Prolonged Left Ventricular Ejection Time in the Post-premature Beat

A Sensitive Sign of Idiopathic Hypertrophic Subaortic Stenosis

By Carl W. White, M.D., and Thomas J. Zimmerman, M.D.

SUMMARY

Failure of the pulse pressure to increase in the post-premature beat is considered characteristic of idiopathic hypertrophic subaortic stenosis (IHSS). The sensitivity and specificity of this response were compared to the change in left ventricular ejection time (LVET) in 12 patients with IHSS, in ten control patients with valvular aortic stenosis (AS) and in five normal subjects. The post-PVC pulse pressure increased in all normals and in nine of the ten patients with AS. In IHSS this response was inconsistent. A positive Brockenbrough sign was seen in only 33%. On the other hand, LVET increased > 20 msec in eleven of twelve patients with IHSS, whereas all normal subjects and all patients with AS showed either decreases in LVET or increases smaller than 20 msec. Prolongation of the LVET during the post-PVC beat > 20 msec appears, therefore, to be a more sensitive sign of IHSS than the corresponding change in pulse pressure.

IDIOPATHIC HYPERTROPHIC SUBAORTIC STENOSIS (IHSS) is a dynamic muscular obstruction to left ventricular ejection which may be induced or increased by a variety of physiologic or pharmacologic interventions. Marked increases in obstruction are known to occur in the post-premature beat, in which the more forceful contraction following the extrasystole results in an augmentation of the left ventricular-aortic pressure gradient. Such augmentation does not differentiate between fixed valvular and dynamic muscular outflow obstruction. Considered characteristic of IHSS, however, is the response of the pulse pressure in the post-premature beat, first described by Brockenbrough and colleagues. Patients with IHSS were noted to exhibit a reduced systemic arterial pulse pressure in the beat following the premature contraction. This contrasted with fixed forms of left ventricular outflow obstruction, in which the post-premature beat showed an increase in pulse pressure. This inverse relationship between arterial pulse pressure and left ventricular systolic pressure in the post-premature beat is generally considered a reliable diagnostic sign of IHSS. Preliminary results, however, suggest that in the milder forms of IHSS this sign may be insensitive.

Prolongation of left ventricular ejection is also common to both valvular aortic stenosis and IHSS. Though nonspecific in the resting state, changes in the left ventricular ejection time (LVET) during pharmacologic intervention have been proposed as a noninvasive screening test for IHSS. There are no studies which compare the LVET in the post-premature beat in these two groups.

The purpose of this investigation was to examine systematically the sensitivity and specificity of the change in pulse pressure and change in left ventricular ejection time in the post-premature beat in patients with IHSS, using patients with valvular aortic stenosis and normal subjects as controls. Differences in responses among these groups may aid in further clinical characterization of this disease.

Materials and Methods

The records of all patients with the diagnosis of IHSS undergoing cardiac catheterization at our institution since 1971 were reviewed. Twelve patients were found to have appropriate catheterization data recorded at paper speeds suitable for evaluation. The diagnosis of IHSS was confirmed by angiography and characteristic hemodynamic or echocardiographic features. Diagnoses with angiography and echocardiography were based upon abnormal systolic approximation of the interventricular septum and anterior leaflet of the mitral valve. Clinical features and hemodynamic abnormalities of patients with IHSS are listed in table 1.

The hemodynamic records of these patients were subsequently examined for the presence of single premature systoles. The extrasystoles were all of ventricular origin and either occurred spontaneously or were deliberately provoked by stimulation of the ventricular endocardium.
LVET in the Post-Premature Beat in IHSS

Clinical and Hemodynamic Characteristics of 12 Patients with IHSS

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>36 ± 5 (SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bifurcations pulse</td>
<td>Rest</td>
</tr>
<tr>
<td>Angiographic mitral insufficiency</td>
<td>Absent</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>73 ± 3</td>
</tr>
<tr>
<td>Peak LV-Ao gradient (mm Hg)</td>
<td>Rest</td>
</tr>
<tr>
<td>Isoproterenol infusion (1-2 μg/min)</td>
<td>88 ± 15</td>
</tr>
<tr>
<td>Amyl nitrite inhalation</td>
<td>52 ± 11</td>
</tr>
<tr>
<td>Exercise (150-300 krm/min)</td>
<td>30 ± 11</td>
</tr>
<tr>
<td>Valsalva (40 mm Hg bronchial pressure)</td>
<td>50 ± 14</td>
</tr>
</tbody>
</table>

LVET in the Post-Premature Beat in IHSS

LVET IN THE POST-PREMATURE BEAT IN IHSS

with a catheter. Tracings showing atrial fibrillation, multiple consecutive extrasystoles, or interpolated extrasystoles were excluded, as were cases where the postextrasystolic electrocardiogram did not show a normal sinus beat. All single premature beats were examined and tabulated. Because of a marked variability in pulse pressure response, two beats per patient were subsequently analyzed. The two beats showing the widest variability in response form the basis of this report. These data were then compared to those obtained from a review of the records of ten patients with valvular aortic stenosis and five normal patients in whom single premature systoles occurred spontaneously during cardiac catheterization. Only one premature beat per patient was generally available for analysis. Cardiac catheterization was done in the normal subjects because of a clinical diagnosis of atypical chest pain. These patients were subsequently determined to have angiographically normal coronary arteries.

Data were recorded at paper speeds of 75-100 mm/sec. Basic heart rate was listed as the control RR interval. The timing of the extrasystoles was expressed as degree of prematurity (RV) measured from the peak of the R wave of the control sinus beat to the beginning of the ventricular depolarization of the extrasystole, and as compensatory pause (VR) measured from the beginning of the QRS complex of the extrasystole to the peak of the R wave of the subsequent sinus beat.

All patients underwent right and left heart catheterization in the postabsorptive state. Left ventricular pressures were measured by the transseptal method or by retrograde arterial catheterization, with care being taken to avoid catheter entrapment. Central aortic pressure was measured in all patients. Simultaneous left ventricular and central aortic pressures were recorded in patients with IHSS and valvular aortic stenosis. Similar pressure recordings were made during the Valsalva maneuver when intrathoracic pressure was sustained at a level of 40 mm Hg, with supine exercise (150-300 Kgm/min) using a bicycle ergometer, during the inhalation of amyl nitrite, and with infusion of isoproterenol 1-2 μg/min. Ejection fractions during sinus rhythm were estimated according to the method of Sandler et al. All patients with ejection fractions <30% were excluded. The peak left ventricular systolic, end-diastolic, and aortic systolic, diastolic and pulse pressures were measured in all patients before and after the extrasystole. The left ventricular-aortic gradient was measured from the peak of the left ventricular pulse contour to the peak aortic pressure.

Left ventricular ejection time was measured from the initial upstroke of the aortic pulse tracing to the incisura. Left ventricular ejection time was not corrected for heart rate as beat to beat changes were examined. The control ejection time and pulse pressure are the mean of the three preceding cycles. LVET and pulse pressure were determined in the same beat.

Results

Heart Rate and Premature Ventricular Contractions

The control heart rate and R-R interval were not statistically different in the three groups. The degree of prematurity (RV) and compensatory pause (VR) for each group are listed in table 2. There were no significant differences in these parameters noted among the three groups.

Left Ventricular-Aortic Pressure Gradients

The resting left ventricular-aortic peak systolic gradient was smaller in IHSS than in aortic stenosis (table 2); however, in the post-premature beat the gradients were not statistically different: 92 ± 10 in IHSS and 118 ± 18 in aortic stenosis. The increase in gradient in the post-premature beat was greater in IHSS than in valvular aortic stenosis (IHSS 48 ± 6 mm Hg, AS 25 ± 5 mm Hg; P < 0.05) but this increase did not result primarily from an increase in left ventricular systolic pressure. The increase in left ventricular systolic pressure was not significantly different in the two groups (IHSS 41 ± 6, AS 24 ± 4).

Pulse Pressure

The increase in pulse pressure from control to post-premature beat averaged 3 ± 2 mm Hg in IHSS, 5 ± 10 in normals and 4 ± 6 in valvular aortic stenosis (fig. 1, table 2). Although there was an average increase in the pulse pressure of the post-premature beat in each group, the increase was statistically significant in valvular aortic stenosis and in normal subjects, but not in IHSS.

The scatter in the post-premature pulse pressure response in IHSS is also shown in figure 1. Four patients had increases in pulse pressure, two had decreases, two showed no change, and in four the response was variable with both increases and decreases in pulse pressure seen in the same record. There was no significant correlation in patients with IHSS between the change in pulse pressure, and resting outflow gradient or the increase in gradient. A fall in pulse pressure occurred in only one of the ten patients with valvular aortic stenosis.

Left Ventricular Ejection Time

The change in LVET in the post-premature beat is shown in figures 2 and 3 and the results are tabulated in figure 4. The left ventricular ejection time in
Table 2

Catheterization Measurements in Patients with IHSS, Valvular Aortic Stenosis, and Normal Subjects

<table>
<thead>
<tr>
<th>Patient</th>
<th>Beat #</th>
<th>PP (mm Hg)</th>
<th>PPVC</th>
<th>C</th>
<th>LV (mm Hg)</th>
<th>LV-Ao gradient (mm Hg)</th>
<th>LVET (msec)</th>
<th>Intervals (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IHSS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A.J.</td>
<td>1</td>
<td>92</td>
<td>94</td>
<td>174/8</td>
<td>234/8</td>
<td>10</td>
<td>92</td>
<td>320</td>
</tr>
<tr>
<td>M.W.</td>
<td>2</td>
<td>56</td>
<td>60</td>
<td>140/6</td>
<td>190/12</td>
<td>13</td>
<td>80</td>
<td>320</td>
</tr>
<tr>
<td>K.B.</td>
<td>2</td>
<td>58</td>
<td>54</td>
<td>136/10</td>
<td>180/8</td>
<td>14</td>
<td>74</td>
<td>330</td>
</tr>
<tr>
<td>W.S.</td>
<td>2</td>
<td>50</td>
<td>56</td>
<td>146/24</td>
<td>170/26</td>
<td>34</td>
<td>56</td>
<td>330</td>
</tr>
<tr>
<td>O.W.</td>
<td>2</td>
<td>46</td>
<td>70</td>
<td>118/10</td>
<td>150/22</td>
<td>12</td>
<td>56</td>
<td>205</td>
</tr>
<tr>
<td>H.B.</td>
<td>2</td>
<td>33</td>
<td>33</td>
<td>133/8</td>
<td>150/8</td>
<td>33</td>
<td>60</td>
<td>300</td>
</tr>
<tr>
<td>T.H.</td>
<td>2</td>
<td>32</td>
<td>52</td>
<td>124/10</td>
<td>159/8</td>
<td>25</td>
<td>78</td>
<td>300</td>
</tr>
<tr>
<td>L.W.</td>
<td>2</td>
<td>44</td>
<td>44</td>
<td>136/7</td>
<td>116/9</td>
<td>25</td>
<td>15</td>
<td>150</td>
</tr>
<tr>
<td>L.L.</td>
<td>2</td>
<td>42</td>
<td>42</td>
<td>129/10</td>
<td>149/18</td>
<td>18</td>
<td>36</td>
<td>170</td>
</tr>
<tr>
<td>W.S.</td>
<td>2</td>
<td>50</td>
<td>48</td>
<td>148/14</td>
<td>229/16</td>
<td>0</td>
<td>110</td>
<td>320</td>
</tr>
<tr>
<td>J.V.</td>
<td>2</td>
<td>26</td>
<td>32</td>
<td>224/16</td>
<td>280/6</td>
<td>152</td>
<td>290</td>
<td>380</td>
</tr>
<tr>
<td>N.S.</td>
<td>2</td>
<td>26</td>
<td>36</td>
<td>240/14</td>
<td>294/8</td>
<td>146</td>
<td>200</td>
<td>350</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td>49</td>
<td>52</td>
<td>160/13</td>
<td>200/14</td>
<td>42</td>
<td>92</td>
<td>297</td>
</tr>
</tbody>
</table>

Assessments

<table>
<thead>
<tr>
<th>Patient</th>
<th>Beat #</th>
<th>PP (mm Hg)</th>
<th>PPVC</th>
<th>C</th>
<th>LV (mm Hg)</th>
<th>LV-Ao gradient (mm Hg)</th>
<th>LVET (msec)</th>
<th>Intervals (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M.D.</td>
<td>3</td>
<td>50</td>
<td>62</td>
<td>184/12</td>
<td>194/16</td>
<td>56</td>
<td>72</td>
<td>360</td>
</tr>
<tr>
<td>G.F.</td>
<td>4</td>
<td>62</td>
<td>76</td>
<td>135/22</td>
<td>142/23</td>
<td>22</td>
<td>23</td>
<td>328</td>
</tr>
<tr>
<td>F.B.</td>
<td>5</td>
<td>74</td>
<td>70</td>
<td>224/22</td>
<td>240/28</td>
<td>88</td>
<td>116</td>
<td>376</td>
</tr>
<tr>
<td>L.H.</td>
<td>6</td>
<td>44</td>
<td>54</td>
<td>220/44</td>
<td>264/42</td>
<td>114</td>
<td>162</td>
<td>316</td>
</tr>
<tr>
<td>F.K.</td>
<td>7</td>
<td>36</td>
<td>50</td>
<td>230/36</td>
<td>262/32</td>
<td>140</td>
<td>170</td>
<td>360</td>
</tr>
<tr>
<td>H.P.</td>
<td>8</td>
<td>27</td>
<td>73</td>
<td>180/36</td>
<td>220/40</td>
<td>—</td>
<td>—</td>
<td>310</td>
</tr>
<tr>
<td>G.O.</td>
<td>9</td>
<td>46</td>
<td>52</td>
<td>240/36</td>
<td>264/36</td>
<td>124</td>
<td>146</td>
<td>416</td>
</tr>
<tr>
<td>G.B.</td>
<td>10</td>
<td>64</td>
<td>88</td>
<td>212/20</td>
<td>262/44</td>
<td>—</td>
<td>—</td>
<td>350</td>
</tr>
<tr>
<td>P.K.</td>
<td>11</td>
<td>48</td>
<td>56</td>
<td>224/16</td>
<td>240/—</td>
<td>100</td>
<td>116</td>
<td>228</td>
</tr>
<tr>
<td>L.K.</td>
<td>12</td>
<td>46</td>
<td>50</td>
<td>220/12</td>
<td>246/16</td>
<td>102</td>
<td>140</td>
<td>360</td>
</tr>
</tbody>
</table>

Mean    | 50     | 63         | 207/25*| 230/29*| 93*      | 118         | 343*         | 337            | 714             | 954            | 458            |

**Statistically significant, P < .05 or CI 95% below IHSS vs AS.

**Statistically significant, P < .05 or CI 95% below IHSS vs Normal.

Abbreviations: IHSS = idiopathic hypertrophic subaortic stenosis; AS = valvular aortic stenosis; PP = pulse pressure; C = control beat; PPVC = post-premature ventricular contraction; LV = left ventricular systolic and end-diastolic pressure; LV-Ao = left ventricular aortic mean gradient; LVET = left ventricular ejection time.

patients with IHSS increased significantly by an average of 48 ± 5 msec during the post-premature beat. In contrast, in valvular aortic stenosis the left ventricular ejection time did not change significantly nor consistently (±3 ± 7 msec). Normal subjects showed a decrease in left ventricular ejection time (−27 ± 7 msec). The change in left ventricular ejection time in the post-premature beat in IHSS is significantly different from both the normal subjects and those with valvular aortic stenosis (P < 0.001). No significant correlation was found between the change in left ventricular ejection time, and the peak outflow gradient or the change in gradient.

The sensitivity of LVET prolongation is shown in figure 4. In the IHSS group the left ventricular ejection time increased more than 22 msec in 11 of 12
LVET IN THE POST-PREMATURE BEAT IN IHSS

Figure 1

Change in pulse pressure of the post-premature beat in patients with IHSS, aortic stenosis, or normal subjects. Connecting vertical bars indicate the maximum variability in the post-PVC response in the same patient.

beat-pairs analyzed. In contrast, no patient with valvular aortic stenosis prolonged the left ventricular ejection time more than 16 msec. None of the normals showed an increase in left ventricular ejection time in the post-premature beat.

A comparison between the percent change in pulse pressure and percent change in left ventricular ejection time in IHSS is shown in figure 5. Pulse pressure in the post-premature beat increased an average of 4% whereas for the left ventricular ejection time the mean increase was 17%. While the response of the pulse pressure in the post-premature beat exhibits considerable variability, showing either increases or decreases, the uniform response of the LVET is prolongation.

Discussion

Although the upstroke time of the resting carotid or aortic pulse tracing in IHSS is characteristically rapid, a prolonged left ventricular ejection time may occur. The resting carotid pulse tracing, however, may not be specific for the diagnosis, requiring at times augmentation of obstruction by pharmacologic stimulation. Our findings suggest that prolongation of the LVET in the post-premature beat in IHSS can also be a useful diagnostic tool — one which is both sensitive and specific. Prolongation of the LVET >20 msec was effective in discriminating IHSS from valvular aortic stenosis. No normal patient showed an increase in the left ventricular ejection time in the post-premature beat.

Outflow obstruction in IHSS is classically considered to be increased by interventions which decrease ventricular volume or increase contractile performance, and to be decreased by reductions in afterload. The contractile performance of the post-premature beat may be increased by 1) postextrasystolic potentiation, "persistence of the positive inotropic effect of activation longer than its negative inotropic effect" and 2) rest potentiation, that increase in strength of beats which follow periods of rest. A similar increase in ventricular contractile performance in both aortic stenosis and IHSS was observed as judged by similar increases in left ventricular systolic pressure. However, the greater change in gradient

Figure 2

Effect of a premature ventricular contraction in IHSS on the pulse pressure and left ventricular ejection time of the subsequent beat.
observed in IHSS reflects the enhancement of obstruction possible only when the obstruction is not fixed. This increase in obstruction appears responsible for the added prolongation of the LVET.

It is also possible that the prolonged LVET might reflect an increase in stroke volume. Studies on changes in ventricular volume in the post-premature beat in IHSS are extremely limited. Rackley and co-workers describe angiographic studies on one post-premature beat in IHSS which revealed that the expected increase in end-diastolic volume in the post-premature beat did not occur, probably reflecting a decrease in compliance. End-systolic volume was decreased, resulting from an increased ejection

---

**Figure 3**

Effect of a premature ventricular contraction on pulse pressure and left ventricular ejection time of the subsequent beat in valvular aortic stenosis.

---

**Figure 4**

Change in left ventricular ejection time of the post-premature beat. Connecting vertical bars indicate maximum variability of the response in the same patient.

---

**Figure 5**

Comparison of the percent change in ejection time and percent change in pulse pressure in patients with IHSS. Small numbers represent beats with identical findings.
fraction with increased stroke volume. Whether the increased stroke volume was ejected into the aorta or into the left atrium was not clear. In contrast, Hernandez and associates, using a velocity catheter in the root of the aorta, and Pierce and coworkers, employing a flow meter around the aorta at the time of surgery, both observed that the forward stroke volume was the same or less in the post PVC beat when compared to other sinus beats in patients with IHSS.13, 14

The exact relationship between the outflow gradient and the LVET remains unclear. In their original series, Braunwald and coworkers found no relation between the peak systolic pressure gradient and the duration of the ejection period.1 Wigle et al., however, noted a direct correlation between the change in LVET and the magnitude of the pressure gradient whether the latter varied spontaneously or followed surgical or pharmacologic intervention.15 In contrast, when an intraventricular pressure difference resulted from catheter entrapment, an inverse correlation was seen. Most recently, Ibrahim et al., studying systolic time intervals in valvular aortic stenosis and IHSS, found that although there was an inverse relationship between the gradient and the isovolumetric contraction time in valvular aortic stenosis, no such correlation existed for IHSS. No single noninvasive parameter in IHSS was found to be of benefit in assessing the degree of obstruction.5

Failure of the pulse pressure to increase in the post-premature beat, frequently termed the Brockenbrough phenomenon, has been considered a hallmark of the hemodynamic diagnosis of IHSS.1 However, the sensitivity and specificity of this sign are not generally recognized. In the original description, a decrease in pulse pressure in the post-premature beat was seen in 11 of 12 patients.2 Braunwald and colleagues found the response abnormal in 45 of 57 patients.1 Gault and Simon found the Brockenbrough sign positive in 18 of 19 patients with IHSS, whereas in eight patients with nonobstructive intraventricular pressure differences produced by catheter entrapment, no positive responses were observed.16 Hancock, however, noted this inverse relationship to be present in only 5 of 14 patients with IHSS, always in association with a large resting gradient, and concluded that an abnormal arterial pulse contour was a more reliable sign of mild muscular subaortic stenosis than the Brockenbrough effect.9

In the present study a marked variability in the pulse pressure response in IHSS was observed. Both increases and decreases in the pulse pressure following a premature beat were seen in the same record. There was no correlation between the resting gradient and the change in pulse pressure in the post-premature beat. A fall in pulse pressure, when seen, was relatively specific for IHSS, being seen in none of the normal patients and in only one of the 10 patients with valvular aortic stenosis (fig. 1). It is apparent, however, that the sensitivity of this sign is lacking. In IHSS, a positive Brockenbrough sign was present consistently in only 33%—4 of the 12 records examined.

The explanation for the smaller frequency of positive Brockenbrough responses in our group is not readily apparent. The magnitude of the response of the gradient to various provocative maneuvers is generally similar to that previously described in IHSS.17 In general, however, the magnitude of the resting gradient is lower in this series than in others reported.1, 18

The variability of pulse pressure responses seen in the post-premature beat may reflect true differences in forward stroke volume perhaps related to the relative prematurity of the ectopic beat. An increase in obstruction, however, would not necessarily result in a decrease in forward stroke volume. The increase in total time for ejection might compensate, allowing an increased stroke volume to be ejected although accompanied by an increase in gradient.

In conclusion, in IHSS a fall in pulse pressure in the post PVC beat, though highly specific, is lacking in sensitivity; that is, a large number of false negative responses are seen. Prolongation of the left ventricular ejection time >20 msec appears, however, to be an equally specific, though much more sensitive, sign and should be considered a reliable diagnostic finding in this dynamic disease.

References


7. SANDLER H, HAWLEY RR, DODGE HT, BAXLEY WA: Calculation of left ventricular volume from single plane (A-P) angiocardiograms. (abstr) J Clin Invest 44: 1094, 1965


9. LYLE DP, BANCROFT WH Jr, TUCKER M, EDDLEMAN EE Jr:


Prolonged left ventricular ejection time in the post-premature beat. A sensitive sign of idiopathic hypertrophic subaortic stenosis.
C W White and T J Zimmerman

Circulation. 1975;52:306-312
doi: 10.1161/01.CIR.52.2.306

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1975 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/52/2/306

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/