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ORIGINAL SCIENTIFIC PAPER

Evaluation of three-dimensional right ventricular function and reverse remodelling in patients undergoing percutaneous mitral valve repair for functional mitral regurgitation: insights from a multicentre Italian registry

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ABSTRACT

Background: The predictive role of right ventricular dysfunction (RVD) in patients with functional mitral regurgitation (FMR) undergoing transcatheter edge-to-edge repair (TEER), as well as RV remodelling following the procedure, remains uncertain. We evaluated the prognostic impact of pre-procedural three-dimensional (3D) right ventricular ejection fraction (RVEF) in patients with FMR. Additionally, we assessed the RV reverse remodelling (RVRR) based on 3D volumes and ejection fraction six months after the procedure.

Methods: Data from 74 patients treated with TEER for FMR were prospectively collected. Pre-procedural RVD, defined as 3D RVEF ≤45%, was observed in 47 patients (63.5%). Patients were divided into three groups according to pre-procedural 3D-RVEF: no RVD (No-RVD, RVEF >45%, $n=27$), mild-to-moderate RVD (MRVD, RVEF 31-45%, $n=36$), and severe RVD (SRVD, RVEF ≤30%, $n=11$).

Results: Patients with SRVD demonstrated a significant higher rate of all-cause mortality compared with the other two groups ($p=0.04$) and RVEF ≤ 30% was associated with all-cause death, independently of left ventricular ejection fraction (LVEF) and left atrial volume index (LAVi) (HR: 3.72, 95% CI 1.12–12.30, $p=0.03$). At 6-month follow-up, only patients with pre-procedural MRVD showed a significant reduction in 3D RV volumes and an improvement in RVEF compared to baseline ($p<0.05$).

Conclusions: RVD was common among patients undergoing mitral TEER for FMR. Those with pre-procedural SRVD had worse mid-term survival compared to patients with MRVD and No-RVD. The group with MRVD was the only one to demonstrate an RVRR six months after the procedure.

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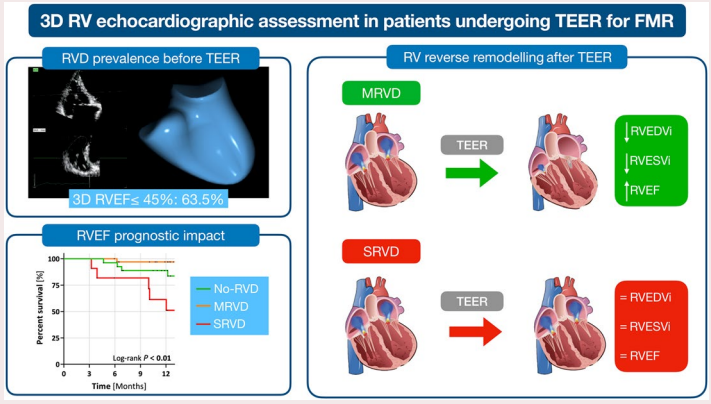
GRAPHICAL ABSTRACT

3D RV echocardiographic assessment in patients undergoing mitral TEER for FMR. Top-left panel: 3D RV reconstruction using semi-automated software and prevalence of RVD defined by 3D-echocardiography (3D RVEF ≤ 45%). Bottom-left panel: Survival curve of patients undergoing mitral TEER, stratified by categories of systolic disfunction (No-RVD, MRVD, SRVD). Right-panel: The impact of mitral TEER procedure on RV reverse remodelling, in terms of volumes and ejection fraction, is observed only in patients with MRVD and not in those with SRVD. 3D: threedimensional; FMR: functional mitral regurgitation; MRVD: mild-to-moderate rightventricular dysfunction; No-RVD: No right ventricular dysfunction; RV: right ventricular; RVD: right ventricular dysfunction; RVEDVi: right ventricular end-diastolic volume index; RVEF: right ventricular ejection fraction; RVESVi: right ventricular end-systolic volume index; SRVD: severe right ventricular dysfunction; TEER: transcatheter edgeto-edge repair.



Abbreviations: FAC: Fractional area change; FMR: Functional mitral regurgitation; FWL: Free wall longitudinal strain; HF: Heart failure; LV: Left ventricular; LVEF: Left ventricular ejection fraction; MRVD: Mild-to-moderate right ventricular dysfunction; No-RVD: No right ventricular dysfunction; NT-proBNP: N-terminal pro-B-type natriuretic peptide; NYHA: New York Heart Association; RV: Right ventricular; RVD: Right ventricular dysfunction; RVEF: Right ventricular ejection fraction; PASP: Pulmonary artery systolic pressure; RVRR: Right ventricular reverse remodelling; SRVD: Severe right ventricular dysfunction; s' TDI: Systolic wave velocity at tissue Doppler imaging; TAPSE: Tricuspid annular plane systolic excursion; TEER: Transcatheter edge-to-edge repair; 2D: Two-dimensional; 3D: Three-dimensional

Introduction

Functional mitral regurgitation (FMR) is among the most frequent valvular heart disease in Europe [1] and the United States [2] and it is associated with poor prognosis and high burden of hospitalisation for heart failure (HF) [3–6]. When left untreated, FMR imposes chronic volume overload on left chambers and causes left ventricular (LV) dilation and dysfunction, elevation of left atrial pressure, development of pulmonary hypertension and tricuspid regurgitation and, finally, right ventricular dysfunction (RVD) [7].

According to the most recent guidelines [1,2], transcatheter edge-to-edge repair (TEER) may be considered in selected symptomatic patients suffering with severe FMR, not eligible for surgery and fulfilling the COAPT inclusion criteria [8–10]. In the COAPT trial, the evidence of a moderate or severe RVD was one of the exclusion criteria. However, almost 50% of patients undergoing mitral TEER has a variable degree of RVD in daily clinical practice [11,12]. Previous studies showed that RVD, assessed by two-dimensional (2D) parameters, and impaired right ventricular (RV)-to-pulmonary arterial coupling are determinants of adverse outcomes after mitral TEER [12–17]. The prevalence and the prognostic role of pre-procedural RVD, assessed by three-dimensional (3D) RV ejection fraction (RVEF), have not yet been evaluated. Moreover, few studies have described the effect of mitral TEER on RV dimensions and systolic function after the procedure, with some conflicting data [18–23]. The aim of this study was to evaluate the prevalence and the prognostic impact of pre-procedural RVD, assessed by means of 3D echocardiography, in patients with FMR undergoing TEER, as well as changes in RV volumes and ejection fraction at 6-month follow-up after the procedure.

Methods

Study population

Data from consecutive patients with symptomatic moderate-to-severe or severe FMR, who underwent TEER with MitraClip (Abbott Vascular, Santa Clara, CA, USA), or Pascal System (Edwards Lifesciences, Irvine, California) and had a baseline echocardiogram, including a comprehensive 3D assessment of the RV, were prospectively collected in a dedicated registry at six Italian centres between February 2021 and April 2022

After Heart Team discussion, all patients were carefully selected in presence of high-grade ventricular or atrial FMR, feasible mitral valve anatomy for transcatheter repair and symptoms (NYHA class II-IV) despite optimal medical therapy for HF, including cardiac resynchronisation therapy, if indicated. Patients without analysable baseline echocardiograms, comprehensive of RV 3D assessment, were excluded from the study.

All patients present in the study signed written informed consent after receiving an oral and written explanation of the issues concerning the procedure, data collection and subsequent analysis. The investigation conforms with the principles outlined in the Declaration of Helsinki.

Echocardiographic assessment

All patients underwent a transthoracic echocardiographic examination, including a 3D RV analysis, at hospital admission and before discharge. Whenever possible, a 6-month follow-up, including clinical and echocardiographic evaluation, was performed at each participating centre. Echocardiographic measurements were performed according to the ASE/EAE recommendations [24,25]. At the end of each exam, a 3D full-volume of the right ventricle was acquired from a modified four-chamber apical view or RV focused view. To maximise the frame rate of the acquisition (to reach at least 20 frames per second), the lateral width and the depth of the image sector were reduced as much as possible and, whenever feasible (patients in regular sinus rhythm and able to cooperate with breath-holding), a multi-beat acquisition was used. The multislice display was used to ensure that the entire chamber volume and borders were included in the analysis. In each centre, a dedicated cardiologist, with expertise in advanced echocardiography, finally analysed the 3D datasets using EchoPac software (GE Vingmed Ultrasound AS, Horten, Norway) or TomTec Imaging Systems (Unterschleissheim, Germany) to measure RV volumes and ejection fraction.

Reproducibility

Intra-observer and inter-observer variability for the 3D manual measurements of RVEF and RV volumes was assessed in a sample of 15 randomly selected patients. Two investigators separately measured the same 3D loops, and one investigator repeated the analysis two weeks later, blinded to the previous measurements (Table S1).

Endpoint assessment

Mitral Valve Academic Research Consortium definition of acute technical success was applied. Clinical endpoints were obtained from medical reports and/or phone calls. The primary endpoint was considered the impact of RVD, assessed *via* 3D RVEF, on all-cause mortality after mitral TEER. The secondary endpoint was the assessment of RV reverse remodelling (RVRR) in terms of 3D volumes and ejection fraction at 6-month follow-up after the procedure.

Definition and grading of RV dysfunction

RVD was defined as RVEF ≤45% [24]. To evaluate the prognostic impact of RVD in patients with severe FMR undergoing TEER, the population was divided into three groups according to the RVEF: no RVD (No-RVD, RVEF >45%), mild-to-moderate RVD (MRVD, RVEF >30 ≤ 45%) and severe RVD (SRVD, RVEF ≤30%). These partition values of RVEF were derived from previous literature [26].

RV reverse remodelling assessment

To assess the presence of RVRR (volumes and ejection fraction) after mitral TEER procedure, the population was stratified based on pre-procedural RVD using the previously described classification. Paired comparisons of echocardiographic variables at baseline, discharge, and follow-up were performed across the three RVD groups to assess potential significant differences over time.

Statistical analysis

Normality of continuous data was tested with the Shapiro-Wilk test: normally distributed variables were expressed as mean ± standard deviation (SD), whereas non-normally distributed variables were presented as median [interquartile range]. Categorical variables were reported as absolute values and corresponding percentages.

Differences in continuous variables were assessed using 1-way analysis of variance (ANOVA) or the Kruskal–Wallis test. Categorical variables were compared with Chi-square test. Paired comparisons between variables at baseline, discharge, and follow-up were performed using the paired-sample Student's t-test or the Wilcoxon signed-rank test, as appropriate.

Adverse events were reported as the observed number of events and as Kaplan-Meier estimated rates. Event-free survival up to 1-year was evaluated using the unadjusted Kaplan-Meier method, and survival among subgroups was compared using the log-rank test (Cox-Mantel test). Cox proportional hazards regression analysis was used to identify predictors of the primary clinical endpoint, expressed as hazard ratio (HR) with 95% confidence interval (CI) and p values. A p value <0.05 was considered statistically significant.

The Statistical analyses were performed by two investigators using SPSS software version 28.0.0 (SPSS Inc., Chicago, IL) and GraphPad Prism software version 8 (GraphPad, Inc, San Diego, CA).

Results

Between February 2021 and April 2022, 74 patients underwent a mitral TEER procedure at six Italian centres and had a baseline echocardiogram that included a comprehensive 3D assessment of the RV (32% from IRCCS Policlinico San Donato, 19% from ASST Spedali Civili of Brescia, 15% from Azienda Ospedaliero-Universitaria Pisana, 15% from A.O.U. Policlinico 'G. Rodolico San Marco' of Catania, 11% from Sant'Orsola-Malpighi Hospital of Bologna, 8% from IRCCS San Raffaele Hospital).

Overall, pre-procedural RVD (i.e. RVEF ≤ 45%) was found in 47 patients (63.5% of the population). According to pre-procedural RV systolic function, 36.5% of patients ($n = 27$) showed No-RVD, 48.6% ($n = 36$) MRVD and 14.9% ($n = 11$) SRVD.

Baseline clinical characteristics

Baseline clinical characteristics of the entire cohort and by groups of RVD are summarised in Table S2.

The median age of our population was 78 years (IQR: 72–82), 68.9% of whom were male. No significant differences in terms of age ($p = 0.70$) and gender ($p = 0.09$) were found among groups. All patients presented with HF-related symptoms, and 72.3% of the cases were in NYHA class III or IV. The group with MRVD more frequently had a history of percutaneous coronary intervention ($p = 0.01$). Interestingly, patients with SRVD had a higher prevalence of chronic obstructive pulmonary disease compared with the other groups (No-RVD 22.2% vs MRVD 16.7% vs SRVD 54.5%, $p = 0.03$). No significant differences among groups were observed in terms of surgical risk, NYHA class, and number of devices implanted (pacemaker, implantable cardioverter-defibrillator, cardiac resynchronisation therapy).

The baseline median N-terminal brain natriuretic peptide (NT-proBNP) was 2810 pg/ml (IQR:1304–7852); patients with higher degree of RVD had a higher NT-proBNP value ($p < 0.01$). Patients received the maximum tolerated guideline-directed medical therapy, including renin-angiotensin system inhibitors (63.5%), beta-blockers (85.1%) and mineralocorticoid receptor antagonists (59.4%). All patients took loop-diuretic therapy (100%) at a median dosage of 75 mg (IQR: 50–125).

Baseline echocardiographic characteristics

Baseline echocardiographic characteristics of the entire cohort and by groups of RVD are summarised in Table 1. The aetiology of FMR was predominantly ventricular (81.0% of patients) of which 50.0% ischaemic and 31.0% non-ischaemic, and atrial in the remaining 18.9% of patients. Median values of effective regurgitant orifice area and regurgitant volume were 0.3 cm^2 (IQR: 0.3–0.4) and 51 mL (IQR: 40–65), respectively.

There were significant differences between groups in terms of LV dilation (for both diameters and volumes) and dysfunction (LV ejection fraction (LVEF): No-RVD 36 (33–49)%, MRVD 36 (30–44)%, SRVD 27 (25–31)%, $p = 0.01$), left atrial dilation (left atrial volume index (LAVi): No-RVD 55 (46–76) mL/m^2, MRVD 61 (51–72) mL/m^2, SRVD 75 (68–93) mL/m^2, $p < 0.01$) and estimated pulmonary artery systolic pressure (PASP) (No-RVD 43 ± 14 mmHg, MRVD 48 ± 14 mmHg, SRVD 66 ± 13 mmHg, $p < 0.01$). All the 2D and 3D parameters regarding RV dimensions (basal and mid-ventricular diameters, 3D end-diastolic and end-systolic volumes), systolic function (tricuspid annular plane systolic excursion, (TAPSE), systolic wave velocity at tissue Doppler imaging (s' TDI), fractional area change (FAC), RV free wall longitudinal strain (FWLS), RVEF, RV stroke volume index), and RV-pulmonary arterial coupling (TAPSE/PASP) resulted significantly different between the groups (TAPSE: $p = 0.03$, all the other parameters: $p < 0.01$). In particular, RV basal and mid-diameters, 3D RV volumes, TAPSE/PASP, FAC, FWLS, RVEF resulted to be significantly different in the group with SRVD compared with the other two groups (paired comparisons between groups: SRVD vs No-RVD: p value < 0.05; SRVD vs MRVD: p value < 0.05). No difference in the grade of tricuspid regurgitation was found between groups ($p = 0.79$).

Table 1. Baseline echocardiographic characteristics of the entire study cohort and of the three groups identified according to pre-procedural RV systolic function.

Variables		Total population ($n=74$)	No-RVD ($n=27$)	MRVD ($n=36$)	SRVD ($n=11$)	p value
MR aetiology, n (%)						
Ischaemic ventricular FMR		37 (50.0)	12 (44.4)	20 (55.6)	5 (45.4)	0.61
Non-ischaemic ventricular FMR		23 (31.0)	8 (29.6)	10 (27.8)	5 (45.4)	
Atrial FMR		14 (18.9)	7 (25.9)	6 (16.7)	1 (9.0)	
MR degree, n (%)	3+	20 (27.0)	12 (44.4)	7 (19.4)	1 (9.0)	0.07
	4+	54 (73.0)	15 (55.5)	29 (80.6)	10 (90.9)	
VC, mm		7 [6, 8]	7 [7, 8]	7 [6, 9]	7 [6, 8]	0.73
EROA, cm^2		0.3 [0.3, 0.4]	0.3 [0.3, 0.4]	0.4 [0.3, 0.4]	0.3 [0.3, 0.4]	0.18
Regurgitant volume, ml		51 [40, 65]	49 [38, 64]	61 [44, 67]	47 [41, 58]	0.26
Mean gradient, mmHg		2.0 [1.0, 2.0]	2.0 [1.0, 2.4]	2.0 [1.0, 2.0]	1.0 [1.0, 1.8]	0.31
LVEDD, mm		61 ± 9	61 ± 10	59 ± 9	68 ± 7$^{\square}$	**0.03**
LVESD, mm		51 ± 11	49 ± 10	50 ± 11	61 ± 8*$^{\square}$	**0.01**
LVEDVi, mL/m^2		100 ± 37	100 ± 33	92 ± 35	127 ± 44$^{\square}$	**0.02**
LVESVi, mL/m^2		65 ± 31	62 ± 27	59 ± 28	91 ± 37*$^{\square}$	**0.01**
LVEF, %		35 [30, 43]	36 [33, 49]	36 [30, 44]	27 [25, 31]	**0.01**
E/e'		14 [10, 20]	13 [8, 15]	14 [10, 20]	22 [10, 29]	0.09
LAVi, mL/m^2		62 [52, 75]	55 [46, 76]	61 [51, 72]	75 [68, 93]*$^{\square}$	**<0.01**
TR degree, n (%)	≤2	34 (46)	13 (48)	17 (47)	4 (36)	0.79
	>2	40 (54)	14 (52)	19 (53)	7 (64)	
TAPSE, mm		18 ± 4	19 ± 3	18 ± 5	15 ± 3 *	**0.03**
PASP, mmHg		49 ± 16	43 ± 14	48 ± 14	66 ± 13*$^{\square}$	**<0.01**
TAPSE/PASP, mm/mmHg		0.38[0.28, 0.52]	0.50[0.32, 0.58]	0.38[0.29, 0.48]	0.25[0.18, 0.28]*$^{\square}$	**<0.01**
S' TDI, cm/s		10 ± 2	11 ± 2	10 ± 2	9 ± 3*	**<0.01**
FAC, %		37 ± 10	44 ± 7	36 ± 7§	26 ± 8*$^{\square}$	**<0.01**
RV FWLS, %		−18 ± 6	−22 ± 6	−17 ± 5§	−11 ± 5*$^{\square}$	**<0.01**
RV basal diameter, mm		42 [38, 49]	39 [36, 46]	41 [38, 47]	58 [51, 62]* $^{\square}$	**<0.01**
RV mid diameter, mm		34 [29, 39]	31 [26, 35]	34 [30, 39]	45 [39, 53]* $^{\square}$	**<0.01**
3D RVEDV, mL		135 ± 48	113 ± 31	129 ± 28	209 ± 63*$^{\square}$	**<0.01**
3D RVEDVi, mL/m^2		76 ± 28	64 ± 18	72 ± 17	117 ± 37*$^{\square}$	**<0.01**
3D RVESV, mL		81 ± 42	53 ± 19	79 ± 18§	157 ± 45*$^{\square}$	**<0.01**
3D RVESVi, mL/m^2		46 ± 24	30 ± 11	44 ± 11§	88 ± 27*$^{\square}$	**<0.01**
3D RVEF, %		42 ± 11	54 ± 7	39 ± 4§	24 ± 4*$^{\square}$	**<0.01**
3D RVSVi, mL/m^2		30 ± 9	34 ± 9	28 ± 8§	29 ± 12	**<0.01**
3D RVEF/PASP, %/mmHg		0.99 ± 0.49	1.41 ± 0.49	0.88 ± 0.25§	0.38 ± 0.08*$^{\square}$	**<0.01**

No RVD (No-RVD): 3D RVEF > 45%; Mild-to moderate RVD (MRVD): 30% < 3D RVEF ≤ 45%; Severe RVD (SRVD): 3D RVEF ≤ 30%.
Data are presented as mean ± SD, median [IQR] or n (%).
§Mild-to moderate RVD vs No RVD: p value < 0.05; *Severe RVD vs No RVD: p value < 0.05; $^{\square}$Severe RVD vs Mild-to-moderate RVD: p value < 0.05.
Bold values indicate significance.
3D: three-dimensional; E/e': early mitral inflow velocity to mitral annular early diastolic velocity at tissue Doppler imaging ratio; EROA: effective regurgitant orifice area; FAC: fractional area change; FMR: functional mitral regurgitation; FWLS: free wall longitudinal strain; LAVi: left atrial volume index; LVEDD: left ventricular end-diastolic diameter; LVEDVi: left ventricular end-diastolic volume index; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; LVESVi: left ventricular end-systolic volume index; MR: mitral regurgitation; RV: right ventricular; RVD: right ventricular dysfunction, RVEDVi: right ventricular end-diastolic volume index; RVEF: right ventricular ejection fraction; RVESVi: right ventricular end-systolic volume index; RVSVi: right ventricular stroke volume index; S' TDI: systolic wave velocity at tissue Doppler imaging; PASP: pulmonary arterial systolic pressure; TAPSE: tricuspid annular plane systolic excursion; TR: tricuspid regurgitation; VC: vena contracta.

Procedural results

Acute technical success was achieved in 71 patients (96.0%). New-generation MitraClip devices were the most frequently used (89.1%). One, two or three devices were implanted in 41 (55.4%), 31 (41.9%), and 2 (2.7%) patients, respectively. No statistically significant differences were observed among the three groups in terms of procedural and in-hospital outcomes (Table S3).

Clinical outcomes and survival analysis

During a median follow-up of 12.5 (10.4–17.7) months, 15 patients died (20.3%), of which 10 (13.5%) for cardiovascular causes (Table S4). Patients with SRVD demonstrated a significant higher rate of all-cause mortality compared with the other two groups (No-RVD 22.1%, MRVD 11.1%, SRVD 45.4%, $p=0.04$). The rate of hospitalisation for HF was observed in 12 patients (16.2%) with no differences between groups ($p=0.47$).

The Kaplan-Meier curve analysis showed that patients with SRVD had a significantly lower survival probability compared with the other two groups (Log rank p value <0.01) (Figure 1). At univariable Cox regression, SRVD, assessed by 3D RVEF (3D RVEF ≤30%: HR: 5.91, 95% CI 1.91–18.30, $p<0.01$), LVEF (HR: 0.93, 95% CI 0.86–0.99, $p=0.03$) and LAVi (HR: 1.03, 95% CI 1.00–1.06, $p=0.03$) were potential predictor of all-cause death. 2D parameters assessing RV systolic function (TAPSE, TAPSE/PASP, FWLS) did not show to predict mortality in our population (Table 2). At multivariable Cox proportional hazard analysis, RVEF ≤ 30% was

associated with all-cause death, independently of LVEF and LAVi (HR: 3.72, 95% CI 1.12–12.30, $p=0.03$) (Table 2).

RVRR after mitral TEER procedure

Paired comparisons between the echocardiographic characteristics evaluated before mitral TEER, at discharge, and at 6-month follow-up were available for 82.4% ($n=61$) of the study population and are presented for the entire population (Table S5) and per groups of pre-procedural RVD (Tables 3–5).

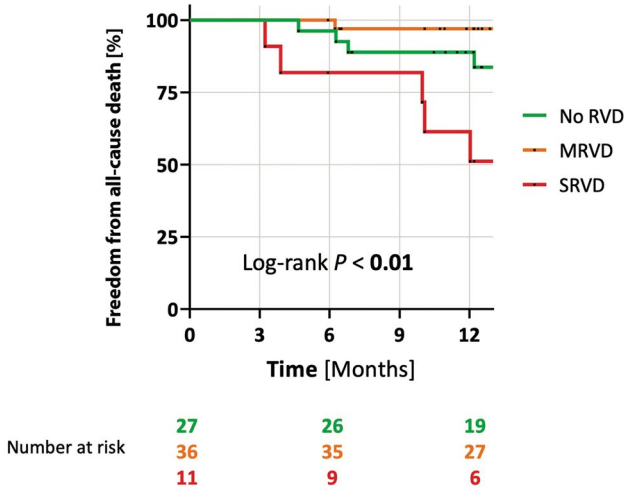


Figure 1. The Kaplan–Meier survival curve analysis of patients undergoing mitral transcatheter edge-to-edge repair (TEER) according to pre-procedural degree of right ventricular dysfunction (RVD), defined by three-dimensional right ventricular ejection fraction (RVEF): No RVD (No-RVD, RVEF >45%), mild-to-moderate RVD (MRVD, RVEF >30 ≤ 45%) and severe RVD (SRVD, RVEF ≤30%).

Interestingly, only patients with pre-procedural MRVD showed a reduction in 3D volumes at 6-month follow-up compared to baseline ($p<0.05$, Table 4), while this did not happen in patients with No-RVD and SRVD (Tables 3 and 5). RV diameters (basal and mid-ventricular) did not change during the follow-up in any RVD group (Tables 3–5). 3D RVEF improved after 6-month from mitral TEER procedure only in patients with MRVD at baseline (3D RVEF: Baseline 40 (36–41) %, Discharge 42 (36–46) %, 6-months 44 (38–47) %, $p<0.01$; 6-months vs Baseline: $p<0.05$; Table 4, Graphic Abstract). All 2D parameters assessing RV function (TAPSE, s' TDI, FAC, RV FWLS) did not change during the follow-up, even when they are analysed per groups of RVD (Tables 3–5). A significant reduction in tricuspid regurgitation degree was observed only in patients with No-RVD at baseline ($p=0.02$, Table 3). Pulmonary pressures (PASP) reduced significantly during the follow-up, except in the group with SRVD at baseline (Tables 3–5 and Table S5). An acute improvement in RV-pulmonary arterial coupling at discharge was observed in the groups with No-RVD and MRVD (TAPSE/PASP: Discharge vs Baseline $p<0.05$), but this was not confirmed at 6-month follow-up (Tables 3 and 4).

Regarding left chambers, LAVi showed a decrease over the 6-months period only in the group with MRVD ($p<0.01$, Table 4), whereas there was no significant change in LV volumes and systolic function in any group. Finally, a sustained reduction in mitral regurgitation degree was observed at 6-month follow-up, with 86.7% of patients exhibiting residual mitral regurgitation ≤2 (Table S5), confirming the high rate of good result of the procedure.

Table 2. Univariable and multivariable cox regression analysis for the baseline predictors of all-cause of death after mitral TEER.

	Univariable analysis		Multivariable analysis	
Variables	HR (95% CI)	*p* value	HR (95% CI)	*p* value
Age (y)	1.05 (0.97, 1.13)	0.23		
Female sex (n)	1.24 (0.42, 3.64)	0.69		
NYHA III-IV	3.02 (0.68, 13.4)	0.15		
Atrial fibrillation	0.91 (0.33, 2.50)	0.85		
CKD	2.29 (0.64, 8.19)	0.20		
COPD	1.77 (0.60, 5.18)	0.30		
TAPSE < 15 mm	0.64 (0.14, 2.83)	0.56		
RV FWLS < −18%	1.52 (0.55, 4.21)	0.42		
3D RVEF ≤ 30%	5.91 (1.91, 18.3)	**<0.01**	3.72 (1.12, 12.33)	**0.03**
TAPSE/PASP < 0.36	1.99 (0.71, 5.56)	0.19		
PASP, mmHg	1.02 (0.99, 1.05)	0.26		
LVEF, %	0.93 (0.86, 0.99)	**0.03**	0.94 (0.88, 1.01)	0.07
LAVi, ml/m^2	1.03 (1.00, 1.06)	**0.03**	1.02 (0.99, 1.05)	0.17

Bold values indicate significance.
CI: confidence interval; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; HR: hazard ratio; LAVi: left atrial volume index; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; PASP: pulmonary arterial systolic pressure; RVEF: right ventricular ejection fraction; RVFWLS: right ventricular free wall longitudinal strain; TAPSE: tricuspid annular plane systolic excursion; TEER: transcatheter edge-to-edge repair; 3D: three-dimensional.

Table 3. Paired comparison between the echocardiographic characteristics at baseline, discharge and 6-month follow-up for the study group without RVD (No-RVD, $n = 27$).

Variables		n (%)[a]	Baseline	Discharge	6-months	p value
MR degree, n (%)	≤2	22 (81.5)	0 (0.0)	20 (90.9)	20 (90.9)	**<0.01**
	>2		22 (100.0)	2 (9.1)	2 (9.1)	
VC, mm		13 (48.1)	7 [7, 9]	3 [2, 4] [§]	3 [3,4]*	**<0.01**
Mean gradient, mmHg		16 (59.3)	1.5 [1.0, 2.9]	3.0 [2.0, 3.8] [§]	3.0 [2.0, 3.8]*	**<0.01**
LVEDD, mm		20 (74.1)	60 ± 10	60 ± 10	58 ± 9	0.07
LVESD, mm		14 (51.9)	47 ± 11	48 ± 10	46 ± 13	0.47
LVEDVi, mL/m^2		20 (74.1)	98 ± 32	98 ± 35	91 ± 29	0.21
LVESVi, mL/m^2		18 (66.7)	60 ± 22	60 ± 25	56 ± 24	0.28
LVEF, %		20 (74.1)	38 [33, 47]	40 [33, 61]	42 [36,52]	0.11
LAVi, mL/m^2		16 (59.3)	53 [43, 78]	57 [48, 76]	48 [36, 78]	0.79
TR degree, n (%)	≤2	21 (77.8)	11 (52.4)	16 (76.2)	19 (90.5)	**0.02**
	>2		10 (47.6)	5 (23.8)	2 (9.5)	
TAPSE, mm		19 (70.4)	19 [17, 21]	18 [17, 23]	17 [16, 21]	0.27
PASP, mmHg		20 (74.1)	43 ± 15	39 ± 11[§]	37 ± 13*	**0.01**
TAPSE/PASP, mm/mmHg		18 (66.7)	0.45 ± 0.17	0.50 ± 0.17[§]	0.53 ± 0.25	0.14
S′ TDI, cm/s		17 (63.0)	11 [10, 13]	11 [10, 12]	11 [10, 13]	0.46
FAC, %		15 (55.6)	47 ± 7	45 ± 7	44 ± 8	0.26
RV FWLS, %		18 (66.7)	−22.4 ± 5.9	−22.0 ± 4.8	−21.3 ± 5.3	0.35
RV Basal diameter, mm		20 (74.1)	42 ± 7	42 ± 7	41 ± 6	0.37
RV Mid diameter, mm		17 (63.0)	31 ± 5	32 ± 5	32 ± 6	0.37
3D RVEDVi, mL/m^2		22 (81.5)	64 ± 19	64 ± 16	60 ± 13	0.28
3D RVESVi, mL/m^2		22 (81.5)	29 ± 11	30 ± 11	28 ± 8	0.49
3D RVEF, %		22 (81.5)	55 ± 7	53 ± 9	54 ± 8	0.54
3D RV SVi, mL/m^2		22 (81.5)	35 ± 9	34 ± 9	31 ± 8	0.06

Data are presented as mean ± SD, median [IQR] or n (%).
Bold values indicate significance.
3D: three-dimensional; EROA: effective regurgitant orifice area; FAC: fractional area change; FWLS: free wall longitudinal strain; LAVi: left atrial volume index; LVEDD: left ventricular end-diastolic diameter; LVEDVi: left ventricular end-diastolic volume index; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; LVESVi: left ventricular end-systolic volume index; MR: mitral regurgitation; RV: right ventricular; RVD: right ventricular dysfunction: RVEDVi: right ventricular end-diastolic volume index; RVESVi: right ventricular end-systolic volume index; RVEF: right ventricular ejection fraction; RVSVi: right ventricular stroke volume index; S′ TDI: systolic wave velocity at tissue Doppler imaging; PASP: pulmonary arterial systolic pressure; TAPSE: tricuspid annular plane systolic excursion; TR: tricuspid regurgitation; VC: vena contracta.
[a]Data availability for paired comparison with respect to the overall numerosity of patients in the No RVD group (27 patients).
[§]Discharge vs Baseline: p value < 0.05; *6-months vs Baseline: p value < 0.05.

Discussion

In a real-world multicentre registry of symptomatic high-risk patients with moderate-to-severe or severe FMR undergoing mitral TEER, we found the following:

i. pre-procedural RVD, defined as 3D RVEF ≤45%, was common, involving 63.5% of patients.
ii. significant differences between RVD group in terms of LV dilation and dysfunction, left atrial dilation, estimated PASP and NT-proBNP values.
iii. patients with pre-procedural SRVD, defined as 3D RVEF ≤30%, despite the technical success of the procedure, reported a higher rate of all-cause mortality during a mid-term follow-up when compared with the groups of patients with MRVD and No-RVD.
iv. 3D RVEF ≤30% proved to be a predictor of poor mid-term survival after mitral TEER (independent of LVEF and LAVi).
v. mitral TEER induced a substantial reduction in RV volumes and an improvement in RVEF at 6-month follow-up only in patients with pre-procedural MRVD.
vi. RV 2D parameters assessing RV systolic function (TAPSE, TAPSE/PASP, FWLS) were not predictors of mortality in our population and showed no significant variability during follow-up.

RVD in patients with FMR underdoing mitral TEER

RVD is recognised as an important determinant of several cardiovascular diseases and its prognostic role in patients with HF and FMR has been widely demonstrated [3].

In patients with chronic severe FMR, RV function may be reduced due to long-standing pressure-overload caused by the increase in left atrial filling pressure and the changes in pulmonary vasculature. Post-capillary pulmonary hypertension develops first, then chronically increased pressures may eventually lead to a combined form as well [14]. This results in RV negative remodelling, which includes RV dilatation and consequent increased tricuspid regurgitation. Several studies reported that RVD, assessed by 2D parameters (TAPSE, s′ TDI, FWLS), and RV-to-pulmonary arterial coupling (TAPSE/PASP) are predictors of adverse clinical outcomes in mitral TEER recipients [12–15,18,23,27,28]. It

Table 4. Paired comparison between the echocardiographic characteristics at baseline, discharge and 6-month follow-up for the study group with mild-to-moderate RVD (MRVD, $n = 36$).

Variables		n (%)[a]	Baseline	Discharge	6-months	p-value
MR degree, n (%)	≤2	33 (91.7)	0 (0.0)	32 (97.1)	28 (84.8)	**<0.01**
	>2		33 (100.0)	1 (2.9)	5 (14.7)	
VC, mm		13 (36.1)	8 ± 2	3 ± 1[§]	4 ± 2*[ǂ]	**<0.01**
Mean gradient, mmHg		30 (83.3)	2.0 [1.0, 2.0]	4.0 [3.0, 5.0][§]	3.0 [2.0, 4.0]*	**<0.01**
LVEDD, mm		33 (91.7)	59 ± 9	59 ± 9	59 ± 9	0.81
LVESD, mm		29 (80.6)	50 ± 11	49 ± 11	50 ± 11	0.80
LVEDVi, mL/m^2		33 (91.7)	94 ± 35	91 ± 31	93 ± 31	0.58
LVESVi, mL/m^2		33 (91.7)	61 ± 28	59 ± 25	60 ± 30	0.82
LVEF, %		33 (91.7)	35 [20, 43]	35 [31, 42]	37 [30,46]	0.58
LAVi, mL/m^2		31 (86.1)	61 [50, 73]	55 [47, 66][§]	57 [51, 62]	**<0.01**
TR degree, n (%)	≤2	33 (91.7)	16 (48.5)	19 (57.6)	25 (75.8)	0.07
	>2		17 (51.5)	14 (42.4)	8 (24.3)	
TAPSE, mm		33 (91.7)	18 [16, 21]	18 [16, 19]	17 [15, 20]	0.28
PASP, mmHg		33 (91.7)	48 ± 14	39 ± 9[§]	42 ± 13	**<0.01**
TAPSE/PASP, mm/mmHg		32 (88.9)	0.38 [0.30, 0,50]	0.49 [0.38, 0.60][§]	0.40 [0.34, 0.54]	0.06
S' TDI, cm/s		21 (58.3)	10 [9, 11]	10 [10, 12]	10 [9, 11]	0.24
FAC, %		24 (66.7)	35 ± 6	39 ± 8	35 ± 9	0.17
RV FWLS, %		26 (72.2)	−18.3 ± 4.1	−18.3 ± 4.3	−18.2 ± 5.1	0.98
RV Basal diameter, mm		33 (91.7)	41 [38, 45]	43 [38, 47]	41 [38, 47]	0.41
RV Mid diameter, mm		23 (63.9)	34 [28, 38]	34 [29, 40]	34 [32, 42]	0.96
3D RVEDVi, mL/m^2		29 (80.6)	67 [57, 87]	71 [56, 88]	67 [56, 90]*	**0.04**
3D RVESVi, mL/m^2		29 (80.6)	41 [34, 50]	43 [30, 52]	39 [32, 48]*	**0.04**
3D RVEF, %		29 (80.6)	40 [36, 41]	42 [36, 46]	44 [38, 47]*	**<0.01**
3D RV SVi, mL/m^2		29 (80.6)	28 ± 8	29 ± 8	30 ± 10	0.30

Data are presented as mean ± SD, median [IQR] or n (%).
Bold values indicate significance.
3D: three-dimensional; EROA: effective regurgitant orifice area; FAC: fractional area change; FWLS: free wall longitudinal strain; LAVi: left atrial volume index; LVEDD: left ventricular end-diastolic diameter; LVEDVi: left ventricular end-diastolic volume index; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; LVESVi: left ventricular end-systolic volume index; MR: mitral regurgitation; RV: right ventricular; RVD: right ventricular dysfunction: RVEDVi: right ventricular end-diastolic volume index; RVESVi: right ventricular end-systolic volume index; RVEF: right ventricular ejection fraction; RVSVi: right ventricular stroke volume index; S' TDI: systolic wave velocity at tissue Doppler imaging; PASP: pulmonary arterial systolic pressure; TAPSE: tricuspid annular plane systolic excursion; TR: tricuspid regurgitation; VC: vena contracta.
[a]Data availability for paired comparison with respect to the overall numerosity of patients in the Mild-to-moderate RVD group (36 patients).
[§]Discharge vs Baseline: p value < 0.05; *6-months vs Baseline: p value < 0.05; [ǂ]6-months vs Discharge: p value < 0.05.

is well known that RV quantitative assessment by 2D echocardiography is challenging due to its complex shape, and 3D echocardiography can overcome the inherent limitations of 2D analysis [29]. New 3D echocardiographic semi-automated software, adapted for RV cavity border detection, have demonstrated good correlation with cardiac magnetic resonance for the calculation of RV volumes and ejection fraction being at the same time more available, less expensive and time-consuming [30,31]. Moreover, 3D RVEF was independently associated with unfavourable outcomes in various cardiovascular diseases (e.g. ischaemic and non-ischaemic cardiomyopathies, valvular diseases, pulmonary hypertension) [32–34]. For these reasons, we evaluated RV dimensions and function by adding 3D analysis to the conventional 2D evaluation. As described in previous literature [12,13], our 3D echocardiographic analysis confirmed that RVD is present in more than 50% of patients with FMR undergoing TEER in clinical practice, although patients with moderate or severe RVD were excluded from COAPT trial. To assess the prognostic impact of pre-procedural RVD, we divided our population according to the degree of RVD [26]. Significant differences between groups of RVD emerged in terms of LV dilation and dysfunction, left atrial dilation, estimated PASP and NT-proBNP values. Patients with pre-procedural SRVD, defined as RVEF ≤30%, showed a significantly lower survival probability compared with patients with MRVD or No-RVD. In a multivariable Cox regression model, RVEF ≤30% arose as the only parameter of RV systolic function able to predict all-cause mortality (independently of LVEF and LAVi) after mitral TEER at a mid-term follow-up. On the other hand, 2D parameters of RV systolic function, known in literature to have a prognostic impact in patients undergoing mitral TEER (TAPSE, TAPSE/PASP, FWLS) [13,15,35], did not predict mortality in our population.

Although a possible explanation for the lack of correlation between 2D parameters assessing RVD and all-cause death in our population was the low number of patients included, we can hypothesise that 3D RVEF might better stratify patients who can have a prognostic benefit from mitral TEER procedure as compared with classical 2D parameters.

The effects of mitral TEER procedure on RVRR

In the literature, there is conflicting evidence about the effect of mitral TEER on RV dimensions and systolic function. An RV remodelling in terms of reduction of

Table 5. Paired comparison between the echocardiographic characteristics at baseline, discharge and 6-month follow-up for the study group with severe RVD (SRVD, $n = 11$).

Variables		*n* (%)[a]	Baseline	Discharge	6-months	*p-value*
MR degree, n (%)	≤2	6 (54.5)	0 (0.0)	6 (100.0)	5 (83.3)	**<0.01**
	>2		6 (100.0)	0 (0.0)	1 (16.7)	
VC, mm		4 (36.4)	7 [6, 9]	3 [2, 3] [§]	4 [3,6]	**<0.01**
Mean gradient, mmHg		5 (45.5)	1.0 [1.0, 1.0]	3.0 [2.0, 3.0]	3.0 [2.0, 3.0]	**0.03**
LVEDD, mm		6 (54.5)	63 [59, 69]	63 [58, 70]	61 [53, 70]	0.88
LVESD, mm		6 (54.5)	56 [52, 61]	56 [53, 65]	51 [46, 65]	0.15
LVEDVi, mL/m^2		6 (54.5)	108 [81, 142]	107 [75, 148]	97 [74, 153]	0.71
LVESVi, mL/m^2		6 (54.4)	75 [57, 110]	84 [54, 122]	58 [38, 125]	0.20
LVEF, %		6 (54.4)	26 [22, 33]	23 [16, 32]	31 [19, 48]	0.33
LAVi, mL/m^2		6 (54.5)	73 [67, 80]	72 [57, 80]	64 [40, 85]	0.64
TR degree, n (%)	≤2	6 (54.5)	3 (50.0)	5 (83.3)	5 (83.3)	0.33
	>2		3 (50.0)	1 (16.7)	1 (16.7)	
TAPSE, mm		5 (45.5)	14 [10, 16]	13 [10, 16]	14 [12, 17]	0.43
PASP, mmHg		5 (45.5)	55 [53, 73]	34 [25, 59]	45 [23, 78]	0.09
TAPSE/PASP, mm/mmHg		5 (45.5)	0.25 [0.16, 0,28]	0.43 [0.17, 0.63]	0.31 [0.15, 0.74]	0.23
S' TDI, cm/s		4 (36.4)	9 [7,11]	10 [7, 12]	10 [8, 11]	0.35
FAC, %		5 (45.5)	25 [19, 28]	30 [22, 34]	25 [23, 41]	0.53
RV FWLS, %		4 (36.4)	−12.0 [−14.3, −9.0]	−11.5 [−12.8, −8.8]	−12.5 [−15.8, −10.0]	0.78
RV Basal diameter, mm		5 (45.5)	56 [49, 61]	56 [46, 63]	47 [41, 56]	0.88
RV Mid diameter, mm		5 (45.5)	40 [34, 52]	42 [28, 46]	37 [30, 48]	0.91
3D RVEDVi, mL/m^2		5 (45.5)	122 [92, 133]	101 [85, 155]	82 [65, 122]	0.58
3D RVESVi, mL/m^2		5 (45.5)	97 [74, 98]	62 [51, 109]	48 [38, 81]	0.12
3D RVEF, %		5 (45.5)	23 [18, 30]	30 [26, 36]	36 [25, 41]	0.40
3D RV SVi, mL/m^2		5 (45.5)	25 [19, 36]	35 [25, 47]	30 [20, 39]	0.37

Data are presented as mean ± SD, median [IQR] or n (%).
Bold values indicate significance.
3D: three-dimensional; EROA: effective regurgitant orifice area; FAC: fractional area change; FWLS: free wall longitudinal strain; LAVi: left atrial volume index; LVEDD: left ventricular end-diastolic diameter; LVEDVi: left ventricular end-diastolic volume index; LVEF: left ventricular ejection fraction; LVESD: left ventricular end-systolic diameter; LVESVi: left ventricular end-systolic volume index; MR: mitral regurgitation; RV: right ventricular; RVD: right ventricular dysfunction; RVEDVi: right ventricular end-diastolic volume index; RVESVi: right ventricular end-systolic volume index; RVEF: right ventricular ejection fraction; RVSVi: right ventricular stroke volume index; S' TDI: systolic wave velocity at tissue Doppler imaging; PASP: pulmonary arterial systolic pressure; TAPSE: tricuspid annular plane systolic excursion; TR: tricuspid regurgitation; VC: vena contracta.
[a]Data availability for paired comparison with respect to the overall numerosity of patients in the Severe RVD group (11 patients).
[§]Discharge vs Baseline: p value < 0.05.

diameters [36] and 3D volumes [18,36] after mitral TEER procedure has never been described for years. Recently, Stolz et al. described a significant reduction of RV end-diastolic volumes at follow-up compared to baseline and demonstrated that patients who had a reduction in 3D RV end-diastolic volume >14% had a trend towards improved survival prognosis after mitral TEER [37].

Regarding RV systolic function, observational studies showed an improvement in RV longitudinal (TAPSE) [20] and global (RVEF) [18] systolic function after successful mitral TEER. Sauter et at. showed an improvement in RVEF only in patients with pre-procedural reduced RVEF (<35%) [18]. In contrast, other reports revealed no change in RV function in terms of TAPSE [18], s' TDI [18], FAC [18,20] and RVEF [36].

In our study, only patients with pre-procedural MRVD demonstrated a significant reduction in 3D RV volumes and an improvement in RVEF after 6 months from the mitral TEER as compared to baseline, whereas the diameters did not change probably due to their lower capability to assess RV complex geometry. Moreover, a sustained decrease in pulmonary pressures was observed after mitral TEER, expect for the groups with pre-procedural SRVD. This finding is in line with previous studies [19,20,37,38] and suggest that mitral TEER induces positive hemodynamic responses in pulmonary circulation pressures reducing consequently RV pressure and volume overload.

Clinical implications

To the best of our knowledge, this is the first study to evaluate the prognostic role of RVEF and to demonstrate the added value of 3D RV echocardiography in mitral TEER recipients (Graphical abstract). This advanced approach could be useful, in daily clinical practice, thanks to the new 3D echocardiographic software, which are more available and less time-consuming.

In the COAPT trial, moderate to severe RVD was a criterion of exclusion for mitral TEER [8], but the echocardiographic parameters used were not specified. To overcome the intrinsic limitations of assessing RV through 2D parameters and to better define RV role in candidates for mitral TEER, we prospectively collected complete echocardiographic data adding RV 3D evaluation.

3D RVEF ≤30% was the only RV parameter to predict all-cause mortality (independently from LVEF and LAVi) in our prospective registry. Moreover, patients with SRVD did not show a reduction in pulmonary pressures and a RVRR after mitral TEER procedure.

Thus, SRVD is a condition from which it may be difficult to recover and 3D RVEF ≤30% may represent a more reliable criterium to include or exclude candidates for mitral TEER procedure than 2D parameters.

The subgroup of patients with pre-procedural MRVD had survival rates comparable to patients with No-RVD after mitral TEER procedure. Interestingly, it was the only subgroup to demonstrate a RVRR 6-months after the procedure, suggesting that these patients may derive a benefit from mitral TEER procedure. The prognostic impact of this RV remodelling has been recently described [37] and it requires further attention and more extensive investigation.

Limitations

The present study has some limitations that should be acknowledged.

First, the small sample size of our population. However, there are only a few data in literature regarding the role of 3D RV echocardiography in patients undergoing mitral TEER.

Second, the number of excluded patients due to inadequate echocardiographic window for RV 3D analysis was not collected in all the centres. However, the feasibility rate of 3D RV assessment at IRCCS Policlinico San Donato was 86%, which is consistent with the literature (feasibility rates ranging from 85% to 96%) [39,40].

Third, an independent core lab to assess the echocardiographic exams was not available, although 3D analysis was performed by highly experienced cardiologist at each participating centre.

Conclusion

In patients undergoing mitral TEER for FMR, the occurrence of RVD, defined *via* 3D-echocardiography, was common in daily clinical practice. Patients with pre-procedural SRVD, defined as RVEF ≤30%, had worse mid-term survival after the procedure compared to patients with MRVD and No-RVD. Additionally, patients with SRVD did not show significant changes in pulmonary pressures, RV volumes, and RV function at the 6-month follow-up. Conversely, patients with pre-procedural MRVD experienced a reduction in RV volumes and an improvement in RVEF at the 6-month follow-up suggesting that these patients may benefit from the procedure. These findings highlight the importance of incorporating a comprehensive 3D echocardiographic assessment of RV function into the diagnostic workup before and after mitral TEER.

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References

[1] Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J. 2022;43(7):561–632. doi: 10.1093/eurheartj/ehab395.
[2] Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA guideline for the management of patients with valvular heart disease: executive summary: a report of the American College of Cardiology/American Heart Association Joint Committee on clinical practice guidelines. Circulation. 2020;77(4):450–500.
[3] Goliasch G, Bartko PE, Pavo N, et al. Refining the prognostic impact of functional mitral regurgitation in chronic heart failure. Eur Heart J. 2018;39(1):39–46. doi: 10.1093/eurheartj/ehx402.
[4] Lancellotti P, Oury C. News and innovations in heart failure. Acta Cardiol. 2024;79(6):637–641. doi: 10.1080/00015385.2024.2401225.
[5] Lancellotti P, NguyenTrung M-L, Ribeiro Coelho S, et al. Top-notch insights into heart failure. Acta Cardiol. 2024;79(4):415–418. Acta Cardiologica doi: 10.1080/00015385.2024.2373535.
[6] Lancellotti P, Ancion A. Advancing heart failure management: innovations and future directions. Acta Cardiol. 2024;79(8):861–865. doi: 10.1080/00015385.2024.2432182.
[7] Lancellotti P, Dulgheru R. Advancing strategies for valvular heart disease and pulmonary hypertension: insights and perspectives. Acta Cardiol. 2024;79(9):973–977. doi: 10.1080/00015385.2024.2436769.
[8] Stone GW, Lindenfeld J, Abraham WT, et al. Transcatheter Mitral-Valve Repair in Patients with Heart Failure. N Engl J Med. 2018;379(24):2307–2318. doi: 10.1056/NEJMoa1806640.
[9] Adamo M, Fiorelli F, Melica B, et al. COAPT-like profile predicts long-term outcomes in patients with secondary mitral regurgitation undergoing mitraclip implantation. JACC Cardiovasc Interv. 2021;14(1):15–25. doi: 10.1016/j.jcin.2020.09.050.
[10] Rietz M, Aminian A, Droogmans S, et al. Transcatheter edge-to-edge mitral valve repair as a bridge to optimal

guideline-directed medical therapy. Acta Cardiol. 2022;77(7):655–657. doi: 10.1080/00015385.2021.1917795.
[11] Bedogni F, Testa L, Rubbio AP, et al. Real-world safety and efficacy of transcatheter mitral valve repair with mitraclip: thirty-day results from the Italian Society of Interventional Cardiology (GIse) Registry Of Transcatheter Treatment of Mitral Valve RegurgitaTiOn (GIOTTO). Cardiovasc Revasc Med. 2020;21(9):1057–1062. doi: 10.1016/j.carrev.2020.01.002.
[12] Truong VT, Ngo TNM, Mazur J, et al. Right ventricular dysfunction and tricuspid regurgitation in functional mitral regurgitation. ESC Heart Fail. 2021;8(6):4988–4996. doi: 10.1002/ehf2.13558.
[13] Karam N, Stolz L, Orban M, et al. Impact of right ventricular dysfunction on outcomes after transcatheter edge-to-edge repair for secondary mitral regurgitation. JACC Cardiovasc Imaging. 2021;14(4):768–778. doi: 10.1016/j.jcmg.2020.12.015.
[14] Meijerink F, de Witte SM, Limpens J, et al. Prognostic value of pulmonary hypertension, right ventricular function and tricuspid regurgitation on mortality after transcatheter mitral valve repair: a systematic review and meta-analysis. Heart Lung Circ. 2022;31(5):696–704. doi: 10.1016/j.hlc.2021.11.017.
[15] Lupi L, Italia L, Pagnesi M, et al. Prognostic value of right ventricular longitudinal strain in patients with secondary mitral regurgitation undergoing transcatheter edge-to-edge mitral valve repair. Eur Heart J Cardiovasc Imaging. 2023;24(11):1509–1517. doi: 10.1093/ehjci/jead103.
[16] Italia L, Adamo M, Lupi L, et al. Percutaneous edge-to-edge mitral valve repair: beyond the left heart. J Am Soc Echocardiogr. 2021;34(10):1038–1045. doi: 10.1016/j.echo.2021.05.013.
[17] Shamekhi J, Sugiura A, Spieker M, et al. A staging classification of right heart remodelling for patients undergoing transcatheter edge-to-edge mitral valve repair. EuroIntervention. 2022;18(1):43–49. doi: 10.4244/EIJ-D-21-00667.
[18] Neuser J, Buck HJ, Oldhafer M, et al. Right ventricular function improves early after percutaneous mitral valve repair in patients suffering from severe mitral regurgitation. Front Cardiovasc Med. 2022;9:830944. doi: 10.3389/fcvm.2022.830944.
[19] Adamo M, Inciardi RM, Tomasoni D, et al. Changes in right ventricular–to–pulmonary artery coupling after transcatheter edge-to-edge repair in secondary mitral regurgitation. JACC Cardiovasc Imaging. 2022;15(12):2038–2047. doi: 10.1016/j.jcmg.2022.08.012.
[20] Giannini C, Petronio AS, De Carlo M, et al. Integrated reverse left and right ventricular remodelling after MitraClip implantation in functional mitral regurgitation: an echocardiographic study. Eur Heart J Cardiovasc Imaging. 2014;15(1):95–103. doi: 10.1093/ehjci/jet141.
[21] Van Riel ACMJ, et al. Percutaneous mitral valve repair preserves right ventricular function. J Am Soc Echocardiogr. 2014;27:1098–1106.
[22] Sauter RJ, Patzelt J, Mezger M, et al. Conventional echocardiographic parameters or three-dimensional echocardiography to evaluate right ventricular function in percutaneous edge-to-edge mitral valve repair (PMVR). IJC Heart and Vasculature. 2019;24:100413. doi: 10.1016/j.ijcha.2019.100413.
[23] Caiffa T, De Luca A, Biagini E, et al. Impact on clinical outcomes of right ventricular response to percutaneous correction of secondary mitral regurgitation. Eur J Heart Fail. 2021;23(10):1765–1774. doi: 10.1002/ejhf.2316.
[24] Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28(1):1–39.e14. doi: 10.1016/j.echo.2014.10.003.
[25] Lang RM, Badano LP, Tsang W, et al. EAE/ASE recommendations for image acquisition and display using three-dimensional echocardiography. J Am Soc Echocardiogr. 2012;25(1):3–46. doi: 10.1016/j.echo.2011.11.010.
[26] Muraru D, Badano LP, Nagata Y, et al. Development and prognostic validation of partition values to grade right ventricular dysfunction severity using 3D echocardiography. Eur Heart J Cardiovasc Imaging. 2020;21(1):10–21. doi: 10.1093/ehjci/jez233.
[27] Osteresch R, Diehl K, Kühl M, et al. Impact of right heart function on outcome in patients with functional mitral regurgitation and chronic heart failure undergoing percutaneous edge-to-edge-repair. J Interv Cardiol. 2018;31(6):916–924. doi: 10.1111/joic.12566.
[28] Popolo Rubbio A, Testa L, Granata G, et al. Prognostic significance of right ventricle to pulmonary artery coupling in patients with mitral regurgitation treated with the MitraClip system. Catheter Cardiovasc Interv. 2022;99(4):1277–1286. doi: 10.1002/ccd.30044.
[29] Knight DS, Grasso AE, Quail MA, et al. Accuracy and reproducibility of right ventricular quantification in patients with pressure and volume overload using single-beat three-dimensional echocardiography. J Am Soc Echocardiogr. 2015;28(3):363–374. doi: 10.1016/j.echo.2014.10.012.
[30] Otani K, Nabeshima Y, Kitano T, et al. Accuracy of fully automated right ventricular quantification software with 3D echocardiography: direct comparison with cardiac magnetic resonance and semi-automated quantification software. Eur Heart J Cardiovasc Imaging. 2020;21(7):787–795. doi: 10.1093/ehjci/jez236.
[31] Muraru D, Spadotto V, Cecchetto A, et al. New speckle-tracking algorithm for right ventricular volume analysis from three-dimensional echocardiographic data sets: validation with cardiac magnetic resonance and comparison with the previous analysis tool. Eur Heart J Cardiovasc Imaging. 2016;17(11):1279–1289. doi: 10.1093/ehjci/jev309.
[32] Nagata Y, Wu VC-C, Kado Y, et al. Prognostic value of right ventricular ejection fraction assessed by transthoracic 3D echocardiography. Circ Cardiovasc Imaging. 2017;10(2):641088. doi: 10.1161/CIRCIMAGING.116.005384.
[33] Sabe MA, Sabe SA, Kusunose K, et al. Predictors and prognostic significance of right ventricular ejection fraction in patients with ischemic cardiomyopathy. Circulation. 2016;134(9):656–665. doi: 10.1161/CIRCULATIONAHA.116.022339.

[34] Vitarelli A, Barillà F, Capotosto L, et al. Right ventricular function in acute pulmonary embolism: a combined assessment by three-dimensional and speckle-tracking echocardiography. J Am Soc Echocardiogr. 2014;27(3): 329–338. doi: 10.1016/j.echo.2013.11.013.

[35] Kaneko H, Neuss M, Weissenborn J, et al. Prognostic significance of right ventricular dysfunction in patients with functional mitral regurgitation undergoing MitraClip. Am J Cardiol. 2016;118(11):1717–1722. doi: 10.1016/j.amjcard.2016.08.054.

[36] Gripari P, Tamborini G, Bottari V, et al. Three-dimensional transthoracic echocardiography in the comprehensive evaluation of right and left heart chamber remodeling following percutaneous mitral valve repair. J Am Soc Echocardiogr. 2016;29(10):946–954. doi: 10.1016/j.echo.2016.06.009.

[37] Stolz L, Weckbach LT, Doldi PM, et al. Right ventricular reverse remodeling following mitral valve transcatheter edge-to-edge repair. JACC Cardiovasc Imaging. 2023;16(7):988–990. doi: 10.1016/j.jcmg.2023.01.007.

[38] Adamo M, Pagnesi M, Ghizzoni G, et al. Evolution of tricuspid regurgitation after transcatheter edge-to-edge mitral valve repair for secondary mitral regurgitation and its impact on mortality. Eur J Heart Fail. 2022; 24(11):2175–2184. doi: 10.1002/ejhf.2637.

[39] Maffessanti F, Muraru D, Esposito R, et al. Age-, body size-, and sex-specific reference values for right ventricular volumes and ejection fraction by three-dimensional echocardiography: A multicenter echocardiographic study in 507 healthy volunteers. Circ Cardiovasc Imaging. 2013;6(5):700–710. doi: 10.1161/CIRCIMAGING.113.000706.

[40] Addetia K, Muraru D, Badano LP, et al. New directions in right ventricular assessment using 3-dimensional echocardiography. JAMA Cardiol. 2019;4(9):936–944. doi: 10.1001/jamacardio.2019.2424.