

Predictive Value of TAPSE/PASP Ratio for Clinical Outcomes in MitraClip Recipients

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Abstract

For patients with severe mitral regurgitation (MR) who cannot tolerate surgery, transcatheter mitral valve repair (TMVR) has become a dependable therapeutic choice. Despite procedural success, many continue to experience heart failure (HF) admissions and mortality over mid-term follow-up. A growing body of research highlights right ventricular (RV)–pulmonary arterial (PA) interaction as an important determinant of prognosis in HF. This investigation explored whether the tricuspid annular plane systolic excursion (TAPSE) to pulmonary artery systolic pressure (PASP) ratio—an echocardiographic index of RV–PA coupling—could predict outcomes in individuals treated with the MitraClip system (Abbott, California, USA). Data were drawn from a multicenter registry of 228 consecutive patients who underwent successful TMVR using MitraClip. Participants were stratified into two cohorts according to a median TAPSE/PASP ratio of 0.35. The principal composite endpoint consisted of all-cause mortality and HF-related readmission. The mean participant age was 72.5 ± 11.5 years, and 154 (67.5%) were men. Subjects with $\text{TAPSE/PASP} \leq 0.35$ experienced significantly more frequent HF rehospitalizations and deaths (Log-Rank = 8.844, $p = 0.003$). Multivariate Cox analysis identified TAPSE/PASP, along with the STS Score, as an independent determinant of the composite outcome. The ratio outperformed individual measures of TAPSE or PASP in predictive value. The TAPSE/PASP ratio represents a simple yet powerful non-invasive marker for prognostic assessment in TMVR patients and may enhance both risk evaluation and procedural selection for MitraClip implantation.

Keywords: MitraClip, Transcatheter mitral repair, Mitral insufficiency, Pulmonary hypertension, Right ventricle–pulmonary artery interaction, echocardiography

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Introduction

Over the last decade, transcatheter mitral valve repair (TMVR) using the MitraClip system (Abbott; Menlo Park, CA, USA) has evolved into a well-established therapeutic strategy for individuals with severe mitral regurgitation (MR) who present a high surgical risk [1–4]. The appropriateness of TMVR is determined by a Heart Team,

which performs an individualized assessment covering procedural feasibility, anticipated clinical benefits, and potential risks [5,6]. Conventional surgical prediction scores contribute to this process but often lack precision when applied to MitraClip populations [2,7]. Consequently, contemporary evaluation also considers additional prognostic markers identified in earlier investigations [8–11]. Despite these refinements, a

considerable proportion of patients continue to experience mortality and HF rehospitalization within the first post-procedural year [2,3, 8–11], even after successful clip implantation. Thus, improving predictive accuracy and refining selection criteria to minimize non-beneficial interventions remain urgent goals.

Patients with advanced MR frequently present with pulmonary hypertension (PH) and right ventricular (RV) impairment, both of which are established predictors of poorer outcomes [12–14]. Although the coexistence of these conditions sometimes leads to procedural exclusion, prior studies have shown that carefully chosen individuals may still benefit from TMVR, often demonstrating marked reductions in pulmonary pressures and evidence of RV reverse remodeling [14–16].

In recent years, the coupling between the right ventricle and the pulmonary artery (RV–PA coupling) has gained attention as a valuable prognostic determinant in both heart failure (HF) and pulmonary hypertension (PH) contexts [17–19]. This physiological parameter reflects how effectively the RV adapts to its afterload and may reveal early signs of impending RV failure [17–20]. Clinically, this adaptation can be quantified non-invasively through the ratio of TAPSE to PASP [19–22]. Despite its increasing use in other cardiovascular populations, its role as a prognostic index in patients undergoing MitraClip implantation has not yet been thoroughly studied.

Accordingly, the present work aimed to determine whether the baseline TAPSE/PASP ratio could enhance prognostic stratification in individuals undergoing successful transcatheter mitral valve repair (TMVR) with the MitraClip system.

Materials and Methods

Study design and participants

Between June 2012 and June 2018, 228 consecutive individuals who underwent transcatheter mitral valve repair (TMVR) using the MitraClip device were recruited across 17 Spanish medical centers.

All information originated from the Spanish MitraClip Registry, a nationwide multicenter database supervised by the Interventional Cardiology Division of the Spanish Society of Cardiology.

Eligible participants exhibited primary or secondary mitral regurgitation (MR), graded 3+ (moderate–severe) or 4+ (severe) via pre-intervention echocardiography.

Only patients with persistent heart failure (HF) symptoms despite optimal guideline-based therapy were included.

At each institution, a multidisciplinary Heart Team reviewed every case and determined that TMVR represented the most suitable therapeutic strategy.

Clinical follow-up was prospectively organized and consisted of periodic examinations, laboratory assessments, and echocardiograms.

The analysis incorporated only those who had comprehensive baseline imaging and successful TMVR defined by a residual MR $\leq 2+$.

The protocol received approval from the ethics boards of all participating hospitals, and each subject provided written informed consent prior to inclusion.

Echocardiographic evaluation

Mitral regurgitation was classified as none, mild (1+), moderate (2+), moderate–severe (3+), or severe (4+), according to regurgitant volume and effective regurgitant orifice area.

Tricuspid annular plane systolic excursion (TAPSE) was quantified using M-mode imaging in the apical four-chamber view, representing the longitudinal displacement of the annulus from end-diastole to end-systole.

Right ventricular systolic pressure (RVSP) was derived from the peak tricuspid regurgitant jet velocity, applying the simplified Bernoulli equation.

Right atrial pressure (RAP) was estimated based on inferior vena cava diameter and collapsibility and was added to the trans-tricuspid gradient to obtain pulmonary artery systolic pressure (PASP).

Each echocardiographic measure was averaged over three cardiac cycles in sinus rhythm and three to five in atrial fibrillation.

Right heart catheterization

A subset of patients underwent right heart catheterization (RHC) via brachial or femoral venous access, according to physician preference.

Standard hemodynamic data were collected following routine invasive protocols.

Endpoint definitions and procedural criteria

The MitraClip implantation technique followed previously reported methodology [1], performed under continuous transesophageal echocardiographic guidance.

Procedural success was defined as achieving an MR reduction to $\leq 2+$.

Functional capacity was recorded using the New York Heart Association (NYHA) classification at baseline and during follow-up.

The primary composite outcome consisted of all-cause mortality and HF-related rehospitalization within the first year, including in-hospital deaths.

Each event was also analyzed independently as a secondary endpoint, with HF rehospitalizations recorded from discharge onward.

Complications and short-term outcomes were described following Mitral Valve Academic Research Consortium (MVARC) definitions [23], encompassing pericardial

effusion, air embolism, chordal rupture, catheter thrombosis, partial clip detachment, bleeding (BARC criteria), vascular complications, myocardial infarction, acute kidney injury, pulmonary embolism, stroke, in-hospital death, and 30-day HF readmission.

Statistical procedures

Categorical data were reported as numbers and percentages, while continuous variables were expressed as mean $\pm$ standard deviation.

Participants were stratified based on the median TAPSE/PASP ratio (0.35).

Group comparisons were performed using the Chi-square, unpaired t-test, or Mann–Whitney U test, as appropriate.

Kaplan–Meier curves were generated for survival analysis and compared with the Log-Rank test.

Variables with $p \leq 0.10$ in univariate testing, along with established prognostic factors from prior studies, were entered into a multivariate Cox regression model after checking for collinearity.

Model discrimination was evaluated using Harrell's C-statistic, and proportional hazards assumptions were confirmed.

Correlations between TAPSE/PASP and hemodynamic measurements were analyzed using the Pearson correlation coefficient.

A p -value < 0.05 was regarded as statistically significant. Analyses were conducted using SPSS version 21.0 (IBM Corp., Chicago, IL, USA).

Results

A total of 228 patients were studied, with a mean age of 72.5 ± 11.5 years; 154 (67.5%) were male.

Most were severely symptomatic (NYHA class III/IV, 86.8%) and displayed moderate procedural risk (STS score 5.8 ± 5.3 ; EuroSCORE-II 8.5 ± 7.9).

Mitral regurgitation was severe in 187 (82.1%) and moderate-to-severe in 41 (17.9%).

Etiology was secondary in 147 of 225 (65.3%), primary in 50 (22.2%), mixed in 28 (12.3%), with 3 unclassified cases.

Procedural success was achieved in all subjects, with an average of 1.5 ± 0.6 clips per patient.

Following repair, MR grade 0–1+ was recorded in 147 (64.5%), and 2+ in the remainder.

Baseline data by TAPSE/PASP ratio

The median TAPSE/PASP was 0.35, consistent with previously described thresholds for RV–PA uncoupling in heart failure cohorts [19,20,24,25].

Patients below this cutoff (≤ 0.35) demonstrated higher-grade tricuspid regurgitation (3–4+), lower TAPSE, elevated PASP, and increased left atrial v-wave pressure, as well as higher PASP values measured via RHC (Table 1). No other significant baseline differences were detected between groups.

Table 1. Baseline characteristics according to TAPSE/PASP

Variable	TAPSE/PASP ≤ 0.35 (n = 114)	TAPSE/PASP > 0.35 (n = 114)	Entire Cohort (n = 228)	p-value
Clinical Characteristics				
Age (years)	71.8 $\pm$ 11.8	73.3 $\pm$ 11.2	72.5 $\pm$ 11.5	0.327
Male sex, n (%)	81 (71.1)	73 (64.0)	154 (67.5)	0.258
Hypertension, n (%)	79 (69.3)	86 (76.1)	165 (72.7)	0.250
Diabetes mellitus, n (%)	40 (35.1)	34 (29.8)	74 (32.5)	0.396
Atrial fibrillation, n (%)	68 (59.6)	65 (58.0)	133 (58.8)	0.893
Glomerular filtration rate (mL/min/1.73 m ²)	58.2 $\pm$ 24.8	64.0 $\pm$ 26.1	60.9 $\pm$ 25.4	0.164
Chronic kidney disease stage 3b–5, n (%)	42 (36.8)	33 (28.9)	75 (32.9)	0.205
Ischemic heart disease, n (%)	61 (53.5)	52 (45.6)	113 (49.6)	0.400
Previous PCI, n (%)	41 (36.0)	35 (30.7)	76 (33.3)	0.699
Previous CABG, n (%)	25 (21.9)	17 (14.9)	42 (18.4)	0.156
Extracardiac arteriopathy, n (%)	16 (14.0)	19 (16.7)	35 (15.4)	0.512
Prior cardiac surgery, n (%)	38 (33.3)	24 (21.1)	62 (27.2)	0.113
COPD, n (%)	25 (21.9)	24 (21.1)	49 (21.5)	0.872
NYHA III–IV/IV, n (%)	101 (88.6)	97 (85.1)	198 (86.8)	0.433
NT-proBNP (pg/mL)	4821.6 $\pm$ 6364	4715.2 $\pm$ 5715	4762.2 $\pm$ 5990	0.915
EuroSCORE II	8.7 $\pm$ 8.3	8.2 $\pm$ 7.6	8.5 $\pm$ 7.9	0.589
STS Score	5.4 $\pm$ 5.2	6.3 $\pm$ 5.5	5.8 $\pm$ 5.3	0.244
Medical Therapy, n (%)				
Beta-blockers	86 (76.8)	90 (78.9)	176 (77.9)	0.695
Mineralocorticoid antagonists	72 (64.3)	60 (52.6)	132 (58.4)	0.076
ACE inhibitors / ARB / ARNI	86 (76.8)	84 (73.7)	170 (75.2)	0.589
Diuretics	108 (96.4)	109 (95.6)	217 (96.0)	0.754
Baseline Echocardiography				
LVEDD (mm)	60.7 $\pm$ 9.9	61.0 $\pm$ 10.4	60.9 $\pm$ 10.1	0.838
LVESD (mm)	49.9 $\pm$ 12.5	49.9 $\pm$ 12.6	49.9 $\pm$ 12.5	0.975
Indexed LVEDV (mL/m ²)	93.4 $\pm$ 34.3	90.9 $\pm$ 34.6	92.1 $\pm$ 34.4	0.623

Indexed LVESV (mL/m ²)	56.6 ± 31.0	55.2 ± 31.3	55.8 ± 31.1	0.762
LVEF (%)	39.3 ± 14.9	41.4 ± 15.5	40.4 ± 15.3	0.283
Indexed LA volume (mL/m ²)	58.3 ± 21.2	62.3 ± 26.8	60.3 ± 24.2	0.291
MR grade IV, n (%)	94 (82.5)	98 (86.7)	187 (82.1)	0.373
Regurgitant volume (mL)	60 ± 24.9	58.8 ± 19.2	59.5 ± 22.3	0.828
Effective regurgitant orifice (mm ²)	42.6 ± 16.9	43.6 ± 18.5	43.1 ± 17.6	0.741
Indexed LVEDV / ERO (mL/mm ²)	2.5 ± 1.4	2.5 ± 1.3	2.5 ± 1.4	0.979
MR etiology, n (%)				0.439
Primary	22 (19.3)	28 (25.2)	50 (22.2)	
Secondary	79 (69.3)	68 (61.3)	147 (65.3)	
Mixed	13 (11.4)	15 (13.5)	28 (12.4)	
Tricuspid regurgitation, n (%)				<0.001
Grade 0–1	35 (30.7)	63 (55.3)	98 (43.0)	
Grade 2	29 (25.4)	28 (24.6)	57 (25.0)	
Grade 3	29 (25.4)	17 (14.9)	46 (20.2)	
Grade 4	21 (18.4)	6 (5.3)	27 (11.8)	
TAPSE (mm)	14.4 ± 3.3	19.5 ± 3.7	16.9 ± 4.3	<0.001
PASP (mmHg)	57.7 ± 11.9	40.2 ± 11.1	48.9 ± 14.4	<0.001
TAPSE / PASP	0.26 ± 0.1	0.52 ± 0.16	0.39 ± 0.18	<0.001
Right Heart Catheterization				
Right atrial pressure (mmHg)	9.8 ± 4.8	8.5 ± 6.1	9.1 ± 5.5	0.520
LA mean pressure (mmHg)	25 ± 25.5	17.4 ± 7.6	20.7 ± 18.0	0.116
LA v-wave pressure (mmHg)	42.9 ± 13.8	29.8 ± 15.5	36.0 ± 15.9	0.010
Δ LA mean pressure (mmHg)	6.2 ± 6.6	5.8 ± 7.4	5.9 ± 7.1	0.848
Δ LA v-wave pressure (mmHg)	21.6 ± 15.7	12.8 ± 12.9	16.4 ± 14.6	0.081
PCW pressure (mmHg)	18.4 ± 7.0	19.0 ± 7.9	18.7 ± 7.3	0.833
Mean PA pressure (mmHg)	30.7 ± 12.4	29.5 ± 10.9	30.2 ± 11.5	0.795
Systolic PA pressure (mmHg)	52.7 ± 18.9	41.1 ± 13.9	47.1 ± 17.4	0.016
PA pulse pressure (mmHg)	28.6 ± 13.6	23.2 ± 6.8	26.0 ± 11.0	0.214
Cardiac index (mL/min/m ²)	2.3 ± 0.6	2.1 ± 0.6	2.2 ± 0.6	0.342
Pulmonary vascular resistance (WU)	2.9 ± 1.5	3.2 ± 1.2	3.1 ± 1.3	0.651
Transpulmonary gradient (mmHg)	12.6 ± 7.6	10.8 ± 3.7	11.8 ± 6.1	0.442
Diastolic pressure gradient (mmHg)	2.9 ± 3.7	2.6 ± 2.5	2.7 ± 3.2	0.847
PA compliance (mL/mmHg)	2.4 ± 1.2	2.5 ± 1.3	2.4 ± 1.2	0.756

* Information available for 225 patients; φ data derived from 26 patients; γ data derived from 51 patients.

Abbreviations:

ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; ARNi = angiotensin receptor neprilysin inhibitor; CABG = coronary artery bypass graft; COPD = chronic obstructive pulmonary disease; LA = left atrium; LVEDD = left ventricular end-diastolic diameter; LVEDV = left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic diameter; LVESV = left ventricular end-systolic volume; MR = mitral regurgitation; PA = pulmonary artery; PASP = pulmonary artery systolic pressure; PCI = percutaneous coronary intervention; PCW = pulmonary capillary wedge pressure; STS-Score = Society of Thoracic Surgeons score; TAPSE = tricuspid annular plane systolic excursion; WU = Wood units.

The relationship between right ventricular to pulmonary artery (RV–PA) coupling and invasive hemodynamic measures was examined using the TAPSE/PASP ratio as a non-invasive surrogate. Correlation analyses employed the Pearson coefficient to evaluate the strength and direction of associations. Findings showed that patients

with higher TAPSE/PASP ratios exhibited increased PA compliance, whereas lower ratios were associated with elevated PA pulse pressure, higher PASP, and increased LA v-wave pressures. These results suggest that TAPSE/PASP provides a useful, non-invasive estimate of RV adaptation to pulmonary afterload (**Table 2**).

Table 2. Correlation of TAPSE/PASP with invasive right heart catheterization parameters

RHC Parameter	Association with TAPSE/PASP	Significance (p)
Right atrial mean pressure (mmHg)	−0.102	0.606
Left atrial mean pressure (mmHg)	−0.197	0.142
Left atrial V-wave mean (mmHg)	−0.324	0.047
Pulmonary capillary wedge pressure (mean, mmHg)	−0.203	0.299
Pulmonary artery mean pressure (mmHg)	−0.236	0.246
Pulmonary artery systolic pressure (mmHg)	−0.373	0.007
Pulmonary artery pulse pressure (mmHg)	−0.423	0.028
Cardiac index (mL/min/m ²)	−0.003	0.988
Pulmonary vascular resistance (Wood units)	−0.103	0.615
Transpulmonary gradient (mmHg)	−0.168	0.412
Diastolic pressure gradient (mmHg)	0.067	0.742
Pulmonary artery compliance (mL/mmHg)	0.418	0.030

Abbreviations: TAPSE = tricuspid annular plane systolic excursion; PASP = pulmonary artery systolic pressure; PA = pulmonary artery; PCW = pulmonary capillary wedge pressure; RHC = right heart catheterization; WU = Wood units.

Clinical outcomes

During follow-up, with a median duration of 260 days (interquartile range: 115–394), 71 of 228 patients (31.1%) experienced the composite primary endpoint. When analyzed by TAPSE/PASP ratio, the incidence was higher in those with $\text{TAPSE/PASP} \leq 0.35$ (40.4%) compared to patients with $\text{TAPSE/PASP} > 0.35$ (21.9%), reaching statistical significance ($p = 0.003$). This composite outcome comprised 61 hospital admissions for heart failure (26.8%) and 22 deaths from any cause (9.6%). Of these deaths, 12 occurred in patients with prior HF hospitalization and 2 during the initial hospital stay, with cardiovascular events contributing to 10 deaths (45.5%). Certain baseline characteristics were associated with higher event rates. Patients with diabetes mellitus had more frequent endpoints (45.1% vs. 26.8%, $p = 0.006$), as did patients with baseline NYHA functional class III–IV/IV (94.4% vs. 83.4%, $p = 0.024$). The STS-Score was slightly elevated among patients reaching the endpoint (7.1 ± 6.4 vs. 5.3 ± 4.7 , $p = 0.059$), but this difference did not achieve statistical significance (Table S1). Lower TAPSE and TAPSE/PASP ratios were observed in patients experiencing events, whereas PASP values were similar across groups. Overall, procedural and device-

related complications were uncommon and did not vary significantly by outcome, except for in-hospital mortality and 30-day HF readmissions (Table S2).

Follow-up data revealed that patients with baseline $\text{TAPSE/PASP} \leq 0.35$ were more likely to remain in advanced NYHA III–IV/IV functional class (39.5% vs. 25.7%, $p = 0.045$). Among those whose TAPSE/PASP remained ≤ 0.35 after successful TMVR, 55.9% were in advanced functional class, compared with 27.8% for patients whose TAPSE/PASP improved above 0.35 ($p = 0.004$). Notably, nearly two-thirds of patients initially below the 0.35 threshold had a TAPSE/PASP ratio above 0.35 when reassessed post-procedure (Table S3).

Survival and multivariable analysis

Kaplan–Meier survival estimates indicated that patients with $\text{TAPSE/PASP} \leq 0.35$ had a significantly higher likelihood of reaching the primary composite endpoint (Log-Rank 8.844, $p = 0.003$; **Figure 1a**). When examining heart failure hospitalizations separately, events remained more frequent in the low TAPSE/PASP group (Log-Rank 7.810, $p = 0.005$; **Figure 1b**). In contrast, all-cause mortality did not differ based on TAPSE/PASP ratio (Log-Rank 0.002, $p = 0.962$; **Figure 1c**).

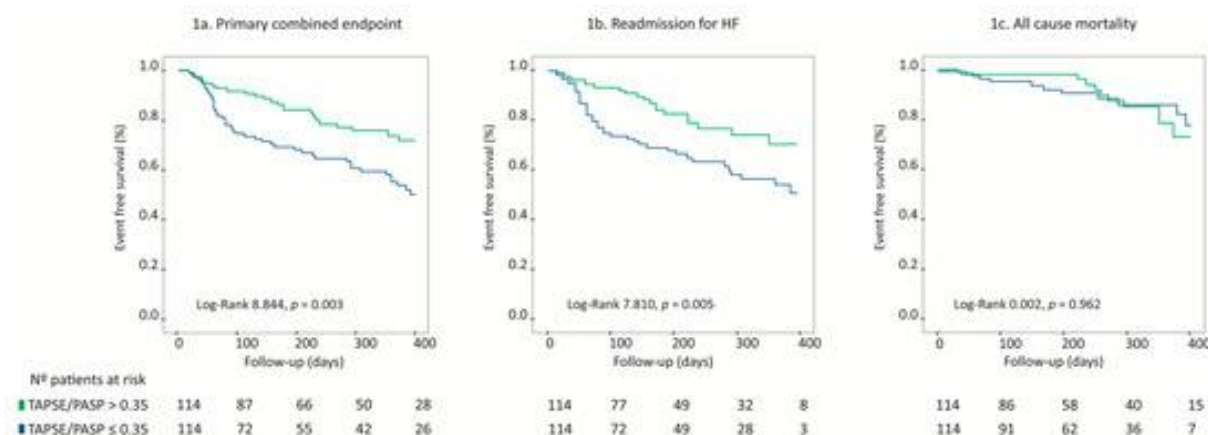


Figure 1. Kaplan–Meier curves illustrating the effect of TAPSE/PASP ratio on outcomes: (a) Primary composite endpoint elevated in $\text{TAPSE/PASP} \leq 0.35$, (b) Higher HF hospitalization rates for $\text{TAPSE/PASP} \leq 0.35$, (c) No significant differences in all-cause mortality

A Cox proportional hazards model was employed to evaluate the independent prognostic value of TAPSE/PASP. Variables with $p < 0.10$ in univariate analysis were included, and TAPSE and PASP were excluded from the final model due to collinearity.

Multivariate analysis confirmed that TAPSE/PASP ratio independently predicted the primary endpoint (HR 2.0; 95% CI: 1.13–3.53, $p = 0.017$), alongside STS-Score (HR 1.05; 95% CI: 1.01–1.10, $p = 0.024$) (**Table 3**).

Table 3. Multivariate Cox Regression Analysis

Factor	β -Coefficient	Hazard Ratio	95% Confidence Interval	Significance (p)
Diabetes Mellitus	0.442	1.56	0.92–2.64	0.101
NYHA Functional Class III–IV/IV	0.722	2.06	0.73–5.84	0.175
$\text{TAPSE/PASP} \leq 0.35$	0.693	2.0	1.13–3.53	0.017
STS Score	0.050	1.05	1.01–1.10	0.024
Tricuspid Regurgitation Grade III–IV/IV	0.091	1.09	0.62–1.92	0.750

Left Ventricular Ejection Fraction (LVEF)	−0.003	0.99	0.98–1.01	0.765
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Abbreviations: FC = functional class; NYHA = New York Heart Association; LVEF = left ventricular ejection fraction; PASP = pulmonary artery systolic pressure; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation; SE = standard error; STS-Score = Society of Thoracic Surgery Score

Remarkably, the prognostic significance of TAPSE/PASP persisted regardless of whether mitral regurgitation was primary, secondary, or mixed in origin. When patients were grouped by MR type, Kaplan–Meier curves revealed that those with a TAPSE/PASP ratio ≤ 0.35 experienced a greater incidence of the composite primary endpoint across primary MR (**Figure 2a**), secondary MR (**Figure**

2b), and mixed MR (**Figure 2c**) subgroups (Log-Rank = 8.749, $p = 0.003$).

Adding MR etiology into a multivariable Cox regression confirmed that a TAPSE/PASP ≤ 0.35 independently predicted the primary endpoint (HR 2.19; 95% CI 1.18–3.85, $p = 0.012$), together with STS-Score (HR 1.05; 95% CI 1.01–1.10, $p = 0.021$).

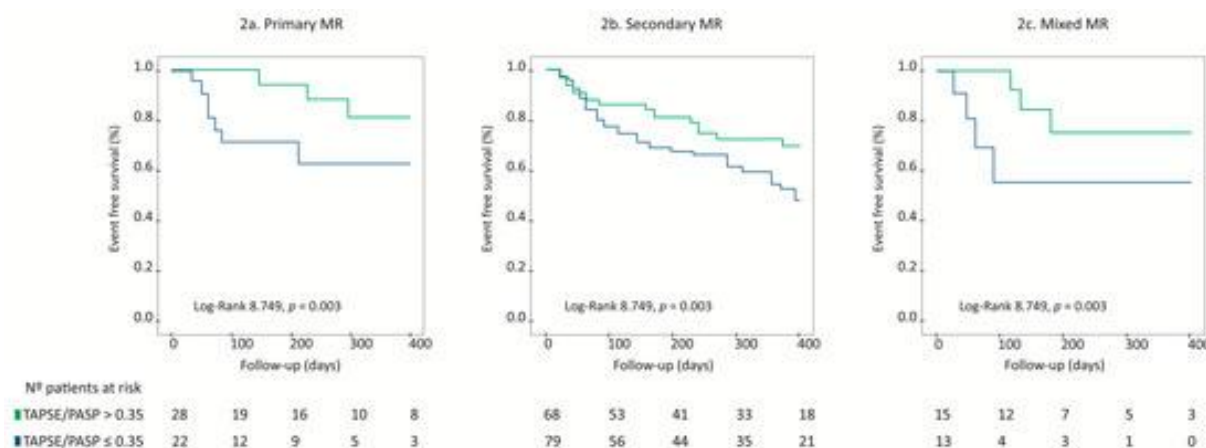


Figure 2. Kaplan–Meier survival analysis according to TAPSE/PASP ≤ 0.35 , separated by MR etiology. Panels show primary MR (a), secondary MR (b), and mixed MR (c). In all subgroups, lower TAPSE/PASP values were linked to higher rates of the composite endpoint

Discussion

To the best of our knowledge, this work is the first to explore how the TAPSE/PASP ratio predicts outcomes in individuals who successfully underwent TMVR using the MitraClip device. Within our cohort, the TAPSE/PASP index proved to be an independent prognostic factor for the combined primary endpoint of heart failure rehospitalizations and overall mortality, together with the STS-Risk Score. More importantly, multivariate Cox regression indicated that TAPSE/PASP provided greater prognostic precision than TAPSE or PASP when analyzed separately.

In recent years, the interaction between the right ventricle (RV) and pulmonary artery (PA) has been recognized as an essential determinant of prognosis in heart failure [19–21]. The most accurate assessment of RV–PA coupling is the ratio of right ventricular end-systolic elastance to effective arterial elastance (E_{es}/E_a) [17,26]. However, this method requires invasive right heart catheterization and specialized tools, which limit its use in everyday practice. The TAPSE/PASP ratio has been introduced as a simple, non-invasive alternative for evaluating RV–PA interaction [19–22,27]. This composite index reflects the RV’s ability to generate force and adapt to pressure overload, integrating the information provided by TAPSE

(longitudinal shortening) and PASP (afterload) [19,21]. Therefore, this ratio can identify subtle reductions in RV functional reserve [26], explaining its superior prognostic capability.

Our observations align with earlier research showing that TAPSE/PASP carries prognostic significance across multiple heart failure and pulmonary hypertension populations [19–22], as well as in patients with severe aortic stenosis treated with transcatheter aortic valve replacement [28]. In our data, TAPSE/PASP demonstrated a clear linear relationship with pulmonary artery compliance and pulse pressure—two invasive parameters that indicate the elasticity of the pulmonary circulation. These correlations further validate the use of TAPSE/PASP as a practical non-invasive marker of RV–PA coupling.

The TAPSE/PASP ratio also correlated inversely with baseline left atrial (LA) v-wave pressure. This pattern likely reflects greater atrial stiffness in individuals with more impaired RV–PA coupling. Previous investigations have reported a connection between reduced LA reservoir capacity, RV–PA uncoupling [24], and poorer functional status [29,30]. In agreement, our data show that a TAPSE/PASP ratio ≤ 0.35 , either before or after TMVR, was associated with worse functional class during follow-up.

The identification of reliable and accessible prognostic parameters is particularly important in patients considered for MitraClip implantation, since they often have advanced stages of heart failure and multiple comorbidities. Earlier studies have linked adverse outcomes in this group to several indicators, including bi-ventricular dysfunction, increased LV chamber dimensions, pulmonary hypertension, significant tricuspid regurgitation, and advanced symptomatic class [3,9–15,31].

Our findings expand upon these prior reports by emphasizing TAPSE/PASP as a novel and valuable measure that enhances prognostic classification in TMVR recipients, independent of the cause of mitral regurgitation. This is relevant in light of the inconsistent conclusions of the COAPT and MITRA-FR trials regarding MitraClip efficacy in secondary MR [32,33]. Several factors, including excessive LV dilatation and smaller regurgitant volumes, may explain the lack of benefit seen in MITRA-FR [34]. Furthermore, the COAPT study enrolled participants with lower pulmonary pressures and better RV function, whereas MITRA-FR included individuals with more severe RV dysfunction and pulmonary hypertension—differences that may account for their contrasting results. In this context, evaluating TAPSE/PASP as a non-invasive representation of RV–PA interaction could help clinicians more accurately identify which patients with secondary MR may benefit from MitraClip therapy.

The STS-Score, which integrates multiple established risk variables, also demonstrated independent prognostic relevance in our analysis, though its predictive strength was less than that of TAPSE/PASP. Combining both metrics could improve pre-procedural evaluation and outcome prediction in TMVR candidates. Notably, conventional prognostic markers such as LVEF and LV volumes did not add predictive value in this dataset—though this should be interpreted cautiously, as most participants exhibited only mildly reduced LVEF and mildly to moderately enlarged LV volumes. Severe tricuspid regurgitation, observed in 11.8% of the sample, also failed to predict outcomes, which might relate to smaller LV sizes and higher LVEF among these cases.

Despite these results, TAPSE/PASP alone did not predict overall mortality, likely due to the relatively small number of deaths and the predominance of non-cardiac causes. Therefore, larger multicenter studies with extended follow-up and adequate power to assess mortality and other hard endpoints are required to substantiate these preliminary findings.

Limitations

This study has several noteworthy limitations. To begin with, it was an observational investigation relying on a

retrospective review of a multicenter registry. Therefore, typical restrictions associated with this design—such as potential confounding variables, as well as selection or follow-up bias—cannot be entirely ruled out. Additionally, no centralized core laboratory was available to evaluate imaging or procedural results, and event adjudication was not independently verified. Consequently, firm conclusions regarding the prognostic capacity of the TAPSE/PASP ratio in forecasting cardiovascular adverse outcomes cannot be drawn solely from this study, and further large-scale, well-powered prospective trials are necessary to validate these findings. Another limitation is that right heart catheterization (RHC) was performed only in a limited portion of the overall cohort, based on the treating physician’s judgment. While this reflects real-world practice, it also means that a systematic invasive evaluation of right heart pressures through RHC was not conducted, similar to most prior studies assessing prognostic indices in patients undergoing MitraClip therapy. Therefore, the possibility that hemodynamic variables exerted a stronger impact on clinical outcomes cannot be entirely excluded. Nevertheless, non-invasive markers used in this research—such as the TAPSE/PASP ratio and echocardiographic PASP estimation—have previously been validated against invasive reference standards [24,26,29]. In our cohort, echo-derived PASP demonstrated a strong correlation with invasively measured PASP ($r = 0.592$, $p < 0.0001$), supporting the reliability of the non-invasive approach employed.

Conclusions

In this group of heart failure patients with significant mitral regurgitation successfully treated with transcatheter mitral valve repair using the MitraClip system, the TAPSE/PASP ratio was identified as an important prognostic marker for the primary composite outcome of HF-related readmissions and all-cause mortality, independent of MR etiology or tricuspid regurgitation severity. Notably, TAPSE/PASP demonstrated stronger prognostic power compared with either of its individual components (TAPSE or PASP) when assessed separately. Consistent with earlier studies, the TAPSE/PASP ratio also exhibited significant correlations with other measures of RV–PA coupling, including pulmonary artery compliance and pulse pressure, further underscoring its value as a non-invasive indicator of right-sided cardiopulmonary interaction.

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References

- Feldman T, Foster E, Glower DD, Kar S, Rinaldi MJ, Fail PS, Smalling RW, Siegel R, Rose GA, Engeron E, et al. Percutaneous repair or surgery for mitral regurgitation. *N Engl J Med*. 2011;364(15):1395–406.
- Sorajja P, Vemulapalli S, Feldman T, Mack M, Holmes DR Jr, Stebbins A, Kar S, Thourani V, Ailawadi G. Outcomes with transcatheter mitral valve repair in the United States: an STS/ACC TVT Registry report. *J Am Coll Cardiol*. 2017;70(19):2315–27.
- Ailawadi G, Lim DS, Mack MJ, Trento A, Kar S, Grayburn PA, Glower DD, Wang A, Foster E, Qasim A, et al. One-year outcomes after MitraClip for functional mitral regurgitation. *Circulation*. 2019;139(1):37–47.
- Maisano F, Franzen O, Baldus S, Schäfer U, Hausleiter J, Butter C, Ussia GP, Sievert H, Richardt G, Widder JD, et al. Percutaneous mitral valve interventions in the real world: early and 1-year results from the ACCESS-EU study. *J Am Coll Cardiol*. 2013;62(12):1052–61.
- Baumgartner H, Falk V, Bax JJ, De Bonis M, Hamm C, Holm PJ, Iung B, Lancellotti P, Lansac E, Rodriguez Muñoz D, et al. 2017 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J*. 2017;38(36):2739–91.
- Otto CM, Nishimura RA, Bonow RO, Carabello BA, Erwin JP 3rd, Gentile F, Jneid H, Krieger EV, Mack M, McLeod C, et al. 2020 ACC/AHA Guideline for the management of patients with valvular heart disease: Executive summary. *J Am Coll Cardiol*. 2021;77(4):450–500.
- Kortlandt FA, van't Klooster CC, Bakker AL, Swaans MJ, Kelder JC, de Kroon TL, Rensing BJ, Eefting FD, van der Heyden JA, Post MC. Predictive value of surgical risk scores for mortality in percutaneous mitral valve repair. *Neth Heart J*. 2016;24(8):475–80.
- Puls M, Lubos E, Boekstegers P, von Bardeleben RS, Ouarrak T, Butter C, Zuern CS, Bekerredjian R, Sievert H, Nickenig G, et al. One-year outcomes and predictors of mortality after MitraClip therapy: results from the German TMVI registry. *Eur Heart J*. 2016;37(8):703–12.
- Baldi C, Citro R, Silverio A, Di Maio M, De Rosa R, Bonadies D, Verolino G, Esposito L, Mastrogiorganni G, Di Muro MR, et al. Predictors of outcome in heart failure with severe functional mitral regurgitation undergoing MitraClip treatment. *Int J Cardiol*. 2019;284:50–8.
- Capodanno D, Adamo M, Barbanti M, Giannini C, Laudisa ML, Cannata S, Curello S, Immè S, Maffeo D, Bedogni F, et al. Predictors of clinical outcomes after edge-to-edge percutaneous mitral valve repair. *Am Heart J*. 2015;170(2):187–95.
- Nickenig G, Estevez-Loureiro R, Franzen O, Tamburino C, Vanderheyden M, Lüscher TF, Moat N, Price S, Dall'Ara G, Winter R, et al. Percutaneous mitral valve edge-to-edge repair: in-hospital results and 1-year follow-up. *J Am Coll Cardiol*. 2014;64(9):875–84.
- Al-Bawardy R, Vemulapalli S, Thourani VH, Mack M, Dai D, Stebbins A, Palacios I, Inglessis I, Sakhuja R, Ben-Assa E, et al. Association of pulmonary hypertension with outcomes of transcatheter mitral valve repair. *JAMA Cardiol*. 2020;5(1):47–56.
- Osteresch R, Diehl K, Kühl M, Fiehn E, Schmucker J, Backhaus T, Fach A, Wienbergen H, Hambrecht R. Impact of right heart function on outcome in chronic heart failure undergoing MitraClip. *J Interv Cardiol*. 2018;31(6):916–24.
- Tigges E, Blankenberg S, von Bardeleben RS, Zürn C, Bekerredjian R, Ouarrak T, Sievert H, Nickenig G, Boekstegers P, Senges J, et al. Implication of pulmonary hypertension in MitraClip patients: results from the TRAMI registry. *Eur J Heart Fail*. 2018;20(4):585–94.
- Godino C, Salerno A, Cera M, Agricola E, Fragasso G, Rosa I, Oppizzi M, Monello A, Scotti A, Magni V, et al. Evolution of right ventricular dysfunction after successful MitraClip implantation. *Int J Cardiol Heart Vasc*. 2016;11:90–8.
- Kottenberg E, Dumont M, Frey UH, Heine T, Plicht B, Kahlert P, Erbel R, Peters J. The minimally invasive MitraClip procedure under general anaesthesia: effects on pulmonary circulation and RV function. *Anaesthesia*. 2014;69(8):860–7.
- Tello K, Dalmer A, Axmann J, Vanderpool R, Ghofrani HA, Naeije R, Roller F, Seeger W, Sommer N, Wilhelm J, et al. Reserve of right ventricular-arterial coupling in chronic overload. *Circ Heart Fail*. 2019;12(1):e005512.
- Vanderpool R, Pinsky M, Naeije R, Deible C, Kosaraju V, Bunner C, Mathier MA, Lacomis J, Champion HC, Simon MA. RV–PA coupling predicts outcome in pulmonary hypertension. *Heart*. 2015;101(1):37–43.
- Guazzi M, Bandera F, Pelissero G, Castelvécchio S, Menicanti L, Ghio S, Temporelli PL, Arena R. TAPSE/PASP relationship in heart failure: index of RV contractile function. *Am J Physiol Heart Circ Physiol*. 2013;305(9):H1373–81.
- Santas E, Palau P, Guazzi M, de la Espriella R, Miñana G, Sanchis J, Bayes-Genís A, Lupón J,

- Chorro FJ, Núñez J. RV–PA coupling as indicator of risk in HFpEF. *Am J Cardiol.* 2019;124(4):567–72.
21. Guazzi M, Dixon D, Labate V, Beussink-Nelson L, Bandera F, Cuttica MJ, Shah SJ. RV contractile function and coupling in HFpEF. *JACC Cardiovasc Imaging.* 2017;10(10):1211–21.
22. Tello K, Wan J, Dalmer A, Vanderpool R, Ghofrani HA, Naeije R, Roller F, Mohajerani E, Seeger W, Herberg U, et al. Validation of TAPSE/sPAP ratio for RV–arterial coupling in severe PH. *Circ Cardiovasc Imaging.* 2019;12(9):e009047.
23. Stone GW, Adams DH, Abraham WT, Kappetein AP, G  n  reux P, Vranckx P, Mehran R, Kuck KH, Leon MB, Piazza N, et al. MVARC: endpoint definitions for TMVR trials. *J Am Coll Cardiol.* 2015;66(3):308–21.
24. Guazzi M, Naeije R, Arena R, Corr   U, Ghio S, Forfia P, Rossi A, Cahalin LP, Bandera F, Temporelli P. Echocardiography of RV–arterial coupling and CPET to predict outcome in HF. *Chest.* 2015;148(1):226–34.
25. Gorter TM, van Veldhuisen DJ, Voors AA, Hummel YM, Lam CSP, Berger RMF, van Melle JP, Hoendermis ES. RV–vascular coupling in HFpEF and pulmonary hypertension. *Eur Heart J Cardiovasc Imaging.* 2018;19(4):425–32.
26. Vonk Noordegraaf A, Westerhof BE, Westerhof N. Relationship between the right ventricle and its load in pulmonary hypertension. *J Am Coll Cardiol.* 2017;69(2):236–43.
27. Masarone D, Errigo V, Melillo E, Valente F, Gravino R, Verrengia M, Ammendola E, Vastarella R, Pacileo G. Effects of sacubitril/valsartan on RV–arterial coupling in HFrEF. *J Clin Med.* 2020;9(10):3159.
28. Sultan I, Cardounel A, Abdelkarim I, Kilic A, Althouse AD, Sharbaugh MS, Gupta A, Xu J, Fukui M, Simon MA, et al. RV–PA coupling in patients undergoing TAVI. *Heart.* 2019;105(2):117–21.
29. Sugimoto T, Bandera F, Generati G, Alfonzetti E, Bussadori C, Guazzi M. Left atrial function dynamics during exercise in HF. *JACC Cardiovasc Imaging.* 2017;10(10):1253–64.
30. Hussain I, Mohammed SF, Forfia PR, Lewis GD, Borlaug BA, Gallup DS, Redfield MM. Impaired RV–PA coupling and sildenafil effect in HFpEF: RELAX trial. *Circ Heart Fail.* 2016;9(1):e002729.
31. Pascual I, Carrasco-Chinchilla F, Benito-Gonzalez T, Li CH, Avanzas P, Nombela-Franco L, Pan M, Serrador-Frutos A, Freixa X, Trillo-Nouche R, et al. Transcatheter mitral repair for functional MR by LV function. *J Clin Med.* 2020;9(6):1792.
32. Stone GW, Lindenfeld J, Abraham WT, Kar S, Lim DS, Mishell JM, Whisenant B, Grayburn PA, Rinaldi M, Kapadia SR, et al. COAPT Investigators. Transcatheter mitral-valve repair in heart failure. *N Engl J Med.* 2018;379(24):2307–18.
33. Obadia JF, Messika-Zeitoun D, Leurent G, Iung B, Bonnet G, Piriou N, Lef  vre T, Piot C, Rouleau F, Carri   D, et al. MITRA-FR Investigators. Percutaneous repair or medical treatment for secondary mitral regurgitation. *N Engl J Med.* 2018;379(24):2297–306.
34. Grayburn PA, Sannino A, Packer M. Proportionate and disproportionate functional mitral regurgitation: conceptual framework. *JACC Cardiovasc Imaging.* 2019;12(2):353–62.