Clinical and Hemodynamic Studies of Myocardial Fibrosis

By Robert E. Nye, Jr., M.D., Frank W. Lovejoy, Jr., M.D., and Paul N. Yu, M.D.

In many instances myocardial fibrosis mimics constrictive pericarditis so closely, both hemodynamically and clinically, that the diagnosis can be made with certainty only at operation or autopsy. In the 3 cases presented here certain distinctions can be made that suggest that the differentiation can sometimes be made by careful analysis of pressure contours from the right heart.

Extensive replacement of myocardium by fibrous tissue produces a syndrome of intractable heart failure that clinically resembles chronic constrictive pericarditis in many ways. M-shaped complexes in the right atrial pressure pattern, and an early diastolic dip and high end-diastolic plateau in the right ventricular pattern, similar to those originally described in constrictive pericarditis,¹-⁴ have been found also at cardiac catheterization of patients with myocardial fibrosis.⁵-⁷ Since surgery is helpful only in the former disease, the possibility of differentiating these 2 conditions is attractive. This paper presents clinical and hemodynamic data in 2 patients with myocardial fibrosis, and in a third patient with myocardial fibrosis made as a probable diagnosis at exploration, in an attempt to determine whether any useful differential points can be found.

Methods

Venous cardiac catheterization was carried out in the usual way, 1 or 2 hours after a light breakfast, by introducing a no. 7 or no. 8 long, single-lumen, Courand catheter through an antecubital vein. Intracardiac pressure was measured with a pressure transducer* and recorded on a 4-channel direct-writing oscillograph.† Mean pressures were measured by planimetric integration of records for 2 (or sometimes 1) respiratory cycle. The arbitrary zero level for all pressures was 6.5 cm. behind the angle of Louis, with the patient supine. Oxygen consumption was measured continuously in an open circuit system, with room air as the inspired gas. Cardiac output was determined by the direct Fick principle. Blood oxygen and carbon dioxide contents were measured with the Van Slyke manometric apparatus.

Case Reports

Case 1. S. B., a 33-year-old male engineer had been in good health until December 1953, when he developed a fever associated with a harsh systolic apical murmur and 1 conjunctival petechia and was hospitalized. There was no leukocytosis, but β hemolytic streptococci were cultured from blood. Treatment with 2.4 million units of penicillin per day was begun. During the next 2 months his fever gradually subsided, but tachycardia persisted, and a gallop rhythm appeared. The heart began to enlarge and the murmur changed in character. There was an episode of thrombophlebitis of the right leg and another suggesting infarction of the spleen. Digitalis was administered. Acute rheumatic fever was suspected but there was no response to salicylate administration, and the serum concentration of alpha-1 and alpha-2 globulin was normal.

The patient was discharged in March 1954 and re-admitted in May 1954 complaining of cough, breathlessness, nausea, vomiting, and diarrhea. There were further cardiac enlargement, intensification of the apical systolic murmur, hepatomegaly, and marked elevation of venous pressure (250 mm. saline). There were no pulmonary rales or peripheral edema. Temperature, white blood count, and erythrocyte sedimentation rate were normal. Constrictive pericarditis was suspected, and he was transferred to Strong Memorial Hospital for investigation. On admission he appeared very ill and orthopneic.

* Statham Laboratories, Inc.
† Stanborn Poly-Viso Cardiote
Clubbing, cyanosis, and edema were absent. The cervical veins were markedly distended. The lungs were unremarkable. The heart was enlarged to the left and right, and a triple rhythm and harsh preordial systolic murmur were noted. The second pulmonic sound was accentuated and split. The blood pressure was 110/95. The liver edge was felt 10 cm. below the costal margin, and there were signs of ascites. The spleen was not palpable.

The electrocardiogram (fig. 1) revealed sinus rhythm, right axis deviation, vertical electric position, and inversion of T waves in leads 2, 3, aVR, and V1 to V6. Fluoroscopically there was generalized cardiac enlargement, with moderately active pulsation of both ventricles. A telerentgenogram of the chest is shown in figure 2.

Cardiac catheterization was performed on June 4 (table 1). The principal findings were oxygen unsaturation of arterial blood, postcapillary pulmonary hypertension, marked reduction of cardiac output, and right ventricular failure. The pressure contour of the right ventricle (fig. 3) consisted of an elevated systolic peak, an early diastolic dip descending below the baseline during inspiration, and a high end-diastolic plateau approaching, or in a few tracings equaling, one third of the systolic pressure. The right atrial pressure contour (fig. 3) contained small a and c waves. The c wave was followed by a prominent y descent, followed by a rapid rise to an end-diastolic plateau, matching the ventricular contour. During inspiration the base of the y descent increased in depth, but there was little or no respiratory variation in mean pressure.

Exploratory thoracotomy was performed on June 8, 1954. The pericardial sac contained about 200 ml. of straw-colored fluid, but no pericardial constriction was found. The day following operation the patient suddenly became semiconscious and died 4 hours later.

Autopsy revealed healed mitral valvulitis, complicated by rupture of 1 or 2 chordae tendineae. The myocardium was largely replaced by dense scar tissue in the lower portion of the septum and over the apex, (fig. 4) and to a lesser extent elsewhere. Both ventricles were hypertrophied and dilated. The coronary arteries were widely patent. Acute pulmonary infarcts and an old splenic infarct were noted. The viscera were the seat of chronic passive congestion.

Case 2. E. K., a 48-year-old male printing-press operator, was hospitalized in December 1953 complaining of dyspnea, orthopnea, nonproductive cough, abdominal distention, ankle swelling, fatigue, night sweats, weakness, and weight loss, which had begun 18 months previously. He had been treated with digitalis and mercurial diuretics, but he had become refractory to treatment.

The principal findings on examination and investigation were as follows. There was no fever. The neck veins were distended. There were rales over the lower third of both lung fields and a right pleural effusion. The heart was enlarged and the rhythm was irregular due to frequent premature contractions. The second pulmonic sound was mildly accentuated. A grade II systolic blowing murmur was

[Fig. 1. Electrocardiograms of 3 patients with myocardial fibrosis.]
B. patients heard clubbing.

There was reduced serum electrolyte and protein concentrations. Serum cholesterol was reduced to 83 mg. per cent, (normal 150 to 200), and the icterus index was 25. These abnormalities were attributed to Laennec's cirrhosis on the basis of a history of heavy alcohol intake. The cephalin flocculation test was negative and the albumin-globulin ratio was normal.

The electrocardiogram disclosed first degree atrioventricular block and multifocal premature ventricular beats. X-ray revealed generalized cardiac enlargement, right pleural effusion, and questionable pneumonitis in the left lower lobe.

Treatment with conventional measures, including large doses of thiamine parenterally, produced some improvement and the lungs became free of rales.

During the succeeding year the patient had 3 hospital admissions for progressive symptoms of dyspnea and edema. Fever was absent except for 1 occasion, due to an associated respiratory infection. Physical findings remained virtually unchanged except that the pulmonary rales gradually disappeared. Several abdominal paracenteses and 1 thoracentesis yielded clear fluid with temporary relief. Laboratory findings were essentially unchanged. Venous pressure was 220 mm. saline. Circulation times were arm-to-lung (ether), 25 seconds and arm-to-tongue (Decholin), 32 seconds. Electrocardiograms revealed atrial flutter and then established atrial fibrillation.

By February 1955 he was severely incapacitated. Physical findings were similar to those described a year before, except that the lungs were clear.

The electrocardiogram (fig. 1) revealed atrial fibrillation.

### Table 1.—Myocardial Fibrosis

<table>
<thead>
<tr>
<th></th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
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<tbody>
<tr>
<td></td>
<td>Rest</td>
<td>Exercise</td>
<td>Rest</td>
</tr>
<tr>
<td>Per cent arterial O₂</td>
<td>81</td>
<td>95</td>
<td>80</td>
</tr>
<tr>
<td>saturation</td>
<td></td>
<td></td>
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<tr>
<td>O₂ consumption, ml./</td>
<td>144</td>
<td>97</td>
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<tr>
<td>M²/min</td>
<td></td>
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<tr>
<td>A-V O₂ difference, ml.</td>
<td>90</td>
<td>57</td>
<td>80</td>
</tr>
<tr>
<td>L</td>
<td></td>
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<tr>
<td>Cardiac index, L/</td>
<td>1.6</td>
<td>1.7</td>
<td>2.3</td>
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<tr>
<td>M²/min</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Heart rate, beats/min</td>
<td>118</td>
<td>79</td>
<td>100</td>
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<tr>
<td>Stroke index, ml./M²/beat</td>
<td>14</td>
<td>21</td>
<td>23</td>
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<tr>
<td>Pressure, mm. Hg</td>
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<tr>
<td>Pulmonary arterial</td>
<td>22</td>
<td>26</td>
<td>27</td>
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<tr>
<td>wedge, mean</td>
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<td></td>
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<tr>
<td>Pulmonary artery,</td>
<td>48</td>
<td>44</td>
<td>47</td>
</tr>
<tr>
<td>mean</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Right ventricle,</td>
<td>51/17</td>
<td>60/14</td>
<td>44/12</td>
</tr>
<tr>
<td>S/D</td>
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<td></td>
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<td>Right atrium, mean,</td>
<td>18</td>
<td>10</td>
<td>21</td>
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<tr>
<td>Resistance, dynes.-cm.</td>
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<tr>
<td>Total pulmonary</td>
<td>1300</td>
<td>930</td>
<td>580</td>
</tr>
<tr>
<td>Pulmonary vascular</td>
<td>700</td>
<td>240</td>
<td>60</td>
</tr>
<tr>
<td>Total systemic</td>
<td>2600</td>
<td>2260</td>
<td>1760</td>
</tr>
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fibrillation and inversion of T waves in the left precordial leads. On fluoroscopy there was a generalized cardiac enlargement with diminished pulsation. A teleradiogram of the chest is shown in figure 2.

Cardiac catheterization disclosed reduced cardiac output with moderate pulmonary hypertension at rest (table 1). Brief leg exercises produced marked widening of the A-V oxygen difference and accentuated the pulmonary hypertension. Arterial oxygen saturation was normal at rest but decreased during exercise. The right ventricular pressure contour, (fig. 3) consisted of an elevated systolic pressure, an early diastolic dip, which descended below the baseline during inspiration, and a gradually rising diastolic pressure. During the longer diastolic pauses the pressure reached a plateau, but this was less than one third the systolic pressure. The atrial pattern was not M-shaped, since the rise in pressure from the trough of the y descent to the next c wave was relatively gradual. There was little or no respiratory variation except in the depth of the y descent. Exercise doubled the right atrial pressure without significantly altering the pattern.

Although these findings were considered to be atypical for constrictive pericarditis, exploratory thoracotomy was advised. At operation no pericardial constriction or adhesions were found. The myocardium had a mottled gray appearance suggesting fibrosis. Both ventricles were enlarged and pulsed well.

After discharge the patient did fairly well at home for about 3 months, under his physician’s care, but then developed increasing failure. Digitalis therapy was difficult because of various abnormal cardiac rhythms. The patient collapsed and died suddenly at home in October 1955.

At autopsy there were bilateral hydrothorax and ascites. Dense focal pericardial adhesions were found at the site of the previous exploration. The heart was hypertrophied and dilated in all chambers, weighing 580 Gm. There was diffuse fibrosis of the myocardium (fig. 4). There was no inflammation or active necrosis. The heart valves were normal. Other findings included an organized thrombus in the left atrium, an old infarct of the spleen and an organizing infarct of the left lower lobe of the lung, a small caseous tuberculous lesion of the right upper lobe of the lung, and portal cirrhosis of the liver. No conclusion was reached about the cause of the myocardial disease.

Case 3. The following case is presented briefly as a probable instance of myocardial fibrosis. M. H., a 48-year-old housewife, had had breathlessness and edema for 1 year. The edema had progressed to include the body wall and face. Her physician noted persistent albuminuria, but failed to induce improvement with digitalis, mercurial diuretics, and acetazolamide (Diamox).

On examination she had generalized edema, a hoarse voice and dry skin. Cardiac enlargement and a soft precordial systolic murmur were noted. The pulmonic second sound was loud and split. There were a few rales at the left lung base. The blood pressure was 124/80. The liver was enlarged.

An electrocardiogram showed first degree A-V block (fig. 1). There was generalized cardiac enlargement with poor pulsations as judged from fluoroscopy, and hilar congestion, but no calcium (fig. 2). There was moderate albuminuria, and a serum albu-
min/globulin ratio was 3-2/3.1. Other studies of renal, hepatic, and thyroid function were normal.

Cardiac catheterization (table 1 and fig. 3) revealed low cardiac output that did not rise with exercise. There was mild postcapillary pulmonary hypertension, also unaffected by exercise. The end-diastolic to systolic pressure ratio in the right ventricle was less than one third, and the dip went below the baseline in inspiration. The right atrial mean pressure was only mildly elevated, considering the degree of disability, and the contour showed considerable respiratory variation in amplitude.

At exploration, the pericardium was normal. The myocardium was pale, suggesting chronic myocarditis to the surgeon. The patient recovered satisfactorily from the operation, but 2 months later the failure began to increase rapidly and she died at home. No autopsy was performed.

**DISCUSSION**

Most authors have concluded that no reliable distinction can be made between myocardial fibrosis and constrictive pericarditis on the basis of the catheterization findings. This is not surprising, since the mode of production of the abnormal pulse contours is generally agreed to be the same in the 2 diseases. Indeed, similar abnormal patterns have also been reported in endocardial fibrosis, funnel chest, and pericardial tamponade. In the 3 cases presented here, however, certain distinctions of a quantitative nature may be made, whose recognition may in the future save some, but not all, patients with myocardial fibrosis an unnecessary thoracotomy.

The following comparison is made with 6 cases of constrictive pericarditis studied by us, since our findings are in general agreement with other published accounts of constrictive pericarditis.

First, the early diastolic dip in the right ventricular pressure tracings usually did not reach the atmospheric pressure baseline in constrictive pericarditis, (5 of our 6 cases) whereas it reached or went below the baseline in all our cases of myocardial fibrosis.

Second, the end-diastolic pressure in the right ventricle was equal to or above one third of the systolic pressure in all our cases with
constrictive pericarditis. In only 1 of our patients with myocardial fibrosis did the diastolic pressure barely achieve this height, and then only in 1 or 2 out of several tracings.

Third, the right atrial mean pressure tended to be higher in patients with constrictive pericarditis than in those comparably disabled by myocardial fibrosis. Thus, 5 of our 6 patients with constrictive pericarditis had a mean right atrial pressure more than 16 mm. Hg. The sixth patient, whose right atrial mean pressure was 12 mm. Hg, was only mildly disabled. In contrast, the pressures in the fibrosis patients, all of whom were severely disabled, were only 10, 12, and 18 mm. Hg respectively.

Fourth, the right atrial pressure contour was less typical in fibrosis than in pericarditis. In the latter disease, the y descent was followed by a rapid upstroke and plateau, following the ventricular pattern and forming with the x descent the so-called W or M complex; and the only variation that occurred with respiration was a slight increase in the depth of the y descent during inspiration. In the patients with fibrosis, the respiratory variation in the depth of the y descent was slightly greater, and in 1 patient (case 3) there was also an increase in the positive deflections during inspiration, although the mean pressure did not fluctuate significantly. In another patient (case 2) whose ventricular pattern was not typical of constrictive pericarditis, the atrial pattern also contained a gradual, rather than an abrupt, rise after the y descent, so that the pattern came to resemble that seen in other types of severe heart failure.

To summarize the differential points, constrictive pericarditis should be strongly suspected when the right ventricular end-diastolic pressure is clearly and consistently one third the systolic or more, the early diastolic dip does not reach atmospheric pressure, the right atrial mean pressure is above 15 mm. Hg, there is little or no respiratory variation in mean atrial pressure or in the shape of the atrial pressure contour, and when there is an abrupt rise and high plateau after y descent, forming an atrial M or W complex. The less well these criteria are fulfilled, the more likely the lesion is to be myocardial fibrosis. Some overlapping may occur in either direction in some of these criteria, but we have not yet encountered a patient among our own cases or in the literature, with constrictive pericarditis, whose end-diastolic to systolic ratio in the right ventricle was less than one third. When this ratio is well below one third, therefore, myocardial fibrosis may be most strongly suspected. The converse is not always true, since Hetzel and co-workers² have presented tracings from a patient whose right ventricular pressure appears to be between 50 and 65 mm. Hg systolic and about 25 mm. Hg end-diastolic. The mean atrial pressure appears over 20 mm. Hg and does not vary with respiration. This patient was subjected to exploratory thoracotomy and the pericardium was found to be normal. No cause for the heart failure was discerned. Balchum, McCord, and Blount⁴ and Sawyer and co-workers¹¹ have also presented proved cases of myocardial fibrosis with end-diastolic pressure in the right ventricle more than half the systolic.

The size of the heart, the vigor of its pulsations, and the absence of pericardial calcification cannot be relied on to distinguish between myocardial fibrosis and constrictive pericarditis, since many patients with proved constrictive pericarditis have cardiac enlargement without marked decrease in the amplitude of the beat and without calcification.

SUMMARY

Three patients are presented with intractable heart failure. Two had proved myocardial fibrosis. The probable diagnosis of myocardial fibrosis in the third patient is based on the operative findings.

Many clinical and hemodynamic features strongly suggested constrictive pericarditis, particularly the right ventricular and right atrial pressure contours, although the pericardium was normal at operation.

The differentiation can sometimes be made on quantitative grounds. Severely disabled patients with right ventricular end-diastolic to systolic pressure ratios clearly less than one third, and with right atrial mean pressures well below 15 mm. Hg, are unlikely to have constrictive pericarditis. Any considerable respiratory variation in right atrial pressure contour
increases the likelihood that the diagnosis is myocardial fibrosis rather than constrictive pericarditis, as does the observation that the right ventricular early diastolic dip goes below the baseline. If these observations are confirmed and extended, it may become feasible to spare certain of these patients unnecessary thoracotomy. Patients with converse findings should be explored, even though cases of myocardial fibrosis will be included.

**SUMMARIO IN INTERLINGUA**

Es presentate tres patientes con intractabile disfallimento cardiac. Duo hhabeva demonstratamente fibrosis myocardial. In le tertia patiente le diagnose probable de fibrosis myocardial es basate super le constatationes operatori.

Multa aspectos clinic e hemodynamic eseva forte indicios de pericarditis constrictive, specialmente le contornos del pression dextero-ventricular e dextero-atrial, ben que le pericarcto eseva normal al operation.

Le differentiation pote a vices facer se super le base de factores quantitativa. Severemente invalide patientes con proportiones inter le pression dextero-ventricular termino-diastolic e le pression systolic amontante a valores claramente infra un tertio e con pressiones dextero-atrial medie amontante a valores claramente infra 15 mm Hg non es probable victims de pericarditis constrictive. Omne grado considerabile de variation respirator in le contorno del pression atrial augmenta le probabilitate que le diagnose deberea esser fibrosis myocardial plusosto que pericarditis constrictive. Le mesmo es ver quando le depression initio-diastolic dextero-ventricular descedente a infra le linea de base.

Si iste observationes es confirmate e extendite, il va forsan devenir possibile evitar thoracotomias innecessari in certes de iste patientes. Patientes con constituentes contrari deberea esser subjicite a operationes exploratorii, mismo si isto signifca que casos con fibrosis myocardial es includite.

**ACKNOWLEDGMENT**

We are grateful to Dr. Roger Terry for the pathologic studies on case 1. We wish to express our appreciation and thanks to Dr. Morris Missal for the permission to study case 2, and to Dr. Milton G. Bohrod for the autopsy findings of the same case. We are indebted to Dr. Donald Jones for referring case 3 to us for study. Dr. E. B. Mahoney performed the exploratory thoracotomy on all 3 cases.

**REFERENCES**


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