Myocardial Injury After Transcatheter Mitral Valve Replacement Versus Surgical Reoperation

Mauricio Felippi de Sá Marchi, MD[a,b], Vitor Emer Egypto Rosa, MD, PhD[a], Pedro Felipe Gomes Nicz, MD[a], José Honório de Almeida Palma da Fonseca, MD, PhD[a], Pedro Calomeni[a], Fernando Chiodini, MD[a], Roney Orismar Sampaio, MD, PhD[a], Pablo Maria Alberto Pomerantzeff, MD, PhD[a], Marcelo de Campos Vieira, MD, PhD[a], Flávio Tarasoutchi, MD, PhD[a], Nicolas M. Van Mieghem, MD, PhD[b], Fábio Sandoli de Brito, Jr., MD, PhD[a], Alexandre Abizaid, MD, PhD[a], and Henrique Barbosa Ribeiro, MD, PhD[a,*]

This study aimed to evaluate the incidence and clinical implications of myocardial injury, as determined by cardiac biomarker increase, in patients who underwent mitral bioprosthesis dysfunction treatment with transcatheter mitral valve replacement (TMVR) versus surgical mitral valve replacement reoperation (SMVR-REDO). Between 2014 and 2023, 310 patients with mitral bioprosthesis failure were included (90 and 220 patients for TMVR and SMVR-REDO, respectively). Multivariable analysis and propensity score matching were performed to adjust for the intergroup differences in baseline characteristics. Creatinine kinase-MB (CK-MB) and cardiac troponin I (cTn) were collected at baseline and 6 to 12, 24, 48, and 72 hours after intervention. The cardiac biomarkers values were evaluated in relation to their reference values. The outcomes were determined according to the Mitral Valve Academic Research Consortium criteria. CK-MB and cTn increased above the reference level in almost all patients after SMVR-REDO and TMVR (100% vs 94%, respectively), with the peak occurring within 6 to 12 hours. SMVR-REDO was associated with a two- to threefold higher increase in cardiac biomarkers. After 30 days, the mortality rates were 13.3% in the TMVR and 16.8% in the SMVR-REDO groups. At a median follow-up of 19 months, the mortality rates were 21.1% in the TMVR and 17.7% in the SMVR-REDO groups. Left ventricular ejection fraction, estimated glomerular filtration rate, CK-MB, and cTn were predictors of mortality. In conclusion, some degree of myocardial injury occurred systematically after the treatment of mitral bioprosthetic degeneration, especially after SMVR, and higher CK-MB and cTn levels were associated with increased cumulative late mortality, regardless of the approach. **(Am J Cardiol 2024;214:8−17)**

Keywords: mitral, valve dysfunction, bioprosthetic valve degeneration, transcatheter mitral valve replacement, myocardial injury, transapical, transseptal, mitral valve surgery

Surgical mitral valve repair and replacement are frequently performed cardiac procedures. In the last decades, there has been an increased use of bioprosthetic (BP) valves implantation in favor of mechanical valves.[1] Surgical mitral valve replacement reoperation (SMVR-REDO) is the gold standard for BP dysfunction.[2] Still, this procedure poses a noteworthy myocardial injury risk, as determined by cardiac creatine kinase-MB (CK-MB) mass and cardiac troponin increase, likely because of the use of aortic cross-clamping and cardioplegia.[2,3] Hence, transcatheter mitral valve replacement (TMVR) has emerged as a minimally invasive alternative, yielding fewer periprocedural complications than SMVR-REDO.[4] Nonetheless, there is a lack of studies specifically evaluating myocardial injury in patients who underwent TMVR versus SMVR-REDO and their impact on the clinical outcomes. Furthermore, the proposed cut-off points used in the Mitral Valve Academic Research Consortium (M-VARC) to define significant myocardial injury are not clinically validated for neither TMVR nor SMVR-REDO.[5,6] The objectives of this study were to evaluate the incidence, predictors, and clinical outcomes of myocardial injury in patients with severe mitral BP valve dysfunction who underwent TMVR versus SMVR-REDO.

Methods

From January 2014 and March 2023, a total of 310 consecutive patients with severe mitral BP dysfunction were included, of whom 90 underwent TMVR (68 transapical [TA] and 22 transseptal [TS]) and 220 underwent SMVR-

[a]Heart Institute (InCor), Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo (HC-FMUSP), São Paulo, Brazil; and [b]Department of Interventional Cardiology, Thoraxcenter, Erasmus University Medical Center, Rotterdam, The Netherlands. Manuscript received September 26, 2023; revised manuscript received and accepted December 9, 2023.

Dr. de Sá Marchi is supported by a PhD research grant from CNPq, Conselho Nacional de Desenvolvimento Científico e Tecnológico−Brasil.

See page 16 for Declaration of Competing Interest.

*Corresponding author.

E-mail address: henrique.ribeiro@hc.fm.usp.br (H.B. Ribeiro).

0002-9149/
https://doi.org/10.1016/j.amjcard.2023.12.009

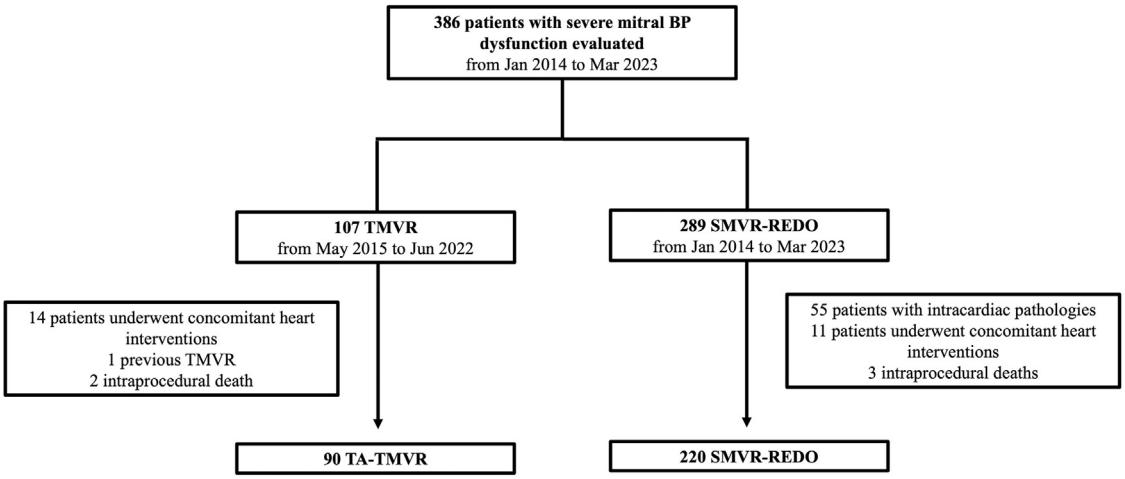

Figure 1. Study flowchart.

REDO. All TMVR and SMVR-REDO procedures were performed by the same heart team at a single center. Figure 1 shows the flow diagram of the study population. The exclusion criteria included the following: (1) patients with intracardiac pathologies that contraindicated transcatheter treatment, such as infective endocarditis or intracardiac thrombus, (2) concomitant heart interventions, (3) previous implant of a transcatheter mitral valve, (4) dysfunctional mitral ring and mitral annular calcification, and (5) transcatheter edge-to-edge repair. The study was approved by the ethics committee and the need for written informed consent from individual patients was waived because of the retrospective and anonymous nature of the study.

Patients who underwent TA and TS were grouped into a single category of patients who underwent TMVR. The baseline co-morbidities were defined according to the Society of Thoracic Surgeons (STS) criteria, and the clinical outcomes were defined according to the M-VARC criteria.[5,6] Clinical follow-up was carried out by clinical visits and/or through phone contact at 1 month, 6-to-12 months after transcatheter aortic valve replacement and yearly thereafter for both groups. Complete late clinical follow-up was available in all patients.

Blood samples were collected before intervention and between 6 to 12 hours, 12 to 24 hours, 24 to 48 hours, and 48 to 72 hours after mitral intervention. At least 1 measure of CK-MB and cardiac troponin I (cTn) was performed at each time point. cTn examinations between 2014 and February 2020 were performed with ADVIA Centaur XP Contemporary Sensitive Troponin I Assay, with a reference value of 0.04 ng/ml for both genders. After February 2020, cTn examinations were performed using ADVIA Centaur XP High Sensitivity Troponin I, with a reference value of 40 ng/L for women and 58 ng/L for men, respectively. The upper limits of normal (ULN) values were based on the ninety-ninth percentile in a healthy population and presented a coefficient of variation of <10%. Myocardial injury was defined as an increase in CK-MB and/or cTn above the ULN (up to 72 hours) after the intervention.[6,7] The degree of biomarkers increase was calculated by dividing CK-MB and/or cTn level by the ULN, and this was expressed as n-fold of increase.

Doppler echocardiographic examination was performed before mitral intervention, upon hospital discharge, and at late follow-up. The images were analyzed by 2 experienced cardiologists and BP dysfunction was defined according to the current guidelines.[8,9] Severe BP stenosis was defined as a calculated mitral prosthesis area $\leq$1.0 cm^2 or mean transmitral gradient $\geq$10 mm Hg, and mitral regurgitation was defined by integrating several doppler and quantitative findings.[10] Mitral regurgitation severity was classified according to the American Society of Echocardiography guideline as none/trace, mild, moderate, or severe.[11]

The Heart Team, which includes clinical cardiologists, interventional cardiologists, echocardiographers, and cardiac surgeons, evaluated each patient's needs and circumstances to determine the most appropriate treatment strategy. TA-TMVR was performed under general anesthesia through TA access with Braile Inovare (n = 68) (Braile Biomedical, São Paulo, Brazil) valves, as previously demonstrated.[12] Inovare is a balloon-expandable valve with a chromium-cobalt stent frame with 6 sizes, ranging from 20 to 30 mm.[12] All of the TS access were also performed under general anesthesia using the SAPIEN 3 (n = 21) and SAPIEN 3 Ultra (n = 1) valves. SMVR-REDO procedures were performed using traditional transatrial access under general anesthesia and extracorporeal circulation. The type and size of BP were chosen at the discretion of the operators.

Categorical variables were reported as n (%). Continuous variables were expressed as mean SD or median (interquartile range), as appropriate. Group comparisons were made using Student's *t* test or Mann−Whitney *U* test for continuous variables and chi-square test for categorical variables. Propensity score matching (PSM) analysis using a 2-to-1 matching process was performed to adjust for the intergroup (TMVR versus SMVR-REDO) differences in baseline characteristics, using the algorithm of nearest-neighbor method matching by the R package MatchIt. The variables used for the matching process were age, hypertension, dyslipidemia, previous coronary artery bypass graft, atrial fibrillation,

estimated glomerular filtration rate (eGFR), EuroScore II, and STS. For the CK-MB and cTn analysis, normality assumption was verified using Anderson−Darling tests. The increase in values of CK-MB and cTn were logarithmically transformed to normalize distributions. Generalized linear model repeated measures analysis was used to evaluate variation of biomarkers, and the Tukey test was used for post hoc analyses. A linear regression analysis was conducted after standardizing cardiac biomarkers by assessing the n-fold increase (calculated by dividing the serum levels by the ULN for each kit) to identify the predictors of increased cardiac biomarker values. Continuous variables were checked for linearity assumption using distribution quartiles and fractional polynomials. Univariable and multivariable Cox proportional hazards models were used to determine predictors of cumulative 30-day and late overall mortality. Variables with a probability value <0.10 were candidates for construction of multivariable regression models. The mortality rates were presented using Kaplan−Meier estimates, and comparisons between groups were made using the logarithmic rank test. Younden index was used to identify the best accuracy point for 30-day and late mortality in the receiver operating characteristic analysis. The results were considered significant with $p < 0.05$. Analyses were made using SPSS 24 (IBM, Armonk, New York) and R Statistical Software 4.2.2 (Foundation for Statistical Computing, Vienna, Austria).

Results

Baseline clinical, echocardiographic, and laboratory characteristics of the study population are listed in Table 1. Patients in the TMVR group were older than in the SMVR-REDO group ($p < 0.001$) and presented a greater burden of co-morbidities, such as higher rates of hypertension, dyslipidemia, atrial fibrillation, lower eGFR, and coronary artery bypass graft history (all with $p < 0.05$). Therefore, patients who underwent TMVR presented higher STS Predicted Risk of Mortality score (5.8 [3.8 to 9.5] vs 2.7 [1.7 to 5.0]%, respectively, $p < 0.001$) and EuroSCORE II (7.8 [4.6 to 11.5] vs 4.4 [3.0 to 6.7]%, respectively, $p < 0.001$). There were no differences in baseline echocardiographic variables, except for a higher left ventricular mass index in TMVR group than in the SMVR-REDO group (103 [90 to 132] g/m^2 vs 91 [71 to 106] g/m^2, respectively, $p < 0.001$). Baseline and procedural characteristics of the PSM population (TMVR and SMVR-REDO) are listed in Table 2 and were well balanced according to the major baseline characteristics.

The median peak values of CK-MB and cTn at each time point within 72 hours after mitral intervention, stratified according to approach (TMVR group vs SMVR-REDO), are shown in Figure 2. The levels of CK-MB and cTn increased in 94.4% of patients who underwent TMVR and in all SMVR-REDO cases, with a median increase of 7.72-fold (4.41 to 16.63) for CK-MB and 200.2-fold (115.50 to 398.75) for cTn, peaking at 6 to 12 hours after both procedures. This increase was significantly higher in the SMVR-REDO group than in the TMVR group, both for CK-MB (9.74 [6.55 to 14.71] vs 3.79 [2.34 to 4.89], respectively, $p < 0.001$) and cTn (258.97 [131.94 to 458.44] vs 118.25 [61.28 to 210], respectively, $p < 0.001$). The degree of increase in CK-MB and cTn according to the approach (TMVR group vs SMVR-REDO) expressed by folds-of-increase are depicted in Figure 3. The median peak values of CK-MB and cTn at each time point within 72 hours after mitral intervention and the degree of increase in CK-MB and cTn according to approach expressed by folds-of-increase stratified according to approach (TMVR group vs SMVR-REDO) in a PSM population are shown in Supplementary Figure 1 and according to a subanalysis of TMVR (TS-TMVR vs TA-TMVR groups) in Supplementary Figure 2. Importantly, TA-TMVR was related with a 2-fold higher increase in CK-MB and cTn with respect to TS-TMVR ($p < 0.05$).

The baseline and procedural variables associated with a higher degree of myocardial injury are listed in Supplementary Table 1. The multivariable analysis demonstrated that baseline left ventricular ejection fraction (LVEF) and SMVR-REDO were independent predictors of CK-MB increase ($p < 0.05$). Regarding cTn, SMVR-REDO was the only independent predictor of increase ($p < 0.05$). In patients who underwent SMVR-REDO, a multivariable subanalysis showed that the independent factors associated with greater increase in CK-MB levels were LVEF and duration of extracorporeal circulation ($p < 0.05$). Concerning cTn, a higher increase in cTn was only predicted by the duration of extracorporeal circulation ($p = 0.018$), as listed in Supplementary Table 2.

The procedural and 30-day outcomes of the overall study population and according to approach are listed in Table 3. Patients in the TMVR group had a shorter hospital stay, had lower rates of major bleeding, and required fewer blood transfusions than patients in the SMVR-REDO group. Yet, echocardiography at 30 days revealed that patients who underwent SMVR-REDO presented lower maximal and mean mitral gradients than those who underwent TMVR. There were no left ventricular outflow tract obstructions in the TMVR group.

The 30-day and late overall mortality did not differ between TMVR and SMVR-REDO groups. Within 30 days after mitral intervention, 48 patients (15%) died: 11 (12%) in TMVR group and 37 (17%) in the SMVR-REDO group ($p = 0.554$). The cumulative mortality rate was 19% in a median follow-up of 19.1 (3.1 to 37.9) months, 19 (21.1%) in the TMVR group and 39 (17.7%) in the SMVR-REDO group, with no difference between groups on long-term follow-up (hazard ratio [HR] 0.86, 95% confidence interval [CI] 0.49 to 1.49, $p = 0.59$). In the propensity-matched cohort, 9 patients (17%) in the TMVR group and 26 (26%) in the SMVR-REDO group died (HR 1.46, 95% CI 0.78 to 2.76, $p = 0.24$) (Figure 4).

Table 4 lists the univariable and multivariable analysis of predictors of 30-day and late cumulative mortality, with 2 models adjusted by CK-MB and cTn, respectively. In model 1, for 30-day mortality, a greater increase in CK-MB (HR 1.012, 95% CI 1.006 to 1.018, $p < 0.001$) and eGFR (HR 0.982, 95% CI 0.969 to 0.996, $p = 0.009$) were independent predictors of mortality. In model 2, a greater increase in cTn (HR 1.001, 95% CI 1.001 to 1.002, $p < 0.001$) and eGFR (HR 0.978, 95% CI 0.965 to 0.991, $p = 0.001$) were independent predictors of 30-day mortality.

Table 1
Baseline clinical and echocardiographic characteristics of the study population

	Overall (n = 310)	TMVR (n = 90)	SMVR-REDO (n = 220)	*p* value
Clinical variables				
Age, years	56.2 ± 13.9	67.3 ± 11.2	51.6 ± 12.2	< 0.001
Female sex	213 (68.7)	62 (68.9)	51 (68.6)	1.000
NYHA				0.839
Class I/II	38 (12.3)	10 (11.1)	28 (12.7)	
Class III/IV	272 (87.7)	80 (88.9)	192 (87.3)	
Angina	14 (4.5)	7 (7.9)	7 (3.2)	0.126
Etiology				0.131
Rheumatic	215 (70.7)	54 (63.5)	161 (73.5)	
Mitral valve prolapse	29 (9.5)	8 (9.4)	21 (9.6)	
Other	60 (19.7)	23 (27.1)	37 (16.9)	
Hypertension	135 (43.5)	50 (55.6)	85 (38.6)	0.009
Diabetes	36 (11.6)	15 (16.7)	21 (9.5)	0.114
Dyslipidemia	88 (28.4)	38 (42.2)	50 (22.7)	< 0.001
COPD	17 (5.5)	7 (7.8)	10 (4.5)	0.277
Atrial fibrillation	186 (60)	66 (73.3)	120 (54.5)	0.003
Cerebrovascular disease	48 (15.5)	17 (18.9)	31 (14.1)	0.375
eGFR < 60 mL/min/1.73 m^2	131 (42.3)	62 (68.9)	69 (31.4)	< 0.001
CABG	16 (5.2)	12 (13.3)	4 (1.8)	< 0.001
PCI	6 (1.9)	3 (3.3)	3 (1.4)	0.362
Pacemaker	19 (6.1)	9 (10)	10 (4.5)	0.120
Hospitalization in the last 30 days	83 (26.9)	22 (25)	61 (27.7)	0.730
Time since last surgery, years	11.7 ± 5.6	12.5 ± 5.4	11.4 ± 5.6	0.129
Number of previous surgeries	1 [1-2]	1 [1 - 2]	1 [1 - 2]	0.615
STS-PROM score, %	3.64 [1.99 − 5.81]	5.81 [3.79 − 9.52]	2.72 [1.69 − 4.97]	< 0.001
EuroSCORE II, %	4.95 [3.39 − 8.44]	7.84 [4.64 − 11.54]	4.36 [3 − 6.73]	< 0.001
Echocardiographic variables				
Left atrium diameter, mm	54 [48 − 61]	55 [48 − 63]	53 [48 − 60]	0.137
LVEF, %	61 [56 − 66]	60 [55 − 65]	62 [56.50 − 66]	0.181
LVESD, mm	33 [30 − 38]	33.5 [29.7 − 39]	33 [30 − 37]	0.622
LVEDD, mm	51 [46 − 55]	51 [45 − 56]	50.5 [46 − 55]	0.748
LVMI, g/m^2	96 [75 − 112]	103 [90 − 132]	91 [71 − 106]	< 0.001
Mitral valve area, cm^2	1.06 ± 0.43	1.07 ± 0.44	1.05 ± 0.43	0.129
Max mitral gradient, mmHg	25 [19 − 30]	24 [18 − 28]	25 [20 − 30]	0.130
Mean transmitral gradient, mmHg	10 [8 − 15]	10 [8 − 13]	11 [9 − 15]	0.129
Moderate/severe mitral regurgitation	121 (56)	51 (61)	70 (53)	0.363
PASP, mmHg	60.5 ± 21.6	60.7 ± 18.2	60.4 ± 23.0	0.935
Moderate/severe right ventricular dysfunction	71 (33)	33 (39)	38 (29)	0.157

Values are n (%), mean ± SD or median [IQR].

CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration; EuroSCORE 2 = European System for Cardiac Operative Risk Evaluation predicted risk of in-hospital mortality; LVEDD = left ventricular end-diastolic diameter; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic diameter; LVMI = left ventricular mass index; NYHA = New York Heart Association; PASP = pulmonary artery systolic pressure; PCI = percutaneous coronary intervention; SMVR-REDO = surgical reoperation of the mitral valve; STS-PROM = Society of Thoracic Surgeons Predicted Risk of Mortality; TMVR = transcatheter mitral valve replacement.

Regarding late cumulative mortality, model 1 demonstrated that a greater increase in CK-MB (HR 1.013, 95% CI 1.007 to 1.019, p <0.001), eGFR (HR 0.984, 95% CI 0.972 to 0.997, p = 0.013), and LVEF (HR 0.975, 95% CI 0.951 to 1.000, p = 0.048) were independent predictors of mortality. In model 2, for late cumulative mortality, a greater increase in cTn (HR 1.001, 95% CI 1.001 to 1.002, p <0.001), eGFR (HR 0.982, 95% CI 0.970 to 0.994, p = 0.004), and LVEF (HR 0.040, 95% CI 0.951 to 0.999, p = 0.040) were variables related to greater mortality.

Using the Youden index, a 10-fold increase in CK-MB best predicted 30-day (area under the curve [AUC] 0.64, 95% CI 0.55 to 0.73, p = 0.046) and late cumulative mortality (AUC 0.58, 95% CI 0.49 to 0.67, p = 0.046), as shown in Supplementary Figure 3. Furthermore, a 500-fold increase in cTn best predicted 30-day (AUC 0.73. 95% CI 0.66 to 0.81, p = 0.040) and late cumulative mortality (AUC 0.69, 95% CI 0.61 to 0.77, p = 0.041).

A 10-fold increase of CK-MB and a 500-fold increase of cTn were associated with overall mortality, regardless of the approach, with an HR of 1.72 (95% CI 1.030 to 2.89, p = 0.04) and 3.87 (95% CI 2.31 to 6.48, p <0.001), respectively, as shown in Figure 5.

Compared with the immediate postmitral intervention measurements, the LVEF at late follow-up remained similar

Table 2
Baseline clinical and echocardiographic characteristics of the propensity-matched population

	Overall (n = 158)	TMVR (n = 53)	SMVR-REDO (n = 99)	*p* value
Clinical variables				
Age, years	60.6 ± 10.4	62.5 ± 11.2	59.5 ± 9.9	0.100
Female sex	103 (67.8)	39 (73.6)	64 (64.6)	0.346
NYHA				0.287
Class I/II	22 (10.5)	8 (15.1)	8 (8.1)	
Class III/IV	136 (89.5)	45 (84.9)	91 (91.9)	
Angina	10 (6.3)	7 (9.0)	3 (3.8)	0.317
Etiology				0.629
Rheumatic	105 (69.1)	36 (67.9)	69 (69.7)	
Mitral valve prolapse	15 (9.9)	4 (7.5)	11 (11.1)	
Other	32 (21.1)	13 (24.5)	19 (19.2)	
Hypertension	71 (46.7)	25 (47.2)	46 (46.5)	1.000
Diabetes	19 (12.5)	6 (11.3)	13 (13.1)	0.949
Dyslipidemia	50 (32.9)	19 (35.8)	31 (31.3)	0.699
COPD	11 (7.2)	3 (5.7)	8 (8.1)	0.826
PASP > 60 mmHg	61 (40.1)	20 (37.7)	41 (41.4)	0.789
Atrial fibrillation	107 (70.4)	41 (77.4)	66 (66.7)	0.234
Cerebrovascular disease	29 (19.1)	10 (18.9)	19 (19.2)	1.000
eGFR < 60 mL/min/1.73 m^2	84 (55.3)	31 (58.5)	53 (53.5)	0.679
CABG	7 (4.6)	3 (5.7)	4 (4)	0.962
PCI	5 (3.3)	2 (3.8)	3 (3)	1.000
Pacemaker	12 (7.9)	7 (13.2)	5 (5.1)	0.144
Hospitalization in the last 30 days	53 (35.1)	13 (25.0)	40 (40.4)	0.088
Time since last surgery, years	12.1 ± 5.7	11.6 ± 5.2	12.5 ± 6	0.364
Number of previous surgeries	2 [1 - 2]	2 [1 - 3]	1 [1 - 2]	0.016
STS-PROM score, %	4.38 [3.06 - 6.54]	4.56 [3.42 - 7.06]	4.29 [2.8 - 5.85]	0.144
EuroSCORE II, %	6.14 [4.06 - 9.21]	7.38 [4.48 - 10.46]	5.89 [3.71 - 8.6]	0.093
Echocardiographic variables				
Left atrium diameter, mm	54 [49 - 60]	54.5 [48.7 - 63]	53.5 [49 - 59]	0.232
LVEF, %	61 [55.5 - 66]	60 [55 - 65.2]	62 [56 - 66]	0.502
LVESD, mm	32 [30 - 37]	33.5 [30 - 38]	33 [30 - 36]	0.460
LVEDD, mm	50 [45 - 54]	49 [44 - 55]	50 [45 - 54]	0.927
LVMI, g/m^2	96 [75 - 111.5]	98 [83.5 - 114]	93 [70.5 - 108]	0.136
Mitral valve area, cm^2	1.02 ± 0.43	1.1 ± 0.5	1 ± 0.4	0.505
Max mitral gradient, mmHg	24 [19 - 29]	24 [19.7 - 29]	24 [19 - 29.7]	0.773
Mean transmitral gradient, mmHg	10 [9 - 14.7]	10 [9 - 13.2]	10 [9 - 15]	0.975
Moderate/severe mitral regurgitation	61 (58.7)	31 (60.8)	30 (56.6)	0.815
PASP, mmHg	61.4 ± 22.4	60.2 ± 18.3	62.1 ± 24.3	0.639
Moderate/severe right ventricular dysfunction	35 (33.7)	18 (35.3)	17 (32.1)	0.889

Values are n (%), mean ± SD or median [IQR].

in the TMVR and SMVR-REDO groups (59 [49.5 to 64] and 60 [52.5 to 65], respectively, p = 0.390). Notably, slightly higher values of mean transmitral gradients were observed in TMVR than in SMVR-REDO, 6 (5 to 7) versus 5 (4 to 7) mm Hg, respectively (p = 0.009).

Discussion

The main findings were as follows: (1) mitral reinterventions (TMVR and SMVR-REDO) were systematically associated with certain degree of myocardial injury, (2) SMVR-REDO and the duration of extracorporeal circulation were the main predictors of CK-MB and cTn increase, (3) greater levels of myocardial injury were independently correlated with higher mortality at 30-day and late follow-up, irrespective of the approach, and (4) CK-MB increase ≥10-fold and cTn ≥500-fold from baseline are relevant thresholds for defining clinically relevant myocardial injury.

Cardiac surgery systematically generates substantial increase in cardiac biomarkers, particularly, in combined procedures and valve reinterventions.[13,14] Minimally invasive interventions, such as transcatheter aortic valve implantation, have been shown to significantly reduce cardiac biomarkers release, most likely because of the avoidance of aortic cross-clamping and cardioplegia.[15,16] However, no study to date had specifically compared the release in cardiac biomarkers in patients who underwent TMVR versus SMVR-REDO. To the best of our knowledge, this study is the first to demonstrate that both approaches are related to a systematic increase in CK-MB and cTn, peaking at 6 to 12 hours, with SMVR-REDO presenting with a 2- to 3-fold higher fold of increase than TMVR.

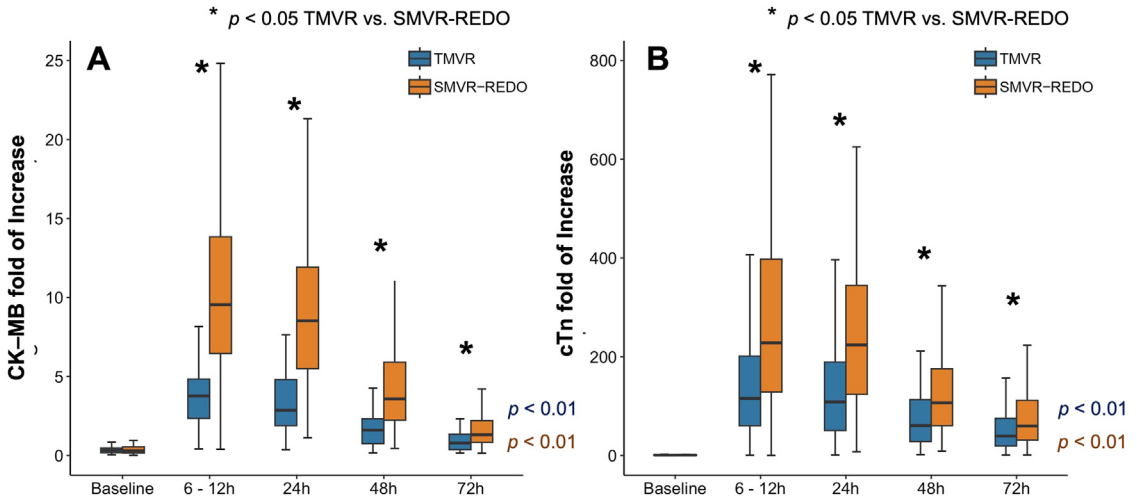

Figure 2. Cluster boxplot with the median changes in CK-MB (*A*) and cTn (*B*) levels after TMVR versus TMVR-REDO. Changes in CK-MB (*A*); and cTn (*B*); levels within the 72 hours after TMVR versus SMVR-REDO. Values are expressed as median (25th to 75th interquartile range) of fold of increase.

Baseline LVEF was significantly related to higher CK-MB and cTn increases, regardless of the approach, indicating the important role of ventricular dysfunction and myocardial compromise in the genesis of myocardial injury.[16,17] Likewise, the significant association of greater CK-MB release to the number of previous surgical interventions and hospitalization in the last 30 days further reinforces the extent of direct myocardial damage as a factor linked to myocardial injury.[18,19] In this study, most patients who underwent TMVR were treated using TA access, which is a known risk factor for myocardial injury.[20] This is likely because of the apex myocardial necrosis associated with large bore catheters.[7] TS approach for TMVR procedures has emerged as a less traumatic strategy, which precludes thoracotomy and apical puncture, potentially leading to less myocardial injury.[21,22] Despite the limited number of patients, this study demonstrated this reduction. However, larger studies are necessary to confirm such findings. Finally, in the surgical cohort, duration of extracorporeal circulation and aortic cross-clamping were factors associated with myocardial injury, underlining the importance of minimizing or even avoiding surgical procedures in patients with compromised ventricles, as previously described in previous studies in the transcatheter aortic valve implantation field.[16]

Myocardial injury has a detrimental prognostic impact in a variety of transcatheter and surgical cardiac interventions.[15,16,23] Accordingly, greater increases of CK-MB and cTn levels were associated with increased 30-day and long-term mortality, irrespective of the approach. The mortality rates were similar between TMVR and SMVR-REDO in the overall population and occurred predominantly in the acute phase, which is consistent with studies comparing these 2 strategies in high-risk patients who underwent mitral valve reintervention.[2,24] In the study population, patients in TMVR group were older and presented a higher burden of co-morbidities, yielding a 2-fold greater STS Predicted Risk of Mortality and EuroSCORE II, a finding consistent with previous reports.[24] The mortality rates were statistically similar between TMVR and SMVR-REDO, even after PSM for baseline characteristics was performed, which is consistent with a recently published meta-analysis comparing these 2 strategies.[24] However, the TMVR group experienced less periprocedural

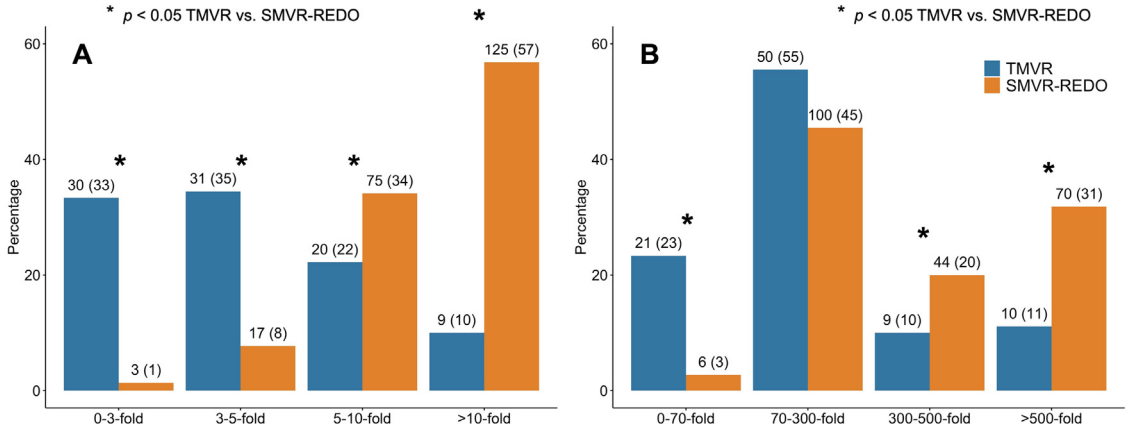

Figure 3. Degree of increase in CK-MB (*A*) and cTn (*B*) levels after TMVR versus SMVR-REDO. Cardiac biomarker changes are grouped according to the percent of patients in the TMVR versus SMVR-REDO according to fold of increase.

Table 3
Procedural and 30-day outcomes of the study population

	Overall (n = 310)	TMVR (n = 90)	SMVR-REDO (n = 220)	*p* value
Procedural outcomes				
Technical success*	261 (96)	81 (93.1)	180 (97.3)	0.111
Extracorporeal circulation, minutes	-	-	105.5 ± 25.6	-
Aortic cross-clamping, minutes	-	-	83.1 ± 20.9	-
Cardiac tamponade	3 (1)	1 (1.1)	2 (0.9)	1.000
Conversion to open surgery	4 (1.3)	4 (4.5)	-	-
Intrahospital mortality	48 (15.5)	11 (12.2)	37 (16.8)	0.400
Hospitalization ICU, days	8 [5 - 15]	9 [5 − 15.5]	8 [5 − 15]	0.974
Hospitalization total, days	11 [7 - 20]	9 [5.5 − 16.5]	12.5 [8 - 21]	< 0.001
30-day outcomes				
Mortality	49 (15.8)	12 (13.3)	37 (16.8)	0.554
NYHA functional class				1.000
Class I/II	236 (93.3)	71 (93.4)	165 (93.2)	
Class III/IV	17 (6.7)	5 (6.6)	12 (6.8)	
New onset atrial fibrillation	31 (10)	4 (4.4)	27 (12.3)	0.061
Cerebrovascular event	3 (1)	-	3 (1.4)	0.559
Acute Kidney Injury*	78 (25.2)	18 (20)	60 (27.3)	0.232
Infection	88 (28.4)	22 (24.4)	66 (30)	0.398
Reintubation	23 (7.4)	7 (7.8)	16 (7.3)	1.000
Endocarditis	2 (0.6)	-	2 (0.9)	1.000
Permanent pacemaker	15 (4.8)	1 (1.1)	14 (6.4)	0.076
Rehospitalization	17 (6.7)	7 (9.1)	10 (5.7)	0.469
eGFR, mL/min/1.73 m^2	64 ± 24.9	53 ± 24.0	70 ± 23.4	< 0.001
In-hospital echocardiographic variables				
Left atrium size, mm	52 [47 - 57]	53 [48 − 57.2]	52 [46 − 57.5]	0.262
LVEF, %	60 [52.5 - 64]	59 [52 - 64]	60 [52.7 - 64]	0.533
LVESD, mm	32 [29.7 - 37]	32 [30 - 37]	32 [29 - 37]	0.728
LVEDD, mm	49 [45 - 53]	49 [45 - 53]	49 [44.5 - 53]	0.826
LVMI, g/m^2	94 [74 - 109]	100 [78- 119]	88 [71.5 − 106]	0.006
Mitral valve size, cm^2	1.79 ± 0.66	1.66 ± 0.52	2 ± 0.80	0.061
Max mitral gradient, mmHg	13 [10 - 16]	15 [11 − 20]	12 [10 - 15]	< 0.001
Mean mitral gradient, mmHg	5.1 [4 - 7]	6 [5 − 9.9]	5 [4 - 7]	< 0.001
Moderate/severe mitral regurgitation	2 (0.9)	1 (1.2)	1 (0.8)	1.000
PASP, mmHg	44.8 ± 19.9	52.6 ± 16.9	41.4 ± 20.2	< 0.001
Moderate/severe right ventricle dysfunction	70 (32.7)	31 (37.3)	39 (29.8)	0.316
30-day laboratorial variables				
Hemoglobin, g/dL	10.1 ± 1.9	9.7 ± 2.2	10.2 ± 1.8	0.035
Creatinine, mg/dL	1 [0.8 - 1.2]	1.1 [0.9 - 1.5]	0.9 [0.8 - 1.2]	< 0.001
Platelets, mm^3	207000 [142500 - 294750]	138000 [113000 - 188000]	251000 [184000 - 351000]	< 0.001

Values are n (%), mean (± SD) or median [IQR]. Technical success, measured at exit from the catheterization laboratory, as: I. Absence of procedural mortality; II. Successful access, delivery, and retrieval of the device delivery system; III. Successful deployment and correct positioning of the first intended device; and IV. Freedom from emergency surgery or reintervention related to the device or access procedure.

ICU = intensive care unit; other abbreviations as in Table 1.

* Following M-VARC criteria:

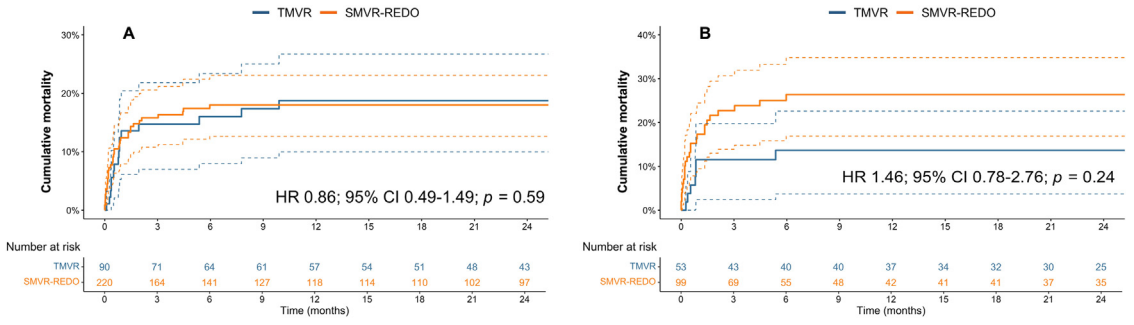

Figure 4. Long-term Kaplan−Meier cumulative mortality according to the approach TMVR versus SMVR-REDO for the overall population (*A*) and for the propensity-matched cohort (*B*).

Table 4
Univariable and multivariable analyses for 30-day and cumulative mortality

Variable	Univariable analysis		Multivariable Analysis	
	HR (95% CI)	*p* value	HR (95% CI)	*p* value
30-day mortality				
Model 1 - CK-MB				
Age	1.017 (0.996 - 1.038)	0.109	1.006 (0.982 - 1.029)	0.639
eGFR	0.983 (0.971 - 0.994)	0.003	0.982 (0.969 - 0.996)	0.009
Max fold CK-MB	1.009 (1.004 - 1.015)	0.001	1.012 (1.006 - 1.018)	<0.001
NYHA	1.584 (0.968 − 2.651)	0.073	1.616 (0.993 − 2.630)	0.054
Model 2 - cTn				
Age	1.017 (0.996 - 1.038)	0.109	1.007 (0.982 - 1.031)	0.600
eGFR	0.983 (0.971 - 0.994)	0.003	0.978 (0.965 - 0.991)	0.001
Max fold cTn	1.001 (1.000 - 1.001)	<0.001	1.001 (1.001 - 1.002)	<0.001
NYHA	1.584 (0.968 − 2.651)	0.073	1.615 (0.988 - 2.640)	0.056
Cumulative mortality				
Model 1-CK-MB				
Age	1.027 (1.008 - 1.047)	0.005	1.016 (0.993 - 1.040)	0.163
eGFR	0.981 (0.970 - 0.991)	<0.001	0.984 (0.972 − 0.997)	0.013
Max fold CK-MB	1.009 (1.003 - 1.014)	0.005	1.013 (1.007 - 1.019)	<0.001
LVEF	0.974 (0.951 - 0.997)	0.028	0.975 (0.951 − 1.000)	0.048
NYHA	1.562 (1.019 − 2.392)	0.041	1.540 (0.977 − 2.428)	0.063
COPD	2.604 (1.181 − 5.740)	0.018	1.590 (0.695 − 3.641)	0.272
Model 2 - cTn				
Age	1.027 (1.008 - 1.047)	0.005	1.019 (0.995 - 1.043)	0.131
eGFR	0.981 (0.970 - 0.991)	<0.001	0.982 (0.970 − 0.994)	0.004
Max fold cTn	1.001 (1.000 - 1.001)	<0.001	1.001 (1.001 - 1.002)	<0.001
LVEF	0.974 (0.951 - 0.997)	0.028	0.975 (0.951 - 0.999)	0.040
NYHA class	1.562 (1.019 − 2.392)	0.041	1.563 (0.987 − 2.475)	0.057
COPD	2.604 (1.181 − 5.740)	0.018	1.484 (0.654 − 3.367)	0.345

HR = hazard ratio; other abbreviations as in Table 1.

complications and a shorter hospital, a finding also observed in contemporary TMVR studies.[4]

Finally, the optimal threshold for defining clinically relevant myocardial injury after mitral BP dysfunction intervention is unsettled.[23] For instance, M-VARC recommends the cut-off value of 10-fold of increase in CK-MB and a 70-fold of increase in cTn, based on a modification of the Society for Cardiac Angiography and Interventions criteria for clinically relevant periprocedural myocardial infarction and the third universal definition of myocardial infarction.[6,25,26] However, these values have never been validated in the context of mitral reintervention. In the present study, a similar cutoff for CK-MB increase was observed, which provides evidence for M-VARC value. Nonetheless, the results showed a much higher cTn optimal cutoff than what was proposed in M-VARC.[5,6] M-VARC cTn cut-off point of 70-fold of increase is disputable, with reported values of approximately 500-fold in higher-risk patients who underwent nontranscatheter aortic valve replacement/noncoronary artery bypass graft operations.[14] This threshold has also been observed in this cohort, in which 500-fold of cTn increase best predicted the 30-day and late mortality. It is, however, important to consider that inconsistencies in studies involving cardiac biomarkers studies are attributable, at least in part, to the different assays used and the various patient populations. Further studies with more patients and

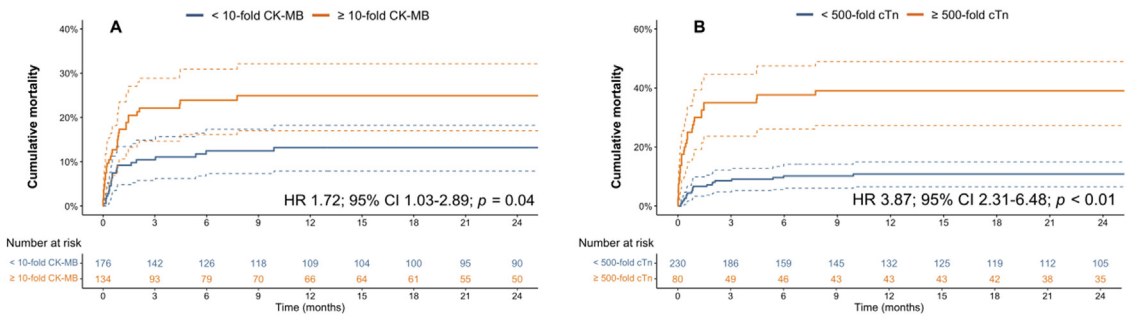

Figure 5. Long-term Kaplan−Meier cumulative mortality according to the percentiles of CK-MB (*A*) and cTn (*B*) increase after the procedure.

events also comparing the approaches of TMVR should further confirm such findings and determine the best cutoff in clinical practice.

This study has some limitations. First, it is an observational analysis with inherent selection bias and significant between-group differences that may not have been accounted, despite performing propensity match scoring and multivariable analysis. Yet, it is important to emphasize that the study population reflects clinical practice, in which patients referred for TMVR are generally older and at a higher operative risk than patients who underwent SMVR-REDO. In addition, patients with concomitant coronary artery disease interventions have been excluded from the analysis; therefore, a conclusion on the potential impact of its presence on cardiac biomarkers magnitude of increase cannot be established.

In conclusion, TMVR and SMVR-REDO resulted in increased CK-MB and cTn levels, with a **2- to 3-fold** higher increase in SMVR-REDO than in TMVR. Higher CK-MB and cTn levels were associated with increased late mortality, regardless of the choice of intervention. Lastly, this study demonstrated that a CK-MB increase ≥10-folds and cTn ≥500-fold from baseline appear to be the optimal thresholds to define clinically relevant myocardial injury after the procedure.

Declaration of competing interest

Dr. José Honório de Almeida Palma da Fonseca is proctor and has received research grant from Braile Biomédica. Dr. Van Mieghem is consultant and has received research grant from Edwards Lifesciences. Dr. Abizaid is proctor for Boston Scientific and has received research grant from Medtronic. Dr. de Brito Jr is proctor for Edwards Lifesciences, Medtronic, and Boston Scientific and received research grant from Medtronic. Dr. Ribeiro is proctor for Edwards Lifesciences, Medtronic, and Boston Scientific and received research grant from Medtronic. The remaining authors have no competing interest to declare.

CRediT authorship contribution statement

Mauricio Felippi de Sá Marchi: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Visualization, Writing – original draft, Writing – review & editing. **Vitor Emer Egypto Rosa:** Conceptualization, Methodology, Supervision, Writing – review & editing. **Pedro Felipe Gomes Nicz:** Data curation, Investigation, Writing – review & editing. **José Honório de Almeida Palma da Fonseca:** Resources, Writing – review & editing. **Pedro Calomeni:** Data curation, Formal analysis, Methodology, Writing – review & editing. **Fernando Chiodini:** Data curation, Investigation, Writing – review & editing. **Roney Orismar Sampaio:** Resources, Writing – review & editing. **Pablo Maria Alberto Pomerantzeff:** Resources, Writing – review & editing. **Marcelo de Campos Vieira:** Resources, Writing – review & editing. **Flávio Tarasoutchi:** Resources, Writing – review & editing. **Nicolas M. Van Mieghem:** Supervision, Writing – review & editing. **Alexandre Abizaid:** Supervision, Writing – review & editing. **Henrique Barbosa Ribeiro:** Conceptualization, Methodology, Project administration, Supervision, Writing – review & editing.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2023.12.009.

1. Gammie JS, Chikwe J, Badhwar V, Thibault DP, Vemulapalli S, Thourani VH, Gillinov M, Adams DH, Rankin JS, Ghoreishi M, Wang A, Ailawadi G, Jacobs JP, Suri RM, Bolling SF, Foster NW, Quinn RW. Isolated mitral valve surgery: the Society of Thoracic Surgeons adult cardiac surgery database analysis. *Ann Thorac Surg* 2018;106:716–727.
2. Zubarevich A, Szczechowicz M, Zhigalov K, Rad AA, Vardanyan R, Easo J, Roosta-Azad M, Kamler M, Schmack B, Ruhparwar A, Wendt D, Weymann A. Surgical redo mitral valve replacement in high-risk patients: the real-world experience. *J Card Surg* 2021;36:3195–3204.
3. Doenst T, Berretta P, Bonaros N, Savini C, Pitsis A, Wilbring M, Gerdisch M, Kempfert J, Rinaldi M, Folliguet T, Yan T, Stefano P, Van Praet F, Salvador L, Lamelas J, Nguyen TC, Dinh NH, Färber G, Di Eusanio M. Aortic cross-clamp time correlates with mortality in the mini-mitral international registry. *Eur J Cardiothorac Surg* 2023;63.
4. Eleid MF, Wang DD, Pursnani A, Kodali SK, George I, Palacios I, Russell H, Makkar RR, Kar S, Satler LF, Rajagopal V, Dangas G, Tang GHL, McCabe JM, Whisenant BK, Fang K, Kaptzan T, Lewis B, Douglas P, Hahn R, Thaden J, Oh JK, Leon M, O'Neill W, Rihal CS, Guerrero ME. 2-year outcomes of transcatheter mitral valve replacement in patients with annular calcification, rings, and bioprostheses. *J Am Coll Cardiol* 2022;80:2171–2183.
5. Stone GW, Vahanian AS, Adams DH, Abraham WT, Borer JS, Bax JJ, Schofer J, Cutlip DE, Krucoff MW, Blackstone EH, Généreux P, Mack MJ, Siegel RJ, Grayburn PA, Enriquez-Sarano M, Lancellotti P, Filippatos G, Kappetein AP, Mitral Valve Academic Research Consortium (MVARC). Clinical trial design principles and endpoint definitions for transcatheter mitral valve repair and replacement: part 1: Clinical trial design principles: a consensus document from the mitral valve Academic Research Consortium. *J Am Coll Cardiol* 2015;66:278–307.
6. Stone GW, Adams DH, Abraham WT, Kappetein AP, Généreux P, Vranckx P, Mehran R, Kuck KH, Leon MB, Piazza N, Head SJ, Filippatos G, Vahanian AS, Mitral Valve Academic Research Consortium (MVARC). 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;66:308–321.
7. Ribeiro HB, Dahou A, Urena M, Carrasco JL, Mohammadi S, Doyle D, Le Ven F, Allende R, Amat-Santos I, Paradis JM, DeLarochellière R, Puri R, Abdul-Jawad Altisent O, del Trigo M, Campelo-Parada F, Pibarot P, Dumont É, Rodés-Cabau J. Myocardial injury after transaortic versus transapical transcatheter aortic valve replacement. *Ann Thorac Surg* 2015;99:2001–2009.
8. Lancellotti P, Pibarot P, Chambers J, Edvardsen T, Delgado V, Dulgheru R, Pepi M, Cosyns B, Dweck MR, Garbi M, Magne J, Nieman K, Rosenhek R, Bernard A, Lowenstein J, Vieira ML, Rabischoffsky A, Vyhmeister RH, Zhou X, Zhang Y, Zamorano JL, Habib G. Recommendations for the imaging assessment of prosthetic heart valves: a report from the European Association of Cardiovascular Imaging endorsed by the Chinese Society of Echocardiography, the Inter-American Society of Echocardiography, and the Brazilian Department of Cardiovascular Imaging. *Eur Heart J Cardiovasc Imaging* 2016;17:589–590.
9. Zoghbi WA, Chambers JB, Dumesnil JG, Foster E, Gottdiener JS, Grayburn PA, Khandheria BK, Levine RA, Marx GR, Miller FA Jr, Nakatani S, Quiñones MA, Rakowski H, Rodriguez LL, Swaminathan M, Waggoner AD, Weissman NJ, Zabalgoitia M, American Society of Echocardiography's Guidelines and Standards Committee; Task Force on Prosthetic Valves; American College of Cardiology Cardiovascular Imaging Committee; Cardiac Imaging Committee of the American Heart Association; European Association of Echocardiography; European Society of Cardiology; Japanese Society of Echocardiography;

Canadian Society of Echocardiography; American College of Cardiology Foundation; American Heart Association; European Association of Echocardiography; European Society of Cardiology; Japanese Society of Echocardiography; Canadian Society of Echocardiography. Recommendations for evaluation of prosthetic valves with echocardiography and Doppler ultrasound: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Task Force on Prosthetic Valves, developed in conjunction with the American College of Cardiology Cardiovascular Imaging Committee, Cardiac Imaging Committee of the American Heart Association, the European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography and the Canadian Society of Echocardiography, endorsed by the American College of Cardiology Foundation, American Heart Association, European Association of Echocardiography, a registered branch of the European Society of Cardiology, the Japanese Society of Echocardiography, and Canadian Society of Echocardiography. *J Am Soc Echocardiogr* 2009;22:975–1014. quiz 82−84.

10. Simonato M, Whisenant B, Ribeiro HB, Webb JG, Kornowski R, Guerrero M, Wijeysundera H, Søndergaard L, De Backer O, Villablanca P, Rihal C, Eleid M, Kempfert J, Unbehaun A, Erlebach M, Casselman F, Adam M, Montorfano M, Ancona M, Saia F, Ubben T, Meincke F, Napodano M, Codner P, Schofer J, Pelletier M, Cheung A, Shuvy M, Palma JH, Gaia DF, Duncan A, Hildick-Smith D, Veulemans V, Sinning JM, Arbel Y, Testa L, de Weger A, Eltchaninoff H, Hemery T, Landes U, Tchetche D, Dumonteil N, Rodés-Cabau J, Kim WK, Spargias K, Kourkoveli P, Ben-Yehuda O, Teles RC, Barbanti M, Fiorina C, Thukkani A, Mackensen GB, Jones N, Presbitero P, Petronio AS, Allali A, Champagnac D, Bleiziffer S, Rudolph T, Iadanza A, Salizzoni S, Agrifoglio M, Nombela-Franco L, Bonaros N, Kass M, Bruschi G, Amabile N, Chhatriwalla A, Messina A, Hirji SA, Andreas M, Welsh R, Schoels W, Hellig F, Windecker S, Stortecky S, Maisano F, Stone GW, Dvir D. Transcatheter mitral valve replacement after surgical repair or replacement: comprehensive midterm evaluation of valve-in-valve and valve-in-ring implantation from the VIVID registry. *Circulation* 2021;143:104–116.
11. Zoghbi WA, Adams D, Bonow RO, Enriquez-Sarano M, Foster E, Grayburn PA, Hahn RT, Han Y, Hung J, Lang RM, Little SH, Shah DJ, Shernan S, Thavendiranathan P, Thomas JD, Weissman NJ. Recommendations for noninvasive evaluation of native valvular regurgitation: a report from the American Society of Echocardiography developed in collaboration with the Society for Cardiovascular Magnetic Resonance. *J Am Soc Echocardiogr* 2017;30:303–371.
12. da Costa LPN, Palma JH, Barbosa Ribeiro H, Sampaio RO, Viotto G, Medeiros Santos R, Freitas Tenório D, Saito VT, Egypto Rosa VE, Pinho Moreira LF, Tarasoutchi F, Pomerantzeff PM, Biscegli Jatene F. Transcatheter mitral valve-in-valve implantation: reports of the first 50 cases from a Latin American Centre. *Interact Cardiovasc Thorac Surg* 2020;30:229–235.
13. Mastro F, Guida P, Scrascia G, Rotunno C, Amorese L, Carrozzo A, Capone G, Paparella D. Cardiac troponin I and creatine kinase-MB release after different cardiac surgeries. *J Cardiovasc Med (Hagerstown)* 2015;16:456–464.
14. Devereaux PJ, Lamy A, Chan MTV, Allard RV, Lomivorotov VV, Landoni G, Zheng H, Paparella D, McGillion MH, Belley-Côté EP, Parlow JL, Underwood MJ, Wang CY, Dvirnik N, Abubakirov M, Fominskiy E, Choi S, Fremes S, Monaco F, Urrútia G, Maestre M, Hajjar LA, Hillis GS, Mills NL, Margari V, Mills JD, Billing JS, Methangkool E, Polanczyk CA, Sant'Anna R, Shukevich D, Conen D, Kavsak PA, McQueen MJ, Brady K, Spence J, Le Manach Y, Mian R, Lee SF, Bangdiwala SI, Hussain S, Borges FK, Pettit S, Vincent J, Guyatt GH, Yusuf S, Alpert JS, White HD, Whitlock RP, VISION Cardiac Surgery Investigators. High-sensitivity troponin I after cardiac surgery and 30-day mortality. *N Engl J Med* 2022;386:827–836.
15. Michail M, Cameron JN, Nerlekar N, Ihdayhid AR, McCormick LM, Gooley R, Niccoli G, Crea F, Montone RA, Brown AJ. Periprocedural myocardial injury predicts short- and long-term mortality in patients undergoing transcatheter aortic valve replacement. *Circ Cardiovasc Interv* 2018;11:e007106.
16. Ribeiro HB, Nombela-Franco L, Muñoz-García AJ, Lemos PA, Amat-Santos I, Serra V, de Brito FS, Abizaid A, Sarmento-Leite R, Puri R, Cheema AN, Ruel M, Nietlispach F, Maisano F, Moris C, Del Valle R, Urena M, Abdul Jawad Altisent O, Del Trigo M, Campelo-Parada F, Jimenez Quevedo P, Alonso-Briales JH, Gutiérrez H, García Del Blanco B, Perin MA, Siqueira D, Bernardi G, Dumont É, Côté M, Pibarot P, Rodés-Cabau J. Predictors and impact of myocardial injury after transcatheter aortic valve replacement: a multicenter registry. *J Am Coll Cardiol* 2015;66:2075–2088.
17. Koifman E, Garcia-Garcia HM, Alraies MC, Buchanan K, Hideo-Kajita A, Steinvil A, Rogers T, Ben-Dor I, Pichard AD, Torguson R, Gai J, Satler LF, Waksman R. Correlates and significance of elevation of cardiac biomarkers elevation following transcatheter aortic valve implantation. *Am J Cardiol* 2017;120:850–856.
18. Yong ZY, Wiegerinck EM, Boerlage-van Dijk K, Koch KT, Vis MM, Bouma BJ, Henriques JP, Cocchieri R, Piek JJ, de Mol BA, Baan J. Predictors and prognostic value of myocardial injury during transcatheter aortic valve implantation. *Circ Cardiovasc Interv* 2012;5:415–423.
19. Havers-Borgersen E, Butt JH, Strange J, Carranza CL, Køber L, Fosbøl EL. Mortality and rehospitalization after mitral valve surgery as a function of age and key comorbidities. *Am Heart J* 2023;258:140–148.
20. Ribeiro HB, Larose É, de la Paz Ricapito M, Le Ven F, Nombela-Franco L, Urena M, Allende R, Amat-Santos I, Dahou A, Capoulade R, Clavel MA, Mohammadi S, Paradis JM, De Larochellière R, Doyle D, Dumont É, Pibarot P, Rodés-Cabau J. Myocardial injury following transcatheter aortic valve implantation: insights from delayed-enhancement cardiovascular magnetic resonance. *EuroIntervention* 2015;11:205–213.
21. Eleid MF, Whisenant BK, Cabalka AK, Williams MR, Nejjari M, Attias D, Fam N, Amoroso N, Foley TA, Pollak PM, Alli OO, Pislaru SV, Said SM, Dearani JA, Rihal CS. Early outcomes of percutaneous transvenous transseptal transcatheter valve implantation in failed bioprosthetic mitral valves, ring annuloplasty, and severe mitral annular calcification. *JACC Cardiovasc Interv* 2017;10:1932–1942.
22. Guerrero M, Vemulapalli S, Xiang Q, Wang DD, Eleid M, Cabalka AK, Sandhu G, Salinger M, Russell H, Greenbaum A, Kodali S, George I, Dvir D, Whisenant B, Russo MJ, Pershad A, Fang K, Coylewright M, Shah P, Babaliaros V, Khan JM, Tommaso C, Saucedo J, Kar S, Makkar R, Mack M, Holmes D, Leon M, Bapat V, Thourani VH, Rihal C, O'Neill W, Feldman T. Thirty-day outcomes of transcatheter mitral valve replacement for degenerated mitral bioprostheses (valve-in-valve), failed surgical rings (valve-in-ring), and native valve with severe mitral annular calcification (valve-in-mitral annular calcification) in the United States: data from the Society of Thoracic Surgeons/American College of Cardiology/Transcatheter Valve Therapy Registry. *Circ Cardiovasc Interv* 2020;13:e008425.
23. Lurati Buse GA, Koller MT, Grapow M, Bolliger D, Seeberger M, Filipovic M. The prognostic value of troponin release after adult cardiac surgery - a meta-analysis. *Eur J Cardiothorac Surg* 2010;37:399–406.
24. Ismayl M, Abbasi MA, Mostafa MR, Aboeata A, Vora AN, Ben-Dor I, Anavekar NS, Goldsweig AM. Meta-analysis comparing valve-in-valve transcatheter mitral valve replacement versus redo surgical mitral valve replacement in degenerated bioprosthetic mitral valve. *Am J Cardiol* 2023;189:98–107.
25. Moussa ID, Klein LW, Shah B, Mehran R, Mack MJ, Brilakis ES, Reilly JP, Zoghbi G, Holper E, Stone GW. Consideration of a new definition of clinically relevant myocardial infarction after coronary revascularization: an expert consensus document from the Society for Cardiovascular Angiography and Interventions (SCAI). *J Am Coll Cardiol* 2013;62:1563–1570.
26. Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction, Katus HA, Lindahl B, Morrow DA, Clemmensen PM, Johanson P, Hod H, Underwood R, Bax JJ, Bonow RO, Pinto F, Gibbons RJ, Fox KA, Atar D, Newby LK, Galvani M, Hamm CW, Uretsky BF, Steg PG, Wijns W, Bassand JP, Menasché P, Ravkilde J, Ohman EM, Antman EM, Wallentin LC, Armstrong PW, Simoons ML, Januzzi JL, Nieminen MS, Gheorghiade M, Filippatos G, Luepker RV, Fortmann SP, Rosamond WD, Levy D, Wood D, Smith SC, Hu D, Lopez-Sendon JL, Robertson RM, Weaver D, Tendera M, Bove AA, Parkhomenko AN, Vasilieva EJ, Mendis S. Third universal definition of myocardial infarction. *Circulation* 2012;126:2020–2035.