmacologic support. J Cardiothorac Vasc Anesth 2017;31:702–6.

28. Freixa X, Hernández M, Farrero M, et al. Levosimendan as an adjunctive therapy to MitraClip implantation in patients with severe mitral regurgitation and left ventricular dysfunction. Int J Cardiol 2016;202:517–8.

29. Almendarez M, Gurm HS, Mariani J, et al. Procedural strategies to reduce the incidence of contrast-induced acute kidney injury during percutaneous coronary intervention. J Am Coll Cardiol Intv 2019;12:1877–88.

30. Körber MI, Scherner M, Kuhr K, et al. Acute kidney injury following percutaneous edge-to-edge vs. minimally invasive surgical mitral valve repair: incidence, predictors and prognostic value. EuroIntervention 2018;13:1645–51.

31. Abuelo JG. Normotensive ischemic acute renal failure. N Engl J Med 2007;357:797–805.

32. Karkouti K, Wijeysundera DN, Yau TM, et al. Acute kidney injury after cardiac surgery: focus on modifiable risk factors. Circulation 2009;119:495–502.

33. McKinlay J, Tyson E, Forni LG. Renal complications of anaesthesia. Anaesthesia 2018;73 Suppl 1:85–94.

34. Kothandan H, Vui KH, Ho VK, et al. Anesthesia management for MitraClip device implantation. Ann Card Anaesth 2014;17:17–22.

35. Arai T, Morice M-C, O'Connor SA, et al. Impact of pre- and post-procedural anemia on the incidence of acute kidney injury and 1-year mortality in patients undergoing transcatheter aortic valve implantation (from the French Aortic National CoreValve and Edwards 2 [FRANCE 2] Registry). Catheter Cardiovasc Interv 2015;85:1231–9.

36. Karkouti K, Grocott HP, Hall R, et al. Interrelationship of preoperative anemia, intraoperative anemia, and red blood cell transfusion as potentially modifiable risk factors for acute kidney injury in cardiac surgery: a historical multicentre cohort study. Can J Anesth 2015;62:377–84.

37. Padmanabhan H, Brookes MJ, Nevill AM, Luckraz H. Association Between Anemia and Blood Transfusion With Long-term Mortality After Cardiac Surgery. Ann Thorac Surg 2019;108:687–92.

38. Freixa X, Estévez-Loureiro R, Carrasco-Chinchilla F, et al. Initial results of combined mitraclipâ® implantation and left atrial appendage occlusion. J Heart Valve Dis 2017;26:169–74.

39. Puls M, Tichelbäcker T, Bleckmann A, et al. Failure of acute procedural success predicts adverse outcome after percutaneous edge-to-edge mitral valve repair with MitraClip. EuroIntervention 2014;9:1407–17.

40. Paranskaya L, D'Ancona G, Bozdag-Turan I, et al. Residual mitral valve regurgitation after percutaneous mitral valve repair with the MitraClip® system is a risk factor for adverse one-year outcome. Catheter Cardiovasc Interv 2013;81:609–17.

KEY WORDS acute kidney injury, MitraClip, mitral edge-to-edge repair, mortality, outcomes, renal insufficiency

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