Ventriculographic Patterns and Hemodynamics in Primary Myocardial Disease

By Thomas H. Kreulen, M.D., Richard Gorlin, M.D., and Michael V. Herman, M.D.

SUMMARY
Thirty-four patients with primary myocardial disease were studied and classified into three distinct types based on their left ventriculogram. Each had unique ventriculographic characteristics and findings. Type I patients with a normal contraction pattern and an elevated left ventricular end-diastolic pressure. Type II A are patients with a hypertrophic pattern without obstruction to outflow while Type II B patients have outflow obstruction. Type III A are patients with generalized hypokinesis. Type III B have a similar contraction pattern but in addition show asynergy. Analysis of the right ventriculogram in seven patients showed changes paralleling those seen in the left ventricle, including asynergic patterns of contraction. The electrocardiogram and chest roentgenogram were found to be sensitive but nonspecific indicators of disease. The short-term prognosis was excellent with type I and poor with type III while type II patients had an intermediate prognosis.

Additional Indexing Words:
Hypertrophy Left ventricular mass Right ventricle Asynergy
Congestive heart failure

The existence of primary myocardial disease has been recognized for more than 100 years. Nevertheless, the underlying pathophysiology of these disorders remains obscure. This has led to difficulty in classifying the cardiomyopathies and earlier studies have done so on the basis of what was known concerning their etiology. More recently, classifications have been proposed which are based on clinical, hemodynamic, and ventriculographic criteria. In 1961 Goodwin described three groups of patients with primary myocardial disease and termed them congestive, obstructive, and restrictive. In 1963 Braunwald added as a subgroup ventricular hypertrophy without obstruction. In 1970 Goodwin modified his previous classification emphasizing two major types, congestive and hypertrophic, and mentioning two rare types, constrictive and obliterative.

It is the purpose of this study to review the hemodynamic and ventriculographic data in a group of patients with primary myocardial disease and to present a classification of these disorders based on ventriculographic patterns of contraction.

Methods
Thirty-four patients with primary myocardial disease were studied. The etiology was idiopathic in 26 patients, alcohol was a possible cause in seven patients, and sarcoidosis was present in one patient. There were 24 males and 10 females with ages from 20 to 69 and a mean age of 43 years. Seven patients found to be normal at diagnostic catheterization served as controls.

The criteria for the diagnosis of primary myocardial disease are listed in Table I. All patients demonstrated abnormal ventricular function manifested either by a hemodynamic or ventriculographic abnormality.

Abnormal hemodynamics were considered to be present if the resting left ventricular end-diastolic pressure was 13 mm Hg or greater, or if the left ventricular end-diastolic pressure during exercise exceeded 18 mm Hg. The ventriculogram was considered abnormal if there was an increased end-diastolic volume, increased left ventricular mass, or abnormal systolic motion pattern when compared to the control group.

Standard hemodynamic parameters were measured in all patients. The existence of left ventricular outflow obstruction was excluded by isoproterenol infusion and the response to a premature contraction. Selective coronary cinearteriography was performed by either the Sones or Judkins technic. Left ventriculography, biplane (30° right anterior oblique, 60° left anterior oblique) in eight patients and single plane in 26 patients, was accomplished using a Siemens 10–5-in. or a General Electric 9–6-in. dual-field image-intensifier system. A power injection into the left ventricle

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Table 1
Criteria for Diagnosis of Primary Myocardial Disease

<table>
<thead>
<tr>
<th>I.</th>
<th>Abnormal ventricular function</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Hemodynamics</td>
</tr>
<tr>
<td>a.</td>
<td>LVEDP at rest &gt; 13, or</td>
</tr>
<tr>
<td>b.</td>
<td>LVEDP at rest &lt; 13, but exercise</td>
</tr>
<tr>
<td>2.</td>
<td>Ventriculogram</td>
</tr>
<tr>
<td>a.</td>
<td>Increased end-diastolic volume</td>
</tr>
<tr>
<td>b.</td>
<td>Increased LV mass</td>
</tr>
<tr>
<td>c.</td>
<td>Abnormal motion pattern</td>
</tr>
<tr>
<td>II.</td>
<td>Normal selective coronary cinearteriogram</td>
</tr>
<tr>
<td>III.</td>
<td>No primary valvular disease</td>
</tr>
<tr>
<td>IV.</td>
<td>No congenital heart disease</td>
</tr>
<tr>
<td>V.</td>
<td>No hypertension</td>
</tr>
</tbody>
</table>

Using 35–50 ml of contrast agent was made through a multiholed catheter passed retrograde through the aortic valve. Cine films were recorded at 60–100 frames/sec using 16-mm film. Calibration of the ventricular image size was made with a 1-cm grid filmed at the level of the left ventricle with the same tube image-intensifier distance as used during ventriculography. The ventricular image was directly traced and analyzed. A frame-by-frame motion analysis was done. No extrasystolic beats or those immediately following an extrasystolic beat were used. End-diastolic and end-systolic frames were analyzed in detail as illustrated in figure 1. Chamber areas were planed and the lengths directly measured. Wall thickness was measured from the lower third of the anterior wall in the right anterior oblique projection in end-diastole. Subsequent calculations were carried out as illustrated in figure 2. Chamber volume was calculated according to a modification of the method of Dodge et al. In the single-plane studies, Drao was substituted for D130 in the formula. Left ventricular mass was calculated according to the method of Rackley et al. Eccentricity was calculated from a standard geometric formula. In this method eccentricity can vary between 0 and 1 with the smaller numbers representing a more round geometric shape. Biplane right ventriculograms were performed in seven patients utilizing the same technic as in the left ventriculograms. Cine films were recorded in the same projections as for the left ventricle. A frame-by-frame motion analysis was done using the midpoint of the pulmonic valve and the apex as the long axis of the right ventricle. The electrocardiograms and chest roentgenograms of all patients were reviewed. Left ventricular hypertrophy was diagnosed according to the criteria of Sokolow and Lyon. Right ventricular hypertrophy was diagnosed according to the criteria of Milnor. Clinical follow-up through both the patient and his physician was carried out when possible. Clinical status, progression of disease, and survival were determined.

Results

Ventriculographic Patterns

The morphology of the left ventriculogram was distinct enough to allow identification of five separate patterns of contraction (table 2, fig. 3). Type I, a completely normal contraction pattern associated with an elevated left ventricular end-diastolic pressure was observed in seven patients. Type II A, found in 11 patients, is a hypertrophic pattern characterized by a normal size and shape of the ventricular cavity, increased wall thickness, increased papillary muscle size, heavy trabeculation, and a uniform contraction with occasional apical obliteration. Type II B are patients who have hypertrophy with outflow obstruction. They were not analyzed in this study and have been reported in previous communications. The ventricles of these patients are similar to type II A except for a slightly smaller sized cavity, an unusual shape which is typically tongue or banana-like in appearance, and an increased shortening of the transverse.
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Table 2

Classification of Primary Myocardial Disease

<table>
<thead>
<tr>
<th>Type</th>
<th>Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Normal contraction pattern and abnormal hemodynamics</td>
</tr>
<tr>
<td>II</td>
<td>Hypertrophy without outflow obstruction</td>
</tr>
<tr>
<td></td>
<td>Hypertrophy with outflow obstruction</td>
</tr>
<tr>
<td>III</td>
<td>Generalized hypokinesis</td>
</tr>
<tr>
<td></td>
<td>Asynergy</td>
</tr>
</tbody>
</table>

diameter in relation to the long axis during systole. Type III A includes six patients with a pattern of generalized hypokinesis having a dilated, rounded chamber which shows uniformly poor motion of all points along the ventricular inner surface. Type III B consists of 10 patients who demonstrated the same ventriculographic characteristics as type III A but, in addition, had asynergy, i.e. localized abnormalities of contraction. These abnormal zones of contraction were similar to those seen in patients with coronary artery disease which have shown a reduction of both end-diastolic and end-systolic volumes associated with an increased ejection fraction. Type III A and type III B were identical in their mechanical-hemodynamic findings and characterized by an increased end-diastolic volume, decreased ejection fraction, increased left ventricular mass, and decreased eccentricity (more round geometric shape). The left ventricular end-diastolic pressure was elevated to a variable degree in all types (on exercise, if not at rest) and was not useful in separating one group from another.

Hemodynamic and Mechanical Correlations

In the entire group of patients there was a tendency for the ventricle to assume a more round geometric shape, i.e. decreased eccentricity, as the end-diastolic volume increased (fig. 5). Furthermore, the ventricles with a rounder geometric shape

Mechanical and Hemodynamic Findings

In addition to a distinctive visual appearance of the left ventriculogram, each group could be characterized by quantitative mechanical and hemodynamic findings (table 3; figs. 3 and 4).

Type I had an elevated left ventricular end-diastolic pressure only. Type II A had an increased left ventricular mass but a normal ejection fraction and eccentricity. The end-diastolic volume, although slightly reduced, was not significantly different from normal. Type II B has been analyzed in previous studies which have shown a reduction of both end-diastolic and end-systolic volumes associated with an increased ejection fraction. Type III A and type III B were identical in their mechanical-hemodynamic findings and characterized by an increased end-diastolic volume, decreased ejection fraction, increased left ventricular mass, and decreased eccentricity (more round geometric shape). The left ventricular end-diastolic pressure was elevated to a variable degree in all types (on exercise, if not at rest) and was not useful in separating one group from another.
Table 3

Ventriculographic Findings in Primary Myocardial Disease

<table>
<thead>
<tr>
<th>Pt (type and no.)</th>
<th>EDV index (ml/m²)</th>
<th>Ejection fraction</th>
<th>LV mass index (g/m²)</th>
<th>Eccentricity (diastole)</th>
<th>LVEDP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal N = 7</td>
<td>100.7 ± 6.8</td>
<td>91.5 ± 0.80</td>
<td>5.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>I N = 7</td>
<td>106.4 ± 6.6</td>
<td>98.5 ± 0.76</td>
<td>16.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>II A N = 11</td>
<td>13.4 ± 0.05</td>
<td>7.3 ± 0.01</td>
<td>0.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>III A and B N = 16</td>
<td>218.4 ± 0.25</td>
<td>32.0 ± 0.03</td>
<td>1.7</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

and hence a larger end-diastolic volume) had a lower ejection fraction (fig. 6). There was no relation between end-diastolic volume and end-diastolic pressure (fig. 7). Figure 8 illustrates the relationship between the angiographically determined stroke volume and end-diastolic volume. The isobars represent the mean normal ejection fraction and 2 sp about the mean. Types III A and B exhibit an abnormally low ejection fraction while the remaining groups did not differ from control.

Right Ventriculograms

A biplane right ventriculogram was performed in seven patients. Three patients were type II A, one was type III A, and three were type III B. All of the right ventriculograms paralleled the respective left ventriculograms in the pattern of contraction.

In addition, there were two patients with type III B who had had clinical evidence of right-sided heart failure and in one of these there was no pulmonary hypertension at the time of study. The

VENTRICULOGRAPHIC FINDINGS IN PRIMARY MYOCARDIAL DISEASE

Ventriculographic findings in primary myocardial disease.
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ventriculograms and hemodynamic data of this patient are illustrated in figure 9. This patient exhibited severe biventricular dysfunction and asynergy.

Electrocardiographic Findings

Six of the 34 patients had a normal electrocardiogram. Four of these were type I and two were type II A. The most common finding was ST-T wave abnormalities which were nonspecific and occasionally simulated ischemic changes. Coronary artery disease may even be mimicked as evidenced by an unequivocal pattern of anterior wall myocardial infarction in two patients with type II A and an inferior wall infarction in one patient with type III A.

Chest Roentgenograms

All patients with type I had a normal chest film. Three of 11 patients with type II A also had a normal chest film. The remaining eight patients demonstrated cardiomegaly involving primarily the left ventricle. Only one of 16 patients with type III had a normal chest film. The remaining 15 patients had cardiomegaly usually of the generalized type which was occasionally confused with a pericardial effusion. The mean cardiothoracic ratio was 0.56 for type II A and 0.60 for types III A and B.

Clinical Follow-up

Clinical follow-up was obtained in 31 patients (table 5). Three patients were lost to follow-up. The single death in the patient with type I was attributed to noncardiac causes. The short-term prognosis for life and lack of disability with type I is favorable and somewhat less favorable with type II A whereas 75% of patients with type III A and B were either dead or had developed progressive heart failure (class III or IV) at the end of 3 years.

Discussion

This study shows that the cardiomyopathies can be classified on the basis of the left ventriculogram. Such a classification is valuable for several reasons. First, it provides a clear separation of patients into groups with specific hemodynamic-mechanical characteristics. Second, there is an association between the ventriculographic classification and the clinical course. Patients with types I and II have a favorable outlook over a 3-year period whereas 75% of patients with type III either died or developed progression of their disease over a similar period. Authors not using a classification similar to ours have emphasized that the clinical course is a highly
variable one punctuated by sudden death. It has been shown that the presence of clinical congestive heart failure and elevation of the mean ventricular diastolic pressure both adversely affect prognosis. Another study suggested that heart size, blood pressure, and alcoholic intake have no influence on prognosis. However, Goodwin's studies, as well as our data, show that a ventriculographic classification separates patients into distinct prognostic categories which can aid in future analysis of natural history as well as therapeutic intervention. Third, appropriate classification of patients provides a rational basis for therapy. As yet, the ultimate course of patients with type I is not known and simple observation seems advisable. Patients with type II B have been improved with beta-adrenergic blockade both because of its antianginal effect and possibly due to increased ventricular compliance. It is not yet known whether such treatment may be effective in type II A. Prolonged bed rest and intensive medical therapy have been advocated for patients with type III. Fourth, it is hoped that this classification will aid in the identification of specific etiologic factors in patients with primary myocardial disease.
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Table 4
Electrocardiographic Findings in Primary Myocardial Disease

<table>
<thead>
<tr>
<th>Findings</th>
<th>Type I (no.)</th>
<th>Type II A (no.)</th>
<th>Type III A and B (no.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal ECG</td>
<td>4</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>ST-T abnormality</td>
<td>2</td>
<td>9</td>
<td>16</td>
</tr>
<tr>
<td>Atrial flutter, fibrillation</td>
<td>0</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>LVH</td>
<td>0</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>RVH</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Infarction pattern</td>
<td>0</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>LBBB</td>
<td>0</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>RBBB</td>
<td>1</td>
<td>1</td>
<td>3</td>
</tr>
</tbody>
</table>

The classification of patients with an elevated left ventricular end-diastolic pressure into a cardiomyopathic group may be questioned. However, previous studies have shown that the left ventricular end-diastolic pressure in normal patients does not exceed 12 mm Hg.27 Further evidence of abnormal ventricular function was obtained in one patient by atrial pacing. This is illustrated in figure 10 which shows pulsus alternans with atrial pacing at a rate of 120 but a normal pulse pressure with the pacemaker turned off. The underlying abnormality in this group of patients seems to be a change in ventricular volume-pressure relations, i.e. a decrease in ventricular compliance with preservation of a normal contraction pattern. Their ultimate classification remains uncertain, however. It is possible that they represent the earliest forms of types II and III or the end stage of a mild viral myocarditis.

Types III A and III B were identical in their hemodynamic-mechanical findings but differed in the nonuniform nature of the disease process as seen on the ventriculograms in the asynergy group. Asynergy has also been found in 50% of patients with Bantu cardiomyopathy.28 This asynergy is identical to that seen in patients with coronary artery disease10 but is always associated with significant overall impairment of ventricular contraction as judged by the ejection fraction. The finding of asynergy in patients with coronary artery disease is readily explained by the patchy distribution of the vascular lesions but the cardiomyopathic process tends to be a diffuse one.29 This paradox is not readily explained but could be related to one of several factors including the occurrence of coronary artery emboli originating from a mural thrombus. Electrocardiographic evidence of infarction might be anticipated in patients in type III B, but no such cases were found. It is also possible that the asynergy seen may not be so much related to a myocardial lesion as to an endocardial lesion. It is known that patients with endomyocardial fibrosis have patchy lesions which are possibly related to organization of endocardial thrombi.30, 31 Such a lesion could restrict motion of the ventricular wall and lead to localized areas of hypokinesis. Left bundle-branch block, present in three patients with asynergy, has been shown not to be a factor in the development of asynergy.32

The present classification of primary myocardial disease is a modification of Goodwin's classification.7 The identification of patients with abnormal hemodynamics and a normal contraction pattern represents a group of patients who are dissimilar to what has been called the constrictive (restrictive) pattern. The patients with abnormal hemodynamics did not have either clinical or laboratory signs resembling pericardial disease. All patients who did present with constrictive signs had ventriculographic abnormalities which fit into our classification as either type III A or B. The differential diagnosis of primary myocardial disease from pericardial disease may also present difficulty but can frequently be resolved by ventriculographic analysis. Patients with type II A had a tendency toward smaller end-diastolic volumes but this was not statistically significant. It has been shown that patients with type II B have both a reduction in end-diastolic volume and an increased ejection fraction.17, 19 Patients with type III are equivalent to the congestive group of Goodwin. In addition, we have divided them into subtypes A and B depending on the presence of asynergy. Goodwin has also described an obliterator group which refers specifically to patients with endomyocardial fibrosis.7 Their angiocardiograms have been described as showing a small, deformed ventricular chamber with a poor contraction33 but ventricular volumes were not calculated. We have not included these patients in our classification because it is not a disease seen in the United States or have direct

Table 5
Clinical Follow-up in Primary Myocardial Disease

<table>
<thead>
<tr>
<th>Findings</th>
<th>Type I (no.)</th>
<th>Type II (no.)</th>
<th>Type III (no.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean follow-up</td>
<td>33</td>
<td>40</td>
<td>37</td>
</tr>
<tr>
<td>Clinically well</td>
<td>5</td>
<td>7</td>
<td>3</td>
</tr>
<tr>
<td>Progressive CHF</td>
<td>0</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Deceased</td>
<td>1</td>
<td>2</td>
<td>6</td>
</tr>
<tr>
<td>Lost to follow-up</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

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Figure 10

Pulsus alternans with atrial pacing in a patient with type I.

ventriculographic measurements been reported. However, they would probably best fit into an additional group (type IV?) which has both a reduction in end-diastolic volume and ejection fraction.

It is not known whether the separation of patients into these types will be maintained with time. The long-range course of the group with a normal contraction pattern is certainly not yet known. The fate of the other groups is better understood. Goodwin has shown that cavity size remains a constant feature of types II and III. The ventricular mass in the generalized hypokinesis and asynergy groups is similar to that found in the hypertrophic group. However, it seems likely that in the hypertrophic group myocardial hypertrophy is a primary process whereas in the generalized hypokinesis and asynergy groups myocardial hypertrophy is a response secondary to ventricular dilation and increased wall stress. Thus, it appears that once a patient can be classified as either type II or III he will maintain the ventriculographic characteristics of that type, whereas the eventual classification of type I patients is still uncertain.

The tendency for the larger ventricles to assume a rounder shape is a phenomenon which is probably not unique to the cardiomyopathies. Decreasing eccentricity (a rounder shape) with increasing end-diastolic volume is probably related to increased wall tension with increased volume as well as alteration of the myocardial architecture by the disease process. Ventricles with the lowest eccentricity had the lowest ejection fractions reflecting their poor ventricular performance. The lack of correlation between end-diastolic volume and left ventricular end-diastolic pressure is common to many forms of heart disease suggesting that compliance abnormalities vary considerably and is a phenomenon which is independent of pump function.

The right ventriculographic abnormalities found in this study suggest that the disease process follows a similar pattern in both ventricles. Of considerable interest is the presence of right-sided heart failure in the patient with normal pulmonary artery pressures and severe right ventricular dysfunction, including severe asynergy of contraction. This suggests that right ventricular dysfunction alone can lead to right heart failure. Selective failure of the right ventricle has been reported in cardiomyopathy previously and is well known to occur in patients with endomyocardial fibrosis. Experimental destruction of the right ventricle in dogs has been shown not to produce any changes in right atrial or pulmonary artery pressures. More recent studies have shown no change in resting hemodynamic performance of the right ventricle in dogs following right coronary artery ligation but evidence of right ventricular failure develops when pulmonary artery impedance increases. This apparent discrepancy between the experimental and clinical data is not fully understood but may relate to factors such as increased patient activity (increased right ventricular work) or an increased intravascular volume.

Although the electrocardiographic changes in primary myocardial disease are not specific, a normal electrocardiogram in the presence of primary myocardial disease is uncommon. Most of the normal electrocardiograms were seen in the group with a normal contraction pattern. The electrocardiogram was an insensitive indicator of left ventricular hypertrophy. Previous studies have shown that the majority of all patients with cardiomyopathy and over 80% of the hypertrophic group have electrocardiographic changes of left ventricular hypertrophy. An infarction pattern was seen in three patients. Although this finding has been noted in patients with type III previously, it has been particularly common in patients with type II B. We did not encounter such cases in type III B. The reasons for this are not clear but could be related to the presence of endocardial fibrosis rather than a myocardial lesion to account for the asynergy.

The chest roentgenogram, although normal in type I patients, was a sensitive indicator of abnormality in types II A and III. The findings
were nonspecific but useful in identifying the presence of cardiac disease. When the electrocardiogram and chest roentgenogram are considered together, all but one patient demonstrated an abnormality. Thus, the combination of an electrocardiogram and chest roentgenogram, although not specific, is highly sensitive to the presence of cardiac disease in types II A and III. This could partly be related to patient selection since the majority of the patients were referred. However, these abnormalities were infrequent in type I patients. Therefore, the diagnosis of primary myocardial disease cannot be excluded by a normal electrocardiogram and chest roentgenogram.

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