Thirty-Month Follow-Up of Resting and Postexercise Apexcardiogram in Asymptomatic Subjects

By Wilbert S. Aronow, M.D.

SUMMARY

Ninety-eight asymptomatic subjects who had a resting and postexercise apexcardiogram and maximal treadmill stress test (MTST) were clinically evaluated 30 months later. Two of six subjects (33%) with an initially abnormal resting apexcardiogram and two of 92 subjects (2.2%) with an initially normal resting apexcardiogram developed coronary heart disease within 30 months. Three of 15 subjects (20%) with an initially abnormal postexercise apexcardiogram and one of 83 subjects (1.2%) with an initially normal postexercise apexcardiogram developed coronary heart disease within 30 months. Two of four subjects (50%) with an initially abnormal resting apexcardiogram and MTST and two of 94 subjects (2.1%) without both an initially abnormal resting apexcardiogram and MTST developed coronary heart disease within 30 months. Three of seven subjects (43%) with an initially abnormal postexercise apexcardiogram and MTST and one of 91 subjects (1.1%) without both an initially abnormal postexercise apexcardiogram and MTST developed coronary heart disease within 30 months. An abnormal resting apexcardiogram, postexercise apexcardiogram, or MTST correlated with an increased incidence of subsequent coronary heart disease. An abnormal postexercise apexcardiogram plus an abnormal MTST correlated best with an increased incidence of subsequent coronary heart disease.

Additional Indexing Words:
Electrocardiography  Apexcardiography  Exercise

Benchimol and Dimond\(^1\) reported that the a-wave ratio measured in an apexcardiogram after a double Master's test was very helpful in distinguishing between normal subjects and patients with arteriosclerotic heart disease. We\(^2\) reported that 98 of 100 asymptomatic subjects (98%), mean age 51 \(\pm\) 6 years, had a satisfactory apexcardiogram at rest and after performing a double Master's test. Six of these 98 asymptomatic subjects (6.1%) had an abnormal resting a-wave ratio of \(\pm\) 15%. Fifteen of these 98 asymptomatic subjects (15.3%) had an abnormal postexercise a-wave ratio of \(\pm\) 20%.

Follow-up data from asymptomatic subjects who have had a resting and postexercise apexcardiogram need to be obtained to determine the value of these tests in predicting latent coronary heart disease. Therefore, we are reporting 30-month follow-up clinical data on our 98 subjects who had a satisfactory resting and postexercise apexcardiogram. In addition, the 98 subjects had a repeat resting and postexercise apexcardiogram at their 30-month follow-up.

We have reported elsewhere that an abnormal maximal treadmill stress test performed in 100 asymptomatic subjects, including the 98 subjects reported in this paper,\(^2,^3\) was significantly correlated with an increased incidence of subsequent coronary heart disease.\(^4\) The maximal treadmill stress test was performed in these subjects 1 hour after they completed the double Master's test. Therefore, we have also analyzed our data to determine the correlation between an abnormal maximal treadmill stress test plus an abnormal resting or postexercise apexcardiogram with the subsequent development of coronary heart disease.

Methods and Materials

The 98 asymptomatic subjects who previously had a satisfactory resting and postexercise apexcardiogram\(^2\) were followed for 30 months. They included 97 men and one woman who were between ages 40 and 67, with a mean age of 53.5 \(\pm\) 6 years, at the 30-month follow-up. All 98 subjects had a repeat resting and postexercise apexcardiogram at their 30-month follow-up. None of them was on any medication at the time of the tests. All 98 subjects had a blood pressure below 140/90 mm Hg and no evidence of valvular disease at
the time of their initial resting apexcardiogram. All 98 subjects had a blood pressure below 150/100 mm Hg and no evidence of valvular disease at the time of their 30-month follow-up resting apexcardiogram. Tests were performed at least 2 hours after a light meal. All 98 subjects had simultaneous electrocardiograms, by lead II, apexcardiograms, and phonocardiograms recorded in the left lateral decubitus position at the maximum apical impulse at rest and for 2 min immediately after performing a double Master's test.

The equipment used consisted of an eight-channel Poly-Beam recorder (Sanborn-Hewlett-Packard-350 series) coupled to a multichannel oscilloscope. Apexcardiograms were recorded with a pulse wave, linear piezoelectric transducer (Sanborn 21051D) connected to a Sanborn dynamic microphone (Sanborn 62-1500-C16) used for recording heart sounds. The pulse-wave transducer was acoustically coupled to the bell of the dynamic microphone by a short length of rubber tubing attached to a side-opening lumen of the sound microphone bell. In this way, the apexcardiograms and phonocardiograms were recorded simultaneously from the same site. The pulse-wave transducer was connected to an AC preamplifier (Sanborn 350-3200A) of the Poly-Beam recorder. The band-pass filter was set to 0.1 for the lower limit and to 40 for the upper limit. The pulse-wave transducer used to record the apexcardiogram reproduced an electric signal that was proportional to the changing pressure in the tubing. The heart sounds were recorded with a frequency response between 25 and 400 Hz.

The pickup bell of the sound microphone connected with the linear pulse-wave transducer was placed directly over the maximum apical impulse and was held in position by hand with slight-to-moderate pressure applied to the chest wall. The tracings were usually recorded at the end of expiration. Precautions were taken to insure that the patients did not perform the Valsalva maneuver. The tracings were recorded at a paper speed of 75 mm/sec with time lines of 0.04 sec.

The postexercise apexcardiograms used for analysis were the earliest acceptable tracings performed after exercise. Acceptable tracings were not usually obtained within 1 min after exercise. If the resting or postexercise tracings were not acceptable, the entire procedure was repeated on another morning.

The a-wave ratio was measured in the resting apexcardiogram (fig. 1) and in the postexercise apexcardiogram. The total amplitude of the tracing was measured, as illustrated in figure 1, from the E-point to the O-point. The a-wave ratio (%) was determined by dividing the amplitude of the a wave by the E-O amplitude and multiplying this result by 100. All measurements recorded represented the mean value of measurements made in three consecutive cardiac complexes.

The apexcardiograms were reviewed by the author after the study was completed. He did not know from whom the tracings under review were obtained.

The 98 subjects had a treadmill stress test performed 1 hour after their postexercise apexcardiogram. The 94 asymptomatic subjects had a maximal treadmill stress test as previously reported. Four subjects who now had angina performed a submaximal treadmill stress test.

Figure 1

Simultaneous recording of the resting apexcardiogram, heart sounds at the apex, and electrocardiogram in a normal subject. Paper speed, 75 mm/sec; time mark = 0.04 sec; a = a wave in the apexcardiogram; E-O wave = total amplitude of the apexcardiogram; 1 = first heart sound; 2 = second heart sound; 3 = third heart sound; 4 = fourth heart sound; a-wave ratio (%) = a-wave amplitude/E-O amplitude × 100.

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The treadmill stress tests were performed as previously described. Leads I, aVF, and V₅ were recorded in the supine and standing positions before exercise. A multistage uninterrupted treadmill stress test similar to that described by Doan and associates was then performed. The patients were monitored with lead V₅ throughout exercise with an oscilloscope. Leads V₅, aVF, and I were recorded in that order each minute during exercise, continuously after 75% of the predicted maximal heart rate was reached, immediately after exercise in the upright and supine positions, and in the supine position every minute after exercise for at least 6 min. Blood pressures were recorded before and after exercise.

The asymptomatic subjects were exercised until they reached 100% of their predicted maximal heart rate or exhaustion. Three of the four subjects with angina pectoris exercised until the onset of angina; the fourth subject with angina pectoris exercised until he reached 90% of his maximal predicted heart rate.

The criterion for an abnormal exercise test was 1.0 mm or more of ischemic S-T-segment depression below the resting level, with either the S-T segment extending horizontally for at least 0.08 sec or with downward sloping of the S-T segment.

The electrocardiograms were reviewed by the author after the study was completed. He did not know from whom the tracings under review were obtained.

Results

Ninety-four of the 98 asymptomatic subjects (95.9%) experienced no clinical manifestations of coronary artery disease during the 30-month follow-up period. Four of the 98 asymptomatic subjects (4.1%) developed angina pectoris during the 30-month follow-up period. Two of these four subjects had significant three-vessel disease visualized by coronary angiography, and one of these two subjects had experienced a transmural myocardial infarction. One subject with angina had significant two-vessel disease visualized by coronary angiography. The fourth subject with angina had a 75% occlusion of his left anterior descending coronary artery visualized by coronary angiography.

Table 1 shows that two of the six subjects (33%) who initially had a resting a-wave ratio of at least 15% developed angina pectoris due to angiographically documented significant coronary artery disease within the 30-month follow-up period. One of these two subjects also had experienced a transmural myocardial infarction. Two of the 92 subjects (2.2%) who initially had a normal resting a-wave ratio developed angina pectoris due to angiographically documented significant coronary artery disease within the 30-month follow-up period.

The data in table 1 were analyzed using a chi-square test. Asymptomatic subjects with an initially abnormal a-wave ratio in the resting apexcardiogram were more likely to develop coronary heart disease within 30 months than asymptomatic subjects with a normal a-wave ratio in the resting apexcardiogram (chi-square = 13.97, P < 0.001).

Of the six asymptomatic subjects who initially had an abnormal resting a-wave ratio in their resting apexcardiogram, two subjects (33%) developed coronary heart disease and had an abnormal a-wave ratio in their 30-month follow-up resting apexcardiogram. One of the these six subjects (17%) remained asymptomatic and had a normal a-wave ratio in his 30-month follow-up resting apexcardiogram. Three of these six subjects (50%) remained asymptomatic and had an abnormal a-wave ratio in their 30-month follow-up resting apexcardiogram.

Of the 92 asymptomatic subjects who initially had a normal a-wave ratio in their resting apexcardiogram, two subjects (2.2%) developed coronary heart disease and had an abnormal a-wave ratio in their 30-month follow-up resting apexcardiogram. One of these 92 asymptomatic subjects (1.1%) remained asymptomatic and had an abnormal a-wave ratio in his 30-month follow-up resting apexcardiogram. Eighty-nine of these 92 asymptomatic subjects (96.7%) remained asymptomatic and had a normal a-wave ratio in their 30-month follow-up resting apexcardiogram.

Table 2 indicates that three of the 15 subjects (20%) who initially had a postexercise a-wave ratio of at least 20% developed angina pectoris due to angiographically documented significant coronary artery disease within the 30-month follow-up period. One of these three subjects also had

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Table 1

<table>
<thead>
<tr>
<th>Subject</th>
<th>Incidence of coronary artery disease developing within 30 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal subjects with an initially abnormal resting apexcardiogram (N = 6)</td>
<td>2</td>
</tr>
<tr>
<td>Normal subjects with an initially normal resting apexcardiogram (N = 92)</td>
<td>2</td>
</tr>
</tbody>
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experienced a myocardial infarction. One of the 83 subjects (1.2%) who initially had a normal postexercise a-wave ratio developed angina pectoris due to angiographically documented significant coronary artery disease within the 30-month follow-up period.

The data in table 2 were analyzed using a chi-square test. Asymptomatic subjects with an initially abnormal postexercise a-wave ratio were more likely to develop heart disease within 30 months than normal subjects with a normal postexercise a-wave ratio (chi-square = 11.46, P < 0.001).

Of the 15 subjects who initially had an abnormal postexercise a-wave ratio, three subjects (20%) developed coronary heart disease and had an abnormal a-wave ratio in their 30-month follow-up postexercise apexcardiogram. Four of these 15 subjects (27%) remained asymptomatic and had a normal a-wave ratio in their follow-up postexercise apexcardiogram. Eight of these 15 subjects (53%) remained asymptomatic and had an abnormal a-wave ratio in their follow-up postexercise apexcardiogram.

Of the 83 asymptomatic subjects who initially had a normal postexercise a-wave ratio, one subject (1.2%) developed coronary heart disease and had an abnormal a-wave ratio in his follow-up postexercise apexcardiogram. Three of these 83 asymptomatic subjects (3.6%) remained asymptomatic and had an abnormal a-wave ratio in their follow-up postexercise apexcardiogram. Seventy-nine of these 83 asymptomatic subjects (95.2%) remained asymptomatic and had a normal a-wave ratio in their follow-up postexercise apexcardiogram.

Table 2

<table>
<thead>
<tr>
<th>Subject</th>
<th>Incidence of coronary artery disease developing within 30 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal subjects with an initially abnormal postexercise apexcardiogram (N = 15)</td>
<td>3 20</td>
</tr>
<tr>
<td>Normal subjects with an initially normal postexercise apexcardiogram (N = 83)</td>
<td>1 1.2</td>
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</tbody>
</table>

Table 3

<table>
<thead>
<tr>
<th>Subject</th>
<th>Incidence of coronary artery disease developing within 30 months</th>
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</thead>
<tbody>
<tr>
<td>Normal subjects with an initially abnormal resting apexcardiogram and maximal treadmill stress test (N = 4)</td>
<td>2 50</td>
</tr>
<tr>
<td>Normal subjects without both an initially abnormal resting apexcardiogram and maximal treadmill stress test (N = 94)</td>
<td>2 2.1</td>
</tr>
</tbody>
</table>

Table 3 shows that two of four asymptomatic subjects (50%) who initially had both an abnormal maximal treadmill stress test and an abnormal a-wave ratio in their resting apexcardiogram developed angina pectoris due to angiographically documented significant coronary artery disease within the 30-month follow-up period. One of these two subjects also had experienced a myocardial infarction. Two of the 94 subjects (2.1%) who did not initially have both an abnormal maximal treadmill stress test and an abnormal a-wave ratio in their resting apexcardiogram developed angina pectoris due to angiographically documented significant coronary artery disease within the 30-month period.

The data in table 3 were analyzed using a chi-square test. Asymptomatic subjects with both an initially abnormal maximal treadmill stress test and an abnormal resting a-wave ratio were more likely to develop coronary heart disease within 30 months than normal subjects without both an abnormal maximal treadmill stress test and an abnormal resting a-wave ratio (chi-square = 22.46, P < 0.001).

Table 4 shows that three of seven asymptomatic subjects (43%) who initially had both an abnormal treadmill stress test and an abnormal a-wave ratio in their postexercise apexcardiogram developed angina pectoris due to angiographically documented significant coronary artery disease within the 30-month follow-up period. One of these three subjects also had experienced a myocardial infarction.
infarction. One of the 91 subjects (1.1%) who did not initially have both an abnormal maximal treadmill stress test and an abnormal postexercise a-wave ratio developed angina pectoris due to angiographically documented significant coronary artery disease within the 30-month follow-up period.

The data in table 4 were analyzed using a chi-square test. Asymptomatic subjects with both an initially abnormal maximal treadmill stress test and an abnormal postexercise a-wave ratio were more likely to develop coronary heart disease within 30 months than normal subjects without both an abnormal maximal treadmill stress test and an abnormal postexercise a-wave ratio (chi-square = 28.95, P < 0.001).

None of the individuals who had an abnormal maximal treadmill stress test, an abnormal resting apexcardiogram, or an abnormal postexercise apexcardiogram had hypertension.

Discussion

The a wave of the apexcardiogram reflects the left ventricular filling wave associated with the impact of blood upon the left ventricular wall during left atrial contraction.8 Benchimol and Dimond1 stated that patients with an ischemic left ventricle have an increased resistance to distensibility, causing the left ventricular end-diastolic pressure to rise, requiring a more vigorous left atrial contraction. Tavel and his associates9 found that a resting a-wave ratio in the apexcardiogram of ≥15% indicated forceful and voluminous left atrial contraction, arising in response to an elevated left ventricular end-diastolic pressure.

Voigt and Friesinger10 pointed out that the a-wave ratio in the apexcardiogram is influenced by the level of the left ventricular end-diastolic pressure, left ventricular volume, and left ventricular compliance. These investigators found that the a-wave ratio in the apexcardiogram reflected the left ventricular a wave caused by atrial systole. They pointed out that the a-wave ratio in the apexcardiogram predicted the magnitude of the left ventricular a wave more accurately than the left ventricular end-diastolic pressure. These investigators also found that an a-wave ratio in the resting apexcardiogram of ≥15% was associated consistently with an elevated left ventricular end-diastolic pressure, but that a normal a-wave ratio could not be used as evidence for a normal left ventricular end-diastolic pressure.

Our data show that two of six asymptomatic subjects (33%) who had an initially abnormal a-wave ratio in their resting apexcardiogram developed subsequent coronary heart disease within 30 months compared to two of 92 asymptomatic subjects (2.2%) who initially had a normal resting a-wave ratio. We also found that three of 15 asymptomatic subjects (20%) who had an initially abnormal a-wave ratio in their postexercise apexcardiogram developed subsequent coronary heart disease within 30 months compared to one of 83 asymptomatic subjects (1.2%) who initially had a normal postexercise a-wave ratio. These data suggest that the resting and postexercise apexcardiogram may be a sensitive indicator of decreased left ventricular compliance due to latent myocardial disease.

The author is reporting elsewhere4 that an abnormal maximal treadmill stress test was correlated in our asymptomatic subjects with an increased probability of developing subsequent clinical coronary heart disease (chi-square = 14.16, P < 0.001). Furthermore, our data show that two of four asymptomatic subjects (50%) who initially had both an abnormal maximal treadmill stress test and an abnormal resting a-wave ratio developed subsequent coronary heart disease within 30 months compared to two of 94 asymptomatic subjects (2.1%) who initially did not have both an abnormal maximal treadmill stress test and an abnormal resting a-wave ratio. Our data also show that three of seven asymptomatic subjects (43%) who initially
had both an abnormal maximal treadmill stress test and an abnormal postexercise a-wave ratio developed subsequent coronary heart disease within 30 months compared to one of 91 asymptomatic subjects (1.1%) who initially did not have both an abnormal maximal treadmill stress test and an abnormal postexercise a-wave ratio. More data need to be obtained to determine whether an abnormal resting or postexercise apexcardiogram in the absence of an abnormal maximal treadmill stress test will correlate with an increased probability of developing subsequent clinical coronary heart disease.

However, our data indicate that the predictive value of an abnormal postexercise apexcardiogram plus an abnormal maximal treadmill stress test (chisquare = 28.95) is greater than the predictive value of the maximal treadmill stress test alone (chisquare = 14.16) in identifying individuals who will develop subsequent clinical coronary heart disease. Three of our 13 asymptomatic individuals (23.1%) who initially had an abnormal maximal treadmill stress test developed coronary heart disease within 30 months.4 One of our 87 asymptomatic subjects (1.1%) who initially had a normal maximal treadmill stress test developed coronary heart disease within 30 months.4 Therefore, the risk ratio of coronary heart disease incidence in negatives to coronary heart disease incidence in positives is 23.1/1.1 or 19.3 for the maximal treadmill stress test. Our data show that the highest risk ratio is 43/1.1 or 39.1 for the postexercise apexcardiogram plus the maximal treadmill stress test, indicating that the postexercise apexcardiogram plus the maximal treadmill stress test yield the best prognostic index.

In conclusion, our data show that an abnormal maximal treadmill stress test, an abnormal a-wave ratio in the resting apexcardiogram, and an abnormal a-wave ratio in the postexercise apexcardiogram in asymptomatic subjects may reflect clinically silent myocardial ischemia and is significantly correlated with an increased incidence of subsequent coronary heart disease. The presence of both an abnormal maximal treadmill stress test and an abnormal a-wave ratio in the postexercise apexcardiogram had the best predictive value in predicting subsequent coronary heart disease.

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