Augmentation of Left Ventricular Contraction Pattern in Coronary Artery Disease by an Inotropic Catecholamine

The Epinephrine Ventriculogram

By Howard R. Horn, M.D., Louis E. Teichholz, M.D., Peter F. Cohn, M.D., Michael V. Herman, M.D., and Richard Gorlin, M.D.

SUMMARY

In order to assess potential improvement in abnormal left ventricular (LV) wall motion, eighteen subjects — sixteen with obstructive coronary artery disease and LV asynergy and two with no evidence of organic heart disease — were studied by cardiac catheterization and cineangiography. Ventriculograms were performed at rest and during a constant infusion of l-epinephrine (EPI) at 1-4 µg/min after an average of nine minutes steady state. EPI infusion induced augmentation of LV contraction pattern in both normal subjects and in all normal zones in the sixteen subjects with asynergy, and in no instance was contraction in a normal zone rendered abnormal. Eleven of sixteen patients showed improved contraction in previously asynergic areas, two of whom also demonstrated paradoxical motion in an abnormal zone. Of a total of forty-four resting asynergic zones, twenty-three exhibited an improved contraction pattern with EPI; one showed depressed contraction, two demonstrated both an increase and deterioration in the same zone (paradoxical motion), and eighteen showed no change. Quantitative motion analysis generally corroborated these qualitative ventriculographic observations. Heart rate, LV systolic pressure and LV end-diastolic pressure increased slightly with EPI, but were not significantly changed from control values. While there was wide variation in end-diastolic volume in the subjects with asynergy, EPI resulted in an increase in both stroke volume and ejection fraction, the latter significantly (P < 0.05). In the four subjects who subsequently underwent aneurysmectomy, preoperative lack of improvement with EPI correlated with a pathologic diagnosis of fibrosis. Other than angina pectoris of brief duration in two subjects, EPI provoked no untoward reactions, arrhythmias or complications. It is concluded that LV motion abnormalities can be improved or changed in certain cases by the inotropic stimulus of EPI, suggesting residual contractile ability; the agent may differentiate between zones of potentially functional cardiac muscle and frank fibrosis.

Additional Indexing Words:

Asynergy
Ischemia
Left ventriculography
Ejection fraction

A VENTRICULOGRAM may exhibit either generally poor contraction or localized zones of segmental dysfunction. This may represent either the permanent end-result of a chronic disease process, such as replacement fibrosis, or a transient and potentially reversible state, in which the cardiac muscle is momentarily functioning poorly. The latter may stem from a variety of causes, such as the applied hemodynamic load, pharmacologic depression of contractility or clinically unrecognized transient ischemia.

Thus, a resting ventriculogram if severely abnormal may not provide sufficient data on the true potential of that heart for contraction. A better appraisal may be provided if further contractile reserve can be elicited by an inotropic intervention.

In order to assess if contractile reserve can be provoked and analyzed, several positive inotropic stimuli have been applied during the course of ventriculography to determine to what degree a poorly functioning ventricle or myocardial segment can be made to contract more extensively. Whether such contraction can occur without such excessive stimulation remains to be determined. Furthermore it is not
known if correction of a basic cardiac defect, such as
valve replacement or restoration of deficient myocardial
blood supply, will permit return of function to a
level higher than in the pretreatment state.
The first agent under investigation has been l-
epinephrine and the objectives have been 1) to assess
potential change in segmental left ventricular motion
abnormalities; 2) to examine inotropic stimulation as a
method of determining contractile reserve; and 3) to
distinguish reversible from potentially irreversible
asynergy.

Methods
Eighteen subjects, sixteen with obstructive coronary
artery disease and left ventricular asynergy and two with no
evidence of organic heart disease, were studied by
diagnostic cardiac catheterization, left ventriculography,
and selective coronary arteriography. Informed consent
was obtained in all patients, and selective coronary
arteriography was performed by the Sones or Judkins
techniques. A subject was considered to have significant or
obstructive coronary atherosclerosis if single or multiple
stenoses of seventy-five percent or greater of the arterial
lumen of a major vessel were present. Half of the subjects
had single plane (right anterior oblique projection) ven-
triculograms and half were studied in the biplane mode.
Conventional hemodynamic variables were measured im-
mEDIATELY prior to angiographic studies. Specific details of
procedures utilized in this laboratory have been previously
reported.1,2 Twenty or more minutes after the last injection
of contrast agent a second ventriculogram was performed
during a constant infusion of l-epinephrine at 1-4 ug/min
after an average of 9 min (range 5-17) steady state of pulse
and blood pressure as previously established by Sullivan and
Gorlin.3
Each ventriculogram was interpreted qualitatively for
determination of which areas were asynergic. Asynergy was
defined as localized abnormalities of ventricular wall motion
and was classified as akinesis, a total lack of motion;
dyskinesis, paradoxical systolic expansion of a zone; or local
hypokinesis, decrease in the expected local motion.4 In addi-
tion, quantitative angiographic methods were employed to
obtain volumetric and ejection fractions, utilizing modifi-
cations of the method of Dodge et al.5 Segmental motion
analysis was accomplished by calculating the conventional
major and minor axes, as previously described by this
laboratory and illustrated in figures 6-9.5 These figures are
graphic illustrations of ventricular silhouettes in the 30-
degree right anterior oblique projection in the resting and
epinephrine state; the arrows indicate the change in ventri-
cular dimensions from end-diastole to end-systole; and,
the major and minor axes, L and D1-D3 respectively, are
shown with their respective values listed for percent shortening from end-diastole to end-systole. The apex and
mid-aortic valve were used as fixed reference points.
In the present study both qualitative and quantitative
motion analyses were confined to the right anterior oblique
projection. The septal and posterolateral zones seen in the
left anterior oblique view are rarely asynergic without cor-
responding involvement of either the anterior, apical, or in-
ferior zones in the right anterior oblique view.5
The data were analyzed by the paired t-test.

Results
Qualitative Analysis of Ventricular Asynergy
The qualitative results are demonstrated in figure 1
and described in table 1. Both of the normal subjects
showed a symmetrically augmented left ventricular contraction pattern with epinephrine, and all sixteen
patients with coronary artery disease demonstrated
enhanced contraction in previously normal resting
zones. Eleven of sixteen patients showed improved
contraction in previously asynergic areas, two of the
eleven also demonstrating paradoxical motion in an
abnormal zone; five of sixteen patients exhibited no
change in asynergic areas with epinephrine.
When analyzed in terms of the total of sixty-four
zones, twenty-three of forty-four areas of asynergy ex-
hibited an improved contraction pattern with epinephrine, one showed depressed contraction, two
demonstrated both an increase and deterioration in
the same zone (paradoxical motion), and eighteen
showed no change. The single zone with depressed
contraction was part of a paradoxical expansive motion
induced by epinephrine (patient H.B.). All normal
zones at rest had augmented contraction with
epinephrine. Asynergy of the basal region was not
observed, and in all cases epinephrine increased the
g rigor of basal contraction. The other four normal
resting zones were all inferior in location and all
demonstrated enhanced contraction (table 1). None of
these four subjects had obstructive disease in coronary
arteries supplying the inferior surface of the left ven-
tricle.

Hemodynamics
The effects of epinephrine on heart rate, left
ventricular systolic pressure and left ventricular end-
diastolic pressure are summarized in table 2 and il-
lustrated in figure 2. In both the normal subjects and
the patients with coronary artery disease in whom
these measurements were available, all three variables
beta stimulation of the changes in these changes slightly increased with epinephrine stimulation, but these changes were not significant. The variable changes in heart rate and blood pressure are typical of the epinephrine response with its mixed alpha and beta stimulation of peripheral vascular beds.* While left ventricular end-diastolic pressure showed little change with epinephrine in most patients, a striking increase was noted in two of the subjects with coronary artery disease, both of whom (J. H. and H. M.) developed angina pectoris at the time.

**Table 1**

**Effect of Epinephrine on Left Ventricular Contraction Pattern**

<table>
<thead>
<tr>
<th>CAD Pts</th>
<th>Anterior</th>
<th>Zone of left ventricle</th>
<th>Zone of left ventricle</th>
<th>Basal</th>
<th>Number asynergic zones per patient</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>R</td>
<td>E</td>
<td>R</td>
<td>E</td>
<td>R</td>
</tr>
<tr>
<td>G.B.</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>G.C.</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>N</td>
</tr>
<tr>
<td>E.B.</td>
<td>+</td>
<td>↑</td>
<td>+</td>
<td>↑</td>
<td>+</td>
</tr>
<tr>
<td>M.A.</td>
<td>+</td>
<td>↑</td>
<td>+</td>
<td>0</td>
<td>N</td>
</tr>
<tr>
<td>H.M.</td>
<td>+</td>
<td>↑</td>
<td>+</td>
<td>↑</td>
<td>+</td>
</tr>
<tr>
<td>M.N.</td>
<td>+</td>
<td>↑</td>
<td>+</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>N.Y.</td>
<td>+</td>
<td>*↑</td>
<td>+</td>
<td>↑</td>
<td>+</td>
</tr>
<tr>
<td>J.H.</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>J.L.</td>
<td>+</td>
<td>↑</td>
<td>+</td>
<td>↑</td>
<td>+</td>
</tr>
<tr>
<td>A.C.</td>
<td>+</td>
<td>↑</td>
<td>+</td>
<td>↑</td>
<td>+</td>
</tr>
<tr>
<td>J.O.</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>+</td>
</tr>
<tr>
<td>H.B.</td>
<td>+</td>
<td>*↑</td>
<td>+</td>
<td>↑</td>
<td>+</td>
</tr>
<tr>
<td>J.E.</td>
<td>+</td>
<td>↑</td>
<td>+</td>
<td>↑</td>
<td>+</td>
</tr>
<tr>
<td>M.T.</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>N</td>
</tr>
<tr>
<td>W.P.</td>
<td>+</td>
<td>↑</td>
<td>+</td>
<td>↑</td>
<td>+</td>
</tr>
<tr>
<td>C.B.</td>
<td>+</td>
<td>0</td>
<td>+</td>
<td>0</td>
<td>N</td>
</tr>
</tbody>
</table>

Total asynergic 16 16 12 0 44

A 8 7 8 — 23
B 0 1 0 — 1
C 2 0 0 — 2
D 6 8 4 — 18

Total normal 0 0 4 16 20

A — — 4 16 20

Total zones 64

Abbreviations: CAD = coronary artery disease; R = rest; E = epinephrine; + = asynergy present; N = normal contraction; ↑ = improved contraction; ↓ = depressed contraction; 0 = no change in contraction; * = increased and decreased contraction in same zone (with paradox); A = number of zones exhibiting increased contraction with EPI; B = number of zones exhibiting decreased contraction with EPI; C = number of zones exhibiting both increase and decrease (same zone); D = number of zones exhibiting no change in contraction with EPI.

**Volume Studies**

Table 2 and figure 3 demonstrate the effects of epinephrine on the quantitative angiographic variables, end-diastolic volume, stroke volume, and ejection fraction. In the two normal subjects minimal changes occurred in end-diastolic volume while stroke volume and ejection fraction increased. While there was wide variation in end-diastolic volume in the coronary artery disease group, epinephrine infusion resulted in an increase in both stroke volume and ejection fraction, the latter significantly (P < 0.05). Despite these directional changes in stroke volume and ejection fraction as a group, there was considerable individual variation. No change occurred in ejection fraction in some patients who nevertheless
Table 2
Effects of Epinephrine on Left Ventricular Hemodynamics and Angiocardiographic Determinations

<table>
<thead>
<tr>
<th></th>
<th>EDV (ml/m²)</th>
<th>SV (ml/m²)</th>
<th>EF</th>
<th>HR (beats/min)</th>
<th>LVSP (mm Hg)</th>
<th>LVEDP (mm Hg)</th>
<th>% Axis Shortening</th>
</tr>
</thead>
<tbody>
<tr>
<td>F.W.</td>
<td>78</td>
<td>74</td>
<td>45</td>
<td>53</td>
<td>0.58</td>
<td>0.72</td>
<td>76</td>
</tr>
<tr>
<td>M.M.</td>
<td>72</td>
<td>82</td>
<td>59</td>
<td>72</td>
<td>0.82</td>
<td>0.88</td>
<td>75</td>
</tr>
<tr>
<td>Mean</td>
<td>75</td>
<td>78</td>
<td>52</td>
<td>63</td>
<td>0.70</td>
<td>0.80</td>
<td>71</td>
</tr>
<tr>
<td>± se</td>
<td>±3.0</td>
<td>±4.0</td>
<td>±7.0</td>
<td>±9.5</td>
<td>±0.12</td>
<td>±0.08</td>
<td>±4.0</td>
</tr>
</tbody>
</table>

Coronary Artery Disease

<table>
<thead>
<tr>
<th></th>
<th>EDV (ml/m²)</th>
<th>SV (ml/m²)</th>
<th>EF</th>
<th>HR (beats/min)</th>
<th>LVSP (mm Hg)</th>
<th>LVEDP (mm Hg)</th>
<th>% Axis Shortening</th>
</tr>
</thead>
<tbody>
<tr>
<td>G.B.</td>
<td>177</td>
<td>156</td>
<td>49</td>
<td>51</td>
<td>0.27</td>
<td>0.33</td>
<td>82</td>
</tr>
<tr>
<td>G.C.</td>
<td>100</td>
<td>120</td>
<td>47</td>
<td>49</td>
<td>0.47</td>
<td>0.41</td>
<td>77</td>
</tr>
<tr>
<td>E.B.</td>
<td>115</td>
<td>135</td>
<td>46</td>
<td>56</td>
<td>0.40</td>
<td>0.42</td>
<td>80</td>
</tr>
<tr>
<td>M.A.</td>
<td>157</td>
<td>134</td>
<td>58</td>
<td>39</td>
<td>0.37</td>
<td>0.30</td>
<td>98</td>
</tr>
<tr>
<td>H.M.</td>
<td>154</td>
<td>175</td>
<td>32</td>
<td>60</td>
<td>0.21</td>
<td>0.34</td>
<td>69</td>
</tr>
<tr>
<td>M.N.</td>
<td>111</td>
<td>93</td>
<td>39</td>
<td>30</td>
<td>0.36</td>
<td>0.35</td>
<td>102</td>
</tr>
<tr>
<td>N.Y.</td>
<td>167</td>
<td>212</td>
<td>52</td>
<td>75</td>
<td>0.31</td>
<td>0.36</td>
<td>83</td>
</tr>
<tr>
<td>J.H.</td>
<td>169</td>
<td>193</td>
<td>87</td>
<td>101</td>
<td>0.52</td>
<td>0.52</td>
<td>64</td>
</tr>
<tr>
<td>J.L.</td>
<td>187</td>
<td>236</td>
<td>47</td>
<td>130</td>
<td>0.25</td>
<td>0.55</td>
<td>76</td>
</tr>
<tr>
<td>A.C.</td>
<td>130</td>
<td>99</td>
<td>30</td>
<td>40</td>
<td>0.23</td>
<td>0.41</td>
<td>90</td>
</tr>
<tr>
<td>J.O.</td>
<td>164</td>
<td>159</td>
<td>38</td>
<td>38</td>
<td>0.23</td>
<td>0.24</td>
<td>60</td>
</tr>
<tr>
<td>H.B.</td>
<td>226</td>
<td>202</td>
<td>76</td>
<td>70</td>
<td>0.34</td>
<td>0.35</td>
<td>58</td>
</tr>
<tr>
<td>J.E.</td>
<td>248</td>
<td>224</td>
<td>68</td>
<td>63</td>
<td>0.27</td>
<td>0.28</td>
<td>84</td>
</tr>
<tr>
<td>M.T.</td>
<td>151</td>
<td>149</td>
<td>54</td>
<td>68</td>
<td>0.34</td>
<td>0.46</td>
<td>66</td>
</tr>
<tr>
<td>W.P.</td>
<td>89</td>
<td>85</td>
<td>29</td>
<td>37</td>
<td>0.33</td>
<td>0.43</td>
<td>67</td>
</tr>
<tr>
<td>C.B.</td>
<td>128</td>
<td>136</td>
<td>52</td>
<td>66</td>
<td>0.41</td>
<td>0.49</td>
<td>71</td>
</tr>
<tr>
<td>Mean</td>
<td>155</td>
<td>157</td>
<td>50</td>
<td>61</td>
<td>0.33</td>
<td>0.39</td>
<td>77</td>
</tr>
<tr>
<td>± se</td>
<td>±10.8</td>
<td>±11.7</td>
<td>±4.0</td>
<td>±6.4</td>
<td>±0.02</td>
<td>±0.02</td>
<td>±3.2</td>
</tr>
</tbody>
</table>

P Value NS NS < 0.05 NS NS NS NS

Abbreviations: R = rest; E = epinephrine; EDV = end-diastolic volume; SV = stroke volume; EF = ejection fraction; HR = heart rate; LVSP = left ventricular systolic pressure; LVEDP = left ventricular end-diastolic pressure; Axes as illustrated in figures 4-7.

*Angina pectoris occurred.
EPINEPHRINE VENTRICULOGRAM

Figure 3
Effect of l-epinephrine on end-diastolic volume index (EDVI), stroke index (SI), and ejection fraction (EF). CAD = coronary artery disease.

demonstrated augmented localized contraction in previously asynergic areas with epinephrine. End-diastolic volume and ejection fraction did not vary together, and changes in volume did not correlate with changes in heart rate or in afterload, as judged by systolic pressure. End-diastolic volume increased in the two patients who developed angina and increased end-diastolic pressure. The increase in stroke volume in patients E. B. and J. H. may have been due to augmented end-diastolic volume rather than augmented contractility.

Quantitative Motion Analysis

Motion studies generally corroborated the qualitative ventriculographic observations. These values (percent axis shortening) are summarized in table 2 and will be illustrated in the following representative case examples showing the four typical ventriculographic responses to epinephrine.

1. Figure 4 depicts an augmented contraction pattern in a normal subject during epinephrine infusion, as evidenced by increased shortening along minor axes D1 - D3. The ejection fraction increased from 0.82 to 0.88 in this case.

2. Figure 5 illustrates one of the patients with coronary disease in whom no change occurred in an asynergic area with epinephrine stimulation. Of note is the lack of change in the area of anteroseptal akinesis, although contraction in the normal inferior and basal zones were enhanced, as was the case in all normal resting zones in coronary disease subjects. Ejection fraction changed from 0.41 to 0.49 in this subject with epinephrine. The pathology report on tissue obtained at the time of this patient’s aneurysmectomy described "extensive old myocardial infarction with fibrosis and marked thinning of the wall."

3. Figure 6, in contrast, represents a patient with coronary disease in whom epinephrine induced augmentation of contraction in a previously asynergic zone. Note the striking improvement in the area of anteroseptal hypokinesis with attendant improvement in normal zones as well. This is well supported by the augmented shortening of D0 and L axes. There was a marked increase in ejection fraction from 0.25 to 0.55 in this subject.

4. Figure 7 illustrates both improvement and deterioration of contraction in the same patient induced by epinephrine. Note the augmented contraction in the areas of high anterior and inferior hypokinesis but with exaggeration of the degree of anterior dyskinesis. The latter is illustrated by the outgoing arrows and axis lengthening. Ejection fraction in this case changed from 0.31 to 0.36.

Intraoperative and Pathological Observations

Table 3 describes the intraoperative observations and tissue diagnosis, where available, of the thirteen patients who underwent cardiac surgery for their coronary artery disease.

Of the six subjects who showed improvement with epinephrine in a zone of asynergy, all showed normal muscular contraction in this zone at the time of operation, 4 with apparently normal muscle and 2 with a mixture of muscle and fibrosis on inspection. Of the 7 patients who showed no improvement in asynergy, with epinephrine 6 were observed to have a frank thin
walled aneurysm or dense fibrotic scar and 1 showed mixed muscle and fibrosis with poor local contraction. Only 1 exhibited a classical bulge on ventriculogram different in configuration from that of the left ventricle. Operative inspection was required to diagnose resectable aneurysm. No postmortem descriptions are available as no mortality has occurred to date.

Safety of the Epinephrine Ventriculogram
Angina pectoris occurred without sequelae in two patients while receiving epinephrine (H. M. and J. H.) and terminated within one-two minutes of cessation of infusion. Otherwise there were no untoward reactions, arrhythmias or complications.

Discussion
Review and Background
Earlier studies in this laboratory have defined and classified disturbances in left ventricular wall motion (asynergy), and have elucidated their contribution to ventricular dysfunction in coronary artery disease. In examining the defects responsible for asynergy it was found that, in some cases, there is replacement of ventricular muscle by fibrous scar. In others, normal muscle is interspersed with fibrosis, and in some cases muscle may be structurally normal but fails to shorten for a variety of reasons.\(^6\),\(^7\) In addition to ischemia, other potential causes for myocardial depression and asynergy in the setting of the cardiovascular laboratory must be considered, such as the administration of radiographic contrast agent, sedative drugs, and other aspects of the catheterization procedure itself.

The potential reversibility of depression and asynergy of the ischemic myocardium is of considerable practical importance. In the setting of acute experimental ischemia, hypokinesis and paradoxical systolic expansion consistently occur after temporary occlusion of the coronary artery, and motion of the hypoxic myocardium is recovered if the occlusion is promptly removed.\(^8\),\(^9\) Furthermore, in man, it has been reported that coronary artery bypass graft surgery in the preinfarction syndrome improved marked left ventricular hypokinesis and akinesis, along with ejection fraction and other derived indices of myocardial contractility.\(^10\) Similar results have been reported in chronic stages of ischemic heart disease where persistent alterations may exist in one area of the ventricle due to frank fibrosis, while other areas of myocardium may be reversibly damaged and capable of improvement if blood flow is restored. In one study of ventricular wall motion following aortocoronary venous bypass surgery, 51% (19 of 37) of deficits of ventricular wall motion were improved following surgery. In this study hypokinesis was improved in 70% (17 out of 24 instances) with a normal contraction restored in nearly one-half of the cases; but akinesis was improved in only 15% (2 out of 13 instances).\(^11\) Bourassa has recently summarized postoperative experience and concluded that revascularization does not necessarily improve left ventricular function.\(^12\) Presumably restoration of function might be possible although not proven if the zone of asynergy was composed of muscle or muscle interspersed with fibrosis. Frank aneurysm and scar would not be expected to improve.

What is required is some means to predict beforehand which portions of the ischemic left ventricle are potentially capable of improvement. Various

Table 3

<table>
<thead>
<tr>
<th>Zones of asynergy: response to epinephrine</th>
<th>1. Improvement</th>
<th>2. No improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fibrosis</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Segmental</td>
<td>1</td>
<td>Aneurysm or fibrosis</td>
</tr>
<tr>
<td>Global</td>
<td>1</td>
<td>Poor local contraction</td>
</tr>
<tr>
<td>Normal</td>
<td>4</td>
<td></td>
</tr>
</tbody>
</table>

Circulation, Volume XLIX, June 1974
interventions have been employed during cineventriculography to better define wall motion abnormalities in coronary artery disease, and in particular to provoke potential areas of asynergy not present at rest. This has been termed "stress ventriculography." One example is the induction of temporary segmental ischemia by atrial pacing; this study demonstrated that major abnormalities of segmental motion of the wall of the ventricle may be induced by the ischemic stress of an increased heart rate. In another study, propranolol, or a beta-adrenergic blocking agent was shown to induce or accentuate zones of asynergy, presumably by causing a certain degree of myocardial depression.

Present Study

In the present study, however, the objective was to determine if segmental and/or global left ventricular contraction pattern could be improved if abnormal at rest. Thus, a mechanism to augment contraction was required, and the agent selected was l-epinephrine. This is a positive inotropic agent which increases cardiac output, stroke volume, and systolic ejection rate without a significant change in blood pressure or heart rate; and, acting as a secondary coronary vasodilator, it increases coronary blood flow. It was felt that l-epinephrine might be a safer agent in the heart of subjects with coronary artery disease because it increases inotropic state while lacking the primary coronary vasoconstrictor effect of norepinephrine and the potentially marked chronotropic and peripheral vasodilating effect of isoproterenol.

In a human study such as this the problems inherent in the methodology and approaches must be recognized. Intracardiac injection of angiographic contrast materials induces two changes; hypervolemia and myocardial depression, as evidenced by elevation of left ventricular end-diastolic pressure and reduced left ventricular function curves in patients with coronary heart disease. Maximal hemodynamic changes occur within one to three minutes after contrast injection and values return to preangiographic levels within fifteen to twenty minutes. For this reason we allowed twenty minutes as a minimum rest period before proceeding with the second (epinephrine) ventriculogram. Whether such augmented osmolalitv and hypervolemia may persist beyond a 20 minute period in certain patients and thereby induce a larger ventricular size during the epinephrine state cannot be determined with certainty. The reproducibility of the angiographically-determined ejection fraction and end-diastolic volume derived from two left ventriculograms done during the same catheterization and at comparable hemodynamic state is ± 0.05 and ± 27 ml, respectively in our laboratory.

In our study the positive inotropic effects of epinephrine on wall motion are well demonstrated by the augmented or hyperdynamic contraction pattern of the entire left ventricle in the normal subjects and of all normal zones in the sixteen subjects with asynergy. In no instance was contraction in such a normal zone rendered abnormal. Eleven of sixteen subjects showed improved contraction in twenty-three of forty-four asynergic areas. Two of these eleven patients also demonstrated paradoxical motion in an abnormal zone. These effects on contraction pattern were achieved without a significant change in heart rate, left ventricular systolic pressure or left ventricular end-diastolic pressure, confirming previous hemodynamic studies. And in six subjects preoperative lack of improvement with epinephrine correlated with a pathologic diagnosis of myocardial fibrosis or frank aneurysm.

Animal studies of the differential effect of catecholamines on ischemic and nonischemic portions of myocardium showed that although the nonischemic myocardium responded to norepinephrine, metaraminol and isoproterenol with augmented contraction, the ischemic zone showed an increase in the amplitude of paradoxical systolic expansion. Similar results were found in another study of acute ischemia in dogs in which the systemic administration of the inotropic agents, isoproterenol and calcium, increased the degree of early systolic bulging with some augmentation of later shortening. Why the human subject with asynergy exhibited augmented contraction more often than paradoxical expansion is unexplained.

Further recent data, from studies employing pacing techniques in animals, indicate that the initial improvement in contraction of ischemic myocardium secondary to inotropic interventions may be attenuated; and, it is possible that segmental performance might eventually become depressed due to increasing energy requirements in the absence of an augmented coronary flow. In the present study, the only one in which epinephrine was the inotropic agent, the second ventriculogram was performed after an average of 9 minutes of infusion. Variation in the duration of infusion did not elicit any particular pattern of response.

In theoretically examining the present level of knowledge about myocardial segmental viability in coronary heart disease, the first issue to consider is the status of the tissue: is it viable muscle, frank fibrosis or a combination of the two? If scar or fibrosis, contraction would not be expected under any circumstances...
as demonstrated by the patients described in table 3. On the other hand, if viable muscle is present, it may or may not contract. Contraction, here, may not occur for a variety of reasons, such as loss of excitation-contraction coupling mechanism or a variety of other causes. Finally, muscle may be found to contract, but only 1) with intense inotropic stimulation, as with epinephrine, and not under normal operating conditions particularly if mass is inadequate or perhaps, 2) by restoration of blood flow to ischemic muscle.

The data from this study show that left ventricular motion abnormalities can be improved or changed in certain cases by the inotropic stimulus of epinephrine, suggesting potential residual contractile ability or available inotropic reserve. Furthermore, the agent may differentiate between non-contraction or malfunctioning zones of cardiac muscle (“chronic reversible ischemia”) and frank fibrosis by inducing contraction in such resting abnormal areas. Epinephrine appears capable of identifying those patients with coronary artery disease in whom asynergy is potentially reversible, but whether this means portions of the ischemic heart are capable of recovery once blood flow is restored is as yet unknown.

Insufficient time has elapsed since this study was initiated to permit any definitive statements regarding the subjects who underwent surgery and their postoperative ventricular function and contraction pattern. Therefore, it remains to be determined whether this particular intervention, the “epinephrine ventriculogram,” will provide a preoperative means of defining the potential benefit of revascularization surgery on left ventricular contraction.

However, the data from this study do strongly support the transient clinical use of epinephrine as a safe inotropic agent in ischemic heart disease, not only where hemodynamic improvement is necessary, but especially in those situations where ventricular asynergy may be an important factor. For example, patients with extensive left ventricular asynergy are known to be at higher than average risk during cardiac surgery, whether or not augmentation of left ventricular wall motion in such patients will correlate with improved prognosis is currently being investigated.

Acknowledgment

We wish to thank Dr. Thomas Ryan and associates of Boston University Medical School for kindly supplying appropriate data on patient A.C.

References


18. KAVANAGH-GRAY D: Left ventricular end-diastolic pressures following selective coronary arteriography. Am Heart J 84: 629, 1972

19. COHN PF, HORN HR, TEICHOLZ LE, KREULEN TH, HERMAN MV, GORLIN R: Effects of angiographic contrast medium on left ventricular function in coronary artery disease. Am J Cardiol 32: 21, 1973


24. Puris, B.R.: Effect of drugs on myocardial contractility in
the intact dog and in experimental myocardial infarction.
Am. J. Cardiol. 21: 886, 1968

of residual function of ischemic muscle by inotropic agents.
Circulation 46 (suppl II): II-147, 1972


ventricular ejection fraction as a prognostic guide in the sur-
gical treatment of coronary and valvular heart disease. Am. J.
Cardiol, In press
Augmentation of Left Ventricular Contraction Pattern in Coronary Artery Disease by an Inotropic Catecholamine: The Epinephrine Ventriculogram

HOWARD R. HORN, LOUIS E. TEICHHOLZ, PETER F. COHN, MICHAEL V. HERMAN and RICHARD GORLIN

_Circulation_. 1974;49:1063-1071
doi: 10.1161/01.CIR.49.6.1063

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1974 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/49/6/1063

 Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

 Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

 Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org/subscriptions/