Diastolic Heart Sounds and Filling Waves in Coronary Artery Disease

By Peter F. Cohn, M.D., Pantel S. Vokonas, M.D., Richard A. Williams, M.D., Michael V. Herman, M.D., and Richard Gorlin, M.D.

SUMMARY
One hundred thirty selected patients with chest pain syndromes were studied by apex- and phonocardiography as well as by cardiac catheterization, selective cine coronary arteriography, and cine left ventriculography. Ninety-three patients had coronary artery disease; 37 did not. Abnormal graphic studies were found in 42 patients with coronary artery disease and three patients with normal coronary arteriograms. These abnormalities correlated well with the presence of elevated left ventricular end-diastolic pressure. Third heart sounds were found less frequently than fourth heart sounds and/or abnormal apexcardiographic a waves, but when present were usually associated with a depressed cardiac index. Diagnostically, over 90% of all patients with chest pain who exhibited graphic abnormalities had significant coronary atherosclerosis. Normal graphic studies did not rule out coronary artery disease, but did indicate adequate left ventricular function since only 5% of patients with normal graphic studies had elevated left ventricular end-diastolic pressure combined with a low cardiac index.

Additional Indexing Words:
Chest pain syndrome Coronary arteriography
Fourth heart sound  Third heart sound
Left ventricular end-diastolic pressure  Apexcardiographic a wave

Fourth heart sounds, abnormal left atrial filling waves, and (to a lesser extent) third heart sounds are commonly recorded by graphic techniques in patients with coronary artery disease. However, extensive correlations of these clinical findings with both hemodynamic and angiographic data have not been previously reported. In the present study, cardiac catheterization, selective cine coronary arteriography, and cine left ventriculography served as a baseline for the evaluation of relationships between abnormal apex- and phonocardiographic findings and (1) left ventricular dysfunction and (2) the presence and extent of coronary arterial disease.

Materials and Methods
Patient Selection
The study population consisted of 130 patients requiring evaluation of a chest pain syndrome. Ninety-three were shown by angiography to have coronary artery disease. In order to avoid attributing the graphic findings to the effects of other forms of heart disease or to the action of drugs, we used the following criteria for the selection of patients: all were suspected clinically of having coronary artery disease uncomplicated by other disorders such as severe hypertension, valvular disease, and primary myocardial disease; none received propranolol within 24 hr of the tests; and no digitalized subjects were included.

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Also excluded were subjects whose electrocardiograms exhibited prolonged P-R intervals.

Clinical Material
Radiologic evidence of left ventricular enlargement and electrocardiographic evidence of transmural myocardial infarction were both determined by standard diagnostic criteria. Age and sex of patients were also recorded.

Catheterization and Angiographic Procedures
All patients were evaluated by cardiac catheterization and angiographic procedures similar to those reported previously from this laboratory. Pertinent data obtained included measurement of left ventricular end-diastolic pressure at high sensitivity (normal value \( \leq 12 \) mm Hg). Cardiac output was measured via the indocyanine green dye technique (normal value \( \geq 2.5 \) liters/min/m\(^2\)). High quality cine coronary arteriograms were obtained on 16 mm Ilford Pan F film with either 6-inch or dual field General Electric or Siemens image intensifier X-ray systems. Stenosis of greater than 75% of a vessel lumen was considered significant. For purposes of this study, patients who exhibited lesser degrees of intramural disease were included under the classification of "normal coronary arteriograms." Thirty-three of the 37 patients in this category, however, had coronary arteriograms completely free of even minor irregularities. Cine left ventriculograms were obtained and evaluated by the method of Herman et al., and the term "asynergy" was used to define any significant abnormality of left ventricular wall motion.

Apex- and Phonocardiographic Studies
Apex- and phonocardiographic studies were usually obtained on the day preceding catheterization and will be subsequently referred to in the text as "graphic studies." Phonocardiograms were recorded at 50–100 Hz (both at and medial to the apex) with a Hewlett-Packard piezo-electric crystal microphone and Sanborn heart sound preamplifier (model 350-1700B). Phonocardiograms were recorded during expiration at the point of maximal impulse, with the patient in a left lateral position, via a conical cup 2.5 cm in diameter connected by a 5-inch rubber tubing to an enclosed diaphragm. This in turn was connected to a Sanborn ECG preamplifier (model 350-3200). Complete descriptions of technique and recording equipment have been reported previously. All tracings were recorded with a simultaneous lead II electrocardiogram at a paper speed of 75 mm/sec, using a Sanborn Series 564 system with a Polybeam recorder. Graphic and hemodynamic parameters were examined in the resting, nonanginal state.

Criteria for Identification of Abnormal Sounds and Impulses
Since no patients had chronic lung disease or cor pulmonale, abnormal heart sounds were presumed to be left ventricular in origin. The third heart sound is a low frequency sound coinciding with the rapid filling phase of ventricular diastole. It is recorded 0.10 to 0.20 sec after the aortic component of the second sound and often corresponds to a rapid filling wave on the apexcardiogram (fig. 1). The major vibrations of the fourth heart sound usually occur 0.12 to 0.17 sec after the onset of the P wave of the electrocardiogram, coincidental with the a wave of the apexcardiogram. These vibrations usually precede the onset of the QRS complex, except in instances of short P-R intervals. Unless the P-R interval is prolonged, the fourth heart sound is normally inaudible, although some small, insignificant vibrations can be recorded on the phonocardiogram at low frequency ranges. Significant (abnormal) vibrations have greater amplitude and pitch, and constitute the clinically audible fourth heart sound. They are readily recorded, even at medium frequency ranges (fig. 1).

Figure 1
Normal and abnormal apex- (ACG) and phonocardiograms (PCG). The record of a patient without third \( (S_3) \) or fourth \( (S_4) \) heart sounds and with both a normal rapid filling wave \( (RFW) \) and atrial filling wave \( (A) \), is contrasted with the prominent rapid filling and A waves seen in a subject with both a third and fourth heart sound. In this latter subject, PCG sensitivity has been increased to better demonstrate the abnormal sounds. This patient also has the extrasystolic bulge \( (E') \) usually associated with a ventricular aneurysm (and subsequently demonstrated at catheterization). Other abbreviations: \( S_1 = \) first heart sound; \( S_2 = \) second heart sound; \( E = \) systolic ejection point; \( O = \) opening of mitral valve.

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Table 1

Interrelationships Between Graphic Abnormalities and Clinical, Arteriographic, and Hemodynamic Findings

<table>
<thead>
<tr>
<th>Graphic studies</th>
<th>Clinical material</th>
<th>Arteriography</th>
<th>Hemodynamics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age*</td>
<td>No. of men</td>
<td>No. with MI†</td>
</tr>
<tr>
<td>Patients with CAD (93)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Abnormal graphics (42)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$S_2$</td>
<td>46</td>
<td>35</td>
<td>22</td>
</tr>
<tr>
<td>$S_2 + S_1$ (Abnormal ACG a wave)</td>
<td>46</td>
<td>35</td>
<td>22</td>
</tr>
<tr>
<td>$S_1$ (Abnormal ACG a wave)</td>
<td>46</td>
<td>35</td>
<td>22</td>
</tr>
<tr>
<td>Normal graphics (51)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with normal coronary arteriograms (37)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abnormal graphics (3)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>$S_2$</td>
<td>52</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>$S_2 + S_1$ (Abnormal ACG a wave)</td>
<td>52</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>$S_1$ (Abnormal ACG a wave)</td>
<td>52</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Normal graphics (34)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total group (130)</td>
<td>45</td>
<td>19</td>
<td>2</td>
</tr>
</tbody>
</table>

*Mean age (ranges were identical in both groups, 35–66 years).
†Determined by ECG.
‡Determined by X-ray.

Abbreviations: MI = myocardial infarction; LVE = left ventricular enlargement; 3VD, 2VD, 1VD = three-vessel disease, etc.; LVEDP = left ventricular end-diastolic pressure; Cl = cardiac index; LV ASYN = left ventricular asynergy; CAD = coronary artery disease; $S_3 = third heart sound; S_4 = fourth heart sound; ACG = apexcardiogram.
The criteria employed for the evaluation of the apexcardiographic a wave are those of Benchimol and Dimond and others who found the amplitude of the normal a wave to be rarely more than 15% of the distance between the zenith (E point) and the nadir (O point) of the apexcardiographic tracing, even after exercise. (Similar quantification does not exist for the rapid filling wave, which is usually not so well defined as the a wave.) Large a waves are considered to represent abnormal atrial filling of the ventricle, and are the apexcardiographic equivalents of audible (or readily recorded) fourth heart sounds. Since one abnormality may occasionally be recorded in the absence of the other, patients were studied with both apex- and phonocardiography.

Results

Results are presented in table 1.

Clinical Material

Mean age was similar in patients with and without significant coronary atherosclerosis. Males constituted 87% of the patients with coronary artery disease and 54% of the patients with normal coronary arteriograms. Patients with normal coronary arteriograms rarely had either ECG evidence of a transmural myocardial infarction or radiologic evidence of left ventricular enlargement. These findings were present in 41% and 26%, respectively, of the patients with coronary artery disease.

Coronary Arteriography

Thirty-seven of the 130 patients (28%) had normal or nearly normal coronary arteriograms. Of the 93 patients with coronary artery disease, 54 (58%) had three-vessel disease, 22 (24%) had two-vessel disease, and 17 (18%) had one-vessel disease.

Hemodynamics

Four of the 37 patients (11%) with normal coronary arteriograms had elevated left ventricular end-diastolic pressures. Two of these patients also had subnormal cardiac indices, and one had left ventricular asynergy. Left ventricular asynergy was also found in one patient with normal end-diastolic pressure. By contrast, 37 of the 93 patients with coronary artery disease (40%) had elevated left ventricular end-diastolic pressures, and 19 of the 37 also had depressed cardiac indices. Left ventricular asynergy was present in 40 of the diseased patients, and these were usually the same patients who had elevated end-diastolic pressures.

Graphic Studies

Abnormal graphic findings were recorded in 45 of the 130 patients. The most frequent finding was a fourth heart sound and/or an abnormal apexcardiographic a wave, occurring in 34 of 45 patients (75%). Nine of the 45 subjects (20%) had combined third and fourth heart sounds. Isolated third heart sounds were found in only two of the patients (5%).

Graphic-Clinical Correlations

Patients with coronary artery disease who had abnormal graphic studies exhibited a 50% frequency of myocardial infarction and a 33% frequency of left ventricular enlargement. Although the corresponding figures in patients with coronary artery disease and normal graphic studies were less (32% and 20%, respectively), these differences did not achieve statistical significance.

Graphic-Arteriographic Correlations

Three of the 45 patients (7%) with abnormal graphic studies had completely normal coronary arteriograms. The other 42 patients had significant coronary artery disease. There was no significant correlation between number of vessels diseased and type of abnormal graphic recordings, although three-vessel disease was found in nine of the 11 patients with third heart sounds.

Graphic-Hemodynamic Correlations

Almost all patients with third heart sounds had elevated left ventricular end-diastolic pressure, depressed cardiac indices, and left ventricular asynergy. By contrast, 70% of patients with isolated fourth heart sounds and/or abnormal apexcardiographic a waves had elevated left ventricular end-diastolic pressure, approximately the same number had asynergy, and only 24% had both an elevated end-diastolic pressure and a low cardiac index. Seven of the 85 patients with normal graphic studies had elevated end-diastolic pressures;
four of these also had depressed cardiac indices. Left ventricular asynergy was found in 12 patients with normal graphic studies, 11 of whom had coronary artery disease.

**Pathophysiology of Graphic Abnormalities**

Figure 2 illustrates the types of left ventricular pressure tracings recorded in patients with normal and abnormal graphic studies, as well as the average left ventricular mean and end-diastolic pressures. The greatest pressure elevations were seen in patients with third heart sounds.

**Discussion**

Previous reports in the literature have noted that patients with coronary artery disease often have abnormal heart sounds ("gallops") and atrial filling waves at rest. If not present at rest they may appear during angina, with exercise, and after a myocardial infarction. Elevated left ventricular end-diastolic pressures have been found in conjunction with these auscultatory or graphic abnormalities. Hemodynamic abnormalities are often labile, however, and diastolic filling sounds may diminish with sedation, dehydration, the administration of hypotensive drugs, nitroglycerin, the use of abdominal binders, or other maneuvers that reduce ventricular filling and lower diastolic pressure. In other cardiovascular diseases in which graphic abnormalities are found, elevated end-diastolic pressures are also common.

Despite these observations, certain issues require further elucidation: (1) the prevalence of these graphic abnormalities (documented during a resting baseline state) in an extensive series of symptomatic patients with and without morphologically proven coronary atherosclerosis and (2) the usefulness of these findings both in diagnosis of coronary artery disease and in assessment of hemodynamic status. The relationship between abnormal graphic studies and elevated left ventricular pressures...
end-diastolic pressure has been amply supported in the present study, even though measurements were not taken simultaneously. In a patient population deliberately limited to those individuals suspected clinically of having uncomplicated coronary artery disease, 41 of 130 subjects had elevated left ventricular end-diastolic pressure. Similarly, 45 of the 130 subjects had graphic abnormalities. Forty-two of these patients had coronary artery disease. Despite the lability of hemodynamic findings, hemodynamic and graphic abnormalities were found in the same patients in the great majority of cases. These patients usually had left ventricular asynergy as well, confirming earlier reports of a high frequency of graphic abnormalities in patients with disturbances of left ventricular wall motion.\textsuperscript{16, 21} Although it is a nonspecific finding in cardiac disease, the presence of a graphic abnormality can be of value to the clinician when he is considering patients who present with the differential diagnosis of chest pain uncomplicated by cardiac drugs or other types of heart disease. Even in those patients it is limited in that it reflects presence rather than extent of coronary arterial disease—82% of patients with coronary artery disease in this study had multivessel disease, yet only 45% had graphic abnormalities. Thus, graphic studies may be normal in patients with extensive vascular lesions and adequate left ventricular function; conversely, patients with strategically placed lesions in single vessels (particularly in the left anterior descending artery) may have abnormal left ventricular function\textsuperscript{22} and, hence, abnormal graphic recordings. Patients with abnormal graphic studies had a higher frequency of both left ventricular enlargement and prior transmural myocardial infarction than did patients with normal graphic studies, but this was not statistically significant. Even though a normal graphic study cannot rule out coronary artery disease, it does provide the clinician with an assessment of the patient’s hemodynamic status. In our series, only 5% of patients with normal graphic studies had both an elevated left ventricular end-diastolic pressure and a low cardiac index.

The finding of abnormal graphic studies (and elevated left ventricular end-diastolic pressure) in symptomatic patients with normal coronary arteriograms suggests that some patients with chest pain but without significant coronary atherosclerosis may have an (as yet) ill-defined cardiomyopathy. Aronow et al.\textsuperscript{29} recently reported a 15% frequency of abnormal heart sounds in asymptomatic and presumably normal subjects in the age group 40 to 60 years. None of these “normal” subjects had been studied either hemodynamically or angiographically; therefore, the significance of their findings in relation to the present study is uncertain.

It is worth commenting on the pathophysiologic basis of these abnormal graphic recordings. In a simultaneous apexcardiographic-hemodynamic study, Vorgt and Freisinger\textsuperscript{20} reported that abnormal apexcardiographic \textit{a} waves correlated well with elevated left ventricular end-diastolic pressures, but only when the latter were due to large atrial filling waves. Thus, pressure elevations due to filling abnormalities in early diastole may or may not be associated with prominent atrial filling waves and their corresponding graphic abnormalities (fourth heart sounds and/or abnormal apexcardiographic \textit{a} waves), but may instead be associated with prominent rapid filling waves and third heart sounds (fig. 2). In patients with coronary artery disease, as well as in those with aortic stenosis\textsuperscript{18} and cardiomyopathies,\textsuperscript{19} there is a greater prevalence of low cardiac indices in those subjects with third heart sounds than in those with only fourth heart sounds or abnormal apexcardiographic \textit{a} waves (table 1). These differences may account for the more ominous prognosis usually associated with the third heart sound.\textsuperscript{1, 2}

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