Bilateral Internal Mammary Artery Grafting Enhances Survival in Diabetic Patients: A 30-Year Follow-Up of Propensity Score-Matched Cohorts

Running title: Dorman et al.; IMA Grafting in Diabetic Patients

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Journal Subject Codes: [7] Chronic ischemic heart disease; [36] CV surgery: coronary artery disease; [191] Other diabetes
Abstract:

**Background**—The prevalence of diabetes is increasing at an unprecedented rate, affecting nearly 8% of the population. Previous studies have demonstrated a potential benefit for surgical over interventional revascularization in this group of patients. Similarly, studies have shown the superiority of bilateral internal mammary artery (BIMA) grafting over single internal mammary artery (SIMA) grafting in select populations. However, concerns regarding sternal wound infection (SWI) have discouraged the use of BIMA grafting in diabetics. Therefore, we studied the long-term results of BIMA vs. SIMA grafting in a large population of diabetic patients in which BIMA grafting was broadly applied.

**Methods and Results**—Between February 1972 and May 1994, 1107 consecutive diabetic patients underwent coronary artery bypass grafting (CABG) with either SIMA (n=646) or BIMA (n=461) grafting. Optimal matching using propensity score-matching was used to create matched SIMA (n=414) and BIMA (n=414) cohorts. Cross-sectional follow-up (6 weeks to 30.1 years, mean 8.9 years) determined long-term survival. There was no difference in operative mortality (OM) sternal wound infection (SWI) or total complications between matched SIMA and BIMA groups (OM: 10/414; 2.4% vs. 13/414; 3.1%, P=0.279; SWI 7/414; 1.7% vs. 13/414; 3.1%; P=0.179); total complications 71/414, 17.1% vs. 71/414, 17.1%, P=1.000). Late survival was significantly enhanced with the use of BIMA grafting (median survival SIMA 9.8 years vs. BIMA 13.1 years; P=0.001). Use of BIMA was found to be associated with late survival on Cox regression (P=0.003).

**Conclusions**—BIMA, compared with SIMA, grafting in propensity score-matched patients provides diabetics with enhanced survival without any increase in perioperative morbidity or mortality.

**Key words**: CABG; diabetes mellitus; follow-up studies; long-term outcomes; bilateral internal mammary artery
Introduction

Diabetes currently afflicts 25.8 million people in this county, approximately 8.3% of the U.S. population. The prevalence has more than doubled in the past decade, and current estimates predict an incidence between one in five and one in three Americans by the year 2050. The burden of disease associated with diabetes is dramatic: adults with diabetes are two to four times more likely to have cardiovascular disease than those without it, and at least 65% will die from it. The national burden of cardiovascular disease due to diabetes is increasing at an unprecedented rate. The nature of cardiovascular disease in diabetics is clinically challenging, as it tends to be extensive, with multivessel involvement. Perhaps it is for this reason that surgical revascularization has been reported to be well suited for the diabetic patient.

Numerous clinical trials have demonstrated a survival benefit for bilateral (BIMA), compared with single (SIMA) internal mammary artery bypass grafting, for patients with multivessel disease. However, there remains considerable reluctance to use this surgical approach in diabetic patients because of concerns regarding the risk of deep sternal wound infection (SWI). We therefore studied the results of a thirty year follow-up of unmatched and propensity score-matched diabetic patients who underwent SIMA or BIMA grafting in a cohort in which BIMA grafting was extensively applied.

Patients and Methods

Patient Population

From February 1972 through May 1994, 1107 consecutive diabetic patients underwent isolated coronary artery bypass grafting (CABG) with either a SIMA (n=646) or BIMA (n=461). Diabetic patients in the study included those who were treated with either hypoglycemic agents
or insulin. Excluded from the study group were patients with concomitant cardiovascular procedures, and those in whom only one distal graft was performed. This study was presented to the Institutional Review Board and a waiver of the requirement for informed patient consent was granted.

The coronary and perioperative risk factors as well as preoperative angiographic findings for unmatched and propensity-matched diabetic patients are summarized in Table 1. Although SIMA and BIMA patients had markedly different risk factor profiles, there were no significant differences in any of the risk factors in propensity score-matched groups.

**Operative Data**

Details of the operative technique used in the present series, including IMA mobilization, orientation, and reconstruction in BIMA grafting have been previously discussed. The IMA was dissected as an isolated pedicle from the chest wall free from surrounding muscle and fascia. The vein is initially dissected but subsequently removed to allow maximal length and versatility. All side branches are cauterized carefully or clipped as necessary. Since 1989, combined antegrade and retrograde infusion methods of cardioplegia were implemented to enhance myocardial protection during the operation. Cardiopulmonary bypass was used in all operations. The left IMA, either as a sequential or isolated graft was preferentially anastomosed to the left anterior descending coronary artery. The right IMA was used for grafting either the right or left system, as previously discussed in detail. The operative data for unmatched and propensity-matched diabetic patients, by group, are presented in Table 2. Operative variables were comparable between matched groups with the exception of a greater cross-clamp time in BIMA vs. SIMA patients (73.8±23.1 vs. 69.4±4.5; P=0.009).

**Data Sources**

Perioperative data were entered prospectively in a standardized manner into a clinical database,
according to the guidelines of the Society of Thoracic Surgeons Adult Cardiac Surgery Database. Follow-up information was obtained through comprehensive questionnaires and by telephone interview with surviving patients, family members or the patient’s personal physician and entered into the follow-up component of the database.

Statistical Analysis

Demographic and clinical data are presented as frequency distributions and simple percentages. Values of continuous variables are expressed as mean ± standard deviation. In unmatched patient cohorts, univariate analysis of selected preoperative and postoperative discrete variables was accomplished by Chi-square with the appropriate degrees of freedom or Fisher’s exact test to assess the equality of proportions. Two-sample t-tests were used to test for the equality of means in continuous variables. To assess differences in matched cohorts, the McNemar test was used to test categorical variables and paired t-tests for continuous variables.

To control for measured potential confounders in the dataset a propensity score was generated for each patient from a multivariable logistic regression model based on 14 demographic/c clinical preoperative covariates as independent variables with treatment type (SIMA vs. BIMA) as a binary dependent variable (Table 1 in the online-only Data Supplement). The resulting propensity score represented the probability that a patient underwent BIMA grafting in CABG. BIMA patients were then matched to SIMA patients in a 1:1 ratio using a Rosenbaum optimal matching algorithm. This approach minimized the overall distance between observations and was conducted using Mahalanobis distance within propensity score calipers (no matches outside the calipers). The quality of the match was assessed by comparing selected baseline characteristics in propensity score-matched patients.

To identify variables associated with hospital mortality in unmatched patients, an initial logistic regression model was developed using 21 preoperative and intraoperative
demographic/clinical variables (Table 2 in the online-only Data Supplement). The final logistic regression model included 4 covariates. Conditional logistic regression was used to determine the independent effects of selected demographic/clinical variables on hospital mortality in propensity score-matched patients.

Cox proportional hazards regression model was used to discern the influence of multiple clinical variables on late survival for patients discharged from the hospital in unmatched and propensity-score matched cohorts (Table 3 in the online-only Data Supplement). Regression coefficients and hazard ratios with 95% confidence intervals were calculated to determine the relative influence of each covariate on the survivor function. Coefficients were computed by the method of maximum likelihood.

Actuarial survival estimates (including operative deaths) were calculated according to the method of Kaplan and Meier using time zero as the date of operation and late death as the endpoint in unmatched patient cohorts. The equality of survival distribution was tested with the log-rank algorithm. Moreover, a Cox proportional hazards regression model stratified on matched pairs was used to estimate treatment effect and cumulative survival between groups. All P-values reported are two-sided and are not adjusted for multiple testing. A probability value of \( \leq 0.050 \) was considered to indicate significant differences between measurements. All analyses were performed using Number Cruncher Statistical Systems software (Version 8, Copyright 2012, NCSS, Kaysville, UT) and STATA (Version 12, Copyright 2012, StataCorp LP, College Station, TX).

Results

Hospital Morbidity
The overall incidence of postoperative morbidity for the two unmatched diabetic groups was low. No complications were experienced in 79.3% (512/646) of the SIMA patients or in 83.1% (383/461) in the BIMA group, (P=0.111). The number of complications was similar in propensity score-matched groups, with each group 82.9% (343/414) being free of complications (Table 3). A between-group comparison revealed that the prevalence of deep SWI was not affected by the type of IMA grafting used in unmatched patients (P=0.144) or in propensity score-matched diabetic patients (P=0.174).

**Hospital Mortality**

Hospital mortality rate was defined as death which occurred during the operation or the hospitalization in which the procedure was performed or after discharge from the hospital but within 30 days of the surgical procedure, unless the cause was unrelated to the operation. The overall hospital mortality rate for all diabetic patients was 4.4% (49/1107). The hospital mortality rate for unmatched SIMA patients was 5.4% (35/646) and 3.0% (14/461) for BIMA patients (Odds Ratio [OR]=1.79; 95% Confidence Interval [CI] 0.95 to 3.51; P=0.058). This difference approached statistical significance. The hospital mortality rate for propensity score-matched SIMA patients was 4.6% (19/414) and 3.1% (13/414) for BIMA patients (P=0.279). The McNemar test for comparison of paired proportions in hospital mortality confirmed no significant differences between groups (OR=1.545; 95% CI 0.68 to 3.65; P=0.257).

The use or non-use of BIMA grafting was not found to be associated with hospital mortality in unmatched patients (Table 4). Moreover, conditional logistic regression analysis for propensity score-matched patients confirmed the insertion of the intra-aortic balloon pump preoperatively or intraoperatively to be associated with an increased risk of hospital mortality (OR=5.33; 95% CI 2.55 to 11.15; p<0.001).
Long Term Follow-up

Follow-up data for the unmatched patient groups were collected on 94.6% of SIMA (611/646) and 97.0% of BIMA patients (447/461). In propensity score-matched patient groups, follow-up data was collected on 95.4% of SIMA (395/414) and 96.9% of BIMA patients (401/414) who were discharged from the hospital. In unmatched patients, the mean follow-up was 9.4±5.7 years (range, 6 weeks to 30.9 years; median 9.3, IQR 4.9-13.0) in SIMA and 11.4±5.3 years (range, 6 weeks to 29.8 years) in BIMA patients. Cumulative follow-up was 5754.0 patient-years for the SIMA and 5117.1 patient-years for the BIMA group. The average duration of follow-up for propensity score-matched hospital survivors was 9.9 years (range, 6 weeks to 24.0 years) in SIMA and 11.3 years (range, 6 weeks to 29.8 years) in BIMA patients. The cumulative follow-up was 3902.3 patient-years for the SIMA group and 4520.9 patient-years for the BIMA group.

To identify independent factors associated with late death, a Cox proportional hazards regression model was created to measure the effects of various prognostic factors on time-to-response (operation to late death) (Table 3 in the online-only Data Supplement). Among unmatched SIMA and BIMA diabetic patients, there were 10 covariates associated with late mortality: 5 preoperative, 1 intraoperative and 4 postoperative variables. In propensity score-matched patients, there were 6 covariates associated with late mortality: 4 preoperative, 1 intraoperative and 1 postoperative (Table 5). Surgical approach, SIMA vs. BIMA grafting, was found to be an independent factor associated with late death in unmatched (P=0.021) and propensity score-matched patients (P=0.003).

Survival estimates for unmatched SIMA and BIMA diabetic patients are shown in Figure 1A. The median survival for SIMA was 8.8 years (95% CI, 8.1 to 9.6) compared with 13.4 years
(95% CI, 12.2 to 14.0) for BIMA patients. The equality of survival distribution for the two unmatched patient groups demonstrated a significant difference (P<0.001).

In the propensity score-matched groups (Figure 1B), the median survival for SIMA patients was 9.8 years (95% CI, 8.6 to 10.5) compared with 13.1 years (95% CI, 12.2 to 13.9) for BIMA patients. Comparison of the survival distribution for these two groups of propensity score-matched diabetic patients demonstrated a significant difference (P<0.001). These results provide further evidence of the survival benefits achieved in diabetic patients with BIMA grafting.

To discern the influence of age on the survival benefits from BIMA grafting, unmatched patients were stratified into those <65 years of age and those >=65 years of age at the time of surgery. In SIMA patients <65 years of age, the median survival time was 13.2 years (CI 10.98 to 15.42) compared with 17.6 years (CI 14.67 to 18.99) for BIMA patients. The equality of survival distribution for patients <65 years of age demonstrated a significant survival advantage for BIMA patients (P=0.006; Figure 2A). In patients >=65 years of age, the median survival time for SIMA patients was 8.1 years (CI 7.32 to 9.26) compared with 10.6 years (CI 9.43 to 12.16) for BIMA patients. A comparison of the survival distribution for these two groups of patients demonstrated a significant survival advantage for BIMA patients (P=0.014; Figure 2B).

Comment

Despite consistently favorable reports regarding the long-term benefits of BIMA grafting,9-11 the Society of Thoracic Surgeons National Database reports that less than 4% of patients undergoing CABG surgery currently receive the benefits of BIMA grafting.16 Surgical reluctance to use BIMA grafting has been particularly noteworthy among diabetic patients, due to concerns
regarding an increased risk of SWI.\textsuperscript{12} Herein we report enhanced long-term survival advantage for BIMA grafting in a large cohort of consecutive multi-graft diabetic CABG patients in whom BIMA grafting was liberally applied.

As with any retrospective surgical experience, clinical decisions are made based on a host of complex interacting factors. Therefore, the cohort of patients in whom SIMA grafting was selected tended to be older, more acutely ill, and associated with more preoperative comorbid conditions. However, even after propensity score-matching, which controlled for each of the identifiable risk factors, a survival advantage was demonstrated in BIMA patients. These results were further confirmed by multivariable Cox regression which clearly showed that BIMA grafting was associated with long-term survival in unmatched and propensity score-matched patients. Similar results have been previously reported in smaller groups of patients with a shorter duration of follow-up.\textsuperscript{17-19} Unlike those reports, the survival benefit herein observed did not appear to be influenced by patient age at the time of surgery.\textsuperscript{20}

The absence of significant difference in the SWI rate among BIMA patients may represent a Type II error that could have become significant with a larger cohort of patients. However, it should be noted, that the study population (N=1107) was sufficiently robust to demonstrate a clear survival advantage for BIMA patients, but not a significant difference in SWI. Moreover, previous studies have also failed to find a significant increase in SWI with BIMA grafting in diabetics.\textsuperscript{21,22} Differences reported in the literature may likely be due less to statistical variance rather than to surgical technique. All IMA’s in this study were harvested using a skeletonized technique, which has been demonstrated to better preserve sternal blood flow\textsuperscript{23-25} and to reduce the risk of SWI.\textsuperscript{26,27} Similarly, early reports of increased postoperative bleeding\textsuperscript{28} and pulmonary morbidity\textsuperscript{29} with BIMA grafting have not been substantiated by
subsequent studies\textsuperscript{30,31} and were not evident in the present study.  

Numerous studies have suggested a survival advantage for CABG over percutaneous coronary intervention for diabetic patients, presumably due to completeness of revascularization in a milieu of extensive and diffuse coronary artery disease with which these diabetic patients present.\textsuperscript{7,8} There is no indication that revascularization was significantly more complete in the matched SIMA vs. BIMA patients in this study.  Certainly the well-documented improved long-term patency of IMA vs. saphenous vein grafts may have played a crucial role in providing this survival benefit.  However, there may be other contributing physiologic reasons as well. The IMA has been demonstrated to have enhanced production of endothelium-derived nitrous oxide\textsuperscript{32-35} which may play an important role in ameliorating diabetes-induced endothelial dysfunction and susceptibility to progressive atherosclerosis and subsequent cardiac events.

Although impressive for their longevity and consistency, the results of the present study nonetheless are limited by its retrospective nature.  Even though propensity score-matching is a well-described technique for “leveling the playing field” in retrospective studies, and in this study risk factors were closely matched, there remains the possibility of confounding variables not accounted for in the data set. Moreover, the use of propensity score-matching limited the sample size to those patients who could be matched.  The advantage of clinical registries is that they reflect aggregate surgical experience as it is practiced, without the rigid selection of prospective randomized studies.  However, results will nonetheless ultimately require confirmation from prospective randomized trials, which are considered the “gold standard.”\textsuperscript{36}  Certain technical issues need to be recognized as well.  In addition to the skeletonized method of IMA harvest, this cohort made extensive use of in-situ grafts (98%).  Therefore, comparison with studies using free IMA and or “Y” and “T” graft configurations may not be applicable.
This long-term retrospective study addresses patients, many of whom were operated on over two decades ago. Risk profiles and surgical outcomes of CABG surgery have changed dramatically during that time period, with increasing patient risk and decreasing operative mortality.\textsuperscript{37} Can we be certain that the ability to apply BIMA grafting in the modern era would be equivalent to the outcomes observed in this study? Have improvements in perioperative care and medical therapy ameliorated or even eliminated the survival benefits observed? More recent studies with both on-\textsuperscript{19} and off-pump\textsuperscript{17} CABG suggest that these results have been replicable in today’s modern surgical era.

The limitations of the data-gathering approach did not allow us to make a more careful assessment of several potentially important factors. First, we were not able to distinguish between insulin-dependent and non-insulin dependent patients in any of our analyses. Secondly, all of these patients were operated upon prior to the routine application of careful perioperative glycemic control. Thirdly, we have no information regarding the adequacy of medical therapy for these patients over the many years of follow-up. However, we have no a priori reason to suspect that any of these factors would necessarily bias the results toward one group or the other.

Lastly, the cross-sectional nature of the follow-up did not permit accurate prospective evaluation of major adverse cardiac events (MACE). Although the historical recollection of patients alive at follow-up did not demonstrate a difference in the occurrence of late cardiac events between groups, this information is limited to patients alive at follow-up and is unverified, and therefore may not be reliable. Nonetheless, the strong historical evidence of improved event-free survival with BIMA grafting would certainly not lead us to suspect a higher incidence of MACE in BIMA patients.\textsuperscript{38-40}

In summary, propensity score-matched BIMA compared with SIMA diabetic patients
experienced improved long-term survival without any increase in perioperative morbidity or mortality. The magnitude of this benefit appears to be sufficient to eliminate the negative influence of diabetes on long-term survival in this cohort of patients. Given the documented benefits of CABG in diabetic patients with extensive coronary artery disease, BIMA grafting is the procedure of choice in those patients in whom the operation is technically feasible.

Acknowledgments: All authors had access to and have reviewed all of the data and agree with the conclusions herein presented. Authors would like to acknowledge the assistance of Debra Guest EdD for her assistance in compilation of the manuscript.

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Conflict of Interest Disclosures: None

References:


Table 1. Comparison of Preoperative Variables and Risk Factors for Unmatched and Propensity Score-Matched Diabetic Patient Groups

<table>
<thead>
<tr>
<th>Variables*</th>
<th>Unmatched Diabetic Patients</th>
<th>Propensity-Matched Diabetic Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SIMA</td>
<td>BIMA</td>
</tr>
<tr>
<td>No. of patients</td>
<td>646</td>
<td>461</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>451</td>
<td>371</td>
</tr>
<tr>
<td>Female</td>
<td>195</td>
<td>90</td>
</tr>
<tr>
<td>Age (y)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>67.7±8.3</td>
<td>63.6±9.0</td>
</tr>
<tr>
<td>Age groups (y)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;50</td>
<td>19</td>
<td>44</td>
</tr>
<tr>
<td>50-59</td>
<td>105</td>
<td>104</td>
</tr>
<tr>
<td>60-69</td>
<td>269</td>
<td>216</td>
</tr>
<tr>
<td>70-79</td>
<td>230</td>
<td>94</td>
</tr>
<tr>
<td>≥80</td>
<td>23</td>
<td>3</td>
</tr>
<tr>
<td>Preoperative coronary risk factors</td>
<td></td>
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</tr>
<tr>
<td>Family history of CAD</td>
<td>310</td>
<td>256</td>
</tr>
<tr>
<td>Hypertension</td>
<td>118</td>
<td>35</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>77</td>
<td>33</td>
</tr>
<tr>
<td>Smoking history</td>
<td>337</td>
<td>275</td>
</tr>
<tr>
<td>Perioperative risk factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>24</td>
<td>6</td>
</tr>
<tr>
<td>Cerebrovascular disease</td>
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<td>8</td>
</tr>
<tr>
<td>Peripheral artery disease</td>
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<td>13</td>
</tr>
<tr>
<td>Prior myocardial infarction</td>
<td>379</td>
<td>256</td>
</tr>
<tr>
<td>History of chronic heart failure</td>
<td>124</td>
<td>63</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>485</td>
<td>296</td>
</tr>
<tr>
<td>Preoperative coronary angiography</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3-Vessel disease</td>
<td>545</td>
<td>583</td>
</tr>
<tr>
<td>Impaired ejection fraction (&lt;0.50)</td>
<td>248</td>
<td>222</td>
</tr>
</tbody>
</table>

*Numbers in parentheses are percentages.

SIMA=single internal mammary artery; BIMA=bilateral internal mammary artery; SD=standard deviation; CAD=coronary artery disease.
Table 2. Comparison of Operative Data for Unmatched and Propensity Score-Matched Diabetic Patient Groups.

<table>
<thead>
<tr>
<th>Variables*</th>
<th>Unmatched Diabetic Patients</th>
<th>Propensity-Matched Diabetic Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SIMA</td>
<td>BIMA</td>
</tr>
<tr>
<td>No. of patients</td>
<td>646 (100.0)</td>
<td>461 (100.0)</td>
</tr>
<tr>
<td>Total grafts</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Distal coronary artery grafts</td>
<td>2036 (100.0)</td>
<td>1551 (100.0)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>3.2±0.9</td>
<td>3.4±0.9</td>
</tr>
<tr>
<td>Range</td>
<td>2-6</td>
<td>2-6</td>
</tr>
<tr>
<td>Cardiopulmonary bypass time</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perfusion time (min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>119.9±45.9</td>
<td>118.6±45.2</td>
</tr>
<tr>
<td>Range</td>
<td>30-504</td>
<td>40-391</td>
</tr>
<tr>
<td>Aortic cross clamp time (min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>68.5±23.9</td>
<td>74.8±24.1</td>
</tr>
<tr>
<td>Range</td>
<td>10-237</td>
<td>15-200</td>
</tr>
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</table>

Numbers in parentheses are percentages; SIMA=single internal mammary artery; BIMA=bilateral internal mammary artery; SD=standard deviation; CAD=coronary artery disease.

Table 3. Comparison of Hospital Complications for Unmatched and Propensity Score-Matched Diabetic Patient Groups

<table>
<thead>
<tr>
<th>Complication</th>
<th>Unmatched (N=1,107)</th>
<th>Propensity Score-Matched (N=828)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SIMA</td>
<td>BIMA</td>
</tr>
<tr>
<td>No. of patients</td>
<td>646 (100.0)</td>
<td>461 (100.0)</td>
</tr>
<tr>
<td>Reoperation for bleeding</td>
<td>19 (2.9)</td>
<td>10 (2.2)</td>
</tr>
<tr>
<td>Pulmonary insufficiency</td>
<td>63 (9.8)</td>
<td>26 (5.6)</td>
</tr>
<tr>
<td>Cerebral vascular accident</td>
<td>13 (2.0)</td>
<td>8 (1.7)</td>
</tr>
<tr>
<td>Perioperative myocardial infarction</td>
<td>31 (4.8)</td>
<td>20 (4.3)</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>35 (5.4)</td>
<td>13 (2.8)</td>
</tr>
<tr>
<td>Low cardiac output</td>
<td>20 (3.1)</td>
<td>12 (2.6)</td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>22 (3.4)</td>
<td>14 (3.0)</td>
</tr>
<tr>
<td>Gastrointestinal disorder</td>
<td>13 (2.0)</td>
<td>9 (2.0)</td>
</tr>
<tr>
<td>Deep sternal infection</td>
<td>10 (1.5)</td>
<td>13 (2.8)</td>
</tr>
</tbody>
</table>

*Numbers in parentheses are percentages; SIMA=single internal mammary artery; BIMA=bilateral internal mammary artery.
Table 4. Multivariable Analysis of Factors Associated With Hospital Mortality in Unmatched Diabetic Patients (N=1107) Undergoing Single Internal Mammary Artery and Bilateral Internal Mammary Artery Grafting

<table>
<thead>
<tr>
<th>Variables</th>
<th>β Estimate</th>
<th>SE</th>
<th>OR (95% CI)</th>
<th>p Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at operation</td>
<td>0.0543</td>
<td>0.020</td>
<td>1.06 (1.01 – 1.10)</td>
<td>0.003</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>0.7865</td>
<td>0.329</td>
<td>2.20 (1.15 – 4.18)</td>
<td>0.020</td>
</tr>
<tr>
<td>Intra-aortic balloon pump</td>
<td>1.0042</td>
<td>0.332</td>
<td>2.73 (1.42 – 5.23)</td>
<td>0.003</td>
</tr>
<tr>
<td>Perfusion time</td>
<td>0.0101</td>
<td>0.002</td>
<td>1.01 (1.01 – 1.01)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Only significant variables (P<0.050) are listed.
SIMA=single internal mammary artery; BIMA=bilateral internal mammary artery; SE=standard error; OR=odds ratio; CI=confidence interval.
Table 5. Variables Influencing Late Mortality by Cox Regression Analysis in Unmatched and Propensity Score-Matched Single Internal Mammary Artery and Bilateral Internal Mammary Artery Patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Unmatched (N=1,107) SIMA/BIMA Diabetic Patients</th>
<th>Propensity-Matched (N=828) SIMA/BIMA Diabetic Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Regression Coefficient</td>
<td>SE</td>
</tr>
<tr>
<td>Preoperative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at operation</td>
<td>0.0545</td>
<td>0.005</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>0.5393</td>
<td>0.099</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>0.7424</td>
<td>0.152</td>
</tr>
<tr>
<td>Surgical history</td>
<td>0.4939</td>
<td>0.132</td>
</tr>
<tr>
<td>Renal dysfunction b</td>
<td>0.5595</td>
<td>0.212</td>
</tr>
<tr>
<td>Intraoperative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BIMA use</td>
<td>-0.1854</td>
<td>0.081</td>
</tr>
<tr>
<td>Postoperative</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cardiac arrest</td>
<td>0.7368</td>
<td>0.280</td>
</tr>
<tr>
<td>Low cardiac output</td>
<td>0.6762</td>
<td>0.231</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0.4587</td>
<td>0.178</td>
</tr>
<tr>
<td>Pulmonary insufficiency</td>
<td>0.5534</td>
<td>0.143</td>
</tr>
</tbody>
</table>

*Only significant variables (P<0.050) are listed. b Noted as creatinine ≥ 2.0 mg/dL.
SIMA=single internal mammary artery; BIMA=bilateral internal mammary artery; HR=hazard ratio; CI=confidence interval.
Figure Legends:

Figure 1. A. Actuarial survival estimates of unmatched diabetic patients who underwent single internal mammary artery coronary artery bypass grafting and bilateral internal artery mammary coronary artery bypass grafting. B. Actuarial survival estimates of propensity score-matched diabetic patients who underwent single internal mammary artery coronary artery bypass grafting and bilateral internal artery mammary coronary artery bypass grafting.

Figure 2. A. Actuarial survival estimates of unmatched diabetic patients <65 years of age who underwent single internal mammary artery coronary artery bypass grafting and bilateral internal artery mammary coronary artery bypass grafting. B. Actuarial survival estimates of unmatched diabetic patients >=65 years of age who underwent single internal mammary artery coronary artery bypass grafting and bilateral internal artery mammary coronary artery bypass grafting.
Number at risk
SIMA Diabetes  646  555  490  417  356  280  193  119  80  50  29
BIMA Diabetes  461  425  401  373  330  289  228  141  82  39  13
% Survival by Years After Operation

Number at risk

<table>
<thead>
<tr>
<th></th>
<th>SIMA Diabetes &lt;65</th>
<th>BIMA Diabetes &lt;65</th>
</tr>
</thead>
<tbody>
<tr>
<td>SIMA Diabetes</td>
<td>166 154 137 126 118 98 83 59 45 25 16</td>
<td>BIMA Diabetes</td>
</tr>
</tbody>
</table>
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0.0

Number at risk

<table>
<thead>
<tr>
<th></th>
<th>SIMA Diabetes &gt;=65</th>
<th>BIMA Diabetes &gt;=65</th>
</tr>
</thead>
<tbody>
<tr>
<td>Years After Operation</td>
<td>Number at risk</td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>248</td>
<td>228</td>
</tr>
<tr>
<td>2</td>
<td>210</td>
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<td>99</td>
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<tr>
<td>12</td>
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<td>9</td>
</tr>
<tr>
<td>20</td>
<td>5</td>
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</table>

100.0% Survival

% Survival

0 2 4 6 8 10 12 14 16 18 20

Years After Operation

SIMA Diabetes >=65

BIMA Diabetes >=65
Bilateral Internal Mammary Artery Grafting Enhances Survival in Diabetic Patients: A 30-Year Follow-Up of Propensity Score-Matched Cohorts
Malcolm J. Dorman, Paul A. Kurlansky, Ernest A. Traad, David L. Galbut, Melinda Zucker and George Ebra

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Supplemental Material
Supplemental Table 1: Covariates Used to Generate Propensity Score.

Preoperative variables

1. Age at operation
2. Cerebrovascular disease
3. Congestive heart failure
4. Dyslipidemia
5. Impaired ejection fraction (<0.50)
6. Family history of coronary artery disease
7. Hypertension
8. Male gender
9. Peripheral artery disease
10. Prior myocardial infarction
11. Renal dysfunction
12. Smoking history
13. 3-Vessel disease
14. Unstable angina
Supplemental Table 2: Covariates Used to Predict In-Hospital Mortality.

Preoperative variables

1. Age at operation
2. Cerebral vascular disease
3. Congestive heart failure
4. Dyslipidemia
5. Impaired ejection fraction (<0.50)
6. Family history of coronary artery disease
7. Hypertension
8. Intra-aortic balloon pump
9. Left main disease (>0.50)
10. Male gender
11. Peripheral artery disease
12. Prior myocardial infarction
13. Renal dysfunction
14. Smoking history
15. Surgical history
16. Surgical urgency
17. 3-Vessel disease
18. Unstable angina

Intraoperative variables

19. Conduit (SIMA vs. BIMA)
20. Distal grafts
21. Perfusion time (min)
Supplemental Table 3: Covariates used to predict late mortality.

Preoperative variables

1. Age at operation
2. Unstable angina
3. Congestive heart failure
4. Cerebrovascular disease
5. Dyslipidemia
6. Family history of coronary artery disease
7. Hypertension
8. Impaired ejection fraction (<0.50)
9. Intra-aortic balloon pump
10. Left main disease (>0.50)
11. Male gender
12. Peripheral artery disease
13. Prior myocardial infarction
14. Renal dysfunction
15. Smoking history
16. Surgical history
17. Surgical urgency
18. 3-Vessel disease

Intraoperative variables

19. Conduit (SIMA vs. BIMA)
20. Distal grafts
21. Perfusion time

Postoperative variables

22. Cardiac arrest
23. Deep sternal wound infection
24. Gastrointestinal disorder
25. Low cardiac output
26. Myocardial infarction
27. Pulmonary insufficiency
28. Renal insufficiency