Necropsy Studies in Myocardial Infarction with Minimal or No Coronary Luminal Reduction Due to Atherosclerosis

By R. S. Eliot, M.D., G. Baroldi, M.D., and A. Leone, M.D.

SUMMARY
A postmortem study was conducted on the hearts of 10 patients who died with a typical clinical picture of acute myocardial infarction within 25 days of onset of symptoms. The coronary arterial systems of the patients revealed minimal or no luminal reduction due to coronary atherosclerosis or other cause. These cases contribute to the understanding of the pathogenesis of acute myocardial infarction in that they document the presence of typical acute myocardial infarction in the absence of chronic or acute coronary arterial obstruction. They further suggest that the hearts of those dying of typical myocardial infarction show minimal or no coronary disease in approximately 7% when studied as described.

Additional Indexing Words:
Myocardial infarct  Minimal coronary luminal reduction  Normal coronaries

Both angina pectoris and myocardial infarction have been clinically demonstrated in patients with angiographically patent coronary arteries by many investigators.1-19 The number of necropsy cases remains small.5, 20-22 The need for further pathological documentation has been emphasized by Burchell23 and James24 among others. It is the purpose of this communication to investigate the incidence of death and the necropsy findings in this condition.

Methods and Materials
Out of a total of 10 cases 5 were men and 5 were women (table 1). Ages ranged from 36-81 years. The three American cases (all females) were selected from a necropsy experience of 20 cases followed with known angiographically patent coronary arteries and objective signs of myocardial ischemia or necrosis. Each presented at termination with typical subendocardial infarction.

The seven Italian cases were drawn from 100 consecutive autopsies performed in persons dying within 25 days of the onset of typical clinical manifestations of acute myocardial infarction. These 100 represented the total consecutive deaths from the Coronary Care Unit experiences of the University of Milan and the Center of Clinical Physiology of the University of Pisa, and were obtained over a two-year period.20 Three Italian cases had previously undergone selective coronary angiography with apparent normal findings. A variety of predisposing factors and other clinical findings were present (table 1). All presented with typical features of acute myocardial infarction.

In each case, it was possible to demonstrate coagulation necrosis employing routine hematoxylin and eosin (H & E) staining, elastic van Gieson, and Movat technique. From the histologic standpoint, the type of infarction was defined as:
1) massive, when all the cells of the infarcted zone with a maximum diameter greater than 5 mm were necrotic,
2) confluent, when multiple necrotic foci tended to join together with some separation of the foci by apparently viable myocardium, and
3) focal, when the lesions appeared as small, unique or multiple microfoci of coagulation necrosis, scattered in normal tissue.

No patient was included in whom typical clinical symptoms were unaccompanied by histologic confirmatory features.26

Prior to opening the heart, coronary luminal studies were performed in three of the Italian cases by selective injection of BaSO₄ solution at a pressure compatible with normal arterial pressures.25, 27 In all cases prior to opening the heart, the coronary arteries were studied by serial section at 3 mm intervals. Following this, the left ventricle was cut into 1 cm transverse sections. Employing a polar planimeter, the area of infarction was evaluated for each slice and the percentage of involvement of the left ventricle was calculated. Histological lumen evaluation was done next by utilizing a micrometer. The average diameter of the lumen and the percentage of the lumen stenosis was calculated with reference to the normal lumen of the vessel.28 Finally, multiple random ventricular samples were taken for histologic study.

Results
The heart weights averaged 464 grams (range 320–630 g). The histologic age of the infarction
Table 1

Sex, Age, Other Main Clinical Findings

<table>
<thead>
<tr>
<th>No.</th>
<th>Sex</th>
<th>Age</th>
<th>Clinical data</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Italian cases</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>M</td>
<td>46</td>
<td>Four severe episodes of angina pectoris in past 7 yr. Bilateral intermittent causalgia.</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>46</td>
<td>Chronic glomerulonephritis and hypertension.</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>63</td>
<td>Cigarette smoker* (2 packs/day). No cardiac symptoms.</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>72</td>
<td>Diabetes, successfully controlled with insulin. Episodes of cardiac failure 3 yr before.</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>81</td>
<td>None available</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>47</td>
<td>Menopause 2 yr before. Cigarette smoker* (1 pack/day). No cardiac symptoms.</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>66</td>
<td>None available</td>
</tr>
<tr>
<td><strong>U.S. cases</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>F</td>
<td>36</td>
<td>Cigarette smoker* (2 packs/day). Angina pectoris for 2 yr (3-6 episodes per week).</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>37</td>
<td>Cigarette smoker* (3 packs/day). Vague atypical chest pain and hyperventilation syndrome for 5-6 yr.</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>40</td>
<td>Nonsmoker, moderate obesity, no known complaints prior to acute myocardial infarction.</td>
</tr>
</tbody>
</table>

*More than 10 years.

There were four transmural and six subendocardial infarcts (fig. 1). Five were massive, three were focal, and two were confluent (fig. 2). The involvement of the left ventricle averaged 18% (range 5-33%). Lumen stenosis (fig. 3) was completely absent in six, 20% reduced in one coronary artery of one case, and 40-50% reduced in single arteries of two separate cases (table 2). Luminal area was 40-50% reduced in two arteries of one case. Histologic studies revealed the typical features of acute myocardial infarction in each instance. In all cases the cardiac valves were normal. Microfocal subendocardial fibrosis was present in all but one case.

Discussion

As noted (table 2), all but two of the hearts were above normal weight, yet only case 2 (table 1) demonstrated hypertension or any explanation for increased heart weight. Although angiographic techniques may minimize or occasionally mask coronary arterial stenosis or obstruction, the opportunities for such errors at necropsy are minimized. It is well recognized that histologic evaluation of coronary lumen stenosis is exaggerated when compared to clinical coronary angiographic study. In the hearts described herein, coronary disease was minimal or absent. Accordingly, the possibility of missing a major obstruction was very small.

When one defines the histologic characteristics of normal coronary arteries, one must recall the minor changes in intima which can be observed. Specifically, there is some intimal thickening due to proliferation of fibrous connective tissue, elastic tissue, and smooth muscle cells. This hyperplastic thickening, variously interpreted as early atherosclerosis or physiological hemodynamic changes or aging or an inflammatory response, is present at birth and increases with age. The features are not those of typical or obvious atherosclerosis. Angiography in older adults with these findings will demonstrate ectatic coronary vessels. Thus, the condition is not associated with lumen reduction.

The possibility of missing a thrombus, which underwent rapid autolysis in vivo or after death, is not confirmed by experimental and human data.

Although extensively reviewed, no histologic evidence of small vessel disease was found in either normal or infarcted areas apart from that secondary to myocardial necrosis. The histologic findings were those typical of the various stages of myocardial infarction.

According to the Italian study carried out in 100

![Figure 1](image-url)

**Figure 1**

A. (Case 6) Early focal subendocardial infarct left ventricle-septum and postero-medial papillary muscle. Size of the infarct was calculated to be less than 10% of the left ventricular mass. B. (Case 5) Transmural massive infarct, posterior left ventricle. Size of the infarct — 22%. Rupture of the heart.
Table 2

<table>
<thead>
<tr>
<th>N</th>
<th>Heart weight (gm)</th>
<th>Histolog age (days)</th>
<th>Site</th>
<th>Location</th>
<th>Infarct</th>
<th>Histolog. type</th>
<th>Extension % LV</th>
<th>Subendoocard. fibrosis</th>
<th>Maximum lumen stenosis %*</th>
<th>Length stenosis (mm)</th>
<th>Other main pathologic findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>630</td>
<td>2</td>
<td>Total LV septum</td>
<td>subendocardial</td>
<td>focal</td>
<td>5</td>
<td>confluent</td>
<td>no</td>
<td>—</td>
<td>—</td>
<td>Stenosing atherosclerosis</td>
</tr>
<tr>
<td>2</td>
<td>420</td>
<td>12</td>
<td>Anterior LV septum</td>
<td>transmural</td>
<td>massive</td>
<td>16</td>
<td>no</td>
<td>no</td>
<td>—</td>
<td>—</td>
<td>Chronic glomerulonephritis</td>
</tr>
<tr>
<td>3</td>
<td>490</td>
<td>20</td>
<td>Total LV</td>
<td>subendocardial</td>
<td>confluent</td>
<td>10</td>
<td>focal</td>
<td>40% LAD</td>
<td>2</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>4</td>
<td>600</td>
<td>4</td>
<td>Total LV</td>
<td>transmural</td>
<td>massive</td>
<td>33</td>
<td>confluent</td>
<td>no</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>5</td>
<td>530</td>
<td>4</td>
<td>Posterior LV</td>
<td>transmural</td>
<td>massive</td>
<td>22</td>
<td>focal</td>
<td>50% RCA</td>
<td>4</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>6</td>
<td>450</td>
<td>2</td>
<td>Total LV septum</td>
<td>subendocardial</td>
<td>focal</td>
<td>5</td>
<td>focal</td>
<td>no</td>
<td>3</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>7</td>
<td>420</td>
<td>2</td>
<td>Total LV septum</td>
<td>transmural</td>
<td>massive</td>
<td>31</td>
<td>focal</td>
<td>50% LAD</td>
<td>3</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>8</td>
<td>320</td>
<td>2</td>
<td>Anterior LV septum</td>
<td>subendocardial</td>
<td>focal</td>
<td>12</td>
<td>confluent</td>
<td>20% LAD</td>
<td>3</td>
<td>—</td>
<td>Rupture posterior myocardial papillary muscle</td>
</tr>
<tr>
<td>9</td>
<td>415</td>
<td>3</td>
<td>Posterior LV</td>
<td>subendocardial</td>
<td>massive</td>
<td>25</td>
<td>confluent</td>
<td>no</td>
<td>3</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>10</td>
<td>375</td>
<td>2</td>
<td>Total LV</td>
<td>subendocardial</td>
<td>massive</td>
<td>18</td>
<td>confluent</td>
<td>no</td>
<td>2</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

*All cases showed a coronary pattern of "right preponderance" type.
consecutive cases, the frequency of an infarct without morphologic evidence of an acute occlusion and without pre-existent severe coronary disease approximates 7%. This figure confirms observations employing plastic casts of the coronary arteries (including histologic features) in cases of acute myocardial infarction.

References


Figure 2

Myocardial coagulation necrosis, typical of myocardial infarct without evidence of myocytolysis. A. Acute focal infarct (H & E x 140). B. Acute confluent infarct (H & E x 160). C. Acute massive infarct (H & E x 20).

Figure 3

Demonstrates maximum degrees of obstruction. A-B. (Case 1) Left anterior descending branch (A) and left circumflex branch (B) demonstrating mild intimal thickening without lumen stenosis (H & E x 50). C. (Case 4) Mild thickening of the intima with normal lumen of the left anterior descending branch. D. (Case 6) 40 percent lumen stenosis of the right coronary artery.
AUTOPSIES IN INFARCTS WITHOUT OCCLUSION


27. World Health Organization, Techn Rep Ser, 1970, No. 441, p 18


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