Effect of Age and Sex on Left Atrial Morphology and Function


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Aims: Left atrial function is abnormal in a wide range of cardiac diseases. This study was designed to assess the effects of normal ageing and sex on left atrial morphology and function.

Methods and Results: Echocardiography was performed in 123 subjects (age 57 ± 19 years, range 22 to 89 years, 59 women) with no evidence of cardiovascular disease. M-mode derived left atrial size, B-mode derived left atrial maximal and minimal volumes, and the volume at onset of atrial systole (P-volume) were measured. Left atrial filling, active and passive emptying volumes and ejections fractions, and expansion index were calculated.

Subjects were divided into four groups according to age. Left atrial diameter increased with age, with significantly smaller left atrial size in younger subjects. The oldest subjects had significantly higher (P < 0.05) left atrial minimal, maximal and P-volume indices. Filling volume index was highest in the oldest subjects (21.9 ± 5.6 ml/m²). Passive emptying volume index was the lowest in those of middle age (10.5 ± 2.8 ml/m²). Active emptying volume index progressively increased with age (P < 0.001). Left atrial expansion index and active emptying fraction were not different between the age groups. There was significant difference in passive emptying fraction (P < 0.001) with highest values in the youngest (44.7 ± 7.3%) and lowest values in the oldest subjects (33.6 ± 4.4%).

Conclusions: Age- and sex-related reference values of echocardiographic indices of left atrial morphology and function are reported. Ageing is associated with left atrial dilatation. Left atrial conduit function deteriorates with age while reservoir and pump function are maintained. Left atrial anteroposterior diameter is smaller in women than in men, but overall left atrial function is not influenced by sex.

Key Words: left atrial function; left atrial dilatation; female; male; ageing; echocardiography.

Introduction

In the normal heart the left atrium acts as a reservoir, a conduit, and a pump. Impairment of left atrial function has been documented in many cardiac conditions including sick sinus syndrome[1], dilated cardiomyopathy[2,3] and heart failure[4-6]. Patients who undergo electrical cardioversion for atrial fibrillation also have transient left atrial impairment[7,8].

Disturbances of left atrial function can have significant effects on overall cardiac performance. Preserved left atrial contraction helps maintain left ventricular end-diastolic pressure without a significant increase in left atrial pressure. Left atrial failure, in contrast, leads to symptoms of heart failure due to high left atrial pressure.

Left atrial function can be assessed both invasively and by non-invasive methods including electrocardiography, echocardiography, cardiac magnetic resonance imaging and left atrial catheterization[9].

This study was designed to assess the effects of physiologic ageing and sex on left atrial morphology and function. Despite some technical difficulties and limitations[10], given the ubiquitous availability and ease of use of echocardiography, M-mode and B-mode echocardiography and cardiac Doppler studies were chosen as the study methods.
Methods

The study population initially comprised 143 individuals (age 59 ± 18 years, range 22 to 89 years) identified from the lists of randomly selected local general practices. Subjects with no recent (less than 1 year) visits to their general practitioner and no chronic illnesses, and taking no regular medication, were invited to attend for echocardiography. Of these, 123 individuals (age 57 ± 19 years, range 22 to 89 years, 59 women) were selected after the exclusion of patients with echocardiographic evidence of left ventricular systolic dysfunction or significant valve disease. All subjects had no symptoms or history of cardiovascular disease, normal physical examinations and electrocardiograms. The informed consent of all the study subjects was obtained, and the study was approved by the locally appointed research ethics committee.

Each subject underwent full echocardiographic examination using commercially available equipment (GE Vingmed Vivid Five scanner) equipped with a 2·5 MHz phased array transducer and a software analysis system (Echopac 6·3, GE Vingmed) running on a Power Macintosh personal computer. All recordings were obtained during normal respiration. The echocardiographic study was performed by the same experienced investigator (NPN).

Left ventricular end-diastolic and end-systolic volumes were measured using the modified Simpson’s rule, and corresponding volume indices were obtained by correcting for body surface area. Left ventricular ejection fraction was calculated with the standard formula. Left atrial anteroposterior diameter was measured at end-systole from B-mode guided M-mode echocardiographic images obtained in the parasternal long-axis view as recommended by the American Society of Echocardiography[11].

Apical four-chamber and two-chamber views were used to assess left atrial morphology using B-mode echocardiography. Left atrial volumes were measured by digitized planimetry of the left atrial cavity at mitral valve opening (maximal volume), at onset of atrial systole (P wave of ECG, P-volume) and at mitral valve closure (minimal volume), as shown in Fig. 1. The volumes were derived using the formula: \( V = 8 \cdot A_4 \cdot A_2 / 3 \cdot \pi \cdot L \)[12], where \( A_4 \) and \( A_2 \) are left atrial areas in the apical four-chamber and two-chamber views and \( L \) is left atrial long axis (averaged from the two apical views).

To characterize the three phases of left atrial activity, the following variables were calculated: left atrial passive emptying volume (maximal volume – P-volume) and left atrial passive emptying fraction (passive emptying volume/maximal volume × 100%) both representing left atrial conduit function, left atrial active emptying volume (P-volume – minimal volume) and left atrial active emptying fraction (active emptying volume/P-volume × 100%) to assess left atrial pump function, left atrial filling volume (maximal volume – minimal volume) and left atrial expansion index (filling volume/minimal volume × 100%) for left atrial reservoir function. All volumes were corrected for body surface area.

Left atrial kinetic energy was calculated with the use of the formula: \( 0·5 \times \rho \times \text{left atrial active emptying volume} \times v^2 \), where \( \rho = 1·06 \text{ g cm}^{-3} \) (the density of blood), \( v = \text{peak Doppler velocity of atrial transmitral filling (A)} \)[13].

Recordings of mitral flow velocities were made using pulsed Doppler from an apical four-chamber view with the sample volume positioned between tips of the mitral leaflets in diastole. Peak velocity of early filling (E) and peak A velocity were measured and the E/A ratio was calculated.

Results are presented as mean ± SD. The echocardiographic data between age groups were compared by analysis of variance followed by the Newman–Keuls test. Unpaired Student’s t-tests were used to compare the data between men and women. A \( P \) value less than 0·05 was considered to be significant.

Results

Subjects were classified into four age groups: Group 1 consisted of 29 subjects (14 women) aged 20 to 39 years, Group 2, 30 subjects (14 women) aged 40 to 59 years, Group 3, 47 subjects (20 women) aged 60 to 79 years, and Group 4, 17 subjects (10 women) ≥ 80 years of age. Echocardiographic and physical data are presented in Table 1. Younger volunteers were taller leading to a lower body surface area with age. The oldest age group was characterized by the lowest heart rate. There were no differences in left ventricular end-diastolic and end-systolic volume indices and left ventricular ejection fraction between the age groups.

Doppler indices of transmitral flow showed that E velocities decreased, while A velocities increased with ageing. As a result, the E/A ratio progressively declined from the youngest group to the oldest one.

Effects of Age

Left atrial dimensions (according to M-mode) and left atrial volume indices (as assessed by B-mode echocardiography) in different age groups are shown in Table 2. There was a tendency to an increase in left atrial diameter with age, with smaller left atrial size in Group 1 compared with other groups. The oldest subjects had higher left atrial minimal, maximal and P-volume indices. Left atrial filling, passive emptying and active emptying volume indices were also different between the groups. Left atrial filling volume index was highest in Group 4, while left atrial passive emptying volume index was lowest in Group 2. Left atrial active emptying volume index progressively increased with age.

Left atrial expansion index and left atrial active emptying fraction were not different between the age groups. However, there was a significant reduction in left atrial passive emptying fraction with increasing age. Figure 2 shows the effect of age on left atrial kinetic energy. There was a tendency to an increase in left atrial passive emptying volume index, while volume index progressively increased with age.

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energy. The index progressively increased with ageing with all inter-group differences significant ($P<0.05$).

**Effects of Sex**

Table 3 summarizes sex-related differences in echocardiographic indices of left atrial function. In this study, women had lower body surface areas than men due to both shorter heights and lower body weights. They also had lower left atrial dimensions at end-systole (P-volume) and at mitral valve closure (minimal volume). Despite demographic distinctions, there were no sex-related differences between men and women in any of...
Table 1. General and echocardiographic characteristics

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
<th>Group 4</th>
<th>F (ANOVA)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>20–39 years</td>
<td>40–59 years</td>
<td>60–79 years</td>
<td>≥80 years</td>
<td></td>
</tr>
<tr>
<td>BSA, m²</td>
<td>1.86 ± 0.22</td>
<td>1.88 ± 0.16</td>
<td>1.80 ± 0.17</td>
<td>1.71 ± 0.18*†‡</td>
<td>3.81§</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>71.17 ± 10.11</td>
<td>65.90 ± 11.80</td>
<td>67.12 ± 9.41</td>
<td>62.97 ± 8.17*</td>
<td>2.68§</td>
</tr>
<tr>
<td>LV EDV index, ml/m²</td>
<td>56.08 ± 11.03</td>
<td>53.34 ± 11.83</td>
<td>52.75 ± 10.64</td>
<td>58.71 ± 12.32</td>
<td>1.47</td>
</tr>
<tr>
<td>LV ESV index, ml/m²</td>
<td>21.43 ± 5.31</td>
<td>21.01 ± 5.30</td>
<td>20.75 ± 6.17</td>
<td>25.02 ± 6.65</td>
<td>2.38</td>
</tr>
<tr>
<td>LV EF, %</td>
<td>61.91 ± 4.71</td>
<td>60.49 ± 5.02</td>
<td>60.89 ± 8.06</td>
<td>57.55 ± 5.28</td>
<td>1.76</td>
</tr>
<tr>
<td>E, cm/s</td>
<td>82.48 ± 11.76</td>
<td>76.16 ± 12.76</td>
<td>67.51 ± 11.52*</td>
<td>63.41 ± 14.29*</td>
<td>12.95§</td>
</tr>
<tr>
<td>A, cm/s</td>
<td>54.09 ± 11.77</td>
<td>67.59 ± 13.62*</td>
<td>77.68 ± 17.92*‡</td>
<td>84.65 ± 13.33*‡</td>
<td>10.60§</td>
</tr>
<tr>
<td>IVRT, ms</td>
<td>68.00 ± 11.53</td>
<td>86.36 ± 17.89*</td>
<td>89.64 ± 22.55*</td>
<td>91.65 ± 21.16*</td>
<td>9.18§</td>
</tr>
<tr>
<td>DT, ms</td>
<td>222.21 ± 46.32</td>
<td>217.07 ± 43.54</td>
<td>224.06 ± 50.63</td>
<td>263.53 ± 56.94*†‡</td>
<td>3.81§</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>1.57 ± 0.36</td>
<td>1.17 ± 0.29*</td>
<td>0.90 ± 0.24†‡</td>
<td>0.76 ± 0.20*‡</td>
<td>44.07§</td>
</tr>
</tbody>
</table>

*P<0.05 compared to Group 1; †P<0.05 compared to Group 2; ‡P<0.05 compared to Group 3; §P<0.05; ¶P<0.001 between groups (ANOVA).

Table 2. Echocardiographic indices of left atrial function

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
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<td>40–59 years</td>
<td>60–79 years</td>
<td>≥80 years</td>
<td></td>
</tr>
<tr>
<td>LA diameter, cm</td>
<td>3.51 ± 0.51</td>
<td>3.99 ± 0.54*</td>
<td>4.12 ± 0.43*</td>
<td>4.19 ± 0.51*</td>
<td>11.17†‡</td>
</tr>
<tr>
<td>LA Vmax index, ml/m²</td>
<td>9.31 ± 2.39</td>
<td>9.33 ± 3.45</td>
<td>9.86 ± 3.81</td>
<td>12.44 ± 3.38†‡</td>
<td>3.78§</td>
</tr>
<tr>
<td>LA Vmin index, ml/m²</td>
<td>16.18 ± 3.41</td>
<td>16.47 ± 4.91</td>
<td>17.98 ± 5.64</td>
<td>22.76 ± 5.61†‡</td>
<td>7.27†‡</td>
</tr>
<tr>
<td>LA Vmax index, ml/m²</td>
<td>29.37 ± 5.38</td>
<td>26.96 ± 6.79</td>
<td>29.75 ± 7.02</td>
<td>34.32 ± 8.31†‡</td>
<td>4.24§</td>
</tr>
<tr>
<td>LA Vmin index, ml/m²</td>
<td>20.05 ± 3.82</td>
<td>17.63 ± 3.79</td>
<td>19.88 ± 4.11</td>
<td>21.88 ± 5.59†</td>
<td>4.04§</td>
</tr>
<tr>
<td>LA Vp index, ml/m²</td>
<td>13.19 ± 3.64</td>
<td>10.49 ± 2.84*</td>
<td>11.76 ± 2.82</td>
<td>11.55 ± 3.46</td>
<td>3.63§</td>
</tr>
<tr>
<td>LA Vp index, ml/m²</td>
<td>6.87 ± 1.44</td>
<td>7.15 ± 2.03</td>
<td>8.12 ± 2.44*</td>
<td>10.33 ± 2.94†‡</td>
<td>10.11†‡</td>
</tr>
<tr>
<td>LA EL, %</td>
<td>4.01 ± 0.94</td>
<td>206.6 ± 60.1</td>
<td>219.4 ± 65.2</td>
<td>179.7 ± 29.5</td>
<td>2.60</td>
</tr>
<tr>
<td>LA PEF, %</td>
<td>4.79 ± 0.73</td>
<td>39.25 ± 6.94*</td>
<td>40.03 ± 7.06*</td>
<td>33.62 ± 5.37†‡</td>
<td>9.54§</td>
</tr>
<tr>
<td>LA AEF, %</td>
<td>4.82 ± 0.53</td>
<td>44.35 ± 8.36</td>
<td>45.83 ± 7.85</td>
<td>45.43 ± 5.65</td>
<td>1.12</td>
</tr>
</tbody>
</table>

*P<0.05 compared to Group 1; †P<0.05 compared to Group 2; ‡P<0.05 compared to Group 3; §P<0.05; ¶P<0.001 between groups (ANOVA).

LA, left atrial; Vmax, minimal volume; Vp, volume at onset of atrial systole (P wave of ECG); Vmax, maximal volume; Vp, filling volume; Vp, passive emptying volume; Vae, active emptying volume; E, expansion index; PEF, passive emptying fraction; AEF, active emptying fraction.

indices of left atrial morphology and function measured with B-mode echocardiography (Table 3).

Discussion

Left Atrial Morphology

Left atrial size is considered a sensitive indicator of cardiac dysfunction and can serve as a prognostic indicator[14–16]. However, left atrial size may also change with age. It is therefore important to take into account age-related changes when left atrial morphology is evaluated in patients with cardiac disease.

Left atrial morphology is conventionally assessed at end-systole using B-mode guided M-mode echocardiography. However, left atrial diameter may be an inaccurate surrogate for left atrial volume. The discrepancy between left atrial anteroposterior dimensions and volumes becomes increasingly important as the left atrium dilates, because small increases in left atrial diameter may reflect significant increases in left atrial volume[10].

B-mode echocardiographic measurement of left atrial volumes may be relatively complicated and time consuming, but it gives more reliable information on left atrial morphology, provided the quality of echo images is acceptable.

According to B-mode assessment in this study, left atrial volumes did not change significantly until late age. This increase was not demonstrated with M-mode data on left atrial diameter, which could be explained by a non-uniform dilatation of the left atrium[17].

Left Atrial Reservoir Function

During ventricular systole the left atrium acts as a reservoir collecting blood from the pulmonary veins. The ability of the left atrium to function in this way is an important determinant of cardiac output[13] and is

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determined by left atrial contraction and relaxation and also by the displacement of the mitral annulus during left ventricular contraction[19].

We did not find any signs of deterioration of left atrial reservoir function with age. Left atrial expansion index did not significantly change with age. This persistence of left atrial reservoir function might be an important factor in maintaining cardiac output during normal ageing.

Table 3. Echocardiographic indices of left atrial function in men and women

<table>
<thead>
<tr>
<th></th>
<th>Men</th>
<th>Women</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>57·6±18·7</td>
<td>56·7±19·6</td>
<td>0·807</td>
</tr>
<tr>
<td>BSA, m²</td>
<td>1·95±0·13</td>
<td>1·68±0·12</td>
<td>0·000</td>
</tr>
<tr>
<td>LA Vmin index, ml/m²</td>
<td>9·82±3·60</td>
<td>10·08±3·39</td>
<td>0·687</td>
</tr>
<tr>
<td>LA Vmax index, ml/m²</td>
<td>29·12±7·14</td>
<td>30·07±7·01</td>
<td>0·467</td>
</tr>
<tr>
<td>LA Vp index, ml/m²</td>
<td>17·61±5·31</td>
<td>18·06±5·49</td>
<td>0·646</td>
</tr>
<tr>
<td>LA Vfil index, ml/m²</td>
<td>19·30±4·13</td>
<td>19·99±4·58</td>
<td>0·392</td>
</tr>
<tr>
<td>LA Vpe index, ml/m²</td>
<td>11·52±2·92</td>
<td>12·01±3·59</td>
<td>0·417</td>
</tr>
<tr>
<td>LA Vae index, ml/m²</td>
<td>7·78±2·30</td>
<td>7·98±2·63</td>
<td>0·664</td>
</tr>
<tr>
<td>LA EI, %</td>
<td>211·8±54·8</td>
<td>212·6±63·7</td>
<td>0·938</td>
</tr>
<tr>
<td>LA PEF, %</td>
<td>39·92±6·32</td>
<td>40·26±8·80</td>
<td>0·813</td>
</tr>
<tr>
<td>LA AEF, %</td>
<td>44·98±7·71</td>
<td>44·40±6·71</td>
<td>0·659</td>
</tr>
</tbody>
</table>

BSA, body surface area; LA, left atrial; Vmin, minimal volume; Vmax, maximal volume; Vp, volume at onset of atrial systole (P wave of ECG); Vfil, filling volume; Vpe, passive emptying volume; Vae, active emptying volume; EI, expansion index; PEF, passive emptying fraction; AEF, active emptying fraction.

Left Atrial Conduit Function

The left atrium acts as a conduit during the phase of early left ventricular diastolic filling. Therefore, an important determinant of left atrial conduit function is the rate of left ventricular relaxation, which deteriorates with ageing[20].

In this study, left atrial passive emptying fraction, highest in young healthy subjects, significantly declined in middle age groups with a further decline in the oldest subjects, confirming deterioration of left atrial conduit function with age. These changes corresponded to the well-described age-related reversion in E/A ratio, which was also observed in our study population. Left atrial passive emptying volume index also declined with age, although less significantly.

Left Atrial Pump Function

Although only 25% or less of left ventricular stroke volume normally enters the ventricle during atrial systole[21], the role of left atrial pump function becomes increasingly important as left ventricular diastolic function deteriorates. Ageing leads to reduced left ventricular diastolic function[22] both due to prolonged left ventricular relaxation[20] and impairment of left ventricular passive properties[23]. Studies performed with the use of Doppler assessment of transmitral flow demonstrated augmentation of left atrial contribution to transmitral flow[24]. Similar findings were found in the present study. However, the use of Doppler spectrum of left ventricular
diastolic filling for the assessment of left atrial function is limited because Doppler velocities are determined by the mitral valve pressure gradient, and therefore reflect both left ventricular and left atrial properties.

The findings obtained with B-mode echocardiography showed that left atrial active emptying fraction remained unchanged with age, which suggests preserved left atrial pump function. Left atrial active emptying volume index increased with age. This, in the presence of left atrial dilatation, is probably a consequence of the effect of the Starling mechanism. An increase in left atrial active contractile performance with age was further confirmed by a progressive increase in left atrial kinetic energy, a recently proposed non-invasive index of left atrial stroke work[13].

**Effect of Sex**

Although left atrial anteroposterior diameter was smaller in women than in men, we did not find any difference between sexes on B-mode derived left atrial volumes as well as indices of left atrial reservoir, conduit or pump function. Therefore, in healthy subjects of different ages sex seems not to affect left atrial performance.

**Limitations of the Study**

Limitations of M-mode echocardiographic measurement of anteroposterior left atrial dimension are well described[10,25]. Nevertheless, we used it in this study, because the method is still widely used both in research and clinical practice. The principal method of the assessment of left atrial function in this study was B-mode echocardiography. Although this method has been validated against invasive techniques[23], its main limitations are associated with the subjective character of left atrial endocardial border tracing, the use of geometric approximations, and insufficient quality of echocardiographic images in some cases. The use of automatic border detection with recently developed acoustic quantification technique may have the potential to overcome some of these limitations[25]. Three-dimensional echocardiography and cardiac magnetic resonance imaging can improve the accuracy of the assessment of left atrial morphology and function, but are not widely available.

**Conclusions**

Age- and sex-related reference values of echocardiographic indices of left atrial morphology and function are reported. Ageing is associated with left atrial dilatation. Left atrial conduit function deteriorates with age while reservoir and pump function are maintained. Left atrial anteroposterior diameter is smaller in women than in men but overall left atrial function is not influenced by sex.

**Acknowledgements**

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**References**


