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Echocardiographic Assessment of a Normal Adult Aging Population

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SUMMARY Echocardiograms were performed on 105 male participants in the National Institute on Aging's volunteer Longitudinal Study Program. All subjects (25-84 years of age) were physically active and had no evidence of hypertension or cardiovascular disease. Measurements were made of the initial diastolic (E-F) slope of the anterior mitral valve leaflet, the aortic and left ventricular cavity dimensions, and the thickness of the posterior left ventricular wall. Fractional shortening of the minor semi-axis of the left ventricle and the velocity of circumferential fiber shortening were also determined.

AS THE NUMBER AND PROPORTION of aged individuals in the population increases, knowledge of normal physiologic changes associated with aging becomes more important. Cardiovascular disease states can only be identified in an aging population, in fact, with reference to age-adjusted normals. However, characterization of the effect of age on cardiovascular structure and function is difficult because of the necessity to exclude those elderly subjects with cardiovascular disease and because invasive studies are associated with increased risk to these patients. Noninvasive phonocardiographic and carotid pulse tracing studies have indicated a prolongation of mechanical systolic and diastolic time periods with increasing age.1,2 The effect of age on the ballistocardiogram has also been thought to indicate prolonged ejection.4 Invasive studies using stroke volume and cardiac output as indicators of resting left ventricular function have been inconclusive. Most studies have shown a
decline with increasing age but pulmonary wedge pressures, which were measured in one study, were also lower in the older group. Invasive studies also introduce stress which may alter baseline performance. Thus it is difficult to determine if observed age differences are due to intrinsic alterations in baseline function or to alterations in the response to stress.

The echocardiogram is particularly suited to study the effect of age on the heart. It provides anatomic information which is unobtainable by any other technique in living individuals. This study describes the effect of aging on several echocardiographic parameters obtained from normal individuals. The study population is unique in that there is a high level of assurance that the individuals are free of overt cardiovascular disease. The information obtained is applicable to aging research and also provides standards with which echocardiographic changes in aged individuals with pathologic conditions can be compared.

Methods

Echocardiograms were obtained from participants in the National Institute on Aging volunteer Longitudinal Study Program. These individuals have had complete examinations and electrocardiograms at approximately eighteen month intervals. All subjects studied were physically active males (although not active athletes) and showed no evidence of chest wall abnormalities, coronary artery, valvular, or hypertensive disease. Hypertension was defined as blood pressure greater than 140/90 mm Hg on repeated baseline determinations over a 48 hour period. All participants were in normal sinus rhythm and none met electrocardiographic criteria for left ventricular hypertrophy. None were taking medication known to influence cardiac function.

All subjects underwent submaximal treadmill stress tests which were negative. The exercise test started with each individual walking on a horizontal treadmill. Stepwise increments in the load every minute were accomplished by elevating the treadmill angle. The electrocardiogram was monitored and recorded using chest leads with electrical axes corresponding to those of limb leads 1, 2, and 3 and chest leads V1, V5, V6, and V7. The test was continued to 90% of the mean age-specific heart rate unless the subject experienced chest pain, unusual weakness or dizziness, or the electrocardiogram disclosed evidence of ischemia, ventricular arrhythmias, or serious conduction abnormalities. The electrocardiographic criterion for a positive test was 0.1 mV or more horizontal or downward sloping ST depression below the level of the PR segment during or following the test.

Echocardiograms were obtained with a Smith-Kline Ekoline machine and recorded on a Honeywell 1856 strip chart recorder. The participants were either supine or rotated into the left lateral position. The depth calibration was checked each day with a plexiglass standard. Measurements were made of the initial portion of the E-F slope of the anterior mitral valve leaflet, the aortic root and left ventricular cavity dimensions, and the thickness of the posterior left ventricular wall. The E-F slope was measured from those complexes which exhibited the greatest slope and amplitude and in which the posterior leaflet was also visible. The aortic root dimension was measured from those complexes in which the aortic valve leaflets were clearly seen and at the time of the inscription of the electrocardiographic Q wave. Left ventricular recordings were selected which demonstrated the posterior mitral valve chordae and in which the posterior left ventricular endocardial and left-sided septal structures were clearly seen as continuous echoes in systole and diastole. Diastolic cavity and wall thickness measurements were made at the time of the Q wave inscription. The systolic cavity was measured at the time of the most anterior motion of the posterior endocardial echo. Ejection time was measured in three ways, as the time from: 1) the initial to maximum anterior systolic motion of the posterior left ventricular wall; 2) the peak of the R wave to the maximum anterior systolic motion of the posterior wall less 50 msec; and 3) the upstroke to the incisura of the carotid pressure pulse tracing. Fractional shortening of the minor semi-axis was calculated as (diastolic dimension − systolic dimension)/diastolic dimension. Velocity of circumferential fiber shortening was calculated as mean VCF = (diastolic dimension − systolic dimension)/(diastolic dimension × ejection time). It was determined in a subset of records that the beat-to-beat variation in six beats was not different from that in three beats and subsequent analyses of data were made using the mean value of each parameter from three nonconsecutive beats. Measurements were made to the nearest millimeter. The coefficient of beat-to-beat variation in each parameter is as follows: mitral valve slope, 6%; aortic root dimension, 4%; left ventricular diastolic wall thickness, 6%; left ventricular systolic wall thickness, 2%; left ventricular diastolic dimension, 2%; left ventricular systolic dimension, 2%; and ejection time, 4%

The relationship between age and the obtained echocardiographic parameters was analyzed using linear regression analysis. The regression equation, the standard error of estimate, the coefficient of correlation, and the significance of the correlation coefficient were determined. Since cardiac dimension measurements may be related to body size, these parameters and those derived from them were also expressed per square meter of body surface area and the relationship of these to age was assessed. Subjects were also divided into three 20-year age brackets: group I, aged 25–44 years; group II, aged 45–64 years; and group III, aged 65–84 years. The means and standard errors of each group for echo variables were calculated and the significance of any difference between the groups was assessed using the Student’s t-test.

Results

Echocardiograms were obtained from 105 subjects. Group III has fewer subjects than the other groups, in part because of an increased incidence of cardiovascular and pulmonary disease in the older population, and greater difficulty in obtaining satisfactory echocardiograms in the group. An example of a typical echocardiogram is given in figure 1.

The effect of age on the studied parameters, as determined by separating the participants into 20 year groups, is presented in table 1. The scatter diagrams, in which the linear correlation between the parameter and age is depicted, are presented in the figures.

The E-F slope of the anterior mitral valve leaflet was
measured in 105 subjects. It was found to decrease with increasing age (table 1, fig. 2). The mean slope for group I is 102.3 mm/sec; for group II, 79.0 mm/sec (P < 0.001); and for group III, 67.1 mm/sec (P < 0.001 vs group I). In all tracings, the posterior leaflet moved in a direction opposite to that of the anterior leaflet. The aortic root diastolic dimension was obtained from 89 participants and increased slightly with increasing age (table 1). The mean dimension for group I is 30.9 mm; for group II, 32.0 mm; and for group III, 32.9 mm (P < 0.05 vs group I). Left ventricular diastolic and systolic wall thickness per m² body surface area increased as well with advancing age (fig. 3). The average diastolic wall thickness is 4.3 mm/m² for group I, 5.0 mm/m² for group II (P < 0.01), and 5.7 mm/m² for group III (P < 0.001 vs group I). Systolic wall thickness was 7.6 mm/m² in group I, 9.2 mm/m² in group II (P < 0.001), and 10 mm/m² in group III (P < 0.001 vs group I). Although the blood pressure of all subjects was normal, the older group had higher systolic pressures than the other two groups. The systolic pressure was 118 ± 2 mm Hg for group I, 120 ± 3 mm Hg for group II and 132 ± 3 mm Hg for group III. Despite this difference in blood pressure there was no correlation between systolic blood pressure and wall thickness/m² by multivariant analysis. Heart rate did not vary with age and was 66 ± 2, 64 ± 3, and 62 ± 3 beats per min in groups I, II, and III, respectively. Left ventricular systolic and diastolic cavity dimensions as well as calculated velocity of circumferential fiber shortening and fractional shortening of the minor semi-axis did not vary with age (table 1). Left ventricular ejection time as measured by three methods is given in table 2. There is no age difference in ejection time by any method of measurement. Ejection time measured from the initial anterior motion of the posterior wall, which was used in the calculation for VCF in each subject, was nearly identical to that measured from the carotid pulse tracing. Ejection time measured from the peak of the R wave to maximum anterior systolic motion of the posterior wall minus 50 msec was consistently higher than that obtained by the other two methods.

**Table 1. Mean Values of Three Age Groups for the Studied Echocardiographic Parameters**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group I (35-44 yr)</th>
<th>Group II (45-64 yr)</th>
<th>Group III (65-84 yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mitral valve E-F slope (mm/sec)</td>
<td>102.3 ± 3.7 (52)</td>
<td>79.0 ± 3.8 (35)*</td>
<td>67.1 ± 5.2 (18)†</td>
</tr>
<tr>
<td>Aortic root diastolic (mm)</td>
<td>30.9 ± 0.6 (45)</td>
<td>32.0 ± 0.6 (34)</td>
<td>32.9 ± 0.8 (17)‡</td>
</tr>
<tr>
<td>LV wall thickness (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>15.4 ± 0.5 (33)</td>
<td>17.6 ± 0.7 (15)</td>
<td>18.8 ± 0.6 (12)*</td>
</tr>
<tr>
<td>Diastolic</td>
<td>8.7 ± 0.3 (33)</td>
<td>9.8 ± 0.5 (16)</td>
<td>10.7 ± 0.5 (13)*</td>
</tr>
<tr>
<td>Systolic/m²</td>
<td>7.6 ± 0.3 (33)</td>
<td>9.2 ± 0.3 (15)†</td>
<td>10.0 ± 0.4 (12)‡</td>
</tr>
<tr>
<td>Diastolic/m²</td>
<td>4.3 ± 0.1 (33)</td>
<td>5.0 ± 0.2 (16)*</td>
<td>5.7 ± 0.2 (13)‡‡</td>
</tr>
<tr>
<td>LV dimension (mm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic</td>
<td>34.4 ± 1.1 (37)</td>
<td>32.1 ± 0.89 (17)</td>
<td>32.1 ± 1.4 (11)</td>
</tr>
<tr>
<td>Diastolic</td>
<td>51.8 ± 1.03 (37)</td>
<td>50.8 ± 1.3 (17)</td>
<td>51.2 ± 1.4 (11)</td>
</tr>
<tr>
<td>Systolic/m²</td>
<td>17.3 ± 0.5 (37)</td>
<td>16.7 ± 0.5 (17)</td>
<td>16.8 ± 0.6 (11)</td>
</tr>
<tr>
<td>Diastolic/m²</td>
<td>26.0 ± 0.5 (37)</td>
<td>26.4 ± 0.6 (17)</td>
<td>27.0 ± 0.7 (11)</td>
</tr>
<tr>
<td>Fractional shortening of the minor semi-axis</td>
<td>.34 ± .01 (37)</td>
<td>.36 ± .01 (17)</td>
<td>.37 ± .02 (11)</td>
</tr>
<tr>
<td>VCF (cire/sec)</td>
<td>1.17 ± .04 (37)</td>
<td>1.23 ± .04 (17)</td>
<td>1.30 ± .08 (11)</td>
</tr>
</tbody>
</table>

*P <0.01, †P <0.001, ‡P <0.05 as compared with group I.
§P <0.05 as compared with group II.
The number of subjects is given in parentheses next to the mean and SEM.
Discussion

The closure rate of the anterior leaflet of the mitral valve is thought to be proportional to the rate of left ventricular filling in early diastole.\textsuperscript{16} The decreased E-F slope found with increasing age, therefore, may indicate that the rate of early diastolic filling diminishes with advanced age. Diminished early diastolic filling is also suggested by the findings of Luisada and associates of an age-associated increase in the E-F interval and in the interval between the second heart sound and the peak of the E wave.\textsuperscript{16} Derman\textsuperscript{20} also found a decrease in the angle formed at the E point with advanced age. This decline could reflect a limitation in the rate of opening valve motion imposed by age-associated changes in either the mitral valve or the left ventricle. Winters\textsuperscript{21} has reported that the closure rate of diseased valves is related to the presence of valve thickening, and pathologic studies\textsuperscript{22, 23} have described age-associated sclerosis and thickening of valve leaflets. Hence, an age-associated change in the leaflets themselves may account for the decreased E-F slope.

Alternatively, an age-associated decline in the ability of the left ventricle to accommodate large amounts of blood in early diastole could also result in decreased early diastolic filling. Such a change could be attributed to delayed left ventricular relaxation or increased left ventricular stiffness. Harrison and associates\textsuperscript{1} found that the isovolumic relaxation time in man increased by 40\% between the third and ninth decade. They attributed this to a slower rate of ventricular relaxation. Animal studies as well have indicated that aging is associated with a prolonged relaxation time and increased contraction duration.\textsuperscript{24, 25} This age change may be due to alterations in active state properties.\textsuperscript{26} Increased myocardial\textsuperscript{27} and chamber\textsuperscript{28} stiffness in aged animals has also been described and could cause delayed ventricular diastolic filling. Increased myocardial stiffness may result from changes in elastic or viscous properties.\textsuperscript{29} Greater wall thickness as well as age-associated alterations in the amount of collagen and fibrous tissue in aged myocardium\textsuperscript{30} may contribute to an increase in chamber stiffness. Any or all of these conditions occurring in man could limit the rate of left ventricular filling in early diastole.

Group mean comparisons indicated that the diastolic aortic root dimension increases with advancing age although the correlation coefficient was low but still significant. Pathologic studies have also reported an increase with age in aortic diameter and volume.\textsuperscript{31} This tends to compensate for the increased aortic stiffness associated with aging\textsuperscript{32} since a larger aorta undergoes a smaller radius change for a given volume injected into it. However, the larger blood-filled aorta at end-diastole requires the heart to accelerate blood against larger inertial forces when systole begins, and from this standpoint increases impedance. The amount and composition of elastin and collagen which also change with age\textsuperscript{33, 34} contribute to aortic impedance. The ability of the aorta to relax in response to catecholamines diminishes with

\begin{table}
\centering
\begin{tabular}{|l|c|c|c|}
\hline
 & Group I (25-44 yr) & Group II (45-64 yr) & Group III (65-84 yr) \\
 & (msec) & (msec) & (msec) \\
\hline
Carotid upstroke to incisura & 296 ± 3 (37) & 293 ± 4 (17) & 297 ± 6 (11) \\
Initial to maximal systolic anterior & & & \\
motion of posterior LV wall & 292 ± 4 (37) & 302 ± 5 (17) & 296 ± 9 (11) \\
Peak R wave to maximal systolic & & & \\
Anterior motion of posterior LV wall & 319 ± 5 (37) & 330 ± 7 (17) & 316 ± 10 (11) \\
less 50 msec & & & \\
\hline
\end{tabular}
\caption{Mean Values of Three Age Groups for Left Ventricular Ejection Time}
\end{table}

The number of subjects is given in parentheses next to the mean and SEM.
advancing age and may also result in increased impedance during exercise. In addition to changes in the aorta itself, age-associated changes in the size, stiffness, and arteriolar tone of the peripheral vascular bed may result in an increase in total vascular resistance and therefore impedance during both rest and exercise. Increased impedance over a long period of time would be expected to result in the age-associated increase in wall thickness with unchanged cavity dimension observed in this investigation. Sjogren has also reported increased diastolic wall thickness with advanced age. Left ventricular hypertrophy, which would decrease wall stress, may therefore represent an adaptation to a chronic state of increased impedance to left ventricular ejection.

Fractional shortening of the minor semi-axis and velocity of circumferential fiber shortening, as determined by echocardiography, correlate well with angiographically obtained data. Inasmuch as these parameters can be viewed as gross indices of cardiac performance, the lack of any age-associated changes indicate no striking decline in cardiac performance with age in the resting state. Previous studies utilizing resting cardiac output and stroke volume as indicators of performance have shown conflicting results. It is generally agreed that resting heart rate does not vary with age. Some studies have shown a decrease in stroke volume with age. However, it is unclear whether the older individuals in these studies were free of cardiovascular or hypertensive disease and were physically active. Some of the studies suggesting an age-associated decline in stroke volume were obtained with pulmonary or brachial artery catheters in place. There is some question as to whether this represents the resting state. This is an important consideration since it is generally agreed that the perception of stress and/or the capacity of the cardiovascular system to react to a catecholamine-mediated response to stress may be diminished with advancing age. In a less stressful, noninvasive situation, Proper and Wall measured stroke volume by precordial counters following intravenous injection of labelled material. They reported no age-associated changes in a group of 500 men aged 20 to 70 years.

In the present study, the echocardiograms were performed with the individuals at rest in a room which was darkened for better visualization of the oscilloscope images. All of the individuals were physically active and capable of exercising on the treadmill to their predicted submaximal heart rate without electrocardiographic evidence of ischemia. Thus, the physically active condition of our older individuals, as well as more nearly baseline conditions for the study, may account for the lack of an age-associated decline in calculated indices of baseline cardiac performance in this study as compared with others. It should be noted, however, that the determination of dimension changes by echocardiography may be less accurate than other derived parameters because of reliance upon a distance measurement between the interventricular septum and one area of the left ventricular posterior wall. Movements along this line may not be as representative of the entire left ventricle in some age groups as it is in others. In addition, lateral resolution problems due to an inability to completely focus ultrasonic waves over the entire depth range of the beam may distort left ventricular septal and endocardial echoes.

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Echocardiographic Measurement of Right Ventricular Wall Thickness

A New Application of Subxiphoid Echocardiography

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SUMMARY The feasibility of subxiphoid echocardiography to measure the thickness of the right ventricular wall (RVWT) was investigated. In 87 (90.6%) of the 96 patients studied, adequate visualization of the echoes from the right ventricular wall was obtained using the subxiphoid technique.

RVWT averaged 0.34 ± 0.08 cm (mean ± 1 SD), ranging from 0.2 to 0.5 cm in 25 normal individuals. This was not significantly different from the values in the left ventricular overload group (0.36 ± 0.10 cm). However, the RVWT was increased significantly (P < 0.001) in the combined group (0.62 ± 0.18 cm), the right ventricular (RV) pressure overload group (0.60 ± 0.13 cm) and the RV volume overload group (0.53 ± 0.11 cm).

Thirty-two patients underwent diagnostic right heart catheterization which revealed a good correlation between the RVWT measured echocardiographically and the right ventricular peak systolic pressure (r = 0.84).

Subxiphoid echocardiography was considered to be useful in diagnosing right ventricular hypertrophy in adults.

THE RECENT DEVELOPMENT AND IMPROVEMENT of echocardiographic instruments has facilitated noninvasive assessment of cardiac function and evaluation of anatomical abnormalities of the heart. One of the most important achievements has been echocardiographic assessment of the dimensions of cardiac structures.1, 2 However, evaluation of ventricular wall thickness has been limited to the left ventricle. Assessment of the right ventricular wall remains outside the scope of echocardiographic study, except in infants and young patients who have a thin chest wall,3, 4 because of interference by the gaseous tissue of the lung and because of problems due to the physical properties of ultrasound. Only the right ventricular dimension described by Popp et al.5 was found to be a clue to the estimation of the size of the right ventricle, the value of which increases in patients with atrial septal defect or tricuspid insufficiency.

Chang et al.6 reported that subxiphoid echocardiography was useful in emphysematous or aged patients for recordings of the mitral valve and the left ventricular posterior wall. The present study was undertaken to examine the feasibility of echocardiographic measurement of right ventricular wall thickness by the subxiphoid method.

Patients and Methods

Ninety-six patients were examined; nine were excluded due to unsatisfactory echocardiographic visualization of the right ventricular wall. The clinical data of the remaining 87 patients are summarized in table 1. The patients were divided into four groups: normal, left ventricular overload, combined, and right ventricular overload. The normal group included 25 patients with no evidence of cardiopulmonary disorders. There were 15 males and 10 females ranging in age from 17 to 58 years (mean 32.9 years). The left ventricular (LV) overload group included 15 males and seven females aged 20-77 years (mean 56.4 years). The combined group

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