

ORIGINAL RESEARCH

Transcatheter Mitral Valve Repair With the MitraClip Device for Prior Mitral Valve Repair Failure: Insights From the GIOTTO-FAILS Study

Arturo Giordano , MD, PhD; Paolo Ferraro, MD; Filippo Finizio , MD; Nicola Corcione , MD; Michele Cimmino , MD; Giuseppe Biondi-Zoccai , MD, MStat; Paolo Denti , MD; Antonio Popolo Rubbio , MD; Anna Sonia Petronio , MD; Antonio L. Bartorelli, MD; Annalisa Mongiardo, MD; Salvatore Giordano , MD; Francesco De Felice , MD; Marianna Adamo , MD; Matteo Montorfano , MD; Cesare Baldi, MD; Giuseppe Tarantini , MD; Francesco Giannini , MD; Federico Ronco, MD; Ida Monteforte , MD; Emmanuel Villa , MD; Maurizio Ferrario, MD; Luigi Fiocca, MD; Fausto Castriota, MD; Angelo Squeri , MD; Corrado Tamburino , MD; Francesco Bedogni, MD

BACKGROUND: Minimally invasive mitral valve repair has a favorable risk–benefit profile in patients with significant de novo mitral regurgitation. Its role in patients with prior mitral valve repair is uncertain. We aimed to appraise the outcome of patients undergoing transcatheter edge-to-edge repair (TEER) with prior transcatheter or surgical mitral valve repair (SMVR).

METHODS AND RESULTS: We queried the Italian multicenter registry on TEER with MitraClip, distinguishing naïve patients from those with prior TEER or (SMVR). Inhospital and long-term clinical/echocardiographic outcomes were appraised. The primary outcome was the occurrence of death or rehospitalization for heart failure. A total of 2238 patients were included, with 2169 (96.9%) who were naïve to any mitral intervention, 29 (1.3%) with prior TEER, and 40 (1.8%) with prior SMVR. Several significant differences were found in baseline clinical and imaging features. Respectively, device success was obtained in 2120 (97.7%), 28 (96.6%), and 38 (95.0%, $P=0.261$) patients; procedural success in 2080 (95.9%), 25 (86.2%), and 38 (95.0%; $P=0.047$); and inhospital death in 61 (2.8%), 1 (3.5%), and no ($P=0.558$) patients. Clinical follow-up after a mean of 14 months showed similar rates of death, cardiac death, rehospitalization, rehospitalization for heart failure, and their composite (all $P>0.05$). Propensity score–adjusted analysis confirmed unadjusted analysis, with lower procedural success for the prior TEER group (odds ratio, 0.28 [95% CI, 0.09–0.81]; $P=0.019$) but similar odds ratios and hazard ratios for all other outcomes in the naïve, TEER, and SMVR groups (all $P>0.05$).

CONCLUSIONS: In carefully selected patients, TEER can be performed using the MitraClip device even after prior TEER or SMVR.

Key Words: MitraClip ■ mitral regurgitation ■ mitral valve repair ■ transcatheter edge-to-edge repair ■ transcatheter mitral valve repair

See Editorial by Dong et al.

Mitral regurgitation is a common cause of morbidity and mortality worldwide, and poses several challenges, especially when significant comorbidities coexist.^{1–4} While surgical mitral valve repair (SMVR) has been considered the gold-standard treatment of mitral regurgitation for several decades,

Correspondence to: Giuseppe Biondi-Zoccai, MD, MStat, Department of Medical-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Corso della Repubblica 79 Latina, Italy. Email: gbiondizoccai@gmail.com

This article was sent to Amgad Mentias, MD, Associate Editor, for review by expert referees, editorial decision, and final disposition.

Supplemental Material is available at <https://www.ahajournals.org/doi/suppl/10.1161/JAHA.123.033605>

For Sources of Funding and Disclosures, see page 11.

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CLINICAL PERSPECTIVE

What Is New?

- Transcatheter mitral edge-to-edge repair is becoming an established alternative to surgical mitral valve repair in patients at increased surgical risk with suitable anatomic features.
- While initially reserved for individuals without prior mitral repair, transcatheter mitral edge-to-edge repair can also be performed in carefully selected patients with prior surgical or transcatheter mitral valve repair.
- Despite a lower procedural success in patients with prior transcatheter mitral valve repair in comparison to naïve patients, transcatheter mitral edge-to-edge repair is associated with favorable results for other short-term outcomes and also for long-term events in patients with prior transcatheter or surgical mitral valve repair.

What Are the Clinical Implications?

- Transcatheter edge-to-edge repair can be safely and effectively performed using the MitraClip device even in carefully selected patients with a clinical history of prior transcatheter or surgical mitral valve repair.

Nonstandard Abbreviations and Acronyms

GIOTTO	Glse Registry of Transcatheter Treatment of Mitral Valve Regurgitation
GIOTTO-FAILS	Glse Registry of Transcatheter Treatment of Mitral Valve Regurgitation-FAILureS
SMVR	surgical mitral valve repair
TEER	transcatheter edge-to-edge repair

its invasiveness is still a limitation, especially in patients at increased surgical risk.^{5,6} Transcatheter edge-to-edge repair (TEER) was introduced several years ago as a minimally invasive alternative to SMVR in carefully selected cases, and, despite some inconsistencies between pivotal trials, TEER has become a mainstay in the management of mitral regurgitation.⁷⁻¹⁰

While these premises hold robustly in patients with de novo mitral regurgitation, individuals with prior SMVR or TEER represent a uniquely challenging setting.^{11,12} First, they are typically at high surgical risk because of advanced age, coexistent cardiovascular conditions, or substantial comorbidities.¹³ Second, leaflet anatomy

may be significantly distorted and thus limit treatment options. Third, the presence of an annular ring or a previous clip may lead to increased transmitral valve gradients.¹⁴ Fourth, left ventricular dysfunction commonly accompanies failing mitral valve repairs, and thus may limit patient resilience as well as long-term prognosis after discharge.¹⁵

While several reports on TEER after failed SMVR or TEER are available, their scope and focus may limit generalization and warrant further research. Thus, we aimed to utilize the multicenter Italian Society of Interventional Cardiology GIOTTO (Glse Registry of Transcatheter Treatment of Mitral Valve Regurgitation) to compare patients naïve to any mitral valve intervention with patients who had prior TEER or SMVR.¹⁶

METHODS

Details of the GIOTTO on TEER with MitraClip (Abbott Vascular) have been reported elsewhere in detail, as well as in the corresponding [ClinicalTrials.gov](https://clinicaltrials.gov/ct2/show/study/NCT03521921) entry (NCT03521921).^{16,17} Briefly, the study protocol was approved by each participating site's institutional review board and the patients provided written informed consent and were included in case TEER was attempted, without any exclusion criteria except for lack of consent to participate. Accordingly, all analyses followed an intention-to-treat principle.

Indications for TEER were as per routine care and, thus, significant mitral regurgitation and valve anatomy suitable for TEER with MitraClip as per transthoracic and transesophageal echocardiography. Current clinical practice guidelines, recommendations, and consensus statements were duly followed in the diagnostic, planning, procedural, and follow-up phases. Procedures were performed under systematic transesophageal echocardiographic guidance and either deep sedation or general anesthesia at the operator's discretion. Given the protracted enrollment in the study over several years, different MitraClip generations were used, from NT to NTr and XTr.

Clinical follow-up, echocardiographic follow-up, and ancillary medical management were performed according to standard care and ongoing guidelines, with direct visits every 1 to 3 months up to 12 months, and then every 12 months. Similarly, transthoracic echocardiography was routinely repeated to evaluate cardiac dimensions, function, and valve features. Mitral Valve Academic Research Consortium recommendations were used for the adjudication of events, with short-term outcomes including device success, procedural success, death, bailout mitral valve surgery, partial device detachment, device embolization, bleeding, vascular complication, stroke, transient ischemic attack, cardiac tamponade, myocardial infarction, and total hospital stay (Data S1). Notably, left ventricular ejection

Table 1. Baseline Features Comparing Patients Naïve to Mitral Valve Intervention With Patients Who Had Prior TEER or SMVR

Feature	Naïve	Prior TEER	Prior SMVR	Overall <i>P</i> value	Subgroup <i>P</i> value*
Patients, n	2169	29	40
Age, y	75.9±9.1	73.2±9.4	70.0±12.2	<0.001	0.234
Women	795 (36.7)	12 (41.4)	14 (35.0)	0.835	0.623
Body mass index, kg/m ²	25.3±4.3	25.8±5.4	25.0±4.6	0.733	0.509
Mitral disease cause				<0.001	<0.001
Degenerative	677 (31.2)	6 (20.7)	27 (67.5)		
Functional dilated	639 (29.5)	14 (48.3)	8 (20.0)		
Functional ischemic	616 (28.4)	8 (27.6)	3 (7.5)		
Mixed	237 (10.9)	1 (3.5)	2 (5.0)		
NYHA class IV	187 (8.7)	4 (13.8)	0	0.001	<0.001
Logistic EuroSCORE	14.7±12.7	18.5±17.9	11.7±9.9	0.320	0.194
EuroSCORE II	6.6±6.3	7.0±4.6	7.3±5.6	0.703	0.769
STS score	5.1±5.4	5.5±5.2	2.4±2.1	0.068	0.018
Prior pacemaker implantation				0.136	0.025
No	1318 (60.8)	12 (41.4)	29 (72.5)		
Monocameral	200 (9.2)	2 (6.9)	4 (10.0)		
Bicameral	334 (15.4)	7 (24.1)	4 (10.0)		
Biventricular	317 (14.6)	8 (27.6)	3 (7.5)		
Prior ICD implantation	667 (30.8)	13 (44.8)	7 (17.5)	0.050	0.017
Diabetes				0.350	0.106
No	1601 (73.8)	19 (65.5)	35 (87.5)		
Diet therapy	56 (2.6)	1 (3.5)	1 (2.5)		
Noninsulin drug therapy	287 (13.2)	6 (20.7)	2 (5.0)		
Insulin therapy	225 (10.4)	3 (10.3)	2 (5.0)		
Dyslipidemia	727 (33.5)	10 (34.5)	9 (22.5)	0.347	0.290
Hypertension	1575 (72.6)	22 (75.9)	25 (62.5)	0.328	0.300
Smoking history	313 (14.4)	6 (20.7)	6 (15.0)	0.545	0.542
Carotid artery disease				0.640	1
No	1987 (91.6)	29 (100)	38 (95.0)		
<50% Stenosis	135 (6.2)	0	1 (2.5)		
50%–79% Stenosis	41 (1.9)	0	1 (2.5)		
>79% Stenosis	6 (0.3)	0	0		
Peripheral artery disease	164 (7.6)	1 (3.5)	4 (10.0)	0.615	0.389
Aortic valve disease				0.451	0.112
None	1542 (71.1)	22 (75.9)	24 (60.0)		
Mild stenosis	50 (2.3)	1 (3.5)	1 (2.5)		
Moderate stenosis	35 (1.6)	1 (3.5)	0		
Aortic regurgitation	510 (23.5)	5 (17.2)	15 (37.5)		
Mixed aortic valve disease	32 (1.5)	0	0		
Prior myocardial infarction	717 (33.1)	6 (20.7)	4 (10.0)	0.002	0.302
Prior hospitalization for heart failure	1220 (56.3)	20 (69.0)	13 (32.5)	0.004	0.004
Syncope	90 (4.2)	0	1 (2.5)	0.780	1
Coronary artery disease	892 (41.1)	9 (31.0)	9 (22.5)	0.032	0.579
Prior coronary revascularization	226 (32.2)	3 (37.5)	2 (28.6)	0.911	1
Prior cardiac surgery	463 (21.4)	9 (31.0)	40 (100)	<0.001	<0.001
Mitral annuloplasty	0	0	8 (20.0)

(Continued)

Table 1. Continued

Feature	Naïve	Prior TEER	Prior SMVR	Overall <i>P</i> value	Subgroup <i>P</i> value*
Coronary artery bypass grafting	305 (14.1)	7 (24.1)	4 (10.0)	0.233	0.182
Heart transplantation	6 (0.3)	0	1 (2.5)	0.197	1
Hemoglobin, g/dL	12.3±1.8	12.1±1.3	13.1±1.6	0.070	0.029
Hematocrit, %	38±5	38±4	39±4	0.374	0.543
Platelet count	208±73	215±75	197±63	0.694	0.397
Estimated GFR, mL/min per 1.73m ²	48.3±24.7	54.2±19.5	62.3±27.8	<0.001	0.184
Formal contraindications to surgical repair					
Porcelain aorta	9 (0.4)	0	0	1	1
Neoplasia	65 (3.0)	0	1 (2.5)	1	1
Hostile chest	56 (2.6)	1 (3.5)	3 (7.5)	0.095	0.634
Frailty	634 (29.2)	14 (48.3)	11 (27.5)	0.089	0.127
Neurologic disability	39 (1.8)	0	1 (2.5)	0.717	1
Collagenopathy	10 (0.5)	0	0	1	1
Other	365 (16.8)	7 (24.1)	14 (35.0)	0.009	0.430
Cirrhosis	5 (0.2)	0	0	1	1
Dialysis	43 (2.0)	0	0	1	1
COPD	327 (15.1)	6 (20.7)	7 (17.5)	0.555	0.764

Values are expressed as number (percentage) or mean±SD unless otherwise indicated.

COPD indicates chronic obstructive pulmonary disease; GFR, glomerular filtration rate; ICD, implantable cardioverter defibrillator; NYHA, New York Heart Association; and STS, Society of Thoracic Surgery.

*Comparing patients with prior transcatheter edge-to-edge repair (TEER) vs those with prior surgical mitral valve repair (SMVR).

fraction, mitral valve gradient, mitral regurgitation grade, and systolic pulmonary artery pressure were systematically assessed before discharge.¹⁸ Long-term clinical outcomes included death, mitral valve surgery, heart transplantation, endocarditis, rehospitalization, and heart failure (HF) grade. Follow-up imaging details included left ventricular ejection fraction, mitral valve gradient, mitral regurgitation grade, tricuspid regurgitation grade, and systolic pulmonary artery pressure.

Descriptive analysis was based on reporting mean±SD and count (percentage) for continuous and categorical variables, respectively. Unadjusted inferential analysis was based on ANOVA, with post hoc Student *t* test, Fisher exact test, logistic regression, Cox proportional hazard analysis, Kaplan-Meier curves, and log-rank test, as appropriate. In particular, binary logistic regression was used to appraise the association between in-hospital outcomes (ie, device success, procedural success, and in-hospital death) considered as dependent variables, and several independent variables, iteratively. Cox proportional hazard analysis was used to appraise the association between outcomes occurring over time (ie, death, cardiac death, rehospitalization, rehospitalization for HF, HF, death or rehospitalization, and cardiac death or rehospitalization for HF) and several independent variables, iteratively. Notably, adjusted analysis was performed using binary logistic regression and Cox proportional hazard analysis, as appropriate, leveraging nonparsimonious propensity scores using an inverse probability of treatment weighting approach.¹⁹

Notably, all outcomes were analyzed only individually, with the exceptions of death, cardiac death, rehospitalization, and rehospitalization for HF, which were analyzed individually, as well as 2 composites: death or rehospitalization and cardiac death or rehospitalization for HF. Statistical significance was set at the 0.05 2-tailed level, without multiplicity adjustment. Computations were performed with Stata 13 (StataCorp LLC). The data that support the findings of this study are available from the corresponding author upon reasonable request.

RESULTS

A total of 2238 patients were included, with 2169 (96.9%) naïve to any mitral valve intervention, 29 (1.3%) with prior TEER with MitraClip, and 40 (1.8%) with prior SMVR (Table 1). Notably, no device different from the MitraClip was previously used in any patient. Focusing on baseline features, there were significant differences in terms of cause, with degenerative mitral regurgitation more common in patients with prior SMVR, while functional dilated mitral regurgitation was more common in the TEER group ($P<0.001$). Similarly, New York Heart Association functional class IV was higher in patients with prior TEER and, to a lesser extent, patients naïve to intervention ($P=0.001$). Patients naïve to mitral valve intervention more frequently had a history of myocardial infarction ($P=0.002$) and coronary artery disease ($P=0.032$), whereas those with prior TEER more

Table 2. Procedural Results Comparing Patients Naïve to Mitral Valve Intervention With Those Who Had Prior TEER or SMVR

Feature	Naïve	Prior TEER	Prior SMVR	Overall <i>P</i> value	Subgroup <i>P</i> value*
Patients	2169	29	40
Systolic BP at baseline, mmHg	117±19	112±19	111±20	0.148	0.898
Systolic BP at end of procedure, mmHg	117±18	110±13	120±20	0.047	0.015
Fluoroscopy time, min	1.5±3.7	2.2±5.1	2.0±7.8	0.510	0.942
Device time, min	2.8±2.1	2.4±1.4	2.3±1.0	0.149	0.818
Operating room time, min	6.2±3.2	5.7±2.5	6.1±1.8	0.632	0.434
Intubation time, min	1.6±11.7	1.5±5.8	1.5±5.0	0.997	0.956
Failed MitraClip implantation	13 (0.6)	0	0	1	1
Total MitraClip number				<0.001	0.798
1	857 (39.5)	21 (72.4)	26 (65.0)		
2	1103 (50.9)	7 (24.1)	13 (32.5)		
3	184 (8.5)	1 (3.5)	1 (2.5)		
4	14 (0.7)	0	0		
5	1 (0.1)	0	0		
MitraClip NT				<0.001	1
1	423 (34.6)	18 (78.3)	11 (78.6)		
2	658 (53.8)	4 (17.4)	2 (14.3)		
3	129 (10.5)	1 (4.4)	1 (7.1)		
4	10 (0.8)	0	0		
MitraClip NTr				0.694	0.429
1	249 (67.1)	2 (66.7)	4 (100)		
2	110 (29.7)	1 (33.3)	0		
3	7 (1.9)	0	0		
4	1 (0.3)	0	0		
MitraClip XTr				0.413	0.598
1	499 (66.6)	3 (75.0)	11 (50.0)		
2	228 (30.4)	1 (25.0)	11 (50.0)		
3	19 (2.5)	0	0		
4	1 (0.1)	0	0		
Pulmonary vein flow at end of procedure				0.002	0.013
Physiologic	942 (43.4)	5 (17.2)	16 (40.0)		
Blunted	143 (6.6)	1 (3.5)	0		
Diastolic	85 (3.9)	4 (13.8)	1 (2.5)		
Inverted	111 (5.1)	5 (17.2)	1 (2.5)		
Reduced systolic function at inspection at end of procedure	102 (4.7)	1 (3.5)	1 (2.5)	1	1
Mitral regurgitation at end of procedure				0.035	0.068
None	1374 (63.4)	14 (48.3)	28 (70.0)		
Mild	692 (31.9)	9 (31.0)	11 (27.5)		
Moderate	68 (3.1)	4 (13.8)	1 (2.5)		
Severe	35 (1.6)	2 (6.9)	0		
Smoke-like effect	140 (6.5)	2 (6.9)	2 (5.0)	0.925	1
ECG changes	251 (11.6)	7 (24.1)	4 (10.0)	0.132	0.182
Atrial fibrillation	190 (8.8)	4 (13.8)	4 (10.0)	0.486	0.712
Ventricular tachycardia/fibrillation	1 (0.1)	0	0	1	1
Device success	2120 (97.7)	28 (96.6)	38 (95.0)	0.261	1
Procedural success	2080 (95.9)	25 (86.2)	38 (95.0)	0.047	0.230
Procedural death	5 (0.2)	0	0	1	1

Values are expressed as number (percentage) or mean±SD unless otherwise indicated.

BP indicates blood pressure.

*Comparing patients with prior transcatheter edge-to-edge repair (TEER) vs those with prior surgical mitral valve repair (SMVR).

commonly had prior hospitalization for HF ($P=0.004$). Finally, renal function was less impaired in patients with prior SMVR ($P<0.001$). Echocardiographic features were significantly different as well, including left ventricular end-diastolic diameter, end-systolic diameter, end-diastolic volume, end-systolic volume, left ventricular ejection fraction, mitral regurgitation severity, mitral valve gradient, presence of flail leaflet, and tricuspid regurgitation grade (all $P<0.05$; [Table S1](#)).

Procedural details and results were largely similar in the groups, despite a higher number of MitraClip devices being implanted in naïve patients ($P<0.001$), including NT devices ($P<0.001$), higher severity of residual mitral regurgitation ($P=0.035$), and lower postprocedural

systolic blood pressure ($P=0.047$) in patients with prior TEER, and a higher prevalence of postprocedural physiologic pulmonary vein flow in naïve patients ($P=0.002$) ([Table 2](#)). Notably, rates of device success appeared similar in the 3 groups, while procedural success was lower in those with prior TEER ($P=0.047$).

Inhospital results were largely similar, including rates of death, stroke, myocardial infarction, bleeding, and vascular complication (all $P>0.05$; [Table 3](#)). Although left ventricular ejection fraction and mitral valve gradient appeared different, such discrepancies largely depended on baseline differences.

Long-term management details are provided in [Table S2](#) and long-term outcomes in [Table 4](#). Of note,

Table 3. Inhospital Clinical and Imaging Outcomes Comparing Patients Naïve to Mitral Valve Intervention With Patients Who Had Prior TEER or SMVR

Feature	Naïve	Prior TEER	Prior SMVR	Overall <i>P</i> value	Subgroup <i>P</i> value*
Patients	2169	29	40
Inhospital death	61 (2.8)	1 (3.5)	0	0.558	0.420
Stroke	0	0	0	1	1
Transient ischemic attack	0	0	1 (2.5)	0.031	1
Cardiac tamponade	5 (0.2)	0	0	1	1
Myocardial infarction	1 (0.1)	0	0	1	1
Bailout mitral valve surgery	6 (0.3)	0	0	1	1
Partial device detachment	14 (0.7)	0	0	1	1
Device embolization	9 (0.4)	0	0	1	1
Any bleeding	19 (0.9)	1 (3.5)	0	0.348	0.420
Minor bleeding	11 (0.5)	1 (3.5)	0	0.161	0.420
Major bleeding	5 (0.2)	0	0	1	1
Disabling bleeding	3 (0.1)	0	0	1	1
Red blood cell transfusion	14 (0.7)	0	0	1	1
Any vascular complication	15 (0.7)	1 (3.5)	0	0.215	0.420
Minor vascular complication	9 (0.4)	1 (3.5)	0	0.134	0.420
Major vascular complication	6 (0.3)	0	0	1	1
Vessel perforation	5 (0.2)	0	0	1	1
Femoral pseudoaneurysm	2 (0.1)	0	0	1	1
Total hospital stay, d	7.6±7.9	7.2±6.4	9.7±19.9	0.251	0.525
Left ventricular ejection fraction at discharge, %	42.5±14.8	33.2±12.6	49.3±13.7	<0.001	<0.001
Mitral gradient at discharge, mmHg	3.4±1.6	4.0±1.7	4.8±3.5	<0.001	0.278
Mitral gradient at least 5 mmHg at discharge	179 (8.3)	4 (13.8)	5 (12.5)	0.281	1
Change in mitral gradient from baseline to discharge, mmHg	1.0±1.4	2.0±1.6	2.1±4.9	0.075	0.583
Mitral regurgitation at discharge				0.245	0.472
1+	1215 (57.6)	13 (46.4)	23 (57.5)		
2+	735 (34.9)	10 (35.7)	13 (32.5)		
3+	121 (5.7)	5 (17.9)	3 (7.5)		
4+	37 (1.8)	0	1 (2.5)		
Systolic pulmonary artery pressure, mmHg at discharge	41±11	46±12	40±15	0.049	0.076

Values are expressed as number (percentage) or mean±SD unless otherwise indicated.

*Comparing patients with prior transcatheter edge-to-edge repair (TEER) vs those with prior surgical mitral valve repair (SMVR).

Table 4. Long-Term Outcomes Comparing Patients Naïve to Mitral Valve Intervention With Patients Who Had Prior TEER or SMVR

Feature	Naïve	Prior TEER	Prior SMVR	Overall <i>P</i> value	Subgroup <i>P</i> value*
Patients	2169	29	40
Follow-up, mo	18.7±16.4	13.5±12.4	15.5±13.6	0.110	0.520
Death	531 (24.5)	8 (27.6)	5 (12.5)	0.195	0.131
Cardiac death	283 (13.1)	5 (17.2)	3 (7.5)	0.483	0.266
Mitral valve surgery	24 (1.1)	0	1 (2.5)	0.545	1
Heart transplantation	9 (0.4)	0	0	1	1
Endocarditis	5 (0.2)	0	0	1	1
Rehospitalization	278 (12.8)	5 (17.2)	5 (12.5)	0.744	0.732
Rehospitalization for HF	224 (10.3)	4 (13.8)	4 (10.0)	0.734	0.712
HF	260 (12.0)	5 (17.2)	4 (10.0)	0.581	0.477
Death or rehospitalization	670 (30.9)	10 (34.5)	9 (22.5)	0.482	0.290
Cardiac death or rehospitalization for HF	448 (20.7)	7 (24.1)	7 (17.5)	0.817	0.554
NYHA class				0.654	0.659
I	272 (17.5)	2 (11.8)	3 (13.0)		
II	932 (59.8)	10 (58.8)	16 (69.6)		
III	330 (21.2)	5 (29.4)	3 (13.0)		
IV	25 (1.6)	0	1 (4.4)		
Left ventricular ejection fraction, %	40.9±14.3	30.3±7.2	47.8±10.1	0.001	<0.001
Mitral gradient, mmHg	3.9±1.8	4.7±2.3	5.5±3.4	<0.001	0.516
Change in mitral gradient from baseline to follow-up, mmHg	1.5±1.6	1.5±1.3	2.2±4.8	0.551	0.789
Change in mitral gradient from discharge to follow-up, mmHg	0.3±1.6	0.7±1.9	0.5±1.3	0.358	0.621
Mitral regurgitation				0.513	0.220
1+	533 (41.3)	5 (31.3)	12 (54.6)		
2+	520 (40.3)	9 (56.3)	7 (31.8)		
3+	172 (13.3)	2 (12.5)	1 (4.6)		
4+	67 (5.2)	0	2 (9.1)		
Tricuspid regurgitation				0.603	1
1+	31 (2.6)	1 (6.3)	1 (5.9)		
2+	549 (46.2)	7 (43.8)	8 (47.1)		
3+	462 (38.9)	6 (37.5)	5 (29.4)		
4+	147 (12.4)	2 (12.5)	3 (17.7)		
Systolic pulmonary artery pressure, mmHg	40.9±11.6	44.7±14.2	37.4±12.2	0.214	0.131

HF indicates heart failure; and NYHA, New York Heart Association.

Values are expressed as number (percentage) or mean±SD unless otherwise indicated.

*Comparing patients with prior transcatheter edge-to-edge repair (TEER) vs those with prior surgical mitral valve repair (SMVR).

after a mean follow-up of 18 months, there were no significant differences in the rates of death, cardiac death, mitral valve surgery, rehospitalization, HF, or their key composites (all $P>0.05$; [Figures 1–3](#)). Echocardiography follow-up confirmed that results accrued during the index hospitalization were well maintained during the subsequent follow-up, with very low rates of severe mitral regurgitation, especially in nonnaïve patients.

Exploratory adjusted analysis, despite being limited by the small sample size of the nonnaïve groups, confirmed that the outcome of patients with prior TEER

and those with prior SMVR was similar to that of naïve individuals for all key outcomes, including death, cardiac death, rehospitalization, rehospitalization for HF, HF, and their most relevant composite (all $P>0.05$; [Table 5](#); [Table S3](#)).

Finally, even opting for sensitivity purposes for a more penalizing 2-tailed 0.005 cutoff to adjust for multiple testing, the main findings as reported in [Table 5](#) remained consistent. The only shift in significance was limited to the borderline difference in procedural success at unadjusted analysis as reported in [Table 2](#),

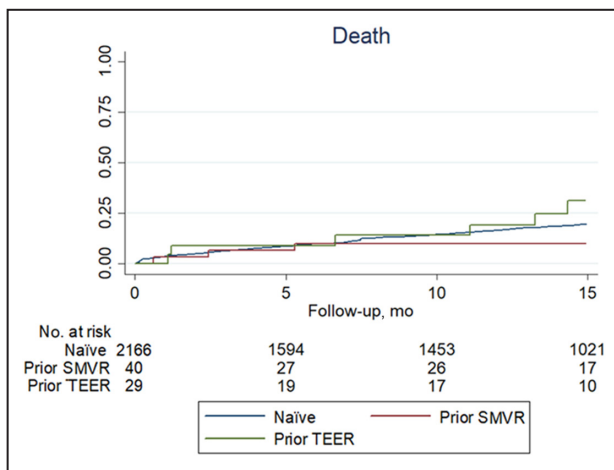


Figure 1. Failure curves for death comparing patients naïve to mitral valve intervention with those who underwent prior transcatheter edge-to-edge repair (TEER) or prior surgical mitral valve repair (SMVR) (naïve vs TEER groups, $P=0.282$; TEER vs SMVR groups, $P=0.089$; and naïve vs SMVR groups, $P=0.257$).

which was no longer significant according to this more demanding threshold.

DISCUSSION

The management of patients with prior TEER or SMVR represents a substantial challenge. While awaiting the completion of prospective randomized trials on this niche area of cardiovascular practice, our observational evidence describes current practice and may be helpful in guiding decision-making. Notably, we found that <4% of patients undergoing TEER in the current

era report a history of TEER or SMVR. Significant differences among these 2 groups and naïve patients are apparent in terms of presenting features, including age, mitral regurgitation cause, history of myocardial infarction, and coronary artery disease. These differences are accompanied by significant variation in echocardiography features, with patients with prior TEER typically exhibiting worse remodeling patterns and more depressed systolic function. Nevertheless, clinical results in the 3 groups appear similar, at early as well as long-term follow-up, and even taking into account baseline differences. These results indicate that TEER can be safely offered in patients with prior TEER or prior SMVR, with favorable expectations for functional echocardiography and clinical improvement.

The evidence in favor of TEER continues to accrue, and these scientific and scholarly successes are mirrored by an ongoing growth in the use and confidence of this minimally invasive approach to treat mitral regurgitation.²⁰ While it is evident that intervention timing and patient selection have an impact on acute and long-term outcomes as much as technical skills,^{9,21} the confidence in TEER translates into its extension to patients who previously were considered suboptimal candidates. In such a setting, patients with prior TEER or SMVR constitute a small but inherently challenging niche. Clinical, anatomical, and technical issues are more relevant in these patients, and failures or suboptimal results are all possible. Indeed, procedural success was lower in patients with prior TEER, despite similar rates of acute device success. Irrespectively, clinical outcomes and echocardiographic findings at follow-up were reassuring, suggesting that repeat TEER or TEER after failed SMVR remain safe and may provide meaningful clinical benefits even at longer follow-up. It is also worth mentioning that most patients, regardless of the index intervention, received only one MitraClip, and an NT type, and yet there was a significant increase in transmitral gradients (actually more pronounced in patients with prior surgery). Indeed, the risk of significant gradient after implantation of a third MitraClip might be the main reason for limiting to only one MitraClip during the redo procedure. Yet, as a result of ongoing technological refinements, such as the introduction of the G4 system, it is plausible to expect further expansion of indications and improved results in the current and future eras.²²

Despite the validity of our detailed analysis, several unanswered questions remain. They include how to best select patients, how to gauge short- and long-term results, how to follow individuals, when and why considering subjects for a redo TEER (which might in some cases come as a third TEER), how to combine TEER with other transcatheter mitral valve techniques (eg, transcatheter annuloplasty), and how to combine the benefits of transcatheter repair with maximization

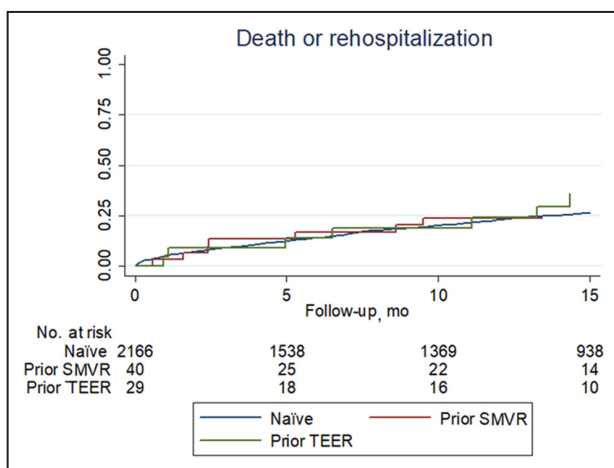


Figure 2. Failure curves for the composite of death or rehospitalization comparing patients naïve to mitral valve intervention with those who underwent prior transcatheter edge-to-edge repair (TEER) or prior surgical mitral valve repair (SMVR) (naïve versus TEER groups, $P=0.303$; TEER vs SMVR groups, $P=0.249$; and naïve and SMVR groups, $P=0.720$).

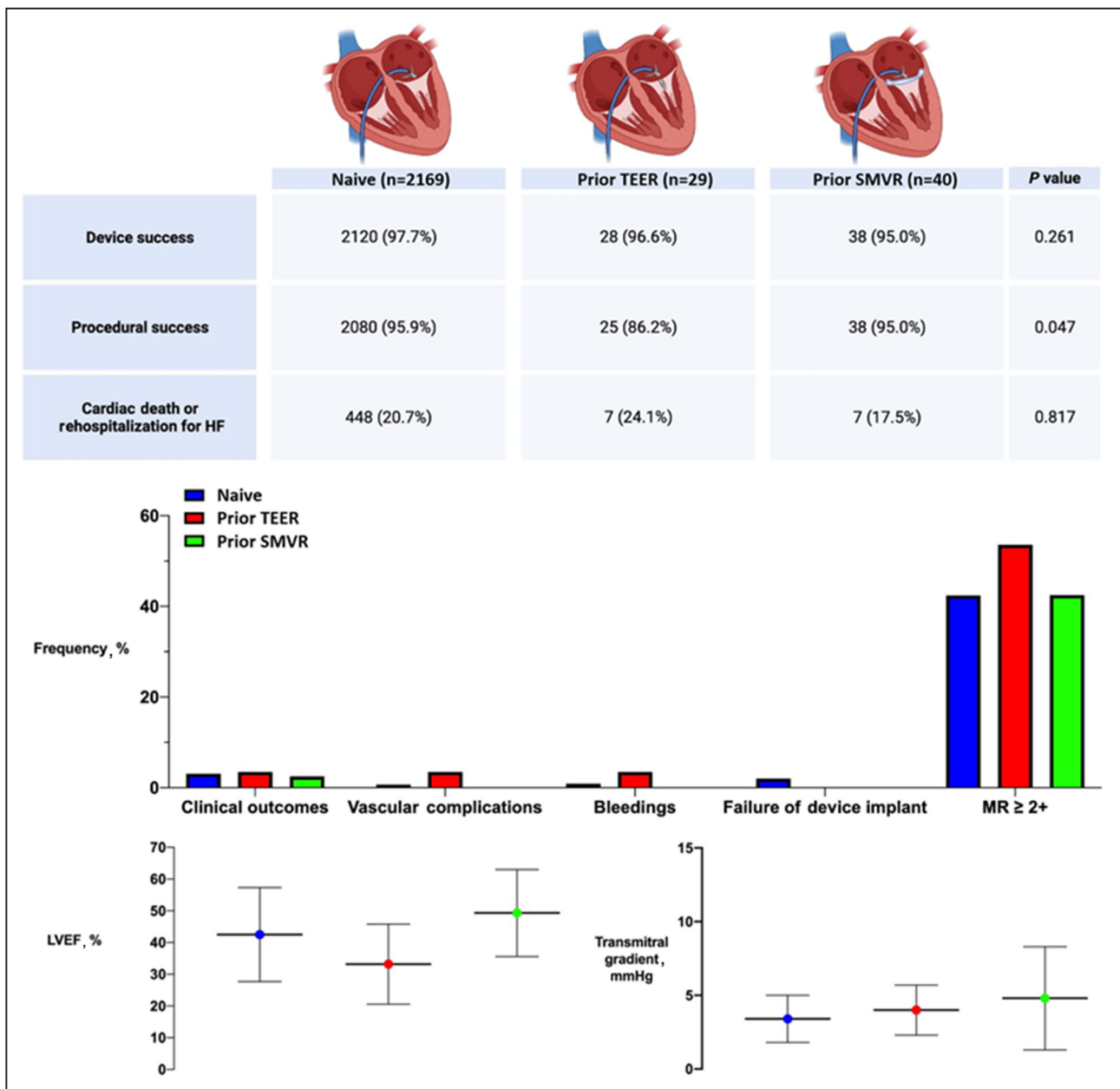


Figure 3. Summary of the GIOTTO-FAILS (Glise Registry of Transcatheter Treatment of Mitral Valve Regurgitation-FAILureS) study.

Clinical outcomes represent the composite of in-hospital death, stroke, transient ischemic attack, cardiac tamponade, myocardial infarction, or bailout mitral valve surgery. HF indicates heart failure; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; SMVR, surgical mitral valve repair; and TEER, transcatheter edge-to-edge repair.

of medical therapy in the era of novel drugs such as sodium-glucose transport protein 2 inhibitors and glucagon-like peptide 1 receptor agonists.

Furthermore, several key limitations of the present work should be noted. Clearly, the observational design is a distinct weakness and the same applies to the small sample size, especially for the subset of patients with prior TEER. In addition, the enrollment of patients over several years is another limitation and the ensuing inclusion of patients treated with different

device generations. Furthermore, this registry was designed as a single-device study, and thus no patient received other available TEER technologies (eg, Pascal [Edwards Lifesciences]), nor transcatheter approaches other than TEER for transcatheter repair, such as Cardioband (Edwards Lifesciences) or AccuCinch (Ancora Heart), to name just a few. Future studies are also warranted to appraise the consistency of the present results in other settings and on tricuspid valve disease.²³ In addition, several important details (eg, time

Table 5. Unadjusted and Adjusted Analyses

Outcomes and comparisons	Unadjusted effect estimates*			Adjusted effect estimates*		
	TEER vs naïve	TEER vs SMVR	SMVR vs naïve	TEER vs naïve	TEER vs SMVR	SMVR vs naïve
Device success	OR=0.65 (0.09–4.85), <i>P</i> =0.672	OR=1.47 (0.13–17.07), <i>P</i> =0.756	OR=0.44 (0.10–1.87), <i>P</i> =0.266	OR=0.76 (0.10–5.80), <i>P</i> =0.788	OR=1.18 (0.99–1.40), <i>P</i> =0.067	OR=0.54 (0.12–2.48), <i>P</i> =0.429
Procedural success	OR=0.27 (0.09–0.79), <i>P</i> =0.016	OR=0.33 (0.06–1.93), <i>P</i> =0.218	OR=0.81 (0.19–3.42), <i>P</i> =0.778	OR=0.28 (0.09–0.81), <i>P</i> =0.019	OR=0.76 (0.10–5.80), <i>P</i> =0.788	OR=0.84 (0.19–3.69), <i>P</i> =0.815
Inhospital death	OR=1.23 (0.17–9.22), <i>P</i> =0.837	OR=1.20 (0.16–8.94), <i>P</i> =0.862
Death	HR=1.47 (0.73–2.95), <i>P</i> =0.282	HR=2.84 (0.85–9.42), <i>P</i> =0.089	HR=0.60 (0.25–1.45), <i>P</i> =0.257	HR=1.29 (0.64–2.61), <i>P</i> =0.477	HR=2.57 (0.76–8.70), <i>P</i> =0.129	HR=0.84 (0.35–2.05), <i>P</i> =0.708
Cardiac death	HR=1.64 (0.68–3.98), <i>P</i> =0.273	HR=3.55 (0.69–18.31), <i>P</i> =0.130	HR=0.66 (0.21–2.06), <i>P</i> =0.475	HR=1.43 (0.59–3.51), <i>P</i> =0.427	HR=2.84 (0.52–15.57), <i>P</i> =0.229	HR=0.90 (0.35–3.43), <i>P</i> =0.881
Rehospitalization	HR=1.66 (0.69–4.03), <i>P</i> =0.259	HR=1.44 (0.42–4.99), <i>P</i> =0.562	HR=1.17 (0.49–2.84), <i>P</i> =0.723	HR=1.17 (0.48–2.88), <i>P</i> =0.723	HR=1.15 (0.32–4.18), <i>P</i> =0.832	HR=1.44 (0.59–3.51), <i>P</i> =0.416
Rehospitalization for HF	HR=1.61 (0.60–4.33), <i>P</i> =0.346	HR=1.44 (0.36–5.76), <i>P</i> =0.606	HR=1.12 (0.42–3.02), <i>P</i> =0.819	HR=1.10 (0.40–2.99), <i>P</i> =0.854	HR=0.99 (0.23–4.37), <i>P</i> =0.994	HR=1.36 (0.51–3.68), <i>P</i> =0.539
HF	HR=1.74 (0.72–4.22), <i>P</i> =0.219	HR=1.77 (0.48–6.61), <i>P</i> =0.393	HR=0.97 (0.36–2.61), <i>P</i> =0.953	HR=1.23 (0.50–3.01), <i>P</i> =0.652	HR=1.32 (0.33–5.27), <i>P</i> =0.690	HR=1.21 (0.45–3.25), <i>P</i> =0.709
Death or rehospitalization	HR=1.39 (0.74–2.59), <i>P</i> =0.303	HR=1.73 (0.68–4.38), <i>P</i> =0.249	HR=0.89 (0.46–1.71), <i>P</i> =0.720	HR=1.12 (0.59–2.10), <i>P</i> =0.732	HR=1.50 (0.58–3.90), <i>P</i> =0.401	HR=1.09 (0.56–2.11), <i>P</i> =0.792
Cardiac death or rehospitalization for HF	HR=1.39 (0.66–2.94), <i>P</i> =0.384	HR=1.61 (0.54–4.79), <i>P</i> =0.394	HR=0.99 (0.47–2.09), <i>P</i> =0.976	HR=1.08 (0.51–2.30), <i>P</i> =0.838	HR=1.31 (0.42–4.05), <i>P</i> =0.644	HR=1.28 (0.60–2.70), <i>P</i> =0.524

HF indicates heart failure; SMVR, surgical mitral valve repair; and TEER, transcatheter edge-to-edge repair.

*Reported as odds ratios (ORs) or hazard ratios (HRs), as appropriate, with accompanying 95% CIs.

span from mitral surgery to TEER or details of such surgery) were not collected. While comprehensive, the application of nonparsimonious propensity scores may not account for all unmeasured differences, and residual confounding due to features that were not explicitly collected should be borne in mind.

In conclusion, TEER can be safely and effectively performed using the MitraClip device even in carefully selected patients with a clinical history of TEER or SMVR. Despite a lower yet still reasonable procedural success rate in patients with prior TEER, short- and long-term outcomes appear similar, comparing patients naïve to mitral valve intervention with patients who had prior TEER or SMVR, even accounting for baseline differences. Whether results of TEER in such a challenging setting can be further ameliorated by combining TEER with other transcatheter repair techniques remains to be formally tested in dedicated clinical studies.

ARTICLE INFORMATION

Received November 17, 2023; accepted February 8, 2024.

Affiliations

Unità Operativa di Interventistica Cardiovascolare, Pineta Grande Hospital, Castel Volturno, Italy (A.G., F.F., N.C., M.C.); Unità Operativa di Emodinamica, Santa Lucia Hospital, San Giuseppe Vesuviano, Italy (P.F.); Department of Medico-Surgical Sciences and Biotechnologies, Sapienza University of Rome, Latina, Italy (G.B.); Mediterranea Cardiocentro, Naples, Italy (G.B.); Department of Cardiac Surgery, Vita-Salute San Raffaele University, IRCCS San Raffaele Scientific Institute, Milan, Italy (P.D.); Department of Cardiology, IRCCS Policlinico San Donato, San Donato Milanese, Milan, Italy (A.P.R., F.B.); Cardiothoracic and Vascular Department, University Hospital Pisa, Pisa, Italy (A.S.P.); Centro Cardiologico Monzino, IRCCS, Milan, Italy (A.L.B.); Department of Biomedical and Clinical Sciences, University of Milan, Milan, Italy (A.L.B.); Division of Cardiology, Department of Medical and Surgical Sciences, "Magna Graecia" University, Catanzaro, Italy (A.M., S.G.); Division of Interventional Cardiology, Azienda Ospedaliera S. Camillo Forlanini, Rome, Italy (F.D.F.); Cardiac Catheterization Laboratory and Cardiology, ASST Spedali Civili di Brescia, Brescia, Italy (M.A.); Department of Medical and Surgical Specialties, Radiological Sciences, Public Health University of Brescia, Brescia, Italy (M.A.); Interventional Cardiology Unit, IRCCS San Raffaele Scientific Institute, Vita Salute San Raffaele University, Milan, Italy (M.M.); Thoracic-Vascular Department, San Raffaele University Hospital, Milan, Italy (M.M.); Heart Department, University Hospital "Scuola Medica Salernitana", Salerno, Italy (C.B.); Department of Cardiac, Thoracic and Vascular Science, Interventional Cardiology Unit, University of Padua, Padua, Italy (G.T.); Division of Cardiology, IRCCS Ospedale Galeazzi—Sant'Ambrogio, Milan, Italy (F.G.); Interventional Cardiology, Department of Cardio-Thoracic and Vascular Sciences, Ospedale dell'Angelo, AULSS3 Serenissima, Venezia, Italy (F.R.); Divisione di Cardiologia, A.O. dei Colli, Ospedale Monaldi, Naples, Italy (I.M.); Cardiac Surgery Unit and Valve Center, Poliambulanza Foundation Hospital, Brescia, Italy (E.V.); Division

of Cardiology, Fondazione IRCCS Policlinico S. Matteo, Pavia, Italy (M.F.); Cardiovascular Department, Papa Giovanni XXIII Hospital, Bergamo, Italy (L.F.); Interventional Cardiology Unit, GVM Care & Research, Maria Cecilia Hospital, Cotignola, Italy (F.C., A.S.); and Division of Cardiology, Centro Alte Specialità e Trapianti (CAST), Azienda Ospedaliero-Universitaria Policlinico-Vittorio Emanuele, University of Catania, Catania, Italy (C.T.).

Sources of Funding

The GIOTTO is sponsored by the Italian Society of Invasive Cardiology, with an unrestricted grant by Abbott Vascular.

Disclosures

M.A. has received speaker fees from Abbott Structural Heart. G.B.-Z. has consulted for Amarin, Balméd, CardioNovum, Crannmedical, Endocore Lab, Eukon, Guidotti, Innovheart, Meditrial, Microport, Opsens Medical, Terumo, and Translumina, outside the present work. The remaining authors have no disclosures to report.

Supplemental Material

Data S1

Tables S1–S3

References 24,25

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