Response of the Left Ventricle in Coronary Artery Disease to Postextrasystolic Potentiation

By Robert I. Hamby, M.D., Agop Aintabilian, M.D., B. George Wisoff, M.D., and Marvin L. Hartstein, M.D.

SUMMARY

Left ventricular volumes and contractile patterns were evaluated during the first sinus beat after a compensatory pause resulting from ventricular arrhythmia and were compared to the second sinus beat (control beat) in order to evaluate the effect of postextrasystolic potentiation. Twelve patients had no evidence of heart disease (group I). Fifty patients had coronary artery disease and included 14 patients (group IIa) with no prior myocardial infarction and a normal left ventricular contractile pattern and 19 patients (group IIb) with an abnormal contractile pattern. Seventeen patients (group IIc) had a documented transmural myocardial infarction as well as an abnormal left ventricular contractile pattern. In all patients the first postextrasystolic sinus beat, when compared to the second sinus beat, demonstrated increases in stroke volume and ejection fraction and decrease in end-systolic volume. There were no qualitative changes in the contractile pattern in the immediate postextrasystolic beat in the patients with normal left ventricular function. In both group IIb and group IIc the changes in end-systolic volume, stroke volume and ejection fraction were significantly greater than observed in groups I and IIa. Abnormal wall segments present in the control beat in groups IIb and IIc demonstrated after postextrasystolic potentiation a normal contractile pattern, improved pattern or no change when compared to the control beat. Abnormal wall segments were more likely to revert to normal as a result of postextrasystolic potentiation in group IIb than group IIc. Akinesia was less likely to revert completely to normal than hypokinesia. In 20 of 24 patients the changes in contractile pattern after aortocoronary bypass surgery corresponded to those observed as a result of postextrasystolic potentiation.

Additional Indexing Words:
Asynergy
Left ventricular function
Coronary artery surgery
Myocardial infarction
Ejection fraction

Abnormal contraction of left ventricular segments is a characteristic finding in patients with coronary artery disease. Such localized abnormal contractility probably represents the morphologic basis for the disturbed hemodynamics which accompany coronary artery disease. With the introduction of aortocoronary bypass surgery it became relevant to determine whether such disturbances in myocardial wall movement in the individual patient are irreversible. There is some evidence, based on postoperative studies after aortocoronary bypass surgery, that in some patients localized disturbances of wall movement may represent a reversible functional abnormality presumably resulting from chronic ischemia.

It has previously been noted that abnormal contractile patterns accompanying chronic ischemia may show evidence of improvement after administration of epinephrine and nitroglycerin. The present report describes the effect of postextrasystolic potentiation on left ventricular function in patients with arteriosclerotic heart disease. Evidence will be presented to demonstrate that in many patients the localized disturbance in contraction may be completely reversible and accompanied by improvement in left ventricular function. Furthermore, the changes in wall movement accompanying postextrasystolic potentiation will be compared with the findings observed after aortocoronary bypass surgery.

Methods

Studies were performed on 62 patients as part of a work-up to evaluate recurrent chest pain. Twelve patients (group I) were found to have normal hemodynamics and normal left ventricular angiographic studies by criteria previously reported. The remaining 50 patients (group II), all of whom had angina pectoris, were found to have coronary artery disease on selective coronary angiography and were divided in three groups. Group IIa consisted of 14 patients with no prior history of myocardial infarction. The elec-
trocardiogram on admission revealed no evidence of previous myocardial infarction and left ventricular angiography demonstrated a normal contractile pattern (synergy). Group IIb consisted of 19 patients without prior history of myocardial infarction and whose electrocardiogram on admission did not suggest prior myocardial infarction. However, all patients in group IIb had an abnormal contractile pattern (asynery) on left ventricular angiographic study. The types of asynergy noted included localized absence of wall movement (akinesia) and diminished localized wall movement (hypokinesia) during systole. Group IIc consisted of 17 patients who had a history of prior myocardial infarction documented by abnormal Q waves in the electrocardiogram. The admitting electrocardiogram was diagnostic of an inferior myocardial infarction in nine patients, anterior in six and combined anterior and inferior infarctions in two patients. All 17 patients in group IIc had left ventricular angiograms demonstrating abnormal contractile pattern.

Cardiac catheterization was performed in the fasting state and consisted of right and transseptal combined with retrograde left heart catheterization. Pressures were measured in all chambers of the heart and cardiac output was obtained by the direct Fick principle. Left ventricular angiograms were obtained in the right anterior oblique position by injecting 0.50 to 0.75 ml/kg of 90% sodium meglumine diatrizoate over two seconds using a power injector (Viamonte-Hobbs) into the left ventricle through either the transseptal or retrograde catheter. A tracing of lead II of the electrocardiogram was superimposed in the right upper corner of each cine frame (Cinetrace, Electronics for Medicine). Cineangiograms were taken with a 35 mm camera at 60 frames/sec. The X-ray equipment utilized for this study included a dual field 6 inch, 3000 gain, 9 inch, 6000 gain image intensifier (General Electric) with a 35 mm (Photomechanism) synchronous camera utilizing a grid control X-ray tube. When the left ventricular angiogram was completed a grid of known dimension was positioned at the approximate location of the left ventricle and a short film strip taken to permit correction due to magnification. After the completion of the left ventricular angiographic study, selective coronary angiograms were performed. Left ventricular volumes were obtained by the area length method and regression equation of Kasser and Kennedy. The cine films were projected with a 35 mm projector (Vanguard Instrument Corp.) on a ground glass screen. The area of the left ventricular cavity was obtained utilizing an electronic digitizer (Graf/Pen, Science Accessories Corp.) interfaced to a digital computer (Hewlett-Packard) for calculating volumes. The left ventricular end-diastolic volume index (EDV) and ejection fraction determined in 20 patients with normal left ventricles using this method were 69 ± 19 ml/m² and 0.68 ± 10, respectively. All results were expressed as the mean ± one standard deviation of the mean with comparisons between groups determined using unpaired Student's t-test.

During selective left ventricular angiography it is common for the injection of contrast material to be accompanied by catheter-induced ventricular ectopic beats. At the completion of the injection of contrast material the ventricular arrhythmia is followed by a compensatory pause and subsequent normal sinus beats. In the calculation of ventricular volumes the first sinus beat after the compensatory pause is ignored since it is recognized that the first postextrasystolic sinus beat may have a different volume and ejection fraction compared to subsequent sinus beats. Depending on several factors, including heart rate and the interval separating the ectopic beat from the first normal sinus beat, the postextrasystolic beat may have a larger volume than the second sinus beat. In the present study the injection of contrast material lasted two seconds and was accompanied by one to three ventricular ectopic beats. At the completion of the injection of contrast material there followed a compensatory pause followed by normal sinus rhythm. The first and second beats (2 to 3½ sec after the beginning of injection of contrast material) after the compensatory pause were utilized to calculate left ventricular volumes. The first sinus beat after the compensatory pause was designated the postextrasystolic beat while the second beat was designated the control beat. The control beat was assumed to represent the normal contractile mechanism and volume for each patient. Patients were selected for this study if ventricular arrhythmia (1 to 3 ventricular ectopic beats) occurred during injection of contrast material, followed by a compensatory pause which was at least one-and-a-half times the R-R interval of subsequent sinus intervals. Furthermore, sufficient contrast material had to remain in the left ventricle after the postextrasystolic beat to permit the determination of the ventricular volumes in the control beat.

Ventriculograms were evaluated by the superimposition of the end-diastolic and end-systolic silhouette utilizing the mid-aortic valve and apex as fixed points. Since two consecutive beats (postextrasystolic and control beat) were compared with each other, no attempt was made to correct for rotation of the heart or downward displacement of the base. One transverse hemiaxis was drawn which bisected at right angles the line defining the long axis (mid-aortic-to-apex) of the heart. A normal left ventricular contraction was accompanied by at least a 20% shortening of the long axis and a 50% shortening of the transverse hemiaxis. A quantitative comparison between the control beat and the postextrasystolic beat was made on the basis of the percent increase of shortening of the hemiaxis and long axis.

Twenty-four patients in groups IIb and IIc were restudied two to four weeks after aortocoronary bypass surgery in the same laboratory utilizing techniques previously described. Five of these patients had single, twelve double and seven triple vein bypass procedures which included 25 grafts to the left anterior descending, 19 to the right coronary and nine to the circumflex artery. All grafts were demonstrated to be patent.

In order to determine the reliability of the method for calculating the volumes of two consecutive beats, the angiograms of 38 patients were reviewed in which there was no interruption of the sinus rhythm by ectopic beats. Comparison of two such consecutive sinus beats in these 38 patients demonstrated excellent reproducibility in the calculation of the end-diastolic volume (r = 0.985), end-systolic volume (r = 0.984), stroke volume (r = 0.987) and ejection fraction (r = 0.990).

Results

The mean left ventricular hemodynamics of the control beat for the groups studied are shown in table 1. The only abnormality noted in group IIa was an elevated left ventricular end-diastolic pressure (>11 mmHg) in five patients. Twelve patients in group IIb had an elevated left ventricular end-diastolic pressure and four had an abnormal ejection fraction (<0.50).
In group IIc the left ventricular end-diastolic pressure was elevated in ten, the end-diastolic volume abnormal (>100 ml/m²) in three and the ejection fraction less than 0.50 in seven patients.

Figures 1 and 2 compare the volume studies and ejection fractions in the control beat and the postextrasystolic beat in the groups studied. The directional changes in the postextrasystolic beat compared to the control beat were the same in all the groups; however, the magnitude of the changes revealed significant group differences (table 2). In all the groups there was an increase in the end-diastolic volume and a decrease in the end-systolic volume resulting in an increase in stroke volume and ejection fraction of the postextrasystolic beat. As indicated in table 2, comparing group I with group IIa revealed no significant difference between the changes in the end-systolic volume, stroke volume and ejection fraction in the postextrasystolic beat compared to the control beat. However, in groups IIb and IIc the changes in end-systolic volume, stroke volume and ejection fraction noted in the postextrasystolic beat were significantly greater compared to changes observed in groups I and IIa (table 2). There was no significant difference comparing group IIb with group IIc. Figures 3 and 4 show a continuous frame-by-frame plot of the volumes of the postextrasystolic and control beats demonstrating that the changes observed in end-systolic volume,

<table>
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<th>Table 1</th>
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<tr>
<td><strong>Left Ventricular Hemodynamics of Patients Studied</strong></td>
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<tr>
<td>-----------------------------------------------</td>
</tr>
<tr>
<td><strong>Number</strong></td>
</tr>
<tr>
<td>Group I</td>
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<td>Group II</td>
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<td>a</td>
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<td>b</td>
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<td>c</td>
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</table>

*Significant difference compared to group I (P < 0.01).
†Significant difference compared to group I and group IIa (P < 0.005).
‡Significant difference compared to group I and group IIa (P < 0.001).

**Figure 1**
A comparison of the end-diastolic and end-systolic volumes of the control beat (CB) and the postextrasystolic beat (PESB) for the groups studied. Note that in all the groups the end-diastolic volume is greater and the end-systolic volume is smaller in the PESB than the CB. These changes result in an increase in the stroke volume in the PESB as compared to the CB. Each point represents the mean for each group studied. SEM = standard error of the mean.

**Figure 2**
A comparison of the ejection fraction in the control beat and the postextrasystolic beat for the groups studied. Note that the ejection fraction of the PESB in group IIb is the same as group I and group IIa. Each point represents the mean for each group studied. SEM = standard error of the mean.

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stroke volume and ejection fraction were not entirely dependent on a change in end-diastolic volume.

The over-all contractile pattern in the postextrasystolic beat when compared to that of the control beat revealed no qualitative difference in group I and group IIa (fig. 5). However, the abnormal wall segments present in the control beat in groups IIb and IIC demonstrated either normal or improved contractile pattern (fig. 6) or no change in contractility (fig. 7) in the postextrasystolic beat. In 12 of 19 patients (63%) in group IIb and 3 of 17 patients (18%) in group IIC the postextrasystolic beat demonstrated a normal contractile pattern. In these 15 patients in groups IIb and IIC demonstrating a normal contractile pattern in the postextrasystolic beat there was a 24.6 ± 9.2% increased shortening of the hemiaxis and an 8.8 ± 7.2% increased shortening of the long axis. In the remaining seven patients in group IIb the contractile pattern of the postextrasystolic beat, although not normal, did improve as evident by a 10 ± 5.1% increased shortening of the hemiaxis and a 4.1 ± 3.8% increased shortening of the long axis compared to the control beat. In the 14 patients in group IIC who did not have a normal contractile pattern in the postextrasystolic beat, eight demonstrated improvement in contractile pattern as evident by a 12 ± 8.3% increased shortening.

Table 2
Comparison of Postextrasystolic Beat and Control Beat

<table>
<thead>
<tr>
<th>Change in</th>
<th>End-systolic volume</th>
<th>Stroke volume</th>
<th>Ejection fraction</th>
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<tr>
<td></td>
<td>(ml)</td>
<td>(%)</td>
<td>(ml)</td>
</tr>
<tr>
<td>Group I</td>
<td>3 ± 2</td>
<td>12 ± 8</td>
<td>20 ± 8</td>
</tr>
<tr>
<td>Group II</td>
<td>a 4 ± 2</td>
<td>12 ± 4</td>
<td>19 ± 6</td>
</tr>
<tr>
<td></td>
<td>b 16 ± 7†</td>
<td>29 ± 11†</td>
<td>33 ± 11†</td>
</tr>
<tr>
<td></td>
<td>c 19 ± 11†</td>
<td>24 ± 13*</td>
<td>39 ± 13†</td>
</tr>
</tbody>
</table>

The above figures represent the mean and ±1 standard deviation of the difference between the control beat and the postextrasystolic beat. First column represents the absolute difference and the second column the percentage (%) change from control.

*Statistically significant compared to group I and IIa (P < 0.01).
†Statistically significant compared to group I and IIa (P < 0.005).
‡Statistically significant compared to group I and IIa (P < 0.001).

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PostExtrasystolic Beat
EDV 214
ESV 50
SV 165
EF 0.77

Control Beat
EDV 184
ESV 49
SV 135
EF 0.73

Figure 5
Angiographic study of a patient in group IIa (normal hemodynamics and volume study with double vessel coronary artery disease) demonstrating the contractile pattern in the postextrasystolic beat and control beat. It is evident that there is no significant qualitative change in the contractile pattern of the postextrasystolic beat compared to the control beat.

Figure 6
Comparison of the contractile patterns of control beats (on left) with those of postextrasystolic beats (on right). The outer silhouette is the end-diastolic phase and the inner silhouette is the end-systolic phase. In patients 1 and 2 there is complete reversibility of the abnormal contractile pattern in the control beat evident in the postextrasystolic beat. In patients 3 and 4 the abnormal contractile pattern present in the control beat is not reversible, but improvement is evident in the postextrasystolic beat.
postoperative study demonstrated a normal contractile pattern (fig. 8). In both the postextrasystolic beat and postoperative study there was no change in contractile pattern in six patients and improvement in five others. In four patients the observations noted in the postextrasystolic beat did not correspond to those found at the postoperative study (fig. 8). Figure 9 shows two examples of improvement in contractile pattern in the first postextrasystolic beat and after successful aortocoronary bypass surgery.

![Diagram](image-url)

**Figure 7**
Comparison of the contractile pattern of the control beat with that of the postextrasystolic beat. This patient had an electrocardiogram demonstrating an inferolateral myocardial infarction. The contractile pattern is not altered in the postextrasystolic beat. The postextrasystolic beat does demonstrate an increase in the end-diastolic volume and stroke volume with a slight increase in the injection fraction.

**Discussion**

Left ventricular angiographic studies are commonly utilized to determine left ventricular volumes and contractile patterns with coronary artery disease. Such studies are commonly associated with catheter-induced ventricular arrhythmias during the injection of the contrast material followed at the termination of the injection by a compensatory pause and normal sinus rhythm. It is generally appreciated that the first sinus beat after the compensatory pause is not representative of the left ventricular function and contractile pattern in a given study and as such is not utilized in the evaluation of left ventricular volumes and contractile patterns. The present study evaluated, in a selected group of patients, the ventricular volume and contractile pattern in both the first and second sinus beats after a compensatory pause. A control

![Diagram](image-url)

**Figure 8**
Relation between postextrasystolic potentiation preoperatively and postoperative result in 24 patients. All 24 patients had asynergy demonstrated preoperatively in the control beat (CB). In 20 patients the postoperative contractile pattern was similar to that observed preoperatively in the postextrasystolic beat. In four patients there was no agreement between the postoperative contractile pattern and the postextrasystolic beat preoperatively.

**Figure 9**
Two examples of studies demonstrating the preoperative contractile pattern (control beat and postextrasystolic beat) with that of the postoperative study.
series demonstrated the reproducibility of ventricular volume determination in two consecutive sinus beats not preceded by a ventricular arrhythmia. One of the difficulties encountered in the present study was the requirement that sufficient amounts of contrast material remain in the left ventricle after the first postextrasystolic beat to permit determination of the end-diastolic and end-systolic volumes in the second beat. Patients with abnormal or low ejection fractions were more likely to have sufficient contrast material remaining in the left ventricle to permit reliable determination of left ventricular volumes in the second beat after the compensatory pause.

This study indicates that after a compensatory pause, left ventricular function and contractile pattern may be significantly altered from the subsequent sinus beat. Our observations are consistent with the phenomena of postextrasystolic potentiation and are similar to the findings of Dyke and coworkers. The latter group studied postextrasystolic potentiation in 15 patients with coronary artery disease by electrically introducing anextrasystole with an R-wave coupled stimulator. It has been shown previously that a premature beat followed by a compensatory pause results in an increase in the contractile force of the first beat following the pause. This phenomenon has been termed postextrasystolic potentiation. Its basic mechanism is not known. The magnitude of the changes noted after the compensatory pause is dependent directly on the prematurity of the extrasystolic beat and the subsequent lengthening of the compensatory pause. Thus postextrasystolic potentiation may not be angiographically demonstrable in cases not having a long enough compensatory pause after a ventricular arrhythmia. In the present study it was appreciated that in order to obtain a consistent inotropic response of the first postextrasystolic beat the compensatory pause should be at least one-and-a-half times the R-R interval of subsequent sinus beats. The Frank-Starling mechanism may be proposed as playing a contributory mechanism responsible for the increased contractility of the first postextrasystolic beat compared to the second beat. Karliner and coworkers observed that abrupt alterations in cycle length in patients with atrial fibrillation were accompanied by changes in contractility which could be directly attributed to the Frank-Starling mechanism. In the present study 51 patients demonstrated an increase in the end-diastolic volume of the first postextrasystolic beat compared to the second sinus beat. This is illustrated in figure 3. An increased end-diastolic volume of the first postextrasystolic beat resulted in an increased ejection fraction when compared to the next sinus beat. However, as illustrated in figure 4, there were 11 patients in the present study in whom no change occurred in the end-diastolic volume of the first postextrasystolic beat compared to the second sinus beat. In spite of the lack of change in the end-diastolic volume there was an increase in the ejection fraction of the first sinus beat, compared to the second sinus beat, as a result of a decrease in the end-systolic volume of the former beat. Observations in animals indicate that the increase in contractility after a compensatory pause is not dependent on an increase in left ventricular distending pressure or changes in end-diastolic volume. These observations indicate that altered preload need not play any role in the inotropic response after a compensatory pause. Finally acute changes in afterload have been observed to affect cardiac performance. Although this could not be evaluated in the present study, the observations by Beck and associates would indicate that the postextrasystolic ventricular pressure response probably does not play a role in the present study.

In the present study the postextrasystolic response of the normal left ventricle included a variable increase in the end-diastolic volume and a decrease in the end-systolic volume resulting in an increase in the stroke volume and ejection when compared to the control beat (figs. 1 and 2). These changes were in no way different from those observed in the group of patients with normal left ventricular function and coronary artery disease (group IIa). The most striking changes noted in the first postextrasystolic beat were in the patients with abnormal left ventricular contractile patterns in the control beat (groups IIb and c). This is consistent with previous observations indicating that postextrasystolic potentiation is most readily demonstrated when myocardial function is significantly impaired. The findings observed in group IIb suggest that abnormal left ventricular function in patients with coronary artery disease and no prior myocardial infarction is potentially completely reversible (fig. 2). In the patients with prior transmural myocardial infarction (group IIc) the mean ejection fraction attained a normal level in the first postextrasystolic beat, but still did not reach that of the other groups (fig. 2).

The over-all contractile pattern of the postextrasystolic beat in the patients with normal left ventricular function revealed no significant qualitative changes when compared to the control beat (fig. 5). This was in sharp contrast to the response seen in the patients whose control beats demonstrated varying degrees of asynergy. In no patient did the contractile pattern deteriorate in the postextrasystolic beat: it either became normal (fig. 6, patients 1 and 2), improved (fig. 6, patients 3 and 4) or revealed no change (fig. 7) when compared to the control beat. The observation that 63% of the patients in group IIb
demonstrated a normal contractile pattern in the postextrasystolic beat compared to only 18% in group IIc indicates that abnormal myocardial segments not associated with a transmural myocardial infarction are potentially reversible. These findings are consistent with our previous observations that reversibility of abnormal myocardial segments after aortic coronary bypass surgery is dependent on whether or not the patient has evidence of previous myocardial infarction. 

It is evident from our observations that residual left ventricular function can be detected in patients with coronary artery disease by their response to postextrasystolic potentiation. The limited experience in 24 patients from groups IIb and IIc studied after aortic-coronary bypass surgery (fig. 8) suggests that the response of an abnormal myocardial segment to postextrasystolic potentiation may be useful in predicting the response of such a segment to aortic-coronary bypass surgery. Preoperative evaluation, which includes the response of the heart to postextrasystolic potentiation, can also be useful in determining the degree of revascularization that should be performed. It seems to us that if a particular myocardial segment demonstrates an irreversible contractile segment in response to postextrasystolic potentiation, probably as a result of extensive myocardial fibrosis, little can be expected from revascularization of such a wall. An R-wave coupled stimulator or paired pulse stimulation is a reasonable and predictable method for obtaining postextrasystolic potentiation and would thus be useful in detecting residual myocardial function in patients with coronary artery disease. 

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References


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