

Research Article

The Mean Transmitral Gradient in Pure Mitral Stenosis: Is It an Element of Severity or an Indicator of Tolerance in Severe Mitral Stenosis?

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Abstract

Background: Rheumatic Mitral Stenosis (MS) remains a frequent valvulopathy in developing countries.

Objectives: Our aims were to evaluate the existence of a direct correlation between the Mean Transmitral Gradient (MTG) and the severity of MS in patients with severe or very severe MS, as well as to analyze the different parameters that condition the MTG.

Methods and Results: Between January and December 2014, 50 patients (41.7 years of average age, 75% were females) were enrolled for pure and severe or very severe Mitral Stenosis (MS) in the Cardiology department of Ibn Rochd University hospital. All patients underwent complete clinical evaluation with a 12-lead ECG and transthoracic echocardiography. We first studied the correlation between the Mitral Valve Surface (MVS) and the MTG. We then separately analyzed two groups of patients: those with a MTG <10 mmHg (group 1) and those with a MTG≥10 mmHg (group 2). For each group, we performed a univariate correlation of MTG with the clinical, electrocardiographic and echocardiographic data. 64% of patients had a severe MS and 36% had a very severe MS. 52% had a MTG <10mmHg and 48% had a MTG≥10mmHg, 80% of patients in group 1 were dyspneic stage II of the NYHA classification and 70% of patients in group 2 were dyspneic stage III (41%) or IV (29%) of the NYHA classification, which means the existence of a significant correlation between MTG and severity of dyspnea. The analytical study of heart rate and the presence of cardiac failure in relation to the MTG showed a significant correlation. The study of sPAP in both groups revealed the existence of a statistically significant correlation ($r = 0.518$ and $P < 0.001$) between sPAP and MTG.

Discussion: The MTG is a good indicator of mitral stenosis tolerance, but it is imperfectly reflecting its severity as it depends on several hemodynamic parameters. Authentic severe MS may exist with MTG <10 mmHg, which is why the value of the MTG should never be interpreted alone.

Keywords: Mean Transmitral Gradient; Mitral Valve Area; Severe Mitral Stenosis

rheumatic valvulopathies remain widespread, and where severe forms of MS can exist at an early age.

However, industrialized countries have seen the emergence in recent years of new etiologies of MS; in particular the drug and / or toxic induced valvular disorders. Therefore, the echocardiographic evaluation of MS and, above all, the definition of impartial criteria to conclude the severity of MS are still relevant.

International scientific communities [1] define MS as "Severe" by a Mitral Valve Area (MA) $\leq 1.5 \text{ cm}^2$ and as "Very severe" by a mitral valve area $< 1 \text{ cm}^2$ with a Mean Transmural Gradient (MTG) $> 10 \text{ mmHg}$. Despite the inconsistency regarding the cut-off value of the Mean Transmural Gradient (MTG), which defines the severity of MS and its variation according to several factors such as heart rate, regularity of heart rhythm, co-existing valvulopathies and cardiac output, the MTG is still included in the recommendations as a criterion for MS severity.

Objectives

Our aim was to:

Assess the existence of a direct correlation between mean transmural gradient and the severity of the mitral stenosis in patients with severe MS (primary criteria). Analyze the parameters influencing the mean transmural gradient (secondary criteria).

Methods

We conducted a prospective monocentric study over a one-year period (January 2014 to December 2014) including all patients enrolled for severe or very severe Mitral Stenosis (MS) in the Cardiology department of Ibn Rochd University hospital of Casablanca.

Patients were excluded if they had any of the following features:

- A mild or moderate mitral stenosis.
- A significant mitral regurgitation or aortic valvular disease associated to mitral stenosis.
- Any other congenital or acquired heart disease associated to MS.

We collected demographic data, symptoms, cardiovascular risk factors and medical history such as embolic events or previous surgical procedures. All patients underwent a complete physical examination, a 12-lead electrocardiogram and a Transthoracic Echocardiography (TTE) performed by an experienced operator using GE VIVID7. The latter allowed the analysis of :

- The quality of valvular apparatus and sub valvular mitral apparatus,
- Valvular mitral area assessed by planimetry,
- Mean transmural gradient,
- Left and right atrial area by planimetry,
- Left ventricular ejection fraction measured by M-mode Teichholz and biplane Simpson's method,

- Right ventricular function,
- Tricuspid Regurgitation (TR)
- Right Ventricle-Right Atrium (RV-RA) gradient from TR flow
- Right atrial pressure estimated from diameter and collapsibility of inferior vena cava.

The mitral valve area was measured by planimetry, with 3 measurements at least. MTG was measured by tracing the anterograde mitral flow obtained by continuous Doppler on the mitral orifice, by means of at least 3 measurements in sinus rhythm and 5 measurements in case of atrial fibrillation.

Initially, we studied the correlation between the mitral valve area and MTG. Then, we analyzed separately two groups of patients: those with a MTG $< 10 \text{ mmHg}$ (group 1) and those with a gradient $\geq 10 \text{ mmHg}$ (group 2). For each group we proceeded to a univariate correlation of MTG and the stage of dyspnea according to the NYHA classification, heart rate, heart failure, rhythmic regularity, left atrial area measured by planimetry, RV function, importance of tricuspid regurgitation and systolic Pulmonary Artery Pressure (sPAP).

The analysis was performed by SPSS software version 20.

Results

Fifty patients presenting a severe or very severe MS were enrolled at the cardiology department of Ibn Rochd university hospital in Casablanca over a one-year period (January 2014 to December 2014).

The average age of our patients was 41.7 years with extremes ranging from 22 to 66 years of age. 30 patients (60%) were < 45 years of age, 19 patients (38%) were between 45 and 65 years of age, and 1 patient (2%) was over 65 years of age.

There was a female predominance in our study (sex ratio: 0.25).

One cardiovascular risk factor was found among 36% of patients. 4 patients (8%) were smokers, 2 patients were diabetics (4%), 5 patients were hypertensive (10%) and 7 women were postmenopausal (14%). 20% of our patients presented a systemic embolism event (10 patients), 5 patients (10%) had undergone a Percutaneous Balloon Mitral Commissurotomy (PBMC) and 2 patients (4%) a Surgical Closed Mitral Commissurotomy (SCMC). In our study, 2 patients were pregnant at the second trimester. The first was dyspneic stage II of the NYHA and the other one was dyspneic stage III of the NYHA. 64% of patients had a severe MS and 36% had a very severe MS. (Table 1)

CHARACTERISTICS	
Total of patients	50
Mean age (years)	41.7
< 45 years	30 patients (60%)
between 45 to 65 years	19 patients (38%)
> 65 years	1 patient (2%)
Sex ratio (male/ woman)	0.25
Cardiovascular risk factors	18 patients (36%)
Smoking	4 patients (8%)
Diabetes	2 patients (4%)
Hypertension	5 patients (10%)
Menopause	7 patients (14%)
History of Stroke	10 patients (20%)
Heart rate	
<60 bpm	1 patient (2%)
Between 60 to 100 bpm	36 patients (72%)
>100 bpm	13 patients (26%)
Dyspnea (NYHA stage)	
Stage I of NYHA	1 patient (2%)
Stage II of NYHA	
28 patients (56%)	
Stage III of NYHA	
14 patients (28%)	
Stage IV of NYHA	7 patients (14%)
Duration of symptoms	
< 2 years	31 patients (62%)
≥2 years	19 patients (38%)
Heart failure	7 patients (14%)
ECG	
Sinus Rhythm (SR)	26 patients (52%)
Atrial Fibrillation	24 patients (48%)
Severe MS<1.5 cm ²	32 patients (64%)
Very severe MS <1 cm ²	18 patients (36%)

Table 1: Demographics and Clinical Characteristics of the Studied Cases.

Among all patients, 52% (26 patients) had a MTG <10 mmHg and 48% had a mean gradient ≥10 mmHg, which suggests there isn't a direct correlation between severity of MS and MTG due to the presence of authentic severe or very severe MS with MTG <10 mmHg (Pearson coefficient $r = -0.137$). (Table 2)

	MA<1.5 cm ²	MA<1 cm ²	Number of patients	Pearson coefficient
GROUP 1 : MTG <10 mmHg	15	11	26	-0.137
GROUP 2 : MTG ≥10 mmHg	17	7	24	

Table 2: Correlation between Mitral Area (MA) and Mean Transmural Gradient (MTG).

Concerning dyspnea, 80% of patients in group 1 were dyspneic stage II of the NYHA classification, 70% of patients in group 2 were dyspneic stage III (41%) or IV (29%) of the NYHA classification. 80% of the latter group had a MTG ≥10 mmHg, which means there is a significant correlation between MTG and severity of dyspnea ($r = 0.586$ and $p < 0.001$).

The analytical study of heart rate and the presence of heart failure compared with the MTG showed a significant correlation. In fact, among all patients of group 1, 96% had a HR between 60 and 100 bpm and none of them presented a heart failure. In group 2, 54% (13 patients) had a HR >100 bpm and 7 of them (53%) presented a left heart failure.

Regarding the regularity of the rhythm, 53% of patients in group 1 (14 patients) had a Regular Sinus Rhythm (RSR) and 46% (12 patients) had an atrial fibrillation. In group 2, half of the patients had RSR and the other half an atrial fibrillation, which means the absence of a statistically significant correlation between regularity of the rhythm and the MTG in our study ($r = 0.038$).

The analysis of systolic Pulmonary Artery Pressure (sPAP) in both groups revealed a statistically significant correlation between sPAP and MTG ($r = 0.518$ and $p < 0.001$). In fact, in group 1, 65% of patients (17 patients) had a normal sPAP <35 mmHg, 23% (6 patients) had a moderate pulmonary hypertension with a sPAP between 35 and 50 mmHg; only 11% (3 patients) had a sPAP >50 mmHg. In group 2, only 12% (3 patients) had a normal sPAP <35 mmHg, 45% (11 patients) had a moderate pulmonary hypertension with a sPAP between 35 and 50 mmHg; 41% of patients (10 patients) had a sPAP more than 50 mmHg.

Finally, by analyzing the right ventricular (RV) function, we did not find a statistically significant correlation between RV function and MTG ($r = -0.002$). In group 1, 84% of the cases (22 patients) had a good or conserved RV function, 15% (4 patients) had an average RV function. In group 2, RV function was good or conserved in 92% of patients and reduced in 8% (2 patients) (Table 3).

	Mean gradient<10 mmHg (number of patients)	Mean Gradient≥10 mmHg (number of patients)	Pearson's correlation coefficient (R)
Mitral area (severe or very severe MS)	26	24	-0.137
Dyspnea			
Stage II	21	7	
Stage III	4	10	
Stage IV	0	7	0.586*
Heart rate			
<60 bpm	1	0	
Between 60 and 100bpm	25	11	
>100 bpm	0	13	0.615*
Systolic pulmonary artery pressure			
<35 mmHg	17	3	
Between 35 to 50 mmHg	6	11	
>50 mmHg	3	10	0.518*
RV Function			
Good	18	17	
Conserved	4	5	-0.002
Average	4	0	
Reduced	0	2	
ECG			
Regular sinus Rhythm	14	12	
Atrial fibrillation	12	12	0.038
Heart failure	0	7	-0.420*

* These data were statistically significant correlation.

Table 3: Correlation between Collected Transmural Mean Gradient and Physical, Electrocardiographic, Echocardiographic Parameters.

Discussion

As the incidence of rheumatic disease in western countries decreased, mitral stenosis has become rarer and has also changed in clinical presentation, occurring in older patients with more altered valvular anatomy. However, in developing countries, rheumatic mitral stenosis remains the most common cause [2].

Other causes of MS include: mitral annular calcification, seen in elderly or dialysis dependent patients, radiation valvulitis, congenital causes (e.g., parachute mitral valve, double orifice mitral valve, supra-mitral ring) systematic inflammatory disorders such systemic lupus erythematosus or antiphospholipid syndrome, carcinoid heart disease or endomyocardial fibrosis [3-5]. In our study, rheumatic etiology was the cause of MS in all our patients.

Echocardiography is the main diagnostic imaging modality to evaluate mitral valve obstruction and assess the severity of MS as well as valve morphology [6]. The evaluation of the severity of MS is based on the measurement of three main parameters: MVA, mean Doppler gradients, and pulmonary artery pressure [4,6,7]. However, according to 2017 ESC/EACTS guidelines for the management of valvular heart disease, valve area using planimetry is the reference measurement of MS severity, whereas MTG and pulmonary pressures reflect its consequences and have a prognostic value [8].

Several methods can be used to estimate the MVA and must often be carried out jointly. It can be measured directly by planimetry, which is the method of choice; it must be performed precisely in parasternal short-axis view at the tip of the mitral leaflets in mid-diastole and requires an experienced operator [6,9]. MVA can be also estimated indirectly by the pressure half time or PHT, continuity equation and Proximal Isovelocity Surface Area (PISA). PHT is a simple and less time-consuming method, but not always reliable particularly in elderly patients, concomitant aortic stenosis or regurgitation, in case of atrial fibrillation and isn't valid immediately after a percutaneous mitral commissurotomy, sole reliance on PHT to determine the severity of MS should be discouraged [6,9,10]. Continuity equation is also relatively simple yet invalid in case of associated aortic or mitral regurgitation and atrial fibrillation. PISA is considered complex and requires an angle correction (angle formed between the valve leaflets). New imaging modalities like tridimensional echocardiography or CT scan are interesting and seem less operator dependent [9].

In this study, we measured the MVA by the planimetry technique in all patients. Nearly half of our patients (48%) were in atrial fibrillation, which made the measurement by PHT method invalid. According to the 2014 valvular heart disease guidelines and 2017 guideline update, MS is considered very severe if $MVA \leq 1 \text{ cm}^2$, severe if it's $\leq 1.5 \text{ cm}^2$ [4]. The measurement of the MTG is simple; it uses continuous Doppler and it is less prone to errors since the gradients are derived from direct measurement of the velocity of the transmural flow.

Tracking this flow is easily identified using continuous-wave Doppler through the MV from an apical four-chamber view. By tracing the Doppler-derived diastolic transmural flow and using the simplified Bernoulli equation to convert velocities into pressures, the MTG is obtained [4]. Doppler measurements (trans-valvular gradients) using the continuous-wave Doppler signal across the

MV show good correlation with invasive measurements using trans-septal catheterization [10]. The ASE 2009 has considered MTG as an orientation element to severe MS if the gradient is $> 10 \text{ mmHg}$ without including it in its definition [11].

However, MTG has not been included in the criteria for assessment of MS severity in the 2014 AHA/ACC Guideline for the management of patients with valvular heart disease and in the 2017 AHA/ACC Guideline update [4]. According to The ESC 2012, the severity of MS is defined by a $MVA < 1 \text{ cm}^2$ and a $MTG > 10 \text{ mmHg}$, as long as this gradient is interpreted according to heart rate and in patients in sinus rhythm [12].

In our study, 52% of patients had a $MTG < 10 \text{ mmHg}$ and 42% of them had a very severe MS, suggesting no direct correlation between a $MVA < 1 \text{ cm}^2$ or $\leq 1.5 \text{ cm}^2$ and a $MTG > 10 \text{ mmHg}$; thus, authentic MS, even very severe, can be seen despite a $MTG < 10 \text{ mmHg}$. The common point between different guidelines is the great variation of MTG depending on several hemodynamic parameters in particular regularity of the rhythm, heart rate, cardiac output and the existence of associated mitral regurgitation [1,11-13].

It should be noted that our study focused on pure severe MS, without any other significant co-existing valvular disease, and that all patients had a normal or conserved systolic left ventricular function, so the correlation of MTG with cardiac output and mitral regurgitation has not been analyzed. Heart rate is the main factor influencing MTG because it increases in case of tachycardia. In fact, at measuring MTG, heart rate must be reported on the echocardiography report [11].

Regularity of the rhythm is another determining parameter of MTG because the latter increases in case of tachyarrhythmia and during a short cycle of atrial fibrillation. It is commonly accepted that in case of atrial fibrillation, it is necessary to average the results of 5 to 10 cycles with the least possible variation of the R-R space and to reassess the patient when heart rate is slower [13]. This led some teams to consider the «corrected mitral gradient» which represents the value of the MTG over heart rate [14]. In our study, the analysis of the correlation between the regularity of the rhythm and the MTG was not statistically significant. Indeed, 53% of patients who had a $MTG < 10 \text{ mmHg}$ was in regular sinus rhythm (RSR) and 46% (12 patients) were in atrial fibrillation. Regarding patients with a $MTG \geq 10 \text{ mmHg}$, the half were in RSR and the other half in atrial fibrillation. This can be explained by the fact that only a third of patients who were in atrial fibrillation had a heart rate > 100 beats per minute (bpm), compared with 62% who had a HR between 60 and 100 bpm.

However, MTG is rather an indicator of hemodynamic tolerance of MS. Indeed, in our study, we found a significant correlation between MTG and severity of dyspnea, occurrence of heart failure and pulmonary hypertension, which confirms the recent guidelines stating that MTG reflects the consequences of MS [8].

Conclusion

Mean transmural gradient is a good indicator of tolerance of mitral stenosis, but it doesn't reflect very well its severity as it depends on many hemodynamic parameters. Authentic very severe mitral stenosis can exist with transmural mean gradient <10 mmHg; which is why the value of MTG can't be individually interpreted.

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