

# Assessment of Mitral Stenosis by Doppler Echocardiography - Influence of Regurgitation on Doppler Pressure Half-Time -

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## 승모판 협착증의 Doppler 심초음파 소견 : - 동반된 승모판 폐쇄부전 및 대동맥판 폐쇄부전이 승모판 혈류의 Pressure Half-Time 측정에 미치는 영향 -

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### 국문 초록

승모판 협착증에서 Doppler 심초음파로 승모판구 면적을 측정할 때 일반적으로 pressure half time(PHT)을 이용하고 있다.

그러나 동반되어 있는 승모판 폐쇄부전이나 대동맥판 폐쇄부전 혈류가 승모판 혈류의 PHT에 미치는 영향에 대한 연구는 드문 실정이다. 이에 저자들은 203례의 승모판 협착증 환자를 대상으로 연구하여 다음과 같은 결과를 얻었다. 전체 환자중 승모판 협착증만 있었던 레는 90례, 승모판 폐쇄부전이 동반되어 있는 레는 45례, 대동맥판 폐쇄부전이 있었던 레는 54례, 승모판 폐쇄부전과 대동맥판 폐쇄부전증이 있었던 레는 14례 이었다.

Doppler 심초음파도의 승모판구 면적 지표인 PHT은 이면성 심초음파도에서 측정된 승모판구 면적과 다음과 같은 상관관계가 있다.

전체 환자군  $r=0.903$ , 승모판 협착증만 있었던 환자군  $r=0.924$ , 승모판 폐쇄부전 동반군  $r=0.867$ , 대동맥판 폐쇄부전 동반군  $r=0.911$ , 승모판 폐쇄부전과 대동맥판 폐쇄부전 동반군  $r=0.843$  이었다.

이상의 결과로 승모판 협착증에서 승모판 혈류의 Doppler 심초음파도에서 PHT로 측정하는 방법은 동반된 승모판 폐쇄부전이나 대동맥판 폐쇄부전에 의해 영향을 받지 않고 정확히 승모판구 면적을 측정할 수 있는 유용한 방법으로 생각되었다.

### = Abstract =

Mitral pressure half-time(PHT) is widely used as an independent measure of mitral valve area (MVA) in patients with mitral stenosis. However,

few data exist regarding the effect of mitral regurgitation and aortic regurgitation on the validity of this method. Two hundreds and three patients with mitral stenosis were studied by Doppler echocardiography and 2 dimensional echocardiography(2

DE) to assess whether mitral regurgitation and aortic regurgitation affected the calculation. Ninety patients had mitral stenosis only, 45 patients were combined with mitral regurgitation, 54 patients were combined with aortic regurgitation and 14 patients were combined with both mitral and aortic regurgitation group. Doppler PHT and 2DE estimates of MVA correlated well in total patients ( $r=0.903$ ) and mitral stenosis only group ( $r=0.924$ ). Good correlations were maintained in patient subgroups combined with mitral or aortic regurgitation ( $r=0.867$  and  $0.911$ , respectively) and both mitral and aortic regurgitation ( $r=0.843$ ). Thus, measurement by Doppler PHT may reflect accurately the MVA as determined by 2DE regardless of presence of mitral and/or aortic regurgitation.

**KEY WORDS :** Mitral stenosis • Pressure half-time method • Mitral regurgitation • Aortic regurgitation.

## INTRODUCTION

Mitral stenosis is the most common valvular heart disease. The estimation of the mitral valve area (MVA) is essential for the evaluation and treatment in patients with mitral stenosis. Cardiac catheterization has been used for a long time to calculate the mitral valve area, but it has some limitations in cases associated with mitral regurgitation, atrial fibrillation, low cardiac output, and most of all catheterization has a definite morbidity and mortality<sup>1-5</sup>).

The noninvasive assessment of mitral stenosis by measuring transmitral pressure gradient or stenotic valve area has been developed. Two-dimensional echocardiography (2DE) is the most widely used method for noninvasive quantification of mitral valve area in patients with mitral stenosis<sup>6-9</sup>). However, when the mitral valve is extensively distorted or severely calcified or both, accurate measurement of the mitral valve area by 2DE may not

be possible<sup>9-11</sup>).

Doppler echocardiographic measurement of pressure half-time (PHT) has been widely accepted for the noninvasive estimation of the MVA in patients with mitral stenosis<sup>12-21</sup>). Hatle et al<sup>18</sup>) developed the pressure half-time method for estimating the mitral valve area. Previous observations made in the cardiac catheterization laboratory demonstrated that the severity of mitral stenosis is directly proportional to the time required for the pressure gradient to fall to one half of its original value. The pressure half-time can be easily determined from continuous wave Doppler spectrum. The mitral valve area obtained using the pressure half-time method have been shown to correlate quite well with cardiac catheterization measurements and relatively unaffected by changes in the other hemodynamic parameters, such as after load, left ventricular filling pressure, heart rate and left atrial and ventricular compliance.

However, recently some investigators<sup>22,23</sup>) have demonstrated that hemodynamic changes cause variations in the pressure gradient across the stenotic valve. In most clinical situations, increase in the pressure will typically decrease atrial and ventricular compliance. However when anatomic shape or physiological changes have independently changed either pressure or compliance, then the PHT method estimates of mitral valve area could be erroneous. And also the PHT is longer in patients with mitral regurgitation, and the PHT is shorter with exercise.

This study evaluates the influence of mitral and/or aortic regurgitation on the determination of Doppler echocardiographic indices for mitral valve area calculation in patients with mitral stenosis.

## SUBJECTS AND METHODS

Two hundreds and three patients with mitral stenosis were included in this study. Fiftysix patients

**Table 1.** Age and sex distribution of patients group

Age	Male	Female	Total
~19	2	1	3
20~29	7	11	18
30~39	11	19	30
40~49	9	40	49
50~59	16	43	59
60~69	8	30	38
70~	3	3	6
Total	56 (27.6%)	147 (72.4%)	203

were male and 147 patients were female. Sixtythree patients were in sinus rhythm. The distribution of age and sex were shown on the Table 1.

Total study population was divided into 4 groups with or without regurgitations. Group 1 was consisted of 90 patients who had mitral stenosis(MS) only. Group 2 was consisted of 45 patients who had MS and mitral regurgitation(MR). Group 3 was consisted of 54 patients who had MS and aortic regurgitation(AR). Group 4 was consisted of 14 patients who had MS with MR and AR.

Two-dimensional echocardiography(2DE) and Doppler echocardiography were obtained using phased-array imaging systems with a 3.5/2.0 MHz transducer with Meridian Echocardiography System. Patients were placed in left lateral decubitus position and electrocardiography were recorded simultaneously.

Two-dimensional echocardiography were obtained in the standard parasternal short-axis view. The smallest orifice of the mitral valve was carefully identified by scanning from the left atrium to the left ventricle and the optimal frame of early diastole was visualized and planimetered to estimate the mitral valve area.

The Doppler mitral valve area was calculated using the pressure half-time method. Diastolic transmitral inflow was identified and distinguished from aortic regurgitation using pulsed Doppler mapping technique. Continuous-wave Doppler was

used to identify the maximal diastolic velocity across the mitral valve from the apical window. A velocity at half-pressure was estimated by  $V/1.4$ , where V is the maximal velocity, and  $V/1.4$  represents the velocity at which the diastolic transvalvular gradient has fallen by one-half. The pressure half-time is the time from peak to half-pressure. Mitral valve area was then determined by dividing 220 by the pressure half-time. In patients with atrial fibrillation, more than 3 signals were averaged from cardiac cycles with a sufficiently long RR interval to readily identify transmitral velocity. Mean pressure gradient, peak pressure gradient and peak velocity were also obtained from transmitral inflow. A Doppler study was considered positive for valve regurgitation if both an audio and spectral signal were clearly present, if the spectral signal displayed turbulent flow and if the spectral signal was present for the duration of more than 50% of either systole or diastole for a given valve. The severity of valve regurgitation was graded on scale from 0 to 4<sup>+</sup> (0 = none, 1<sup>+</sup> = mild, 2<sup>+</sup> = moderate, 3<sup>+</sup> = moderately severe, and 4<sup>+</sup> = severe). In case of more than moderate regurgitation, we considered as presence of aortic or mitral regurgitation in this study.

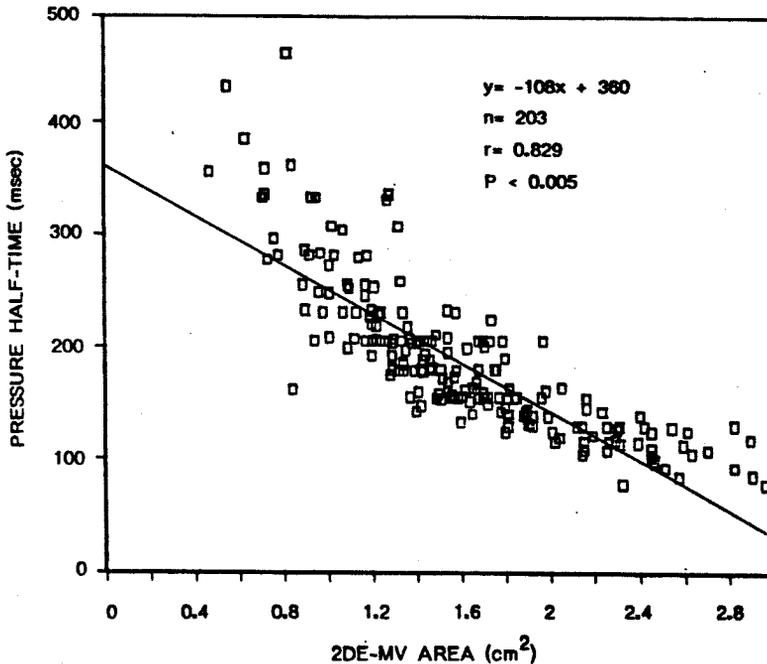
Every measurements from recorded videotapes were obtained from MicroSonics CAD 886 version 2.3 software and HIPAD digitizer which is connected to IBM PC. Linear regression analysis was used to compare each Doppler parameters and standard reference, 2DE-MVA.

## RESULTS

The mean value of mitral valve area of total 203 patients as determined by 2DE(2DE-MVA) was  $1.60 \pm 0.52 \text{cm}^2$  and from the Doppler pressure half-time method was  $1.32 \pm 0.44 \text{cm}^2$ . Pressure half-time, mean pressure gradient, peak pressure gradient and peak velocity were  $187.42 \pm 67.53 \text{msec}$ ,  $7.67 \pm 3.64 \text{mmHg}$ ,  $14.76 \pm 5.52 \text{mmHg}$  and  $1.89 \pm 0.35 \text{m/sec}$  respectively. As compared with standard

**Table 2.** Correlation between 2DE-MVA and Doppler echocardiographic indices in total patients(n=203)

	Mean± S.D	r value	P value
2DE-MVA(cm <sup>2</sup> )	1.60± 0.52		
Doppler indices			
Mitral valve area(cm <sup>2</sup> )	1.32± 0.44	0.903	0.005
Pressure half-time(msec)	187.42± 67.53	0.829	0.005
Mean pressure gradient(mmHg)	7.67± 3.64	0.507	0.005
Peak pressure gradient(mmHg)	14.76± 5.52	0.447	0.005
Peak velocity(m/sec)	1.89± 0.35	0.454	0.005



**Fig. 1.** Correlation between two-dimensional echocardiographic mitral valve area(2DE-MVA) and pressure half-time in total patient.

reference 2DE-MVA, these Doppler derived MVA, PHT, mean pressure gradient, peak pressure gradient and peak velocity were significantly correlated with correlation coefficient  $r=0.903, 0.829, 0.507, 0.447$  and  $0.454$  respectively( $P<0.005$ , Table 2). Fig. 1 and Fig. 2 showed correlation between 2DE-MVA and PHT( $r=0.829, y=-108x+360, P<0.005$ ) or mean pressure gradient( $r=0.507, y=-3.6x+13.4, P<0.005$ ).

In group 1(MS only,  $n=90$ ), the mean value of MVA from 2DE was  $1.51\pm 0.51\text{cm}^2$  and from

Doppler PHT method was  $1.24\pm 0.45\text{cm}^2$ . PHT, mean pressure gradient, peak pressure gradient and peak velocity were  $202.94\pm 76.86\text{msec}, 8.13\pm 3.81\text{mmHg}, 15.23\pm 5.75\text{mmHg}$  and  $1.92\pm 0.36\text{m/sec}$  respectively. As compared with standard reference 2DE-MVA, these Doppler derived MVA, PHT, mean pressure gradient, peak pressure gradient and peak velocity were significantly correlated with correlation coefficients  $r=0.924, 0.845, 0.549, 0.487$  and  $0.496$  respectively( $P<0.005$ , Table 3). Fig. 3 and Fig. 4 shows correlation between 2DE-

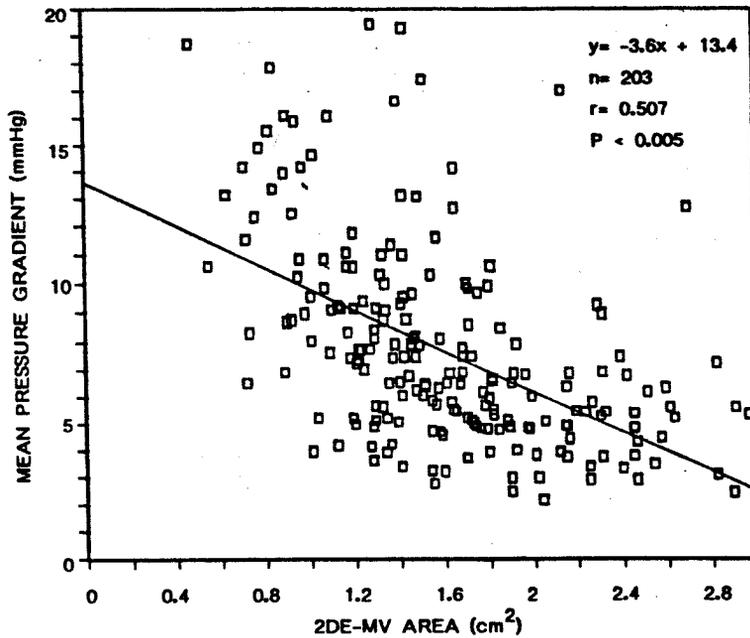


Fig. 2. Correlation between 2DE-MVA and mean pressure gradient in total patient.

Table 3. Correlation between 2DE-MVA and Doppler echocardiographic indices in group I (MS only, n=90)

	Mean $\pm$ S.D	r value	P value
2DE-MVA(cm <sup>2</sup> )	1.72 $\pm$ 0.53		
Doppler indices			
Mitral valve area(cm <sup>2</sup> )	1.44 $\pm$ 0.47	0.867	0.005
Pressure half-time(msec)	167.09 $\pm$ 57.74	0.794	0.005
Mean pressure gradient(mmHg)	7.27 $\pm$ 4.0	0.652	0.005
Peak pressure gradient(mmHg)	14.78 $\pm$ 6.07	0.632	0.005
Peak velocity(m/sec)	1.89 $\pm$ 0.38	0.644	0.005

MVA and PHT( $r=0.845$ ,  $y=-127.6x+396$ ,  $P<0.005$ ) or mean pressure gradient( $r=0.549$ ,  $y=-4.1x+14.4$ ,  $P<0.005$ ).

In group 2(MS+MR,  $n=45$ ), the mean value of MVA from 2DE was  $1.7 \pm 0.53 \text{ cm}^2$  and from Doppler PHT method was  $1.44 \pm 0.47 \text{ cm}^2$ . PHT, mean pressure gradient, peak pressure gradient and peak velocity were  $167.09 \pm 57.74 \text{ msec}$ ,  $7.27 \pm 4.0 \text{ mmHg}$ ,  $14.78 \pm 6.07 \text{ mmHg}$  and  $1.89 \pm 0.38 \text{ m/sec}$  respectively. As compared with standard reference 2DE-MVA, these Doppler derived MVA, PHT, mean pressure gradient, peak pressure gradient and peak velocity were significantly correlated with

correlation coefficients  $r=0.867$ ,  $0.794$ ,  $0.652$ ,  $0.632$  and  $0.644$  respectively ( $P<0.005$ , Table 4). Fig. 5 and Fig. 6 showed correlation between 2DE-MVA and PHT( $r=0.794$ ,  $y=-86x+315$ ,  $P<0.005$ ) or mean pressure gradient( $r=0.652$ ,  $y=-4.9x+15.7$ ,  $P<0.005$ ).

In group 3(MS+AR,  $n=54$ ), the mean value of MVA from 2DE was  $1.60 \pm 0.52 \text{ cm}^2$  and from Doppler PHT method was  $1.32 \pm 0.39 \text{ cm}^2$ . PHT, mean pressure gradient, peak pressure gradient and peak velocity were  $184.24 \pm 58.35 \text{ msec}$ ,  $7.59 \pm 3.16 \text{ mmHg}$ ,  $14.37 \pm 4.97 \text{ mmHg}$  and  $1.87 \pm 0.32 \text{ m/sec}$  respectively. As compared with standard refe-

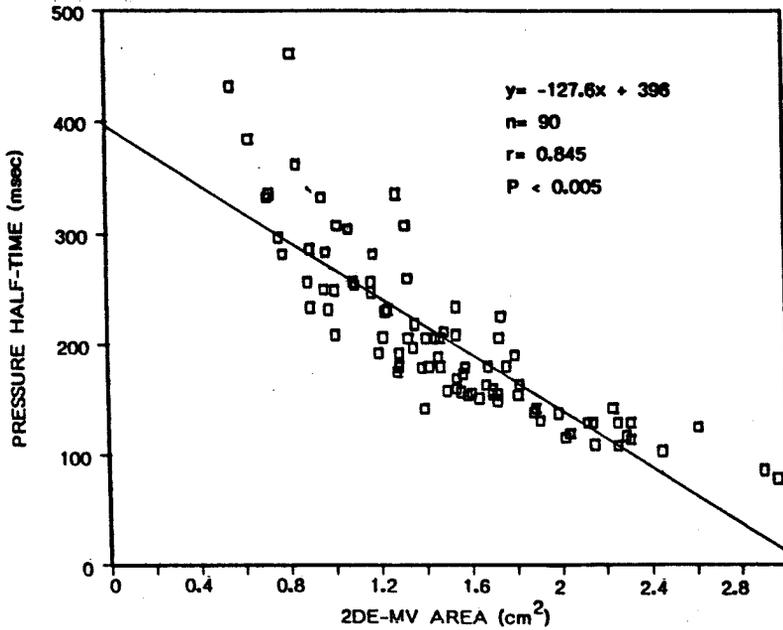


Fig. 3. Correlation between 2DE-MVA and pressure half-time in group I(mitral stenosis only).

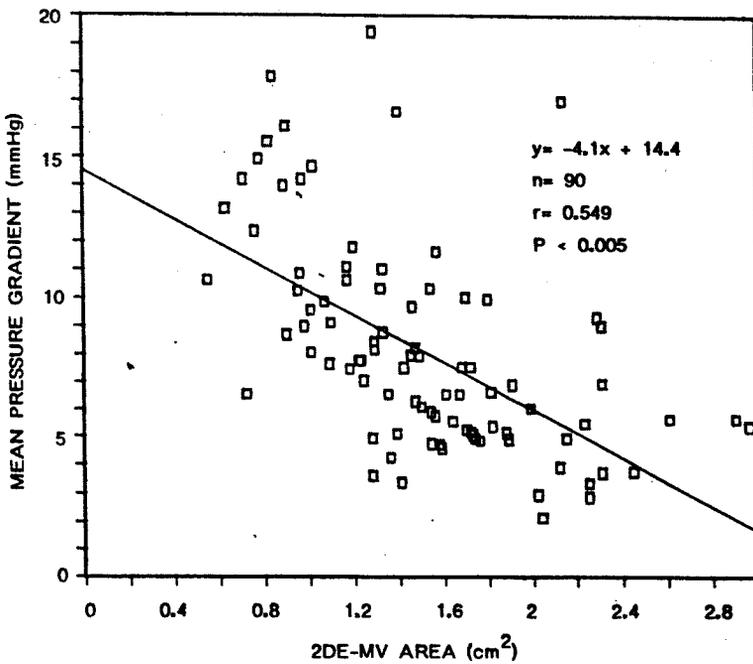


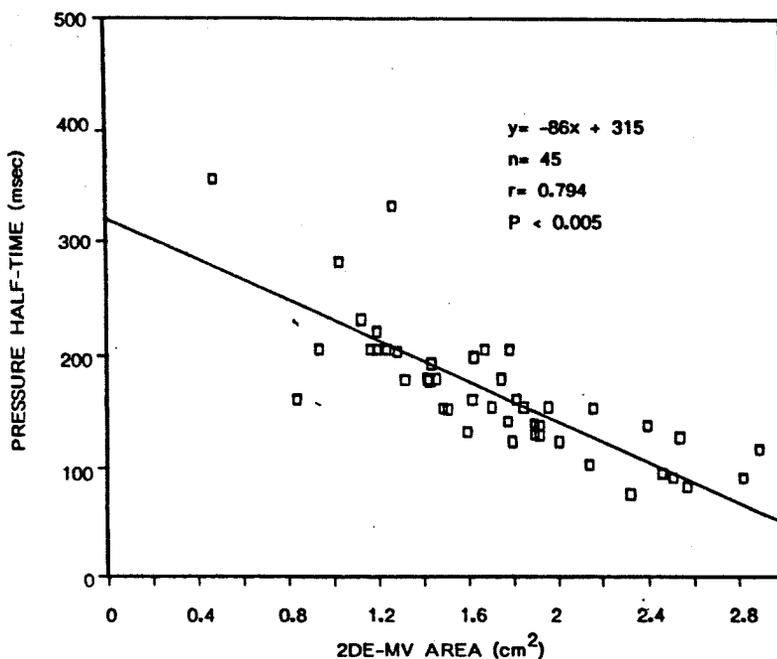
Fig. 4. Correlation between 2DE-MVA and pressure gradient in group I(mitral stenosis only).

rence 2DE-MVE, Doppler derived MVA, PHT and mean pressure gradient were significantly correlated with correlation coefficients  $r=0.911$ ,  $0.851$  and  $0.274$  respectively ( $P<0.005$ ,  $P<0.005$ ,  $P<0.05$ ,

Table 5). But peak pressure gradient and peak velocity were not correlated with 2DE-MVA. Fig. 7 and Fig. 8 showed correlation between 2DE-MVA and PHT ( $r=0.851$ ,  $y=-95x+346$ ,  $P<0.005$ ) or

**Table 4.** Correlation between 2DE-MVA and Doppler echocardiographic indices in group II (MS+MR, n=45)

	Mean $\pm$ S.D	r value	P value
2DE-MVA(cm <sup>2</sup> )	1.51 $\pm$ 0.51		
Doppler indices			
Mitral valve area(cm <sup>2</sup> )	1.24 $\pm$ 0.45	0.924	0.005
Pressure half-time(msec)	202.94 $\pm$ 76.86	0.845	0.005
Mean pressure gradient(mmHg)	8.13 $\pm$ 3.81	0.549	0.005
Peak pressure gradient(mmHg)	15.23 $\pm$ 5.75	0.487	0.005
Peak velocity(m/sec)	1.92 $\pm$ 0.36	0.496	0.005



**Fig. 5.** Correlation between 2DE-MVA and pressure half-time in group II (mitral stenosis + mitral regurgitation).

mean pressure gradient ( $r=0.274$ ,  $y=-1.65x+10.2$ ,  $P<0.05$ ).

In group 4 (MS+MR+AR,  $n=14$ ), the mean value of MVA from 2DE was  $1.82 \pm 0.39 \text{ cm}^2$  and from Doppler PHT method was  $1.41 \pm 0.31 \text{ cm}^2$ . PHT, mean pressure gradient, peak pressure gradient and peak velocity were  $165.21 \pm 39.77 \text{ msec}$ ,  $6.35 \pm 2.77 \text{ mmHg}$ ,  $13.24 \pm 4.23 \text{ mmHg}$  and  $1.80 \pm 0.28 \text{ m/sec}$  respectively. As compared with standard reference 2DE-MVA, Doppler derived MVA and PHT were significantly correlated with correlation

coefficients  $r=0.843$  and  $0.766$  ( $P<0.005$ , Table 6). But mean pressure gradient, peak pressure gradient and peak velocity were not correlated with 2DE-MVA. Fig. 9 and Fig. 10 showed correlation between 2DE-MVA and PHT ( $r=0.766$ ,  $y=-78.9x+308$ ,  $P<0.005$ ) or mean pressure gradient ( $r=0.218$ ,  $y=-1.6x+9.2$ ,  $P>0.05$ ).

## DISCUSSION

Determination of MVA in patients with mitral

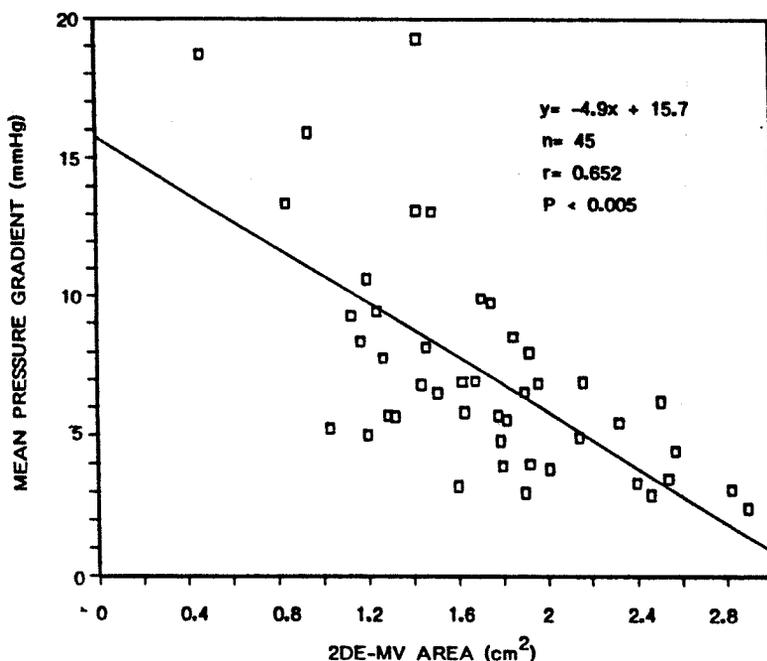


Fig. 6. Correlation between 2DE-MVA and mean pressure gradient in group II (mitral stenosis + mitral regurgitation).

Table 5. Correlation between 2DE-MVA and Doppler echocardiographic indices in group III (MS + AR, n = 54)

	Mean ± S.D	r value	P value
2DE-MVA (cm <sup>2</sup> )	1.60 ± 0.52		
Doppler indices			
Mitral valve area (cm <sup>2</sup> )	1.32 ± 0.39	0.911	0.005
Pressure half-time (msec)	184.24 ± 58.35	0.851	0.005
Mean pressure gradient (mmHg)	7.59 ± 3.16	0.274	0.005
Peak pressure gradient (mmHg)	14.37 ± 4.97	0.227	NS
Peak velocity (m/sec)	1.87 ± 0.32	0.237	NS

NS : Not significant

stenosis has critical importance. The symptoms and signs of mitral stenosis are often difficult to quantify and do not always reflect reductions in MVA<sup>24</sup>). Therefore, the ability to accurately assess MVA by noninvasive techniques is of great meaning to the management of patients with mitral stenosis.

There are several methods reported in the past, to assess the severity of mitral stenosis, including Gorlin's equation, planimetric measurement by 2 DE, the PHT method and the continuity equation<sup>25</sup>).

Previous studies comparing measurements by two-dimensional echocardiography with those by the Gorlin equation with values derived from cardiac catheterization have reported correlation coefficients of  $r=0.83$  to  $0.95^{7,9,10,26,27}$ ). Accordingly, echocardiography is currently the most widely used method for the noninvasive estimation of MVA. In addition, 2DE has been used to plan the type of surgery to be performed in patients with mitral stenosis<sup>8,27,28</sup>), and to assess the adequacy and subsequent course of surgical commissurotomy<sup>29,30</sup>).

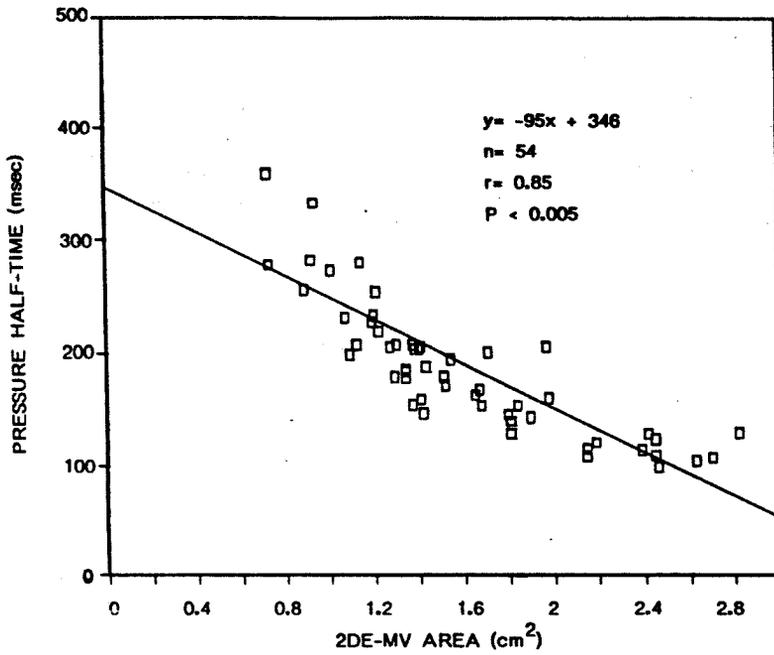


Fig. 7. Correlation between 2DE-MVA and pressure half-time in group III (mitral stenosis + aortic regurgitation).

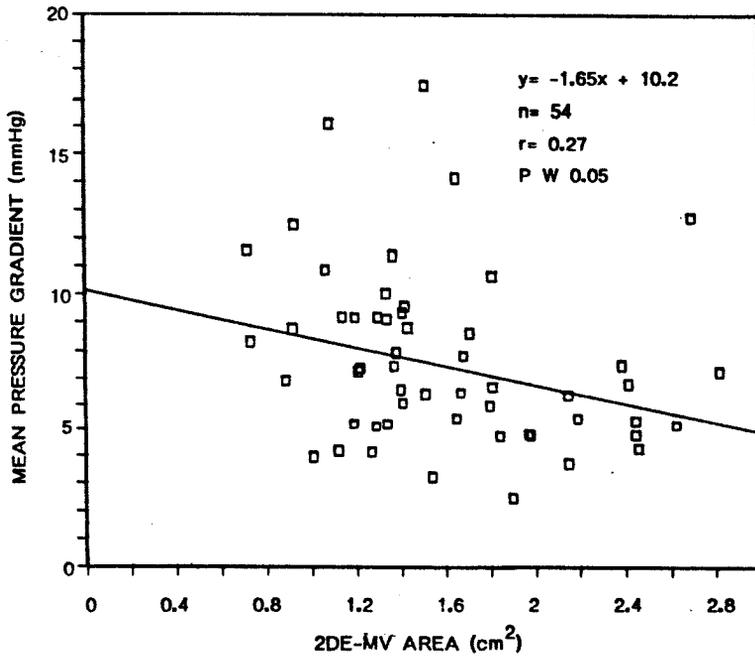
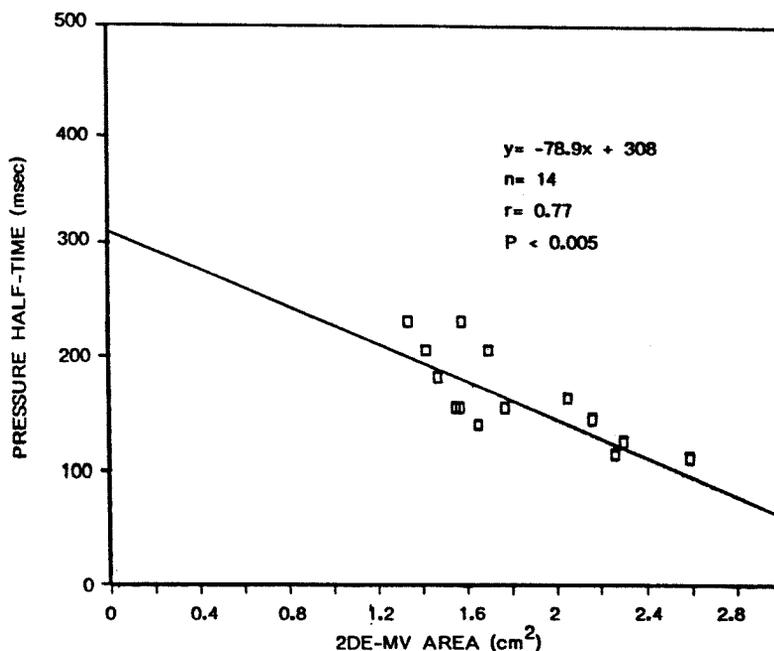


Fig. 8. Correlation between 2DE-MVA and mean pressure gradient in group III (mitral stenosis + aortic regurgitation).

**Table 6.** Correlation between 2DE-MVA and Doppler echocardiographic indices in group IV(MS+MR+AR, n=14)

	Mean± S.D	r value	P value
2DE-MVA(cm <sup>2</sup> )	1.82± 0.39		
Doppler indices			
Mitral valve area(cm <sup>2</sup> )	1.41± 0.31	0.843	0.005
Pressure half-time(msec)	165.21± 39.77	0.766	0.005
Mean pressure gradient(mmHg)	6.35± 2.77	0.218	NS
Peak pressure gradient(mmHg)	13.24± 4.23	0.077	NS
Peak velocity(m/sec)	1.80± 0.28	0.055	NS

NS : Not significant



**Fig. 9.** Correlation between 2DE-MVA and pressure half-time in group IV(mitral stenosis+ mitral regurgitation+ aortic regurgitation).

Therefore, 2DE-MVA used as a standard reference in this study. However, this method is dependent on technically optimal studies, proper gain settings and locating the true orifice in the short-axis view<sup>9)</sup>

The concept of assessing the severity of mitral stenosis by the time required for the early diastolic transmitral gradient to decreased to one-half its maximal value was introduced in 1966 by Libanoff and Rodbard<sup>31)</sup>. Hatle et al<sup>18,19)</sup> used continuous-wave Doppler recordings of transmitral flow velo-

city to determine PHT noninvasively. Hatle postulated that the mitral valve orifice area could be determined by dividing an empirically derived constant of 220 by the Doppler PHT<sup>32)</sup>. The ability of this formula to predict MVA from continuous-wave Doppler data has been validated for both native<sup>11,33)</sup> and prosthetic mitral valves<sup>34,35)</sup>. The constant of 220 used to calculate MVA has been derived empirically in a group of patients with mitral stenosis, and may not be directly applicable

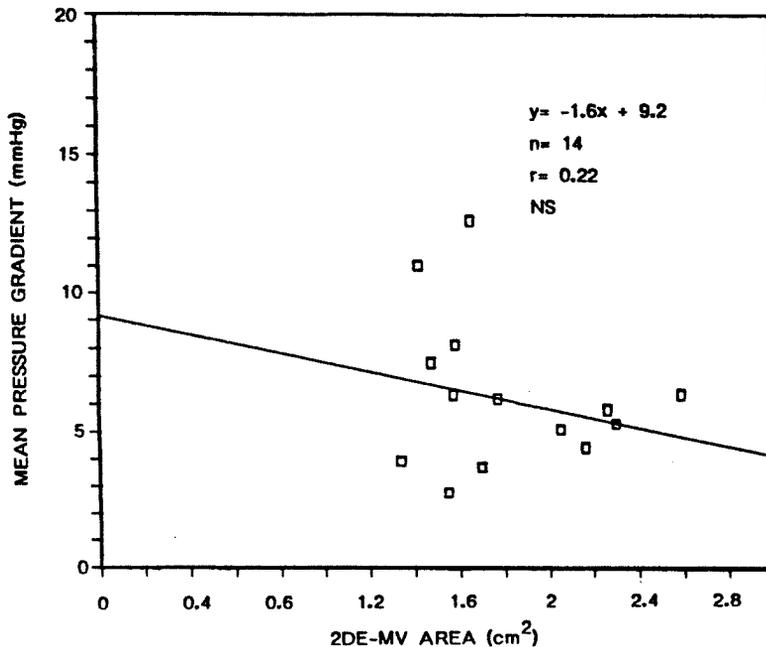


Fig. 10. Correlation between 2DE-MVA and mean pressure gradient in group IV (mitral stenosis + mitral regurgitation + aortic regurgitation).

to individual subjects. In addition, accurate measurement of the PHT is dependent on a clear definition of the envelope of a continuous-wave Doppler signal. Lack of a well defined continuous edge of the Doppler signal can lead to errors in the derivation of measurements of mitral valve size. Potential pitfalls of Doppler include: first, with rapid heart rates or prominent A waves, the slope of early diastolic flow may be disturbed and therefore the diastolic half-time is difficult to measure. Second, in the presence of aortic regurgitation, it can be difficult to record a clear mitral diastolic Doppler spectral envelope. Third, a significant angle error may occur<sup>36</sup>).

Smith et al<sup>11</sup>) used the PHT method to measure MVA, in patients after mitral commissurotomy. They reported that the Doppler PHT was superior to 2DE in estimating MVA in patients who have undergone commissurotomy. But, comparing MVA estimates from the PHT method with catheterization based estimates, they found that the PHT

underestimated the catheterization assessment of the valve area. Thoma et al<sup>22</sup>) reported that the PHT is not an independent inverse measure of MVA but is also directly proportional to net chamber compliance and the square root of the initial transmitral gradient. They have described a theoretical derivation for PHT based on fluid dynamics principles<sup>37</sup>). In this formulation, PHT is predicted to vary inversely with MVA but also to directly with net left atrial and left ventricular compliance and the square root of initial pressure gradient. Thus, in clinical situations where compliance or pressure gradient is changing significantly, theory would predict PHT to be inaccurate. The PHT method of estimation of MVA in left ventricular hypertrophy or ischemia and aortic regurgitation may be inaccurate<sup>25</sup>).

The smaller the transmitral pressure gradient and the larger the transported volume through the valve are for a given area, the longer PHT will be<sup>23</sup>). The prolonged PHT observed in mitral regu-

rgitation<sup>18)</sup>. The degree of inaccuracy seemed to be related to the severity of aortic regurgitation. Although mild aortic regurgitation produced no significant inaccuracies of MVA determined by the PHT method, moderate-to-severe aortic regurgitation produced significant overestimation of MVA<sup>25)</sup>. The effect of aortic regurgitation on PHT may be explained by a steep elevation of left ventricular diastolic pressure and hence a steep reduction in transmitral pressure gradient.

This study addresses the assessment of mitral stenosis complicated with mitral and/or aortic regurgitation by Doppler echocardiographic PHT method. Determination of MVA by Doppler PHT was most significantly correlated with 2DE-MVA. PHT method was reliable even in the presence of mitral and/or aortic regurgitation.

Askenazi<sup>38)</sup> has shown that a reliable estimate of MVA can be made in the presence of mitral regurgitation if a satisfactory left ventricular angiogram with correct calibration is obtained, when heart rate is regular and there is no aortic regurgitation. Bryg et al<sup>39)</sup> reported excellent correlation between MVA estimates from Doppler PHT, catheterization and echocardiographic planimetry in patients with atrial fibrillation and mitral regurgitation.

Other study<sup>40)</sup> showed that Doppler PHT estimates of mitral valve orifice area were accurate even in patients with aortic regurgitation. Severe aortic regurgitation has been shown to result in early closure of the mitral valve when left ventricular pressure increases rapidly and exceeds left atrial pressure during diastole<sup>41,42)</sup>. Accordingly, one could postulated that aortic regurgitation may shorten the PHT and lead to overestimation of MVA by Doppler. However, patients with significant mitral stenosis may be protected from mitral preclosure by elevated left atrial pressure and thickened, relatively immobile leaflets<sup>41,42)</sup>. Thus, lack of influence of aortic regurgitation on the PHT assessment of MVA may reflect the overall severity of mitral

stenosis in this patient population.

This study has some limitations. We did not compare PHT method with cardiac catheterization method known as gold standard to evaluate MVA yet. But it is widely recognized that neither echocardiographic planimetry nor the Gorlin equation is a perfect measure of MVA. And there were many cases of patients associated with mitral and/or aortic regurgitation or atrial fibrillation, the standard reference 2DE-MVA itself might be inaccurate.

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