Fatal Myocardial Infarction Following Carotid Endarterectomy

Three Hundred Thirty-five Patients Followed 6–11 Years After Operation

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Routine coronary angiography has been recommended to all patients undergoing carotid endarterectomy at the Cleveland Clinic since 1978. Patients found to have severe, correctable coronary artery disease (CAD) have been advised to undergo myocardial revascularization as a staged or combined procedure in conjunction with carotid endarterectomy in an attempt to reduce the incidence of fatal myocardial infarction during the postoperative period, and during the late follow-up interval. In order to provide an historic standard with which the results of this approach may eventually be compared, complete follow-up information has been obtained for 95% of 335 consecutive patients who underwent carotid endarterectomy between 1969 and 1973. Fatal myocardial infarction accounted for 60% of early deaths within 30 days of operation and occurred in 1.8% of the entire series. Among the patients who survived operation, the five-year mortality rate was 27%, and the 11-year mortality rate was 48%. Myocardial infarction caused 37% of the deaths that occurred within five years after operation and 38% of the deaths that have occurred within 11 years. Differences in the incidence of fatal myocardial infarction within five years after operation between a group of 116 patients who had no clinical evidence of CAD and a group of 209 patients suspected to have CAD attained statistical significance (p < 0.1) despite the fact that 67 patients suspected to have CAD eventually underwent myocardial revascularization. Improvement in actuarial survival (p < 0.05) and reduction in the late mortality rate (p < 0.01) were statistically significant for the subset of patients with suspected CAD who had aortocoronary bypass graft procedures.

Coronary artery disease (CAD) is the most common cause of early postoperative death and late death following carotid endarterectomy. Ennix and associates recently reported operative mortality rates following carotid endarterectomy of 18.2%, for patients with angina pectoris, and 1.5%, for patients who had no cardiac symptoms. According to several large published series, myocardial infarction is responsible for 50–70% of all late deaths among patients who undergo carotid reconstruction, occurs with even greater frequency among patients who have preoperative evidence of CAD, and accounts for three to five times the number of late deaths caused by stroke. In a series of patients followed for more than five years after carotid endarterectomy performed for transient ischemic attacks (TIA), DeWeese and associates determined late mortality rates of 27% for patients who had no clinical indication of CAD at the time of operation and 56% for those with suspected CAD. Thompson and associates found that myocardial infarction caused 52% of late deaths and stroke only 16% of late deaths in a series of 592 patients followed as long as 13 years after carotid endarterectomy.

Recent reports indicate that patients who have had direct myocardial revascularization with the use of coronary artery bypass grafts experience fewer cardiac complications after subsequent vascular and other major operations than would be expected even in the absence of known CAD. Since patients who have extracranial cerebrovascular disease appear to be at a particularly high risk for late postoperative cardiac complications, routine coronary angiography has been recommended to all patients undergoing carotid endarterectomy at the Cleveland Clinic since 1978. As described in a previous report, severe, correctable coronary artery lesions were documented using this format in 55% of the patients scheduled for abdominal aortic reconstruction who had preoperative evidence of CAD and in 17% of those with nonclinical indication of CAD. Elective myocardial revascularization was performed in 24% of the patients in this in-

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vestigation, and 96 patients underwent aortic reconstruction, with a single postoperative death which was unrelated to CAD. During the same study period, 27% of patients who required carotid endarterectomy also underwent elective myocardial revascularization as a staged or combined procedure to correct severe CAD discovered during routine coronary angiography.

Because routine coronary angiography and, if indicated, myocardial revascularization continue to be recommended without prospective randomization to all patients under consideration for elective peripheral vascular operations at this institution, historic standards will be necessary to evaluate the effect of this approach on late survival. Previous publications described the influence of CAD on survival of 616 patients who had abdominal aortic aneurysm resection or lower extremity revascularization at the Cleveland Clinic between 1969 and 1973. This report presents a series of 335 consecutive patients who required carotid endarterectomy during the same five-year period. Late follow-up information was obtained by telephone contact with each patient, a close surviving family member, or the referring physician and is complete for 95% of the patients.

**Patient Information**

The 335 patients in this series consisted of 235 men and 100 women with an age range of 31–81 years (mean: 60 years). Thirty-seven patients (11%) were less than 50 years of age at the time of operation, 127 patients (38%) were 50–60 years of age, 138 patients (41%) were 60–70 years of age, and 33 patients (10%) were over 70 years of age. The indications for operation are given in Table 1. Previous hemispheric or vertebrobasilar neurologie symptoms had occurred in 252 patients (75%). Eighty-three patients (25%), most of whom were scheduled for elective myocardial revascularization or another peripheral vascular procedure, had asymptomatic carotid bruits and underwent prophylactic carotid re-construction after severe carotid stenosis had been demonstrated by angiography. The 335 patients in this series underwent a total of 390 carotid endarterectomies during the study period, and 105 patients (31%) required another cardiovascular procedure in conjunction with carotid reconstruction.

**Atherosclerotic Risk Factors**

Two hundred thirty patients (69%) had hypertension under medical treatment or blood pressure measurements greater than 150/90 mmHg. Diabetes mellitus under medical treatment, an abnormal glucose tolerance test, or a fasting or two-hour postprandial blood glucose level greater than 120 mg/dl were present in 127 patients (38%). The serum cholesterol value ranged from 50–750 mg/dl (mean: 247 mg/dl) and was greater than 270 mg/dl in 93 patients (28%). The serum triglyceride value ranged from 51–3350 mg/dl (mean: 219 mg/dl) and was greater than 180 mg/dl in 124 patients (37%). A total of 254 patients (76%) either smoked cigarettes or had discontinued their chronic use of cigarettes less than five years before their operations.

**Preoperative Cardiac Status**

No history of previous CAD symptoms or known cardiac disease could be elicited from 175 patients (52%). Historic information obtained from the remaining 160 patients, their families, or their referring physicians, was consistent with previous myocardial infarction in 33 patients (10%), angina pectoris in 68 patients (20%), congestive heart failure in seven patients (3%), arrhythmias requiring medical management in four patients (1%), and two or more of these factors in 48 patients (14%).

The preoperative electrocardiogram (EKG) was normal in 153 patients (46%). Previous myocardial infarction was documented by EKG evidence in 63 patients (19%) while 108 patients (32%) had ischemic myocardial changes within the ST-T segments. Six patients (2%) had arrhythmias on preoperative EKG tracings, and five patients (1%) had two or more abnormal EKG findings.

Considering those features which are most suggestive of CAD by history (previous myocardial infarction, angina pectoris) or by EKG findings (previous myocardial infarction, ischemic myocardial changes), 118 patients (35%) had no preoperative evidence of CAD, 35 patients (10%) had CAD by history alone, 57 patients (17%) had CAD on the basis of EKG findings alone, and 125 patients (38%) had CAD according to both history and EKG information.
of the 105 patients who underwent carotid endarterectomy as a staged operation preceding other planned cardiovascular procedures had fatal complications before the second operation could be performed. The other three deaths attributable to carotid endarterectomy occurred within a group of 230 patients (1.3%) for whom no other operations were anticipated.

**Late Mortality Rate**

Eighteen patients (5%) were lost to follow-up during the maximum observation interval of 11 postoperative years. The principal causes of late mortality among 325 operative survivors in this series are given in Table 2. A total of 155 patients (48%) have died, and myocardial infarction was the principal cause of death in 59 patients (38%). Myocardial infarction was responsible for more than twice the number of late deaths produced by either of the next leading sources of late mortality, stroke or malignant neoplasm.

Complete life table data for the 325 patients who survived operation are given in Table 3. Eighty-seven patients (27%) died within five years of operation. Myocardial infarction was the principal cause of death in 32 patients, accounting for 37% of the deaths and affecting 10% of those patients who survived carotid endarterectomy. Of the 238 patients who lived at least five years after operation, 68 patients (29%) have subsequently died within five to 11 years. Myocardial infarction was responsible for 27 (40%) of these deaths, affecting 11% of the five-year survivors. A total of 59 (18%) of the 325 operative survivors have had fatal myocardial infarctions during the full follow-up interval of 11 years.

Considering the 325 operative survivors in this series, 209 patients had some indication of CAD on the basis of their previous cardiac history or preoperative

**Table 2. Causes of Late Mortality Among 325 Operative Survivors from One to Eleven Years after Operation**

<table>
<thead>
<tr>
<th>Principal Cause of Death</th>
<th>Number</th>
<th>Per Cent of Deaths</th>
<th>Per Cent of Operative Survivors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Myocardial infarction</td>
<td>59</td>
<td>37</td>
<td>18</td>
</tr>
<tr>
<td>Stroke</td>
<td>26</td>
<td>17</td>
<td>8</td>
</tr>
<tr>
<td>Malignant neoplasm</td>
<td>15</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>9</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Aortoenteric fistula</td>
<td>2</td>
<td>1</td>
<td>0.5</td>
</tr>
<tr>
<td>Ruptured aortic aneurysm</td>
<td>1</td>
<td>0.5</td>
<td>0.25</td>
</tr>
<tr>
<td>Intestinal ischemia</td>
<td>1</td>
<td>0.5</td>
<td>0.25</td>
</tr>
<tr>
<td>Other, or unknown</td>
<td>39</td>
<td>26</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>155</td>
<td>100</td>
<td>48</td>
</tr>
</tbody>
</table>

**Results**

**Postoperative Mortality Rate**

A total of ten deaths occurred within 30 days of operation, resulting in a patient mortality rate of 3.0% and a procedure mortality rate of 2.6%. Four of these patients had no complications related to carotid endarterectomy but died following cardiac or other peripheral vascular procedures performed during the same hospital admission. Therefore, carotid reconstruction alone was responsible for a patient mortality rate of 1.8% and a procedure mortality rate of 1.5%. Myocardial infarctions caused six postoperative deaths, and two patients sustained fatal strokes. Another patient died with massive intestinal infarction, and the remaining death was caused by irreversible coagulopathy following subsequent abdominal aortic aneurysm resection.

Preoperative atherosclerotic risk factors or advancing age were not associated with statistically significant differences in postoperative mortality. Three (2.9%)
EKG findings, while 116 patients had no clinical evidence of CAD. Figure 1 presents graphic representation of life table data for these two groups, together with similar information for a normal 1970 male population of the same age (60 years) and for a group of 601 patients with known CAD documented by coronary angiography at the Cleveland Clinic, which has previously been reported by Proudfit and associates. The five- and ten-year survival rates following carotid endarterectomy were 78 and 24% for patients without evidence of CAD, and 70 and 14% for patients suspected to have CAD. Statistical analysis of survival curves determined that late survival of patients in this series who were suspected to have CAD was significantly worse (p < 0.05) than that of the normal male population throughout the entire follow-up interval. Moreover, there was no statistical difference in survival rates during the first eight postoperative years between patients suspected to have CAD in this series and those with proven CAD described by Proudfit. The late survival of patients who had no preoperative evidence of CAD closely approximated that of a normal male population within the first four years after operation, but differences in survival did become significant (p < 0.05) beyond the fifth postoperative year.

The five-year and 11-year incidences of fatal myocardial infarction were 5 and 13% for patients without clinical evidence of CAD, and 12 and 21% for patients suspected to have CAD (p < 0.1). The group of 209 patients suspected to have CAD by history or EKG findings included 67 patients who underwent direct myocardial revascularization with the use of aorto-coronary bypass grafts as staged or combined operations in conjunction with carotid endarterectomy, or as incidental procedures performed during the late follow-up interval. The remaining 142 patients did not receive myocardial revascularization and, with few exceptions, were not evaluated by coronary angiography. Figure 2 contains graphic representation of life table data for these two subsets of patients together with similar information for a normal male population of the same age and the 601 patients with documented CAD reported by Proudfit. Differences in late survival between patients who underwent direct myocardial revascularization and those who did not were statistically significant (p < 0.05) throughout the first eight years after operation. Decline in the slope of the survival curve during the ninth and tenth years after operation for patients who had myocardial revascularization represented three deaths among only seven patients still eligible for consideration, and did not permit accurate statistical analysis. A total of 201 patients were available for follow-up for at least five years after operation. During this interval, there were no significant differences in survival between patients who underwent myocardial revascularization and the normal male population, or between patients with suspected but surgically untreated CAD and the series of patients with documented CAD described by Proudfit. Crude five-year and 11-year mortality rates were 37 and 58% for patients with suspected but surgically untreated CAD, and 15 and 34% for those having myocardial revascularization.

The influence of age at the time of operation on early postoperative mortality rates, five- and 11-year mortality rates, and the incidence of fatal myocardial infarction is shown in Figure 3. As might be expected, advancing age was associated with an increase in late mortality from all causes. Fatal myocardial infarction accounted for 41% of all late deaths affecting 17% of
between patients with a positive cardiac history and abnormal EKG findings and those with no clinical evidence of CAD were highly significant (p < 0.05).

Among preoperative atherosclerotic risk factors, only diabetes mellitus had a limited correlation with late mortality. One hundred twenty-three diabetics and 202 nondiabetics survived carotid endarterectomy. Of these, 43 diabetics (35%) and 44 nondiabetics (22%) died within five years of operation (p < 0.02), and myocardial infarction was the principal cause of death in 14 patients (11%) and 18 patients (9%), respectively. The total 11-year mortality rate was 54% for diabetics and 44% for nondiabetics, and myocardial infarction was the cause of death in 21 and 15%, respectively. With the exception of the five-year mortality rate, no significant differences were identified in these subsets of patients. Mortality rates and the incidence of fatal myocardial infarctions among hypertensive patients were virtually identical to those among patients who did not have hypertension.

**Discussion**

This report concludes a series of three publications describing the impact of CAD upon operative mortality and late survival of all patients who underwent abdominal aortic aneurysm resection,7 lower extremity revascularization,8 and carotid endarterectomy at the Cleveland Clinic between 1969 and 1973. This period of study was selected at the time these investigations were begun in 1979 because a minimum follow-up interval of five years was available for all patients, surgical management and operative mortality were at least comparable to those presently reported, and contemporary medical management of CAD with agents such as propranolol were not arbitrarily excluded from consideration. Late deaths were attributed to myocardial infarction only on the basis of convincing information or death certificates provided by close surviving family members, referring physicians, hospital

### Table 4. Total Incidence of Fatal Myocardial Infarction According to Preoperative Cardiac Status

<table>
<thead>
<tr>
<th>Preoperative Cardiac Status</th>
<th>Patients</th>
<th>Fatal Myocardial Infarction</th>
<th>Postoperative</th>
<th>Late (1–11 Years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative cardiac history and normal EKG</td>
<td>118</td>
<td>Number of Patients</td>
<td>1</td>
<td>0.8</td>
</tr>
<tr>
<td>Previous myocardial infarction or angina by history alone</td>
<td>35</td>
<td>Number of Patients</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Previous myocardial infarction or myocardial changes by EKG alone</td>
<td>57</td>
<td>Number of Patients</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Positive cardiac history and abnormal EKG</td>
<td>125</td>
<td>Number of Patients</td>
<td>5</td>
<td>4.0</td>
</tr>
</tbody>
</table>

Late incidence calculated on the basis of operative survivors.
records, civil authorities, or former employers. The actual incidence of fatal myocardial infarction in this investigation undoubtedly is higher than that reported since the cause of sudden death was considered as unknown and since approximately 5% of patients were lost to follow-up.

The results of this study suggest that late survival among patients who have any indication of CAD on the basis of previous cardiac symptoms or abnormal EKG findings at the time of carotid endarterectomy is more closely comparable to survival demonstrated by patients with significant CAD documented by coronary angiography than to that of the normal population of the same age. Patients with preoperative evidence of CAD sustained a statistically significant number of fatal myocardial infarctions throughout the 11-year follow-up interval, and late death from complications of CAD appeared to be especially prevalent among patients less than 50 years of age at the time of carotid reconstruction. Unlike the 616 patients who underwent aortic aneurysm resection or lower extremity revascularization at this institution during the same period of study, there were no statistically significant differences in actuarial survival between patients suspected to have CAD and those with no clinical evidence of CAD or in the incidence of fatal late myocardial infarction between diabetics and non-diabetics following carotid endarterectomy. This disparity is best explained by the fact that the course of one out of every three patients suspected to have CAD in this report was altered by direct myocardial revascularization performed as a staged or combined procedure in conjunction with carotid endarterectomy, or as an incidental operation during the late follow-up period. Improvement in actuarial survival and reduction in the late mortality rate for patients with suspected CAD who received myocardial revascularization were highly significant and were probably responsible for observed differences between subsets of patients with suspected CAD in this series in comparison to similar patients with aortic aneurysms or lower extremity ischemia.

Although improved patient selection and advances in the technology of intraoperative cerebral protection have enhanced the safety of elective extracranial cerebrovascular repair during the past 15 years, the impact of fatal myocardial infarction on the late survival rate following successful operations has remained remarkably constant. In this report, the postoperative survival rates at five years and at ten years were 73 and 18% for all operative survivors, 78 and 24% for patients without clinical evidence of CAD, and 70 and 14% for those suspected to have CAD who did not undergo myocardial revascularization. Fatal myocardial infarctions caused 37% of the deaths that occurred within five years of operation and 38% of the deaths that occurred within ten years. In 1965, DeBakey and associates reported five-year survival rates of 68% for all patients following extracranial operations, 83% for patients without clinical evidence of CAD, and 64% for patients suspected to have CAD. DeWeese and associates described a five-year survival rate following carotid endarterectomy of 66% and found that myocardial infarction caused 71% of all late deaths involving 24% of their entire series. Thompson and Toole and their associates observed that myocardial infarction accounted for approximately three times the number of late deaths in patients with carotid atherosclerosis than did stroke, irrespective of whether the extracranial disease received surgical correction, medical management, or no treatment at all.

Patients with documented CAD who undergo direct myocardial revascularization have been reported to sustain fewer cardiac complications after subsequent vascular and other major operations than otherwise would be expected. Ennix and associates found that perioperative myocardial infarctions at the time of carotid endarterectomy occurred in 13% of patients who had angina pectoris and in only 0.8% of patients who had no clinical evidence of CAD. In a series of 1238 patients who underwent 1546 carotid procedures, the operative mortality rates were 1.5% for patients without CAD, 18% for patients with angina pectoris who underwent carotid endarterectomy alone, and 3% for patients with angina pectoris who underwent simultaneous carotid endarterectomy and myocardial revascularization. Crawford and associates presented a series of 358 patients who underwent 484 subsequent operations at various intervals following direct myocardial revascularization, including 308 vascular procedures in 232 patients. Only four operative deaths (0.8%) occurred following these subsequent procedures, and only 12 patients (3%) died from cardiac causes within a five-year follow-up period. The five-year actuarial survival for 97 patients with carotid atherosclerosis and CAD was 73% following carotid endarterectomy alone and was 88% following carotid endarterectomy in conjunction with direct myocardial revascularization. Other reports from medical centers with extensive experience with coronary artery bypass indicate that five-year survival rates of 90% or greater may be expected following direct myocardial revascularization even in patients who previously had CAD involving multiple coronary arteries, and that the prospects for extended survival are enhanced if coronary bypass is performed before myocardial damage has occurred.
Considering the ominous implications of CAD in patients with extracranial cerebrovascular disease, routine coronary angiography has been recommended to all patients undergoing carotid endarterectomy at the Cleveland Clinic since 1978. Although late follow-up information is not yet available for patients whose management presently is determined with the use of routine coronary angiography, this report describes an historic control group with which such patients will eventually be compared in an effort to define those patients for whom survey coronary angiography and, if indicated, myocardial revascularization are advisable for safe carotid reconstruction and improved late survival rates.

Acknowledgments

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References