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Right Heart Dysfunction and Clinical Outcomes in Patients with Severe Mitral Regurgitation undergoing MitraClip

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ABSTRACT

Background: *At present, it is unclear whether right heart dysfunction (RHD) predicts adverse outcomes in patients with severe mitral regurgitation (MR) after transcatheter mitral valve repair.*

Methods: *74 consecutive patients treated with MitraClip at our institution were included in the analysis. Right heart catheterization (RHC) hemodynamics were assessed to determine right atrial pressure (RAP), right ventricular diastolic pressure (RVDP), RV +dP/dT, RV systolic pressure (RVSP), mean pulmonary artery pressure (MPAP), right ventricular failure index (RVFI, ratio of RAP to pulmonary capillary wedge pressure (PCWP)), and pulmonary vascular resistance (PVR). Transthoracic echocardiograms were reviewed to determine RA volume index (RAVI), severity of tricuspid regurgitation (TR), RV diameter, tricuspid annular plane systolic excursion (TAPSE), DTI-derived tricuspid lateral annular systolic velocity (RV S'), severity of pulmonic regurgitation (PR), RVSP, PASP, and RFVI. Cox proportional hazard models were utilized to examine the relation between variables and mortality.*

Results: *The median STS risk was 10%. RAP >15 mmHg (HR: 4.1, 95%CI: 1.1-16), RVDP >10 mmHg (HR: 13, 95%CI: 2.5-67), MPAP >40mmHg (HR: 3.5, 95% CI: 1.03-12), RVFI (RA/PCWP) >0.63 (HR: 3.0, 95%CI: 1.04-8.5), and PVR >3 Woods units (HR: 3.5, 95% CI: 1.2-10.1) were significantly associated with increased risk of death. In contrast, none of the echocardiographic variables were predictive of death after MitraClip.*

Conclusions: *Invasively measured reduced RV systolic function (elevated RFVI (RA/PCWP)), elevated RH filling pressures (RAP and RVDP), and pulmonary artery hypertension (elevated MPAP and PVR) may identify patients with severe MR undergoing MitraClip who are at increased risk of adverse outcomes.*

Keywords

Mitral regurgitation, Right heart, Right ventricular dysfunction, Heart failure, Catheterization.

Introduction

Patients with severe, symptomatic mitral valve regurgitation (MR) have increased morbidity and mortality and it is predicted that the prevalence of severe, symptomatic MR will continue to increase [1,2]. Importantly, many patients with severe MR have a high burden of comorbidities thereby making them poor candidates for surgical mitral valve repair or replacement. MitraClip provides percutaneous repair of the mitral valve similar in mechanism to the surgical Alfieri stitch and is approved for patients with severe functional and degenerative MR at high or extreme surgical risk [3,4]. While it is clear that MitraClip reduces the severity of MR and consequent clinical heart failure (HF) burden [3,4], the mechanisms which contribute to poor clinical outcomes in patients after MitraClip are not well delineated. Right heart dysfunction (RHD) is linked with adverse outcomes in patients with coronary artery disease, valvular heart disease, and chronic heart failure [5-9]. Additionally, the ratio of right atrial pressure (RAP) to pulmonary capillary wedge pressure (PCWP) (RA/PCWP) >0.63 has proven to be a strong predictor of mortality in patients with left-sided heart failure [10]. More specifically, the RA/PCWP is a descriptor of the relationship between right and left-sided filling pressures and provides an invasive measure of right ventricular (RV) failure, which we term the RV failure index (RVFI). Presently, the link between RHD and adverse clinical outcomes in patients with severe MR after MitraClip is not entirely understood. Furthermore, no studies have comprehensively examined and compared the relation between parameters of right heart (RH) structure and function assessed on right heart catheterization (RHC) and echocardiography and clinical outcomes in patients with severe MR. Accordingly, we studied the association between both RHC and echo derived measures of RH structure and function and clinical outcomes in patients with severe MR undergoing MitraClip.

Materials and Methods

Patient population

A total of 74 consecutive patients who underwent MitraClip at our institution were included in the analysis. All patients had symptomatic moderate-to-severe or severe MR despite optimal medical therapy and were deemed high surgical risk by a "heart team". Patients were enrolled from 10/01/2014 through 12/31/2018.

MitraClip Procedure

Percutaneous edge-to-edge mitral valve repair was performed as described in detail previously [3,4]. All procedures were performed using a 24 Fr MitraClip device (Abbott Vascular, Santa Clara, CA, USA). All clips were implanted under general anesthesia, fluoroscopic, and transesophageal echocardiographic guidance. The right femoral vein access site was closed using 2 Pre-close sutures. After the procedure, patients were transferred to and managed in our coronary care unit.

Right Heart Catheterization

Pre-MitraClip RHC was performed using a 7F Swan-Ganz catheter to determine right atrial pressure (RAP), right ventricular diastolic pressure (RVDP), right ventricular (RV) end-diastolic pressure (RVEDP), RV +dP/dT, RV systolic pressure (RVSP), pulmonary artery systolic pressure (PASP), mean pulmonary artery pressure (MPAP), pulmonary capillary wedge pressure (PCWP), transpulmonary gradient (TPG), the pulmonary artery pulsatility index (PAPI), RA/PCWP (RVFI), and pulmonary vascular resistance (PVR). Clinically relevant cut-points were defined based on previously reported data or the population mean as follows: RAP>15mmHg, RVDP >10mmHg, RVEDP >15mmHg, RV +dP/dT <400ms, RVSP >40mmHg, PASP >50mmHg, MPAP >40mmHg, PCWP >25mmHg, TPG >12mmHg, PAPI <4.8, RA/PCWP (RVFI) >0.63, and PVR >3 Woods units [10-16].

Echocardiography

Pre-MitraClip transthoracic echocardiograms were reviewed by a board-certified cardiologist, blinded to clinical outcomes, to determine left ventricular ejection fraction (LVEF), various measures of RH structure and function, and severity of valvular regurgitation based on previously published guidelines of the American Society of Echocardiography (ASE) [17-19]. The LVEF was determined based on visual estimation in multiple views including parasternal long-axis, parasternal short-axis, apical 2-chamber, apical 3-chamber, and apical 4-chamber. Right atrial (RA) volume was calculated using the disk summation method in the apical four-chamber view. RA volume was indexed to body surface area to obtain the RA volume index (RAVI). The inferior vena cava (IVC) diameter was measured in its long axis in the subcostal view proximal to the ostium of the RA at end-expiration. The RAP was estimated based on the IVC diameter as described previously [18]. Basal and mid cavity RV diameter was determined in the RV focused apical 4-chamber view at end-diastole. Peak tricuspid regurgitation (TR) jet velocity during systole was determined using continuous wave Doppler interrogation. Estimated RVSP was determined from peak TR jet velocity using the simplified Bernoulli equation where RVSP = $4V^2$, where V is the peak velocity (in meters per second) of the TR jet. Estimated PASP was determined by adding the estimated RVSP and RAP as described previously [17,18]. Tricuspid annular plane systolic excursion (TAPSE) was measured by M-mode echocardiography with the cursor positioned along the lateral aspect of the tricuspid valve annulus in the apical four-chamber view. Doppler tissue imaging (DTI)-derived tricuspid lateral annular systolic velocity (RV S') was measured along the free wall of the RV. Severity of valvular regurgitation was determined qualitatively using color flow Doppler as described previously [19]. Variables were dichotomized based on clinically relevant values, as defined by the ASE guidelines, as follows: RAVI >34ml/m2, RV basal diameter >4.2cm, TAPSE <1.3cm, and RV S' <8s, estimated RVSP >40mmHg, estimated PASP >50mmHg, moderate/severe TR, and moderate/severe PR [17,18]. Echo-RFVI (RA/PCWP) >0.63 was defined as significant based on previously published invasive hemodynamic data [10,13]. Echo-derived PCWP was determined using the previously described formula: PCWP = 1.24 x (E/e') + 1.9, where E = mitral inflow E wave velocity on pulsed-wave Doppler and e' = averaged early diastolic velocity of the mitral annulus obtained by tissue Doppler imaging of the septal and lateral sides of the mitral annulus [20].

Clinical Outcomes

Overall death was defined as any death that occurred during the follow-up period. Cardiovascular death was defined if the cause of death was attributable to myocardial ischemia/infarction, heart failure, or cardiac arrest. Heart failure hospitalization was defined as any hospitalization wherein patients manifested clinical (dyspnea, peripheral edema, pulmonary edema), laboratory (elevated BNP), or radiographic (chest X-ray) evidence of heart failure and/or were treated for congestive heart failure symptoms with oral or intravenous diuretics. All events were adjudicated and co-verified independently by two individuals (R.J.B and T.D.). Event ascertainment occurred via comprehensive chart review of the electronic medical record and review of publicly available obituaries.

Statistical Analysis

Data were summarized as counts (percentages) for categorical variables and mean ± SD for continuous variables. Cox proportional hazard models adjusted for age and sex were utilized to examine the association between right heart structure and function variables and death. Two-sided p-values <0.05 were considered statistically significant. Statistical analysis was performed using STATA statistical software.

Results

Baseline features of MitraClip patients

The baseline clinical characteristics of the MitraClip population are summarized in Table 1. The mean age of patients was 76 ± 12 years with a slight male majority (53%). The patient cohort had a high surgical risk with median STS-PROM of 10%. The burden of systolic and diastolic heart failure was high at 61% and 73%, respectively. The burden of coronary artery disease, systemic hypertension, diabetes mellitus, and atrial fibrillation was 65%, 84%, 28%, and 64%, respectively. The prevalence of clinical HF was high with 92% of patients presenting with New York Heart Association functional class III HF symptomatology. Finally, the mean BNP was 718 ± 822 pg/mL.

Right Heart Catheterization Hemodynamics

Baseline RHC hemodynamic parameters are summarized in Table 2. In general, patients manifested elevated right and left sided filling pressures as well as mild to moderate pulmonary artery hypertension. RAP was mildly elevated at 9.0 ± 5.8 mmHg. RVSP was severely elevated at 50 ± 18 mmHg. RVDP was mildly elevated at 3.5 ± 4.2 mmHg, while the RVEDP was severely elevated (11 ± 6.0 mmHg). PCWP was mildly elevated at 18 ± 7.9 mmHg. The mean PAPI was 4.8 ± 4.1. The mean RFVI (RAP/PCWP) was 0.48 ± 0.22. Finally, the mean PVR was elevated at 3.1 ± 3.0 Woods units.

Echocardiographic Variables

Baseline RH structure and function echocardiographic variables are summarized in Table 3. LV systolic function was mildly reduced with a mean LVEF of 42 ± 17%. RA size was elevated (39 ± 20 ml/m^2). The RV was dilated with a basal linear diameter of 4.4 ± 0.75 cm. Similar to RHC, patients manifested elevated right and left sided filling pressures: RAP (12 ± 3.2 mmHg), RVSP (40 ± 12 mmHg), PASP (52 ± 13 mmHg), and PCWP (25 ± 7.7 mmHg). RV systolic function was reduced with TAPSE of 1.8 ± 0.44 cm and DTI-derived tricuspid lateral annular systolic velocity of 10 ± 2.8 cm/s. Ninety-four percent of patients had moderate or severe MR. Sixty-three percent of patients had moderate or severe TR whereas only 8% of patients had moderate or severe PR.

Table 1: Baseline clinical features of patients undergoing MitraClip.

Age at MitraClip (years)	76 ± 12
Female	35 (47)
Body mass index (kg/m^2)	28 ± 7.5
STS-PROM score	10 ± 7.8
Systolic heart failure	45 (61)
Diastolic heart failure	54 (73)
Coronary artery disease	48 (65)
Hypercholesterolemia	68 (92)
Systemic hypertension	62 (84)
Diabetes mellitus	21 (28)
Atrial fibrillation	47 (64)
Peripheral vascular disease	24 (32)
Cerebrovascular accident	2 (3)
Lung disease	26 (35)
Obstructive sleep apnea	8 (11)
Renal insufficiency	26 (35)
History of smoking	47 (64)
NYHA FC I II III IV	 0 (0) 5 (7) 68 (92) 1 (1)
BNP (pg/mL)	718 ± 822

Values are mean ± SD or n (%).

Table 2: Right heart catheterization hemodynamic variables before MitraClip.

Right atrial pressure (mmHg)	9.0 ± 5.8
Right atrial pressure – V wave (mmHg)	12 ± 6.6
Right ventricular systolic pressure (mmHg)	50 ± 18
Right ventricular diastolic pressure (mmHg)	3.5 ± 4.2
Right ventricular end-diastolic pressure (mmHg)	11 ± 6.0
Pulmonary capillary wedge pressure (mmHg)	18 ± 7.9
Pulmonary capillary wedge pressure – V wave (mmHg)	26 ± 13
Pulmonary artery pulsatility index (PAPI)	4.8 ± 4.1
Right ventricular failure index (RFVI, RAP/PCWP)	0.48 ± 0.22
Pulmonary artery systolic pressure (mmHg)	49 ± 18
Pulmonary artery diastolic pressure (mmHg)	20 ± 10
Mean pulmonary artery pressure (mmHg)	31 ± 13
Transpulmonary gradient (mmHg)	13 ± 9.2
Pulmonary vascular resistance (Woods units)	3.1 ± 3.0
Right ventricular stroke work (g/m/beat)	20 ± 8.3
Right ventricular stroke work index (g/m/beat/m^2)	10 ± 3.8
Mean arterial pressure (mmHg)	80 ± 16
Systemic vascular resistance (dyn*s/cm^5)	1380 ± 616
Pulmonary artery – oxygen saturation (%)	58 ± 9.1
Aorta – oxygen saturation (%)	93 ± 4.5

Values are mean ± SD.

Table 3: Echocardiographic variables prior to MitraClip.

Left ventricular ejection fraction (%)	42 ± 17
Right atrial volume index (ml/m^2)	39 ± 20
Inferior vena cava diameter (cm)	2.4 ± 1.3
Estimated right atrial pressure (mmHg)	12 ± 3.2
Right ventricular diameter – base (cm)	4.4 ± 0.75
Right ventricular diameter – mid (cm)	3.3 ± 0.74
Tricuspid regurgitation systolic velocity (m/s)	3.1 ± 0.48
Estimated right ventricular systolic pressure (mmHg)	40 ± 12
Estimated pulmonary artery systolic pressure (mmHg)	52 ± 13
Estimated pulmonary capillary wedge pressure (mmHg)	25 ± 7.7
Tricuspid annular plane systolic excursion (TAPSE) (cm)	1.8 ± 0.44
DTI-Derived Tricuspid Lateral Annular Systolic Velocity (RV S') (cm/s)	10 ± 2.8
Right ventricular failure index (RFVI, RA/PCWP)	0.52 ± 0.18
Systolic blood pressure (mmHg)	125 ± 19
Severity of tricuspid regurgitation, n (%)	
None	0 (0)
Trivial	10 (16)
Mild	14 (22)
Moderate	19 (30)
Severe	21 (33)
Severity of pulmonic regurgitation, n (%)	
None	18 (28)
Trivial	28 (44)
Mild	13 (20)
Moderate	4 (6)
Severe	1 (2)
Severity of aortic regurgitation, n (%)	
None	29 (45)
Trivial	7 (11)
Mild	20 (31)
Moderate	8 (13)
Severe	0 (0)
Severity of mitral regurgitation, n (%)	
Moderately Severe	22 (34)
Severe	42 (66)

Clinical Outcomes

The median follow-up time of the cohort was 1.2 years. Of the 74 patients in the cohort, 23 (31%) died during the follow-up period, sixteen (22%) died of a cardiovascular death, and fourteen (19%) experienced a hospitalization for acute heart failure (Table 4). Figure 1 summarizes the cumulative incidence of overall death during the follow-up period. The median survival time was 3.3 years.

Table 4: Crude event rates of total death, cardiovascular death, and heart failure hospitalization.

Death, n (%)	23 (31)
Cardiovascular death, n (%)	16 (22)
Heart failure hospitalization, n (%)	14 (19)

Table 5 summarizes the age and gender-adjusted Cox proportional hazard ratios for death following MitraClip by RH structure and function parameters obtained on RHC and echocardiogram. Among the 12 RHC parameters of RH structure and function, 5 were significantly associated with increased risk for death: RAP >15 mmHg (HR: 4.1, 95%CI: 1.1-16), RVDP >10 mmHg (HR: 13, 95%CI: 2.5-67), MPAP >40mmHg (HR: 3.5, 95% CI: 1.03-12), RVFI (RA/PCWP) >0.63 (HR: 3.0, 95%CI: 1.04-8.5), and PVR >3 Woods units (HR: 3.5, 95% CI: 1.2-10.1). Patients with relative RV failure (RVFI (RA/PCWP) >0.63) on RHC manifested significantly increased risk of overall death during the follow-up period (p=0.014) (Figure 2). Likewise, patients with pulmonary artery hypertension (PVR >3 Woods units) had significantly increased risk of overall death (p=0.042) (Figure 3). In contrast, none of the 9 echocardiographic variables of RH structure and function were significantly associated with mortality including: RAVI >34ml/m^2 (HR: 0.81, 95% CI: 0.32-2.1), RV diameter-base >4.2cm (HR: 1.5, 95% CI: 0.44-5.3), TAPSE <1.3cm (HR: 1.1, 95% CI: 0.24-4.9), estimated RVSP >40mmHg (HR: 0.64, 95% CI: 0.25-1.6), estimated PASP >50mmHg (HR 1.3, 95% CI: 0.49-3.6), estimated PASP >70mmHg (HR 0.9, 95% CI: 0.11-6.6), and echo-RVFI (RA/PCWP) >0.63 (HR: 0.89, 95% CI: 0.28-2.9).

Table 5: Age and gender adjusted cox proportional hazard ratios for death following MitraClip.

	Death
Right heart catheterization	
RAP >15mmHg	**4.1 (1.1-16)**
RVDP >10mmHg	**13 (2.5-67)**
RVEDP >15mmHg	1.2 (0.38-4.0)
RV +dP/dT <400ms	1.5 (0.55-3.9)
RVSP >40mmHg	1.0 (0.31-3.5)
MPAP >40mmHg	**3.5 (1.03-12)**
PASP >50mmHg	2.4 (0.84-6.6)
PASP >70mmHg	3.3 (0.90-12.4)
PCWP >25mmHg	0.72 (0.16-3.2)
PAPI <4.8	1.3 (0.43-3.7)
RA/PCWP >0.63	**3.0 (1.04-8.5)**
PVR >3 Woods units	**3.5 (1.2-10.1)**
Echo	
RAVI >34ml/m^2	0.81 (0.32-2.1)
Moderate/severe TR	0.87 (0.34-2.2)
Severe TR	1.1 (0.40-2.8)
RV diameter-base >4.2cm	1.5 (0.44-5.3)
TAPSE <1.3cm	1.1 (0.24-4.9)
RV S' <8cm/s	1.4 (0.42-4.4)
Moderate/severe PR	0.77 (0.16-3.7)
Estimated RVSP >40mmHg	0.64 (0.25-1.6)
Estimated PASP >50mmHg	1.3 (0.49-3.6)
Estimated PASP >70mmHg	0.86 (0.11-6.6)
RA/PCWP >0.63	0.89 (0.28-2.9)

RAP: Right atrial pressure, RVDP: Right ventricular diastolic pressure, RVEDP: Right ventricular end-diastolic pressure, RVSP: Right ventricular systolic pressure, MPAP: Mean pulmonary artery pressure, PASP: Pulmonary artery systolic pressure, PCWP: Pulmonary capillary wedge pressure, PAPI: Pulmonary artery pulsatility index, PVR: Pulmonary vascular resistance, RA: Right atrial, RV: Right ventricle, RAVI: Right atrial volume index, TR: Tricuspid regurgitation, TAPSE: Tricuspid annular plane systolic excursion, PR: Pulmonic regurgitation.

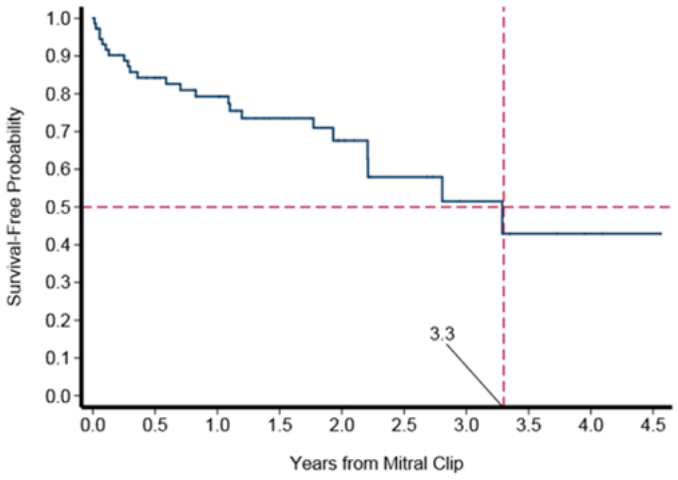

Figure 1: Kaplan-Meier survival curve for cumulative incidence of total death.

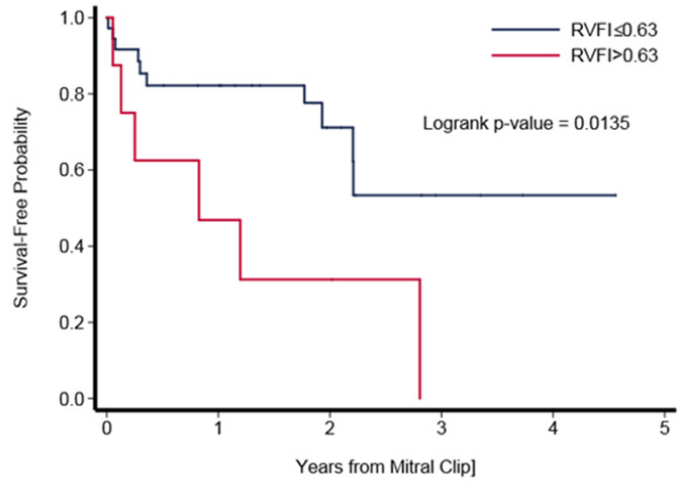

Figure 2: Kaplan-Meier survival curve for cumulative incidence of death by RVFI (RA/PCWP) (≤0.63 vs >0.63).

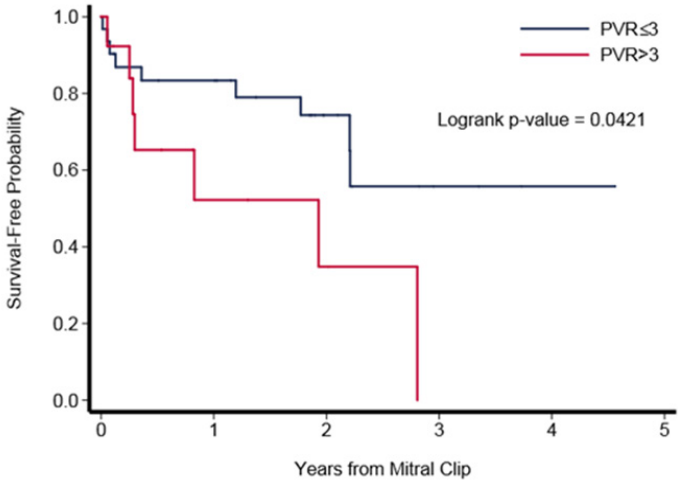

Figure 3: Kaplan-Meier curve for cumulative incidence of death by PVR (≤3 vs >3).

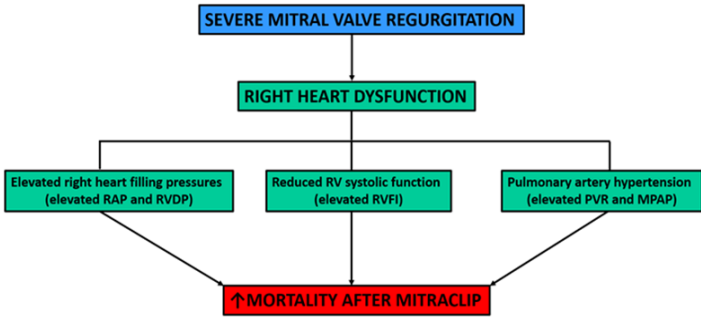

Figure 4: Relationship between severe mitral valve regurgitation, right heart dysfunction, and clinical outcomes following MitraClip.

Discussion

In patients with chronic, severe MR, deleterious right heart (RH) structure and/or function can result from persistently elevated left atrial pressure and consequent pulmonary venous and arterial hypertension which ultimately begets elevated RV afterload. Over time, RV pressure overload results in RH enlargement (RA and RV dilation) and RV dysfunction, which may contribute to adverse clinical outcomes in patients with severe MR. Here, we report, for the first time, that several measures of RH dysfunction on RHC, including RAP >15mmHg, RVDP >10mmHg, RVFI (RA/PCWP) >0.63, MPAP >40mmHg, and PVR >3 Woods units, predicted increased risk of death in patients with severe MR undergoing MitraClip. In contrast, none of the echocardiographic measures, including RAVI >34ml/m^2, TAPSE <1.3cm, RV S' <8cm/s, severity of TR, severity of PR, and RVFI (RA/PCWP) >0.63, were associated with mortality. To our knowledge, this is the first report of comprehensive examination of the relation between several invasive and non-invasive measures of RH structure and function and clinical outcomes after MitraClip in patients with severe MR, demonstrating that several RHC parameters are predictive of adverse events, whereas echocardiographic parameters are not.

To date, 3 studies, in relatively small patient cohorts, have suggested that RV dysfunction or pulmonary hypertension are linked with worse outcomes in patients after MitraClip [21-23]. Importantly, all 3 studies examined the RH purely by echocardiography, whereas we are the first to comparatively examine RH structure and function by both RHC and echo. Furthermore, we studied several echocardiographic variables of RH structure/function that had not been previously examined including: RAVI, RVSP, PASP, severity of PR, and the RVFI (RA/PCWP). Giannini et al. showed that RV S' <9.5 cm/s was associated with increased cardiovascular mortality whereas TAPSE, severity of TR, mid RV diameter, and systolic pulmonary artery pressure were not [21]. In contrast, we did not find an association between an even lower (and presumably more severe measure of RV dysfunction) RV S' and overall mortality. The disparate findings could be due to study sample differences as our patient population was more female and had higher overall LV systolic function. Also, the adjudicated outcomes were different as we examined overall mortality whereas they reported cardiovascular mortality. Matsumoto and co-workers examined the relation between pre-existing pulmonary hypertension, defined

as PASP >50 mmHg on Doppler echo, and all-cause mortality in 91 patients undergoing MitraClip [22]. These investigators reported that a PASP >50mmHg was linked with a significantly increased risk of mortality (HR: 3.7, 95%CI: 1.7-8.5, p=0.002). Of note, the mean PASP was similar between both studies being 51mmHg in their study and 52mmHg in ours. Despite this, we did not observe an association between PASP >50mmHg on echo and mortality (HR: 1.3, 95%CI: 0.49-3.6). The follow-up time in their study was 25 months and 1.2 years in ours, which may explain the difference. Finally, Kaneko and colleagues examined the relation between RV dysfunction, defined by TAPSE <1.5cm, and all-cause mortality in 117 patients with severe MR and LVEF ≤40% [23]. They noted that patients with a TAPSE <1.5cm had a nearly 2-fold increase in mortality (p=0.042). In contrast, we found that using an even lower TAPSE, thereby defining even more severe RV systolic dysfunction, of <1.3cm was not predictive of all-cause mortality (HR 1.1, 95%CI 0.24-4.9). Perhaps the differences between our studies relate to the fact that all patients in their study had an LVEF ≤40%. Hence, their study population had lower baseline LV systology and it may be that the lower LVEF influenced mortality to a greater extent than right heart dysfunction parameters. Despite the differences, our study population paralleled the previous studies [21-23] with respect to mean RV diameter, MPAP, TAPSE, RV S' being similar between the studies. Also, we expanded the number of RH echocardiographic variables by studying RAVI, severity of PR, RVSP, and RA/PCWP. Nevertheless, we did not observe an association between any of the echocardiographic measures of RH structure or function and all-cause mortality after MitraClip.

A novel and interesting aspect of our study is that we are the first to examine the relation between invasive hemodynamic parameters obtained on RHC and clinical outcomes after MitraClip in patients with severe MR. Additionally, we are the first to report that several RHC parameters were predictive of increased mortality after MitraClip including: RAP >15mmHg, RVDP >10mmHg, RVFI (RA/PCWP) >0.63, MPAP >40mmHg, and PVR >3 Woods units. To our knowledge, this is the first report of its kind. Importantly, each of the RHC measures we found to be predictive indicate a different functional aspect of the RH circulation. The elevated RAP and RVDP tell us that elevated right-heart filling pressures predict increased mortality, while the elevated RA/PCWP indicates that reduced RV systolic function is linked with mortality. Finally, the elevated MPAP and PVR supports the notion that pulmonary artery hypertension predicts mortality.

So how can several RHC parameters predict mortality, but not echo parameters? One may think that significant differences exist between the RHC and echo parameters. However, we found that the mean RAP, RVSP, RFVI (RA/PCWP), and PCWP were similar between RHC and echo. Echocardiographic assessment of PCWP in patients with MR is a potential source of error as the calculation involves use of the mitral E/e', which we know is affected by presence and severity of mitral regurgitation. We do not believe echocardiographic ascertainment of RH structure and function was a source of error as our echo values of RV diameter, TAPSE, RV S', and severity of TR were similar to prior studies [21-23]. Perhaps the differences are explained by invasive cardiac cath metrics of right heart physiology being more sensitive measures of RHD in patients with severe MR who undergo MitraClip. Additionally, it may be that the high prevalence of pulmonary hypertension and moderate to severe tricuspid regurgitation in our study overwhelms the ability of echocardiography to discriminate different right heart correlates of mortality. In support of this notion, 63% of our patients had moderate or severe TR.

Limitations

There exist several limitations about this study which must be considered when interpreting our data. First, this is a retrospective cohort study and hence subject to selection and information bias. Second, this is a single-center study with a relatively small cohort of patients and hence we could not probe the relation between RH structure and function and clinical outcomes in Cox models that included further adjustments for potential confounding variables. Third, we had low event rates of heart failure hospitalization and thus could not examine the relation between RH structure and function and this important clinical outcome. Finally, we do not have follow-up RHC data to probe the relation between a change in the RH hemodynamics after MitraClip and overall mortality.

Conclusion

We report that several measures of right heart dysfunction on RHC, including elevated RH filling pressures (elevated RAP and RVDP), reduced RV systolic function (elevated RFVI (RA/PCWP)), and pulmonary artery hypertension (elevated PVR and MPAP), predict increased overall mortality in patients with chronic, severe, symptomatic MR undergoing percutaneous mitral valve repair with the MitraClip system (Figure 4). We contend that comprehensive assessment of right heart physiology utilizing right heart catheterization may help identify patients with severe MR at increased risk of adverse clinical outcomes following MitraClip. Future studies in larger patient cohorts with longer patient follow-up could confirm and extend our hypothesis-generating findings.

References

1. Lung B, Vahanian A. Epidemiology of valvular heart disease in the adult. Nat Rev Cardiol. 2011; 8: 162-172.
2. Trichon BH, Felker GM, Shaw LK, et al. Relation of frequency and severity of mitral regurgitation to survival among patients with left ventricular systolic dysfunction and heart failure. Am J Cardiol. 2003; 91: 538-543.
3. Feldman T, Foster E, Glower DD, et al. Percutaneous repair or surgery for mitral regurgitation. NEJM. 2011; 364: 1395-1406.
4. Stone, GW, Lindenfeld J, Abraham WT, et al. Transcatheter mitral-valve repair in patients with heart failure. NEJM. 2018; 379: 2307-2318.
5. Guglin M, Verma S. Right side of heart failure. Heart Failure Rev. 2012; 17: 511-527.
6. Polak JF, Holman BL, Wynne J, et al. Right ventricular ejection fraction: an indicator of increased mortality in patients

with congestive heart failure associated with coronary artery disease. J Am Coll Cardiol. 1983; 2: 217-224.

7. Ghio S, Gavazzi A, Campana C, et al. Independent and additive prognostic value of right ventricular systolic function and pulmonary artery pressure in patients with chronic heart failure. J Am Coll Cardiol. 2001; 37: 183-188.
8. Kammerlander AA, Marzluf BA, Graf A, et al. Right ventricular dysfunction, but not tricuspid regurgitation, is associated with outcome late and after left heart valve procedure. J Am Coll Cardiol. 2014; 64: 2633-2642.
9. Le Tourneau T, Deswarte G, Foucher-Hossein C, et al. Right ventricular systolic function in organic mitral regurgitation: impact of biventricular impairment. Circulation. 2013; 127: 1597-1608.
10. Lala A, Guo Y, Xu J, et al. Right ventricular dysfunction in acute myocardial infarction complicated by cardiogenic shock: a hemodynamic analysis of the should we emergently revascularize occluded coronaries for cardiogenic shock (SHOCK) trial and registry. J Cardiac Fail. 2018; 24: 148-156.
11. Swan HJ, Ganz W, Forrester J, et al. Catheterization of the heart in man with use of a flow-directed balloon-tipped catheter. N Engl J Med. 1970; 283: 447-451.
12. Nemens EJ, Woods SL. Normal fluctuations in pulmonary artery and pulmonary capillary wedge pressures in acutely ill patients. Heart-Lung. 1982; 11: 393-398.
13. Cipriani M, De Simone V, D'Angelo L, et al. Ventricular assist devices for heart failure: a focus on patient selection and complications. Res Rep in Clin Cardiol. 2014; 5: 199-211.
14. Kern MJ, Lim MJ, Goldstein JA. Hemodynamic Rounds: Interpretation of Cardiac Pathophysiology from Pressure Waveform Analysis. 3rd ed, (Eds), Wiley-Blackwell, Hoboken. 2009.
15. Kern MJ. The Cardiac Catheterization Handbook. 6th ed, (Ed), Elsevier, Philadelphia. 2015.
16. Moscucci M. Grossman and Baim's Cardiac Catheterization, Angiography, and Intervention, 8th ed, Wolters Kluwer/ Lippincott Williams & Wilkins, Philadelphia. 2013; 223.
17. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015; 28: 1-39.
18. Rudksi LG, Lai WW, Afilalo J, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American society of echocardiography. J Am Soc Echocardiogr. 2010; 23: 685-713.
19. Zoghbi WA, Adams D, Bonow RO, et al. Recommendations for noninvasive evaluation of native valvular regurgitation: a report from the American Society of Echocardiography. J Am Soc Echocardiogr. 2017; 30: 305-371.
20. Nagueh SF, Middleton KJ, Kopelen HA, et al. Doppler tissue imaging: a noninvasive technique for evaluation of left ventricular relaxation and estimation of filling pressures. J Am Coll Cardiol. 1997; 30: 1527-1533.
21. Giannini C, Fiorelli F, Colombo A, et al. Right ventricular evaluation to improve survival outcome in patients with severe functional mitral regurgitation and advanced heart failure undergoing MitraClip therapy. International Journal of Cardiology. 2016; 223: 574-580.
22. Matsumoto T, Nakamura M, Yeow WL, et al. Impact of pulmonary hypertension on outcomes in patients with functional mitral regurgitation undergoing percutaneous edge-to-edge repair. Am J Cardiol. 2014; 114: 1735-1739.
23. Kaneko H, Neuss M, Weissenborn J, et al. Prognostic significance of right ventricular dysfunction in patients with functional mitral regurgitation undergoing MitraClip. Am J Cardiol. 2016; 118: 1717-1722.