Assessment of Left Ventricular Diastolic Function and Potential by Quantitative Analysis of Left Ventricular Filling Curves in Patients with Atrial Fibrillation

A New Algorithm for Doppler Echocardiographic Study

Yu-cheng Zhu, M.D.,* Hong Chen, M.D.,* Yong Gu, M.D.,* Qing-yuang Miao, M.D.,* Takashi Oki, M.D.,** Nobuo Fukuda, M.D.,** Arata Iuchi, M.D.,** Tomotsugu Tabata, M.D.,** and Susumu Ito, M.D.,**

Summary

To evaluate left ventricular (LV) diastolic function and potential, LV filling curves for 18 patients with atrial fibrillation (Af) were constructed and their positions and appearance were evaluated quantitatively by analysis of 95% maximal filling volume points and maximal curvature alteration points. The LV filling curves of group A (Af only) lay left superiorly, while those of group B (impaired LV diastolic function) were situated right inferiorly, all bending steeply. The LV filling curves of group C (mitral stenosis) bent slightly. The lowest normal filling volume points and compensation areas were calculated to evaluate LV diastolic function and were demonstrated to be very different in groups A and B. The lowest normal filling volume points of group C were similar to those of group A, but compensation areas were smaller, indicating a lower LV diastolic potential. It is concluded that the 95% maximal filling volume point, maximal curvature alteration point, lowest normal filling volume point and compensation area are effective indices for evaluating not only LV diastolic function but also the diastolic potential. (Jpn Heart J 34: 579–590, 1993)

Key Words:
Left ventricular diastolic function Left ventricular filling curve Echocardiography Atrial fibrillation

Atrial fibrillation (Af) is one of the most common arrhythmias observed clinically and contributes to the high mortality of patients with heart diseases.1,2 Thus it is very important to assess cardiac function in patients with Af.
In this study we focused on left ventricular (LV) diastolic function because impairment of LV diastolic function is a major cause of symptoms\(^5\) and of congestive heart failure\(^4\) in patients with heart disease, and the morphologic characteristics of Doppler echocardiography in diagnosing the impairment\(^5\) are lost during Af because of the absence of effective atrial contraction.

For the assessment of LV diastolic function during Af, the method of averaging cardiac indices during several cardiac cycles is reported to be unsatisfactory because of message loss and inaccuracy.\(^6,7\) LV filling curves have been shown to be effective for assessing diastolic function\(^6,7\) and their construction is facilitated by the constant change in R-R intervals during Af. The procedure can be carried out without atrial pacing, volume load, drug administration, restraint of venous return drainage, etc., which are the usual methods used in cases of sinus rhythm.

However, there is still no accurate and effective method for assessing LV filling curves. In some previous studies, the positions and appearance of LV filling curves were assessed only roughly, while the morphologic characteristics of the impairment of diastolic function were overlooked.

In the present study, the LV filling curves of patients with Af were analyzed quantitatively, and thus both diastolic function and the potential were evaluated.

**MATERIALS AND METHODS**

**Subjects**

The subjects studied were 18 patients with Af, who were divided into 3 groups according to their values for LV end-diastolic pressure (LVEDP), ejection fraction (EF) and maximal mitral valve area (MVA). Group A consisted of 5 patients with Af only, aged 36–49 (45±5.3) years, with a LVEDP of 8±2.1 mmHg, EF of 65.8±4.2% and a normal MVA. Group B consisted of 8 patients with impaired diastolic function, aged 36–79 (56±14) years, 3 with hypertrophic cardiomyopathy, 3 with hypertensive heart disease and 2 with coronary heart disease. Their values for LVEDP (15.9±3.1 mmHg) were higher than normal, but their values for EF (66.2±4.9%) and MVA were within normal limits. Group C consisted of 5 patients with mitral stenosis and Af aged 30–55 (44.6±9.4) years, with normal values for LVEDP (8±2.2 mmHg) and EF (64±3.8%). Patients with severe mitral and aortic regurgitation were excluded from this study. Treatments with beta-receptor exciting and blocking agents, calcium antagonists, vessel dilators and diuretics were suspended for at least 48 hours and treatment with digitalis was stopped 1 week before examination by echocardiography and cardiac catheterization.
Data collection

Each patient was placed in the left lateral recumbent position during echocardiographic examination. The apical four chamber or LV long-axis view was obtained and the sample volume was placed just distal to the tip of the mitral leaflets with the cursor line oriented as parallel as possible to a hypothetical line transversing the LV from the apex to the mitral valve. Slight adjustments in transducer angulation or sample volume were sometimes necessary to maximize the audio and graphic qualities of the Doppler signals. The LV inflow was recorded over 15–30 cardiac cycles at a paper speed of 100 mm/sec during cessation of breathing at the end of deep expiration. The maximal mitral valve area (MVA) was measured at the mitral valve level of the LV short-axis view. The volume of LV inflow \((\text{VLVIF})\) was calculated according to the following formula:8)

\[
\text{VLVIF} = \text{MVA} \times \int v(t) \, d(t) \times \text{CF}
\]

where \(\text{MVA}\) is the maximal mitral valve area, and \(\int v(t) \, d(t)\) is the area under the LV inflow curve (time velocity integral), measured with the aid of an off-line computerized-analysis station equipped with a digitizer and a programmable graphic analyzer. \(\text{CF}\) is the correction factor used for estimating mean mitral valve area from \(\text{MVA}\). An identical \(\text{CF}\) was used in the present study based on the conclusions by Miller et al8) and Stewart et al,9) of the statistical insignificance of the differences between the values of cardiac output derived from average \(\text{CF}\) and those derived using individual \(\text{CF}\)s. \(\text{CF}\) was set at 1 because of the underestimation of cardiac output by 10–15% when a \(\text{CF}\) of 0.77 was used.8)

Construction of the LV filling curve

The data were plotted in a coordinate system whose vertical axis was \(\text{VLVIF}\) and whose horizontal axis was the preceding R-R interval. To prevent significant error of measurements, we excluded R-R intervals of less than 370 msec and the relevant \(\text{VLVIF}\) values. Because of the curvilinear distribution of the data on the draft and the presence of maximal limitation of \(\text{VLVIF}\), the data were processed with the curve fitting method10) and the common formula was as follows:

\[
\text{VLVIF} = k - ax \quad (2)
\]

where \(x\) is the R-R interval, and \(k\), \(a\) and \(b\) are positive constants. The curve fitting efficiency was tested using the least square method and the regression coefficients for the rectified lines from the curves by use of the derived functions are reported.
Analysis of the LV filling curves

95% maximal filling volume point: Because k, a and b are positive numbers, k is the maximal filling volume. The 95% maximal filling volume points were determined by formula (2).

Maximal curvature alteration point: The curvature of the LV filling curve was determined by formula (3):

\[ k = \frac{V_{LVIF}''}{[1 + V_{LVIF}']^\frac{3}{2}} \]  

(3)

where \( V_{LVIF}' \) and \( V_{LVIF}'' \) are the first and second order derivatives, respectively of \( V_{LVIF} \).

\( K' \) (curvature alteration rate) reaches a maximum when \( K'' \) is 0. Through deduction on this basis, \( K' \) was shown to be maximal at \( V_{LVIF}' = -0.3230 \text{ ml/msec/m²} \). Thus, the maximal curvature alteration points were determined.

The maximal curvature alteration point is the maximal turning point of the LV filling curve. Consequently, it was used as the demarcation point to break the LV filling curve into placid and steep limbs. The direction of the placid limb can be determined by the angle of the bowstring drawn from the 95% maximal filling volume point to the maximal curvature alteration point against the horizontal axis because only one arc can be drawn between the 2 points. That is, if the 2 points are given, only one set of data of constants k, a and b can be adopted. Constant k can be determined from the 95% maximal filling volume point, constants a and b can be determined from the maximal curvature alteration point and the alteration rate at this point (−0.3230).

Similarly, the position of the LV filling curve can be determined if the maximal curvature alteration point and 95% maximal filling volume point are known.

Lowest normal filling volume point and compensation area: The lowest normal filling volume point was set at 40 ml/m² according to the normal value limits of the cardiac stroke index in China.\(^{11}\) The relevant R-R interval was determined by formula (2).

The compensation area was the area encircled by the LV filling curve, the horizontal line whose \( V_{LVIF} \) was 40 ml/m² and the vertical line whose R-R interval was 600 msec. It is:

\[ CA = |-t^{600}(k - ab^x) - 40 \times | 600 - t | \]  

(4)

where CA is the compensation area, and t is the R-R interval of the lowest normal filling volume point.

The compensation area was set positive when the \( V_{LVIF} \) at an R-R interval of 600 msec was higher than the normal limit (40 ml/m²), and vice versa (Fig. 1).
Through formula deduction, formula (4) was simplified to:

\[ CA = \left| k \times \Delta x + \frac{\Delta y}{\ln b} - 40 \times \Delta x \right| \]  (5)

where \( \Delta x \) is 600 msec minus the R-R interval whose relevant \( V_{LVIF} \) is 40 ml/m², and \( \Delta y \) is \( V_{LVIF} \) whose relevant R-R interval is 600 msec minus 40.

Comparative statistical analysis: The F test was used for comparison of values among the 3 groups, while Student's t-test was used for comparison of values between 2 groups. Data are expressed as means (M)±standard deviation (SD).

**RESULTS**

LV filling curves of patients with Af (Table I, Fig. 2)

The LV filling curves of all patients with Af fitted well with the exponential function \( V_{LVIF} = k - ab^x \) [all \( p<0.01 \), regression coefficients (r) for the rectified lines from the curves: 0.87±0.05], where k, a and b were all positive numbers, \( h<1 \).

95% maximal filling volume points of LV filling curves (Fig. 3)

significant differences were found in the R-R intervals and \( V_{LVIF} \) at the 95% maximal filling volume points in the 3 groups (all \( p<0.01 \) except for the difference between the R-R intervals in groups A and B, and in the \( V_{LVIF} \) values in groups A and C, \( p<0.05 \)).
Table I. Left Ventricular Filling Curves of Patients with Atrial Fibrillation

<table>
<thead>
<tr>
<th>Group</th>
<th>No.</th>
<th>Age (y)</th>
<th>Function ( V_{LVF} = k \cdot ab^2 )</th>
<th>( p )</th>
<th>( r )</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1</td>
<td>36</td>
<td>( V_{LVF} = 92-1354 (0.99091)^* )</td>
<td>&lt;0.01</td>
<td>0.85</td>
<td>Af only</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>46</td>
<td>( V_{LVF} = 89-1110 (0.99266)^* )</td>
<td>&lt;0.01</td>
<td>0.89</td>
<td>Af only</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>45</td>
<td>( V_{LVF} = 88-1782 (0.99115)^* )</td>
<td>&lt;0.01</td>
<td>0.95</td>
<td>Af only</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>49</td>
<td>( V_{LVF} = 91-1548 (0.99066)^* )</td>
<td>&lt;0.01</td>
<td>0.94</td>
<td>Af only</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>49</td>
<td>( V_{LVF} = 90-1919 (0.99031)^* )</td>
<td>&lt;0.01</td>
<td>0.92</td>
<td>Af only</td>
</tr>
<tr>
<td>B</td>
<td>1</td>
<td>36</td>
<td>( V_{LVF} = 71-2845 (0.99114)^* )</td>
<td>&lt;0.01</td>
<td>0.89</td>
<td>HCM</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>40</td>
<td>( V_{LVF} = 67-1637 (0.99306)^* )</td>
<td>&lt;0.01</td>
<td>0.85</td>
<td>HCM</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>52</td>
<td>( V_{LVF} = 63-1465 (0.99535)^* )</td>
<td>&lt;0.01</td>
<td>0.78</td>
<td>HCM</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>54</td>
<td>( V_{LVF} = 56-1276 (0.99431)^* )</td>
<td>&lt;0.01</td>
<td>0.77</td>
<td>IHHD</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>60</td>
<td>( V_{LVF} = 58-1670 (0.99329)^* )</td>
<td>&lt;0.01</td>
<td>0.88</td>
<td>HHHD</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>62</td>
<td>( V_{LVF} = 57-1719 (0.99321)^* )</td>
<td>&lt;0.01</td>
<td>0.93</td>
<td>IHHD</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>79</td>
<td>( V_{LVF} = 60-1547 (0.99340)^* )</td>
<td>&lt;0.01</td>
<td>0.90</td>
<td>HHHD</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>68</td>
<td>( V_{LVF} = 71-4160 (0.99021)^* )</td>
<td>&lt;0.01</td>
<td>0.85</td>
<td>HHDD</td>
</tr>
<tr>
<td>C</td>
<td>1</td>
<td>30</td>
<td>( V_{LVF} = 84-95 (0.99783)^* )</td>
<td>&lt;0.01</td>
<td>0.89</td>
<td>MS</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>50</td>
<td>( V_{LVF} = 84-62 (0.99843)^* )</td>
<td>&lt;0.01</td>
<td>0.83</td>
<td>MS</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>43</td>
<td>( V_{LVF} = 63-146 (0.99685)^* )</td>
<td>&lt;0.01</td>
<td>0.84</td>
<td>MS</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>46</td>
<td>( V_{LVF} = 84-86 (0.99831)^* )</td>
<td>&lt;0.01</td>
<td>0.87</td>
<td>MS</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>49</td>
<td>( V_{LVF} = 88-197 (0.99622)^* )</td>
<td>&lt;0.01</td>
<td>0.86</td>
<td>MS</td>
</tr>
</tbody>
</table>

Af=atrial fibrillation; HCM=hypertrophic cardiomyopathy; IHHD=ischemic heart disease; HHHD=hypertensive heart disease; MS=mitral stenosis; \( r \)=regression coefficients for the rectified lines from the curves.

Fig. 2. Left ventricular filling curves of patients with atrial fibrillation only (group A), impaired left ventricular diastolic function (group B) and mitral stenosis (group C).

The 95% maximal filling volume points of groups A, B and C were situated left superiorly \((658.00\pm55.81 \text{ msec}, 85.50\pm1.50 \text{ ml/m}^2)\), medially in the horizontal direction but inferiorly \((900.90\pm115.35 \text{ msec}, 59.73\pm5.82 \text{ ml/m}^2)\) and to the right and medially in height \((1430.80\pm329.17 \text{ msec}, 76.37\pm9.41 \text{ ml/m}^2)\), respectively.
Maximal curvature alteration points of LV filling curves (Fig. 3)

There were significant differences between the R-R intervals and $V_{LVIF}$ values at maximal curvature alteration points in groups A and B (each $p<0.01$). Maximal curvature alteration points of group A lay left superiorly ($419.80 \pm 18.24$ msec, $53.38 \pm 5.05$ ml/m²), while those of group B were situated right inferiorly ($517.37 \pm 18.94$ msec, $17.09 \pm 13.18$ ml/m²), and those of group C were in a third subset of the coordinates.

The directions of the placid limbs of groups A and B were $7.52 \pm 0.30$ and $6.45 \pm 0.54$ degrees, respectively. The difference in these values was statistically
significant, but small (<1\(^o\)).

**Lowest normal filling volume points and compensation areas** (Fig. 4)

There was no significant difference between the lowest normal filling volume points in groups A and C (385.20±28.62 vs 385.40±131.83 msec, p>0.05), but the compensation area of group A (6027.00±1622.33 ml×msec/m\(^2\)) was larger than that of group C (2415.40±1701.16 ml×msec/m\(^2\), p<0.01). The lowest normal filling volume point of group B lay to the right of those in groups A and C (626.38±91.02 msec, p<0.01) and the compensation area was negative (-111.75±905.47ml×msec/m\(^2\)).

**DISCUSSION**

Left ventricular (LV) filling curves are thought to be useful in evaluating the filling state of patients with atrial fibrillation (AF). However, in previous studies,\(^{12,13}\) the position and appearance of LV filling were observed roughly, and there had been no precise evaluation of LV diastolic function. In the present study, a new processing algorithm was devised to determine the 95% maximal filling volume point and the maximal turning point, and hence to describe the position and appearance of the LV filling curve. The diastolic compensation ability of LV was evaluated by calculation of the lowest normal filling volume point and compensation area. Furthermore, the calculation was simplified to make it suitable for rapid computational operation.

**LV filling curves**

The LV filling curves of all 18 subjects studied fitted well with the exponential function \(V_{LVIF} = k - ab^x\). This finding is consistent with a report by Oki et al,\(^{14}\) that the peak velocity of the preceding LV inflow is related to the coupling interval of supraventricular premature contraction, and the observation by Nakamura et al\(^{15}\) of a linear correlation between \(dp/dt\) and the preceding R-R interval.

Because the first order derivative of \(V_{LVIF}\) (\(V_{LVIF}'\)) is \(-ab^x\ln b, >0\), the LV filling curve is a monotonically increasing curve. That is, the LV filling volume increases with the length of the preceding R-R interval. Our results are consistent with a report by Shabetai et al,\(^{16}\) of constant increase in the LV volume during the whole diastolic phase in patients with AF.

The second order derivative of \(V_{LVIF}\) (\(V_{LVIF}''\)) is \(ab^x\ln^2 b, <0\). Consequently, with an increase in the R-R interval, the rate of alteration of the LV filling curve decreases and the segment of the LV filling curve becomes flatter.
95% maximal filling points of LV filling curves

The 95% maximal filling points of group B were situated to the right and inferiorly to those of group A. That is, in spite of a lower maximal filling volume, the 95% maximal filling points required longer preceding R-R intervals. The 95% maximal filling points of group C were intermediate in height to those in groups A and B, but required the longest preceding R-R intervals.

Maximal curvature alteration points of LV filling curves

The maximal curvature alteration points of groups A and B were situated in a first subset, those of group A lying superiorly to the left, and those of group B lying inferiorly to the right. Therefore, the placid limbs of group A were located not only superiorly, but also nearer the vertical axis than those of group B. The directions of the placid limbs of groups A and B were almost the same.

In general, the LV filling curves of group A (with normal LV diastolic function) were situated superiorly to the left, while those of group B (with impaired LV diastolic function) were situated inferiorly to the right. In spite of the absence of a self control comparison in the present study, it is reasonable to infer that when a patient with Af suffers impairment of LV diastolic function, the LV filling curve moves almost in parallel to the right and inferiorly (Fig. 5).

The maximal curvature alteration points of group C were situated in a third subset, meaning that all segments of LV filling curves in the first subset were

![Fig. 5. Left ventricular filling curves of 18 patients with atrial fibrillation.](image-url)
placid limbs, presenting a very gentle appearance.

Our results were consistent with a report by Inagaki\(^1\)\(^2\) of a very slow increase in the LV end-diastolic volume in patients with mitral stenosis and Af.

**Lowest normal filling volume points and compensation areas of LV filling curves**

The lowest normal filling volume points and compensation areas are two different but reciprocal indices of the LV diastolic potential. As shown in Figure 6, the two LV filling curves (a3 and c2) had nearly the same compensation areas (4851 vs 4164 ml x msec/m\(^2\)). Curve a3 had a longer lowest normal filling volume point (407 msec) than curve c2 (218 msec), but the compensation area of curve a3 was larger than that of curve c2 when the R-R interval was larger than the lowest normal filling volume point of curve a3. That is, despite the smaller compensation range, curve a3 had a higher compensation efficiency in its compensable area. The differences between these curves were similar to those of runners, those of long-distance runners being suitable for long distances, and those of sprinters being suitable for short distances.

Of the 3 groups, group A had the shortest lowest normal filling volume points, and the largest compensation areas, indicating good LV diastolic function and potential. In contrast, group B had the longest lowest normal filling volume points, presenting a very gentle appearance.
points (more than 600 msec) and negative compensation areas, implying impaired LV diastolic function and potential. The lowest normal filling volume points of group C were similar to those of group A, but the compensation areas were smaller. That is, despite normal LV diastolic function, the diastolic potential was less than that of patients with Af alone.

The following conclusions are drawn from this study:

a) All the LV filling curves fitted well with the exponential function
\[ V_{LVf} = k - ab^x \]
where \( k \), \( a \) and \( b \) are constants and \( x \) is the preceding R-R interval.

b) The 95% maximal filling volume point and maximal curvature alteration point are good indices for describing the position and appearance of the LV filling curves. The LV filling curves of patients with Af only are situated superiorly to the left, while those of patients with impaired diastolic function are situated inferiorly to the right, all bending steeply. The LV filling curves of patients with mitral stenosis are flat, and are in a third subset, transversing the LV filling curves of groups A and B.

c) The lowest normal filling volume point and compensation area are effective indices for describing the diastolic function as well as the potential. Groups A and B were shown to have very different diastolic functions and potentials. Group C had relatively good diastolic function, but a low potential.

**Study limitation**

In assessment of cardiac output in adults, utilization of the mitral valve orifice has been more difficult than that of the aortic site because of the marked changes in valvular cross-sectional area that occur during diastole. In spite of the great efforts that have been made to develop the methods of estimating the mean mitral cross-sectional area from the maximum area and the good correlations that have been acquired between the results determined by the Doppler technique and those by the catheter technique, the underestimation of the cardiac output by means of the Doppler technique remains a problem to be solved.

**REFERENCES**

5. Labovitz AJ, Pearson AC, Louis S: Evaluation of left ventricular diastolic function; clinical relevance
and recent Doppler echocardiographic insights. Am Heart J **114**: 836, 1987


10. Lu SZ: Exponential curve fitting. in Chinese Encyclopaedia of Medicine, Branch of Statistics, ed by Yang SQ, Guo ZC, Shanghai Science and Technology Publishing House, Shanghai, p163, 1986


