Clinical and Laboratory Findings in Patients with Nonobstructive Intraventricular Pressure Differences

By James H. Gault, M.D., and Allan L. Simon, M.D.

SUMMARY
Clinical and laboratory findings were examined in eight patients with nonobstructive intraventricular pressure differences resulting from catheter entrapment in obliterated apical portions of the left ventricular cavity. Cardiorespiratory symptoms were reported by six of the eight patients; three had angina pectoris, and two had experienced syncope. A soft systolic ejection murmur was noted at the cardiac apex or left sternal edge, or at both sites, in each patient at rest or following exercise; no patient had a bifid systolic arterial pulse contour. Paradoxical splitting of the second heart sound with respiration did not occur. In five patients the cardiac index was substantially elevated. In four, an intraventricular pressure difference was present in the basal state, while in the remaining four a pressure difference was elicited by the Valsalva maneuver and isoproterenol. In each patient the arterial pulse pressure consistently increased in the beat following a ventricular extrasystole, and angiographic evidence of left ventricular outflow obstruction was not observed. In all patients, obliteration of the apical portion of the left ventricular cavity during systole was demonstrated angiographically to result from an extreme degree of systolic emptying. Left ventricular hypertrophy was demonstrated angiographically in six patients, four of whom exhibited asymmetric hypertrophy, predominantly involving the interventricular septum. In two patients no abnormality of the left ventricular cavity contour was apparent. These clinical, hemodynamic, and angiographic findings allow differentiation of patients with nonobstructive pressure differences from those with hypertrophic subaortic stenosis.

Additional Indexing Words:
Cavity obliteration  Idiopathic hypertrophic subaortic stenosis

In patients with idiopathic hypertrophic subaortic stenosis (IHSS), the documentation of obstruction to left ventricular outflow and the estimation of its severity are based on the measurement of an intraventricular pressure difference. Experimental studies have shown, however, that intraventricular pressure differences can be recorded in the absence of obstruction, when the catheter tip lies within portions of the left ventricular cavity that are obliterated during systole.¹⁻⁴ A similar phenomenon also can occur in patients.⁵⁻⁸ Therefore, it has become of considerable importance both diagnostically and therapeutically to characterize the clinical and hemodynamic findings in patients having nonobstructive pressure differences, and to determine whether or not such patients can be distinguished from those with IHSS. Accordingly, the clinical and laboratory features in a group of

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patients in whom intraventricular pressure differences could not be ascribed to obstruction were examined and compared with those of patients with IHSS and obstruction to left ventricular outflow.9, 10

Methods

Previous studies have demonstrated an elevated systolic pressure in all portions of the left ventricle proximal to the outflow tract when obstruction exists in the left ventricular (LV) outflow tract.6, 9 Thus, an end-hole catheter introduced from the left atrium into the left ventricle records a pressure exceeding that in the aorta both in the body of the ventricle and in the inflow tract (fig. 1B). If, however, upon withdrawal of the catheter from the body or apex of the left ventricle to the inflow tract, the pressure falls to a level equal to that in the aorta, then outflow tract obstruction cannot exist, and the elevated pressure may be ascribed to catheter entrapment in obliterated portions of the ventricular apex (fig. 1A). The present report describes eight patients in whom the presence of a nonobstructive pressure difference was documented by measurements of apical and inflow tract pressures.

The history, physical examination, electrocardiogram, and phonocardiogram of each patient were assessed. All patients underwent left heart catheterization in the postabsorptive state following premedication with pentobarbital sodium, 100 mg intramuscularly. In seven patients the left heart chambers were entered transseptally,11 while, in one patient, recordings of LV inflow tract pressures were made during withdrawal across the mitral valve of a retrograde arterial catheter. Brachial or femoral arterial pressure was recorded by means of an indwelling Cournand needle. LV and systemic arterial pressures at rest were recorded in each patient, and the cardiac

![Figure 1](image_url)

Simultaneous recordings of left ventricular (LV) and brachial arterial (BA) pressures are shown on withdrawal of an end-hole catheter from the LV apex to the left atrium (LA) in a patient with a nonobstructive pressure difference (panel A) and one with idiopathic hypertrophic subaortic stenosis (IHSS) and obstruction to LV outflow (panel B)
output was measured by the indicator-dilution technic. To confirm the location of the catheter in the inflow tract during LV pressure measurements, continuous pressure recordings were made as the end-hole catheter was withdrawn across the mitral valve. Similar pressure recordings were made in each patient during the Valsalva maneuver, when intrathoracic pressure was sustained at a level of 40 mm Hg, as well as during the intravenous infusion of isoproterenol, 1 to 2 μg/min.

In each patient, an average of five determinations of the change in the systemic arterial pulse pressure in the beat following a ventricular premature contraction (VPC) was made, comparing the first postextrasystolic beat with that immediately preceding the extrasysole. The arterial pulse pressure following a VPC in these patients also was compared with that in 20 patients who did not have significant disease of the LV myocardium.

Biplane angiocardiograms exposed in the frontal and lateral projections following LV injection of contrast material were obtained in six of the eight patients. In the other two patients selective LV cineangiograms were obtained in the right anterior oblique projection.

The observations made in these eight patients were contrasted with the clinical, hemodynamic, and angiographic findings in a reference group of 19 previously studied patients in whom the presence of IHSS was documented by the finding of an elevated pressure both in the apical and inflow regions of the left ventricle (fig. 1B).

Results

Clinical Observations

Four of the eight patients were considered on the basis of clinical, radiographic, and hemodynamic findings to have idiopathic LV myocardial hypertrophy. In two patients, one of whom (E. Mea.) had primary pulmonary hypertension, an elevated LV systolic pressure occurred in the absence of evidence of LV disease. One patient (E. Mer.) had a nonobstructive pressure difference in addition to mild valvular aortic stenosis (peak systolic trans-valvular aortic pressure difference of 10 mm Hg). The remaining patient (P.F.) had undergone ventricular septal myotomy for IHSS with obstruction 10 months previously.

Cardiorespiratory symptoms were reported by six of the eight patients with nonobstructive pressure differences, while in the comparison group of 19 patients with IHSS and LV outflow obstruction, 16 had experienced symptoms. The duration of symptoms ranged from 1 to 15 years (average, 7 years) in the latter group. A cardiac murmur had been detected previously in only three of the eight patients with nonobstructive pressure differences, while previous knowledge of a cardiac murmur was reported by 16 of the 18 patients with IHSS in whom this information could be obtained. Five patients with nonobstructive pressure differences had noted symptoms of congestive heart failure, including dyspnea and edema; one patient had a history of syncope, another, of near-syncopal episodes, and three had histories of angina pectoris. Fifteen patients with obstruction (79%) had experienced symptoms of congestive heart failure; 10 (55%) had angina pectoris, three (16%) had syncope, and six (32%) had near syncope. Thus, symptoms in the two groups of patients were similar. Patient P.F. had been asymptomatic since operative relief of obstruction.

Six of the eight patients with nonobstructive pressure differences exhibited a soft ejection murmur at the cardiac apex or left sternal border at rest; in two of these patients, the location of the murmur suggested an origin in the right ventricular outflow tract. In the remaining two patients, a murmur was elicited by exercise. The murmur was of low intensity, being grade III/VI in only one patient, in whom coincident mild valvular aortic stenosis was documented at cardiac catheterization. A thrill localized to the second left intercostal space was noted in one patient with a nonobstructive pressure difference in whom mild right ventricular outflow obstruction was documented at catheterization. In contrast, a loud apical ejection murmur of grade III/VI intensity or greater was present in all but one of the 19 patients with obstruction and was accompanied by a thrill in nine patients. Paradoxical splitting of the second heart sound with respiration was not observed in any of the patients with nonobstructive pressure differences, but was present in four of the 19 patients with obstruction. An atrial gallop sound was heard in six of the eight
patients with nonobstructive pressure differences and in 15 of the 17 patients with obstruction who were in sinus rhythm. While the systemic arterial pulse exhibited a sharp upstroke in both groups, the bifid systolic contour typical of IHSS was not observed in patients with nonobstructive pressure differences.

LV hypertrophy was demonstrated electrocardiographically in only two patients with nonobstructive pressure differences. Two patients, including P.F., exhibited left bundle-branch block; none had abnormal Q waves. The electrocardiogram revealed LV hypertrophy in 15 of 19 patients with obstruction; in addition, nine patients had abnormal Q waves consistent with ventricular septal hypertrophy.16

**Hemodynamic Findings**

The hemodynamic findings are shown in table 1. All eight patients with nonobstructive pressure differences were in sinus rhythm, with heart rates ranging from 60 to 102/min. The cardiac index was elevated at rest (> 3.5 L/min/m²) in five patients, each of whom exhibited normal LV end-diastolic pressure; in two patients a reduced cardiac index occurred with moderate elevation of the LV end-diastolic pressure. None exhibited elevated systemic arterial pressure.

Four patients exhibited an intraventricular pressure difference at rest ranging from 15 to 87 mm Hg, while in four patients an intraventricular pressure difference was noted only during provocative maneuvers (fig. 2). During the Valsalva maneuver, the pressure difference was augmented in each patient, reaching levels comparable to those observed during the Valsalva maneuver in patients with IHSS and obstruction.

In patients with nonobstructive pressure differences, the arterial pulse contour was consistently normal (fig. 3A) in contrast to the rapid upstroke and prominent tidal wave characteristic of IHSS17 (fig. 3B) observed in 17 of the 19 patients with obstruction. In the other two patients with IHSS who had small resting pressure differences, this abnormality of the arterial pulse contour was noted only in beats immediately following ventricular extrasystoles, when the obstruction was augmented.

The arterial pulse pressure response in the beat following a ventricular extrasystole is shown in a typical patient with a nonobstructive pressure difference and in one with IHSS in figure 3. Figure 4 summarizes the data on all patients, as well as on 20 additional patients without disease of the LV myocardium. The pulse pressure was unchanged or decreased in 18 of 19 patients with obstruction, the change ranging from 0 to −12 mm Hg; in one patient with IHSS, the pulse pressure increased by 5 mm Hg. In contrast, the arterial pulse pressure consistently increased in the beat following a ventricular extrasystole in patients without obstruction, the increase ranging from 5 to 15 mm Hg (fig. 4). In patient P.F.,

### Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>Heart rate (BPM)</th>
<th>Cardiac index (L/min/m²)</th>
<th>RV infund. pressure difference (mm Hg)</th>
<th>LVEDP (mm Hg)</th>
<th>Arterial pressure S/D (mm Hg)</th>
<th>Intraventricular pressure difference (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>O.L.</td>
<td>85</td>
<td>4.07</td>
<td>10</td>
<td>8</td>
<td>112/70</td>
<td>20</td>
</tr>
<tr>
<td>E. Mer.</td>
<td>88</td>
<td>4.20</td>
<td>13</td>
<td>9</td>
<td>138/72</td>
<td>0</td>
</tr>
<tr>
<td>W.C.</td>
<td>78</td>
<td>4.41</td>
<td>2</td>
<td>10</td>
<td>122/67</td>
<td>0</td>
</tr>
<tr>
<td>E. Mea.</td>
<td>85</td>
<td>3.61</td>
<td>0</td>
<td>12</td>
<td>130/64</td>
<td>15</td>
</tr>
<tr>
<td>B.J.</td>
<td>102</td>
<td>2.10</td>
<td>15</td>
<td>23</td>
<td>100/66</td>
<td>87</td>
</tr>
<tr>
<td>V.B.</td>
<td>70</td>
<td>2.25</td>
<td>–</td>
<td>19</td>
<td>95/51</td>
<td>0</td>
</tr>
<tr>
<td>C.J.</td>
<td>60</td>
<td>3.80</td>
<td>8</td>
<td>8</td>
<td>136/72</td>
<td>0</td>
</tr>
<tr>
<td>P.F.</td>
<td>70</td>
<td>3.30</td>
<td>–</td>
<td>8</td>
<td>121/69</td>
<td>73</td>
</tr>
</tbody>
</table>

Abbreviations: RV = right ventricular; infund. = infundibular; LVEDP = left ventricular end-diastolic pressure; S/D = systolic/diastolic; N.D. = not done.
Nonobstructive Intraventricular Pressure

The intraventricular pressure difference, in mm Hg, in each patient with a nonobstructive pressure difference as measured by catheter withdrawal across the mitral valve during the Valsalva maneuver (left panel) and isoproterenol infusion (right panel). The pressure difference in the control state is shown on the left hand side of each panel.

The arterial pulse pressure declined by 12 mm Hg before relief of obstruction, and increased by 5 mm Hg following operation, when a nonobstructive pressure difference was present. The arterial pulse pressure responses in patients with nonobstructive pressure differences were generally comparable to those observed in patients without LV disease, in whom the pulse pressure increases ranged from 9 to 24 mm Hg.

A small pressure difference across the RV outflow tract was demonstrated in five of six patients without LV obstruction in whom this measurement was available and in 11 of 15 patients with LV outflow obstruction. The peak systolic RV inflow-outflow pressure differences in the two groups ranged from 2 to 15 mm Hg and 3 to 15 mm Hg, respectively.

Angiographic Findings (Figs. 5 and 6)

Selective angiograms were obtained in all eight patients. The LV chamber at end-diastole appeared small and the apical portion of the cavity was obliterated during systole in each patient (Fig. 6). Indentation of the supero-anterior aspect of the LV outflow tract and of the inferomedial surface of the LV cavity, indicating hypertrophy of the intraventricular septum, was demonstrated in four of the eight patients; in two of these four patients, asymmetric hypertrophy involved the apical portion of the ventricle as well and essentially obliterated the apex of the ventricle in diastole (Fig. 5A and C). In two patients with angiographic evidence of concentric hypertrophy, in whom LV trabeculation and myocardial wall thickness appeared increased,

Simultaneous recordings of left ventricular (LV) and brachial arterial (BA) pressure pulses are shown in a patient with a nonobstructive pressure difference (panel A) and in a patient with IHSS and obstruction (panel B). In the patient with a nonobstructive pressure difference, the arterial pulse contour is normal, and the arterial pulse pressure is increased in the beat following the ventricular extrasystole. In the patient with IHSS and obstruction, the arterial pulse exhibits a bifid systolic contour, and the arterial pulse pressure declines in the beat following the ventricular extrasystole.

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and in two patients in whom the LV cavity and myocardial wall thickness appeared normal, obliteration of the apex resulted from an extreme degree of systolic emptying (fig. 6). Angiograms in patients with obstructive pressure differences revealed, in addition to asymmetric ventricular hypertrophy, a radiolucent area in the region of the outflow tract, previously described in patients with IHSS and obstruction. This abnormality in the systolic position of the mitral leaflets, which appears to result from apposition of the leading edge of the valve leaflets and the ventricular septum, was not demonstrated in any of our patients with nonobstructive pressure differences. Mitral regurgitation, a relatively common finding in patients with obstruction (nine of 19 patients), was observed in only one of eight patients with nonobstructive pressure differences.

**Discussion**

That catheter entrapment within portions of the LV cavity which are obliterated during systole may result in the recording of an intraventricular pressure difference has been shown in animals and in man initially by Criley and his associates and subsequently by other investigators. The present study indicates that cavity obliteration in man may result from extreme degrees of ventricular emptying in the absence of other evidence of LV disease or may occur in patients with myocardial hypertrophy in whom the aberration in LV function includes rapid and extreme degrees of systolic emptying. It is of particular interest that in four of eight patients in this study in whom a nonobstructive pressure difference was observed, systolic obliteration of the apical portion of the ventricle occurred in the presence of asymmetric hypertrophy, which resulted in a deformity of the LV cavity in two patients, which was not unlike that observed in patients with IHSS. Hypertrophy of the interventricular septum was further suggested in these patients by small pressure differences localized at the right ventricular infundibulum, also commonly observed in patients with IHSS. A nonobstructive pressure difference was documented in one patient whose son exhibited findings consistent with IHSS and obstruction, and in another who 10 months previously had undergone an operation for IHSS with documented obstruction to LV outflow.

Evidence has been presented recently from studies in this laboratory that obstruction to LV outflow may result in patients with IHSS because of distortion of the normal alignment of the papillary muscles by inferior septal hypertrophy, resulting in traction on the mitral leaflets, holding them in the outflow tract against the hypertrophied septum during systole. In the present study, angiographic evidence of papillary muscle malalignment

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*Figure 4*

The average change in arterial pulse pressure in the beat following ventricular extrasystoles, in mm Hg, is shown in patients with nonobstructive pressure differences (triangles) and those with IHSS and obstruction (circles), and these findings are contrasted with observations in 20 patients with no left ventricular disease (squares). Values above the dashed horizontal line indicate an increase and values below, a decrease in pulse pressure following the ventricular extrasystole. Average values for each group are indicated by the solid bars.
Figure 5

Selective left ventricular angiocardiogram obtained in a patient (B.J.) with a nonobstructive pressure difference at rest, showing films exposed in the anteroposterior (panels A and B) and lateral (panels C and D) projections in diastole (left panels) and systole (right panels). The left ventricular cavity is markedly deformed and consists almost entirely of a dilated inflow tract with only a small tongue-like projection representing the apical portion of the chamber in diastole (solid arrows, panels A and C). Hypertrophy of the interventricular septum is suggested by the indentation of the outflow tract seen in the lateral projection (dashed arrow, panel C). During systole, the apical portion of the ventricle is virtually obliterated (arrow, panel D), but the inflow tract is widely patent.

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Selective left ventricular angiocardiogram obtained in a patient (W.C.) with a nonobstructive pressure difference at rest, showing films exposed in the frontal projection (left panels) and lateral projection (right panels) at end-diastole (upper panels) and at end-systole (lower panels). Note that the apical portions of the left ventricular chamber are obliterated during systole. The left ventricular trabeculations are increased, and myocardial wall thickness appeared diffusely increased, consistent with concentric hypertrophy.
and malposition of the mitral leaflets was found in each patient with obstruction, while in the four patients with asymmetric hypertrophy and nonobstructive pressure differences, these abnormalities were not observed. In one of these patients, the asymmetric hypertrophy was less severe than in patients with obstruction, while in two, extreme hypertrophy was present in the apical portion as well as septal region of the left ventricle, and papillary muscle alignment was not distorted. Thus, it appears likely that the severity and localization of hypertrophy dictate the presence of papillary muscle and mitral leaflet displacement, apical obliteration, or both, and consequently the occurrence of obstructive or nonobstructive pressure differences in patients with asymmetric ventricular hypertrophy.

Extreme ventricular emptying also is a feature common to patients with obstructive and those with nonobstructive pressure differences. In patients with IHSS, it often appears that the delivery of a normal stroke volume from the small LV chamber can be accomplished only by complete emptying of the ventricular apex. In the majority of patients with nonobstructive pressure differences in this study, however, this unusual pattern of LV contraction was associated with evidence of a hyperdynamic circulation, particularly an increased cardiac index. Indeed, the clinical features in these patients are similar to those described in patients with the hyperkinetic heart syndrome suggesting that in some patients this syndrome may be a manifestation of an idiopathic hypertrophic state.

Intraventricular pressure differences could be induced or augmented, as in patients with IHSS, by reduction in venous return with increased ventricular systolic emptying during the Valsalva maneuver, or by enhanced sympathetic effect during administration of isoproterenol. The possibility exists that increased sympathetic nervous tone may play a role in the production of intraventricular pressure differences at rest, particularly in patients in whom the LV cavity is not deformed by asymmetric hypertrophy (fig. 6).

It is of interest that all but two patients with nonobstructive pressure differences had significant cardiorespiratory symptoms and that in the two patients with more severe degrees of asymmetric hypertrophy, angina and syncope, or near syncope, occurred. While each patient had a cardiac murmur at rest or with exercise, the murmur generally was soft, having the characteristics of a functional murmur. The murmur did not appear to be related to the intraventricular pressure difference, since murmurs were present in patients in whom no resting pressure difference was found. In no instance did a patient with a nonobstructive pressure difference have an apical murmur accompanied by a thrill, paradoxical splitting of the second heart sound, or a sharp, bifid arterial pulse on direct tracings or indirect carotid recordings, findings characteristic of IHSS with obstruction.

The contour of the LV pressure pulse and the response of the intraventricular pressure difference to the Valsalva maneuver and to isoproterenol were similar in patients with obstructive and nonobstructive pressure differences. However, the two groups could be readily distinguished on the basis of the directly recorded arterial pulse contour and by the arterial pulse pressure response in the beat following a ventricular extrasystole. In particular, the arterial pulse pressure response consistently was normal in patients with nonobstructive pressure differences, while with one exception, in patients with obstruction the arterial pulse pressure declined or was unchanged in the beat following an extrasystole.

The findings of the present study support the contention that obstruction to LV outflow in patients with asymmetric ventricular hypertrophy results in a distinctive complex of clinical and hemodynamic features that can be clearly distinguished from those in patients with nonobstructive pressure differences. That marked symptomatic benefit may result from operations designed to relieve obstruction in patients with IHSS has been well demonstrat-
The observation that severe asymmetric hypertrophy without obstruction may be associated with angina pectoris, syncope, and congestive heart failure, symptoms resembling those which occur in patients with IHSS, emphasizes the importance of determining precisely the nature of the lesion prior to consideration of operative treatment.

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