

## ORIGINAL RESEARCH

## VALVULAR HEART DISEASE

# A Novel Hemodynamic Index Characterizing Mitral Regurgitation Undergoing Transcatheter Edge-to-Edge Repair



## The MPF

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## ABSTRACT

**BACKGROUND** Hemodynamic impact of residual mitral regurgitation (MR) after transcatheter edge-to-edge repair (TEER) is not always univocally measured by transesophageal echocardiographic (TEE) assessment alone. When analyzing TEER procedure result, operators often encounter discrepancy between TEE guidance and invasive hemodynamic monitoring.

**OBJECTIVES** This study sought to investigate the role of invasive hemodynamic monitoring during mitral valve TEER procedure on top of TEE guidance.

**METHODS** We analyzed 78 patients with moderate-to-severe or severe MR who underwent TEER. Mitral pulse pressure fraction (MPF) was extracted from intraprocedural continuous left atrial pressure monitoring. Twenty-three patients with the same grade of MR not undergoing TEER were included as a control group. At follow-up, clinical and functional status in the majority of patients undergoing TEER were reassessed by NYHA classification and the 12-item Kansas City Cardiomyopathy Questionnaire (KCCQ).

**RESULTS** TEER significantly reduced MR burden on both TEE guidance and invasive hemodynamic monitoring. Post-TEER MPF was significantly reduced compared to both pre-TEER setting ( $P < 0.001$ ) and control group ( $P < 0.001$ ). At follow-up, while MR reduction assessed by TEE was associated with an improved functional status in terms of the 12-item KCCQ but not of NYHA classification, a greater reduction in MPF was associated with a significant amelioration of both NYHA classification ( $P = 0.036$ ) and 12-item KCCQ ( $P = 0.032$ ).

**CONCLUSIONS** MPF could provide an immediate estimate of the real hemodynamic impact of MR and a prompt prediction of the functional improvement after TEER. (JACC Adv. 2024;3:101099) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the [Author Center](#).

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**ABBREVIATIONS  
AND ACRONYMS****KCCQ** = Kansas City  
Cardiomyopathy Questionnaire**LAP** = left atrial pressure**MACE** = major adverse cardiac  
events**MPF** = mitral pulse pressure  
fraction**MR** = mitral regurgitation**PCWP** = pulmonary capillary  
wedge pressure**RHC** = right heart  
catheterization**SAP** = systemic arterial  
pressure**TEE** = transesophageal  
echocardiography**TEER** = transcatheter edge-to-  
edge repair

**T**ransesophageal echocardiographic (TEE) guidance throughout transcatheter edge-to-edge repair (TEER) provides valuable information regarding both anatomic device positioning and residual mitral regurgitation (MR) jets. The direct hemodynamic impact of residual MR in the immediate post-TEER setting is not always univocally measured by echocardiographic assessment alone which cannot estimate acute changes in filling pressures and left atrial compliance. Interventional cardiologists often encounter discrepancy between echocardiographic guidance and the immediate hemodynamic result of implanted clip, that is, while the TEE result can be suboptimal requiring additional clipping, further implantation of clips does not always impact the final hemodynamic result.<sup>1</sup>

Invasive continuous left atrial pressure (LAP) monitoring during TEER by means of the manufacturer-provided steerable guide catheter used for optimal device placement has been proven to be a feasible intraoperative tool,<sup>2</sup> although pressure waveform overdamping with consequent pressure underestimation as compared to a dedicated catheter with side holes has been reported.<sup>3</sup> Moreover, intra-procedural measurement of LAP changes showed equivocal association with functional outcomes,<sup>4</sup> while other studies indicated that it can predict clinical outcomes independently from TEE guidance.<sup>5,6</sup>

We therefore sought to investigate the role of invasive LAP monitoring during TEER in terms of clinical outcomes by means of mitral pulse pressure fraction (MPF), a novel index derived from left atrial and systemic arterial hemodynamics.

**METHODS**

**POPULATION.** We conducted a retrospective observational study of 78 patients with moderate-to-severe or severe MR who underwent TEER at our institutions, Policlinico Universitario A. Gemelli IRCCS in Rome and Ospedale Generale Regionale F. Miulli in Acquaviva delle Fonti between September 2017 and August 2022. Patients included in our study were chosen from a larger cohort of patients with at least moderate-to-severe MR referred to our tertiary centers and deemed suitable to undergo TEER after a multidisciplinary team assessment taking into account clinical and procedural aspects.

We collected demographic, clinical, procedural, and outcome data during the index TEER and during

follow-up as outpatient visits or by means of tele-matic clinical assessments (telephone or video calls). Patients with inaccurate or missing baseline medical and procedural reports were excluded from the study population. Furthermore, we collected clinical and procedural data from a control group of 23 patients, extracted from a larger cohort of patients with moderate-to-severe or severe MR who did not undergo TEER in order to compare baseline hemodynamic characteristics with the study population. Our study complied with the Declaration of Helsinki and all patients gave written informed consent before TEER or right heart catheterization (RHC).

**TEER PROCEDURE AND ECHOCARDIOGRAPHIC ASSESSMENT.**

In all cases of the study population, mitral valve TEER was performed using the Abbott Mitraclip System (Abbott Laboratories). TEERs were performed under general anesthesia and using both TEE and fluoroscopic guidance. The 3 main echocardiographic etiologies of MR were included in our study to provide a more comprehensive understanding of the hemodynamics of this condition: organic MR, functional disproportionate MR, and functional proportionate MR. In the echocardiographic setting of functional MR, we adopted the definition proposed by Grayburn et al.<sup>7</sup> to distinguish between proportional and disproportional subtypes of functional MR.

Intraoperative TEE was used to obtain both continuous echocardiographic evaluation of MR and successful TEER. MR was graded quantitatively by a multiparametric approach: preprocedural and immediate postimplantation residual MR were defined as trivial, mild, moderate, moderate-to-severe, and severe. Intraoperative MR reduction was defined by the difference between preprocedural and immediately after TEER MR and subsequently graded into the following 4 classes: worsening of MR, no reduction of MR, minimal reduction of MR, and optimal reduction of MR. Left ventricle ejection fraction was assessed with biplane Simpson's method, right ventricle systolic function expressed by tricuspid annular plane systolic excursion, left atrium volume indexed for body surface area, and pulmonary artery systolic pressure calculated from the peak velocity of the tricuspid regurgitant jet according to the Bernoulli equation plus the estimated right atrial pressure (according to the diameter and inspiratory collapse of the inferior vena cava). Effective regurgitant orifice area was calculated by the proximal isovelocity surface area method.

**INVASIVE PRESSURE ASSESSMENT AND MPF CALCULATION.**

Invasive continuous LAP monitoring TEER was obtained by means of the manufacturer-

provided steerable guide catheter used for optimal device placement and release. We obtained and analyzed LAP tracing of a cycle of at least 10 seconds before and after clip implantation for every patient undergoing TEER procedure. Intraprocedural continuous systemic arterial pressure (SAP) tracing was monitored invasively through the cannulation and the connection of a radial artery to a second pressure line. Regarding LAP tracing, during live TEER procedure, operators usually deal with one single a/c wave displayed by the polygraph as these 2 positive deflections are in close proximity during the cardiac cycle. Mean minimum LAP was defined as the arithmetic mean of a/c wave (c wave in case of atrial fibrillation) and the lowest between x and y descent.

$$\text{mean minimum LAP} = a/c \text{ wave} + x/y \text{ wave} 2$$

MPF is an index derived from both invasive LAP tracing and SAP monitoring. It is calculated dividing the difference between v wave in the LAP tracing and mean minimum LAP, by the systolic arterial pressure which is, in the absence of aortic stenosis, the measure of systolic left ventricular pressure.

$$\text{MPF} = \frac{v \text{ wave} - \text{mean minimum LAP}}{\text{systolic arterial pressure}}$$

MPF expresses the proportion of pressure generated by the left ventricle which affects the left atrium. In other words, MPF is also a measure of the resistance offered by the mitral valve to the blood ejected by the left ventricle. The higher the MPF, the higher the hemodynamic impact of the MR and the lower the continence of the valve. By means of excluding the mean minimum LAP, MPF should be able to dissect the impact of MR from the increased filling pressures that are characteristic for heart failure.

Control group's invasive pressure evaluation was obtained from RHC assessment: hemodynamic data were collected in the form of pulmonary capillary wedge pressure (PCWP) tracings, as surrogate for LAP, and compared to the study population's baseline hemodynamic profile. In all cases, PCWP was obtained through a balloon-tipped 6-F Swan-Ganz catheter. As for the study population, we collected the control group's RHC data during the index RHC procedure and extracted the hemodynamic variables required for MPF's calculation from the PCWP tracings.

**OUTCOMES.** TEER procedural success was assessed as per Mitral Valve Academic Research Consortium criteria.<sup>8</sup> The primary endpoint of the study was the first occurrence of major adverse cardiac events (MACE) defined as the composite of death from any cause and heart failure-related hospitalization. Cardiovascular death was defined by the Mitral Valve

**TABLE 1** Baseline Demographic, Clinical, and Preprocedural Echocardiographic Characteristics

	TEER Population (n = 78)	RHC Control Group (n = 23)	P Value
Age (y)	78 (72.5-83)	72 (60-81)	0.381
Female	32 (41%)	15 (65%)	0.071
BMI (kg/m <sup>2</sup> )	24 (22.8-26.1)	24.6 (22-28)	0.618
Comorbidities			
Diabetes	22 (28%)	4 (17%)	0.357
Hypertension	55 (71%)	14 (61%)	0.832
Hypercholesterolemia	43 (55%)	10 (43%)	0.352
Peripheral vascular disease	11 (14%)	1 (4%)	0.143
COPD	20 (26%)	3 (13%)	0.371
Atrial fibrillation	39 (50%)	13 (56%)	0.684
eGFR (ml/min/1.73 m <sup>2</sup> )	51 (35-70)	51 (35-75)	0.854
Patient history			
Ischemic cardiomyopathy	37 (47%)	4 (17%)	0.036
Previous MI	28 (36%)	4 (17%)	0.189
Previous PCI	32 (41%)	3 (13%)	0.034
Previous CABG	9 (11%)	2 (9%)	0.951
Previous CRT/ICD	22 (28%)	4 (17%)	0.502
Previous stroke	4 (5%)	2 (9%)	0.122
Hospitalization for HF in last 12 mo	30 (38%)	4 (17%)	0.125
NYHA functional class			
I	0	0	
II	10 (13%)	5 (22%)	0.083
III	53 (68%)	15 (65%)	0.863
IV	15 (19%)	3 (13%)	0.284
12-item KCCQ	35 (27.5-50)	40 (35-45)	0.087
Echocardiographic assessment			
Organic MR	29 (37%)	10 (43%)	0.746
Moderate-to-severe MR	18 (23%)	9 (39%)	0.438
Severe MR	60 (77%)	14 (61%)	0.531
EROA MR (cm <sup>2</sup> )	0.39 (0.27-0.55)	0.27 (0.19-0.49)	0.247
LVEF (%)	46 (30-59)	38 (26-62)	0.483
LVEDVi (mL)	77 (56-99)	64.8 (45.5-98.6)	0.134
LVESVi (mL)	35 (24-70)	28 (21-48)	0.103
LAVi (mL)	67 (53-82)	69.2 (61-78,6)	0.473
Estimated sPAP (mm Hg)	50 (35-60)	60 (39-70)	0.698
Moderate-to-severe or severe TR	24 (31%)	12 (52%)	0.018

Values are median (IQR) or n (%).  
 BMI = body mass index; CABG = coronary artery bypass grafting; COPD = chronic obstructive pulmonary disease; CRT = cardiac resynchronization therapy; eGFR = estimated glomerular filtration rate; EROA = effective regurgitant orifice area; HF = heart failure; ICD = implantable cardioverter-defibrillator; KCCQ = Kansas City Cardiomyopathy Questionnaire; LAVi = indexed left atrial volume; LVEDVi = indexed left ventricular end-diastolic volume; LVEF = left ventricular ejection fraction; MI = myocardial infarction; PCI = percutaneous coronary intervention; RHC = right heart catheterization; sPAP = systolic pulmonary artery pressure; TEER = transcatheter edge-to-edge repair; TR = tricuspid regurgitation.

Academic Research Consortium indication.<sup>8</sup> Secondary endpoints were the single components of MACE as well as noncardiovascular death, all-cause hospitalization, cardiovascular hospitalization, myocardial infarction defined according to ESC 4th definition of Myocardial Infarction,<sup>9</sup> stroke, single leaflet TEER device attachment, new cardiac resynchronization therapy, end-stage renal impairment requiring hemodialysis, and functional status at follow-up assessed by means of both the NYHA classification

**TABLE 2 Baseline Hemodynamic Parameters**

	TEER Population (n = 78)	RHC Control Group (n = 23)	P Value
LAP x/y wave	14 (9-17)	20 (17.5-24)	0.001
LAP a/c wave	23 (16-28)	25 (22.5-32.5)	0.304
Mean min LAP	20 (13-23)	22.5 (20-28.5)	0.057
LAP v wave	32 (21-49)	36 (27.5-45)	0.635
Mean LAP	22 (15-27)	27 (22.5-35)	0.034
Mean arterial pressure	79 ± 8	95 ± 17	<0.001
Systolic arterial pressure	121 ± 14	124 ± 27	0.070
MPF	0.104 (0.056-0.208)	0.069 (0.052-0.155)	0.989

Values are median (IQR) or mean ± SD. Hemodynamic variables reported in mm Hg.  
LAP = left atrial pressure; MPF = mitral pulse pressure fraction; RHC = right heart catheterization;  
TEER = transcatheter edge-to-edge repair.

and the validated 12-item version of the Kansas City Cardiomyopathy Questionnaire (KCCQ)<sup>10</sup> considering the summary score of the questionnaire.

**STATISTICAL ANALYSIS.** All patients included in our study were analyzed as pre-TEER, post-TEER, and control group. Comparisons were made among these 3 groups. Continuous variables were reported as median (IQR) (1st and 3rd quartiles) when characterized by a non-normal distribution or as mean ± SD when normally distributed. Categorical variables were expressed as frequencies and percentages. Paired t-test, Wilcoxon test, Mann-Whitney test, or Kruskal-Wallis test were conducted as deemed appropriate. Pearson chi-square test was used to assess differences among categorical variables. Stratified log-rank test was assessed to show the incidence of clinical endpoints and to check for intergroup differences. Probability value of <0.05 ( $P < 0.05$ ) was considered the cutoff showing statistical significance. Univariable Cox regression analysis was employed to investigate potential associations between variables and outcomes in the TEER population of our study. Variables with a probability value of <0.05 in the univariable analysis were further investigated in the multivariable Cox regression analysis where hazard ratio was adjusted for sex, age, body mass index, and left ventricle ejection fraction. Statistical analyses were performed using IBM SPSS Statistics, version 25.0 (SPSS, IBM Corp) and GraphPad Prism, version 9.2.0 (GraphPad Software).

## RESULTS

**BASILINE CLINICAL AND ECHOCARDIOGRAPHIC CHARACTERISTICS.** We collected intraprocedural invasive pressure tracings of 78 patients undergoing

TEER in our centers. Twenty-three patients who underwent RHC were included in the study as a control group. Baseline demographic, clinical, and preprocedural echocardiographic characteristics of patients analyzed in our study are reported in **Table 1**.

Median age in both TEER and control group was comparable and female sex was equally represented. There was no significant difference in baseline clinical characteristics between the 2 groups when considering comorbidities such as diabetes, hypertension, hypercholesterolemia, peripheral vascular disease, chronic obstructive pulmonary disease, and chronic kidney disease. Patients with ischemic cardiomyopathy and previous percutaneous coronary intervention were significantly more prevalent in the TEER group. Baseline functional status as assessed by both the NYHA classification, assessed in all patients at baseline, and the 12-item version of the KCCQ, assessed in 75 out of 78 (96%) patients at baseline, was comparable between the 2 groups. Of note, 87% of patients in the TEER group reported symptoms consistent with NYHA functional classes III/IV and the median 12-item KCCQ before TEER was 35. Functional MR was the most prevalent MR etiology in both groups, accounting for 63% of cases in the TEER group. In the latter, median effective regurgitant orifice area and median left ventricle ejection fraction were 0.39 cm<sup>2</sup> and 46%, respectively. Overall, there was no significant difference between the 2 groups regarding the main echocardiographic parameters, except for the presence of moderate-to-severe or severe tricuspid regurgitation which was more prevalent in the control group undergoing RHC. Despite this difference, median echocardiographic estimation of pulmonary artery systolic pressure was similarly elevated in both groups (50 and 60 mm Hg, in the TEER group and in the control group, respectively). Of note, all patients included in our study showed normal transaortic gradient.

**HEMODYNAMIC ASSESSMENT.** A comparison between baseline hemodynamic parameters is summarized in **Table 2**.

Both x/y wave and mean LAP were more elevated in the control group but there was no significant difference when considering a/c wave, mean minimum LAP, and v wave. Systolic arterial pressure, invasively assessed in the TEER group and noninvasively estimated in the control group, was comparable. Notably, there was no statistically significant difference in terms of baseline MPF (median MPF 0.104 and 0.069 in the TEER and in the control group, respectively).

In the TEER group, the hemodynamic impact of the procedure on the different parameters analyzed is

**TABLE 3 Hemodynamic Parameters in TEER Population (N = 78)**

	Pre-TEER	Post-TEER	Estimated Difference (95% CI)	P Value
LAP x/y wave	14 (9-17)	13 (8-17)	1.18 (-0.112 to 2.479)	0.073
LAP a/c wave	23 (16-28)	18 (13-22)	3.645 (1.867-5.423)	0.001
Mean min LAP	20 (13-23)	16 (10-20)	2.414 (0.962-3.867)	0.001
LAP v wave	32 (21-49)	21 (14-25)	14.289 (10.165-18.413)	0.001
Mean LAP	22 (15-27)	16 (11-21)	5.013 (3.048-6.978)	<0.001
Mean arterial pressure	79 ± 8	80 ± 10	-1.394 (-4.295 to 1.506)	0.341
Systolic arterial pressure	121 ± 14	123 ± 15	-1.565 (-3.571 to 0.439)	0.124
MPF	0.104 (0.056-0.208)	0.04 (0.021-0.069)	0.101 (0.071-0.131)	<0.001

Values are median (IQR) or mean ± SD.  
 LAP = left atrial pressure; MPF = mitral pulse pressure fraction; TEER = transcatheter edge-to-edge repair.

summarized in **Table 3**: TEER significantly reduced several hemodynamic parameters included in our analysis, such as a/c wave, v wave, mean LAP. SAP values were stable throughout the procedure. Median MPF value was significantly reduced after procedure completion and there was no significant difference in median MPF before TEER compared to the median MPF of the control group while we found that median MPF after TEER was significantly lower than both pre-TEER MPF and control group’s MPF (**Tables 2 and 3**).

Overall median change in MPF ( $\Delta$ MPF) was 0.052 (IQR: 0.016-0.148) without any significant difference among the 3 main echocardiographic MR etiologies (0.07 [IQR: 0.03-0.25] in organic MR, 0.04 [IQR: 0.032-0.12] in functional proportionate MR, and 0.03 [IQR: 0.014-0.11] in functional disproportionate MR).

**PROCEDURAL OUTCOMES.** Number and type of clips (MitraClip system) used in our study population are

**TABLE 4 Number of Clips Implanted per MV TEER Procedure and Type of Clips Used in our Study Population**

Number of Clips Implanted (in a Single MV TEER Procedure)	Patients (N = 78)
1 clip	44
2 clips	33
3 clips	1

Type of Clip (MitraClip System)	Total Clips Implanted (Total Clips = 113)
NT	9 (8%)
XT	6 (5%)
NTW	16 (14%)
XTW	31 (27%)
NTR	18 (17%)
XTR	33 (29%)

Values are n or n (%).  
 MV = mitral valve; TEER = transcatheter edge to edge repair.

summarized in **Table 4**. In all but 1 case (98%), a residual post-TEER trivial, mild, or moderate MR was achieved, with a significantly improved MR grade in the post-TEER setting compared to baseline MR ( $P < 0.001$ ). Specifically, an optimal residual post-TEER MR was obtained in 43 cases. Intraprocedural echocardiographic MR reduction assessed by TEE guidance (no reduction vs mild reduction vs optimal reduction in MR grade) was associated with improved 12-item KCCQ ( $P = 0.024$ ) but it did not significantly correlate with improved functional status at follow-up as assessed by NYHA classification ( $P = 0.405$ ) nor with the incidence of MACE after discharge ( $P = 0.585$ ) (**Supplemental Tables 1 to 3**).

Three patients died following TEER during the index hospitalization: one patient developed acute hemodynamic collapse in the cardiovascular intensive care unit while being monitored in the post-procedural setting with echocardiographic evidence of partial clip detachment from posterior mitral valve leaflet; a second death was secondary to fatal SARS-CoV2 infection leading to multiorgan failure; fulminant urosepsis was responsible for the third in-hospital death in the TEER group.

**MPF ASSOCIATION WITH CLINICAL FOLLOW-UP.** Median follow-up after TEER procedure was 372 days (IQR: 151-752 days). Survival time estimates were 865 days (95% CI: 730-998 days) with 18 patients (24%) who died during follow-up after index hospitalization, 4 (5%) of which were cardiovascular deaths. Eight patients (11%) were hospitalized due to heart failure. Six patients (8%) were hospitalized due to cardiac issues other than heart failure. One patient had to undergo cardiac surgery due to a partial clip detachment 8 months after index TEER procedure; the same patient reported new hemodialysis initiation. No patients reported stroke or transient ischemic attack during follow-up and one patient underwent new cardiac resynchronization therapy

<b>TABLE 5 Cox Regression Models on the Relationship Between Hemodynamic Variables and Clinical Outcomes</b>				
	<b>Univariable Analysis</b>		<b>Multivariable Analysis</b>	
	<b>OR (95% CI)</b>	<b>P Value</b>	<b>OR (95% CI)</b>	<b>P Value</b>
<b>Pre-TEER invasive hemodynamic parameters</b>				
LAP x/y wave	0.955 (0.899-1.014)	0.131		
LAP a/c wave	0.992 (0.943-1.044)	0.762		
Mean min LAP	0.975 (0.922-1.032)	0.383		
LAP v wave	0.998 (0.976-1.020)	0.843		
Mean LAP	0.990 (0.947-1.035)	0.658		
MPF	1.739 (0.076-39.975)	0.729		
<b>Post-TEER invasive hemodynamic parameters</b>				
LAP x/y wave	0.998 (0.934-1.065)	0.943		
LAP a/c wave	1.018 (0.958-1.081)	0.564		
Mean min LAP	1.007 (0.944-1.074)	0.832		
LAP v wave	1.017 (0.980-1.055)	0.371		
Mean LAP	1.009 (0.954-1.066)	0.761		
MPF post	148.707 (0.070-31374.092)			
Higher $\Delta$ mean LAP <sup>a</sup>	0.986 (0.483-2.013)	0.970		
Higher $\Delta$ LAP v wave <sup>a</sup>	0.984 (0.608-1.661)	0.984		
Higher $\Delta$ MPF <sup>a</sup>	1.028 (0.506-2.090)	0.940		
<b>At least 2 NYHA Classes Functional Improvement</b>				
	<b>Univariable Analysis</b>		<b>Multivariable Analysis</b>	
	<b>OR (95% CI)</b>	<b>P Value</b>	<b>OR (95% CI)</b>	<b>P Value</b>
<b>Pre-TEER invasive hemodynamic parameters</b>				
LAP x/y wave	0.958 (0.862-1.065)	0.426		
LAP a/c wave	1.024 (0.941-1.115)	0.582		
Mean min LAP	0.997 (0.903-1.101)	0.958		
LAP v wave	1.039 (1.005-1.075)	0.026	1.063 (1.017-1.111)	0.006
Mean LAP	1.052 (0.975-1.135)	0.189		
MPF	100.919 (2.457-4145.860)	0.015		
<b>Post-TEER invasive hemodynamic parameters</b>				
LAP x/y wave	0.982 (0.885-1.089)	0.726		
LAP a/c wave	1.019 (0.931-1.115)	0.679		
Mean min LAP	1.004 (0.909-1.110)	0.934		
LAP v wave	1.003 (0.948-1.062)	0.908		
Mean LAP	0.994 (0.911-1.086)	0.900		
MPF	5.875 (0.001-84306.802)	0.770		
Higher $\Delta$ mean LAP <sup>a</sup>	1.782 (0.581-5.465)	0.313		
Higher $\Delta$ LAP v wave <sup>a</sup>	2.228 (0.894-5.553)	0.085		
Higher $\Delta$ MPF <sup>a</sup>	10.414 (1.330-81.558)	0.026	9.705 (1.162-81.061)	0.036

Continued on the next page

implantation. We did not find any significant relationship between hemodynamic variables included in the Cox regression model and the occurrence of MACE at follow-up (Table 5). Of note, baseline echocardiographic left ventricle end-systolic volume index was the only variable which correlated with MACE occurrence (Supplemental Tables 1 to 3).

We were able to collect functional follow-up data for 62 patients (83%). Forty-five patients (72%) reported improved functional status of  $\geq 1$  functional class as assessed by the NYHA classification, and 44 cases (70%) reported an overall improved functional status consistent with NYHA functional classes I/II,

which was significant as compared with the pre-TEER functional status ( $P < 0.001$ ). Median 12-item KCCQ post-TEER, assessed in 52 patients (67%), was 47 (IQR: 40-66), significantly higher than the baseline 12-item KCCQ ( $P < 0.001$ ).

NYHA class improvement at follow-up was associated with a significantly greater reduction in MPF, defined as a higher  $\Delta$ MPF value, as outlined in the box plot of the Central Illustration. Patients undergoing TEER procedure were further divided in 2 subgroups based on the variation in the 12-item KCCQ summary score before and after the procedure. An increase of  $\geq 20$  points in the KCCQ questionnaire was

**TABLE 5 Continued**

	At least 20 Points in 12-items KCCQ Improvement			
	Univariable Analysis		Multivariable Analysis	
	OR (95% CI)	P Value	OR (95% CI)	P Value
Pre-TEER invasive hemodynamic parameters				
LAP x/y wave	0.887 (0.815-0.965)	0.006	0.863 (0.785-0.950)	0.003
LAP a/c wave	0.953 (0.889-1.021)	0.173		
Mean min LAP	0.921 (0.853-0.994)	0.034	0.903 (0.829-0.984)	0.020
LAP v wave	1.027 (0.998-1.058)	0.070		
Mean LAP	0.990 (0.932-1.053)	0.759		
MPF	220.915 (7.537-6475.190)	0.002	192.269 (4.592-8050.280)	0.006
Post-TEER invasive hemodynamic parameters				
LAP x/y wave	0.943 (0.863-1.030)	0.191		
LAP a/c wave	0.970 (0.891-1.056)	0.482		
Mean min LAP	0.959 (0.878-1.046)	0.343		
LAP v wave	0.989 (0.939-1.042)	0.680		
Mean LAP	0.959 (0.889-1.034)	0.277		
MPF	14.336 (0.001-171645.087)	0.578		
Higher Δ mean LAP <sup>a</sup>	1.923 (0.763-4.842)	0.165		
Higher Δ LAP v wave <sup>a</sup>	2.449 (1.126-5.323)	0.024	2.938 (0.949-9.097)	0.062
Higher Δ MPF <sup>a</sup>	4.984 (1.434-17.319)	0.011	4.035 (1.129-14.416)	0.032

Hemodynamic variables reported in mm Hg and displayed as median (IQR) or mean ± SD. Hazard ratio was adjusted for sex, age, BMI, and LVEF. When assessing follow-up functional outcomes for NYHA classification and 12-item KCCQ version, the models were adjusted for baseline values of these variables. <sup>a</sup>Higher Δ mean LAP, Δ LAP v wave, and Δ MPF values are defined as values exceeding the median value of our study population.  
 Abbreviations as in Tables 1 and 4.

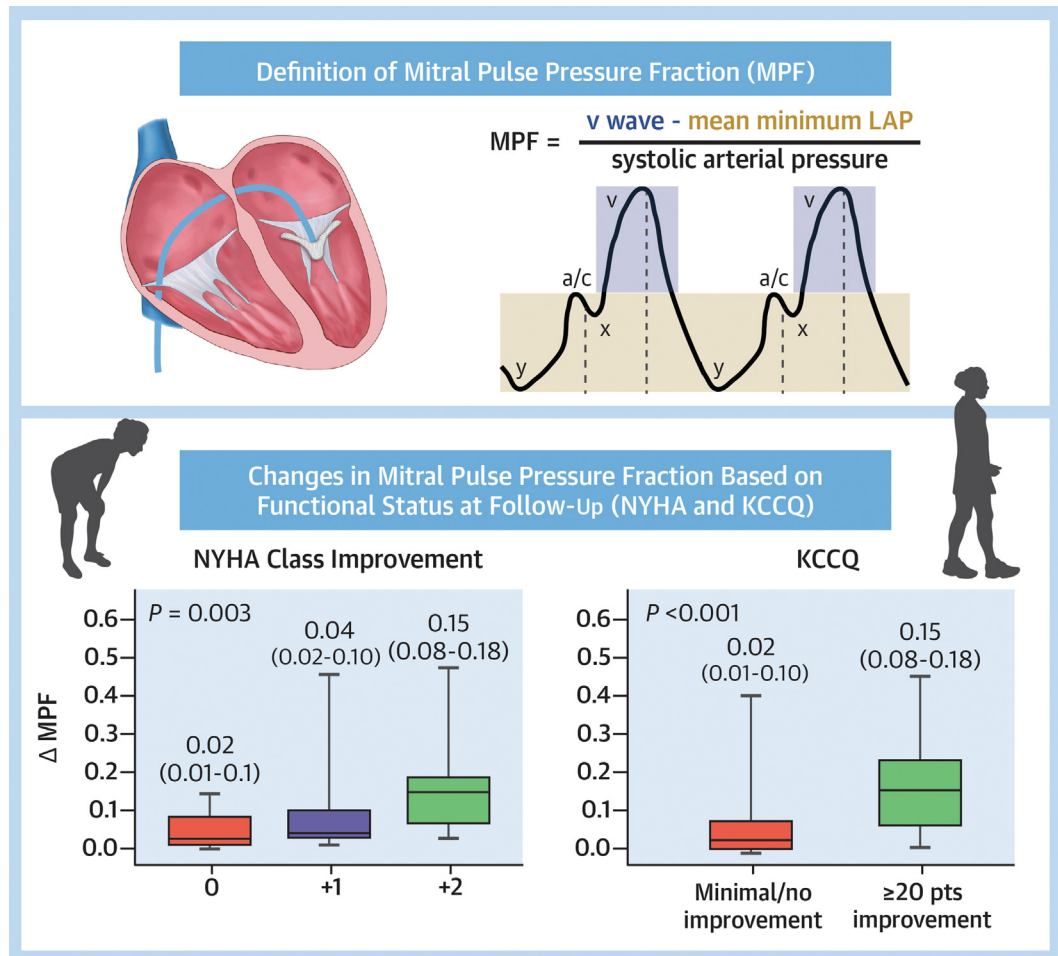
considered as an indicator of a major functional and clinical improvement during follow-up; patients reporting such an improvement showed a higher median ΔMPF, as depicted in the **Central Illustration**. When testing the relationship between variables and improvement in NYHA classification or in 12-item KCCQ at follow-up, higher MPF amplitude variation, defined as values exceeding the median value of MPF variation in our study population, was the only variable showing a significant association at the Cox multivariable analysis with both classifications, while variations in LAP v wave and mean LAP did not attain significant relationship with functional outcomes (**Table 5**).

## DISCUSSION

The hemodynamic response to TEER, highlighted by the improvement of several hemodynamic variables analyzed in our study, including MPF, is consistent with an overall favorable impact of the procedure on the LA dynamics. Preprocedural hemodynamics were comparable with the control group’s PCWP-derived assessment, while post-TEER results showed a significant improvement compared to both pre-TEER and control group’s hemodynamics. MR reduction as assessed by TEE was not associated with enhanced functional status during the follow-up period,

whereas a greater reduction in MPF demonstrated association with improved functional status with a substantial improvement in both NYHA classification and 12-item version of KCCQ.

Optimal procedural echocardiographic MR grade reduction was obtained in the vast majority of patients who underwent TEER procedure and, in all cases, intraprocedural TEE was used as a guidance to implant TEER. Despite improved echocardiographic MR appearance, 9 patients (11%) showed an increased MPF post-TEER with a resultant negative value of ΔMPF, linked to unfavorable LA dynamics and associated with worsening functional status at follow-up compared to cases where higher positive ΔMPF values were obtained. Overall, optimal MPF reduction and higher ΔMPF values were associated with improved functional status at follow-up. Taken together, these considerations, a procedural approach based on both TEE guidance and hemodynamic assessment through MPF variation, could offer incremental decisional benefits over the solely TEE and Doppler-derived indirect assessment of hemodynamics. MPF takes into account different hemodynamic variables capturing acute changes in loading conditions and atrial compliance which cannot be quantitatively and accurately measured by echocardiography,<sup>11</sup> in particular, in the post-TEER mitral valve anatomy<sup>12</sup> where post-TEER fluid dynamics

**CENTRAL ILLUSTRATION** Novel Hemodynamic Index Characterizing Mitral Regurgitation Undergoing Transcatheter Edge to Edge RepairLeone AM, et al. *JACC Adv.* 2024;3(8):101099.

Box plot showing the difference in median MPF after MV TEER when considering patients who reported clinical improvement of 2 or more classes as assessed by the NYHA classification and patients who showed 1 NYHA class improvement or no improvement (bottom left) and patients who showed improved 12-item KCCQ compared to patients who did not gain such a significant clinical improvement (bottom right). KCCQ = Kansas City Cardiomyopathy Questionnaire; LAP = left atrial pressure; MPF = mitral pulse pressure fraction; MV = mitral valve; TEER = transcatheter edge-to-edge repair.

could result in multiple and eccentric regurgitant jets with intraprocedural TEE assessment overestimating residual MR.<sup>13,14</sup> When a discordant result is obtained after TEER, for example, improved hemodynamics with high  $\Delta$ MPF but a suboptimal echocardiographic MR reduction, integrating both data in the decisional process could offer a better choice in terms of functional outcomes rather than just trying to achieve optimal echocardiographic MR reduction amplitude with additional clipping, considering that residual MR is not always independently associated with optimal

hemodynamic response.<sup>15</sup> In line with this principle, Kuwata et al.<sup>6</sup> demonstrated how continuous invasive pressure monitoring during TEER procedure can predict clinical outcomes independently from residual echocardiographic MR. A recent study by Sato et al.<sup>16</sup> further corroborated the integrated approach with echocardiographic and invasive pressure assessment to guide TEER procedure: patients with optimal hemodynamic result after TEER were associated to better outcomes at follow-up compared to other profiles with suboptimal echocardiographic and/or

hemodynamics, the latter including patients with optimal residual echocardiographic MR but with impaired post-TEER LA hemodynamics. Similarly, an early analysis by Gaemperli et al.<sup>17</sup> showed how improved hemodynamics in the post-TEER setting, defined as a significant reduction in mean PCWP, PCWP-estimated v wave, and mean pulmonary artery pressure, were associated with improved outcomes at follow-up. In line with our study's results, functional status improvement as assessed by the 6-minute walk test in a study by Maor et al.<sup>18</sup> was linked to favorable post-TEER hemodynamics, defined by a significant reduction of the v wave.

MR etiologies evaluated by echocardiography appeared to have a comparable response to TEER from a hemodynamic point of view. There was a trend towards higher  $\Delta$ MPF in the organic MR subgroup but it did not reach statistical significance. Larger population size could provide additional information on the association between MR etiology and TEER hemodynamic response. Nonetheless, 2 recently published studies have highlighted how MR etiology is not associated with outcomes in patients undergoing TEER<sup>19,20</sup> in line with the findings of our study.

Regarding technical aspects to obtain MPF monitoring, other than the femoral venous access used for the TEER procedure and the peripheral radial artery cannulation to monitor SAP, we did not have to obtain additional vascular accesses or to retrogradely navigate with vascular catheters into the aorta or left ventricle in order to invasively assess aortic or ventricular pressure. In all cases we analyzed, the steerable guide catheter provided to perform TEER procedure was sufficient to obtain optimal LAP tracing before and after clip implantation. This simplicity of invasive pressure monitoring with the avoidance of adding other intravascular catheters could be a major advantage and increase feasibility and adoption of live MPF calculation. However, a major limitation of the current Mitraclip system is represented by the waveform damping during the final step of the grasping procedure that can limit significantly the accuracy of an invasive pressure-guided intervention. Consequently, the availability of continuous pressure monitoring, by means of a larger guide catheter or of a dedicated transducer, would be warranted to perform a fully pressure-guided optimized TEER.

**STUDY LIMITATIONS.** The primary constraints of our present observational analysis stems from the restricted number of patients included in the study and the limited duration of the follow-up period. LAP

measurement during TEER was performed through the steerable guiding catheter rather than a dedicated atrial catheter: LAP could be over-dampened and there could be a left to right shunt via the interatrial septum after the removal of the steerable guiding catheter. However, considering that all measures were collected before clip insertion and after clip release (but before recrossing the interatrial septum), we suppose that these confounding factors have played a minor role. Moreover, we considered the invasive pressure from the radial artery cannulation as the standard to monitor the intraprocedural systolic pressure, but the former is not a true reflection of LV systolic pressures and could be prone to some degree of overestimation. Furthermore, an increase in systemic vascular resistance can contribute to the elevation of systolic blood pressure. PCWP extracted from RHC was used to calculate MPF in the control group and this invasive parameter could be prone to measurement error and influenced by the hemodynamic condition of patients during RHC. The statistical analysis lacked adjustment for multiple comparisons, emphasizing the need for caution in interpreting the results.

## CONCLUSIONS

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MPF is a novel index providing an immediate estimate of the hemodynamic impact of MR. TEER is an effective treatment of MR, irrespective of the etiology of MR, even in terms of change in MPF. More importantly, the amount of MPF change is favorably correlated to a change in functional status.

Considering the ease of MPF calculation, its integration on top of intraprocedural echocardiographic guidance could offer a prompt and accurate prediction of functional clinical improvement after TEER and a possible hemodynamic guide to intervention.

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## PERSPECTIVES

**COMPETENCY IN PATIENT CARE AND**

**PROCEDURAL SKILLS:** Invasive hemodynamic monitoring during TEER can have incremental intraprocedural value on top of echocardiographic guidance. MPF change after TEER was the only invasive hemodynamic parameter correlated with improved functional status at follow-up as assessed by both NYHA classification and the 12-item

version of KCCQ, independently from the echocardiographic assessment during TEER.

**TRANSLATIONAL OUTLOOK:** Multicenter trials enrolling more patients undergoing TEER could confirm the results of our study and provide additional data on the relationship between invasive hemodynamic monitoring and clinical outcomes.

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**KEY WORDS** invasive hemodynamic monitoring, mitral regurgitation, mitral valve, transcatheter mitral valve edge-to-edge repair

**APPENDIX** For supplemental tables, please see the online version of this paper.