Calculation of Mitral Valve Area in Mitral Stenosis: Comparison of Continuity Equation and Pressure Half Time With Two-Dimensional Planimetry in Patients With and Without Associated Aortic or Mitral Regurgitation or Atrial Fibrillation

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Abstract- Accurate measurement of Mitral Valve Area (MVA) is essential to determining the Mitral Stenosis (MS) severity and to achieving the best management strategies for this disease. The goal of the present study is to compare mitral valve area (MVA) measurement by Continuity Equation (CE) and Pressure Half-Time (PHT) methods with that of 2D-Planimetry (PL) in patients with moderate to severe mitral stenosis (MS). This comparison also was performed in subgroups of patients with significant Aortic Insufficiency (AI), Mitral Regurgitation (MR) and Atrial Fibrillation (AF). We studied 70 patients with moderate to severe MS who were referred to echocardiography clinic. MVA was determined by PL, CE and PHT methods. The agreement and correlations between MVA's obtained from various methods were determined by kappa index, Bland-Altman analysis, and linear regression analysis. The mean values for MVA calculated by CE was 0.81 cm (±0.27) and showed good correlation with those calculated by PL (0.95 cm, ±0.26) in whole population (r=0.771, *P*<0.001) and MR subgroup (r=0.763, *P*<0.001) and normal sinus rhythm and normal valve subgroups (r=0.858, *P*<0.001 and r=0.867, *P*<0.001, respectively). But CE methods didn't show any correlation in AF and AI subgroups. MVA measured by PHT had a good correlation with that measured by PL in whole population (r=0.770, *P*<0.001) and also in NSR (r=0.814, *P*<0.001) and normal valve subgroup (r=0.781, *P*<0.001). Subgroup with significant AI and those with significant MR showed moderate correlation (r=0.625, *P*=0.017 and r=0.595, *P*=0.041, respectively). Bland Altman Analysis showed that CE would estimate MVA smaller in comparison with PL in the whole population and all subgroups and PHT would estimate MVA larger in comparison with PL in the whole population and all subgroups. The mean bias for CE and PHT are 0.14 cm and -0.06 cm respectively. In patients with moderate to severe mitral stenosis, in the absence of concomitant AF, AI or MR, the accuracy of CE or PHT method in measuring MVA is nearly equal. But in the presence of significant AI or MR, PHT method is obviously superior to CE and in the presence of AF neither have sufficient accuracy.

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Introduction

Mitral Stenosis (MS), mainly caused by rheumatic fever, remains a public health challenge in the majority of developing countries such as Iran. Along with clinical data, accurate measurement of Mitral Valve Area (MVA) is essential to determining the MS severity and to achieving the best management strategies for this disease (1). Performing cardiac catheterization, followed by evaluating MVA using Gorlin formula is the gold standard in MVA measurement. Nevertheless, since this method is costly and invasive that may also cause morbidity and mortality, MVA is most often assessed by echocardiography. At this time, Two-Dimensional Planimetry (PL), mitral Pressure Half-Time (PHT) and the Continuity Equation (CE) are the most popular

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methods for non-invasive quantification of MVA in patients with MS, each having its own intrinsic drawbacks (2,3,4,5).

The planimetry method is highly dependent on the examination technique, and several factors such as improper receiver gain settings and inadequate image plane orientation may influence its accuracy. Yet, as it is a direct method with the no need for mathematical modeling, and also because it is less affected by concomitant Mitral Regurgitation (MR), Aortic Insufficiency (AI), and changes in heart rate (2,6), 2-Dimensional Planimetry usually serves as a gold standard for the assessment of MS in routine clinical practices (7), and as the reference method for providing anatomical measurements of the mitral valve orifice (8,9).

The main goal of this study is to determine MVA by Doppler echocardiography in a noninvasive manner utilizing CE and PHT methods and then to compare the accuracy of these two methods with that of 2D planimetry in patients with moderate to severe MS. On the side, we also perform such comparison for three subgroups of patients with atrial fibrillation and with concomitant valvular regurgitation (AI and MR).

Materials and Methods

Study population

From April of 2010 to March of 2011, we studied 70 patients among those who were referred to echocardiography clinics at our tertiary teaching hospital. The inclusion criterion was moderate to severe MS which corresponds to an MVA of less than 1.5 cm^2 measured using 2D planimetry technique. Exclusion criteria, on the other hand, were the presence of surgical commissurotomy or percutaneous balloon mitral valvuloplasty in the patient's history, severe distortion of valve anatomy particularly with severe valve calcification at the tip of the leaflet, and unsatisfactory acoustic window or unstable hemodynamic condition of the patient. Informed consent was obtained from each patient, and the study was approved by the local Ethics Committee of our center.

Echocardiographic examinations and measurements

All the patients underwent 2D and Doppler echocardiography at rest while they were asked to lie in the left lateral decubitus position in order to optimize the quality of the echocardiographic images. The echocardiographic examinations were conducted by an ultrasonography device (VIVID 7, GE-VingMed, Horten, Norway) equipped with a 3.5 MHz transducer and depth was adjusted for the parasternal and apical views. Making use of the modified Simpson method, the ejection fraction was measured at the apical four-chamber view. The left ventricular diameters, as well as the left atrial diameter, were calculated at the parasternal two-dimensional views as recommended by the American Society of Echocardiography (10).

The planimetry method

Using the 2D images of the mitral valve obtained from parasternal short axis view, 2D planimetry of the mitral orifice area was accomplished by an experienced cardiologist. To avoid probable overestimation of the area, the narrowest orifice of mitral valve (i.e., the location of leaflet tip) was identified by means of scanning from the left atrium in the direction of the left ventricular apex (9). The gain was set to the lowest level at which the circumference of the mitral orifice was still visible. Next step was determining the frame for which the mitral orifice was at its maximum opening in early diastole, followed by MVA measurement with the help of the planimetry method. Three and five cycles were recorded in patients with sinus rhythm and atrial fibrillation (AF) respectively. In each case, the mean of the consecutive MVA measurements was used in the calculations. The result served as the gold standard for MVA measurement in this study.

The continuity equation method

Mitral valve area was computed using CE as the ratio of the aortic forward stroke volume over the Trans mitral time-velocity integral, in which the aortic forward stroke volume itself is the product of the cross-sectional area of the aortic annulus and the time-velocity integral of the left ventricular outflow tract (Figure 1). Again, three and five cycles were recorded in patients with sinus and AF rhythm respectively, followed by averaging between the consecutive measurements, with the final result being the mean value for each patient.

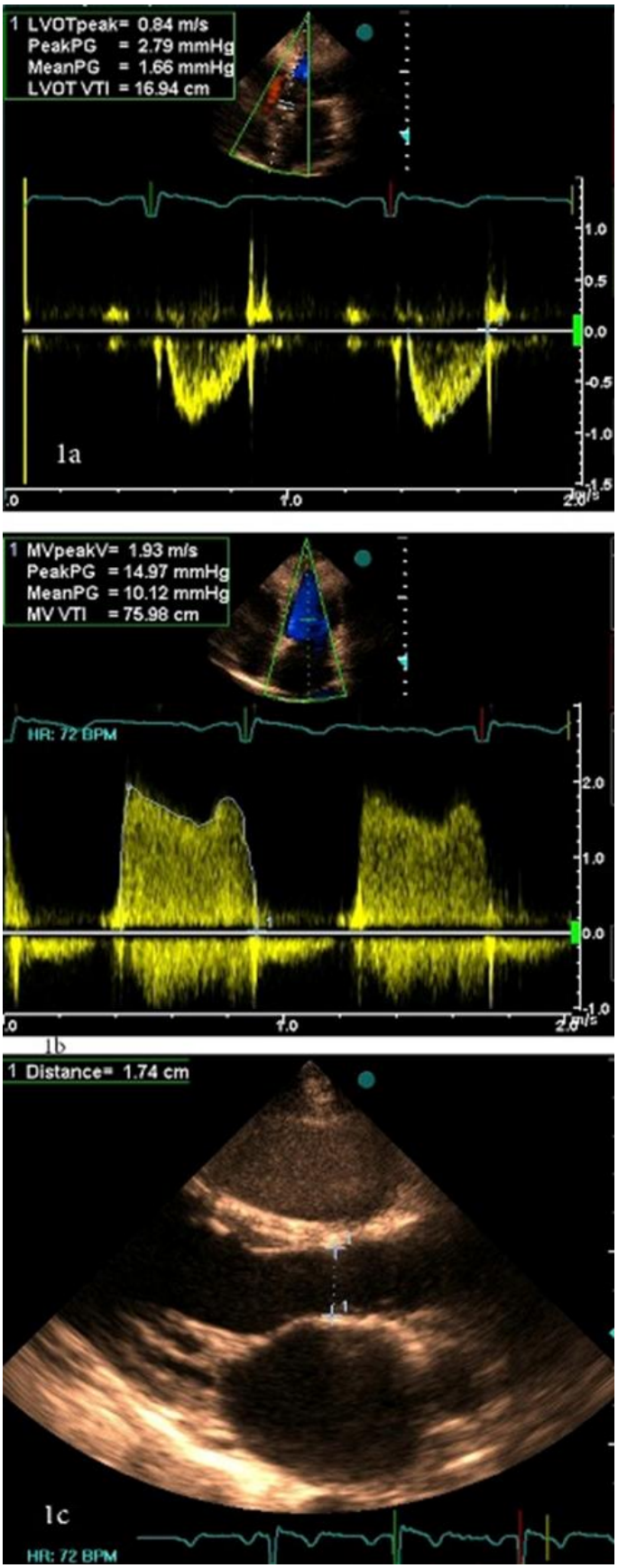

Figure 1. Measurements of LVOT-VTI, and MV-VTI and aortic annulus diameter for calculating mitral valve area by continuity equation method

The pressure half-time method

Using spectral continuous color Doppler traces of the diastolic Transmitral flow, MVA was estimated at the apical four-chamber view (11). The PHT, the time interval between the maximum early diastolic pressure gradient, and the point where the gradient is half the maximum value, were obtained. MVA was calculated as 220 divided by PHT using PHT method. A minimum of five beats was analyzed for each patient.

Statistical analysis

Continuous variables and categorical data are expressed in the form of mean±SD and absolute number (percentage) respectively. The data obtained by three methods were compared and analyzed in several ways. Initially, the kappa coefficient was calculated for the amount of agreement between the two methods in determining severe mitral stenosis (MVA less than 1 cm^2). To do this, MVA variable that was calculated in quantitative form changed to dichotomy variable (1 stands for MVA<1$_{cm^2}$ and 0 for MVA≥1 $_{cm^2}$) and then kappa coefficient was measured between two methods. After that, the correlation between MVA's obtained from PHT and CE methods with PL was determined by linear regression analysis. Finally, the agreement and bias between two methods that are measuring a same quantitative variable (CE vs. PL and PHT vs. PL) also were calculated by Bland-Altman analysis. All the statistical analyses were accomplished with the use of the commercially available package SPSS version 18.0, SPSS, Inc., Chicago, IL, USA

Results

Clinical and echocardiographic characteristics of the patients are summarized in Table 1. The average age of the study population was 42±9 years ranging from 20 to 73 years with 55 participants (78.6%) being women. Sixteen patients (23%) had AF rhythm. Fourteen patients (20%) has at least moderate MR or higher. At least moderate AI was seen in twelve patients (17%).

The mean value of MVA obtained by 2-D planimetry was 0.95±0.26 cm^2 ranging from 0.45 to 1.45 cm^2. The average values of MVA measured by PHT and CE, on the other hand, were 1.01±0.31 cm^2 and 0.81±0.27 cm^2, respectively. Mean of MVA which was obtained by each method are presented in Table 1 based on subgroups. Other echocardiographic data also presented in table 1.

Table 1. Descriptive Data

	Total		Valvular Disease						Rhythm			
			Significant AI		Significant MR		No Significant Regurgitation		NSR		AF	
Number	70	100%	12*	17%	14*	20%	46*	66%	54	77%	16	23%
Age	42	(±9.01)	41.25	(±6.48)	42.07	(±7.13)	42.47	(±10.06)	40.184	(±7.65)	48.25	(±10.60)
Female	55	78%	9	75%	11	79%	36	78%	42	78%	13	81%
EF	48%	(±0.06)	48%	(±0.06)	45%	(±0.08)	49%	(±0.05)	49%	(±0.05)	46%	(±0.07)
LVEDD	4.68	(±0.59)	4.80	(±0.60)	5.02	(±0.45)	4.56	(±0.60)	4.66	(±0.52)	4.75	(±0.80)
LVESD	3.20	(±0.62)	3.16	(±0.60)	3.40	(±0.56)	3.16	(±0.62)	3.11	(±0.52)	3.50	(±0.82)
LAD	4.85	(±0.99)	4.95	(±1.01)	4.91	(±1.11)	4.88	(±1.04)	4.76	(±1.05)	5.15	(±0.73)
LAA	30.37	(±8.17)	30.92	(±10.54)	35.29	(±10.69)	29.53	(±7.40)	29.20	(±8.12)	34.31	(±7.26)
LVOTVTI	18.54	(±3.76)	19.29	(±3.89)	17.99	(±4.44)	18.27	(±3.66)	19.25	(±3.72)	16.12	(±2.85)
RVOTVTI	13.59	(±3.05)	13.25	(±3.72)	12.46	(±3.45)	13.76	(±2.99)	13.80	(±2.84)	12.88	(±3.70)
MVVTI	70.93	(±23.14)	73.89	(±12.06)	71.37	(±23.56)	69.83	(±25.01)	72.30	(±25.40)	66.30	(±12.38)
SYS.PAP	48.14	(±17.36)	54.17	(±22.85)	51.43	(±16.80)	45.76	(±15.42)	46.76	(±18.02)	52.81	(±14.49)
MVA.PL	0.95	(±0.26)	0.83	(±0.20)	1.05	(±0.27)	0.95	(±0.26)	0.95	(±0.28)	0.94	(±0.19)
MVA.CE	0.81	(±0.27)	0.74	(±0.21)	0.76	(±0.33)	0.83	(±0.26)	0.85	(±0.28)	0.67	(±0.18)
MVA.PHT	1.01	(±0.31)	0.86	(±0.31)	1.13	(±0.27)	1.03	(±0.31)	1.03	(±0.34)	0.95	(±0.18)

- Continuous Parameters presented in Value (±SD) and Number and Gender presented in absolute number and percentage format.
- * Two patients had both AI and MR and counted in both groups.

AI : Aortic Insufficiency, MR : Mitral Regurgitation, NSR : Normal Sinus Rhythm, AF : Atrial Fibrillation, EF : Ejection Fraction, LVEDD : Left Ventricle End Diastolic Diameter, LVESD : Left Ventricle End Systolic Diameter, LAD : Left Atrium Diameter, LAA : Left Atrium Area, LVOTVTI : Left Ventricle Outflow Tract Velocity-Time Integral, RVOTVTI : Right Ventricle Outflow Tract Velocity-Time Integral, MVVTI : Mitral Valve Velocity-Time Integral, SYS.PAP : Systolic Pulmonary Artery Pressure, MVA : Mitral Valve Area, PL : Planimetry, CE : Continuity Equation, PHT : Pressure Half Time

Results of the mentioned analysis are presented in Table 2. Kappa coefficient between PL and CE was 0.421 in whole population and -0.11, -0.286, 0.125 in AF, AI and MR subgroups respectively. Kappa coefficient between PL and PHT showed better agreement (than PL and CE) in the whole population and all subgroups. It was 0.658 in the whole population and 0.213, 0.800, 0.300 in AF, AI and MR subgroups respectively.

Table 2. Analytic Data. Comparison of CE and PHT

		Total	Rhythm		Valvular Disease		
			NSR	AF	Sig. AI	Sig. MR	No Sig. Regurgitation
Planimetry vs continuity Equation	**Kappa Coefficient**	0.421	0.495	-0.116	-0.286	0.125	0.646
	Correlation.R (*P*)	0.771 (<0.001)	0.858 (<0.001)	0.287 (0.281)	0.276 (0.385)	0.763 (0.001)	0.867 (<0.001)
	Bland Altman Bias (SD)	0.141 (±0.179)	0.105 (±0.149)	0.264 (±0.223)	0.094 (±0.250)	0.288 (±0.213)	0.123 (±0.135)
Planimetry vs Pressure Half Time	**Kappa Coefficient**	0.658	0.775	0.213	0.800	0.300	0.654
	Correlation.R (*P*)	0.770 (<0.001)	0.814 (<0.001)	0.263 (0.325)	0.595 (0.041)	0.625 (0.017)	0.781 (<0.001)
	Bland Altman Bias (SD)	-0.065 (±0.204)	-0.082 (±0.198)	-0.010 (±0.223)	-0.027 (±0.251)	-0.080 (±0.231)	-0.074 (±0.196)

Sig. AI : Significant Aortic Insufficiency, Sig. MR : Significant Mitral Regurgitation, NSR : Normal Sinus Rhythm, AF : Atrial Fibrillation

The mean values for MVA that were calculated by CE had good correlation with those calculated by PL in whole population (r=0.771, *P*<0.001) and MR subgroup (r=0.763, *P*<0.001). These values showed very good correlation in Normal Sinus Rhythm (NSR) and MS without significant regurgitation subgroups (r=0.858, *P*<0.001 and r=0.867, *P*<0.001, respectively) (Figure 2). But AF and AI subgroups did not show any correlation (r=0.287, *P*=0.281 and r=0.276, *P*=0.385 respectively). Mean values of MVA measured by PHT method had a good correlation with that measured by PL in the whole population (r=0.770, *P*<0.001) and in NSR (r=0.814, *P*<0.001) and MS without significant regurgitation subgroup (r=0.781, *P*<0.001). Subgroup with significant AI and those with significant MR showed moderate correlation (r=0.625, *P*=0.017 and r=0.595, *P*=0.041, respectively)

Bland Altman Analysis showed that CE would estimate MVA smaller in comparison with PL in the whole population and all subgroups (positive values for ($\sum_1^n PL - CE$)) and PHT would estimate MVA larger in comparison with PL in whole population and all subgroups (negative values for ($\sum_1^n PL - PHT$)). Bland Altman graphs illustrated in (Figure 3).

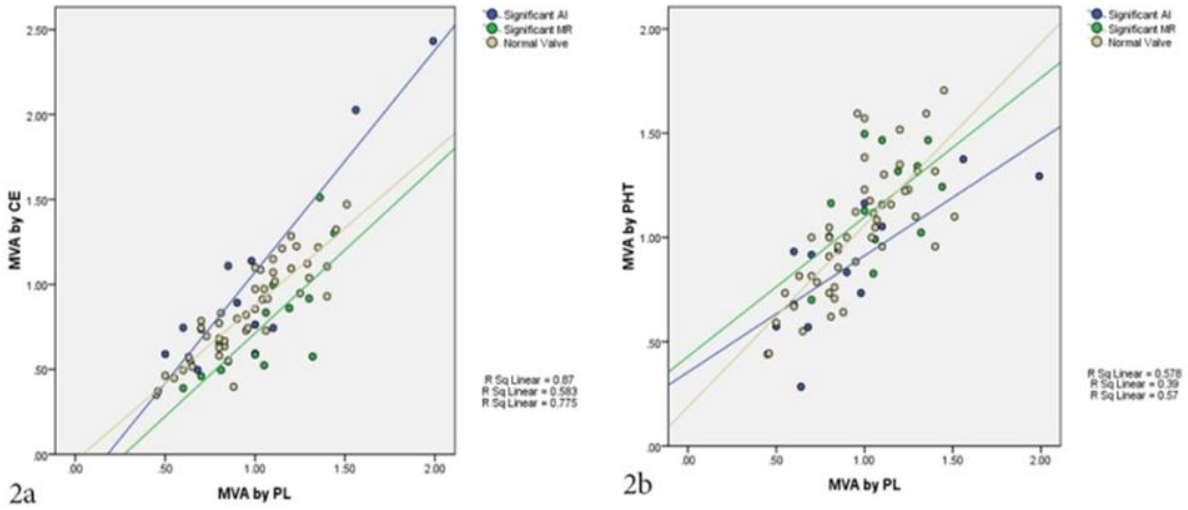

Figure 2. Mitral valve area determined by CE (A) and PHT (B) methods plotted against PL measurements. Different colors represent patients with AI, MR, and Otherwise Normal Valve (Mitral Stenosis without significant regurgitation)

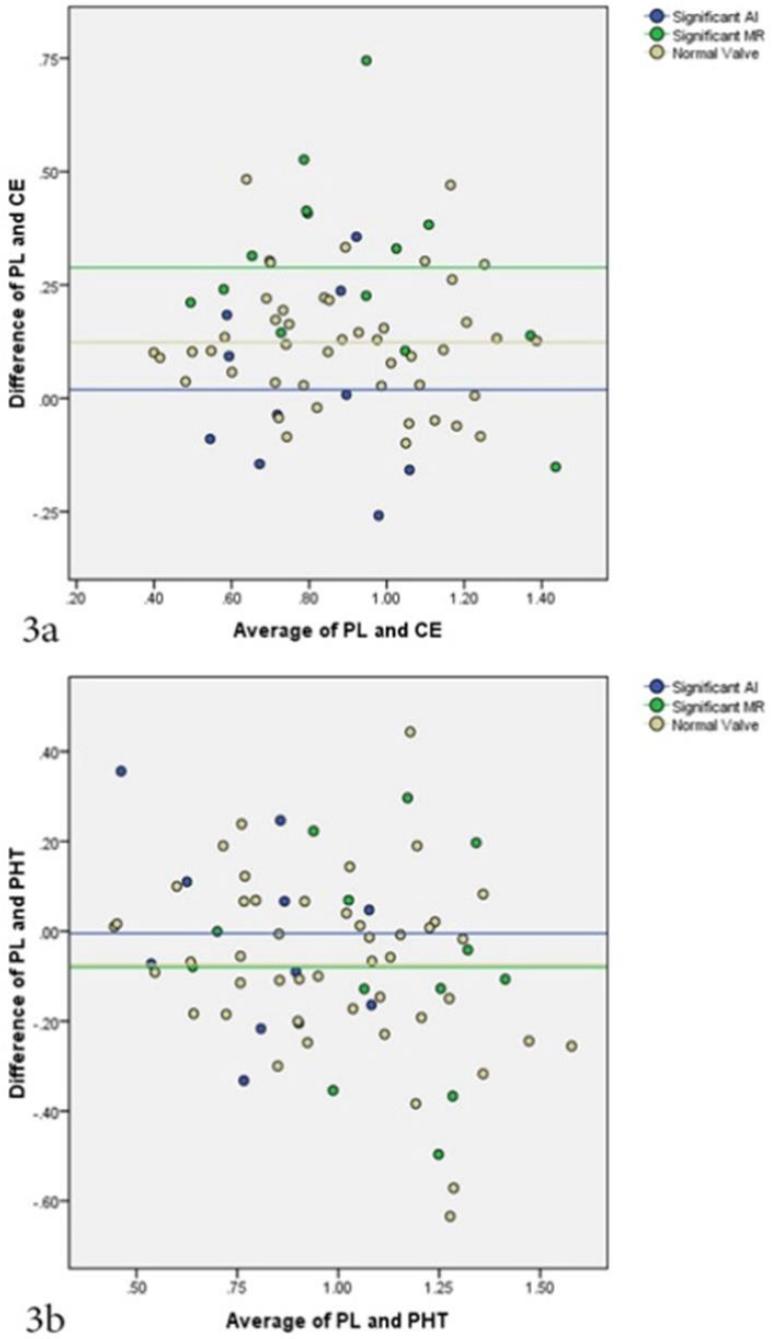

Figure 3. Bland Altman plot for PL.CE (A) and PL.PHT (B). Different colors represent patients with AI, MR and Otherwise Normal Valve (Mitral Stenosis without significant regurgitation)

Discussion

Mitral stenosis severity determination, which relies on the accurate evaluation of MVA, plays crucial prognostic and therapeutic roles in clinical assessment. Cardiac catheterization using the Gorlin formula is an invasive method and therefore its usage must be limited to cases where using echocardiographic methods for MVA measurements yield conflicting results or when there exists discrepancy between echocardiographic and clinical findings (12). Hence, need for an accurate noninvasive method capable of effective MVA assessment is felt among clinicians. Such method must be able to provide an estimate as close as possible to the

actual anatomic values. Direct measurement of MVA by 2D planimetry remains the reference measurement method as it shows excellent correlation with anatomic orifice size (8). However, this technique is highly dependent on operator skills and becomes burdensome quite sometimes (2). Also, the feasibility of the planimetry method is limited as it cannot be applied to almost 5% of patients due to a massive calcification or poor acoustic window (13).

In the present study, we compared the accuracy of the two widely used echocardiographic methods that are used for MVA calculation, namely CE and PHT, using PL as a gold standard.

The continuity equation

It has previously been demonstrated that MVA may be determined accurately by Doppler echocardiography based on the equation of continuity (14). Herein, we applied this method to quantify the MVA in patients with MS and associated AF, MR, and AI. As a result, we found that this method is quite accurate in determining MVA, just in the absence of AF, AI or MR. Among 44 patients in sinus rhythm with mitral stenosis, Derumeaux *et al*., (15) compared CE with planimetry and PHT method, and the results achieved from catheterization using the Gorlin formula. The authors suggested that for evaluating the severity of mitral stenosis, CE was reliable and accurate compared to catheter data and it was superior to PHT method. The sensitivity and specificity of CE for the estimation of MVA<1.5 cm2 were 90% and 100% respectively while those of PHT method were 88% and 91% accordingly. In a recent study, Chu *et al*., (16) also showed that real-time 3-dimensional echocardiography, which provides an accurate measurement of MVA in calcific MS, has a greater correlation with MVA calculated by CE than MVA by PHT (r=0.86 vs. r=0.59, respectively).

Similar to our finding, there are several reports that CE is invalidated by the presence of AI (9,12,17) but Yamagishi *et al*., (18) showed that MVA determined by CE method correlated well with catheterization measurements irrespective of the presence of AI (r=0.91). Nakatani *et al*., (14) also suggested that in the presence of AI, CE method might be more accurate for estimation of MVA, as compared to PHT method

In addition, unlike PHT method, that its accuracy for the measurement of the MVA has been questioned immediately after percutaneous balloon mitral valve dilatation (19), the MVA calculated by the Doppler CE immediately after balloon inflation correlated well (r=0.9) with measurements at catheterization by the Gorlin formula (20) indicating the superiority of CE method over PHT method for this setting. This is possibly because of the dependence of PHT method on physiological parameters such as left atrial and left ventricular compliance that alters abruptly following valvuloplasty (21).

However, CE has several theoretical and practical limitations. First, it is not recommended for routine use in MS because it is technically demanding and needs multiple measurements, increasing the effect of errors (12). Second, this method is dependent on transvalvular flow and can be affected by cardiac output and the presence of MR and AI (9), and therefore it cannot be used in patients with atrial fibrillation or associated significant MR and AI (12).

The pressure half-time

Due to its simplicity, PHT method, proposed by Hatle *et al*., (11), is currently used as a popular Doppler method to noninvasively estimate MVA in the clinical situation. Nevertheless, this technique has some significant limitations. The PHT method used for the estimation of MVA is inaccurate under the conditions of tachycardia, concomitant significant AI or left ventricular dysfunction (14,22,23,24). This method is also inaccurate in the setting of atrial fibrillation and left ventricular stiffness (4,25). Therefore, it is interesting in our study that in the presence of associated valvular abnormalities (Both MR and AI) PHT is still reliable (At least better than CE) to measure MVA, But AF had major impact on its accuracy and its correlation with PL.

Since MS is often concomitant with other valvular heart diseases including AI or MR, and sometimes using PL is really impossible, one has to choose another method such as CE or PHT to calculate MVA. In these circumstances our results are in favor of PHT in comparison to CE; however, more studies should be done to validate these results.

The main limitation of our study is possibly the lack of cardiac catheterization and using Gorlin formula as the standard method for measurement of MVA. Single center study and lack of inter-observer and intra-observer were other limitations; however, our study was conducted in a tertiary referral center admitting patients from all across the country, and all of the echocardiography was done by the single fellowship of echocardiography. As far as we know, this study with seventy patients of at least moderate MS is one of the biggest studies in this field.

In patients with moderate to severe mitral stenosis, in the absence of concomitant AF, AI or MR, the accuracy of CE or PHT method in measuring MVA is nearly equal.

But in the presence of significant AI or MR, PHT method is obviously superior to CE and in the presence of AF neither have sufficient accuracy.

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