Superimposition of Transmural Infarction Following Acute Subendocardial Infarction*

How Frequent?

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Thirty-five consecutive patients with acute subendocardial infarction admitted to the coronary care unit during a 15-month period were identified and analyzed for location of infarction, and for the in-hospital course in terms of recurrent chest pain, the occurrence of a second infarction, and the clinical status at the end of hospitalization. Thirteen patients developed a transmural infarction sometime between 3 and 21 days (average, ten days) after the initial subendocardial infarction. The transmural infarction was defined by a separate episode of severe and prolonged chest pain, late development of QRS alteration, and an appropriate elevation of the creatine phosphokinase concentration. Our experience with acute subendocardial infarction, heretofore regarded as a relatively benign event, indicates that the immediate prognosis of the patient who sustains his first episode of subendocardial infarction is not at all benign, and, indeed, subendocardial infarction frequently heralds transmural infarction within the acute phase of the disease.

Acute subendocardial infarction has heretofore been regarded as a relatively benign event, with an incidence of arrhythmia and other complications of infarction far less than that observed in transmural infarction.1,2

It is the purpose of this report to indicate that the in-hospital experience of 35 consecutive patients with acute subendocardial infarction suggests that the immediate prognosis of the patient who sustains his first episode of subendocardial infarction is not benign and, indeed, frequently heralds transmural infarction within the acute phase of the disease.

**Materials and Methods**

All patients admitted to the coronary care unit of the Brookdale Hospital Medical Center between Dec 1, 1973 and March 1, 1975, a 15-month period, were reviewed. Those patients without prior myocardial infarction who had had an acute episode of chest pain and demonstrated symmetric and deep inversion of the T wave persisting for at least 48 hours and unassociated with abnormalities in the QRS complex and who had elevation of the creatine phosphokinase concentration were considered to have suffered a subendocardial infarction. Thirty-five patients were identified by these criteria as having sustained an acute subendocardial infarction.

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The patients were then analyzed for the location of the subendocardial infarction and for their in-hospital course in terms of complications of the initial infarction, particularly recurrent chest pain, the occurrence of a second infarction, the complications of that infarct, and the clinical status at the end of hospitalization. No attempt at long-term follow up of all the patients was made, although the subsequent course of many was known.

**Results**

Serial electrocardiograms of a typical patient with subendocardial infarction are shown in Figure 1. Of the 35 patients, 13 (37 percent) developed during hospitalization a transmural infarction defined not only by a late development of QRS alteration and an appropriate creatine phosphokinase elevation, but also by a well-defined episode of severe and prolonged recurrent chest pain. These infarctions occurred from 3 to 21 days (average, ten days) after the initial episode. The characteristics and clinical course of the groups who did and did not develop a transmural infarction are shown on Table 1.

It can be noted that the clinical characteristics and risk factors are not different enough to provide a separation of those patients likely to sustain a transmural infarction from those who will not. The difference in sex distribution in the two groups may be a chance variation in a small sample but warrants further assessment. More important, the presence of recurrent brief anginal pain did not provide a separation between the two groups.
Table 1—Clinical Features of Single Subendocardial Infarction and of Subendocardial Infarction with Subsequent Transmural Infarction

<table>
<thead>
<tr>
<th>Features</th>
<th>Single Subendocardial Infarction</th>
<th>Subsequent Transmural Infarction</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>22</td>
<td>13</td>
</tr>
<tr>
<td>Mean age</td>
<td>66</td>
<td>61</td>
</tr>
<tr>
<td>Male/female ratio</td>
<td>15/7</td>
<td>12/1</td>
</tr>
<tr>
<td>Hypertension</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>Diabetes</td>
<td>10</td>
<td>2</td>
</tr>
<tr>
<td>Cigarettes</td>
<td>15</td>
<td>9</td>
</tr>
<tr>
<td>Site of initial infarction on ECG</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>12</td>
<td>9</td>
</tr>
<tr>
<td>Inferior</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Combined</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Recurrence of ischemic pain not including pain of reinfarction</td>
<td>9</td>
<td>6</td>
</tr>
<tr>
<td>Interval to transmural infarction, days</td>
<td>. . .</td>
<td>3-21 (mean, 10)</td>
</tr>
<tr>
<td>Mortality</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Cause of death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1) Cerebrovascular accident</td>
<td>(1) Pump failure accident</td>
<td></td>
</tr>
<tr>
<td>(2) Sepsis</td>
<td>(2) Pump failure</td>
<td></td>
</tr>
</tbody>
</table>

It should also be noted that in this sample of patients with subendocardial infarction, none of whom had a history of prior infarction or electrocardiographic evidence of an old infarction or bundle-branch block, the mortality and morbidity in those patients without superimposed transmural infarction was low (2/22) and was noncardiac in both instances.

**DISCUSSION**

Since the report of Wilson et al. in 1933 on the electrocardiographic changes in experimental myocardial infarction, transmural infarction has been identified electrocardiographically by the presence of Q waves, and the subendocardial infarction has been identified by abnormalities limited to the ST segment and T wave. Although this anatomic correlation is no longer considered precise,4,5 the electrocardiographic separation of infarction has been and continues to be widely used as a prognostic index. In the index of Peel et al., as in others,7,8 the subendocardial label is assigned a low score and an accordingly favorable prognosis. Indeed, the failure to make the separation of infarction into transmural and subendocardial in reporting on the prognosis of acute myocardial infarction has been decried because of the gross differences in prognosis between the two electrocardiographic entities.1,2

In the series reported here, subendocardial infarction was defined electrocardiographically by the symmetric and deep inversion of the T wave unassociated with alteration in the QRS complex and persisting for at least 48 hours. No patient with electrocardiographic changes limited to ST-segment alterations without the symmetric and persistent inversion of the T wave was included in this study.

Thirteen of the 35 patients with subendocardial infarction as so defined developed transmural infarction during the period of hospitalization.

Transmural infarction occurring days to weeks after a well-defined subendocardial infarction is not a new or unique observation, although the frequency with which this occurs is hitherto unreported. In 1945, Rosenbaum et al. reported the electrocardiographic study of two patients who demonstrated electrocardiographic criteria for transmural infarction after subendocardial infarction. An additional report analogous in part to our own is that of Stimmel et al. who described the clinical course of 15 patients with subendocardial infarction, seven of whom developed abnormal Q waves during their early hospitalization but without any other clinical signs of extending infarction. A more comparable example of progression of subendocardial to transmural infarction occurring over a period of weeks is the single case reported by Bell and Fox in their review of the pathogenesis of subendocardial ischemia.

While our observations have focused on the occurrence of transmural infarction after acute subendocardial infarction during a single hospital period, the concept that the clinical course of the subendocardial infarction is benign has only recently been challenged. Two studies involving a large number of patients with subendocardial infarction failed to distinguish either the pattern of complications or the clinical outcome by the electrocardiographic separation of infarction into transmural and subendocardial.15,16 However, these observations are not similar to the findings in our own series where, perhaps because none of our patients had known previous infarction, the in-hospital course of the patient whose infarct remained subendocardial was benign and similar to the course of subendocardial infarction previously described.1,2

Except for fatal arrhythmia, the complications of infarction are those related to size and location of the infarct and are found in patients with transmural infarction or subendocardial infarction with previous transmural infarction or the rare universal subendocardial infarction.14-16 Left ventricular
failure, cardiogenic shock, cardiac rupture, septal perforation, papillary muscular rupture, mural thrombus, and the postmyocardial infarction syndrome are all associated with the presence of transmural infarction.\textsuperscript{16-20} Although free of these mechanical and anatomic complications of transmural infarction, coronary arterial disease in subendocardial infarction may nonetheless be extensive.

A recent angiographic study of the coronary arteries in 32 patients with subendocardial infarction revealed extensive disease in all, with 21 of the 32 having significant double- and triple-vessel disease.\textsuperscript{21}

In the 35 patients reported here, there was a clinical difference neither in the manner of onset of the attack nor in the electrocardiographic changes, including the presence of ventricular arrhythmia, which would have enabled us to distinguish the patient with an uncomplicated subendocardial infarction from the one who went on days or weeks later to transmural infarction.

Because of the mass of evidence available to suggest that myocardial salvage depends on the early therapeutic intervention in the heart attack syndrome,\textsuperscript{22,23} the therapy in the patient with uncomplicated acute subendocardial infarction assumes even greater importance in the perspective of myocardial salvage than does treatment of the patient whose infarct is already transmural. Perhaps, as suggested by Spain\textsuperscript{24} and others,\textsuperscript{25} many heart attacks at inception are limited to multifocal areas of subendocardial necrosis. In the presence of diseased but patent coronary arteries, the subendocardial necrosis may be sufficient with or without accompanying arrhythmias to alter the hemodynamics, disturb perfusion, and set the stage for the superimposition of a thrombus, thereby converting a limited area of multifocal necrosis to a regional or transmural infarction either immediately, as in the typical transmural infarct, or after a substantial time interval, as in the patients described here.

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