Clinical implications of internal mammary artery bypass grafts: the Coronary Artery Surgery Study experience

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ABSTRACT From the Coronary Artery Surgery Study Registry, all patients undergoing initial bypass surgery procedures with independent vein grafts were identified. The 950 patients receiving an internal mammary artery bypass graft were compared with the 6027 patients receiving vein graft alone. Improved survival rates with internal mammary artery grafts were noted at hospitals in which these grafts were performed infrequently as well as those in which the internal mammary artery graft was used frequently. The improved survival was noted in patients with normal (p = .004) as well as impaired (p = .004) ventricular function, in men (p = .0001) as well as women (p = .005), in patients over age 65 (p = .01) as well as younger patients (p < .0001), and in those with (p = .05) or without (p < .0001) critical stenosis of the left main coronary artery. The internal mammary artery bypass graft was an independent predictor of survival (p = .0004) and reduced the risk of dying by a factor of 0.64. It was concluded that the internal mammary artery graft is the bypass vessel of choice and should not be denied any subgroup.


THE INTERNAL mammary artery bypass graft, in use since 1968,1 has been shown to yield superior long-term clinical results as compared with the saphenous vein graft in single-institution follow-up studies at 10 years2 and at 15 years.3 The Coronary Artery Surgery Study (CASS) Registry gives an opportunity to evaluate the clinical follow-up of patients with internal mammary artery bypass grafts from many institutions, including some who used this conduit infrequently.

From 1974 to 1982, 10,121 patients enrolled in the CASS Registry from 15 participating centers (Appendix) underwent coronary artery bypass surgery and formed the basis of this analysis of the long-term benefits of the internal mammary artery bypass.

Methods

Patients were analyzed in two groups: 950 patients with a single internal mammary artery bypass graft with or without additional vein grafts and the 6027 patients with vein grafts alone. Only patients with independent grafts with a single anastomotic site were included. Excluded were patients undergoing repeat operations (n = 2262) or initial bypass with double internal mammary arteries (n = 23), sequential internal mammary arteries (n = 24), Y vein grafts (n = 406), and sequential vein grafts (n = 2429). All vein grafts were reversed autogenous saphenous veins. There were no internal mammary artery implants. The 15 clinical centers were subdivided into three groups according to the frequency of their use of the internal mammary artery bypass, and separate analyses of operative mortality rates and survival rates were determined. Follow-up was obtained by mail and phone interviews according to CASS protocol4 for up to 8 years (mean 5.5 years), with follow-up obtained in 99.5%.

Operative mortality was defined as death that occurred within 30 days of surgery. Coronary artery stenoses were considered significant in the presence of a luminal narrowing of at least 50% reduction in diameter in the left main coronary artery or at least 70% reduction in diameter of any other coronary artery segment. Significant stenosis of the left main coronary artery was considered double-vessel disease. The left ventricular score evaluated the contractility of the five segments of the left ventricle (anterobasal, anterolateral, apical, diaphragmatic, and posterior) as observed from the 30 degree right anterior oblique view during angiography. Contraction was coded as follows: normal, 1; moderate hypokinesis, 2; severe hypokinesis, 3; akinesis, 4; and dyskinesis, 5. The total number of points yielded the left ventricular score. Surgical priority was assessed by each center as elective, urgent, or emergent. Complete revasculari-
zation was considered accomplished when all major vessels with significant stenosis were bypassed.

Statistical analysis. The factors characterizing patients who had internal mammary artery grafts and patients who had vein grafts were compared by discriminant analysis. The analysis was done separately for hospitals that used the internal mammary artery infrequently, occasionally, and frequently. Twenty-nine covariates were used initially with stepwise selection of variables, with the sample size restricted to patients with all covariate values known. To reduce the possibility of bias due to the restricted sample, the stepwise selection was repeated using only covariates with p > .10 in the initial run. These results are reported here. Long-term survival was compared between groups by the log-rank statistic. In our population, patients with internal mammary artery grafts generally required more grafts. To adjust for the bias introduced by comparing patient groups with different graft requirements, each survival analysis was carried out within the strata determined by the number of grafts placed and pooled over the strata. All tests are two sided; p = .05 was considered to be statistically significant.

Results

The 15 clinical centers were subdivided into three groups according to the frequency of their use of the internal mammary artery bypass: group I consisted of eight sites performing 4343 operations but using the internal mammary artery bypass in only 1.1% of operations (range 0 to 3.4%); group II consisted of three sites performing 1145 operations, using the internal mammary artery bypass in 13% of operations (range 9.7% to 14.5%); group III consisted of four sites performing 1489 operations, with the internal mammary artery bypass in 50.5% (range 30.4% to 66.2%) of these operations.

The operative mortality rates (table 1) were not significantly different when an internal mammary graft was used as compared with vein grafts only in either the total group or in the three subgroups. Thus the operative mortality rates were not increased when internal mammary artery grafts were used even by sites at which this form of bypass was rarely used. The 5 year cumulative survival rates (table 1) were better when an internal mammary artery bypass was used than with vein grafts only. The improved survival reached statistical significance in groups II and III but was not significant in group I, possibly because of the very low incidence of the internal mammary bypass. Review of selection criteria by the clinical centers (table 2) for patients with internal mammary artery bypass grafts did not reveal a consistent bias of the sites using the internal mammary bypass less frequently to select less ill patients for this bypass graft. Univariate analysis (table 3) showed that patients in the internal mammary group were younger, had less main coronary artery stenosis of 50% or more, had less impaired left ven-

### TABLE 1

Use of the internal mammary artery graft and operative mortality and 5 year cumulative survival rates

<table>
<thead>
<tr>
<th>Group</th>
<th>Use of internal mammary artery</th>
<th>Operative mortality rate (%)</th>
<th>5 year survival rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Internal mammary artery</td>
<td>Vein graft</td>
</tr>
<tr>
<td>I</td>
<td>49/4343 (1.1%)</td>
<td>0</td>
<td>2.9</td>
</tr>
<tr>
<td>II</td>
<td>149/1145 (13.0%)</td>
<td>2.0</td>
<td>3.8</td>
</tr>
<tr>
<td>III</td>
<td>752/1489 (50.5%)</td>
<td>2.8</td>
<td>3.0</td>
</tr>
<tr>
<td>Total</td>
<td>950/6977 (13.6%)</td>
<td>2.5</td>
<td>3.1</td>
</tr>
</tbody>
</table>

### TABLE 2

Factors selected by discriminant analysis that were more common in patients with internal mammary artery grafts than in patients with vein grafts only (29 factors considered)

<table>
<thead>
<tr>
<th>Group</th>
<th>Factor</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Unstable angina</td>
<td>.001</td>
</tr>
<tr>
<td></td>
<td>Fewer vessels diseased</td>
<td>.003</td>
</tr>
<tr>
<td></td>
<td>No use of nitroglycerin</td>
<td>.004</td>
</tr>
<tr>
<td>II</td>
<td>No use of nitrates</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td></td>
<td>Younger age</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td>.006</td>
</tr>
<tr>
<td></td>
<td>More grafts placed</td>
<td>.03</td>
</tr>
<tr>
<td>III</td>
<td>More grafts placed</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td></td>
<td>Absence of S3 sounds</td>
<td>.0009</td>
</tr>
<tr>
<td></td>
<td>More diseased vessels</td>
<td>.005</td>
</tr>
<tr>
<td></td>
<td>Proximal LAD stenosis ≥70%</td>
<td>.02</td>
</tr>
</tbody>
</table>

### TABLE 3

Univariate analysis of characteristics of the internal mammary artery and vein graft only groups

<table>
<thead>
<tr>
<th>Factor</th>
<th>Internal mammary artery (%)</th>
<th>Vein graft (%)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;65 yr</td>
<td>7.3</td>
<td>10.3</td>
<td>.004</td>
</tr>
<tr>
<td>Left main coronary artery stenosis ≥50%</td>
<td>9.6</td>
<td>13.3</td>
<td>.001</td>
</tr>
<tr>
<td>Left ventricular score ≥10</td>
<td>23.7</td>
<td>30.6</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Proximal left anterior descending stenosis</td>
<td>51.3</td>
<td>44.6</td>
<td>.0001</td>
</tr>
<tr>
<td>Three-vessel disease</td>
<td>46.4</td>
<td>41.6</td>
<td>.006</td>
</tr>
<tr>
<td>Three grafts or more</td>
<td>58.7</td>
<td>44.8</td>
<td>&lt;.0001</td>
</tr>
<tr>
<td>Women</td>
<td>16</td>
<td>17</td>
<td>NS</td>
</tr>
</tbody>
</table>
tricular function, but had more proximal left anterior descending disease and more multivessel disease and required more grafts. The prevalence of women was similar in both groups. Multivariate analysis (table 4) with a Cox regression model with covariates (age, left ventricular function, proximal left anterior descending stenosis, left main coronary artery stenosis, completeness of revascularization, sex, number of vessels diseased, surgical priority, and number of grafts placed) demonstrated that the use of an internal mammary artery graft was an independent predictor of survival (p < .00004) and reduced the risk of dying by a factor of 0.64.

Cumulative survival rates over 7 years (table 5) were better in patients with an internal mammary artery graft both with normal or near-normal ventricular function (p = .004) as well as with impaired ventricular function (p = .004). The presence of an internal mammary artery graft was associated with improved survival in patients with left main coronary stenosis of 50% severity or greater (p = .051) as well as those with stenosis less than 50% (p < .0001). The improved survival rates with an internal mammary artery bypass graft were seen in women (p = .005) as well as men (p < .0001) and in the older (p = .01) as well as the younger patients (p < .0001).

Angina recurred in the first postoperative year in 27% of the group receiving vein grafts only and in 20% of those receiving at least one internal mammary artery graft (table 6). This significant difference decreased with time so that by 3 years of follow-up the recurrence rates no longer reached statistical significance.

**Discussion**

This study involving 15 clinical sites has shown that use of the internal mammary artery graft is an independent predictor of survival after coronary artery bypass surgery. The demonstrated reduction in risk of dying by a factor of 0.64 is remarkably similar to the previously reported findings of reduction in risk of dying by a factor of 0.62 and 0.65. This reduction in risk was noted in centers rarely using the internal mammary artery graft as well as in those commonly using this graft. There was no increased operative mortality rate associated with infrequent use of this graft. Thus benefit can be obtained by well-qualified surgeons relatively inexperienced with the internal mammary artery bypass graft. All surgeons associated with this study are considered well qualified, since all CASS participating centers were required to demonstrate high-quality surgical experience.

Surgeons have been slow to change their selection of conduit to the internal mammary artery graft from the saphenous vein graft, with only 13% of surgeons in 1980 performing internal mammary artery grafts. As recently as 1983, a major center in a review of bilateral internal mammary artery grafting concluded that the saphenous vein was the standard conduit for grafting but bilateral mammary artery grafts should be used when saphenous veins were unsuitable. Some early studies suggested that internal mammary artery flow would be inadequate for large coronary arteries as compared with saphenous veins, but subsequently the ability of the internal mammary artery to adjust to physiologic demands has been demonstrated. The internal mammary artery bypass takes longer to per-

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**TABLE 5**

Cumulative survival rate at 7 years

<table>
<thead>
<tr>
<th>Internal mammary artery</th>
<th>Vein graft</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. of patients</strong></td>
<td><strong>Survival (%)</strong></td>
</tr>
<tr>
<td>Left ventricular score &lt;10</td>
<td>711</td>
</tr>
<tr>
<td>Left ventricular score ≥10</td>
<td>221</td>
</tr>
<tr>
<td>Left main coronary artery stenosis &lt;50%</td>
<td>858</td>
</tr>
<tr>
<td>Left main coronary artery stenosis ≥50%</td>
<td>91</td>
</tr>
<tr>
<td>Men</td>
<td>798</td>
</tr>
<tr>
<td>Women</td>
<td>152</td>
</tr>
<tr>
<td>Age ≤65 yr</td>
<td>881</td>
</tr>
<tr>
<td>Age &gt;65 yr</td>
<td>69</td>
</tr>
</tbody>
</table>
form and needs greater surgical expertise than the saphenous vein graft procedure. Consequently, many surgeons avoid using the internal mammary artery in unstable patients, in those with left main coronary artery stenosis, in elderly patients, and, due to small size, in women. In this study, an improvement in survival associated with the internal mammary artery graft was seen in patients with left main coronary stenosis greater than 50% with impaired ventricular function, in elderly patients, and in women.

Recurrence of angina was less frequent in patients with the internal mammary artery graft for the first few years but decreased with time so that by 3 years there was no difference in the recurrence of angina between patients with the saphenous vein graft and those with the internal mammary artery graft. This lack of sustained benefit might be caused by progression of coronary artery disease or by failure of associated vein grafts. In addition, in view of the improved survival in the group with internal mammary grafts, this group probably included patients with angina who, if they had received only vein grafts, might not have survived long enough to be included in the subgroup with recurrent angina.

The internal mammary artery has been shown at post mortem examination to be remarkably free from atherosclerosis. Microscopic studies have suggested that defects in the internal elastic lamina present in coronary arteries but not internal mammary arteries might be responsible for the marked disparity in atherosclerosis between these vessels. The excellent long-term patency rate of internal mammary artery bypasses and progressive failure rate of saphenous bypass grafts have been well documented from many centers. The internal mammary artery is most commonly anastomosed to the left anterior descending coronary artery and thus gives protection to the most important area of the myocardium. The excellent long-term patency rate is undoubtedly the primary reason for improved surgical survival rates as compared with saphenous vein grafts.

New techniques with the internal mammary artery allow use of this bypass to all segments of the coronary arterial system, by in situ or free grafts and by single or sequential grafts. There will be broader use of this bypass as more surgeons gain expertise in these techniques. Surgeons should be encouraged by this study, which showed benefit to the patients receiving an internal mammary artery bypass at hospitals where this graft was used rarely as well as at those where the procedure was performed frequently. The internal mammary artery bypass graft should be included as a factor of survival when designing new studies or when comparing results among institutions or various therapies. The internal mammary artery bypass graft is the graft of choice for coronary artery disease and should not be denied any subgroup of patients.

Appendix
Cooperating clinical sites
University of Alabama in Birmingham: William J. Rogers, M.D.,* Richard O. Russell, Jr., M.D., Albert Oberman, M.D., and Nicholas T. Kouchoukos, M.D.
Albany Medical College: Eric D. Foster, M.D.,* Julio A. Sosa, M.D.,* Joseph T. Doyle, M.D., Martin F. McKneally, M.D., Joseph B. McIlduff, M.D., Harry Odabashian, M.D., and Thomas M. Older, M.D.
Boston University: Thomas Ryan, M.D.,* David Faxon, M.D., Laura Wexler, M.D., Robert L. Berger, M.D., Donald Weiner, M.D., and Carolyn H. McCabe, B.S.
Loma Linda University: Joan Coggins, M.D.,* Marshfield Medical Foundation, Inc., and Marshfield Clinic: William Myers, M.D.,* Richard D. Sautter, M.D.,* John N. Brownell, M.D., Dieter M. Voss, M.D., and Robert D. Carlson, M.D.
Massachusetts General Hospital: J. Warren Harthorne, M.D.,* W. Gerald Austen, M.D.,* Robert Dinsmore, M.D., Frederick Levine, M.D., and John McDermott, M.D.
Mayo Clinic and Mayo Foundation: Robert L. Frye, M.D.,* Bernard Gersh, M.D., David R. Holmes, M.D., Michael B. Mock, M.D., Hartzell Schaff, M.D., and Ronald E. Vlietstra, M.D.
Miami Heart Institute: Arthur J. Gosselin, M.D.,* Parry B. Larsen, M.D., and Paul Swaye, M.D.
Montreal Heart Institute: Martial G. Bourassa, M.D.,* Claude Goulet, M.D., and Jacques Lesperance, M.D.
New York University: Ephraim Glassman, M.D.,* and Michael Schloss, M.D.
St. Louis University: George Kaiser, M.D.,* J. Gerard Mudd, M.D.,* Robert D. Wiens, M.D., Hendrick B. Barner, M.D., John E. Codd, M.D., Denis H. Tyras, M.D., Valle L. Willman, M.D., and Bernard R. Chatman, M.D.
St. Luke’s Hospital Center: Harvey G. Kemp, Jr., M.D.,* and Airlie Cameron, M.D.
Stanford University: Edwin Alderman, M.D.,* Francis H. Koch, M.D., Paul R. Cipriano, M.D., James F. Silverman, M.D., and Edward B. Stinson, M.D.
Medical College of Wisconsin: Felix Tristani, M.D.,*
Harold L. Brooks, M.D.,* and Robert J. Flemma, M.D.
Yale University: Lawrence S. Cohen, M.D.,* Rene Langou,
M.D., Alexander S. Geha, M.D., Graeme L. Hammond, M.D.,
and Richard K. Shaw, M.D.

Central Electrocardiographic Laboratory, University of
Alabama. L. Thomas Sheffield, M.D.,* David Roitman, M.D.,
and Carol Troxell, B.S.

Coordinating Center, University of Washington. Kathryn
Davis, Ph.D.,* Mary Jo Gillespie, M.S., Lloyd Fisher, Ph.D.,
J. Ward Kennedy, M.D., Richard Kronmal, Ph.D., and Kevin
Cain, Ph.D.

Chairman of the Steering Committee. Thomas Killip,
M.D., Beth Israel Medical Center.

National Heart, Lung and Blood Institute. Eugene R.
Passamani, M.D., Thomas Robertson, M.D., and Peter
Frommer, M.D.

*Principal Investigator

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