

## RESEARCH ARTICLE

# Invasive hemodynamics are equivocal for functional outcomes after MitraClip

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**Abstract**

**Objectives:** To evaluate invasive hemodynamics in assessing MC therapy success as well as evaluate its effectiveness as a predictor of functional outcomes.

**Background:** Mitral regurgitation grade is a poor predictor of functional outcomes after a MitraClip. There is a paucity of data on invasive hemodynamics as a predictor of outcomes.

**Methods:** Sixty-nine patients underwent MC between 2015 and 2018 at the University of Minnesota Medical Center and were retrospectively analyzed. Invasive hemodynamics were performed before and after device deployment with transesophageal echocardiographic guidance. Statistical analysis was performed using STATA version 16. Student's *t* test was used for continuous variables and Pearson's chi-squared test for categorical variables. Mann-Whitney test was performed for continuous variables where data were not normally distributed. Logistic and linear regression were used to investigate relationships between variables and outcomes.

**Results:** A total of 69 patients were included in the study. The mean age was 83 (75-87) years and 38 (55%) were male. Eighty-one percentage had  $\geq$  NYHA III symptoms. Eighty-seven percentage had severe MR. Pulmonary capillary wedge pressure was 20 (15-24). Overall, there was significant improvement in left atrial pressure including mean left atrial pressure index, MR, and NYHA class after MC ( $<.001$ ). There was no significant association between invasive hemodynamics (including left atrial mean pressure index or its reduction rate) and functional outcomes ( $p = \text{NS}$ ). MR grade was also not predictive of functional outcomes.

**Conclusion:** Left atrial pressure may not be a significant predictor of functional outcomes, and, in isolation, may not be an improvement over MR grade.

**KEYWORDS**

left atrial pressure, MitraClip, mitral regurgitation, mitral valve, structural heart disease, valvular heart disease

**Abbreviations:** CI, cardiac index; CO, cardiac output; KCCQ, Kansas City Cardiomyopathy Questionnaire; LAP, left atrial pressure; MC, MitraClip; MR, mitral regurgitation; NYHA, New York Heart Association; STS, Society of Thoracic Surgeons; SVR, systemic vascular resistance; TEE, transesophageal echocardiogram; UMMC, University of Minnesota Medical Center.

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## 1 | INTRODUCTION

Transcatheter mitral valve repair has shown significant promise in the treatment of complex degenerative and functional mitral valve disease since its Federal Food and Drug Administration (FDA) approval in 2013.<sup>1</sup> Recent data have shown that reducing mitral valve regurgitation (MR) with MitraClip (MC) therapy improves mortality and functional outcomes.<sup>2</sup> Greater than mild residual MR after MC has been shown to correlate with poor outcomes and worsening mortality.<sup>3</sup>

However, MR assessment using TEE becomes more difficult after MC deployment, due to the complexity of the mitral valve apparatus and the role of hemodynamics in modifying MR.<sup>4</sup> Recently, analysis of successful implantation with transesophageal echocardiography (TEE) has been put to question.<sup>5</sup> Echocardiographic quantification of residual MR following MC is challenging due to several reasons: presence of the clip itself, eccentricity of MR jets, multiple MR jets, as well as dynamic and altered anatomy of the mitral valve orifice secondary to MC.<sup>4,6</sup> Although TEE may be adequate in estimating the magnitude of

**TABLE 1** Demographics and clinical characteristics

Parameter	Overall (n = 69)	NYHA improved (n = 37)	NYHA unimproved (n = 32)	P
Clinical characteristics				
Age	83 (75-87)	85 (78-89)	79 (75-86)	.224
Female gender	45% (31)	43% (16)	47% (15)	.762
NYHA				.184
I	2.9% (2)	0% (0)	6% (2)	
II	16% (11)	14% (5)	19% (6)	
III	64% (44)	62% (23)	66% (21)	
IV	17% (12)	24% (9)	9.4% (3)	
Body mass index, kg/m <sup>2</sup>	25 (23-29)	24 (23-29)	26 (23-29)	.656
CHF	65% (45)	54% (25)	63% (20)	.659
Myocardial infarction	22% (15)	27% (10)	16% (5)	.252
Prior valve surgery	17% (12)	8% (3)	28% (9)	<b>.029</b>
PCI	29% (20)	24% (9)	34% (11)	.884
CABG	29% (20)	27% (10)	32% (10)	.700
Stroke	8.7% (6)	11% (4)	6.3% (2)	.503
Hyperlipidemia	87% (60)	84% (31)	91% (29)	.400
Hypertension	71% (49)	70% (26)	72% (23)	.884
Diabetes	19% (13)	14% (5)	25% (8)	.224
COPD	38% (26)	41% (15)	34% (11)	.598
Coronary artery disease	88% (61)	84% (31)	94% (30)	.197
Prior CHF hospitalization	65% (45)	68% (25)	63% (20)	.537
Ambulatory cardiogenic shock	45% (31)	36% (12)	59% (19)	<b>.046</b>
Atrial fibrillation	70% (48)	65% (24)	75% (24)	.362
STS score, Repair	6.1 (4.1-9.4)	7.1 (5-11)	4.9 (4.1-7.2)	<b>.026</b>
Creatinine	1.2 (0.9-1.4)	1.2 (0.9-1.5)	1.2 (1.0-1.4)	.217
Echocardiographic parameters				
Degenerative MR	87% (60)	84% (31)	90% (29)	.755
LVEF	55 (44-60)	55 (47-62)	51 (44-59)	.164
LVIDd	5.2 (4.7-5.8)	5.2 (4.8-5.9)	5.0 (4.5-5.6)	.263
LAVI, mL/m <sup>2</sup>	59 (47-70)	59 (47-71)	62 (41-73)	.898
MR grade				.191
III	13% (9)	8 (3)	19% (6)	
IV	87% (60)	92% (34)	81% (26)	

Note: Numbers in boldface indicate *P* values <.05.

Abbreviations: CABG, coronary artery bypass grafting; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; LAVI, left atrial volume index; LVEF, left ventricular ejection fraction; LVIDd, Left ventricular internal diameter end diastole; MR, mitral regurgitation; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; STS, Society of Thoracic Surgeons.

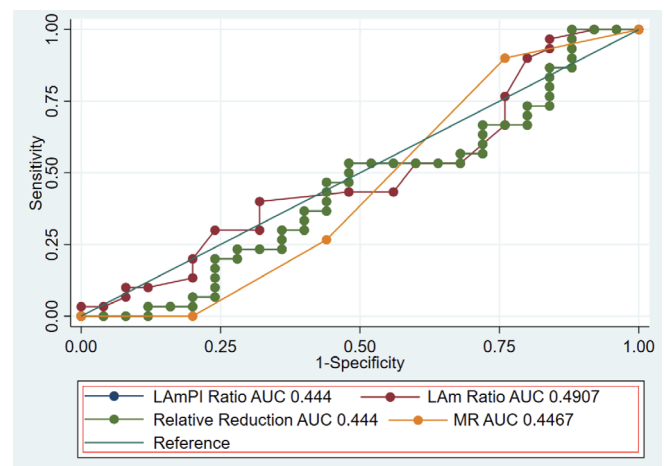
a single regurgitating jet, the complex Doppler flow created by multiple jets after MC implantation leads to a wide range of variability in assessment.<sup>7</sup> Furthermore, volume loading and afterload can also lead to a range of MR values that further attenuate its usefulness.<sup>8,9</sup>

Multiple observational studies have evaluated other means of assessing MR; in particular, using hemodynamics.<sup>10</sup> Both continuous and discontinuous measurements have been used to evaluate MC success based on various measures, both direct and indirect of left atrial pressure (LAP).<sup>5</sup> As a result, hemodynamics have been shown to better correlate with functional outcomes as compared with MR grade alone.<sup>5,11</sup> Moreover, this has led Abbott Vascular to introduce an innovative improvement to the MC mitral repair system that allows continuous measurement of LAP in an attempt to improve these outcomes.<sup>12</sup> However, there is still a paucity of data evaluating the utility of hemodynamics in assessing MC therapy and success, and even fewer studies addressing correlation to functional outcomes.<sup>11,13</sup> The aim of our study is to build on other studies, such as Kuwata et al, and evaluate invasive hemodynamics in the assessment of MC therapy success as well as evaluate its effectiveness as a predictor of functional outcomes.<sup>5</sup>

## 2 | MATERIALS AND METHODS

University of Minnesota Medical Center (UMMC) is a quaternary, 800-bed hospital in Minneapolis, MN. UMMC was an early adopter of the MitraClip procedure with implementation in 2014 and performed almost 100 MC procedures between 2014 and 2019, along with a number of other structural procedures. We retrospectively analyzed 69 consecutive patients undergoing MC at UMMC between 2014 and 2018. Data were obtained from the standard transvalvular therapy (TVT) data collection forms, and additional data were collected from the electronic medical record as needed.

During the MC procedure, continuous LA pressure monitoring was performed using Abbott Vascular's pigtail catheter. This technique has been previously validated in multiple studies.<sup>11,13</sup> Blood pressure was measured invasively using a radial arterial line. Right atrial pressure measurement was performed prior to transeptal puncture. In patients where continuous right heart hemodynamics were present, cardiac output (CO), index (CI), and systemic vascular resistance (SVR) were recorded. LAP indices were calculated in the following manner: left atrial mean pressure index = left atrial mean pressure/systolic blood pressure. Other indices such as left atrial V-wave and A-wave pressure index were calculated in the same manner. LAP (mean, V-wave, A-wave) were also indexed to CO, CI, and SVR



**FIGURE 1** Improvement in NYHA class. This figure shows the outcome value of “Improvement in NYHA Class” with ROC curves and values for LAmP ratio, LAmPI ratio, MR, and relative reduction. Each of the curves is nonsignificant. LAmPI, left atrial mean pressure index; LAm, left atrial mean; MR, mitral regurgitation; AUC, area under the curve

**TABLE 2** Periprocedural characteristics

Parameter	Overall (n = 69)	NYHA improved (n = 37)	NYHA unimproved (n = 32)	P
MVARC bleeding	10% (7)	5% (2)	16% (5)	.161
Major vascular complications	13% (9)	8.1% (3)	19% (6)	.191
Infection	7.2% (5)	5.4% (2)	9.4% (3)	.526
Conversion to surgery	0% (0)	0% (0)	0% (0)	1.000
Technical success	87% (66)	95% (35)	78% (25)	.075
Greater or equal to moderate residual MR at intraprocedural assessment	20% (14)	16% (6)	25% (8)	.295
Greater or equal to moderate residual MR at discharge	29% (20)	92% (9)	34% (11)	.314
Length of stay, days	3 (2-5)	2 (1-4)	4 (2-5)	<b>.043</b>
Clip implantations	1.5 (1-2)	1.5 (1-2)	1.5 (1-2)	.624
Duration of procedural time, min	176 (144-244)	152 (131-198)	197 (165-264)	<b>.003</b>
Fluoroscopy time, min	28 (19-49)	31 (19-34)	43 (24-58)	<b>.033</b>

Note: Numbers in boldface indicate P values <.05.

Abbreviations: MR, mitral regurgitation; MVARC, Mitral Valve Academic Research Consortium; NYHA, New York Heart Association.

**TABLE 3** Invasive hemodynamic parameters

Parameter	Baseline			Post-Procedure		
	NYHA improved (n = 37)	NYHA unimproved (n = 32)	P	NYHA improved (n = 37)	NYHA unimproved (n = 32)	P
PCWP a, mmHg	20 (15-25)	17 (15-22)	.416	14 (9-18)	12 (10-19)	.629
PCWP v, mmHg	31 (23-40)	33 (25-45)	.481	20 (15-26)	25 (19-28)	.206
mPCWP, mmHg	17 (15-24)	20 (14-25)	.446	12 (10-16)	15 (10-19)	.420
LAVpI, mmHg	0.276 (0.205-0.374)	0.299 (0.205-0.381)	.631	0.152 (0.119-0.214)	0.208 (0.187-0.288)	.069
LAmPI, mmHg	0.164 (0.142-0.190)	0.192 (0.119-0.227)	.528	0.100 (0.082-0.137)	0.115 (0.080-0.184)	.374
LA compliance, mL/mmHg	6.15 (3.75-8.53)	5.42 (4.79-6.99)	.911	9.31 (6.69-16.0)	9.90 (4.82-16.0)	.966
SVR, dynes/seconds/cm <sup>-5</sup>	1787 (1029-2080)	1672 (1158-1992)	.670	1596 (1133-2102)	1496 (1075-1886)	.356

Abbreviations: LA, left atrial; LAmPI, left atrial mean pressure index; LAVpI, left atrial V-wave pressure index; mPCWP, mean pulmonary capillary wedge pressure; NYHA, New York Heart Association; PCWP A, pulmonary capillary wedge pressure A wave; PCWP v, pulmonary capillary wedge pressure V wave; SVR, systemic vascular resistance.

where available. LA compliance was calculated using TEE-derived LA volume index/left atrial mean pressure. Left atrial compliance calculation has been previously validated by using invasive hemodynamics combined with echocardiographic measurements.<sup>14</sup> The change in periprocedural hemodynamic parameters was measured as both a delta (pre-procedure value – post-procedure value/pre-procedure value × 100) and a ratio (post-procedure value/pre-procedure value × 100).

Outcomes were assessed according to the Mitral Valve Academic Research Consortium criteria.<sup>15</sup> Device success was defined as implantation of at least one MC device, absence of mortality, freedom from emergent surgery. Follow-up was performed at 30 days, 6 months, and 1 year with functional and echocardiographic evaluation. All echocardiograms were performed and read by level III operators. Baseline and follow-up functional assessment was done according to the New York Heart Association (NYHA) criteria, KCCQ-12 questionnaire, and 6-minute walk test. Outcome endpoints were improvement in NYHA class of  $\geq$  one class, improvement in KCCQ-12 score or 6-minute walk test at 30 days, and freedom from hospitalization due to heart failure on follow-up.

Continuous variables are calculated as mean with SD or as median with interquartile range when appropriate based on normality of the data. These data were analyzed using Student's *t* test or Mann-Whitney test where appropriate. Categorical variables are reported as frequencies and percentages and analyzed using chi-square test or Fisher exact test. Relationships between variables were analyzed using logistic regression. A *P* value  $<.05$  was considered to be statistically significant. STATA version 16 was used for analysis. The study was approved by the Institutional Review Board of the University of Minnesota Medical Center. Individual consent requirement was waived.

### 3 | RESULTS

Sixty-nine patients underwent MC at UMMC from 2014 through 2018, of whom 55% were male. The median age of the study population was 83 years. The median Society of Thoracic Surgeons (STS) score was 7.6 for mitral valve (MV) repair and 9.7 for MV replacement. Grade IV MR was present in 87% and grade III MR in 13% of the population. Exactly 17% of the population had NYHA class IV and 64% NYHA III symptoms prior to MC therapy. The rest of the baseline characteristics are reported in Table 1. Patients were less likely to have improvement in their NYHA functional class if they had prior valve surgeries (*P* = .029) or ambulatory cardiogenic shock (*P* = .046) prior to the procedure. There was also a significant difference between STS score for MV repair between patients whose NYHA class improved and those whose NYHA class did not improve (*P* = .026).

Interestingly, patients with a shorter MC overall procedure time (*P* = .003) and shorter fluoroscopy time (*P* = .03) were more likely to see improvement in their NYHA functional class after the procedure, as seen in Table 2. We do not have direct evidence, but it is possible that patients with a shorter procedure and less radiation time had more straightforward anatomy that made the MC procedure quicker. This will need to be studied more extensively in the future. In retrospective analysis, patients with an improvement in their NYHA functional class also had a shorter length of stay periprocedurally (0.043). There was no significant difference in number of clips placed, procedural complication, or residual MR compared with improved and unimproved functional classes.

Invasive hemodynamics were performed in all patients. There was a significant improvement in both MR grade and invasive hemodynamics after MC therapy. Left atrial mean pressure improved from 20 to 13 mmHg (*P*  $<.001$ ). Similarly, there was a significant improvement in other LAP parameters such as A- and V-waves as well as all pressure

**TABLE 4** Relationship between intraprocedural parameters and NYHA class improvement

Logistic regression model		
	Univariate analysis	
	Odds ratio (95% CI)	P
Pre-procedural invasive hemodynamic parameters		
PCWP a, mmHg	1.04 (0.941-1.15)	.446
PCWP v, mmHg	0.990 (0.950-11.03)	.619
PCWP mean, mmHg	0.981 (0.915-1.05)	.578
LAVPI, mmHg	0.343 (0.005-21.6)	.613
LAmPI, mmHg	0.205 (.0003-136.8)	.633
LA compliance, mL/mmHg	1.06 (0.875-1.28)	.552
SVR, dynes/seconds/cm <sup>-5</sup>	1.00 (0.999-1.001)	.690
Pre-procedural TEE parameters		
MR grade	2.62 (0.597-11.5)	.202
Noninvasive mPG	1.00 (0.788-1.28)	.973
Post-procedural invasive hemodynamic parameters		
PCWP a, mmHg	1.02 (0.944-1.11)	.573
PCWP v, mmHg	0.981 (0.931-1.03)	.485
PCWP mean, mmHg	0.974 (0.902-1.05)	.519
LAVPI, mmHg	0.015 (0.00004-5.26)	.161
LAmPI, mmHg	0.032 (0.00002-50.98)	.360
LA compliance, mL/mmHg	0.997 (0.891-1.12)	.960
SVR, dynes/seconds/cm <sup>-5</sup>	1.00 (0.999-1.002)	.220
Post-procedural TEE parameters		
MR grade	0.532 (0.162-1.75)	.299
Noninvasive mPG	0.824 (0.635-1.07)	.147
Reduction rate of invasive hemodynamic parameters		
PCWP a, mmHg	0.996 (0.979-1.01)	.673
PCWP v, mmHg	0.997 (0.980-1.01)	.737
PCWP mean, mmHg	0.995 (0.980-1.01)	.539
LAVPI, mmHg	0.990 (0.974-1.01)	.261
LAmPI, mmHg	0.993 (0.979-1.01)	.314
LA compliance, mL/mmHg	1.00 (0.975-1.03)	.260

Abbreviations: LA, left atrial; LAmPI, left atrial mean pressure index; LAVPI, left atrial V-wave pressure index; mPCWP, mean pulmonary capillary wedge pressure; mPG, mean pressure gradient; MR, mitral regurgitation; NYHA, New York Heart Association; PCWP A, pulmonary capillary wedge pressure A wave; PCWP V, pulmonary capillary wedge pressure V wave; SVR, systemic vascular resistance.

indexed values (ie, left atrial mean pressure index). There was no difference between baseline and post-procedure systemic pressures. Exactly 29% of patients had residual moderate or severe MR after MC therapy. There was a significant improvement of MR grade post-procedure in 71% of the patients, who had mild, trivial, or no MR post-procedure. Post-procedure left atrial compliance was 9.31 and 9.90, respectively, among those whose NYHA class improved vs those whose class did not improve ( $p = \text{NS}$ ). Figure 1 shows the receiver operating curve of several

hemodynamic variables, indicating that they are neither sensitive nor specific for predicting MC outcomes.

There was no significant association between baseline or post-procedural invasive hemodynamics and functional improvement, or lack thereof, based on NYHA class (Table 3). There was a significant difference between the 6-minute walk test post-procedure between those with improved NYHA function (1100 ft) and those with unimproved NYHA functional class (855 ft) ( $P = .029$ ). There was no significant difference in the pre-procedure 6-minute walk tests, pre-procedure KCCQ-12 score, or post-procedure KCCQ-12 scores between those with improved and unimproved NYHA classes.

When reviewing the relationship between the intraprocedural parameters and improvement in NYHA functional class improvement, there were no parameters that were statistically significant by logistic regression modeling (Table 4). Relationship between intraprocedural parameters and rehospitalization at 30 days can be seen in Table 5. Of invasive hemodynamic parameters, pre-procedural mean pulmonary capillary wedge pressure was the only variable that showed association with rehospitalization at 30 days for heart failure ( $P = .048$ ). Functional parameters associated with rehospitalization included both pre- and post-procedural KCCQ-12 scores ( $P = .021$  and  $P = .005$ , respectively).

Of note, KCCQ-12 score significantly improved from preoperatively ( $P < .001$ ); however, although there was a numerical trend toward improvement in post-procedural 6-minute walk tests, the results were not statistically significant (Table 6).

## 4 | DISCUSSION

The MV apparatus is a very complex structure with multiple different architectural and dynamic facets that incorporates compliance, preload, and afterload to determine its successful function. Its complexity creates multiple points at which pathology can alter one or more of these aspects, affecting its function and leading to MR.<sup>16</sup> Depending on which component is involved, MR can be either degenerative or functional.<sup>17</sup> These categories are then better represented by Carpentier classes of MR, which illustrate the myriad of mechanisms involved in this process.

Historically, surgeons have been most successful with attenuation of degenerative MR as the pathology is primarily in the MV itself and not in the ventricular or atrial part of the apparatus. Moreover, repair, rather than replacement, has delivered the best mortality and functional outcomes if successful in eliminating all MR.<sup>18</sup> Functional MR, while surgically correctable, continues to suffer from inevitable pump failure as the primary mechanism, thus attenuating outcomes.<sup>19</sup> More recently, advances in transcatheter technology have produced a number of percutaneous MV repair and replacement techniques. The most studied of these has been MC therapy, which is based on Alfieri stitch first described in 1991.<sup>20</sup>

Subsequent studies of the MC device in the EVEREST I and II trials showed that successful attenuation of MR is achieved in ~70% of the patient population.<sup>21,22</sup> This is not unexpected given that

**TABLE 5** Relationship between procedural parameters and rehospitalization at 30 days for heart failure

Logistic regression model				
	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	P	95% CI	P
Pre-procedural invasive hemodynamic parameters				
PCWP a, mmHg	0.793 (0.622-1.01)	.063	0.832 (0.500-1.38)	.479
PCWP v, mmHg	0.955 (0.892-1.02)	.181		
PCWP mean, mmHg	0.872 (0.763-0.999)	<b>.048</b>	0.277 (0.320-1.39)	.277
LAVPI, mmHg	0.317 (0.001-128)	.707		
LAmPI, mmHg	0.001 (8.19e-09-40.13)	.190		
LA compliance, mL/mmHg	1.00 (0.835-1.21)	.965		
SVR, dynes/seconds/cm <sup>-5</sup>	0.999 (0.997-1.00)	.120		
Pre-procedural TEE parameters				
MR grade	0.444 (0.073-2.70)	.378		
Noninvasive mPG	0.769 (0.360-1.64)	.498		
Post-procedural invasive hemodynamic parameters				
PCWP a, mmHg	0.995 (0.893-1.11)	.927		
PCWP v, mmHg	0.996 (0.932-1.07)	.911		
PCWP mean, mmHg	1.00 (0.910-1.10)	.973		
LAVPI, mmHg	2.31 (0.002-3235)	.821		
LAmPI, mmHg	0.880 (0.00003-30 385)	.981		
LA compliance, mL/mmHg	0.904 (0.751-1.09)	.286		
SVR, dynes/seconds/cm <sup>-5</sup>	0.999 (0.997-1.00)	.219		
Post-procedural TEE parameters				
MR grade	0.884 (0.187-4.19)	.876		
Noninvasive mPG	0.915 (0.604-1.39)	.675		
Reduction rate of invasive hemodynamic parameters				
PCWP a, mmHg	1.03 (0.987-1.09)	.159		
PCWP v, mmHg	1.01 (0.989-1.04)	.302		
PCWP mean, mmHg	1.02 (0.998-1.05)	.070	1.45 (0.866-2.43)	.157
LAVPI, mmHg	1.01 (0.985-1.03)	.545		
LAmPI, mmHg	1.02 (0.996-1.04)	.114		
LA compliance, mL/mmHg	1.02 (0.985-1.05)	.303		
Pre-procedural functional parameters				
KCCQ-12	0.954 (0.917-0.993)	<b>.021</b>	0.977 (0.927-1.03)	.382
6-minute walk test	0.998 (0.996-1.000)	.128		
Post-procedural functional parameters				
KCCQ-12	0.920 (0.867-0.975)	<b>.005</b>	0.925 (0.869-1.04)	.352
6-minute walk test	0.999 (0.995-1.004)	.908		

Note: Numbers in boldface indicate P values <.05.

Abbreviations: KCCQ, Kansas City Cardiomyopathy Questionnaire; LA, left atrial; LAmPI, left atrial mean pressure index; LAVPI, left atrial V-wave pressure index; mPCWP, mean pulmonary capillary wedge pressure; mPG, mean pressure gradient; MR, mitral regurgitation; NYHA, New York Heart Association; PCWP A, pulmonary capillary wedge pressure A wave; PCWP V, pulmonary capillary wedge pressure V wave; SVR, systemic vascular resistance.

surgeons frequently employ at least two repair methodologies (leaflet resection and annulus reduction) to completely eliminate MR. However, as shown in the COAPT trial, a minimal amount of residual MR may not be an entirely flawed design in the setting of a

failing ventricle as is common in functional MR. The COAPT trial showed that patients with functional MR undergoing MC therapy have not only improved functional status but also improved mortality.<sup>2</sup> As indicated in our study, there are certain groups of patients



**TABLE 6** Comparison of functional parameters

Parameter	Pre-procedure	Post-procedure	P
KCCQ-12	36 (14-52)	74 (63-86)	<b>&lt;.001</b>
6-minute walk test, feet	970 (670-1162)	952 (812-1210)	.113

Note: Numbers in boldface indicate *P* values <.05.

Abbreviations: KCCQ, Kansas City Cardiomyopathy Questionnaire.

who seem less likely to symptomatically benefit from MC, including those with prior valve surgeries, as well as prior episodes of ambulatory cardiogenic shock.

Challenges remain at assessing procedure success based on MR grade alone. This is largely because TEE assessment of MR grade becomes convoluted when MC therapy introduces multiple regurgitant jets.<sup>23,24</sup> No single evaluation of these jets has been shown to adequately correlate with functional or mortality outcomes.<sup>25,26</sup> The PISA method and summation of vena contracta is not reliable in the presence of multiple MR jets created by MC therapy.<sup>27</sup> While 3D TEE imaging enables the operator to measure the vena contracta as well as the EROA directly by 3D planimetry, such measurements can lead to an overestimation after MC therapy.<sup>28</sup> Invasive hemodynamics, which have the advantage of being accurately assessed intraprocedural have advanced to the forefront of this assessment.<sup>29,30</sup> Yet, instant assessment of left atrial pressures is also fraught with inconsistencies as the MV apparatus is heavily dependent on both preload and afterload parameters.<sup>31</sup> As a result, drastic changes in preload and afterload that occur during the MC procedure can not only dramatically change the degree of MR seen TEE, but also the LAP changes seen invasively.<sup>32</sup>

To address this confounder, Kuwata et al indexed the LAP to left ventricular systolic pressure.<sup>5</sup> Based on this evidence, new generation MitraClip systems incorporate continuous LAP measurement functionalities without requiring additional tools such as pigtail catheters. Our study assessed whether findings reported by Kuwata et al could be validated in a sicker cohort with higher pulmonary capillary wedge pressures. Although studies have shown that LAP index is successful at predicting both functional status as well as risk of rehospitalization, more data are needed to address whether other variables are playing a role.<sup>32</sup> The data in this study are significant for a number of reasons; first, there is a larger cohort of patients than in prior studies that have evaluated hemodynamics as a determinant or predictor of outcomes. Second, our findings are consistent with a wealth of earlier data that MC therapy improves left atrial hemodynamics and TEE MR grade. Third, this study is also consistent with the data that MC therapy improves functional outcomes in patients with severe functional MR, including NYHA class, KCCQ, 6-minute walk test, and rehospitalization.<sup>30,32</sup> Most importantly, this study shows that invasive hemodynamics, including indexed values, are not better determinants of functional outcomes, and are similar to MR grade in their predictive capacity.

We also go one step further and introduce the measure of left atrial compliance as a possible predictor of outcomes. In general, left atrial compliance can be problematic as measurement of LAP is often

indirect and pulmonary vein flow is often used as a surrogate.<sup>33</sup> In our study, however, we were able to estimate left atrial compliance with greater accuracy due to invasive hemodynamic measurements. Furthermore, LAP varies with systemic pressure, and as a result, single-point measurements can be ineffective without accounting for systemic changes.<sup>34</sup> As a result, we have also analyzed indexed values of left atrial compliance for both volume and pressure to address these concerns. We do this with the assumption that chronic changes in left atrial compliance as a result of fibrosis due to continuous exposure to high pressures may lead to a worse response in these patients.<sup>35</sup> Low left atrial compliance is generally considered to be <4 mmHg and associated with poor outcomes.<sup>36</sup> Our average compliance was >5, and was not significantly different than both groups. Multiple studies evaluating left atrial compliance in other left atrial pathologies such as atrial fibrillation have shown its role and importance in determining treatment success.<sup>37,38</sup> Despite this, left atrial compliance alone is not a significant predictor of outcomes, although numerically it does appear to be an improvement over the other parameters.

Overall, functional parameters seem to have more consistently significant relationships with NYHA functional class improvement and rehospitalization at 30 days for heart failure. This is possibly related to the fact that both NYHA and KCCQ-12 are subjective measures of patient symptoms; however, 6-minute walk test and rehospitalization are objective measures that provide definable endpoints to support initially subjective assessments.

What is more likely is that none of these variables alone can predict functional outcomes effectively. This intuitively makes sense because it is the combination of all of these parameters that allow the mitral apparatus to function as a single successful dynamic and architectural unit. As a result, improving only one parameter may address a part of the equation, but does not address the pathology as a whole. More data are necessary to define meaningful predictors of successful MV therapy as it relates to functional outcomes as well as patient selection.

Our study has several limitations. First, this is a retrospective cohort analysis of a single-center population. Second, despite having a larger cohort of patients than seen in prior studies, the overall population of the study is relatively small from a moderate volume TMVr center, spanning multiple years and multiple generations of the device, which may affect results.<sup>39,40</sup>

Also of note, between 20% and 30% of patients had residual MR on discharge. This was similar across the group that improved and that did not improve from the standpoint of NYHA class. In our study, given the higher left atrial compliance, it was difficult to assess for outcomes based on these values. Pulmonary vein flow was also not addressed in this study, which should be addressed in subsequent studies. In the future, larger studies will lend more power and show statistical significance in values that only trended toward significance in our study.

## 5 | CONCLUSION

LAP may not be a significant predictor of functional outcomes; and, in isolation, may not be an improvement over MR grade or any other

single predictor of technical success. Integrated markers are necessary to define functional success after MC therapy.

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## CONFLICT OF INTEREST

This manuscript has not been previously published and is not under consideration for publication elsewhere. The authors have no conflicts of interest to disclose.

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All authors have read and approved the manuscript.

Sergey Gurevich had full access to all of the data in the study and takes complete responsibility for the integrity of the data and the accuracy of the data analysis.

## TRANSPARENCY STATEMENT

The lead author affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

## DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author, Sergey Gurevich, upon reasonable request.

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