Impact of Cardiac Rhythm on Mitral Valve Area Calculated by the Pressure Half Time Method in Patients With Moderate or Severe Mitral Stenosis

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Background: The pressure half-time (PHT) method has been widely used to estimate mitral valve area (MVA) in patients with mitral stenosis (MS), in the belief that this simple method provides reliable information on true MVA. However, its limitation has been repeatedly recognized under different circumstances. The aim of this study was to evaluate the effect of cardiac rhythm on PHT-derived MVA calculation in relation to net atrioventricular compliance ($C_n$).

Methods: Patients ($n = 41$) with rheumatic pure moderate or severe MS were consecutively recruited. Eighteen patients with sinus rhythm were allocated to group 1 and the remaining patients with chronic atrial fibrillation to group 2. MVA was obtained using the PHT method and by planimetry (considered the gold standard in this study). $C_n$ was calculated with a previously validated equation.

Results: There were no differences between the 2 groups in terms of age, gender, left ventricular dimensions or ejection fraction, or transmural pressure gradient. Left atrial volume index ($134.6 \pm 106.7$ vs $79.2 \pm 16.8 \text{ mL}^{}$; $P = .003$) and $C_n$ ($6.6 \pm 1.5$ vs $4.7 \pm 1.2 \text{ mL/mm Hg}$; $P < .001$) were higher in group 2 than in group 1. Disagreement of MVA estimation by PHT compared with that by 2-dimensional planimetry was $8.0 \pm 19.2\%$ for group 1 and $-24.9 \pm 13.9\%$ for group 2 ($P = .002$). In addition, the extent of disagreement of PHT-derived MVA compared with that by 2-dimensional planimetry was significantly correlated with $C_n$ ($r^2 = 0.71$, $P < .001$). MVA by the PHT method was estimated to be substantially higher in patients with $C_n$ values < $4 \text{ mL/mm Hg}$, most of whom were in sinus rhythm. Multivariate analysis confirmed the independent association of cardiac rhythm with discrepancy of PHT-derived MVA compared with that by planimetry.

Conclusion: Changes in cardiac rhythm with associated modifications of $C_n$ can alter the accuracy of the PHT method for estimating MVA. Given the limitation described here, 2-dimensional planimetry, not the PHT method, should be used as a primary echocardiographic tool for MVA calculation. (J Am Soc Echocardiogr 2009;22:42-47.)

Keywords: Mitral valve, Stenosis, Compliance, Pressure half-time, Echocardiography

Echocardiographic determinations of mitral valve area (MVA) are of considerable importance to reliably assess the severity of mitral stenosis (MS). Of the several echocardiographic approaches available, 2-dimensional (2D) planimetry and the pressure half-time (PHT) method are currently the most widely used techniques in everyday clinical practice. In particular, since its first application in 1977, the PHT method has gained widespread acceptance for MVA calculations, mainly because of its simplicity and its excellent reproducibility. However, despite these undoubted advantages, it has been repeatedly reported to be inaccurate in a variety of conditions: in the setting of significant aortic valve diseases,4 significant mitral regurgitation,5 tachycardia,6 impaired ventricular compliance,7 immediately after percutaneous mitral commissurotomy,8 and even during pregnancy.9 These shortcomings can be accounted for by the fact that PHT is dependent not only on MVA but also on net atrioventricular compliance ($C_n$) and transmural gradient.4,5 Given the frequent coexistence of atrial fibrillation (AF) and MS10-12 and the fact that AF is associated with a change in $C_n$,13 it appears that chronic AF hampers the accuracy of PHT-derived MVA values, which is of clinical relevance in terms of accurately estimating MS severity and the timely treatment of patients with MS.

Thus, the purpose of this study was to address the effect of cardiac rhythm (especially in relation to $C_n$) on PHT-derived MVA calculations in a consecutive series of patients with pure moderate or severe MS, using 2D planimetry as the reference standard.4,5,14,15

METHODS

Study Subjects

We enrolled 41 patients with diagnoses of pure moderate or severe MS (defined as $\text{MVA} \leq 1.5 \text{ cm}^2$) and without prior experience of
percutaneous mitral commissurotomy. Patients with diabetes mellitus, hypertension, coronary artery disease on preoperative coronary angiography, tachycardia, mitral regurgitation more than mild in degree, aortic stenosis, and/or regurgitation more than mild degree and those with left ventricular (LV) ejection fractions < 50% were excluded. The study protocol was approved by the institutional review board of our hospital. All patients were fully informed about the procedure and gave informed consent before study enrollment.

Echocardiography

All patients underwent comprehensive 2-dimensional and Doppler echocardiography with commercially available equipment (Siemens Sequoia, Siemens Medical Solutions USA, Inc, Mountain View, CA; Vivid 7, GE-Vingmed Ultrasound AS, Horten, Norway). LV end-systolic and end-diastolic diameters and wall thicknesses were measured using M-mode tracings at the midventricular level in the parasternal short-axis plane. Left atrial (LA) volume was measured at end-systole using the biplane Simpson’s method. Systolic pulmonary artery pressure was derived from tricuspid regurgitant jet velocity using the simplified Bernoulli equation, assuming a right atrial pressure of 10 mm Hg.

MVA on 2D planimetry was obtained from the parasternal short-axis view, using the most appropriate image by an experienced cardiologist (Y.-J.K.). To compare MVA values by 2D planimetry with those obtained using the PHT method in a blinded fashion, PHT-derived MVA was measured separately by another experienced cardiologist (H.-K.K.). The percentage differences between MVA values determined using the 2D planimetry and PHT method were calculated as follows:

\[
\frac{\text{[(MVA by the PHT method) } - \text{ MVA by 2D planimetry]} \times 100}{\text{MVA by 2D planimetry}}
\]

\(C_n\) was calculated as previously described\textsuperscript{11,16,17} using the following equation:

\[C_n = 1,270 \times (\text{MVA} / \text{E} - \text{wave downslope}),\]

where \(C_n\) is expressed in milliliters per millimeter of mercury, MVA by the continuity equation is expressed in square centimeters, and the E-wave downslope is expressed in centimeters per square second\textsuperscript{10,16,17}.

All measurements were made over ≥5 consecutive cardiac cycles in patients with sinus rhythm and over ≥7 in those with AF, and averages were used in the final analysis.

Statistical Analysis

Data are expressed as mean ± SD for continuous variables and as number (percentage) for categorical variables. For the comparison of continuous variables between the 2 groups, the independent \(t\) test was used. Fisher’s exact test or the linear-by-linear association test was used to compare frequency ratios between the 2 groups, as appropriate. Pearson’s correlation coefficient was calculated to investigate the correlation of 2 parametric variables. MVA values determined by 2D planimetry and the PHT method were compared using Bland-Altman analysis.\textsuperscript{18} Nonlinear least squares regression analysis was adopted to obtain the constant \(K\) that is best fitted in the equation PHT = \(K/MVA\) by 2D planimetry for patients with sinus rhythm or those with AF, separately.\textsuperscript{3} To demonstrate the independent association between cardiac rhythm or \(C_n\) and the presence or absence of significant disagreement between the PHT-derived MVA values and those by planimetry, we created 2 different models for multivariate logistic regression analysis using a forward conditional stepwise protocol. For the first model, age, MS severity, type of rhythm (sinus vs AF), LA volume index, and \(C_n\) were selected as independent variables, with the presence or absence of significant disagreement between the PHT-derived and planimetry-derived MVA values (defined as a discrepancy of ≥10% between the 2 methods) as a dependent variable. For the second model, an interaction term between type of rhythm and \(C_n\) was additionally chosen along with the independent variables for the first model, with the same dependent variable.

All statistical analyses were performed with the commercially available statistical software package SPSS version 13.0 (SPSS, Inc, Chicago, IL). A \(P\) value < 0.05 was accepted as a cutoff value for statistical significance in all analyses.

RESULTS

Study Patients

Forty-one patients with pure moderate or severe MS (defined as MV area ≤ 1.5 cm\(^2\)) made up the study population. There were 31 women and 10 men (mean age, 50.7 ± 8.4 years; range, 35 to 68 years). Eighteen patients were in sinus rhythm, and 23 were in AF. No patients showed alterations in cardiac rhythm between normal sinus rhythm and AF. Fourteen patients were in New York Heart Association functional class I, 18 were in class II, and 9 were in class III. The mean systolic and diastolic blood pressures were 117 ± 17 and 74 ± 10 mm Hg, respectively, and the mean heart rate was 71 ± 11 beats/min. All patients had normal LV systolic function, with a mean LV ejection fraction of 58 ± 6%.

Clinical and Echocardiographic Data

Clinical and echocardiographic data are shown in Table 1. On the basis of cardiac rhythm, patients were divided into 2 groups: 18 patients with sinus rhythm (group 1) and 23 with AF (group 2). No significant differences were evident between the 2 groups in terms of age and gender. LV end-systolic and end-diastolic dimensions and LV ejection fractions were comparable in the 2 groups. As expected, LA volume index (134.6 ± 106.7 vs 79.2 ± 16.8 mL; \(P = 0.003\)) and \(C_n\) (6.62 ± 1.49 vs 4.68 ± 1.18 mL/mm Hg; \(P < .001\)) were significantly higher in group 2 than in group 1. We found no correlation between LA volume index and \(C_n\), in either group \((r = 0.27, P = .28\) for group 1; \(r = 0.42, P = .07\) for group 2). There was, however, a moderate correlation between the initial maximal pressure gradient or LA volume index and \(C_n\) in all patients \((R = -0.47, P = .002,\) and \(R = 0.55, P = .001,\) respectively). The correlation between the initial maximal pressure gradient and \(C_n\) was more prominent in group 1 \((R = -0.88, P < .001)\) than in group 2 \((R = -0.40, P = .06)\) (\(z = -2.79, P = .005\)).

Although the transmitral mean pressure gradient was similar between the 2 groups \((11.0 ± 3.7 mm Hg for group 1 vs 9.8 ± 3.8 mm Hg for group 2; \(P = .30\)), MVA by the PHT method showed a significantly higher value in group 1 than in group 2 \((1.07 ± 0.17 vs 0.88 ± 0.22 cm\(^2\); \(P = .003\)). In contrast, MVA by planimetry was lower in group 1 than in group 2 \((1.01 ± 0.23 vs 1.18 ± 0.25 cm\(^2\); \(P = .04)\). As a result, PHT-derived MVA values displayed only a moderate correlation with planimetry-derived MVA values, with respective correlation coefficients in groups 1 and 2 of 0.68 \((P = .003)\) and 0.7 \((P < .001)\), but without a statistical difference between the 2 groups \((z = -0.11, P = .91;\) Figure 1).

To examine the effects of cardiac rhythm on PHT-derived MVA estimation, the percentage differences between MVA on 2D planimetry
Table 1 Clinical and echocardiographic data of 41 patients with pure moderate or severe MS

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients with SR (n = 18)</th>
<th>Patients with AF (n = 23)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical data</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (y)</td>
<td>49.4 ± 7.1</td>
<td>51.8 ± 9.3</td>
<td>.38</td>
</tr>
<tr>
<td>Men/women</td>
<td>6/12</td>
<td>4/19</td>
<td>.21</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>10</td>
<td>4</td>
<td>.04*</td>
</tr>
<tr>
<td>II</td>
<td>5</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>3</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>73 ± 11</td>
<td>69 ± 10</td>
<td>.34</td>
</tr>
<tr>
<td><strong>Echocardiographic data</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVIDs (mm)</td>
<td>30.6 ± 3.8</td>
<td>32.1 ± 4.2</td>
<td>.24</td>
</tr>
<tr>
<td>LVIDd (mm)</td>
<td>47.0 ± 4.3</td>
<td>49.6 ± 6.0</td>
<td>.14</td>
</tr>
<tr>
<td>LV ejection fraction (%)</td>
<td>58 ± 7</td>
<td>58 ± 4</td>
<td>.98</td>
</tr>
<tr>
<td>LA volume index (mL/BSA)</td>
<td>79.2 ± 16.8</td>
<td>134.6 ± 106.7</td>
<td>.003</td>
</tr>
<tr>
<td>Transmural mean PG (mm Hg)</td>
<td>11.0 ± 3.7</td>
<td>9.8 ± 3.8</td>
<td>.33</td>
</tr>
<tr>
<td>Initial peak E velocity (m/s)</td>
<td>2.1 ± 0.37</td>
<td>2.1 ± 0.3</td>
<td>.91</td>
</tr>
<tr>
<td>Severe MS†</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MVA (cm²)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>By 2D planimetry</td>
<td>1.02 ± 0.23</td>
<td>1.18 ± 0.25</td>
<td>.04</td>
</tr>
<tr>
<td>By the PHT method</td>
<td>1.07 ± 0.17</td>
<td>0.88 ± 0.22</td>
<td>.003</td>
</tr>
<tr>
<td>Disagreement of MVA values by PHT with reference to that by 2D planimetry (%)</td>
<td>8.0 ± 19.2</td>
<td>-24.9 ± 13.9</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Cn (mL/mm Hg)</td>
<td>4.68 ± 1.18</td>
<td>6.62 ± 1.49</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>sPAP (mmHg)</td>
<td>42.5 ± 13.6</td>
<td>44.5 ± 14.7</td>
<td>.65</td>
</tr>
</tbody>
</table>

BSA, Body surface area; EF, ejection fraction; LVIDd, LV end-diastolic internal dimension; LVIDs, LV end-systolic internal dimensions; PG, pressure gradient; sPAP, systolic pulmonary artery pressure.

*Analysis by linear-by-linear association.
†Defined as MVA < 1 cm² according to 2D planimetry.

MVA Values Obtained by the PHT Method in Relation to Cn

According to Bland-Altman analysis, mean bias and limits of agreement between MVA on 2D planimetry and MVA on PHT for group 1 were 1.05 ± 0.19 and −0.3 to 0.5 cm², respectively, whereas for group 2, these values were 1.03 ± 0.22 and −0.49 to 0.11 cm², respectively (Figure 2), suggesting reasonable agreement between the 2 methods. However, disagreement of the PHT-derived MVA as a function of Cn were found, as depicted in Figure 3 (r² = 0.71, P < .001). Assuming that ±10% variability is acceptable in clinical practice (horizontal green lines in Figure 3), MVA was estimated to be substantially higher in patients with Cn values < 4 mL/mm Hg (Figure 3); on the other hand, MVA values were lower substantially in most patients with chronic AF with reference to those by 2D planimetry.

Only cardiac rhythm emerged as an independent determinant associated with the presence of significant disagreement between the PHT-derived MVA values and those derived on 2D planimetry from MS severity between the 2 methods were found in 7 patients in group 1 (36.8%) and in 12 in group 2 (63.2%).
Table 2: Multivariate stepwise conditional logistic regression analysis of factors that are associated independently with the presence of significant discrepancy between PHT-derived MVA and that derived on 2D planimetry

<table>
<thead>
<tr>
<th>Independent factor</th>
<th>β</th>
<th>exp(β)</th>
<th>P value</th>
<th>95% CI for exp(β)</th>
<th>Multiple R² value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model 1: AF</td>
<td>1.56</td>
<td>4.75</td>
<td>.005</td>
<td>1.62-13.9</td>
<td>0.31</td>
</tr>
<tr>
<td>Model 2: interaction term (Cn by cardiac rhythm)</td>
<td>0.27</td>
<td>1.31</td>
<td>.003</td>
<td>1.09-1.57</td>
<td>0.36</td>
</tr>
</tbody>
</table>

CI, Confidence interval.

the first model. From the second model, the interaction term showed an independent association with the presence of significant disagreement between the PHT-derived MVA values and those derived on 2D planimetry (Table 2), implying that changes in cardiac rhythm with associated modification of Cn have a significant impact on the PHT-derived MVA calculation.

Figure 4 provides 4 representative cases that well exemplify the impact of Cn on the PHT-derived MVA calculation in relation to cardiac rhythm. In a patient with sinus rhythm and Cn < 4 mL/mm Hg (Figure 4A), PHT-derived MVA (63.1%) was markedly higher compared with that by 2D planimetry, whereas in another patient with sinus rhythm and Cn of 4.96 mL/mm Hg (Figure 4B), PHT-derived MVA was the same as that derived by planimetry. On the other hand, in a patient with AF and Cn of 7.02 mL/mm Hg, PHT-derived MVA was lower by 27.1% than that obtained on 2D planimetry (Figure 4C), and in another patient with AF and Cn of 4.95 mL/mm Hg, the extent of disagreement between the MVA values by PHT and 2D planimetry was decreased to 16.5% (Figure 4D).

Determination of the Optimal Parameter K in the Equation PHT = K/MVA by 2D Planimetry

We also attempted to obtain the best value for the empiric constant K (a value of 220 is currently used) in the above formula and achieved best fit using a K value of 209 for MVA derived by 2D planimetry (standard error of estimate, 8.41; 95% confidence interval, 191.2-226.7) for group 1, whereas the value was 288 (standard error of estimate, 10.86; 95% confidence interval, 265.7 to 310.7) for group 2, implying that constant K for group 2 is significantly higher than the currently accepted empirical value of 220.

DISCUSSION

The present study shows in patients with pure moderate or severe MS that (1) cardiac rhythm has a significant influence on the accuracy of PHT-derived MVA assessment, possibly through the intermediary of Cn alteration, as advocated by multivariate forward conditional stepwise logistic regression analysis, and (2) Cn is highly correlated with the extent of disagreement between MVA values derived by PHT and those derived by 2D planimetry. In addition, using a noninvasive echocardiographic approach, we confirmed the invasively obtained earlier finding that Cn is significantly higher in patients with MS and chronic AF compared with those in sinus rhythm.

Impact of Cardiac Rhythm and Cn on MVA Calculation by the PHT Method

PHT is directly dependent not only on MVA but also on Cn and the transmitial pressure gradient,\(^4\,^5\) as shown by the following equation:

\[ \text{PHT} = \left( \frac{11.6 \times \text{Cn} \times \Delta P^{1/2}}{\text{MVA}} \right), \]

where \(\Delta P\) is the initial pressure gradient (in millimeters of mercury), and MVA is effective MVA.\(^1^9\) Although this equation is mathematically very similar to the equation used for Cn calculation, an uncertainty about the influence of change in cardiac rhythm with associated alteration of Cn in a physiological range on the PHT-derived MVA calculation formed the basis of this study. We can recognize that this expression resembles the formula MVA = 220/PHT. If the numerator of the above equation would remain closest to the empirical factor of 220, changes in Cn would invariably cause inverse changes in \(\Delta P^{1/2}\). The fact that previous studies have shown an empirical constant of 220 to be accurate for MVA determination may indicate that the fortuitous balance between Cn and \(\Delta P^{1/2}\) commonly takes place in the clinical setting. Unfortunately, however, this relation is not always true, as shown by the present study, in which the correlation coefficient between Cn and \(\Delta P\) was only moderate (\(r = -0.48, P = .001\)). It has been reported that a few conditions (eg, significant aortic diseases or significant mitral regurgitation,\(^4\,^5\) tachycardia,\(^6\) and the period immediately after commissurotomy\(^8\)) can disrupt the balance between Cn and \(\Delta P^{1/2}\). We previously reported using invasive cardiac catheterization that chronic AF is another condition that modifies Cn in patients with significant MS,\(^1^3\) and this was verified noninvasively in the present study. In our analysis, patients with chronic AF were found to have higher Cn values in contrast to those with sinus rhythm. The rise in Cn led to a lengthening of PHT, in turn underestimating PHT-derived MVA. Furthermore, patients with Cn < 4 mL/mm Hg showed considerable disagreement of the PHT-derived MVA values compared with those derived on 2D planimetry. Of note, all but one of the patients were in sinus rhythm, suggesting that cardiac rhythm has a significant impact on the accuracy of the PHT method through the hidden interplay with Cn.

Clinical Implications

Although patients with chronic AF were found to have a substantially different constant K of 288, we do not propose that the currently used value of 220 be replaced with this new value in patients with chronic AF, because we believe that this constant may be variable depending on the patient group interrogated. Instead, we would like to emphasize the dependence of PHT on factors other than MVA. From the clinical perspective, this issue is of utmost importance when serial, longitudinal MVA assessment is required. A previous study nicely demonstrated the inaccuracy of PHT immediately after percutaneous mitral commissurotomy because of its dependence on Cn.\(^8\) The present study demonstrated that similar understanding can be applied in patients with MS because of the frequent coexistence or new appearance of AF and associated changes in Cn. Therefore, we recommend the use of 2D planimetry as the first choice for MVA determination in clinical practice to avoid the possible influence of Cn on PHT-derived MVA, especially in patients with AF. In particular, thanks to remarkable advances in echocardiographic imaging, this method has been feasible in more than 95% of patients with MS, and even the presence of calcification does not significantly affect the reliability of 2D planimetry.\(^1^4\,^2^0\)

Study Limitations

Several limitations need to be acknowledged. First, we did not have data regarding invasively obtained MVA values using the Gorlin formula as a reference standard. Although the validity of invasively obtained MVA values using the Gorlin formula is generally accepted, errors of 20% to 40% may be encountered.\(^2^1\,^2^2\) Moreover, MVA on 2D planimetry has been shown to be closely correlated with ana-
Changes in cardiac rhythm with associated modifications of $C_n$ can alter the accuracy of PHT-derived MVA in patients with pure moderate or severe MS. Depending on $C_n$, the magnitude of disagreement between MVA derived on 2D planimetry and PHT-derived MVA is variable and cannot be ignored in the clinical setting, especially in terms of the serial follow-up assessments of patients with MS. Given the limitations provided in the present study, 2D planimetry, not the PHT method, should be considered a primary noninvasive echocardiographic tool for estimating MVA.

**CONCLUSIONS**

Changes in cardiac rhythm with associated modifications of $C_n$ can alter the accuracy of PHT-derived MVA in patients with pure moderate or severe MS. Depending on $C_n$, the magnitude of disagreement between MVA derived on 2D planimetry and PHT-derived MVA is variable and cannot be ignored in the clinical setting, especially in terms of the serial follow-up assessments of patients with MS. Given the limitations provided in the present study, 2D planimetry, not the PHT method, should be considered a primary noninvasive echocardiographic tool for estimating MVA.

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