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Percutaneous Mitral Valve Edge-to-Edge Repair

In-Hospital Results and 1-Year Follow-Up of 628 Patients of the 2011–2012 Pilot European Sentinel Registry

Georg Nickenig, MD, PhD,* Rodrigo Estevez-Loureiro, MD, PhD,† Olaf Franzen, MD,‡ Corrado Tamburino, MD, PhD,§ Marc Vanderheyden, MD,‖ Thomas F. Lüscher, MD,¶ Neil Moat, MS,# Susanna Price, MD, PhD,** Gianni Dall'Ara, MD,† Reidar Winter, MD, PhD,†† Roberto Corti, MD,¶ Carmelo Grasso, MD,§ Thomas M. Snow, MD,† Raban Jeger, MD,‡‡ Stefan Blankenberg, MD,§§ Magnus Settergren, MD, PhD,†† Klaus Tiroch, MD,‖‖ Jan Balzer, MD,¶¶ Anna Sonia Petronio, MD,## Heinz-Joachim Büttner, MD,*** Federica Ettori, MD,††† Horst Sievert, MD,‡‡‡ Maria Giovanna Fiorino, MD,§§§ Marc Claeys, MD, PhD,‖‖‖ Gian Paolo Ussia, MD,¶¶¶ Helmut Baumgartner, MD,### Salvatore Scandura, MD,§ Farqad Alamgir, MD,**** Freidoon Keshavarzi, MD,**** Antonio Colombo, MD,†††† Francesco Maisano, MD, PhD,‡‡‡‡ Henning Ebelt, MD,§§§§ Patrizia Aruta, MD,§ Edith Lubos, MD,§§ Björn Plicht, MD,‖‖‖‖ Robert Schueler, MD,* Michele Pighi, MD,† Carlo Di Mario, MD, PhD,† on behalf of the Transcatheter Valve Treatment Sentinel Registry Investigators of the EURObservational Research Programme of the European Society of Cardiology

ABSTRACT

BACKGROUND The use of transcatheter mitral valve repair (TMVR) has gained widespread acceptance in Europe, but data on immediate success, safety, and long-term echocardiographic follow-up in real-world patients are still limited.

OBJECTIVES The aim of this multinational registry is to present a real-world overview of TMVR use in Europe.

METHODS The Transcatheter Valve Treatment Sentinel Pilot Registry is a prospective, independent, consecutive collection of individual patient data.

RESULTS A total of 628 patients (mean age 74.2 ± 9.7 years, 63.1% men) underwent TMVR between January 2011 and December 2012 in 25 centers in 8 European countries. The prevalent pathogenesis was functional mitral regurgitation (FMR) (n = 452 [72.0%]). The majority of patients (85.5%) were highly symptomatic (New York Heart Association functional class III or higher), with a high logistic EuroSCORE (European System for Cardiac Operative Risk Evaluation) (20.4 ± 16.7%). Acute procedural success was high (95.4%) and similar in FMR and degenerative mitral regurgitation (p = 0.662). One clip was implanted in 61.4% of patients. In-hospital mortality was low (2.9%), without significant differences between groups. The estimated 1-year mortality was 15.3%, which was similar for FMR and degenerative mitral regurgitation. The estimated 1-year rate of rehospitalization because of heart failure was 22.8%, significantly higher in the FMR group (25.8% vs. 12.0%, p[log-rank] = 0.009). Paired echocardiographic data from the 1-year follow-up, available for 368 consecutive patients in 15 centers, showed a persistent reduction in the degree of mitral regurgitation at 1 year (6.0% of patients with severe mitral regurgitation).

CONCLUSIONS This independent, contemporary registry shows that TMVR is associated with high immediate success, low complication rates, and sustained 1-year reduction of the severity of mitral regurgitation and improvement of clinical symptoms. (J Am Coll Cardiol 2014;64:875–84) © 2014 by the American College of Cardiology Foundation.

From the *Department of Internal Medicine and Cardiology/Pneumology, University of Bonn, Bonn, Germany; †Department of Cardiology, NIHR Biomedical Research Unit, Royal Brompton Hospital, London, United Kingdom; ‡Department of Cardiology, Rigshospitalet, Copenhagen, Denmark; §Department of Cardiology, Ferrarotto Hospital, Catania, Italy; ‖Department of Cardiology, OLV Ziekenhuis, Aalst, Belgium; ¶Department of Cardiology, University Hospital of Zurich, Zurich, Switzerland; #Cardiac Surgery Department, NIHR Biomedical Research Unit, Royal Brompton Hospital, London, United Kingdom; **Intensive Care Unit, NIHR Biomedical Research Unit, Royal Brompton Hospital, London, United Kingdom; ††Department of Cardiology, Karolinska University Hospital, Stockholm, Sweden; ‡‡Department of Cardiology, University Hospital Basel, Basel, Switzerland; §§Department of

ABBREVIATIONS AND ACRONYMS

CI = confidence interval

DMR = degenerative mitral regurgitation

EuroSCORE = European System for Cardiac Operative Risk Evaluation

FMR = functional mitral regurgitation

LVEF = left ventricular ejection fraction

MR = mitral valve regurgitation

MV = mitral valve

NYHA = New York Heart Association

OR = odds ratio

SPAP = systolic pulmonary artery pressure

TMVR = transcatheter mitral valve repair

Mitral valve surgery is the treatment of choice for patients with severe mitral regurgitation (MR) who develop symptoms and/or demonstrate worsening of left ventricular (LV) function (1) (**Figure 1**); however, a significant number of patients cannot undergo mitral valve (MV) surgery because of their prohibitive surgical risk (2). Previous reports suggest that this may account for approximately one-half

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of the patients being considered for mitral surgery (3,4). The MitraClip system (Abbott Vascular, Santa Clara, California), conceived for transcatheter mitral valve repair (TMVR), received regulatory approval in Europe in 2008 and has already gained widespread clinical application. The system is based on the edge-to-edge repair concept, a technique proposed by Alfieri to simplify surgical treatment in suitable high-risk candidates. The EVEREST II (Endovascular Valve Edge-to-Edge Repair Study II) randomized trial (5) showed that TMVR was less effective than surgery in reducing MR but induced fewer perioperative adverse events and yielded similar improvement in functional status. These results were maintained at 4 years in patients with a successful initial repair (6). Subsequent observational studies with wider clinical and echocardiographic inclusion criteria have confirmed the benefit of TMVR in patients with severe LV dysfunction, patients not responding to cardiac resynchronization therapy, and patients deemed inoperable or at high surgical risk (7–16). The majority of these studies came from a handful of high-volume centers, early in their application of the technique, and included only a small number of selected patients. The TCVT (Transcatheter Valve Treatment Sentinel Pilot Registry) is part of the European Society of Cardiology EuroObservational Research Programme and reports immediate and 12-month follow-up results of 628 consecutive patients treated between January 2011 and December 2012 in 25 centers in 8 European countries. The aim of

General and Interventional Cardiology, Universitäres Herzzentrum Hamburg, Hamburg, Germany; ‖‖Department of Cardiology, Helios Klinikum Wuppertal, Wuppertal, Germany; ¶¶Department of Cardiology, Universitätsklinikum Düsseldorf, Düsseldorf, Germany; ##Cardiac Catheterization Laboratory, Cardiothoracic and Vascular Department, Azienda Ospedaliero Universitaria Pisana, Pisa, Italy; ***Department of Cardiology and Angiology II, Universitäts-Herzzentrum Freiburg, Bad Krozingen, Germany; †††Cardiothoracic Department, Spedali Civili Brescia, Brescia, Italy; ‡‡‡Department of Cardiology and Vascular Medicine, CardioVasculäres Centrum Frankfurt, Frankfurt, Germany; §§§Department of Cardiology, Ospedale Civico ARNAS, Palermo, Italy; ‖‖‖Department of Cardiology, University Hospital Antwerpen, Edegem, Belgium; ¶¶¶Department of Cardiology, Policlinico Tor Vergata, Roma, Italy; ###Department of Cardiology and Angiology, Universitätsklinikum Münster, Münster, Germany; ****Department of Cardiology, Castle Hill Hospital, Cottingham, United Kingdom; ††††Department of Cardiology, Università degli Studi San Raffaele, Milano, Italy; ‡‡‡‡Department of Cardiovascular Surgery, Università degli Studi San Raffaele, Milano, Italy; §§§§Department of Cardiology, Universitätsklinikum Halle/Saale, Halle/Saale, Germany; and the ‖‖‖‖Department of Cardiology, University Clinic Essen, Essen, Germany. Dr. Franzen has received honoraria and a grant from and served on the speakers' bureau for Abbott Vascular. Dr. Lüscher has received a research grant from Abbott. Mr. Moat is a consultant and proctor for Medtronic. Dr. Price has an educational contract with Medtronic; and serves on the medical advisory board for Abbott. Dr. Grasso serves as a proctor for Abbott. Dr. Settergren serves as a proctor and advisory board member for and has received an educational grant from Abbott Vascular. Dr. Petronio serves as a clinical proctor for Medtronic. Dr. Ettori serves as a clinical proctor for Medtronic. Dr. Sievert has received study honoraria, travel expenses, and consulting fees from Abbott, Access Closure, AGA, Angiomed, Aptus, Atrium, Avinger, Bard, Boston Scientific, Bridgepoint, Carag, Cardiac Dimensions, CardioKinetix, CardioMEMS, Cardiox, Celonova, CGuard, Coherex, Contego, Covidien, CSI, CVRx, EndoCross, ev3, FlowCardia, Gardia, Gore, Guided Delivery Systems, Hemoteq, InSeal Medical, Lumen Biomedical, HLT, Lifetech, Lutonix, Maya Medical, Medtronic, NDC, Occlutech, Osprey, Ostial, PendraCare, pfm Medical, Recor, ResMed, Rox Medical, SentreHeart, Spectranetics, SquareOne, Svelte Medical Systems, Trireme, Trivascular, Vascular Dynamics, Venus Medical, Veryan, and Vessix; he has received grant support from Cook and St. Jude Medical; and he has stock options in CardioKinetix, Access Closure, Velocimed, Lumen Biomedical, Coherex, and SMT. Dr. Baumgartner has received travel support from Abbott, St. Jude Medical, and Direct Flow Medical; and travel support and consultant and speaker fees from Edwards Lifesciences. Dr. Maisano serves as a consultant for Abbott, Medtronic, St. Jude Medical, and Valtech Cardio; he receives royalties from Edwards Lifesciences; and he is a cofounder of 4Tech. Dr. Lubos has received honoraria from Abbott. Dr. Plicht receives lecture honoraria and travel grants from Abbott Vascular. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. At the time of the registry, the following companies were supporting the EURObservational Research Programme: Gold—Abbott Vascular, Bristol-Myers Squibb, Pfizer Inc., Boehringer Ingelheim, Daiichi-Sankyo Europe, Menarini International Operations, Novartis Pharma, Sanofi-Aventis, and Servier International. Silver—Amgen and Bayer Pharma. Bronze—Boston Scientific International and Merck & Co., Inc. Data collection was conducted by the EURObservational Research Programme (EORP) department of the European Society of Cardiology by Gerard Gracia. Statistical analyses were performed by Cécile Laroche with the support of Renato Urso. Overall activities were coordinated by Aldo Maggioni, Scientific Coordinator, EORP; Thierry Ferreira, Head of Department, EORP; and the EORP Oversight Committee (Roberto Ferrari, Panos Vardas, Michel Komajda, Fausto Pinto, Angeles Alonso, David Wood, Nikolaos Maniadakis, Patrizio Lancellotti, Carina Blomström-Lundqvist, Stephan Windecker, Stefan Anker, Uwe Zeymer, Aldo Maggioni, and Luigi Tavazzi).

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this report is to present a real-world overview of device use focusing on patient characteristics, clinical indications, techniques, in-hospital outcomes, and 1-year outcomes.

METHODS

Twenty-five centers in 8 European countries contributed to this registry (Online Appendix). They prospectively entered data on consecutive patients from January 2011 (or from the time of ethics committee approval) to December 2012 via a dedicated Internet-based Case Record Form hosted and managed at the European Society of Cardiology Heart House. The EuroObservational Research Programme team generated queries to clean the database and validate entries. A total of 155 of 628 cases (24.6%) were audited on site. This pilot registry received no direct commercial sponsorship from the device manufacturer, which produced the only CE-marked commercially available device for transcatheter MV repair during the study period.

At participating centers, all consecutive patients receiving transcatheter mitral edge-to-edge repair with TMVR were prospectively entered into the registry. The only exclusion criterion was refusal to sign the agreement to enter data, which was approved by the ethics committees of the participating centers.

The MitraClip system is a 4-mm-wide, polyester-covered, cobalt-chromium, V-shaped device with 2 movable arms. With the patient under general anesthesia and with the use of fluoroscopic and transesophageal echocardiographic guidance (17), transseptal puncture is performed, which enables the advancement of a 24-F torqueable sheath from the femoral vein into the left atrium. The MitraClip catheter is then advanced across the MV into the LV with the clip arms opened with a perpendicular orientation to the coaptation line. When the opened arms are withdrawn, the leaflets fall into the clip and are secured between the arms and the grippers, which creates a double-orifice valve. If an acceptable reduction in MR is achieved without a critical increase in transmitral gradient and adequate stability is demonstrated, the clip is detached from the delivery system. In patients with broad regurgitant jets, the use of a second clip is now considered a common technique to improve results (18).

ENDPOINTS AND DEFINITIONS. Procedural success was defined as a reduction in the degree of MR to equal to or less than moderate (≤2+) without complications (5). Clinical and echocardiographic follow-up was performed at discharge and at 1 and 12 months after implantation. For the echocardiographic analysis substudy, we selected centers (15 of 25) with a follow-up rate of at least 90% (n = 383), because we expected positive or negative bias to modify the characteristics of the patients assessed in the remaining centers. Only patients with paired echocardiographic observations during follow-up were included in the analysis (n = 368 [61%]).

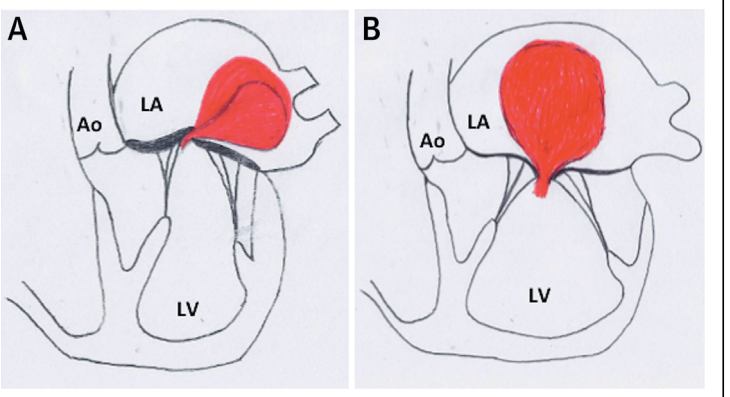


FIGURE 1 Pathogenetic Process of Degenerative and Functional Mitral Regurgitation

(A) Degenerative mitral regurgitation is a consequence of a spectrum of conditions in which morphological changes in the connective tissue of the mitral valve cause structural lesions (such as chordal elongation, leaflet tissue expansion) that prevent normal function of the mitral apparatus, leading to leaflet prolapse. **(B)** Functional mitral regurgitation is a consequence of left ventricular remodeling after myocardial injury (dilated cardiomyopathy, ischemic left ventricular insufficiency, and so on), with enlargement of the left ventricular chamber and mitral annulus, apical and lateral migration of the papillary muscles, leaflet tethering, and reduced closing forces. These processes lead to incomplete coaptation of the leaflets and variable degrees of mitral regurgitation that can fluctuate dynamically as a function of volume status, afterload, heart rhythm, and residual ischemia. The leaflets themselves are normal, and the disease primarily affects the myocardium rather than the valve itself. Ao = ascending aorta; LA = left atrium; LV = left ventricle.

STATISTICAL ANALYSIS. Continuous variables are reported as mean ± SD or as median and interquartile range, as appropriate. Between-group comparisons were made with a nonparametric test (Kruskal-Wallis test). Categorical variables are reported as percentages. Between-group comparisons were made with a chi-square test (Fisher exact test if the expected cell count was <5). Univariate analysis was applied to both continuous and categorical variables. Multivariate logistic regression analysis was used to identify the variables independently associated with the combined endpoint of death or readmission because of heart failure at 1 year. We included all variables correlated with the combined endpoint at $p < 0.1$ or expected from previous studies to influence outcome. Because we used the EuroSCORE (European System for Cardiac Operative Risk Evaluation) as an overall

TABLE 1 Baseline Clinical Characteristics

	Overall (n = 628)	Mixed/ Other (n = 17)	Functional MR (n = 452)	Degenerative MR (n = 143)	p Value*
Age, yrs	74.2 ± 9.7	78.0 ± 8.4	72.8 ± 9.8	78.3 ± 8.5	<0.001
Male	63.1	41.2	67.7	52.5	<0.001
Diabetes mellitus	27.9	11.8	33.1	12.6	<0.001
Hypertension	75.9	88.2	77.6	69.0	0.038
COPD	19.3	11.8	19.8	20.3	0.905
Previous stroke	14.4	17.7	12.8	18.2	0.109
Significant CAD	30.9	29.4	31.9	25.9	0.659
Previous MI	31.2	25.5	37.6	13.3	<0.001
Previous PCI†	15.5	11.8	16.4	14.1	0.515
Previous CABG	32.3	35.3	34.9	21.7	<0.003
Previous valve surgery	10.4	5.9	9.7	11.9	0.459
NYHA functional class					0.004
I	1.6	0.0	1.1	3.5	
II	12.9	23.5	10.4	19.6	
III	68.7	52.9	70.3	63.6	
IV	16.8	23.5	18.2	13.3	
AFib/flutter	31.7	18.8	27.2	50.0	<0.001
LVEF <30%	32.8	12.5	42.0	2.8	<0.001
Baseline SCr, μmol/l	132.0 ± 80.5	115.7 ± 37.2	137.7 ± 88.0	112.6 ± 45.8	0.002
CKD	30.5	17.7	32.8	24.1	0.051
Hemodialysis	9.2	0.0	9.3	10.5	0.634
EuroSCORE	20.4 ± 16.7	15.5 ± 11.2	21.9 ± 17.6	16.3 ± 13.7	0.003

Values are mean ± SD or %. *p Value for comparisons between functional and degenerative mitral regurgitation. †Within 3 months.

AFib = atrial fibrillation; CABG = coronary artery bypass graft surgery; CAD = coronary artery disease; CKD = chronic kidney disease; COPD = chronic obstructive pulmonary disease; EuroSCORE = European System for Cardiac Operative Risk Evaluation; LVEF = left ventricular ejection fraction; MI = myocardial infarction; MR = mitral regurgitation; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; SCr = serum creatinine.

estimation for the risk of patients, we excluded all the components used for its calculation to avoid collinearity. MR severity and New York Heart Association (NYHA) functional class were compared between different time points (baseline, discharge, 1 month, and 12 months) by use of the Bowker test. Changes in echocardiographic measurements between different time points (baseline, discharge, and 12 months) were analyzed with paired Student *t* tests. Survival rates up to 12 months were presented as Kaplan-Meier curves. Differences were considered statistically significant at p values <0.05.

All analyses were performed with SAS statistical software version 9.2 (SAS Institute, Inc., Cary, North Carolina). The multivariate logistic regression analysis was performed with program R (Vienna University of Economics and Business Administration, Vienna, Austria) and the package Hmisc (Vanderbilt University, Nashville, Tennessee).

RESULTS

BASELINE CHARACTERISTICS. Between January 2011 and December 2012, 628 patients (mean age 74.2 ± 9.7 years) were entered into the database. Baseline characteristics for the entire population are displayed in Table 1. The prevalent pathogenesis was functional mitral regurgitation (FMR) (n = 452 [72.0%]). In the overall population, men predominated (63.1%), but patients with degenerative MR (DMR) showed an almost equal distribution of men and women (52% vs. 48%). The vast majority of patients were highly symptomatic (NYHA functional class >III, 85.5%) and at high surgical risk (logistic EuroSCORE 20.4 ± 16.7%). Mean logistic EuroSCORE and prevalence of FMR according to country are displayed in Figure 2. There was a marked heterogeneity among countries with regard to the pathogenesis of MR and the surgical risk of patients selected for TMVR.

PROCEDURAL AND IN-HOSPITAL OUTCOMES. Procedural variables and in-hospital outcomes are displayed in Table 2. Acute procedural success was high (95.4%) and equivalent between groups (p = 0.304). One clip was implanted in the majority of cases (61.4%), 2 clips were implanted in 35.1% of cases, and very few patients received 3 or more clips (2.4%). Patients with DMR tended to receive a greater number of clips than those with FMR (≥2 clips implanted in 62 patients with DMR [44.3%] vs. 162 patients with FMR [36.5%], p = 0.098). Overall, in-hospital mortality was 2.9%

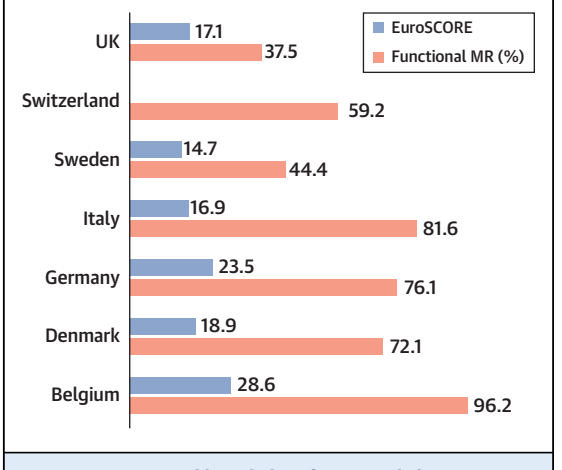


FIGURE 2 Geographic Variation of Mean Logistic EuroSCORE and Prevalence of Functional MR Pathogenesis

There is marked variation between countries with regard to the type of mitral regurgitation (MR) treated and the surgical predicted risk. EuroSCORE = European System for Cardiac Operative Risk Evaluation.

(18 of 628 patients) and ranged between 4.9% (7 of 143 patients) in the DMR group and 2.0% (9 of 452 patients) in the FMR group (p = 0.075). Two patients died in the group with mixed/unknown pathogenesis. Cardiac tamponade and stroke were infrequent (1.1% and 0.2%, respectively). Vascular damage and profuse bleeding that required multiple transfusions were rare (1.1% and 0.7%, respectively). The need for transfusion of at least 1 U of blood was seen in 10.1% of patients.

ECHOCARDIOGRAPHIC DATA AT ADMISSION AND DISCHARGE. Baseline and post-procedural paired echocardiographic data are displayed in Table 3. At baseline, patients with FMR had larger LV volumes (p < 0.001) and a significantly lower LV ejection fraction (LVEF; p < 0.001). By contrast, patients with DMR presented with more severe MR on both semi-quantitative and quantitative echocardiographic parameters. They also had significantly higher systolic pulmonary pressure values (p < 0.001). Echocardiograms obtained before discharge showed a marked reduction in MR less than or equal to moderate in 98.2% of patients, with equivalence between groups (p = 0.910). Overall, a significant reduction in atrial volumes (mean change in left atrial volume 10.4 ml, p = 0.004) and systolic pulmonary artery pressure (SPAP) (mean ΔSPAP 5.8 mm Hg, p < 0.001) was observed at discharge. LVEF showed a small but significant decrease after repair (mean ΔLVEF 1.0%, p = 0.020), especially in the DMR group (ΔLVEF 4.4%, p < 0.001). In both FMR and DMR patients, significant changes were demonstrated in atrial volume and pulmonary pressure. There was a significant increase in the mean transmitral pressure gradient for both types of MR, but without significant differences between groups.

TABLE 2 Procedural/In-Hospital Clinical Outcomes

	Overall* (n = 628)	Functional MR (n = 452)	Degenerative MR (n = 143)	p Value†
Death	2.9	2.0	4.9	0.075
Tamponade	1.1	0.7	1.8	0.298
Stroke	0.2	0.0	0.7	0.241
Severe bleeding	1.1	0.9	2.1	0.368
Transfusion	10.1	9.7	12.4	0.406
Vascular complication requiring intervention	0.7	1.0	0.0	0.581
New-onset atrial fibrillation	11.7	12.6	10.2	0.599
Acute procedural success	95.4	95.8	93.7	0.304
Clip embolization	0.7	0.5	0.9	0.521
Inability to reduce MR	3.5	3.0	4.4	0.387
Implant ≥2 clips	37.5	36.5	44.3	0.098
Procedure duration, min	138.3 ± 67.9	137.2 ± 68.2	132.1 ± 65.6	0.463
Median hospital stay (IQR), d	5 (3–7)	5 (4–7)	5 (3–7)	0.348

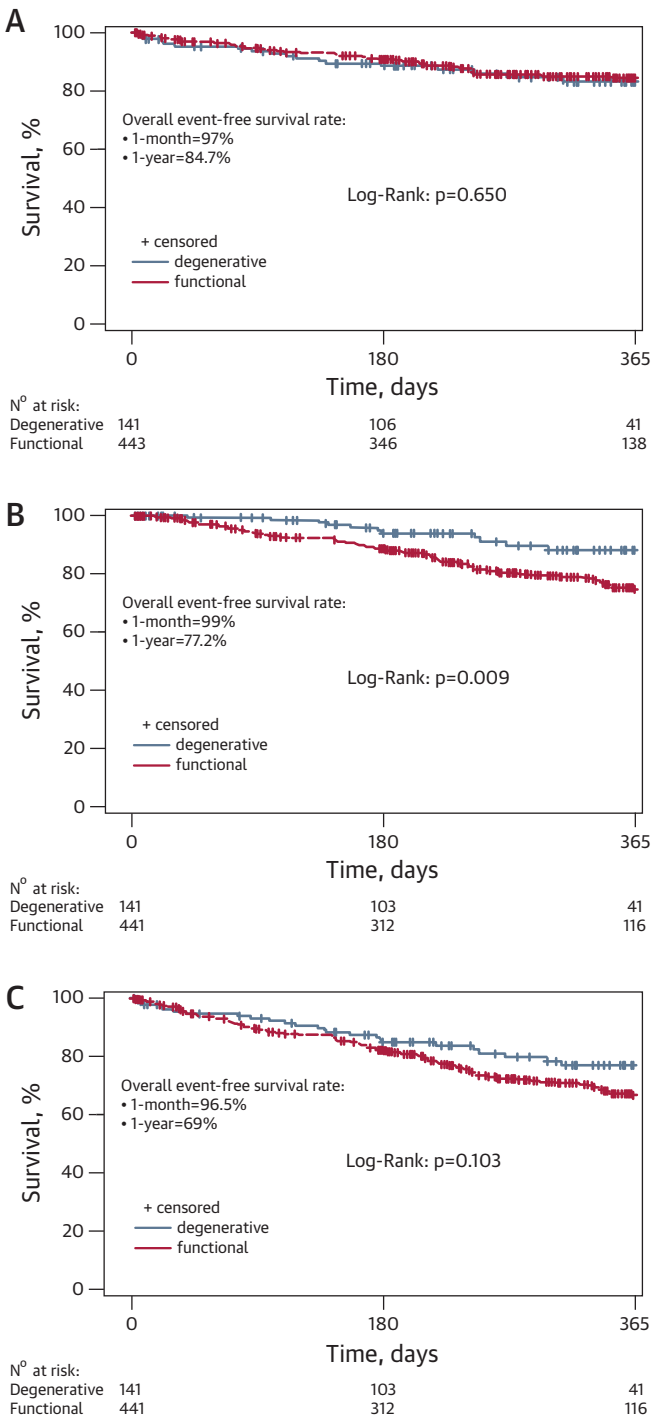
Values are % or mean ± SD, unless otherwise noted. *Includes the 17 mixed/other patients. †p Value for comparisons between functional and degenerative mitral regurgitation.
IQR = interquartile range; MR = mitral regurgitation.

FOLLOW-UP RESULTS: CLINICAL OUTCOMES. Twelve-month clinical follow-up was obtained in 552 patients

TABLE 3 Echocardiographic Variables Before and After TMVR

	Overall (n = 368)				FMR (n = 264)				DMR (n = 85)			
	Pre-Clip	Post-Clip	Δ	p Value	Pre-Clip	Post-Clip	Δ	p Value	Pre-Clip	Post-Clip	Δ	p Value
LVEDV, ml	159.4 ± 86.1	154.8 ± 86.3	4.6	0.119	171.1 ± 90.2	167.0 ± 90.8	4.1	0.212	118.9 ± 57.9	113.1 ± 54.3	5.8	0.265
LVESV, ml	103.0 ± 69.0	102.4 ± 74.6	0.6	0.797	116.3 ± 71.3	114.8 ± 78.4	1.5	0.634	54.0 ± 32.4	56.5 ± 33.4	−2.5	0.313
LA volume, ml	120.8 ± 66.3	110.4 ± 58.1	10.4	0.004	122.5 ± 59.7	113.4 ± 57.9	9.1	0.029	114.1 ± 85.4	99.3 ± 63.2	14.8	0.040
LVEF, %	42.6 ± 15.9	41.6 ± 15.0	1.0	0.020	37.1 ± 13.6	37.0 ± 13.5	0.1	0.792	59.9 ± 9.3	55.5 ± 9.6	4.4	<0.001
Degree of MR, %				<0.001				<0.001				<0.001
None/mild	0.7	72.8			1.0	71.9			0	72.1		
Moderate	13.2	25.4			14.3	26.1			9.8	26.2		
Severe	86.1	1.8			84.7	2.0			90.2	1.6		
MR quantification												
EROA, cm^2	0.43 ± 0.16	–	–		0.42 ± 0.15	–	–		0.46 ± 0.18	–	–	
VC, mm	7.5 ± 2.7	–	–		7.5 ± 2.7	–	–		7.6 ± 2.9	–	–	
RV, ml	53.8 ± 27.6	–	–		51.1 ± 27.7	–	–		62.7 ± 21.3	–	–	
Mean TMG, mm Hg	2.0 ± 1.2	3.4 ± 2.0	−1.4	<0.001	1.9 ± 1.3	3.4 ± 2.1	−1.5	<0.001	2.3 ± 1.3	3.6 ± 1.6	−1.3	0.003
SPAP, mm Hg	46.0 ± 14.5	40.2 ± 11.7	5.8	<0.001	44.2 ± 13.2	39.2 ± 11.2	5	<0.001	53.5 ± 16.9	43.4 ± 12.2	10.2	0.001

Values are mean ± SD or %.
DMR = degenerative mitral regurgitation; EROA = effective regurgitant orifice area; FMR = functional mitral regurgitation; LA = left atrial; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESV = left ventricular end-systolic volume; MR = mitral regurgitation; RV = regurgitant volume; SPAP = systolic pulmonary artery pressure; TMG = transmitral pressure gradient; TMVR = transcatheter mitral valve repair; VC = vena contracta.



CENTRAL ILLUSTRATION **Kaplan-Meier Analysis of Survival Free From Death, Rehospitalization Due to Heart Failure, and Composite of Death and Rehospitalization, Comparing Degenerative Versus Functional Mitral Regurgitation**

(A) Death, **(B)** rehospitalization due to heart failure, **(C)** composite of death and rehospitalization. We observed a significant difference between the 2 types of mitral regurgitation with regard to readmission because of heart failure; however, no differences between groups with regard to death or the composite endpoint were noted.

(88.0%). Median follow-up duration was 346 days (interquartile range: 211-385 days). The estimated 1-year mortality was 15.3%, without significant differences between groups (FMR 15.0% vs. DMR 16.2%, p[log-rank] = 0.650) (**Central Illustration A**). The overall Kaplan-Meier probability of survival at 1 year was 84.7% (SD 1.7%). The estimated 1-year rate of rehospitalization because of heart failure was 22.8% and was significantly higher in the FMR group than the DMR group (25.8% vs. 12%, p[log-rank] = 0.009) (**Central Illustration B**). Conversely, the probability of being free from readmission was 77.2% (SD 2.2%).

At 1 year, the estimated rate of survival free from death or readmission because of heart failure was 69.0% (SD 2.3%). The **Central Illustration C** compares the survival curves of FMR and DMR in terms of death and the composite endpoint of death plus rehospitalization (p[log rank] = 0.103).

The prevalence of different NYHA functional classes during follow-up is shown in **Figure 3**. At 1 month, both FMR and DMR patients exhibited an improvement, with 74.9% (203 of 271 patients) of the former and 76.5% (52 of 68 patients) of the latter showing improvement. This effect persisted over 1 year, with most patients in NYHA functional class II or lower.

Multivariate analysis showed that EuroSCORE (odds ratio [OR]: 1.44; 95% confidence interval [CI]: 1.11 to 1.86; p = 0.006), LVEF <30% (OR: 2.69; 95% CI: 1.64 to 4.42; p < 0.001), and successful clip deployment (OR: 0.12; 95% CI: 0.03 to 0.53; p = 0.005) were independently associated with the composite endpoint at 1 year.

Reintervention at 1 year was observed in 17 patients (3.8%) in the overall population, consisting of an additional MitraClip implantation in 13 patients (2.9% of cases), surgical MV repair in 3 (0.7%), and MV replacement in 1 (0.2%). No significant differences were observed between groups in terms of reintervention.

ECHOCARDIOGRAPHIC FOLLOW-UP. MR reduction at hospital discharge and 1 year is shown in **Figure 4**. At discharge, no significant differences were observed between groups, with lower degrees of MR observed in the FMR group. At 1 year, the rate of recurrence of severe MR in the DMR group was higher, albeit not significantly (6.6% vs. 5.9%, p = 0.965).

At 1 year (**Figure 5**), we observed a slight, nonsignificant reduction in LV end-diastolic volume in patients with DMR but no change in the FMR group. The overall cohort, especially DMR patients, showed a decrease in LVEF (Δ1.4% at 1 year compared with preclip, p = 0.033). Patients with FMR experienced a nonsignificant trend to an improvement in LVEF. Left

atrial volumes decreased significantly, mainly in the FMR group. SPAP showed a persistent significant decrease at 1 year (Δ5.2 mm Hg, $p < 0.001$). Finally, the significant increase in mean transmitral pressure gradient that appeared during the in-hospital evaluation was persistent at 1 year (**Figure 6**).

DISCUSSION

This first report from the mitral cohort of the TCVT European Sentinel registry presents one of the largest independent, contemporary, real-world data collections on the safety and efficacy of MV repair with percutaneous TMVR. Acute procedural success was greater (>90%) than in the initial randomized EVEREST trial but similar to the success observed in more recent registries (10-15,19,20).

This registry also confirms that patients enrolled in contemporary clinical practice are very different from the patients enrolled in the EVEREST clinical trial, which was limited to surgical candidates, mainly with preserved LV function and degenerative valve disease. With regard to the cause of MR, 72% was functional, at variance with EVEREST II (27% prevalence of FMR) but similar to recent registries (66% in TRAMI [Transcatheter Mitral Valve Interventions], 69% in ACCESS-EU [ACCESS-Europe, A Two-Phase Observational Study of the MitraClip System in Europe], and 60% in EVEREST high-risk) (11,13,21). In the present registry, there was a high prevalence of ischemic heart disease, LV dysfunction, and NYHA functional class III or IV (>85% of patients). These features, together with other comorbidities and the old age of the patients, especially in the DMR group, translated into a high logistic EuroSCORE, with an average >20%. The widespread use of TMVR for patients with heart failure and secondary MR is explained by the suboptimal results and high mortality of surgical correction (22-24). In EVEREST II, patients with advanced age, secondary FMR, and depressed LVEF had similar results with TMVR and surgery, compared with previous registries focused on this high-risk group that showed promising results for both MR reduction and functional class improvement (7-9,11,13,21,25).

It is important to stress the overall high acute procedural success (95.4%) achieved with a technically demanding procedure, which was similar between the FMR and DMR groups. Notably, acute procedural success was even higher than in contemporary registries (91% in ACCESS-EU and 94% in TRAMI) (13,21). Greater operator, imaging, and anesthesiology team experience is the most likely explanation for the greater MR reduction with fewer

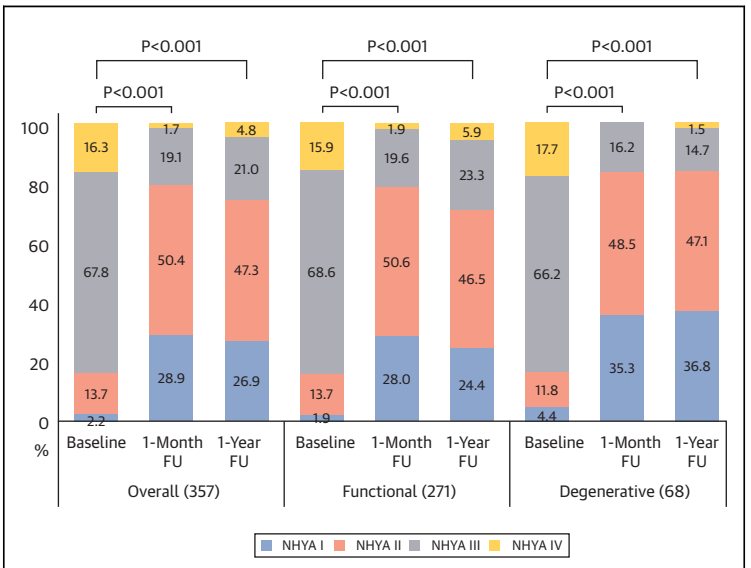


FIGURE 3 NYHA Functional Class at Baseline and at 1-Month and 1-Year Follow-Up

We observed a relevant improvement in New York Heart Association (NYHA) functional class in the overall cohort and for both types of mitral regurgitation (MR). At 1 year, patients with functional MR were more frequently in NYHA functional class III or IV than patients with degenerative MR. FU = follow-up.

complications and a shorter procedure time than in early reports (26). It is important to highlight that almost 38% of patients received more than 1 clip, and nearly half of the patients with DMR required ≥2

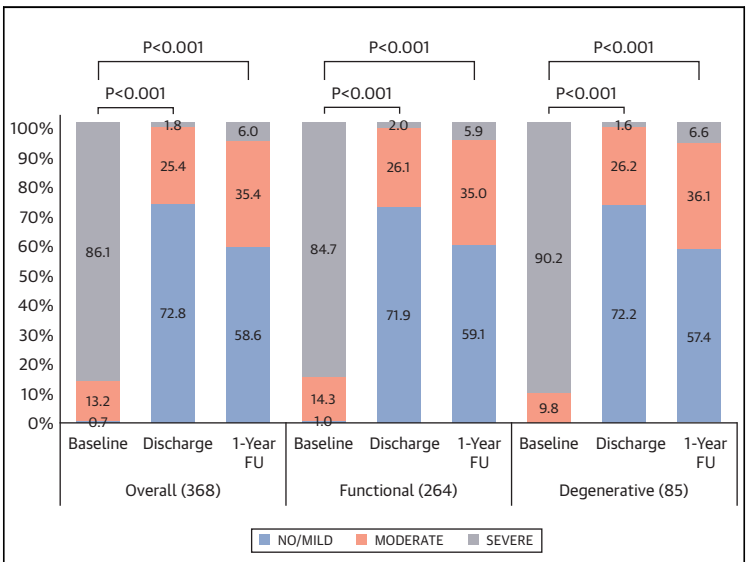


FIGURE 4 Severity of Mitral Regurgitation at Baseline and Follow-Up (Discharge and 1-Year Follow-Up) After TMVR

A significant reduction in the degree of mitral regurgitation was noted, with no difference between functional and degenerative mitral regurgitation. This reduction persisted at 1 year. FU = follow-up; TMVR = transcatheter mitral valve repair.

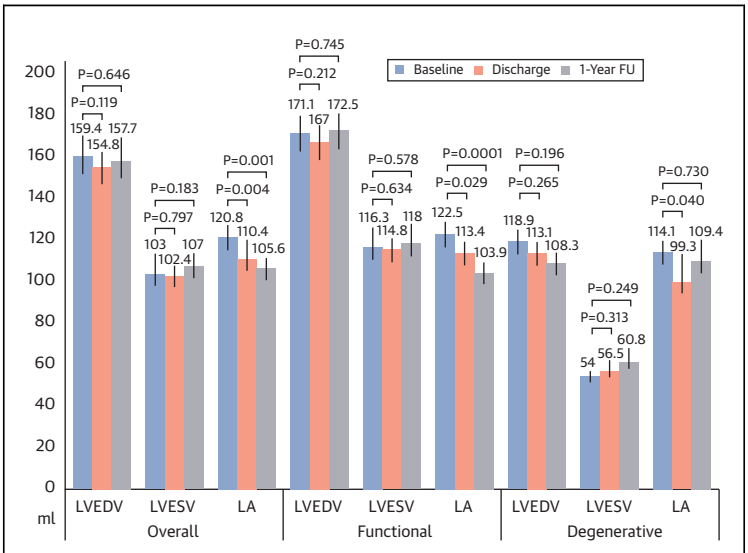


FIGURE 5 Echocardiographic Measurement of Left Ventricular and Left Atrial Volumes at Baseline, Discharge, and 1-Year Follow-Up After TMVR (Paired Data From 368 Patients)

In the overall cohort, a nonsignificant reduction in left ventricular end-diastolic volume (LVEDV) was observed, with a significant reduction in left atrial volume (LA). In functional mitral regurgitation, left ventricular volumes remained stable during follow-up, although a significant reduction in LA was noted. In degenerative mitral regurgitation, the most relevant finding was a reduction in LVEDV over time (nonsignificant). LVESV = left ventricular end-systolic volume; TMVR = transcatheter mitral valve repair.

clips. The EVEREST subanalysis (27) showed that patients with more severe MR (measured by higher regurgitant volumes) were more likely to receive more than 1 clip to achieve an optimal MR reduction, whereas previous data from Franzen et al. (8) showed that in 80% of patients with end-stage heart failure, MR can be successfully treated with a single clip. Successful reduction of MR is of paramount importance to maximize the clinical benefit of the procedure (19,28). With proper patient selection, the implantation of ≥2 clips is not associated with higher gradients or lower MV area at follow-up than the use of just 1 clip (29).

Numerically, in-hospital mortality was lower than in previous registries in high-risk populations (10,11,13,19), with higher rates observed in the DMR than in the FMR group. This finding may be explained by the fact that although patients with DMR had lower logistic EuroSCOREs and therefore expected lower rates of in-hospital adverse events, they were significantly older and had more severe MR and pulmonary hypertension, together with other adverse factors that were not taken into account in the risk score calculation.

The registry confirmed that TMVR confers sustained clinical benefit, with persistent severe MR in 1.8% of cases immediately post-procedure and 6% at 1 year, a long-term improvement already observed in other real-world registries (e.g., 80% MR ≤2+ in ACCESS-EU at 1 year) (12,13,21). Patients with DMR, in whom regurgitant volume plays the key role in the pathophysiology of LV remodeling, showed a considerable although not significant decrease in LV end-diastolic volume. Conversely, in patients with FMR, LV volumes at 1 year presented an increase from the post-procedure values, likely caused by the

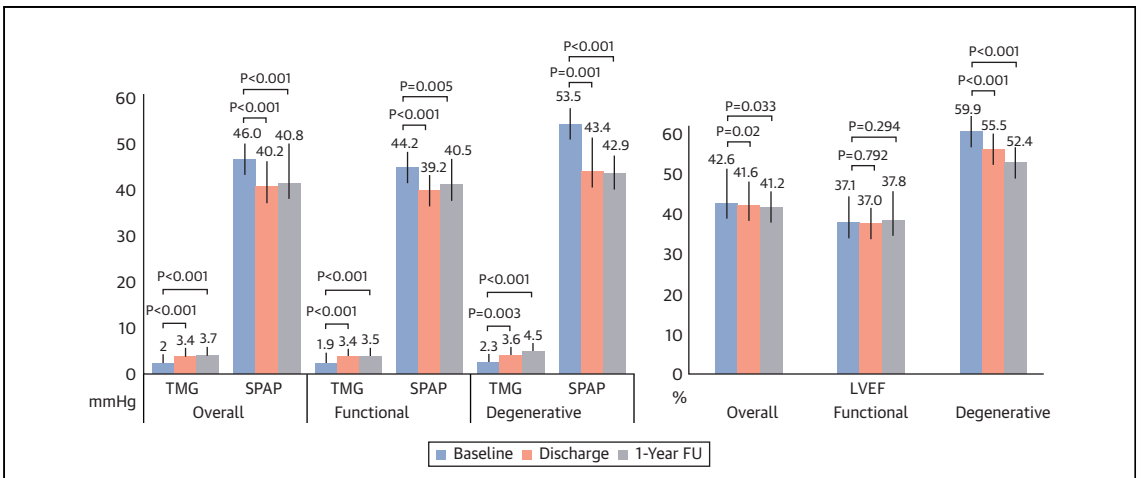


FIGURE 6 Echocardiographic Measurement of Transmitral Pressure Gradient, SPAP, and Ejection Fraction, at Baseline, Discharge, and 1-Year Follow-Up

Significant and persistent reductions in systolic pulmonary artery pressure (SPAP) were observed. After transcatheter mitral valve repair, transmitral pressure gradient (TMG) (mm Hg) increased significantly, although no cases of severe mitral stenosis were reported. LVEF = left ventricular ejection fraction (%).

underlying myocardial disease. The correction of mitral insufficiency alters just 1 of the multiple mechanisms that lead to progressive LV dilation, and LV volumes can remain high despite a significant reverse atrial remodeling after implantation of the clip, a finding that suggests an effective correction of the volume overload. It must be stressed as well that patients with FMR in this trial were treated in an advanced stage of evolution of their disease. With earlier correction of MR, we speculate that a favorable LV remodeling may still occur. Volumetric reductions were more pronounced in the EVEREST trial, which is possibly explained by the inclusion of an older population with more advanced disease in our registry. In addition, the different proportion of patients with DMR and FMR may account for the differences observed between our data and the EVEREST analyses with regard to LV remodeling (30,31).

NYHA functional class showed improvement during follow-up for both FMR and DMR patients, although at 1 year, the proportion of patients with FMR in a more advanced functional class was higher than in patients with DMR. The 1-year mortality rate was comparable to the mortality reported in the most recent registry (21), with no significant difference in the rate of mortality of FMR and DMR patients. The variable with the strongest association with the combined endpoint of death or rehospitalization for heart failure was the inability to implant a clip and reduce MR. This finding was addressed recently in a report from the EVEREST investigators in a subset of patients with DMR: The degree of residual MR after the procedure was linked to a worse outcome, with an increase in the rates of death and rehospitalization because of heart failure (32). Notably, our data and the recently published ACCESS-EU (21) show a 1-year survival that is similar to the rate in the most contemporary trial of surgical correction of FMR but in patients with very high surgical risk (33).

STUDY LIMITATIONS. First, the TCVT registry is a pilot, voluntary registry. Thus, procedural complications, adverse events, and echocardiography parameters are self-reported. Second, despite the extreme simplification of the follow-up data requested, which excluded, for instance, drug regimen, the completeness of follow-up for clinical events (88%) and especially echocardiographic data (61%) is far from ideal. However, the centers compliant with full echocardiographic data entry provided nearly complete entry of their consecutive 368 patients with paired echocardiographic data, a group that is one of the largest series in the literature and reports complete data in terms of serial volumes and atrioventricular gradients, which are essential to understand the effects of TMVR on LV remodeling and MR reduction.

Registries do not eliminate the need for properly randomized controlled trials with external adjudication and core laboratory analysis of data with great subjectivity, such as, for instance, severity of mitral insufficiency. Still, they offer the opportunity to understand whether trial results are applicable to real-life settings and, conversely, help to provide the key outcome measures to design meaningful future controlled studies.

CONCLUSIONS

In this large contemporary registry addressing the effect of TMVR on MR reduction, functional class improvement, and clinical events, both FMR and DMR exhibited an immediate reduction in the severity of MR and improvement in functional class that persisted at 1 year. Procedural and late mortality was low and lower than expected in such a high-risk cohort, without differences between FMR and DMR.

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REPRINT REQUESTS AND CORRESPONDENCE: Dr. Carlo Di Mario, National Institute of Health Research, Cardiovascular Biomedical Research Unit, Royal Brompton Hospital, Sydney Street, SW3 6NP London, United Kingdom. E-mail: c.dimario@rbht.nhs.uk.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Experience in Europe with percutaneous TMVR suggests efficacy in reducing the severity of primary mitral regurgitation with a relatively low complication rate and persistent improvement in functional class in most patients.

TRANSLATIONAL OUTLOOK: The results of randomized trials should provide more information about the value of TMVR as a palliative adjunctive treatment of heart failure patients with severe primary mitral regurgitation refractory to mediation therapy.

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KEY WORDS MitraClip, mitral regurgitation, percutaneous mitral valve repair, registry

APPENDIX For supplemental material, please see the online version of this article.