Spectral Energy of the First Heart Sound in Acute Myocardial Ischemia

A Correlation with Electrocardiographic, Hemodynamic, and Wall Motion Abnormalities

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SUMMARY First heart sound (S₁) energy spectra in isovolumic systole, hemodynamics, and angiographic left ventricular wall motion (LVWM) at rest and with atrial pacing were compared in 27 patients who underwent diagnostic cardiac catheterization and angiography because of chest pain. Eighteen patients were found to have coronary artery disease (CAD) and nine patients, normal coronary arteries. Eleven of the 18 CAD patients (61%) had a mean reduction in the spectral energy of S₁ of 6.5 ± 1.4 (SEM) dB below control (∼52%), during interruption of ischemic stress of rapid atrial pacing, compared to only one of nine patients without CAD (P < 0.05). Only five CAD patients (28%) had an abnormal rise (≥5 mm) in left ventricular end-diastolic pressure (LVEDP) either during or upon interruption of pacing, and six (33%) had ischemic ST-segment depression ≥0.1 mv in the ECG. Similarly two patients free of CAD (22%) had an abnormal increase in LVEDP, and none had ECG evidence of ischemia. Seventeen CAD patients (94%) had segmental LVWM abnormalities at rest or with interruption of pacing, while three patients with normal coronary arteries (33%) had abnormal angiographic LVWM (P < 0.01).

Thus, reduction in S₁ spectral energy is a common accompaniment of myocardial ischemia. In the present study, it was more frequently observed than abnormalities in either the ECG or LVEDP, but was not as consistently seen as segmental left ventricular wall motion abnormalities.

ACUTE MYOCARDIAL ISCHEMIA has been noted in the clinical setting to be associated with reduction in loudness of the first heart sound (S₁). This study was designed to determine whether detailed analysis of the first heart sound during ischemic stress of rapid atrial pacing provides a quantitative measure of changes in energy spectra of S₁.

Several theories have been proposed to explain the mechanism of generation of the first heart sound (S₁). Of the more recent studies, one has supported the acceleration and deceleration theory of Rushmer as the most likely physiologic explanation. An echocardiographic study from our laboratory has shown that, although the timing of mitral valve closure is a critical factor in determining the intensity of S₁, the energy of sound vibrations is probably derived from the force of left ventricular contraction during isovolumic systole.

Sakamoto and associates have reported a nearly linear relationship between the amplitude of S₁ and peak rate of
rise of left ventricular pressure (LV dp/dt) in dogs. Myocardial infarction in man has been shown to cause a shift of the maximum energy of S1 to a lower frequency range,10,11 This finding tends to support the clinical observation of an apparent softening of S1 in acute myocardial infarction.12 The acceleration of blood during the isovolumic portion of S1 sets the entire heart wall-blood system into free vibrations with an intensity determined by the force and velocity of ventricular contraction. The frequency spectrum of these vibrations is determined primarily by the mass and compliance of the vibrating system and is in the range of 10 Hz to 500 Hz. Spectral analysis thus permits isolation of the frequency components of S1 associated with ventricular contraction. Stephens and associates10,11 have shown changes in the frequency spectrum that can be related to various disease states.

The present study focuses on the spectral energy changes of S1, during pacing-induced myocardial ischemia in man. Since ischemia induced by rapid atrial pacing has been found to result in a decrease of left ventricular contractility,13 a corresponding change in the energy distribution of the frequency spectrum of S1 would be expected.

**Material and Methods**

Twenty-seven patients with chest pain syndromes and suspected atherosclerotic coronary artery disease were included in the study. Patients with associated valvular heart disease were excluded. Propranolol and long-acting nitrates were discontinued at least 24 hours prior to study. All patients underwent diagnostic right and either transseptal or retrograde left heart catheterization using standard techniques. A bipolar pacing catheter was positioned in the coronary sinus. Cardiac output was determined in duplicate by the indicator dilution technique, using indocyanine green, as reported previously from our laboratory.14,15 Pressures were obtained using Statham P23Db transducers and were recorded on a direct writing oscillograph (Brush Instruments, Model 480). Measurement of left ventricular end-diastolic pressure (LVEDP) was facilitated by using high gain and rapid paper speed (50–100 mm/sec). LVEDP during transient interruption of rapid pacing was determined by averaging 15–20 consecutive beats starting with the third beat. Cardiac index (CI) and left ventricular stroke work index (LVSWI) were calculated using standard formulae.

Heart sounds were recorded by an air-coupled microphone placed on the chest in the fourth intercostal space adjacent to the left sternal border. The advantages of this microphone are a flat frequency response from 1 to 2500 Hz, optimal acoustic impedance matching to the chest surface, and relative insensitivity to application force. A more detailed description of the characteristics of the microphone has been reported elsewhere.18

A specially designed amplifier (General Electric) with a bandpass of 20–2500 Hz, variable gain of 0–80 dB, and a signal-to-noise ratio greater than 80 dB was used. The heart sound amplifier output and electrocardiographic (ECG) lead V1 were recorded on an FM magnetic tape recorder (Honeywell, Model 7600) at a speed of 15 inches/sec, sufficient to
Table 2. Heart Sound, Hemodynamic, and Angiographic Data of Patients with Normal Coronary Arteries

<table>
<thead>
<tr>
<th>Pt</th>
<th>HR (beats/min)</th>
<th>AS</th>
<th>SAP (mm Hg)</th>
<th>LVEDP (mm Hg)</th>
<th>LVWM</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cont</td>
<td>Max</td>
<td>Int.</td>
<td>dB</td>
<td>%</td>
</tr>
<tr>
<td>MD</td>
<td>120</td>
<td>150*</td>
<td>120</td>
<td>-1.5</td>
<td>-16</td>
</tr>
<tr>
<td>BC</td>
<td>61</td>
<td>143*</td>
<td>60</td>
<td>-0.9</td>
<td>-10</td>
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<tr>
<td>AS</td>
<td>71</td>
<td>137*</td>
<td>67</td>
<td>-0.4</td>
<td>-5</td>
</tr>
<tr>
<td>FDr</td>
<td>80</td>
<td>120*</td>
<td>80</td>
<td>-0.4</td>
<td>-3</td>
</tr>
<tr>
<td>HW</td>
<td>75</td>
<td>150</td>
<td>75</td>
<td>+0.8</td>
<td>9</td>
</tr>
<tr>
<td>CC</td>
<td>83</td>
<td>143</td>
<td>81</td>
<td>+1.2</td>
<td>+15</td>
</tr>
<tr>
<td>EW</td>
<td>80</td>
<td>150</td>
<td>80</td>
<td>+1.8</td>
<td>+24</td>
</tr>
<tr>
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<td>88</td>
<td>143</td>
<td>88</td>
<td>+2.5</td>
<td>+33</td>
</tr>
<tr>
<td>LD</td>
<td>73</td>
<td>150</td>
<td>56</td>
<td>+3.0</td>
<td>+44</td>
</tr>
<tr>
<td>Mean</td>
<td>81</td>
<td>79</td>
<td>+0.7</td>
<td>+10</td>
<td>144/86</td>
</tr>
</tbody>
</table>

*Chest pain during pacing.

Abbreviations: Same as for Table 1.

Data Analysis

A real time spectral analyzer (Spectral Dynamics Corp.) was used to obtain energy spectra of S, for the first 16 patients. In order to facilitate heart sound analysis in the second group of 11 patients, the data were digitized by an analog-to-digital converter and analyzed by a PDP-11 computer (Digital Equipment Corp.) using a fast Fourier transform program. In both methods of heart sound analysis, the sampling interval began 45–50 msec after the onset of the Q wave of the ECG, and was 65 msec in duration. This interval has been reported to correspond to the timing of isovolumic systole in man.19

Eight to 15 beats were analyzed for each patient in the control state and after interruption of the maximum rapid paced rate. The first two beats after interruption of pacing were not selected for analysis in order to avoid effects of increased ventricular filling after the abrupt change in cycle length. The output of both the spectral analyzer and computer represents the average energy spectra of S, for all of the beats analyzed in each state, and was plotted by an X-Y recorder. Changes in the frequency spectra were determined by plotting the difference for each patient over the 20–300 Hz range. This graphic method permitted examination of changes in energy as a function of frequency.

The average change of heart sound energy spectra between control and paced states was computed for each patient in order to correlate heart sound data with hemodynamic and angiographic observations. This mean was obtained by converting the differences in decibels to linear values at intervals of 20 Hz from 20 to 300 Hz. Each patient served as his own control. When groups of patients were compared, only relative changes were used.

The reproducibility of the recording and analysis system was examined by comparing energy spectra of S, at different points in time in ten subjects. This was found to be within 1 dB for a given subject.

The heart sound analysis by the spectral analyzer and the computer employing Fourier transform are equivalent. Therefore, the two groups of patients were combined and statistical analysis was performed by Student's t-test and Chi-square analysis to compare patients with and without coronary artery disease.
Results

The results are presented in tables 1–3. Eighteen patients were found to have occlusive coronary artery disease (CAD). Their data are summarized in table 1. Nine patients were found to have normal coronary arteries and their data are presented in table 2. Figure 1 is a graphic plot of spectral energy versus frequency in a normal subject (A), and for abnormal response in a CAD patient (B).

The mean control cardiac index of the CAD group of $3.1 \pm 0.2$ (SEM) L/min/m² was unchanged at $3.1 \pm 0.2$ L/min/m² during rapid atrial pacing. LVEDP decreased from a control of 11 to 7 mm Hg during rapid pacing, and rose slightly above the control level to 13 mm Hg upon interruption of pacing. Mean LVSWI fell appropriately from $53 \pm 3$ g * m²/m² in the control period to $33 \pm 3$ g * m²/m² during rapid pacing. In the group of nine patients without CAD the average control CI of $2.8 \pm 0.2$ L/min/m² dropped slightly to $2.5 \pm 0.2$ L/min/m² during rapid pacing. Similarly LVEDP fell from 8 mm Hg in the control state to 5 mm Hg during rapid pacing, and increased modestly to 10 mm Hg with interruption of pacing. The LVSWI likewise decreased from $50 \pm 3$ g * m²/m² to $26 \pm 2$ g * m²/m². In no patient did the PR interval during interruption of rapid pacing change more than 0.02 sec over the control.

During interruption of rapid atrial pacing, the 18 CAD patients had a mean reduction in the spectral energy of $S_0$ of $3.4 \pm 1.3$ (SEM) compared to the control level. The nine patients with normal coronary arteries had a mean increase of $0.7 \pm 0.5$ (SEM). Eleven of the 18 CAD group (61%) had a reduction in excess of 1 dB. This exceeds the limits of reproducibility of the method and therefore constitutes a significant decrease. The mean reduction in these 11 patients was $6.5 \pm 1.4$ dB below control (−52%). Only one of nine patients without CAD (M.D.) had a reduction greater than 1 dB. This difference was significant at $P < 0.05$ by Chi-square analysis (table 3).

Five of 18 patients with CAD (28%) had an abnormal rise in LVEDP during or upon interruption of pacing ≤ 5 mm Hg over control10. (table 1). Two of nine patients (22%) with normal coronary arteries (table 2) demonstrated an abnormal increase in LVEDP. The difference between the two groups of patients is not significant (table 3).

Fourteen of 18 patients with CAD were found to have segmental abnormalities in angiographic left ventricular wall motion (LVWM) in the control state, consisting of hypokinesis, akinesis, or dyskinesia. In six of these the LVWM abnormalities increased upon interruption of rapid atrial pacing. Three additional patients with normal LVWM in the control state had abnormalities observed following rapid pacing. In the one remaining patient with normal LVWM in the resting state a second left ventriculogram was not obtained after rapid pacing. The difference in LVWM abnormalities between the CAD and normal coronary group is significant at $P < 0.01$ (table 3).

Six of the 18 CAD patients (33%) had an ischemic ST segment response to atrial pacing (horizontal or downsloping ST depression ≥ 0.1 mV), whereas none of the patients free of CAD had ischemic ST changes. Although ischemic ST depression appears to be specific for CAD in this patient population, the difference between the two groups did not attain statistical significance.

Discussion

Rushmer7 has proposed that acoustic vibrations induced by the acceleration and deceleration of blood within cardiac structures produce heart sounds, rather than closure of valve leaflets per se. Sakamoto and associates8 found a linear relationship between the amplitude of $S_0$ and maximum LV dp/dt in dogs during pharmacologic interventions, myocardial infarction, occlusion of great vessels, volume loading, and hemorrhage. Other investigators9,10 have found changes in the frequency content of $S_0$ in myocardial infarction. Similar changes during transient acute myocardial ischemia have not been reported.

While it is apparent that there is a relationship between left ventricular contractility and spectral energy of $S_0$, during isovolumic systole, other factors must also be involved. For example, evidence of decreased ventricular compliance dur-

![Figure 1](http://circ.ahajournals.org/doi/10.1161/01.CIR.57.3.596)
Reduced compliance should increase the frequency of vibrations induced by the force of contraction, analogous to increasing the stiffness of a damped linear oscillator. Another determinant which has been correlated with the amplitude of $S_1$ is the timing of mitral valve closure. When the valve is closed or nearly closed prior to the onset of systole, the subsequent $S_1$ is reduced in amplitude. This has been shown to occur with prolongation of P-R interval which permits atrioventricular closure of the mitral valve. Whether such a mechanism of premature valve closure may be implicated in presence of ischemia remains to be demonstrated. Partial closure of the valve could be caused by an early rise of pressure in the ischemic, less compliant left ventricle following the atrial systole. Such a mechanism may be evaluated in future studies by obtaining simultaneous echocardiograms with the stress induced ischemia. Thus, there may be opposing factors involved in alterations of the spectral energy of $S_1$ during myocardial ischemia.

Rapid atrial pacing has been shown to be a useful method of evaluating myocardial function in the presence of ischemia in patients with occlusive coronary artery disease. Furthermore, Graber et al. have found a reduction in left ventricular contractility in man characterized by changes in velocity of the contractile element during pacing-induced ischemia. Thus, it is reasonable to expect a reduction in the spectral energy of $S_1$ during reversible myocardial ischemia.

In the present study a reduction in the spectral energy of $S_1$ correlated well with the presence of significant angiographic coronary artery disease. Eleven of 18 CAD patients (61%) were found to have a reduction in the spectral energy of $S_1$ in excess of 1 dB during pacing interruption compared to the control. Only one of nine patients without CAD demonstrated a similar decrease ($P < 0.05$). The mean reduction among the 11 CAD patients was substantial, $6.5 \pm 1.4$ dB or 52%. Nine of the patients had evidence of pacing-induced myocardial ischemia with the development of typical anginal chest pain and/or ischemic ST segment depression on the ECG. The only objective evidence of ischemia in the other two patients was segmental left ventricular wall motion abnormalities induced by atrial pacing. In one of nine patients (M.D.) with normal coronary arteries the modest reduction of 1.5 dB in spectral energy of $S_1$ remained unexplained.

In our laboratory the measurement of LVEDP either during or upon brief interruption of atrial pacing has proved to be an inconsistent finding in the assessment of patients with CAD, in contrast to other reports. This observation is supported by the present study in which only five of 18 CAD patients (28%) were found to have pacing-induced abnormalities in LVEDP. Also two of nine patients with normal coronary arteries (22%) were found to have similar changes in LVEDP. This finding remains unexplained although one of the patients was also found to have abnormal LVWM.

An ischemic flat or downsloping ST segment depression ($\geq 0.1$ mV) was found in only six of 18 patients in the CAD group (33%) and therefore is a relatively less sensitive index of myocardial ischemia.

In our experience the most sensitive index of myocardial ischemia associated with CAD is segmental abnormality of left ventricular wall motion observed either in the resting state or during pacing-induced ischemia. Seventeen of 18 CAD patients (94%) were found to have segmental abnormalities of LVWM either at rest or upon interruption of rapid pacing. The one patient with normal LVWM (H.B.) did not have a second ventriculogram. LVWM abnormalities also occurred in three of nine patients without CAD, suggesting an undefined abnormality of myocardial function. Two of these patients had mitral valve prolapse in which left ventricular contraction abnormalities have been reported.

This study has demonstrated the feasibility of using spectral analysis of the first heart sound in the evaluation of myocardial ischemia. If further studies confirm this finding then reduction in spectral energy of $S_1$ may be used as a useful index of ischemia. In the present study this parameter was more sensitive than abnormalities in LVEDP but not as consistent as segmental left ventricular wall motion abnormalities. This technique of analysis of $S_1$ would be particularly useful as a noninvasive method if similar effects of ischemia are observed with atraumatic interventions such as exercise stress testing.

References

Changes in Plasma Catecholamines and Dopamine Beta-Hydroxylase after Corrective Surgery for Coarctation of the Aorta

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SUMMARY In six patients within 12 hours of surgical correction of aortic coarctation there was a 750% increase in plasma noradrenaline concentrations accompanied by an increase in systolic and diastolic blood pressures. The magnitude of the postoperative increase in noradrenaline concentrations was related to the preoperative level of the pressure gradient across the coarctation. Six months after operation plasma noradrenaline concentrations were still significantly elevated. In nine patients who underwent other types of major surgery there was a small increase in plasma noradrenaline concentrations and a return to levels within the normal range within 24 hours.

Various explanations for the rise in plasma noradrenaline concentrations are considered. In particular the possibility is raised that after surgical correction of aortic coarctation the increased levels indicate a marked increase in sympathetic nervous system activity; this may be mediated by baroreceptor mechanisms and may persist for up to six months after surgery.

THE SURGICAL CORRECTION OF COARCTATION OF THE AORTA is frequently followed by postoperative hypertension and the cause of this is incompletely understood. Increased urinary excretion of catecholamines following resection of aortic coarctation has been shown, and on the basis of this finding, the sympathetic nervous system has been suggested to be the cause of this postoperative increase in blood pressure.1-4 In addition in some patients the surgical correction of coarctation does not bring the blood pressure within the range of normal for the age and sex of the patient.5-8 The reason for this is also not clear.

Changes in the sympathetic nervous system and adrenal medullary activity are reflected in an alteration in plasma noradrenaline and adrenaline concentrations.9 Similarly changes in plasma dopamine-β-hydroxylase (DβH) activity may be used as an index of sympathetic nervous system activity.10

In this study changes in plasma noradrenaline and adrenaline concentrations and DβH activities have been measured before, during, and after surgical correction of aortic coarctation to determine the relationship between postoperative hypertension and the activity of the sympathetic nervous system and adrenal medulla. These patients were re-investigated six months after surgery to assess whether or not their blood pressure had increased and was correlated with an increase in plasma adrenaline and noradrenaline concentrations and DβH activities.

Patients

Aortic Coarctation Group

Three males and three females aged 19.2 ± 4.4 years (mean ± SEM) formed this group (table 1). All underwent preoperative left heart catheterization to determine the degree of narrowing of the coarctation. This is expressed as the peak pressure gradient across the coarctation at the time of systole. Preoperative blood pressure was determined in the right arm using a sphygmomanometer after supine bed rest for 30 min. Preoperative blood samples for plasma adrenaline, noradrenaline, and DβH estimations were taken; patients had not had drugs for at least 72 hours.

Premedication and anesthesia during surgery were the same in all patients and included induction with thiopentone, muscle relaxation with D-tubocurarine, and maintenance of anesthesia with nitrous oxide and oxygen. Following thoracic surgery patients were transferred to the intensive care unit where systolic and diastolic blood pressures were monitored continuously using an intrarterial cannula. Venous blood samples were collected for plasma adrenaline and noradrenaline concentrations and DβH activity estimation immediately before resection of coarctation and immediately after the anastomosis was

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