Detection of Residual Myocardial Function in Coronary Artery Disease Using Post-extra Systolic Potentiation

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SUMMARY

Improved global or segmental wall motion following revascularization suggests potential reversibility of ischemic left ventricular dysfunction in coronary artery disease (CAD). This study evaluates the effectiveness of post-extra systolic potentiation (PESP) to detect latent residual contractile function. Quantitative left ventriculography was performed in 15 patients with CAD (including seven with significant asynergy) and in three normal controls. During the ventriculogram, a single extra-systole was introduced by an R-wave coupled stimulator (R-stimulus interval averaged 398 msec, with an average mA of 2.4). PESP improved segmental axis shortening in 51 of 55 normal axes and 15 of 17 hypokinetic or akinetic axes. It also increased both ejection fraction and mean rate of circumferential fiber shortening in 17 of 18 patients. No significant arrhythmia occurred with this technique. A single interposed beat with PESP in one ventriculogram is a safe, effective method to detect residual potential contractile function in myocardium that may be hypokinetic or akinetic under conditions of the study.

Additional Indexing Words:
Ejection fraction                  Asynergy
Ventricular volumes              Axis shortening

The preoperative detection of ischemic, yet still viable myocardium is critically important since coronary revascularization surgery may correct segmental and ventricular dysfunction in some patients with coronary artery disease, 1, 5 presumably by restoring blood flow to the temporarily compromised myocardium. Segmental areas of myocardium may be hypokinetic or even akinetic during left ventriculography, yet capable of a further contractile response when adequate stimuli are introduced. Response to such stimuli may distinguish between scar and muscle, the latter having the potential for contraction, although it is still uncertain whether reconstitution of blood flow will necessarily bring about the same enhancement of contraction as inotropic stimulation. In addition, evidence of myocardial contractile reserve in the ventricle as a whole may be a useful prognostic sign in patients with depressed ventricular function.

Detection of myocardium which at least has the potential for contraction in patients with coronary artery disease and myocardial dysfunction may be possible by demonstrating augmented contractility following inotropic stimulation. 6 For this purpose, we recently studied the potentiation of contractile state that follows a single ventricular premature contraction (post-extra systolic potentiation or PESP) in acutely ischemic canine myocardium with reversible dysfunction. 6 Segmental shortening and ventricular function were consistently augmented, thus detecting myocardial viability in this preparation.

The present study investigated PESP in patients with coronary artery disease and myocardial dysfunction to determine 1) whether significant latent or residual myocardial function may be present, thereby suggesting the presence of viable ischemic myocardium, and 2) to determine whether PESP is a safe, effective and convenient form of inotropic stimulation.

Methods

After giving informed consent, 18 patients with a chest pain syndrome were evaluated with right and left heart catheterization, including cine left ventriculography and...
selective coronary cineangiography. There was no systematic selection process for this study, nor does it represent a truly consecutive series; instead each patient served as his own control. PESP was studied during the routine left ventriculogram. Following two or three normal sinus beats, a single ventricular premature contraction was introduced using an R-wave coupled stimulator* and a right ventricular bipolar pacing catheter. For each patient, the R-to-stimulus interval and milliamperage of the stimulus were determined as follows: the stimulus was first introduced just prior to the P wave and the milliamperage adjusted to produce a captured beat. The stimulus was then moved back toward the T wave, with its final position determined by the production of a single reproducible extrasystole without subsequent ventricular firing. The average R-stimulus interval was 398 msec (range 320-460 msec) and average milliamperage 2.4 mA (see fig. 1). Quantitative ventriculography was done using a grid-calibration technique and the area-length method of Dodge et al. Briefly, the longitudinal axis (L) and the three transverse axes (D1, D2, D3) were measured, and the area of the ventricular silhouette in the right anterior oblique position planimetered (fig. 2). End-diastolic and end-systolic volumes were derived from the largest and smallest silhouettes, respectively, using the long axis and aortic root as reference points. No attempt was made to correct for rotational movement of the ventricle or displacement of the base, nor was a cast system employed to correct for true volumes. End-diastolic and end-systolic volumes (EDV, ESV), ejection fraction (EF), and mean rate of circumferential fiber shortening (VCF, using axis D2) were calculated to assess over-all ventricular function, and specific axis shortening was used to evaluate segmental function. Data comparison was done between two beats: (1) the sinus beat preceding the ventricular premature contraction; and (2) the PESP beat. The lower limits of normal values for axis shortening and ejection fraction in our laboratory are as follows: for the transverse axis, 20% shortening or greater; for the longitudinal axis, 10% shortening or greater; for the ejection fraction, 0.50 or greater. In this study, a hypokinetic axis was defined as 5-20% shortening (transverse) and

2-10% (longitudinal). An akinetic axis was defined as less than 5% shortening (transverse) and <2% (longitudinal). A dyskinetic axis exhibited lengthening or paradoxical motion. Using these quantitative criteria, only patients with hypokinetic, akinetic, or dyskinetic axes were considered to have evidence of ventricular asynergy.

Biplane studies were not obtained in enough patients to warrant inclusion of data derived from the left anterior oblique (LAO) plane. However, based on previous studies, wall motion is usually better in the LAO view and effects of PESP reported in the present study might be expected to underrepresent biplane values, rather than overestimate them.

Results

Patient Population

As indicated in table 1, of the 15 patients evaluated for a chest pain syndrome were found to have significant coronary artery disease (manifested by greater than 75% narrowing of one or more coronary arteries). Nine patients had prior transmural myocardial infarctions and seven had quantitative evidence of significant asynergy, including four with ejection fractions less than 0.50. Three of these had akinetic or dyskinetic segments as defined previously. Three patients had no significant coronary artery disease and served as "normal" controls.

Effect of PESP on Over-all Ventricular Function

The effect of PESP on ejection fraction for the 15 patients in the study group is shown in figure 3. Ejection fraction improved in each patient, whether normal or with coronary artery disease. Significant improvement after PESP was recorded in the CAD group as a whole. Of the four patients with CAD and an abnormal EF, two showed marked improvement in EF with PESP and two demonstrated changes in EF less than 0.10.

Figure 4 shows the effect of PESP on ESV index and EDV index (panel A) and on VCF (panel B) in 15

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*Developed by Barouh Berkovits of the American Optical Company.
patients with coronary artery disease. Although EDV index increased significantly above the control value, more importantly the ESV index decreased significantly below the control value. Furthermore, as shown in panel B, the mean VCF improved significantly with PESP from 1.45 to 1.87 circ/sec.

Effect of PESP on Segmental Myocardial Function
The effect of PESP on segmental myocardial function is shown in figure 5. There are a total of 72 axes in 18 patients. Panel A depicts the effect of PESP on 55 axes with normal shortening in the sinus beat. Fifty-one of the 55 axes showed increased shortening after PESP; the other four shortened normally but less than during the sinus beat. Panel B depicts the effect of PESP on 11 axes defined as hypokinetic on the sinus beat. There was improvement in nine (including five which reached the normal range); neither of the other two showed paradoxical motion. Panel C shows the effect of PESP on six axes transecting akinetic or dyskinetic zones; all axes improved but only one to the normal range.

Discussion
The results of the present study indicate that PESP can detect latent or residual myocardial function in patients with coronary artery disease and myocardial dysfunction. The inotropic effect of PESP results in improvement of over-all ventricular function with

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**Table 1**

Effects of Post-extra Systolic Potentiation on Angiographic Determinations

<table>
<thead>
<tr>
<th>Patient</th>
<th>EDVI R</th>
<th>EDVI P</th>
<th>ESVI R</th>
<th>ESVI P</th>
<th>EF R</th>
<th>EF P</th>
<th>VCF R</th>
<th>VCF P</th>
<th>D1 R</th>
<th>D1 P</th>
<th>D2 R</th>
<th>D2 P</th>
<th>D3 R</th>
<th>D3 P</th>
<th>L R</th>
<th>L P</th>
</tr>
</thead>
<tbody>
<tr>
<td>R.G.</td>
<td>88</td>
<td>0.80</td>
<td>9</td>
<td>0.93</td>
<td>2.99</td>
<td>3.07</td>
<td>45</td>
<td>50</td>
<td>52</td>
<td>67</td>
<td>58</td>
<td>64</td>
<td>62</td>
<td>63</td>
<td></td>
<td></td>
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<tr>
<td>W.C.</td>
<td>70</td>
<td>0.64</td>
<td>93</td>
<td>0.79</td>
<td>1.65</td>
<td>2.02</td>
<td>40</td>
<td>54</td>
<td>34</td>
<td>41</td>
<td>36</td>
<td>50</td>
<td>22</td>
<td>25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>S.G.</td>
<td>97</td>
<td>0.74</td>
<td>102</td>
<td>0.83</td>
<td>4.72</td>
<td>6.62</td>
<td>44</td>
<td>54</td>
<td>38</td>
<td>53</td>
<td>31</td>
<td>41</td>
<td>34</td>
<td>41</td>
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</table>

Abbreviations: R = regular sinus rhythm; P = post-extra systolic potentiation; EDVI = end-diastolic volume index (ml/m²); ESVI = end-systolic volume index (ml/m²); EF = ejection fraction; VCF = mean rate of circumferential fiber shortening (circ/sec); D1, D2, D3 = transverse axes; L = longitudinal axes. * = myocardial infarction; ** = left ventricular aneurysms, in addition to infarction.
augmented ejection fraction, decreased end-systolic volume index and augmented VCF. Since not all patients in this series had markedly depressed left ventricular function these results may be considered preliminary; however, significant improvement of segmental function was shown by augmentation of shortening in hypokinetic zones, often with improvement to normal ranges, and induced contraction in akinetic or dyskinetic zones, although rarely to normal values. A true fibrous aneurysm would not be expected to contract and presumably increased axis shortening with PESP in akinetic zones is due to enhancement of shortening in nonfibrosed tissue that is either adjacent to or interspersed with scar tissue. This premise is supported by direct observation of the left ventricle of patient RC during surgery: the asynergic area was a mixture of muscle and fibrous scar. Neither of the other two patients with akinetic zones underwent surgery.

Previous studies have employed pharmacologic inotropic stimulation to detect latent or residual myocardial function in ischemic myocardium in both experimental animals and man. Usefulness of these agents is limited, however, because responses may be attenuated or result in secondary ischemic depression of myocardial function. Furthermore, a coronary steal syndrome has been shown to occur with isoproterenol, resulting in further ischemic and contractile depression of deeper myocardial layers while over-all ventricular function was improving. Perhaps most importantly in human subjects, pharmacologic inotropic stimulation necessitates two ventriculograms—an inconvenience which may unnecessarily prolong a study in critically ill patients. Because of the problems associated with pharmacologic inotropic stimulation, additional means of inotropic stimulation were sought. We recently investigated the effect of PESP (a fundamental characteristic of mammalian
cardiac muscle in acutely ischemic myocardium in the dog. Viability of the muscle was subsequently demonstrated because restoration of normal function occurred after re-establishment of coronary blood flow. In these experiments, comparison of pharmacologic inotropic stimulation with PESP showed that only PESP consistently demonstrated muscle viability (i.e., improved segmental and over-all ventricular function) via normalization of the segmental shortening pattern in the ischemic muscle, while pharmacologic inotropic stimulation produced responses which were minimal and inconsistent. In addition to providing more consistent augmentation of muscle when it is acutely ischemic, PESP is safe — with no adverse effects on ventricular rhythm in the canine studies (or in the 18 patients in the present study) — and convenient — requiring only one ventriculogram during catheterization and a simple, inexpensive, and reusable external source of electrical stimulation.

As shown in the present study in patients with coronary artery disease and myocardial dysfunction, detection of augmented contraction following inotropic stimulation may identify viable yet ischemic myocardium, thereby defining preoperatively the areas in which revascularization would reperfuse potentially recoverable muscle. Whether this correlation is dependent on the magnitude, rather than merely the presence of augmentation, and whether augmented function will spontaneously occur following successful revascularization is presently being studied. However, previous experiments have demonstrated that restoration of blood flow can improve segmental as well as over-all ventricular function in acutely ischemic myocardium. Furthermore, reversal of myocardial dysfunction has been demonstrated in some patients following coronary artery bypass graft surgery. Bourassa et al. reported improvement of contractility in 19 of 37 (51%) areas with preoperative hypokinetic or akinetic function. Chatterjee et al. showed correction of segmental dysfunction in the majority of patients studied postoperatively and documented improved over-all ventricular function with increased ejection fraction and a rightward shift in the force-velocity curve.

In addition, demonstration of contractile reserve may be useful as a prognostic sign in those patients with depressed ventricular function, since it is these patients who have the poorest prognosis, whether treated medically or surgically. Thus, demonstration of a better prognosis in those patients with the greatest amount of contractile reserve, as measured by the technique reported in this and related studies, may be of great clinical importance when patients with depressed ventricular function are considered for cardiac surgery.

References


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