The Coronary Arteries and Left Ventricle in Clinically Isolated Angina Pectoris

A Necropsy Analysis

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SUMMARY Certain clinical and morphologic observations are described in 27 patients with severe isolated angina pectoris of either the stable (five patients) or the unstable form (22 patients). Twenty-four patients died during or shortly after cardiac operations designed to relieve angina pectoris and three died during cardiac catheterization. During life none had had clinical evidence of acute myocardial infarction or congestive cardiac failure. At necropsy, each had diffuse, extensive coronary atherosclerosis with severe luminal narrowing: the lumens of at least two, an average of three, of the four major epicardial coronary arteries were narrowed > 75% in cross-sectional area by old atherosclerotic plaques. Despite the severe coronary narrowing, there was little myocardial damage. Left ventricular scarring (excluding papillary muscle) was observed grossly in only 14 (52%) of the 27 patients and in each it involved only a small portion of myocardial wall. The left ventricular cavity was of normal size in all except two patients. The hearts were of normal weight in 15 (56%) patients, and the average increase above the upper range of normal for the other 12 hearts was 19%. Thus, clinically isolated, severe angina pectoris is associated with severe, diffuse luminal narrowing but relatively little myocardial damage.

ALTHOUGH NUMEROUS ANGIOGRAPHIC STUDIES have been performed during life on the coronary arteries and left ventricles of patients with clinically isolated angina pectoris, i.e., no clinical evidence of acute myocardial infarction, congestive cardiac failure, or "resuscitated sudden death," morphologic studies on the coronary arteries and left ventricular myocardium in these patients have not been possible until recently. The reason is that most patients with angina pectoris die either suddenly or from acute transmural myocardial infarction and consequently are placed in the category of sudden coronary death or acute myocardial infarction rather than in the category of angina pectoris. Furthermore, few patients with clinically isolated angina pectoris dying of a noncardiac condition have been evaluated clinically near the time of necropsy examination. The introduction of cardiac catheterization with coronary angiology and the frequent use of the aortocoronary arterial bypass operation have provided an opportunity for morphologic study soon after clinical evaluation. In this report certain clinical and morphologic observations are presented in 27 patients with clinically isolated angina pectoris. Each died during or shortly after an operation to relieve angina pectoris or during cardiac catheterization.

Patients Studied and Methods

The 27 cases were obtained by review of all patients studied in this pathology laboratory who had died during or shortly after cardiac catheterization (three patients) or cardiac operations to relieve angina pectoris (aortocoronary bypass, 21; carotid-sinus stimulator, 2; Vineburg procedure, 1). Patients who had had clinical evidence of acute myocardial infarction before catheterization or cardiac surgery and patients with associated valvular, congenital, primary myocardial (hypertrophic cardiomyopathy) or pericardial heart disease were excluded.

The clinical and necropsy records in all 27 patients were reviewed. From the clinical records, the type of angina pectoris in each patient was judged to be either stable or unstable. Stable angina was defined as anterior thoracic pain, lasting usually 3 to 10 minutes, related to effort and relieved by rest or nitroglycerin. The pattern of occurrence of stable angina did not change although it could vary in severity. Unstable angina was defined as anterior thoracic pain of recent onset (< 1 month before clinical evaluation) or a recent change in the pattern of the pain of stable angina, i.e., worsening of the pain in terms of frequency, severity, intensity and ease of provocation. Nocturnal or rest angina or prolonged angina within three months of death was considered unstable. There was no electrocardiographic or enzymatic evidence of recent acute myocardial infarction in any of the hospitalized patients with either form of angina.

Both the gross hearts and the histologic sections of left ventricle and coronary arteries were re-examined. The coronary arteries were examined in a manner described in detail elsewhere. They were removed intact from the hearts, and each was placed in a separate container of formalin, fixed, decalcified, sectioned at 5 mm intervals, briefly decalcified again, then processed in alcohols and xylene, embedded in paraffin, and two histologic sections from each 5 mm segment were cut, stained, and examined. One section was stained by hematoxylin and eosin and the other by Movat's stain. The degree of narrowing of the cross-sectional area of each of the four major coronary arteries (left main, left anterior descending, left circumflex and right) was graded as follows: < 25%, 25-50%, 51-75% and > 75%.

The ventricular myocardium was examined by making approximately six transverse sections of the ventricles beginning at the cardiac apex and progressing cephalad. The cuts were made parallel to the posterior atrioventricular sulcus. Each of the transverse slices of ventricular myocardium was 1.0 to 1.5 cm in thickness. Gross fibrosis or necrosis was confirmed by histologic examination. From three to eight (average five) histologic sections of left ventricle were examined from each patient.

Results

All 27 patients had severe angina pectoris; each had been in functional class III or IV (New York Heart Association...
The angina pectoris was considered stable in five patients and unstable in 22 patients. Although all 27 patients had undergone cardiac catheterization (including coronary and left ventricular angiography in 26 of them), three died during or shortly after this procedure, and the other 24 died during or after operations to relieve angina pectoris. Thirteen died in the operating room, seven others within 24 hours after operation, two within 48 hours, one at 18 and another at 34 days postoperatively.

**Clinical Features**

The 27 patients ranged in age from 39 to 67 years (average 50); 21 (78%) were men and six were women. Angina pectoris had been present from one to 120 months (average 25): for less than one year in 12 and for more than three years in five. Systemic hypertension (> 140/90 mm Hg) was recorded at some time in 11 patients (41%) and in all it was intermittent; 21 (77%) smoked cigarettes, and 19 (71%) were 10% or more above ideal body weight. The serum lipoprotein pattern, known in 23 patients, was normal in 11 and abnormal in 12: type II hyperlipoproteinemia in seven; type III in one and type IV in four. The heart size was normal by chest roentgenogram in all 27 patients, and in none did the electrocardiogram show evidence of ventricular hypertrophy. None of the 27 patients before cardiac catheterization or cardiac operation had had clinical evidence of acute myocardial infarction, congestive cardiac failure, or a history of successful resuscitation after sudden collapse (ventricular fibrillation).

**Morphologic Features**

The atherosclerotic process was diffuse (fig. 1), involving each 5 mm segment of coronary artery in all 27 patients, and the degree of laminal narrowing by this process was severe in all. The lumens of at least two, and an average of three, of the four major coronary arteries were > 75% narrowed in cross-sectional area by old atherosclerotic plaque in all 27 patients: the left anterior descending in all 27; the right in 26; the left circumflex in 21; and the left main in nine. Seven patients had > 75% narrowing in two arteries, 11 patients in three arteries, and nine patients in all four arteries. The average number of coronary arteries narrowed > 75% was the same in the five patients with stable angina and in the 22 patients with unstable angina, namely, three in each.

The hearts ranged in weight from 320 to 520 g (average 407): for the six women, 320 to 480 (average 375) and for the 21 men, 330 to 520 (average 417). The weight of the heart was normal (350 g or less in women; 400 g or less in men) in 15 (56%) and increased in 12 (44%) patients. The average increase above the normal range for the latter 12 patients was 19%. A history of systemic hypertension was present in seven of the 12 patients with cardiomegaly and in four of the 15 patients with normal sized hearts. The hearts of the five men with stable angina averaged 393 g (range 350-475) and those of the 16 men with unstable angina averaged 424 g (range 350-520).

The left ventricular cavity was judged visually to be of normal size in all but two patients. In one, however, the dilatation almost surely resulted from a large acute myocardial infarction which occurred at the time of aorto-coronary bypass and caused cardiogenic shock during the entire 36-hour postoperative period. The cause of the left ventricular dilatation in the other patient is uncertain, although it was confirmed by angiography which also showed hypokinesis of the apical portion of the left ventricle. The left ventricular end-diastolic pressure in this patient, however, was only 8 mm Hg, his blood pressure was normal, his valves competent, and he never had evidence of congestive cardiac failure. Furthermore, at necropsy no myocardial foci of fibrosis or necrosis were present.

Grossly visible scars were present in the left ventricular walls (excluding papillary muscles) in 14 patients (52%), with stable angina and ten with unstable angina. In only four patients including one with stable and three with unstable angina, however, was the scarring transmural, i.e., extended through more than just the inner one-half of the myocardial wall. In the remaining ten patients, the scarring was non-transmural; in eight it was entirely subendocardial, i.e., limited to the inner one-half of the myocardial wall. The scars in all 14 patients were small, involving less than 20% of the circumference of a transverse section of left ventricle, and none extended more than 2 cm in length on the apical-basal longitudinal dimension of the left ventricle. In none of the 14 patients did the scarring appear to result in thinning of the myocardial wall.

Foci of myocardial necrosis were present in the left ventricular free wall or ventricular septum in four (15%) of the 27 patients. These foci were visible grossly (but confirmed histologically) in three patients and visible by histologic study only in the fourth patient. The acute infarcts were

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**FIGURE 1. The four major coronary arteries at the same magnification (× 16) at sites of maximal narrowing in a 59-year-old woman with pure angina pectoris of seven years’ duration. She died in the operating room after Vineberg procedure. At necropsy, the most proximal 1 cm of the right (R), left circumflex (LC) and left anterior descending (LAD) coronary arteries were greater than 75% narrowed in cross-sectional area. The left main (LM) also was narrowed but not to this extent. The left coronary artery was considerably larger than the right one and supplied the posterior descending coronary arteries. Hematoxylin and eosin stains (R, LM, LC); Movat stain (LAD).**
transmural in two patients and entirely subendocardial in two. In only one patient was the infarct large. This 47-year-old woman died 36 hours after an aortocoronary bypass operation during which time she was in severe shock. Each of the four patients with myocardial necrosis died from 18 to 48 hours after start of the aortocoronary bypass operation. The histologic age of the myocardial necrosis corresponded in each of the four patients to the postoperative time intervals. The myocardial necrosis, therefore, must have been operatively induced and not present before operation.

**Comments**

This study describes the heart at necropsy in 27 patients who during life had angina pectoris of severe degree (unstable in 82%) as the only apparent clinical manifestation of coronary heart disease and who died neither a sudden coronary death, nor from spontaneous acute myocardial infarction. Death in each patient was precipitated by either cardiac catheterization or cardiac operation, and, therefore, during life the only clinical manifestation of myocardial ischemia was angina pectoris. Furthermore, none of the patients had clinical evidence of congestive cardiac failure or associated noncoronary forms of cardiac disease.

The coronary arteries at necropsy in the patients with isolated angina pectoris were relatively uniform, diffusely atherosclerotic, and their lumens were severely narrowed. Of the several hundred histologic sections of coronary arteries examined (approximately 60 per patient) in the 27 patients, all contained atherosclerotic plaques. Furthermore, the lumens of at least two of the four major extramural coronary arteries were > 75% narrowed in cross-sectional area by old atherosclerotic plaques; an average of three of the four major coronary arteries were narrowed to this extent. In a third of the patients the lumens of all four major coronary arteries were narrowed > 75% by atherosclerotic plaque. Thus, in one-third of the patients, the left main coronary artery was severely (> 75%) narrowed and when this degree of narrowing occurred in this artery the lumens of each of the other three coronary arteries were similarly narrowed. In all patients, the lumen of the left anterior descending was > 75% narrowed by atherosclerotic plaque; in 26 of the 27 patients the right was similarly narrowed; and in 21 patients the left circumflex was narrowed to this extent.

Despite the severe coronary narrowing in the patients with isolated angina pectoris, the left ventricles were remarkably free of gross morphologic abnormality. The left ventricular cavity was of normal size in all but two patients, and minimal or mild left ventricular scars were observed grossly in only 14 (52%) of the 27 patients. Obviously, all of these myocardial infarcts were clinically silent. Thus, despite the severe coronary luminal narrowing, the morphologic changes in the left ventricle were mild.

Despite intermittent hypertension in 41% of the 27 patients, the average weight of all 27 hearts was only 5% above the upper range of normal. The range of heart weights was narrow: only one heart weighed more than 500 g and only two less than 350 g.

Whether or not the morphologic observations in the patients described herein would be applicable to those in living patients with clinically isolated angina pectoris is uncertain. It is likely, however, that the present observations are applicable only to patients with severe debilitating angina pectoris, i.e., those with symptoms severe enough to consider or warrant coronary bypass operation, and to those with unstable angina.

Although the patients in the present study had angina pectoris as the only clinical manifestation of coronary heart disease, the extent of the coronary atherosclerosis and the degree of luminal narrowing produced were similar to that observed at necropsy in patients with fatal acute myocardial infarction or sudden coronary death with or without previous angina pectoris. Furthermore, the extent of atherosclerosis and the degree of luminal narrowing produced by it were similar to that observed in patients with severe progressive congestive cardiac failure after healing of an acute transmural myocardial infarct. Thus, the myocardial response to similar degrees of coronary luminal narrowing is highly variable. The two ends of the clinical spectrum of coronary heart disease might be considered to be represented by the patient manifesting only pain (isolated angina pectoris) and the other by the patient with dyspnea (ischemic cardiomyopathy) after healing of an acute myocardial infarct. The explanation for this varied myocardial response to similar degrees of coronary luminal narrowing is uncertain.

Guthrie and associates recently analyzed the degree of coronary narrowing by gross examination in 47 patients with stable (35 patients) or unstable (12 patients) angina and the degree of coronary luminal narrowing in their patients was similar to that described in the 27 patients herein. A history of acute myocardial infarction, however, was present in 60% of their patients, three also had aortic valve disease and nine had mitral regurgitation, indicating that their population did not consist entirely of clinically isolated angina pectoris, although their patients also had died during or shortly after cardiac operation or catheterization.

**References**

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