A life table and Cox regression analysis of patients with combined proximal left anterior descending and proximal left circumflex coronary artery disease: non–left main equivalent lesions (CASS)

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ABSTRACT Combined proximal left anterior descending and proximal left circumflex artery stenoses ≥70% have been referred to as "left main equivalent" lesions. We compared the survival rates of medically treated patients who have this type of coronary anatomic characteristics with the survival rates of patients who have left main coronary artery stenoses ≥70% by use of a stratified life table approach and a Cox regression model. Comparison of the patients with left main coronary artery stenoses with those who have left main equivalent lesions by use of life table analysis and three different calculations of patient exposure time revealed a poorer prognosis for the patients who had left main coronary artery disease (p ≤ .04 for all three methods). The stepwise Cox analysis also determined that patients who had left main artery stenoses had a significantly poorer prognosis than patients who had left main equivalent coronary disease (p = .002), even after consideration of important baseline variables known to affect survival rates. We then compared the patients who had combined proximal left anterior descending and proximal left circumflex artery disease with patients who had combined stenoses ≥70% in the nonproximal left anterior descending and proximal circumflex coronary arteries to determine if location of the left anterior descending stenosis influenced survival rates. The 5 year survival rate was not as high for the patients who had proximal left anterior descending artery disease (55% vs 70%, p = .001). In conclusion, combined proximal left anterior descending and proximal left circumflex artery disease identifies a high-risk (as determined by angiography) patient subset. It is not, however, prognostically equivalent to left main coronary artery disease.

Circulation 68, No. 6, 1163–1170, 1983.

THE PROGNOSIS for patients who have coronary artery disease is determined in part by the number of diseased vessels and the functional state of the left ventricle.1–3 Characteristics of survival are also determined by the location and degree of luminal narrowing, a limitation of the conventional angiographic classification of patient subgroups into groups having single-, double-, and triple-vessel coronary disease.4–6 Several angiographic studies have shown an increased risk of cardiac events in patients who have severe left main coronary artery disease.7,8 Randomized and observational studies of patients with left main coronary artery disease have determined that the risk can be decreased for specific groups of patients who undergo aortocoronary bypass grafting.7,8

Combined proximal left anterior descending and left circumflex coronary artery (left main equivalent [LMEQ]) disease may jeopardize left ventricular myocardium to the same extent as a corresponding degree of left main stenosis. However, the natural history of the LMEQ lesion is not completely understood, in part because of the relative absence of published survival data for large numbers of medically treated patients with LMEQ disease. In the several randomized studies that have been published patients have not been stratified according to presence or absence of LMEQ disease, and it is presently not clear if bypass surgery

Vol. 68, No. 6, December 1983

The Collaborative Study in Coronary Artery Surgery is funded by the National Heart, Lung and Blood Institute, Bethesda, MD.
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Received August 10, 1982; revision accepted August 4, 1983.
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prolongs life in the subgroup of patients with LMEQ disease.9, 10

The aim of the present study is to determine whether LMEQ disease is really equivalent to left main coronary artery disease and to examine the hypothesis that the location of obstruction of the left anterior descending coronary artery is important in determining long-term survival.

Materials and methods

Patients. The Coronary Artery Surgery Study (CASS) registry contains 24,959 patients who underwent coronary angiography between 1975 to 1979 for suspected or proven coronary artery disease. The three groups of patients selected for the present study contain 2619 patients who did not have coronary bypass surgery before enrollment.

The group with LMEQ disease consisted of 1018 patients who had combined stenoses of \( \geq 70\% \) in the proximal left anterior descending and proximal circumflex coronary arteries. Each patient in this group had a stenosis \( \geq 70\% \) in the proximal left anterior descending coronary artery before the first septal perforator and a stenosis \( \geq 70\% \) in the proximal circumflex artery before the first obtuse marginal branch in the absence of left main coronary artery disease.

The group with left main coronary artery (LM) disease contained 859 patients who had stenoses of \( \geq 70\% \) in the left main coronary artery. The third patient group contained 742 patients who had combined stenoses of \( \geq 70\% \) of the left anterior descending coronary artery (distal to the proximal segment) and the proximal circumflex coronary artery and who had no obstructive disease in the proximal left anterior descending or left main coronary arteries (MIDLAD group).

The baseline characteristics for the three patient groups are summarized in table 1. Patient enrollment ended on May 31, 1979. Vital status and coronary bypass surgery statistics as of July 19, 1982 were known in 99\% of patients.

Clinical and catheterization variables. The definition of clinical variables used in the CASS study have been described in previous reports.12 The score for congestive heart failure was calculated based on the number of positive responses when a history of congestive heart failure was obtained, use of diuretics, use of digitalis, and the presence or absence of pulmonary rales on the physical examination at admission (possible score 0 to 4).

Coronary arteriography was performed by either the brachial or femoral technique. Several views of each coronary vessel were used for analysis. The extent of arterial stenosis, defined as the percent of maximal luminal narrowing, was recorded for each of the 27 coronary segments. In this study \( \geq 70\% \) luminal narrowing of a major coronary artery was considered a significant lesion. The score for left ventricular contraction was calculated numerically from a subjective appraisal of the opacified left ventricle in the 30 degree right anterior oblique view. The left ventricle was divided into five segments and each segment was scored from 1 to 6 (1 = normal and 6 = aneurysm). Ejection fraction was calculated with the area-length method.

Data analysis

Life table method. Differences in survival rates among groups were tested by the log-rank (Mantel-Haenszel) statistic13 with three methods of analysis. In the first method, to adjust for the bias that may have been introduced by the high rate of early surgery, medically treated patients were defined as those who did not undergo coronary bypass grafting or those who had very late surgery (method A). In the first year after enrollment, the number of days within which 95\% of the bypass operations were performed was determined for each hospital (average time, 4 months). At each hospital, the patients who underwent coronary bypass surgery within this interval or within 90 days after enrollment were excluded from analysis. Exposure time for the remaining medically treated patients was started from the average time to surgery for that hospital. The patients who died before this cutoff date were excluded from the analysis. This type of analysis removes the unfair bias of early deaths attributed to medical therapy in patients who may have been assigned to undergo surgery.

In a second method of analysis, exposure time was considered to begin from the time of enrollment into the CASS registry. All patients were initially regarded as medically treated. Patients who chose surgical therapy were also regarded initially as medically treated patients. The data for these patients were included until the time of coronary artery bypass grafting. Thus, early deaths before scheduled surgery were considered a failure of medical therapy (method B).

Finally, a third method to calculate exposure time was used to adjust for the high rate of early crossover to surgical therapy (method C). In this analysis, medically treated patients were defined as those who did not undergo coronary bypass grafting within 6 months of coronary angiography. Data from the patients who had coronary bypass surgery after 6 months were withdrawn from the survival analysis beginning at the time of surgery.

Cox regression analysis. The relative importance of the clinical and angiographic variables was assessed with a stepwise Cox survival analysis.14 The effect of group (e.g., those with LM vs LMEQ disease) was analyzed with an indicator variable coded 0 or 1. The Cox analysis was performed in two stages to

### Table 1

Selected clinical and angiographic features of patients

<table>
<thead>
<tr>
<th>Feature</th>
<th>Combined proximal</th>
<th>Combined nonproximal</th>
<th>LM proximal</th>
<th>LM coronary</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>1018</td>
<td>742</td>
<td>859</td>
<td></td>
</tr>
<tr>
<td>Mean age (yr)</td>
<td>57 ± 8 (SD)</td>
<td>56± 9(^a)</td>
<td>57 ± 9</td>
<td></td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>85</td>
<td>82</td>
<td>84</td>
<td></td>
</tr>
<tr>
<td>CCS angina class III, IV (%)</td>
<td>58</td>
<td>54</td>
<td>59</td>
<td></td>
</tr>
<tr>
<td>% CHF</td>
<td>15</td>
<td>15</td>
<td>11(^a)</td>
<td></td>
</tr>
<tr>
<td>Prior MI (%)</td>
<td>61</td>
<td>66(^a)</td>
<td>48(^b)</td>
<td></td>
</tr>
<tr>
<td>RCA stenosis 70% (%)</td>
<td>76</td>
<td>79</td>
<td>72(^a)</td>
<td></td>
</tr>
<tr>
<td>Left coronary dominant (%)</td>
<td>8</td>
<td>6</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Mean EF</td>
<td>0.55 ± 0.17</td>
<td>0.55 ± 0.17</td>
<td>0.58 ± 0.16(^b)</td>
<td></td>
</tr>
<tr>
<td>Mean LV contraction score</td>
<td>10.4 ± 4</td>
<td>9 ± 4</td>
<td>9 ± 4(^b)</td>
<td></td>
</tr>
<tr>
<td>Operated 90 days (%)</td>
<td>65</td>
<td>60(^a)</td>
<td>84(^b)</td>
<td></td>
</tr>
</tbody>
</table>

Combined proximal LAD and proximal Cx Disease vs other groups:

\(^a\) p < .05, \(^b\) p < .01.

\( \text{LAD} = \text{left anterior descending coronary disease} \geq 70\%; \text{LM} = \text{circumflex coronary disease} \geq 70\%; \text{CCS} = \text{Canadian Cardiovascular Society}; \text{CHF} = \text{congestive heart failure}; \text{MI} = \text{myocardial infarction}; \text{RCA} = \text{right coronary artery}; \text{EF} = \text{ejection fraction}; \text{LV} = \text{left ventricle}.\)
increase maximum number of patients available to test the group variable. In the first stage, 33 baseline variables were included to select those most important in influencing survival rates. The second Cox analysis used the selected variables along with the group variable to determine the importance of coronary anatomic characteristics (e.g., those with LM vs LMEQ disease) in the presence of covariates known to influence survival rates. In the stepwise Cox analysis, the variable most related to survival rate is chosen first. At subsequent steps, all remaining variables are considered for possible inclusion in the model; the process ends when the remaining (unselected) variables do not contribute statistically significant (p > .05) information to the model.

The stratified actuarial curves and ranking of the stepwise Cox analyses were analyzed with all three methods (A, B, and C).

**Results**

Actuarial analysis of patient survival rates revealed that the subgroup with LMEQ disease had a survival pattern intermediate between the patient subgroups with LM and MIDLAD disease. The probabilities of 5 year survival were 48% (LM), 54% (LMEQ), and 71% (MIDLAD) (p < .0001) when exposure time was calculated from the average number of days to surgery (method A; figure 1, A). The probabilities of 5 year survival calculated with method B were 46%, 55%, and 70% (p = .0001) for the patients who had LM, LMEQ, and MIDLAD disease, respectively (figure 1, B). The differences among the three patient subgroups remained significant when method C was used. The 5 year survival estimates calculated with method C were 48%, 54%, and 71% (p < .0001) for the patients with LM, LMEQ, and MIDLAD disease, respectively (figure 1, C). The raw data used to calculate the survival estimates with each method are listed in appendix 1.

Since the patient groups were slightly different at baseline, we studied the effect of covariates by stratified actuarial and Cox regression analyses to adjust for the differences in clinical and angiographic characteristics. Each analysis was run with the definition of a medically treated patient according to method A, B, or C. Since the differences among the three subgroups of patients remained significant regardless of the method used, the data presented are those obtained with method B.

**LMEQ vs MIDLAD disease.** The baseline characteristics of the two patient groups were similar at entry into the trial. Although statistically significant differences were observed in mean age, the difference was not clinically important (57 vs 56 years). The prevalence of previous myocardial infarction was greater in the group with MIDLAD disease (p = .04). However, adjustment by stratification by the infarct variable did not change the significance level (p = .0001) of the intergroup comparison. A larger number of patients with LMEQ disease underwent coronary bypass grafting within 90 days. When the patients not undergoing surgery in the two groups were compared, they were similar with respect to baseline variables. Thus, the probability of surviving 5 years with an LMEQ lesion is significantly poorer than that with a MIDLAD le-
sion, even after adjustment for baseline variables (p = .005 for method A, p = .016 for method B, and p = .009 for method C).

Cox regression analysis. To perform a stepwise Cox regression analysis for the patients with LMEQ and MIDLAD disease, seven of 33 baseline variables were selected as independently related to survival rate. The second stepwise Cox analysis of the seven variables and an additional variable that distinguished LMEQ from MIDLAD disease, showed that coronary anatomy (or group) was important even after adjustment for the three entering covariates (table 2). The second analysis increased sample size from 1148 to 1462 patients. The chi-square statistics in table 2 reflect the relative importance of the variables. The scores for congestive heart failure, left ventricular, and mitral regurgitation each affected survival rates more significantly than did group. However, the survival rate for patients who had LMEQ disease was lower (p = .012) even after adjustment for the covariates.

LMEQ vs LM disease. The patients with LM disease had fewer prior infarctions, less congestive heart failure, better left ventricular function, and less obstructive right coronary artery disease at baseline than the patient group with LMEQ disease (table 1). Nevertheless, the survival rate of patients with LMEQ disease was greater than that of the group with LM disease (figure 1). The difference in survival rates between the two groups was apparent primarily in the first year after angiography.

When the patients who did not undergo coronary artery bypass grafting within 90 days were compared, baseline characteristics were similar (p > .05), except for the prevalence of prior infarct; prior infarct was less common in patients who had LM disease (72% vs 61%; p = .02). Thus, the patients who had LM disease had a poorer prognosis even after consideration of baseline variables. When the comparison of survival rates was adjusted for the different proportions of patients with impaired left ventricular function, the 5 year survival rate was significantly lower for the patients who had LM disease (p = .04 for method A, p = .021 for method B, and p = .001 for method C). Data from the 73 patients for whom left ventricular contraction score was not coded were not considered in this latter analysis.

Cox regression analysis. For analysis of the 33 baseline variables plus a group variable that distinguished LMEQ from LM disease, eight covariates and group were selected as variables independently related to survival rates. A second stepwise Cox analysis restricted to the selected nine variables showed that score for congestive heart failure, left ventricular score, and age were most related to survival rates, although group remained significant (p = .002) even after adjustment for the covariates (table 3).

Discussion

The angiographic classification of patients into subsets of those having single-, double-, and triple-vessel coronary disease is simple and provides a useful prognostic guide in the daily management of patients with coronary disease. However, this classification may be somewhat restrictive for individual patients. Some patients with double- and triple-vessel disease have stenoses in the proximal segment(s) of the left coronary artery. The prognosis for the latter group of patients should clearly be considered separately because the amount of left ventricular muscle at risk increases when stenoses are more proximal.

In the present study, combined stenoses of the proximal left anterior descending and proximal circumflex coronary arteries were associated with a lower survival rate than was a corresponding extent of disease in

**TABLE 3**

| Stepwise Cox regression analysis of patients who had LMEQ or LM disease (≥ 70% narrowing) |
|-----------------|-----------------|-----------------|-----------------|-----------------|
| Variable        | Chi-square      | Beta-coefficient |
| CHF score       | 38.15           | .4154           |
| LV score        | 24.39           | .0977           |
| Mitral regurgitation | 16.17    | .4154           |
| Patient group   | 6.282           | .4408           |

CHF = congestive heart failure; LV = left ventricular; Patient group = LMEQ vs MIDLAD.

Final model chi-square statistics were computed with all variables considered together. Chi-square > 3.84 corresponds to p < .05, chi-square > 6.63 to p < .01, and chi-square > 10.81 to p < .001. Exposure time calculated with method B.

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nonproximal left anterior descending coronary artery segments. The 5 year survival rate obtained in the CASS of 55% for patients with LMEQ stenoses of \( \geq 70\% \) is similar to the 54% reported in an abstract by Conley et al.\(^6\) for patients with stenoses of \( \geq 75\% \) and is lower than the 76% reported by Tiras et al.\(^7\) for patients with stenoses of \( \geq 50\% \). In the study by Tiras et al.,\(^8\) patients who had severe left ventricular dysfunction were excluded. The European Coronary Surgery Study reported a higher mortality for medically treated patients who had multivessel disease (including the proximal segment of the left anterior descending coronary artery) compared with the mortality for patients who did not have proximal left anterior descending coronary artery disease.\(^9\) The difference was significant for patients who had double-vessel disease. The probability of 5 year survival was 82% in the European trial (greater than the 55% reported in the CASS study). Population sampling may explain the interstudy differences. The European trial included only candidates for surgery and excluded patients older than 65, those who had severe angina, or those who had poor left ventricular function and an ejection fraction <0.50. The CASS registry included these patients as well as some patients in whom operation could not be considered. In the European study, 50% luminal narrowing was considered important, whereas 70% narrowing was considered significant in the CASS. In the European randomized study of patients undergoing medical vs surgical therapy, the patients assigned to the medical group who received coronary bypass surgery were considered in the calculation of the medical survival estimates to allow comparison with the patients assigned to the surgical group according to the “intention-to-treat” principle.

**Comparison with LM disease.** LM coronary disease is a lesion associated with an increased risk of coronary events.\(^1\) Combined proximal left anterior descending and proximal left circumflex coronary artery (LMEQ) disease is often compared with LM disease because the extent of jeopardized myocardium would be similar if the degree of luminal narrowing were equivalent. However, the two subgroups of patients are clearly different prognostically.\(^15\)\(^,\)\(^6\)\(^,\)\(^8\)\(^,\)\(^9\)\(^,\)\(^19\)\(^,\)\(^20\) In the CASS, LM stenoses of \( \geq 70\% \) were associated with a lower survival rate than LMEQ disease (\( p \leq .04 \)). The difference in survival rates occurred mainly the first year after angiography and was greatest when method C was used. Associated disease in the right coronary artery would not explain the difference since obstructive right coronary disease was less common in the patients with LM disease and the variable of right coronary stenosis of \( \geq 70\% \) was not selected in the stepwise Cox analysis.

The 5 year survival rate of 37% for patients who had LM disease (\( \geq 70\% \) narrowing) calculated with method C in the CASS was similar to the 36% survival rate reported by Conley et al.\(^6\) who used a similar method of life table analysis. Life table analysis that uses method C for observational data may make medical therapy appear less effective than it is, because early deaths that occur within 6 months of angiography and before coronary bypass surgery (if scheduled) are considered to occur in the medical group (appendix 2). This point is illustrated by calculating the survival rates for patients with LM disease with methods A and B, in which 5 year survival rates were 48% and 46%, respectively.

The so-called LMEQ lesion is a heterogeneous entity since there are different coronary anatomic characteristics within this subgroup of patients. A comparison between the two subgroups of patients (LM vs LMEQ) is therefore difficult, particularly when one attempts to match for all variables known to independently affect survival rates.

**Clinical implications.** The observational data reported from this CASS registry study compare three angiographically defined subsets of patients. We selected the LMEQ lesion because the prognostic importance of this angiographic entity has provoked considerable controversy in the literature.\(^15\)\(^,\)\(^19\)\(^,\)\(^20\)

Most of the patients in the present study who had LM, LMEQ, or MIDLAD disease underwent coronary artery bypass grafting. The patients who did not undergo surgery are a selected group and have a tendency to have less severe angina and more impaired left ventricular function than patients who undergo surgery. Thus, the survival rates we report should not be extrapolated to all patients who have LM, LMEQ, or MIDLAD disease without these considerations in mind.

Combined stenoses of the proximal left anterior descending and proximal left circumflex coronary arteries do not constitute a prognostic LMEQ lesion. However, this angiographically defined combination of stenoses does identify a patient subgroup at increased risk of cardiac events compared with patients in whom the left anterior descending stenoses are not proximal. Patients who have combined stenoses in the proximal left anterior descending and proximal left circumflex coronary arteries should be considered independently as a separate group and should not be classified into the conventional angiographic classification of patients with double- or triple-vessel coronary artery disease. This point is particularly important when guidelines
for prognosis are determined or when the effects of therapy, such as coronary artery bypass grafting, are evaluated.

CASS
Cooperating clinical sites

Central Electrocardiographic Laboratory
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APPENDIX 1
Life table statistics for 3 month intervals in patients with MIDLAD, LMEQ, and LM coronary artery disease

<table>
<thead>
<tr>
<th>MIDLAD group</th>
<th>LMEQ group</th>
<th>LM group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alive at start of interval</td>
<td>Died</td>
<td>Withdrawn for CABG</td>
</tr>
<tr>
<td>0-3</td>
<td>742</td>
<td>17</td>
</tr>
<tr>
<td>4-6</td>
<td>282</td>
<td>4</td>
</tr>
<tr>
<td>7-9</td>
<td>246</td>
<td>10</td>
</tr>
<tr>
<td>10-12</td>
<td>231</td>
<td>6</td>
</tr>
<tr>
<td>13-15</td>
<td>214</td>
<td>3</td>
</tr>
<tr>
<td>16-18</td>
<td>208</td>
<td>4</td>
</tr>
<tr>
<td>19-21</td>
<td>201</td>
<td>7</td>
</tr>
<tr>
<td>22-24</td>
<td>193</td>
<td>2</td>
</tr>
<tr>
<td>25-27</td>
<td>174</td>
<td>3</td>
</tr>
<tr>
<td>28-30</td>
<td>156</td>
<td>2</td>
</tr>
<tr>
<td>31-33</td>
<td>154</td>
<td>2</td>
</tr>
<tr>
<td>34-36</td>
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<td>37-39</td>
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<td>40-42</td>
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<td>43-45</td>
<td>97</td>
<td>2</td>
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<tr>
<td>46-48</td>
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<td>49-51</td>
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<td>52-54</td>
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<td>70-72</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>73-75</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

CABG = coronary artery bypass grafting.
Appendix 2

Calculation of life table estimates with different definitions of exposure time. The use of three methods of survival analysis in this article illustrates some of the difficulties in performing observational data analysis of one treatment when patients may at any time change to an alternative treatment, and the change may occur for reasons related to survival. In the present study of medically treated patients, patients may at any time end their medical therapy by having surgery. Patients may choose to have surgery because their symptoms become worse, or they may choose not to have surgery. Both of these conditions may relate to prognosis and complicate the analysis of survival under medical therapy. In this study, the life table 1 year survival estimates by methods A, B, and C for patients who had LM disease (≥70% narrowing) were 78%, 87%, and 65%, respectively. Why was there a drastic increase in mortality with method C? The explanation can be illustrated by the following hypothetical example. In 100 patients, suppose 10 patients die in the first 3 months and nine patients (10%) of the remaining 90 patients die in the next 3 months. Assume none of the patients have coronary bypass surgery during this 6 month period. Figure 2, A, shows the patient experience. The 3 month survival rate is 90% (90/100) and the 6 month survival rate is 81% (81/100). In this situation, methods A, B, and C all estimate the 3 and 6 month survival as 90% and 81%, respectively.

Now suppose another similar group of 100 patients are studied. Again 10 patients (10%) die in the first 3 months, but this time 80 of the 90 remaining patients receive coronary bypass surgery at 3 months. In the next 3 months, one (10%) of the 10 patients who did not receive bypass surgery dies. Figure 2, B, illustrates the patient experience. The survival estimates for methods A, B, and C are shown in figure 3. Method A uses only the 10 patients who are alive at 3 months (the average time to surgery) and, assuming exposure begins at 3 months, estimates the survival at 90% (9/10) over the next 3 months. Method B includes all 100 patients the first 3 months (survival 90/100 or 90%) and only the 10 patients not assigned to surgery the second 3 months [6 months survival rate (90/100) × (9/10) or 81%]. These are the same estimates as in the patient without surgery. Method C excludes the 80 surgically treated patients from the entire analysis, so that the first 3 months survival rate is calculated as 10/20 or 50% and the 6 month survival rate as 9/20 or 45%.

The experience after diagnosis for patients at high risk, such as those with left main coronary disease, in whom coronary

\[\text{PATIENT EXPERIENCE WITH NO CORONARY SURGERY} \]

\[
\begin{array}{c|c|c|c}
\text{Time} & 0 & 3 & 6 \\
\hline
\text{Number alive} & 100 & 90 & 81 \\
\text{Number dead} & 10 (10%) & 9 (10%) & 9 (10%) \\
\text{Observed survival} & 100\% & 90\% \times \frac{9}{10} & 81\% \times \frac{9}{10} \\
\end{array}
\]

\[\text{PATIENT EXPERIENCE IF 8 OF 9 PATIENTS HAVE CORONARY SURGERY AT 3 MONTHS} \]

\[
\begin{array}{c|c|c|c}
\text{Time} & 0 & 3 & 6 \\
\hline
\text{Number alive} & 100 & 90 & 81 \\
\text{Number dead} & 10 (10%) & 9 (10%) & 9 (10%) \\
\text{Observed survival} & 100\% & 90\% \times \frac{9}{10} & 81\% \times \frac{9}{10} \\
\end{array}
\]

\[\text{FIGURE 2. A. Patient experience if no coronary bypass operations are performed. B. Patient experience if eight of nine patients have coronary bypass surgery at 3 months.} \]

bypass surgery improves life expectancy in specific patient subsets is not unlike this example. When both the early mortality and the early surgery rates are high, a definite downward bias for medical survival may appear, as in the preceding example. We suspect this might explain the different survival estimates calculated with method C, as was shown in figure 1, and believe that methods A and B are preferable.

There are other relative strengths and weaknesses of methods A and B beyond the scope of this article. Method A would be particularly appropriate in a nonrandomized observational study when medical and surgical comparisons are made because the medical group exposure time starts (on the average) at the same time as surgery. Since patients are not excluded in method A when they have late surgery, this method is particularly appropriate for comparing a strategy of early elective surgery with a strategy of delayed surgery. Method B and method C do not consider surgical exposure time; that is, after surgery, the survival experience does not contribute to the survival estimates. When the fact and timing of coronary bypass surgery occur independent of future medical risk, and when surgery indeed alters prognosis, method B is especially appropriate. However, there is no perfect method of observational survival analysis, and unless one is willing to make certain assumptions, the estimates provided may contain bias.

References

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12. The Principal Investigators of CASS and their Associates. The National Heart, Lung and Blood Institute Coronary Artery Surgery Study. Historical background, design, methods, the registry, the randomized trial, clinical data base. Circulation 63 (suppl I): 1-11, 1981


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B R Chaitman, K Davis, L D Fisher, M G Bourassa, M B Mock, J Lespérance, W J Rogers, D Fray, D H Tyras and M P Judkins

_Circulation_. 1983;68:1163-1170
doi: 10.1161/01.CIR.68.6.1163

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/68/6/1163

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