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Role of the Mitral Valve Resistance in Evaluation of Mitral Stenosis Severity

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Abstract

Background: Mitral valve resistance (MVR) is an important hemodynamic consequence of mitral stenosis (MS). We aimed to determine whether the mitral valve resistance could be used as a clinically reliable method for estimation of MS severity.

Materials and Methods: Transthorathic echocardiographic study of 128 patients with rheumatic MS to estimate; mitral valve area (MVA); planimerty (2D) and pressure half time (PHT), mitral valve score (MVS), right ventricular systolic pressure (RVSP), mean transmitral pressure gradient (MPG), diastolic filling time(DFT), left ventricular out flow tract diameter(LVOTd) and velocity time integral (LVOT vti), MVR calculated as: MPG/aortic flow ratio [(LVOTd) (LVOTvti)/DFT] in dynes.sec.cm^{-5}.

Results: MVR at cut off values of: ≥105.26 dynes.sec.cm^{-5}, had a sensitivity of 86.7% and a specificity of 74.5% for severe MS, between 76.02 and 105.26 dynes.sec/cm^5 it had a sensitivity of 85.2% and a specificity of 72% for moderate MS, at ≤76.02 dynes.sec/cm^5 it had a sensitivity of 81% and a specificity of 91% for mild MS. MVR in moderate MS; can detect symptomatic patients at a cut off value ≥85.65 dynes.sec/cm^5 with a sensitivity of 87% and a specificity of 100%. MVR had positive correlations with MVS and RVSP (r=0.618 and 0.401), -ve correlations with MVA-2D and PHT (r=-0.559 and -0.284), P<0.01. MVR was an independent predictor of the NYHA functional class (B ± SE0.003 ± 0.001, odds ratio 0.3, P<0.01). NYHA functional class showed the best correlation with MVR (r=0.630, P<0.01).

Conclusion: MVR can be used as a parameter for expression of stenosis severity, and could be used for evaluation of symptomatic moderate MS.

Keywords: Hemodynamics; Mitral valve stenosis; Mitral valve resistance

Introduction

The mitral stenosis (MS) severity is determined by the severity of the impending obstruction; assessed by both mitral valve area (MVA) and mean transmitral diastolic pressure gradient (MPG). However, these conventional stenosis indexes poorly reflect the major hemodynamic consequence of MS [1,2]. Reporting stenosis; as hemodynamic resistance, rather than anatomic area, focus on functional [3] and better reflect the hemodynamic burden rather than anatomic consequences of MS, so it could be used as a severity index in patients with MS [4].

Valvular resistance has been proposed as an alternative measure of stenotic valvular lesions that may be less flow dependent and, thus, superior over valve area calculations for the quantification of aortic stenosis [5]. But no clear threshold of severity in MS [6].

The present study aimed to determine whether the mitral valve resistance estimated by resting transthoracic echocardiography could be used as a clinically reliable method for estimation of the degree of mitral stenosis severity and find out the threshold of severity. We tried to study the relation between MVR at rest and the patient's NYHA functional class in moderate MS (the grey zone).

Materials and Methods

This is a retrospective study, carried out in cardiology department, Zagazig university hospitals, Egypt. Approval was obtained for performing the study from the Ethical Committee of the Faculty of medicine, Zagazig University. Egypt. An informed consent was obtained from all patients after explaining the procedure of the study. We selected 128 patients with rheumatic MS; patients with: atrial fibrillation (AF), shunts, pulmonary stenosis, moderate or severe mitral or aortic regurgitation, impaired left ventricular systolic function and a poor acoustic window were excluded from the study.

All participants were subjected to the following

Complete history taking and thorough clinical examination.

Transthoracic echocardiography (TTE): This was done by a (Hewlett Pakard SONOS 5500) echo-set and 2.5-MHz transducers and was used for 2D and Doppler studies. Patients were examined in the left lateral decubitus position.

The following measures were taken:

a) 2D-echocardiographic (2D-echo) study of the following: The mitral valve score (MVS) (we used the Wilkin's score; of leaflet mobility, thickening, degree of calcification, and subvalvular thickening), the total score is the summation of the 4 items and ranges "between 4 and 16" [6,7].

The left ventricular outflow tract (LVOTd) was estimated in the left parasternal long axis view.

From the left parasternal short-axis view, the mitral valve area by planimerty (MVA-2D) was measured at the leaflet tips, by direct tracing of the mitral orifice, including opened commissures.

b) Pulsed wave-Doppler (PW) interrogation of: The LVOT in the apical-5 chamber view was used to estimate the left ventricular outflow tract velocity-time integral (LVOTvti).

The mitral valve orifice to measure the diastolic filling time (DFT) in the apical 4-chamber view; as the time passed from the beginning of the E wave to the end of the A wave.

c) Continues wave-Doppler (CW) echocardiography of: the mitral valve orifice in the apical 4-chamber view to measure the MVA by pressure half time (MVA-PHT) and the mean transmitral diastolic pressure gradient (MPG).

- **Estimation of the RVSP**=systolic pulmonary artery pressure (sPAP), calculated from the modified Bernoulli equation: RVSP=sPAP=$4V^2$ + right atrial pressure, where 'V' is the maximum velocity of the tricuspid valve regurgitant jet.

- **The Mitral valve resistance was calculated from the equation**: (MVR)=(ΔP/F)=mean transmitral pressure gradient/aortic flow ratio [(cross sectional area LVOT) (LVOTvti)/DFT] and represented as adynes/sec/cm^{-5} [8-10].

Patients were classified into 3 groups according to MS severity: group I; 31 patients with severe MS (where MVA <1 cm^2 and MPG >10 mmHg), group II; 35 patients with moderate MS (MVA 1-1.5 cm^2 and MPG 5-10 mmHg) and group III; 62 patients with mild MS (MVA >1.5 cm^2 and MPG <5 mmHg) [6,9].

Off-line assessment of 2D and Doppler images was performed by two investigators who were blinded to clinical data; the assessment was performed in two separate occasions for each of the investigators.

Statistical Analysis

All data were analyzed using SPSS software statistical package for social science version 16 (SPSS, Inc. Chicago, IL, USA). Results were presented as mean value ± SD for continuous variables and as frequency (%) for categorical variables. Data was tested for normality using the Kolmogorov-Smirnov test. Means were compared using One Way ANOVA test, categorical data were compared using chi-squared test. Pearson correlations between MVR, NYHA class and the other variables were done. Multivariate logistic regression analysis was done to estimate the independent predictors of dyspnea. Determination of cutoff values with associated sensitivity and specificity was performed using Receiver Operating Characteristics (ROC) analysis.

Results

Our study included 128 patients with rheumatic MS; in 3 groups according to the stenosis severity, patients' demographic and clinical characteristics are in Table 1, demographic, clinical and echocardiographic characteristics of the studied groups are in Table 2.

Characteristics	Findings
Age (yrs) range and (mean ± SD)	15-63 (34.1 ± 11.6)
Gender(M/F)%	35/93 (27.3.8/72.7%)
Severe MS	31(24.2%)
Moderate MS	35(27.3%)
Mild MS	62(48.4%)
MVS (mean ± SD)	7.3 ± 1.9
MVA(2D) (mean ± SD) cm2	1.38 ± 0.41
MVA(PHT) (mean ± SD) cm2	1.48 ± 0.78
MPG (mean ± SD)mmHg	10.2 ± 5.1
DFT (mean ± SD)msec	422.3 ± 90.8
LVOTd (mean ± SD)cm	2.07 ± 0.38
RVSP (mean ± SD)mmHg	45.7 ± 22.8
MVR (mean ± SD) dynes.sec/cm5	104.26 ± 69.23

Table 1: Demographic and clinical characteristics of the patients: MS; mitral stenosis, MVS: mitral valve score, MVA (2D): MVA by planimerty, MVA (PHT): MVA by pressure half time, MPG: transmitral mean diastolic pressure gradient, DFT: diastolic filling time, LVOTd: left ventricular out flow tract diameter, RVSP; right ventricular systolic pressure, MVR: mitral valve resistance.

Variables	Group I (severe MS) 31 (24.2%)	Group II (moderate MS) 35 (27.3%)	Group III (mild MS) 62 (48.4%)	P
Age (yrs) (mean ± SD)	29.8 ± 9.75	36.69 ± 13.28	34.79 ± 11.64	0.05 (severe vs. mod and mild)
Gender (M/F)%	6/28 (17.6/82.4%)	11/24 (31.4/68.6%)	16/43 (27.1/72.9%)	0.69
Limiting dyspnea (NYHA ≥II)	30(96.8%)	31(88.6%)	7(11.3%)	0.001 (mild vs. mod and severe)
MVS (mean ± SD)	8.58 ± 2.19	7 ± 0.94	6.89 ± 1.88	0.002 (severe vs. mod and mild)
MVA(2D) (mean ± SD) cm2	0.89 ± 0.09	1.18 ± 0.15	1.74 ± 0.24	0.001 among groups

MVA(PHT) (mean ± SD) cm2	1.0 ± 0.46	1.2 ± 0.17	1.76 ± 0.18	0.001 (mild vs. mod and severe)
MPG (mean ± SD) mmHg	14.3 ± 4.3	10.8 ± 3.9	7.8 ± 4.8	0.001among groups
DFT (mean ± SD) msec	468.58 ± 94.17	429.89 ± 90.98	394.9 ± 79.41	0.01 (severe vs. mild)
LVOTd (mean ± SD) cm	1.86 ± 0.34	2.15 ± 0.34	2.13 ± 0.38	0.002 (severe vs. mod and mild)
RVSP (mean ± SD) mmHg	75.2 ± 32.9	42.8 ± 16.5	43.1 ± 20.7	0.05 (severe vs. mod and mild)
MVR (mean ± SD) dynes.sec/cm5	174.66 ± 81.42	110.41 ± 39.39	65.59 ± 42.36	0.003 among groups

Table 2: Demographic, clinical and Echocardiographic measurements in each group: NYHA; New York Heart Association functional class. Highly significant p<0.01, significant; p ≤0.05, nonsignificant; p>0.05

Patients with severe MS compared to those with moderate and mild MS; were younger (29.8 ± 9.75 vs. 36.69 ± 13.28 and 34.79 ± 11.64 yrs. respectively, P=0.05), had higher MVS (8.58 ± 2.19 vs. 7 ± 0.94 and 6.89 ± 1.88 respectively, P=0.002), with higher RVSP (75.19 ± 32.86 vs. 42.8 ± 16.54 and 43.11 ± 20.72mmHg respectively, P=0.05) and narrower LVOTd (1.9 ± 0.3 vs. 2.2 ± 0.3 and 2.1 ± 0.4 cm respectively, P=0.002).

Patients with mild MS compared to those with moderate and severe MS; had larger MVA-PHT (1.76 ± 0.18 vs. 1.2 ± 0.17 and 1.0 ± 0.46 cm^2 respectively, P=0.001) and lesser NYHA functional class {7(11.3%) vs. 31(88.6%) and 30(96.8%) respectively, P=0.001}.

There were significant differences among groups regarding; MVA -2D (0.89 ± 0.09, 1.18 ± 0.15 and 1.74 ± 0.24 cm^2, P=0.001), MPG (14.34 ± 4.29, 10.75 ± 3.93 and 7.84 ± 4.78 mmHg, P=0.001) and MVR (174.66 ± 81.42 vs. 110.41 ± 39.39 and 65.59 ± 42.36 dynes/sec/cm^5 respectively, P=0.003).

MVR showed positive correlations with; MVS (r=0.618, P=0.001), valve thickness (r=0.733, P=0.002) and RVSP (r=0.401, P=0.002). It correlated negatively with MVA-2D (r=-0.559, P=0.001) and MVA-PHT (r=-0.284, P=0.001), Table 3.

Variables	r	P
NYHA functional class	0.630**	0.001
Valve thickness	0.733**	0.002
MVS	0.618**	0.001
MVA-2D	-0.559**	0.001
MVA- PHT	-0.284**	0.001
MPG	0.820**	0.003
RVSP	0.401**	0.002

Table 3: Correlation of MVR (dynes/sec/cm^5) and other parameters: *Significant correlation, P-value ≤0.05, **highly Significant correlation P-value ≤0.01.

NYHA functional classification showed positive correlations with; MVR (r=0.630, P=0.001), MVS (r=0.508, P=0.002), MPG (r=0.555, P=0.001), RVSP (r=0.218, P=0.031) and negative correlations with MVA-2D (r=-0.758, P=0.005) and MVA-PHT (r=-0.365, P=0.001).

Logistic regression analysis expressed MVR as an independent predictors of the NYHA functional class (B ± SE; 0.003 ± 0.001, 0.3 odds ratio, R=0.797, P=0.003), nearly as powerful as MVA-2D (B ± SE; -1.385 ± 0.106, R=0.758, P=0.002) and more powerful than MVS (B ± SE; 0.076 ± 0.034, R=0.508, P=0.029).

By ROC analysis, MVR at a cut off value ≥105.261 dynes.sec/cm^5 had a sensitivity of 86.7% and a specificity of 74.5%, to detect severe MS; [95% CI 0.827-0.944, area under the curve=0.89, P=0.001], it can detect moderate MS if MVR >76.02 and <105.26 dynes/sec/cm5 with a sensitivity of 85.2% and a specificity of 72%, [95% CI 0.645- 0.847, area under the curve=0.75, P=0.002] and at a cut off value ≤76.02 dynes.sec/cm^5 MVR had a sensitivity of 81% and a specificity of 91%, to detect mild MS; [95% CI 0.816-0.941, area under the curve=0.89, p=0.023], (Figure 1).

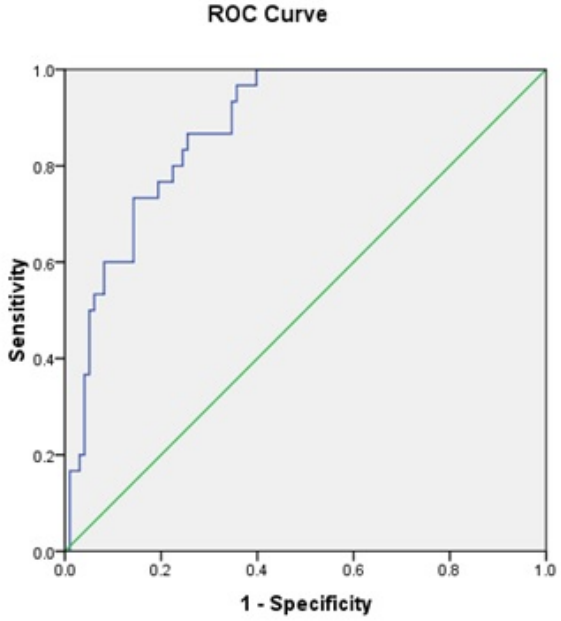

Figure 1: Sensitivity and specificity of MVR in estimation of severe MS. MVR at a cut off value ≥105.26 had a sensitivity of 86.7%, a specificity of 74.5%, to predict severe MS; [area under the curve 0.88 (good predictor), 95% CI 0.818-0.938, p=0.001].

MVR at a cut off value ≥85.65 dynes.sec/cm^5 had a sensitivity of 87% and a specificity of 100%, to detect symptomatic moderate MS;

[area under the curve 0.968 (excellent predictor), 95% CI 0.913-1.022, P=0.001], (Figure 2).

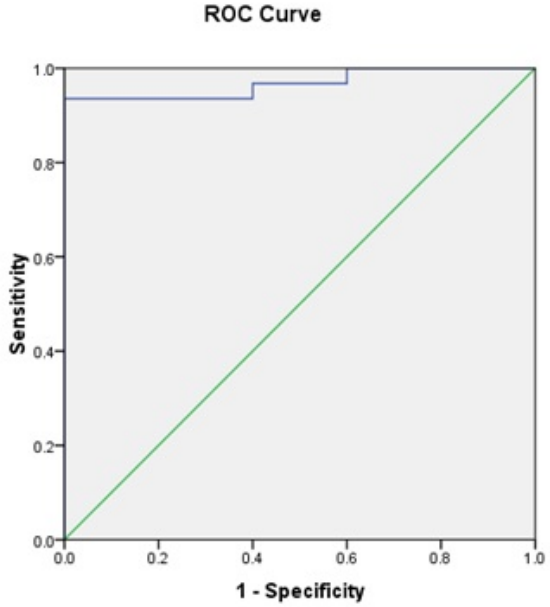

Figure 2: Sensetivity and specificity of MVR in estimation of symptomatic moderate MS. MVR at a cut off value ≥85.65 dynes.sec/cm^5 had a sensitivity of 87%, a specificity of 100%, to detect symptomatic moderate MS; [area under the curve 0.968 (excellent predictor), 95% CI 0.913-1.022, p=0.001].

Discussion

Mitral stenosis (MS) severity is traditionally assessed by the mitral valve area and mean transmitral pressure gradient. However, these indexes fail to reflect the major hemodynamic consequence of MS. Valve resistance (VR) is a physiologic expression of stenosis as it incorporates both the pressure gradient and flow data [11,12]. In aortic stenosis, hemodynamic burden on the left ventricle is closely related to aortic VR but not to the valve area. Accordingly, the MVR may also better reflect the hemodynamic burden of MS and, hence, be an important determinant of pulmonary artery systolic pressure (sPAP) in patients with MS [13]. Valvular resistance is superior over valve area calculations for the quantification of aortic stenosis [5]. But no clear threshold of severity in MS [6].

So we aimed to determine whether the mitral valve resistance estimated by transthoracic echocardiography could be used as a clinically reliable method for estimation of the degree of mitral stenosis severity.

To estimate the severity of the morphological abnormalities in valvular structure, we used the Wilkin score system (anatomical score) with evaluation of leaflet and subvalvular thickness, calcification and valvular mobility. We determined the functional class according to NYHA classification.

We found that patients with severe MS were younger, explained by more severe and aggressive pathology of rehumatic MS affecting young aged, in endemic developing countries, with earlier complain than elderly who neglect and deny, in concordence with Ramakrishna, et al. [11] and Chockalingam, et al. [12] But in contrary to Lung, et al. [13], which could be explained by; patient selection, as we excluded patients with AF; which increases with advancing age in mitral stenosis, also it could be explained depending on the fact that the disease is more aggressive in the developing countries so presented earlier.

The more damaged the valvular structure was, the higher its obstructive effect. Explanations possible for this finding are: first, transformation of potential energy into kinetic energy in the blood volume pushed against the valve during left atrial emptying may be partially absorbed in a less injured and more compliant valve resulting in reduced pressure gradient. Second, the inertia to open fully in diastole may be greater in a more damaged valve with a higher obstructive effect. Third, a more compliant valve may have higher orifice variability than the less compliant ones, exerting a smaller obstructive effect. Fourth, in more damaged valves there would be a summation of resistance in leaflet and subvalvular levels.

We found that the MVR (functional determinant of MS severity) was more in severe MS and correlated with the anatomical determinants of MS (MVA, MVS, valve thickness, MPG and RVSP). Our results were in agreement with Weitzel L, et al. [14,15], Izgi, et al. [10] and Tanboga, et al. [15,16].

To the best of our knowledge, this is the first to study the sensitivity and specificity of resting MVR for grading of mitral stenosis severity. We found that MVR showed near excellent cutoff values to detect severe and mild MS and a good cutoff value to detect moderate MS.

Some patients who are considered asymptomatic adopt their level of exertion and thereby do not get symptoms. Moreover, symptomatic status is subjective; hence an objective tool for risk stratification is required to be implemented in regular follow up of patients with MS, especially in those with moderate MS.

We found that; MVR showed the best correlation with NYHA functional class when compared to the anatomical determinants of MS severity and it is an independent predictor of NYHA class, this explain the major role of MVR in development of dyspnia, thus, MVR could be a complement to the other conventional methods used in assessment of MS. Our results are in agreement with Izgi, et al. [10] and others [17-20].

MVA is flow dependent, more in asymptomatic patients; it appears to be a reliable tool to assess the severity of MS under changing hemodynamic conditions in the majority of asymptomatic patients but to a lesser extent in symptomatic patients [20]. MVR is not flow dependent in the symptomatic patients and thus, may be a better hemodynamic indicator than the valve area in stenotic valvular lesions [11,17,20,21]. Izgi, et al. [10] demonstrated that stress systolic pulmonary artery pressure (sPAP) was the only independent variable which can predict exercise capacity, and he demonstrated that MVR is the strongest and the independent predictor of both resting and stress sPAP, Henriqu, et al. [21] considered MVR as an important index for determining severity of symptoms in patients with severe MS.

Depending on these results we studied the relation between MVR and the patient's NYHA functional class in moderate MS (the grey zone); we found that estimated MVR (at rest) showed an excellent cutoff value to detect NYHA functional class ≥II in moderate MS.

Study Limitations: The present study was limited by the small sample size. We excluded patients who had AF, so as to obtain uniformity in data collection specially DFT. We excluded patients who

had shunts and impaired systolic function to nullify the effect of left ventricular pressure on the MVR.

Conclusion

The mitral valve resistance could be used as a reliable non-invasive parameter to express stenosis severity besides the conventional stenosis indices, and could be used as an objective parameter to confirm the subjective symptomatic moderate MS to provide adequate data supporting, when to intervene or give aggressive medical treatment.

Recommendations

Further research with a large sample size, including AF cases. Follow up and study of MVR and its changes after percutaneous mitral valvuloplasty. We advice to implement MVR as an objective tool for risk stratification in regular follow up of patients with MS, especially in those with moderate MS.

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