PATHOPHYSIOLOGY AND NATURAL HISTORY

MYOCARDIAL INFARCTION

Myocardial infarction in young patients: an analysis by age subsets

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ABSTRACT  We examined, in age subsets, 2643 patients with acute myocardial infarction. Clinical features and 1 year morbidity and mortality were compared in 203 young patients (<45 years), 1671 patients 46 to 70 years old, and 769 elderly patients (>70 years). Ninety-two percent of young patients were men, and a family history of premature coronary artery disease was more common in young patients (41% compared with 28% of middle-aged and 12% of elderly patients). More young patients were currently smoking cigarettes (82% compared with 56% of middle-aged and 24% of elderly patients), and only 8% of young patients had never smoked. Previous myocardial infarction and history of angina pectoris or congestive heart failure were less common (p < .001) in the young patients than in middle-aged and elderly patients. In-hospital mortality was only 2.5% for young patients, compared with 9.0% in middle-aged and 21.4% in elderly patients (both p < .001). Postdischarge 1 year mortality was also strikingly low in young patients, at 2.6% compared with 10.3% in middle-aged and 24.4% in elderly patients. The incidence of reinfarction during the 1 year of follow-up was similar in all subsets. The statistical significance of 65 variables as predictors of 1 year mortality and reinfarction was tested and the following found to be significant (p < .05): hospital discharge on antiarrhythmic drugs, digoxin, or diuretics; history of previous myocardial infarction or congestive heart failure; chest x-ray findings of heart failure; low ejection fraction; and atrial fibrillation. Thus, young patients entering the hospital have an excellent 1 year prognosis, but those with prior infarction in whom there are selected abnormal findings at hospital discharge comprise a subgroup that may benefit from early aggressive management.


THERE IS A relative paucity of information concerning the clinical features, natural history, and prognosis in young patients with acute myocardial infarction. Despite the relatively low frequency of myocardial infarction in the young population, the potential for death and long-term disability make this entity an important clinical problem. A number of studies have examined the epidemiologic features and the coronary arterial anatomy in young adults with evidence of coronary heart disease, and angiographic studies have demonstrated less extensive coronary artery disease than in older patients. We reasoned, therefore, that young patients with myocardial infarction should have not only different presenting features, but also a more favorable early and late prognosis than their older counterparts. Accordingly, in the present study, we divided a large group of patients with acute myocardial infarction into subsets defined by age to examine in detail differences in risk factors, clinical features, morbidity, and mortality.

Methods

Patients. The study group was derived from 2643 patients (admitted within 24 hr of onset of symptoms) with acute myocardial infarction entered prospectively into a computerized data base maintained by The Specialized Center of Research on Ischemic Heart Disease at the University of California San Diego. Patients were entered from 1968 through 1983 and were recruited from University of California San Diego Medical Center (1968–1983, n = 577), San Diego Veterans Administration Medical Center (1980–1983, n = 228), the United States Regional Naval Medical Center in San Diego (1980–1983, n = 423), and Vancouver General Hospital, British Columbia, Canada (1976–1983, n = 1515). We have previously shown simi-
The mean ages of patients in the young, middle-aged, and elderly subsets were 39 ± 5, 60 ± 7, and 77 ± 5 years (mean ± SD, respectively). The number of hours from onset of symptoms to admission did not differ among the three subsets (6.8 ± 6.0, 6.9 ± 5.6, and 7.4 ± 5.6 hr for young, middle-aged, and elderly patients, respectively).

Symptoms on admission to the cardiac care unit did not differ among the groups. The mean stay in the hospital was 14 ± 6 days in the young and middle-aged patients and 16 ± 7 days in the elderly patients.

Clinical and prognostic variables. Procedures used in the acquisition of data and definitions of clinical and prognostic variables are detailed in previous reports.\(^{17, 18}\) We included data from the history, physical examination, laboratory studies, radiographic variables, and the electrocardiogram. Family history was considered positive when asymptomatic coronary artery disease occurred before age 60 in siblings, parents, parent’s siblings, or grandparents. Documented systolic blood pressure of 160 mm Hg or more or diastolic blood pressure of 100 mm Hg or more was considered a history of hypertension. Previous myocardial infarction was documented by electrocardiogram or hospital records. Other historical variables included: a history of angina pectoris (substantial distress of short duration related to exertion or excitement and relieved by nitroglycerin), history of congestive heart failure (shortness of breath on exertion associated with either orthopnea or paroxysmal nocturnal dyspnea), history of diabetes, lipid abnormality, smoking, and chronic obstructive lung disease. Radiographic variables included the grade of pulmonary congestion and the cardiothoracic ratio. Electrocardiographic variables included location of myocardial infarction, and presence or absence of ventricular tachycardia and fibrillation, atrial fibrillation and flutter, atrial and junctional tachycardia, bundle branch blocks, intraventricular conduction delays, and first, second, and complete heart block.

Special studies on discharge, including a radionuclide ejection fraction study and 24 hr ambulatory electrocardiographic monitoring, were obtained in all consenting patients at two hospitals, but were optional at two other hospitals for all patients admitted after 1979. In a subgroup of 756 patients (51%), the left ventricular ejection fraction was determined just before discharge. In another subgroup of 845 patients (61% of patients admitted after 1979), data from 24 hr ambulatory monitoring just before discharge were available. It is difficult to assess to what extent this bias due to patient selection might have influenced our results. We analyzed complex ventricular arrhythmias, when present, and defined them as frequent ventricular beats (more than 1 beat/min or 30 beats/hr), multiform ventricular premature beats, couplets, early ventricular beats (R-on-T phenomenon), or ventricular tachycardia (more than 3 consecutive ventricular premature beats). Heart failure in the cardiac care unit was considered to have occurred when at least two of the following were observed: S<sub>3</sub> gallop, or radiographic evidence of pulmonary congestion. Cardiac arrest, extension, pericarditis, pulmonary and systemic emboli, pneumonia, rupture of the interventricular septum and papillary muscle, cardiomyocarditis, papillary muscle dysfunction, persistent chest pain, hypotension, and shock were coded as complications. Information on the administration of digitalis, diuretics, procaínamide, quinidine, and β-blocking agents at discharge was included in the analysis. Data from the discharge physical examination, chest radiograph, and electrocardiogram were also included for patients studied after 1979.

Follow-up. All patients in this study were followed up by telephone interview at 3, 6, and 12 months after admission. Of patients eligible for 1 year follow-up, over 97% were contacted. The proportion of patients participating in the 1 year follow-up did not differ among the three age groups. Information on deaths was obtained from hospital records and the death certificate. For deaths occurring outside of the hospital, telephone interviews with the personal physician and family members were conducted to clarify details. Of the 597 deaths within 1 year, 33 or 5.5% were noncardiac (0 in young, 14/289 [4.8%] in middle-aged, and 19/298 [6.4%] in elderly patients). Sudden death was defined as that due to documented arrhythmias and when the patient was found dead and no other cause was apparent it was also recorded as sudden death. Cardiac deaths or new nonfatal myocardial infarctions (defined as for the index infarctions) within 1 year were counted as events.

Statistical analysis. Continuous clinical characteristics of patients in the three age subsets were compared by analysis of variance, and categorical variables were compared by computation of a chi-square statistic. When overall significance was achieved, pairwise comparisons were made. Univariate statistical analysis by t test was used to assess differences between young patients with myocardial infarction who suffered an event during the 1 year period of follow-up and those who did not. Survival curves for the three subsets were compared with the Mantel-Cox statistic by use of the Biomedical Computer Programs package of statistical programs (PIL).\(^{19}\)

Results

Young patients comprised 8% of the population, whereas 65% were middle-aged and 27% were elderly patients. Ninety-two percent of young patients were men, compared with 78% of middle-aged and 60% of elderly patients. Features of medical history are compared in table 1. A history of angina pectoris was documented in only 23% of young patients compared with 40% of middle-aged and 48% of elderly patients, and a previous myocardial infarction was noted in only 15% of young patients, about half the incidence observed in middle-aged and elderly patients. Congestive heart failure had occurred in only 3% of young patients, compared with 10% of middle-aged and 21% of elderly patients.

Risk factors. Only 7% of young patients were without risk factors, compared with 15% of middle-aged and 32% of elderly patients (both p < .001). Eighteen
percent of young patients had three or more risk factors compared with only 5% of elderly patients (p < .001) and 16% of middle-aged patients. A family history of coronary artery disease was common in young patients, occurring in 41%, and was recorded for 28% of middle-aged and only 12% of elderly patients (table 1). Histories of hypertension and diabetes were not prominent risk factors in young patients compared with middle-aged and elderly patients, and a history of a lipid abnormality was uncommon in all groups, although it was more often encountered in the young and middle-aged than in older patients (table 1). Smoking histories were strikingly different among the age subsets, as depicted in figure 1. Over 80% of the young patients were smoking at the time of entry into the study, compared with 56% of the middle-aged and 24% of the elderly patients. The number of patients who had never smoked or who had quit smoking increased significantly with advancing age.

**Clinical features.** The relationships between age and infarct type and location are presented in figure 2. Inferior infarctions accounted for 43% and 39% of
Infarctions in the young and middle-aged, and only 30% of infarctions in elderly patients (p < .001). The frequency of anterior infarctions, however, did not differ between age subsets. Non-Q wave infarctions in young patients were uncommon, occurring in 12%, and those of indeterminant location were also unusual, comprising only 2% of infarctions in young patients; these types were seen to increase significantly with increasing age.

The number of days spent in the coronary care unit was similar for young and middle-aged patients (4.6 ± 3.1 and 5.0 ± 3.6), but was significantly less than that for elderly patients (5.8 ± 3.3, p < .001).

When all coded complications were included, complications occurred less often in young patients. Thirty-two percent of young patients had no complications, compared with 21% of both middle-aged and elderly patients (both p < .001). Major complications are list-
ed in table 1. The incidence of congestive heart failure complicating infarction in young patients was 41%, compared with 54% in middle-aged and 71% in elderly patients. The incidence of persistent chest pain and infarct extension did not differ significantly between age subsets (table 1). Shock was unusual in all groups (2% in young patients vs 3% in middle-aged patients and 5% in elderly patients).

Figure 3 summarizes the occurrence of arrhythmias and heart block among the age subsets. Supraventricular arrhythmias increased in frequency with increasing age, occurring in 11% of young, 20% of middle-aged, and 38% of elderly patients. These differences were due to an increase in the frequency of atrial fibrillation with advancing age (5% of young, 12% of middle-aged, and 25% of elderly patients, p < .05 in each instance). The incidence of atrial flutter was similar in each age group (3% of young, 5% of middle-aged, and 7% of elderly patients). Ventricular tachycardia was seen most often in young patients (30% compared with 23% of middle-aged and 21% of elderly patients), but complex premature ventricular complexes on Holter monitoring were more common in older patients. Ventricular fibrillation, however, did not have a predilection for age. Complete heart block was more common in the elderly (10%) compared with the young and middle-aged patients (5% and 6%, respectively).

We analyzed the relationship between arrhythmias detected in the coronary care unit and the administration of antiarrhythmic therapy at discharge. Twenty-eight of the 198 young patients were discharged on antiarrhythmic drugs, and of these, 19 had ventricular tachycardia, four had ventricular fibrillation, and six had supraventricular arrhythmia. However, 65 patients had these documented arrhythmias and did not receive antiarrhythmic drugs at the time of discharge.

Hospital laboratory data and discharge variables are presented in table 1. Cardiothoracic ratios obtained from chest x-rays were similar among young and middle-aged patients with myocardial infarction, and were higher by a small but significant percent in elderly patients. The ejection fraction did not differ significantly among age subsets. Peak creatine kinase was highest in young patients, with large, significant differences observed between all age groups. The leukocyte count was also highest in the young patients, although significant differences between middle and elderly age groups were not observed. Young patients were significantly less likely to be discharged on antiarrhythmic drugs, digitalis, and diuretics than middle-aged or elderly patients. Young and middle-aged patients were discharged on β-blockers more often than elderly patients.

Cardiac catheterization data were available only for patients entered into the data base after 1979. We examined coronary angiograms of the patients within 6 weeks of hospital discharge in an attempt to ensure that the coronary anatomy reflected that present at the time.
of infarction. Coronary anatomy was described with the use of the criteria of the Coronary Artery Surgical Study (CASS).\textsuperscript{20} Of the 190 patients for whom catheterization data were available, only four of the patients had left main disease, and these were in the middle-age group. Characteristics of the coronary anatomy of the remaining patients are listed in table 2. Single- or zero-vessel disease (stenosis $>70\%$ luminal diameter) was present in 63\% (29/46) of young patients, 40\% (49/125) of middle-aged patients, and 20\% (3/15) of elderly patients. Conversely, three-vessel disease was present in only 17\% (8/46) of young patients, 27\% of middle-aged patients, and 33\% of elderly patients.

Data regarding coronary artery bypass surgery were available for patients entered into the data base between 1979 and 1984. Twenty percent of young patients underwent coronary artery bypass surgery in the year after their myocardial infarction, compared with 13\% of middle-aged patients ($p < .04$) and 2\% of elderly patients ($p < .001$). Since coronary bypass operations were reported for up to 1 year after infarction, whereas cardiac catheterization data were examined only within 6 weeks of the index infarction, the number of patients in the coronary bypass group differs from that in the catheterization group.

**Mortality and reinfarction.** Early and late mortality and reinfarction rates are presented in figure 4. Hospital mortality was 2.5\% in young patients, compared with 9.0\% in middle-aged patients and 21.3\% in elderly patients. Postdischarge mortality for patients followed for 1 year was also low in young patients at 2.6\% compared with 10.3\% in middle-aged and 24.4\% in elderly patients. However, the risk of nonfatal reinfarction for patients discharged alive and followed for 1 year was nearly identical among the three groups (5\%, 5\%, and 6\%, respectively).

Figure 5 illustrates the cumulative survival among the three age subsets beginning 24 hr after hospitalization and for up to 1 year after discharge. Ninety-five percent of young patients were alive at 1 year, compared with 88\% of middle-aged patients, and 63\% of elderly patients (both significant, $p < .001$). The percentages of deaths classified as sudden were similar among the three groups.

**Predictors of late (1 year) morbidity and mortality.** Of 65 variables tested as univariate predictors of late (1 year) death or reinfarction in young patients with myocardial infarction, the nine that were shown to be statistically significant ($p < .05$) are listed in table 3. Hospital discharge on antiarrhythmic medication was the number one predictor of an event at 1 year in young patients, followed by a history of a previous myocardial infarction, atrial fibrillation, low ejection fraction, digoxin on discharge, a history of congestive heart failure, chest x-ray findings of pulmonary congestion and increased cardiothoracic ratio, and diuretics on discharge. More patients suffering another event had received \(\beta\)-blockers at discharge compared with those who had no event (43\% vs 32\%), but this was not a statistically significant difference. Due to the small number of patients suffering an event within 1 year in the young group, a multivariate analysis of the top five predictors was performed excluding ejection fraction,

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**TABLE 2**

Number of diseased coronary arteries according to age subset\textsuperscript{a}

<table>
<thead>
<tr>
<th>No. of diseased vessels\textsuperscript{b}</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>YMI</td>
<td>7</td>
<td>22</td>
<td>8</td>
<td>8</td>
<td>45</td>
</tr>
<tr>
<td>MMI</td>
<td>8</td>
<td>41</td>
<td>43</td>
<td>31</td>
<td>123</td>
</tr>
<tr>
<td>OMI</td>
<td>1</td>
<td>2</td>
<td>5</td>
<td>5</td>
<td>13</td>
</tr>
<tr>
<td>Total</td>
<td>16</td>
<td>65</td>
<td>56</td>
<td>44</td>
<td>181</td>
</tr>
</tbody>
</table>

YMI = young patients with myocardial infarction; MMI = middle-aged patients with myocardial infarction; OMI = elderly patients with myocardial infarction.

\textsuperscript{a}Does not include four patients with left main disease (all in MMI) and six patients (one YMI, two MMI, three OMI) with variant or unknown dominance.

\textsuperscript{b}By CASS criteria ($>70\%$ stenosis).
since this was not available for all patients. The number one multivariate predictor of 1 year mortality was receipt of digoxin at the time of hospital discharge, followed by a history of congestive heart failure and atrial fibrillation.

Discussion

Analysis of subsets of patients with acute myocardial infarction has become a widely used method of determining prognosis and identifying high-risk groups that might benefit from aggressive diagnostic and therapeutic measures. The present study of age subsets shows that young patients with myocardial infarction constitute a distinct group with an extremely low hospital mortality and a relatively favorable 1 year prognosis. Young patients accounted for only 8% of the total number of patients with infarction in our series, which is similar to the findings of other studies.

![Figure 5](image-url)  
**FIGURE 5.** Cumulative 1 year survival in the age subsets. Only cardiac deaths were included in the analysis. Most deaths in young patients occurred in the first 90 days and no deaths occurred after day 240. YMI = young patients with myocardial infarction; MMI = middle-aged patients with myocardial infarction; OMI = older patients with myocardial infarction.

### TABLE 3

<table>
<thead>
<tr>
<th>Variable</th>
<th>Event (n = 19)</th>
<th>No event (n = 171)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Receiving antiarrhythmic drug at discharge (%)</td>
<td>43</td>
<td>11</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>History of previous MI (%)</td>
<td>42</td>
<td>13</td>
<td>&lt;.003</td>
</tr>
<tr>
<td>Atrial fibrillation (%)</td>
<td>21</td>
<td>3</td>
<td>&lt;.003</td>
</tr>
<tr>
<td>Ejection fraction value (%)</td>
<td>39 ± 16 (n = 9)</td>
<td>53 ± 13 (n = 60)</td>
<td>&lt;.004</td>
</tr>
<tr>
<td>Digoxin at discharge (%)</td>
<td>50</td>
<td>15</td>
<td>&lt;.004</td>
</tr>
<tr>
<td>History of CHF (%)</td>
<td>16</td>
<td>2</td>
<td>&lt;.009</td>
</tr>
<tr>
<td>Cardiothoracic ratio</td>
<td>0.52 ± 0.07 (n = 11)</td>
<td>0.47 ± 0.05 (n = 95)</td>
<td>&lt;.02</td>
</tr>
<tr>
<td>Pulmonary congestion on CXR (%)</td>
<td>74</td>
<td>43</td>
<td>&lt;.03</td>
</tr>
<tr>
<td>Diuretics at discharge (%)</td>
<td>36</td>
<td>12</td>
<td>&lt;.05</td>
</tr>
</tbody>
</table>

Total variables tested = 65; rank based on p values; p values are based on t test or chi-square. Mean values are ±1 SD.

MI = myocardial infarction; CHF = congestive heart failure; CXR = chest x-ray.

*One hundred ninety of 203 young patients were followed for 1 year and included in this analysis.
Several investigators have suggested that the most potent predisposing risk factors for coronary artery disease should be especially prevalent in this population, and this has generated intense epidemiologic interest.

**Risk factors.** Our study highlights the importance of male sex, family history, and cigarette smoking in young patients with acute myocardial infarction. A previous study has also reported a greater familial influence on the development of myocardial infarction in young compared with older patients and the authors suggested that this influence is mediated by hypertension and familial hyperlipidemia. Although family studies were not performed, we found that a history of hypertension was not a prominent risk factor for acute myocardial infarction in younger patients, a finding also supported by the work of others. A history of lipid abnormality was seen less often in young than in elderly patients, although the overall incidence was small. The true incidence of hyperlipidemia is underestimated in this study, however, since measurements of blood lipids were not obtained. Diabetes was distinctly unusual in our young patients compared with older patients, consistent with the findings of others. Familial influence, therefore, may be a result of subtle abnormalities in lipoprotein metabolism and other ill-defined factors. Our findings demonstrate a closer association of tobacco consumption with the development of myocardial infarction in young patients than in older age groups, consistent with the known significant coronary risk of tobacco consumption.

**Clinical features.** There are conflicting reports concerning the clinical course and natural history of myocardial infarction in young patients. Uhl and Farrel found a more favorable early prognosis for 165 young patients under 40 years of age compared with that for 100 patients over 40 years old, but there were no significant differences in the incidence of ventricular arrhythmias or heart failure; reinfarction rate was not different between young and old patients. Young patients in our study appeared to have more extensive infarctions, as judged by higher peak enzyme levels, a higher incidence of Q wave infarctions, and a higher incidence of ventricular tachycardia compared with those in older patients. Despite these potentially poor prognostic signs, complication rates and mortality were surprisingly low. In young patients we found that prior myocardial infarction and findings consistent with left ventricular dysfunction and/or arrhythmias at discharge were predictive of death or reinfarction within 1 year. Unlike previous reports in the general post-myocardial infarction population, ventricular arrhythmia or bundle branch block in the young patients was not predictive of an event during the first year after infarction. Atrial fibrillation, however, was highly associated with a poor outcome; it has been previously reported to be a prognostic risk factor in the general postinfarction population. Although the subset of patients for whom cardiac catheterization data were available represented a highly selected group, the results are consistent with previous studies that have demonstrated less coronary artery disease in young patients.

There are two obvious biases in the findings concerning arrhythmias. First, results of ambulatory monitoring were available for only 61% of patients admitted after 1979, resulting in selection bias. Second, the impact of antiarrhythmic therapy on 1 year survival is uncertain. Therapy was not uniformly administered to young patients at discharge, since the decision to use antiarrhythmic drugs was made by the patient's physician. Although it is frequently difficult to determine the basis for such a decision, results of our analysis of the relationship between arrhythmias (detected in the coronary care unit) and the administration of an antiarrhythmic drug at discharge were inconsistent. Thus, while arrhythmias in the coronary care unit played an important role in the decision to institute drug therapy in some patients, other factors clearly existed that our study did not address.

**Prognosis.** A favorable 1 year mortality in young patients with myocardial infarction has been reported by others, although not all authors are in agreement. In a follow-up study of 440 patients discharged from the hospital, Vedin et al. found no difference in 1 year mortality between patients less than and older than 55 years of age. Zukel et al. showed a higher first year mortality in patients with myocardial infarction who were below the age of 40, but those who survived had a more favorable long-term prognosis compared with older patients. Such disparate results may be due in part to selection bias and problems inherent in defining natural history retrospectively. We found a strikingly low hospital mortality and a comparatively low 1 year mortality rate in young patients in this large series of consecutive, unselected patients with myocardial infarction. This excellent prognosis was observed despite large myocardial infarctions, with ejection fractions and cardiothoracic ratios that were similar to those in older patients. Older patients, however, had more evidence of multisystem disease, a more frequent history of angina pectoris, myocardial infarction, and congestive heart failure.
and a higher incidence of complicating heart failure and atrioventricular block.

**Therapeutic implications.** Radtke et al.\(^{38}\) obtained favorable results with bypass surgery in 72 patients under 40 years of age (57 of whom had experienced myocardial infarction), including improved return-to-work status and exercise tolerance, despite a reduced graft patency rate. Analysis of our own patients enrolled since 1979 revealed that an increased proportion of young patients underwent coronary bypass surgery, indicating a lower threshold for operative intervention in the young and reluctance to operate on the elderly. Given the low reported incidence of multivessel and left main disease in young patients,\(^{33}\) and the favorable outlook reported herein, it seems unlikely that revascularization had a significant impact on 1 year mortality or reinfarction rate in that study. Recent reports of unfavorable long-term graft patency rates\(^{39,40}\) and the excellent 1 year prognosis that we report herein suggest that the use of revascularization in young patients, except for the management of refractory angina pectoris, should be reexamined. Young patients entering the hospital with a myocardial infarction have an excellent 1 year prognosis, but those with a prior history of infarction, a history of congestive heart failure, and atrial fibrillation during hospitalization comprise a subgroup that may benefit from early aggressive management.

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