Left Main Coronary Artery Stenosis
The Influence of Aortocoronary Bypass Surgery on Survival
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SUMMARY A retrospective study was carried out in 114 unoperated and 197 operated patients having left main coronary artery (LMCA) stenosis ≥ 50%. Including the operative mortality of 9.1%, survival at seven years was significantly greater following pure aortocoronary bypass graft surgery, 77.5% as compared to 48.5% for the unoperated patients (P < 0.01). The surgical mortality was significantly less during the last five years (1972-1976), 6.2% as compared to 17% during 1969-1971 (P < 0.025). The three year survival in patients operated since 1972 was 90.2% as compared to 60.4% for unoperated patients. Survival remained significantly higher in the operated patients when studied as subsets on the basis of the severity of the LMCA stenosis (< 70% as opposed to ≥ 70%), and on the extent of associated obstructive disease of major coronary arteries (0-1 versus 2-3 arteries). It was significantly higher, however, only in operated patients with associated stenosis ≥ 70% of the right coronary artery. Survival was higher following surgery only when the ejection fraction was at least 0.45, or the left ventricular end-diastolic pressure below 20 mm Hg.

LEFT MAIN CORONARY ARTERY (LMCA) STENOSIS was said to have an extremely poor prognosis.1,2 A retrospective study of survival in unoperated and operated patients having LMCA stenosis was carried out in our institution to evaluate the possible beneficial effect of surgery concerning longevity.

Material and Methods
Three hundred and fifty cases of LMCA stenosis reducing the lumen by at least 50% were identified among the 10,000 patients subjected to selective coronary arteriography from January 1968 to December 1976 (3.6%). Excluded were eight patients who died as a consequence of coronary arteriography, 16 patients who had associated valvular or other cardiac anomalies, 21 patients in whom internal mammary artery implantation was achieved with or without aortocoronary bypass surgery, and four patients who had associated left ventricular wall resection. Of the remaining 301 patients, 10 were operated upon after a minimum period of one year on medical therapy and were thus included in the unoperated as well as in the operated cohorts. Because of the changes in clinical and angiographic findings, baseline data were recorded twice for these 10 patients, at the time of entry in the unoperated cohort, and before surgery. The study is thus based on 114 unoperated and 197 operated cases out of a total of 301 patients. There were 267 males and 34 females. Their age varied between 34 and 71 years, with a mean of 49.8 ± 8. The LMCA stenosis reduced the lumen by 50% to 65% in 173 cases and by at least 70% in 128. In 10 patients, complete obstruction of the LMCA was observed (fig. 1). LMCA stenosis without significant narrowing (≥ 50%) of other coronary arteries was present in only 11 cases (3.5%).

Effort angina was graded according to the Canadian Cardiovascular Society classification.3 Unstable angina was considered when one of the following two conditions were present during the preceding month, with or without previous stable angina: 1) a crescendo pattern or rapid progression in severity; 2) unprovoked pain lasting more than 15 minutes. The diagnosis of heart failure was based on objective clinical and radiological signs. Old myocardial infarction was identified on the electrocardiogram in the presence of abnormal Q waves in at least two leads. A downsloping or horizontal depression of at least 1 mm of the ST segment as well as symmetrical inverted T waves were considered as ischemic ECG changes.

Selective coronary arteriography was performed with pre-shaped catheters in most cases. Cineventriculograms were obtained in a 30° right oblique projection. The ejection fraction was calculated by the method described by Kennedy et al.4 in 90 unoperated patients and in 155 operated patients who had technically adequate ventriculograms.

The only detected significant differences between both groups were a lower ejection fraction and a higher left ventricular end-diastolic pressure in patients of the unoperated cohort, as shown in table 1. No significant difference was observed with respect to mean age, duration of clinical manifestations, history of myocardial infarction, incidence of unstable angina, degree of effort angina, presence of congestive heart failure, and resting ECG abnormalities. These baseline characteristics were compared using Student's t-test, Chi-square or Fischer's exact test. Associated involvement of other coronary arteries did not appear to differ, nor was there any difference found in the degree of obstruction of the various coronary arteries (fig. 1).

Saphenous vein aortocoronary bypass was performed in all cases except in two patients who had an internal mammary artery anastomosis. Five patients also had right coronary artery endarterectomy. The mean number of bypasses per patient was 2.5. Postoperative angiographic studies were carried out in 30 patients, 16 to 18 months after surgery as part of postoperative control evaluations in two series of consecutive patients.5 Graft patency was observed in 83.3% (60/72).

Zero time was coronary arteriography for the unoperated patients and surgery for the others. The choice of therapy was not standardized and indications for surgery varied among the participating physicians. Most survivors of the operated group were examined at a special follow-up clinic and information about the unoperated patients was obtained through patient or physician contact. The mean follow-up

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period was 26.2 ± 24 months for the unoperated patients and 28.6 ± 21.9 months for the operated patients.

Survival curves were obtained using the life table method described by Cutler and Ederer\(^a\) (table 2). The significance of differences in survival curves was determined by the Chi-square procedure described by Mantel,\(^b\) and the difference of survival rates at each yearly interval was tested by a Z score.\(^c\) We have not indicated the statistical significance of differences between two groups when effective number of patients exposed to the risk of dying during a yearly interval was below 15.

**Results**

Thirty-four of 114 unoperated patients died during the first five years but no death was recorded during the subsequent three years of observation. The surgical mortality (within the first month) was 9.1% (18/197). It was 17% (9/53) during the first two years and 6.2% (9/144) since 1972 (\(P < 0.025\)). All deaths during the first year interval in the operated patients occurred within the first month. There were 10 late deaths over a seven year period among the operated patients.

The survival curve of operated patients was significantly higher than that of the unoperated patients, as shown in figure 2. The proportion of survivors at seven years was 77.5% in the operated patients, as compared to only 48.5% in the unoperated cohort (table 2). The difference is even greater in patients who have entered the study since 1972, the 3 year survival being 90.2% in the operated patients as compared to 60.4% in the unoperated (fig. 3). No significant difference is observed between the groups of patients treated before 1972.

When the patients were divided on the basis of the severity of narrowing of the LMCA, \(< 70\%\) or \(\geq 70\%\), the differences in survival between the operated and unoperated cohorts remained significant (fig. 4). Similarly, survival was significantly better in operated patients with associated obstructive disease (stenosis \(\geq 50\%\)) of less than two major coronary arteries as well as with involvement of two to three
Figure 2. Survival curves of patients with left main coronary artery stenosis ≥ 50%. In this figure and subsequent ones, the number of patients in each group refers to the number of patients at zero time. The number indicates that the effective number of patients exposed to the risk of dying during that yearly interval in either cohort is less than 15. NS = not significant.

Arteries (fig. 5). Operated patients, however, did not have a significantly greater survival when there was no significant associated disease of the right coronary artery (stenosis ≥ 70%, with right dominant or balanced circulation pattern), as shown in figure 6. Survival curves were significantly different in patients having a significant obstruction of the right coronary artery, a greater survival being observed in the operated cohort.

As shown in figure 7, survival was significantly greater in operated patients having an ejection fraction between 0.45 and 0.59, but it was not significantly different in patients with ejection fractions below 0.45 or above 0.59. The mean ejection fraction was similar in the operated and unoperated cohorts with ejection fractions between 0.45 and 0.59 (0.51 ± 0.04 and 0.52 ± 0.05), and also above 0.59 (0.67 ± 0.05 and 0.67 ± 0.05). It was significantly higher in the operated patients as compared to the unoperated patients for cohorts with ejection fractions below 0.45:

Figure 3. Survival curves of patients with left main coronary artery stenosis ≥ 50% divided on the basis of the time of entry in the study: during the period 1968-1971 in the left panel and during 1972-1976 in the right panel.

Figure 4. Survival curves of patients with LMCA stenosis divided on the basis of the severity of the narrowing, 50 to 65% in the left panel, and ≥ 70% in the right panel.

34.6 ± 8.6 versus 29.8 ± 9.2 (P < 0.05). When patients with an ejection fraction of at least 0.45 are considered, the survival curve is significantly higher for the operated patients (Chi^2 = 6.95; P < 0.01) and the five year survival is 83 ± 12% for the operated cohort as compared to 55 ± 20% for the unoperated cohort (P < 0.03).

Survival was greater in the operated cohort with a left ventricular end-diastolic pressure below 20 mm Hg, but the difference in survival was not significant among patients with a pressure ≥ 20 mm Hg (fig. 8). The mean diastolic pressure was similar (10 ± 3 mm Hg) in operated and unoperated patients for cohorts with pressures below 20 mm Hg, but for cohorts with pressures ≥ 20 mm Hg, it was higher in the unoperated patients (27 ± 4 as compared to 23 ± 3).

Discussion

LMCA stenosis is most commonly associated with significant obstructive disease of other coronary arteries. Of reported cases of LMCA stenosis 0 to 27.6% were isolated lesions, 1, 2, 9-14 an average of 5.8% for these combined cases,
including ours (37/640). Because of its low incidence, it has thus far been impossible to define the natural history of isolated LMCA stenosis. Nonetheless, the prognosis of this lesion associated with involvement of other arteries was initially thought to be extremely poor, a risk of dying during the first year exceeding 40% being reported.12, 16 Most series, however, dealt with small numbers and the observation periods did not exceed two years.1, 2, 10, 15, 16 In our series, as well as in Lim et al.'s study,17 the mortality was highest during the first year after diagnosis and it is less impressive during subsequent years. There is in our series a plateau phenomenon in the survival curve after five years, as previously noted by Humphries et al.18 concerning triple vessel involvement. Although the prognosis is indeed poor, it appears to have been grossly exaggerated. Bruschke et al.9 found a 43% survival rate in 37 patients with LMCA stenosis ≥ 50% over a five year period. Lim et al.19 studied 141 patients for a minimum period of five years and reported a 49% survival, which is similar to that found in our series. Survival in patients having LMCA stenosis is not different from that in patients with triple coronary artery disease, namely 40% to 50% over a five year period.8, 13, 18

The effect of aortocoronary bypass surgery on survival is not clearly defined. Most reports are based on small series of patients and the follow-up periods seldom exceed two years. Many authors conclude that survival does not appear improved by surgery10, 11, 15, 19 and that it should be recommended only for disabling angina. Others suggest that survival may be enhanced and thus surgical management with the hope of prolonging life may be a rational approach.12, 14, 20-23 In a study of LMCA stenosis ≥ 50%, Talano et al.12 reported 82% survival in 89 patients one year after surgery whereas only 61% of 32 medically treated operable patients were still alive (P < 0.05). Cohen and Gorlin20 reported a risk of death at 24 months of 43.6% in 17 medically treated patients as compared to 12.5% in 40 operated patients having narrowing of at least 50% of the LMCA (P < 0.05). It should be noted that over 80% of their patients had a normal ejection fraction. Pichard et al.22 reported 76.1% three year survival in medically treated patients (35/46) as compared to 90.4% in operated patients (47/52) with LMCA stenosis ≥ 70%. In a prospective randomized controlled trial in patients with angina pectoris and left main stenosis ≥ 50%, Takaro et al.23 found a significant difference in cumulative survival rates at 30 months: 65% in 53 medically treated patients as compared to 82% in 60 operated patients.

Most deaths occur early after operation.10, 12, 14, 20 The operative mortality has been reported from 3.4% to 28%.2, 10-15, 19-25 In our experience, it has improved markedly, decreasing from 17% in the first two years of this study to 6.2% during the subsequent five years, that is, during 1972 to 1976 (P < 0.025). Cohen and Gorlin have also noted an improvement from 20% to 6.2%.20 The difference in survival between unoperated and operated patients in our series became apparent with improvement in the operative mortality (fig. 7).

In a study without randomization of patients the difference in survival may be explained by obvious or undetected differences between the cohorts. In our study, the
operated and unoperated cohorts appeared quite similar except for low ejection fractions and a higher left ventricular end-diastolic pressure in the unoperated cohort. In the subgroups with ejection fractions of at least 0.45 or with a left ventricular end-diastolic pressure below 20 mm Hg, these parameters were not different, and survival was still significantly higher in the operated cohorts. Nevertheless, similarity between these subgroups is not certain and the results remain suggestive evidence only.

Our findings are similar in many respects to those observed in the randomized trial reported by Takaro et al. In both studies, surgery appears to improve survival in patients with LMCA stenosis of at least 50%, but there is no evidence that it does so in LMCA stenosis without associated significant disease of the right coronary artery. It is of interest that our study shows in addition that survival remains greater following surgery whether the LMCA stenosis is slight or critical (below 70% as opposed to 70% or greater), and whether associated obstructive disease of other major coronary arteries is slight or extensive (involvement of 0 to 1 artery as compared to associated double or triple vessel disease).

Takaro et al. found a statistically higher survival in operated patients with “some abnormality of left ventricular function,” but not in patients with “a normal left ventricular function.” There were no significant differences, however, in cumulative survival rates of operated and unoperated patients divided in subsets on the basis of an ejection fraction greater or less than 50%. Our study suggests that patients with slight to moderate impairment of left ventricular function, as defined by an ejection fraction between 0.45 and 0.59, seem to have a greater survival following surgery (fig. 7). Although the mean ejection fraction was identical for both cohorts in the 0.45 to 0.59 range, one cannot be entirely certain that these cohorts were at equal risk concerning this parameter taken as an expression of left ventricular function. Survival curves were not different in patients having an ejection fraction of at least 0.60, but this may be due to the small number of such patients in the unoperated cohort. When all patients with an ejection fraction of at least 0.45 are considered, survival is significantly greater in operated patients. On the other hand, survival is not significantly different in patients having an ejection fraction below 0.45, but this finding may not be reliable because the mean ejection fraction is significantly lower in the unoperated cohort and the number of patients involved is small. These comments also apply to the lack of significance between survival curves of operated and unoperated patients having a left ventricular end-diastolic pressure at or above 20 mm Hg. It seems that the influence of left ventricular function with respect to survival is not clear in our study, nor in Takaro et al.’s report. Patients with slight to moderate impairment of left ventricular contraction tend to have an improved survival following surgery, but there is no definite evidence that patients with normal nor with markedly abnormal left ventricular function have the same benefit.

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