Influence of Aging on Cardiac Function Examined by Echocardiography

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We assessed the influence of aging on cardiac function by means of parameters measured by echocardiography. The study group consisted of 494 normal subjects aged 13 to 87 years. We measured the ratio of early filling (E) and atrial contraction (A) transmitral flow velocities (E/A) of left and right ventricular inflow (LV E/A and RV E/A) for assessment of diastolic function. We also measured left ventricular ejection fraction (LVEF), and the ratio of pre-ejection period (PEP) and ejection time (ET) of the left ventricle (PEP/ET) for assessment of systolic function. Both LV E/A and RV E/A decreased significantly with aging while LVEF and PEP/ET remained normal range. The decline rate as aging was greater in LV E/A than in RV E/A. These results showed that both left and right ventricular diastolic function deteriorated with aging while left ventricular systolic function was not noticeably affected by aging. We suggest that indexes of diastolic function are more sensitive than those of systolic function when the natural course is studied in a large population.

In cardiac evaluation, parameters of systolic function index such as stroke volume, cardiac output and ejection fraction are very useful in diagnosis and prognosis of patients with cardiac diseases and in evaluating their response to medical treatment. On the other hand, even though the meanings of systolic and diastolic function of heart are different, it is clear that the diastolic function may contribute to the heart failure in some degree (Braunwald and Ross 1963; Bristow et al. 1970; Gaasch et al. 1976; Grossman and McLaurin 1976; Brutsaert et al. 1985). Echocardiography can easily measure ejection fraction (EF) which is a major index of left ventricular systolic function, by M-mode and B-mode analysis and other parameters of cardiac function from Doppler velocity patterns.

The ratio of early filling (E) and atrial contraction (A) transmitral flow velocities (E/A) measured by Doppler technique is used as a sim-
ple and good index of diastolic function. Recently, E/A is recognized as being useful for the presumption of left ventricular hemodynamics (Appleton et al. 1988; Giannuzzi et al. 1994), classification of cardiac function (Vano-verschelde et al. 1990), and prognostic value (Klein et al. 1991; Shen et al. 1992; Pinamonti et al. 1993; Werner et al. 1994; Xie et al. 1994; Yamamuro et al. 1996). However, left ventricular filling pattern receives strong influence from aging factor seen even in healthy normal subjects which inverse the E/A (Takenaka et al. 1986; Gardin et al. 1987; Graettinger et al. 1987; Klein et al. 1989; Kitzman et al. 1991; Cacciapuoti et al. 1992). In this study, we investigated the relationship between age and some of the parameters in left ventricular systolic and diastolic function using echocardiography.

As right ventricular diastolic function can also be assessed by transtricuspid flow velocity patterns (Klein et al. 1990; Pye et al. 1991; Gatzoulis et al. 1995; Komaki et al. 2003), we also extended our investigation to discuss the correlation of left and right ventricular diastolic functions.

Materials and Methods

Subjects

The study populations were 494 patients (13 – 87 years old) without significant cardiac disease who came to our hospital for echocardiographic examination from May 2000 until March 2002. Patients with atrial fibrillation were excluded. The breakdown is as follow: 232 men (56.4 ± 14.9 years old) and 262 women (59.4 ± 15.8 years old).

Measurement methods

E/A of mitral and tricuspid valves. Transmitral flow velocities at the center position between the tips of anterior and posterior mitral leaflets in apical four-chamber view were recorded by pulsed Doppler technique. Transtricuspid flow velocities at the center position between the tips of anterior and septal leaflets were recorded in a same manner. The peak velocities of early diastolic filling (E) and atrial contraction (A) of both transmitral and transtricuspid valves were measured and E/A ratio for both valve were calculated (Fig. 1).

Left ventricular ejection fraction. Left ventricular wall motion was recorded using M-mode method. Left ventricular internal dimension at end-diastole (LVDd) and left ventricular internal dimension at end-systole (LVDs) were measured and left ventricular EF was calculated based on Teichholz method.

PEP/ET. The opening and closure of aortic valve were recorded using M-mode method. The time from Q wave of electrocardiography until aortic valve opening was considered as pre-ejection period (PEP) and the time from starting of left ventricular ejection until aortic valve closure was considered as ejection period (ET). Both values were measured and PEP/ET ratio was calculated (Fig. 2). We used conventional ultrasound apparatuses (Toshiba SSH-260A, SSH-160A Toshiba, Tokyo) for the echocardiographic examination. Central frequency was

Fig. 1. Examples of left ventricular inflow pattern. A: Normal relaxation pattern (E > A). B: Abnormal relaxation pattern (E < A).
3.5 MHz for M-mode. Central frequency was 2.5 MHz and pulse repetition rate was 4 kHz for the Doppler measurement.

Statistical analysis

Patients were classified according to the age. We calculated the mean ± S.D. (standard deviation) for the transmitral and transtricuspid E/A ratios, EF and PEP/ET ratio according to groups. We also calculated the difference in mean value using analysis of variance (ANOVA). Regression analysis of linear function and secondary function were examined. Correlation coefficient value of transmitral and transtricuspid E/A ratios were higher in the second function but the difference is not significant, for that we used the linear function of regression analysis as it can respond enough and easy to apply to clinical study.

RESULTS

Table 1 shows the average (mean ± S.D.) of each parameter according to age. We also analyzed each parameter according to sex and found that there was no significant difference between male and female for all parameters. Therefore, we only separated the results between male and female for the transmitral and transtricuspid E/A ratio (mean ± S.D.) (Fig. 3).

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Number</th>
<th>Transmitral E/A</th>
<th>Transtricuspid E/A</th>
<th>LVEF (%)</th>
<th>PEP/ET</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20</td>
<td>9</td>
<td>2.28 ± 0.69</td>
<td>1.92 ± 0.63</td>
<td>63.6 ± 5.2</td>
<td>0.31 ± 0.06</td>
</tr>
<tr>
<td>20～29</td>
<td>19</td>
<td>1.75 ± 0.45</td>
<td>1.60 ± 0.37</td>
<td>65.4 ± 5.6</td>
<td>0.30 ± 0.07</td>
</tr>
<tr>
<td>30～39</td>
<td>33</td>
<td>1.62 ± 0.45</td>
<td>1.69 ± 0.64</td>
<td>67.0 ± 4.5</td>
<td>0.32 ± 0.05</td>
</tr>
<tr>
<td>40～49</td>
<td>74</td>
<td>1.31 ± 0.32</td>
<td>1.42 ± 0.39</td>
<td>66.0 ± 5.0</td>
<td>0.32 ± 0.06</td>
</tr>
<tr>
<td>50～59</td>
<td>114</td>
<td>1.06 ± 0.29</td>
<td>1.25 ± 0.36</td>
<td>68.1 ± 5.2</td>
<td>0.32 ± 0.05</td>
</tr>
<tr>
<td>60～69</td>
<td>108</td>
<td>0.86 ± 0.26</td>
<td>1.15 ± 0.32</td>
<td>68.5 ± 6.1</td>
<td>0.30 ± 0.05</td>
</tr>
<tr>
<td>70～79</td>
<td>114</td>
<td>0.76 ± 0.19</td>
<td>1.07 ± 0.27</td>
<td>68.2 ± 5.8</td>
<td>0.31 ± 0.06</td>
</tr>
<tr>
<td>&gt; 79</td>
<td>23</td>
<td>0.73 ± 0.14</td>
<td>0.98 ± 0.25</td>
<td>68.6 ± 4.3</td>
<td>0.30 ± 0.06</td>
</tr>
</tbody>
</table>
Parameters related to diastolic function

Average value of an E/A ratio for the transmitral flow was 2.28 ± 0.69 which was more than 2.0 for subjects below 20 years old and 1.06 ± 0.29 which was more than normal average value of 1.0 for subjects who were in their 50’s. However, we found that E/A ratio for subjects who were in their 60’s was 0.86 ± 0.26 which was below 1.0. The inversion of E wave and A wave was apparent in subjects who were in their 40’s and increase rapidly to the percentage of 45% and 73% for sub-
jects who were in their 50’s and 60’s, respectively, and increase further to more than 90% for sub-
jects who were in their 70’s and 80’s. The correlation coefficient (r) for the transmitral E/A ratio and age was −0.615 (p < 0.001) and was recognized for having weak negative correlation (Fig. 4A).

As for average value of an E/A ratio for the transtricuspid flow, the average value was 2.12 ± 0.70 which was more than 2.0, similar to the transmitral E/A ratio for subjects below 20 years
old and showed tendency to decrease as age increases. However, compared to the transmitral flow, the E/A ratio of trantricuspid flow decreased slowly where for subjects who were in their 70’s, the average value of E/A ratio was 1.06 ± 0.29, which was not below 1.0 and the inversion of E wave and A wave was 40% from overall result. For subjects who were in their 80’s, the inversion of E and A waves was 57% and the average value again was not below 1.0. The correlation coefficient \((r)\) for the trantricuspid E/A ratio and age was \(-0.497\) \((p < 0.001)\) and was recognized for having weak negative correlation (Fig. 4B).

We also investigated the relationship between E/A ratio of transmitral and trantricuspid flow velocities and found positive correlation with correlation coefficient \((r)\) equal to \(+0.588\) \((p < 0.001)\) (Fig. 5).

**Parameters related to systolic function**

In relation to EF, we found no significant difference in the average values of all age groups although we could see a slight increase in average value of EF as age increases. We also found no significant correlation between EF and age from the correlation coefficient \((r)\) was \(+0.168\) (Fig. 6A).

As for PEP/ET ratio, we found no significant difference in all age groups and the average was around 0.3. We also found no significant correlation between PEP/ET and age and the correlation coefficient \((r)\) was \(-0.041\) (Fig. 6B).

Fig. 5. Scattergram showing correlation between transmitral E/A and trantricuspid E/A. \(y = 0.671 + 0.553x, r = +0.588\) \((p < 0.001)\).

Fig. 6. A: Scattergram showing correlation between LVEF and age. Simple regression line is drawn. \(y = 64.157 + 0.060x, r = +0.168\) B: Scattergram showing correlation between PEP/ET and age. Simple regression line is drawn. \(y = 0.320 - 0.00015x, r = -0.041\).
The relationship between LVEF and PEP/ET had weak negative correlation with correlation coefficient ($r$) equal to $-0.168$ ($p < 0.001$).

**DISCUSSION**

In previous studies, evaluation of left ventricular diastolic function has been useful for an early diagnosis of patients with early stage heart failure because diastolic function was often altered when systolic function was preserved (Klein et al. 1991; Shen et al. 1992; Pinamonti et al. 1993; Werner et al. 1994; Xie et al. 1994; Yamamuro et al. 1996). However, diastolic function altered as aging even in healthy subjects. Young healthy subjects showed the ratio around 2.0 but the ratio gradually decreases as aging. At 60 years old, the ratio becomes below 1.0 which is believed as the normal value (Takenaka et al. 1986; Gardin et al. 1987; Graettinger et al. 1987; Appleton et al. 1988; Hatle et al. 1989; Klein et al. 1989; Kitzman et al. 1991; Cacciapuoti et al. 1992). This phenomenon is known as the aging factor in the atonic characteristic of left ventricle.

In this study, we also found that the average ratio showed below 1.0 at the age 60’s. However, the population of the patients with greater A wave than E wave, showing the deterioration of left ventricular diastolic function, was 18% and 45%, at the age 40’s and 50’s, respectively. The percentage rose rapidly to 73% at the age 60’s. Considering individual performance, we believe that the deterioration of left ventricular diastolic function starts as early as age 40’s. An increase in collagen in the pressure-overloaded ventricle is known to cause myocardial stiffness (Conrad et al. 1995; Ho et al. 1996). Thus diastolic dysfunction in aging is due to the increase of interstitial collagen fiber in left ventricular wall.

The same phenomenon was found in the right ventricular diastolic function where one of the parameters, tricuspid annular velocity, is considered. However, the inversion was slower than the transmitral flow. The average was above 1.0 even older than age 70’s. In fact, in age 70’s, the patients with inverted E/A ratio of tricuspid flow had correlation, it is thought that both left and right ventricular diastolic function deteriorate from age 40’s. The difference of degree on diastolic dysfunction may be caused by the effect of pressure-overload was more prominent in left ventricular wall than right ventricle.

Regarding systolic function, aging did not influence EF and thus left ventricular systolic function which is the basis of cardiac pump function is preserved even as age increases.

Recently, tissue Doppler measurement of mitral or tricuspid annular velocity is considered more sensitive and stable method of assessing diastolic function (Tighe et al. 2003). The influence of afterload or valvular disease is smaller in tissue Doppler measurement than conventional flow measurement. In the present study, we evaluated the diastolic function of normal population without cardiac disease. We need to evaluate diastolic function using tissue Doppler technique.

**CONCLUSION**

We found that diastolic function of both left and right ventricles deteriorated as aging while systolic function was not influenced by aging factor. Furthermore, the rate of deterioration was more prominent in left ventricle compared to right ventricular diastolic function.

**References**


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