Letter to the Editor

# Time to peak velocity of aortic flow is useful in predicting severe aortic stenosis 

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Echocardiography has been the gold standard method to evaluate the severity of aortic valvular stenosis (AS) in clinical practice. The calculation of aortic valve area (AVA) by continuity equation is reliable and has been extensively studied in past publications [1-4]. To get the correct AVA by continuity equation, the following parameters must be reliably measured: 1) left ventricular (LV) outflow tract (LVOT) diameter (LVOTd); 2) pulsed wave Doppler signal of the blood flow in the LVOT; and 3) continuous wave Doppler signal of the blood flow at the stenotic aortic valve [5]. However, these measurements could not always be satisfactory. It is well known that moderate AS has fast up-stroke and slow down-stroke but severe AS has more slow up stroke $[6,7]$ (Fig. 1). Therefore, the aim of this study was to determine whether simple time intervals such as time to peak velocity of the blood flow at aortic valve (Tvmax) and left ventricular ejection time (ET), Tvmax/ET, were related to the severity of AS in patients with preserved LV ejection fraction.

We prospectively examined the echocardiograms of 87 AS patients between June 2010 and June 2011. The mean age was 74 years and 49 ( $56.3 \%$ ) subjects were men. The patients who had a thickened aortic valve with AVA less than $2.0 \mathrm{~cm}^{2}$ by continuity equation and with normal sinus rhythm were included. Exclusion

[^0]criteria were more than moderate amount of aortic regurgitation, more than moderate degree of mitral valve disease, serious ECG abnormalities such as atrial fibrillation, LBBB, paced rhythm, and left ventricular ejection fraction $<50 \%$. This study protocol was reviewed and approved by IRB.

Peak and mean pressure gradients at aortic valve were measured, and aortic valvular area (AVA) was calculated by the continuity equation. We defined severe AS as AVA less than $1.0 \mathrm{~cm}^{2}$ and mild AS as more than $1.5 \mathrm{~cm}^{2}$ by continuity equation. In addition, Tvmax, which was defined as the time interval between the onset and the peak velocity of the aortic flow, and left ventricular ejection time (ET) with continuous Doppler technique (Fig. 1) were measured repeatedly with two weak interval by two independent observers without any information of AS severity.

Data were expressed by mean value $\pm$ SD. One way ANOVA and post hoc analysis was performed to compare the parameters among groups. In correlating measured time variables and the AVA, mean pressure gradient (PG) was assessed with Pearson correlation. Linear correlation was used to examine inter-observer and intra-observer agreements. Receiver operating characteristic (ROC) curves were constructed to select the most advantageous cutoff points.

Characteristics of each group are shown in Table 1. In One way ANOVA analysis, various parameters including mean PG, Tvmax, ET, LV wall thickness, ratio of early diastolic mitral inflow velocity (E) to early diastolic septal annular velocity ( $e^{\prime}$ ), i.e. $E / e^{\prime}$, left atrial volume index (LAVI) and Tvmax/LVET show significant difference among groups. But after post hoc tests, only mean PG, Vmax, Tvmax and Tvmax/ET show significant difference among them (Fig. 2). Tvmax and Tvmax/ET became longer with the progression of AS. Tvmax correlated positively with mean $\mathrm{PG}(\mathrm{r}=0.685 ; \mathrm{p}<0.001)$, and negatively with AVA ( $\mathrm{r}=-0.679 ; \mathrm{p}<0.001$ ). But LVET correlated very weakly with AVA and mean PG ( $\mathrm{r}=-0.130,0.249$ respectively). Other than the parameters Tvmax/ET, Tvmax divided by the cardiac cycle length for the correction of the cardiac cycle length variation (Tvmax/RR) also showed significant correlation with AVA or mean PG. But none of those parameters showed better correlation than Tvmax itself (Table 2, Fig. 3). In predicting severe AS, ROC curves were constructed for each of those variable (Fig. 4), where Tvmax (area under ROC curve; 0.928 ) is comparable to mean PG or Vmax (AUC; 0.957, 0.946 respectively) to predict severe AS. Tvmax was also a good predictor for $1.5 \mathrm{~cm}^{2}$ (AUC; 0.857). From ROC curves, the most optimal cutoff values of Tvmax were determined. A Tvmax of $\geq 106 \mathrm{~ms}$ was $76.9 \%$ sensitive and $90 \%$ specific for AVA $<1.0 \mathrm{~cm}^{2}$ (Table 3). Intra-observer


Fig. 1. Comparison of Doppler shapes between moderate and severe AS. Tvmax is longer in severe AS.
and inter-observer correlations $\left(\mathrm{R}^{2}\right)$ for measuring Tvmax were 0.781 and 0.799 respectively.

In the current study, time interval variables of the aortic valve were evaluated in pure AS patients with normal LVEF and sinus rhythm. Time related variables such as Tvmax and Tvmax/ET showed a good correlation with either AVA or mean PG.

Moreover Tvmax had relatively good sensitivity and specificity in predicting severe AS in patients with normal LV systolic function. Therefore, it suggests that a simple time related parameter on echocardiographic study could accurately identify the patients with severe AS.

It is not a surprise that Tvmax was effective in predicting severe AS, because concepts of time intervals for AS severity were introduced before the emergence of the two dimensional echocardiography or Doppler technique. In the absence of echocardiography, ejection time index, time of the peak of systolic murmur, and time to one-half carotid upstroke were measured by physical examination, carotid pulse recording or phonocardiography [8-10]. It was known that prolonged time intervals might be related to the severity of AS.

Javier et al. suggested that the waveform shape may provide an alternative guide to the grade of stenosis. They showed that slow late systolic opening of the stenotic aortic valve was associated with worse

Table 1
Characteristics of study subjects.

|  | Mild ( $\mathrm{N}=31$ ) | Moderate ( $\mathrm{N}=26$ ) | Severe ( $\mathrm{N}=30$ ) | Total ( $\mathrm{N}=87$ ) |
| :---: | :---: | :---: | :---: | :---: |
| Tvmax (ms) | $83.7 \pm 17.4$ | $100 \pm 13.8$ | $118.2 \pm 17.5$ | $99.8 \pm 21.7$ |
| ET (ms) | $296 \pm 31.9$ | $289 \pm 61.5$ | $318 \pm 32.7$ | $302 \pm 44.2$ |
| $V \max (\mathrm{~m} / \mathrm{s})$ | $2.52 \pm 0.33$ | $3.71 \pm 0.63$ | $4.79 \pm 0.56$ | $3.66 \pm 1.09$ |
| Mean PG (mm Hg) | $13.6 \pm 2.96$ | $32.3 \pm 11.2$ | $54.1 \pm 12.3$ | $32.9 \pm 19.6$ |
| AVA ( $\mathrm{cm}^{2}$ ) | $1.57 \pm 0.19$ | $1.13 \pm .0 .21$ | $1.76 \pm$ 0.0.18 | $1.16 \pm 0.39$ |
| LVEDD (mm) | $50.6 \pm 4.97$ | $50.8 \pm 4.66$ | $53.5 \pm 5.63$ | $51.0 \pm 5.13$ |
| LVESD (mm) | $28.5 \pm 4.03$ | $29.6 \pm 3.84$ | $32.2 \pm 4.58$ | $29.5 \pm 4.33$ |
| IVS (mm) | $9.91 \pm 1.73$ | $10.8 \pm 2.01$ | $12.3 \pm 1.84$ | $10.7 \pm 2.04$ |
| LVPW (mm) | $9.83 \pm 1.56$ | $10.6 \pm 1.76$ | $12.2 \pm 1.48$ | $10.5 \pm 1.84$ |
| EF (\%) | $72.0 \pm 8.19$ | $72.0 \pm 7.48$ | $68.6 \pm 9.24$ | $70.9 \pm 8.46$ |
| Heart rate (beats/min) | $67.3 \pm 9.66$ | $63.9 \pm 9.21$ | $65.9 \pm 13.1$ | $66.2 \pm 10.0$ |
| E wave ( $\mathrm{m} / \mathrm{s}$ ) | $0.69 \pm 0.233$ | $0.701 \pm 0.190$ | $0.798 \pm 0.313$ | $0.714 \pm 0.244$ |
| A wave (m/s) | $0.943 \pm 0.234$ | $0.902 \pm 0.176$ | $0.862 \pm 0.229$ | $0.917 \pm 0.221$ |
| E/A ratio | $0.760 \pm 0.197$ | $0.822 \pm 0.409$ | $0.985 \pm 0.562$ | $0.820 \pm 0.359$ |
| $\mathrm{e}^{\prime}(\mathrm{cm} / \mathrm{s})$ | $0.0617 \pm 0.0169$ | $0.0559 \pm .0206$ | $0.0504 \pm .0165$ | $0.0580 \pm 0.0182$ |
| $\mathrm{E} / \mathrm{e}^{\prime}$ | $11.8 \pm 4.94$ | $13.9 \pm 5.29$ | $16.2 \pm 6.25$ | $13.2 \pm 5.53$ |
| DT (ms) | $252 \pm 69.2$ | $258 \pm 89.5$ | $271 \pm 71.3$ | $257 \pm 74.7$ |
| LAVI ( $\mathrm{cm}^{3} / \mathrm{m}^{2}$ ) | $30.1 \pm 9.88$ | $33.0 \pm 13.3$ | $38.9 \pm 14.1$ | $32.7 \pm 12.2$ |
| Tvmax/ET | $0.284 \pm 0.057$ | $0.338 \pm 0.044$ | $0.376 \pm 0.039$ | $0.334 \pm 0.060$ |
| Age (yr) | $74.8 \pm 9.54$ | $72.8 \pm 11.4$ | $74.2 \pm 9.58$ | $74.0 \pm 10.3$ |
| BSA ( $\mathrm{m}^{2}$ ) | $1.69 \pm 0.186$ | $1.64 \pm 0.198$ | $1.70 \pm 0.247$ | $1.68 \pm 0.202$ |

Tvmax; time to peak velocity, ET; left ventricular ejection time, Vmax; maximal velocity of aortic flow, PG; pressure gradient, AVA; aortic valve area, LVEDD; LV end diastolic dimension, LVESD; LV end systolic dimension, IVS: interventricular septum, LVPW; LV posterior wall, EF; ejection fraction, E wave and A wave; peak velocity of early filing and during atrial contraction respectively, $\mathrm{e}^{\prime}$; peak velocity of mitral annulus during early filling, DT; deceleration time, LAVI; left atrial volume index, BSA; body surface area.

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