Bilateral internal thoracic artery grafting improves long-term survival in patients with reduced ejection fraction: A propensity-matched study with 30-year follow-up

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Objective: Bilateral internal thoracic artery (BITA) grafting has been shown to improve long-term survival after coronary artery bypass grafting. However, there has been reluctance to use this technique in higher-risk patients. Patients with reduced ejection fraction (EF) have been shown to present a higher operative risk and reduced long-term survival. We studied the perioperative and long-term results of BITA versus single internal thoracic artery grafting (SITA) in a large population of patients with reduced EF in whom BITA grafting was broadly applied.

Methods: Between February 1972 and May 1994, 4537 consecutive patients in whom EF was recorded underwent SITA (2340) or BITA (2197) grafting. Prospectively collected clinical data recorded EF categorically as less than 0.30 (group I; n = 233), 0.30 to 0.50 (group II; n = 1256), or greater than 0.50 (group III; n = 3048). Multivariable analyses were performed to determine correlates of operative and late mortality. Optimal matching using propensity scoring was used to create matched SITA and BITA cohorts: group I, SITA and BITA, n = 87 each; group II, SITA and BITA, n = 448 each; group III, SITA and BITA, n = 1137 each. Equality of survival distribution was tested by the log-rank algorithm.

Results: There was no difference in operative mortality between matched SITA and BITA groups (group I: SITA vs BITA, 10.3% vs 6.9%, $P = .418$; group II: 4.7% vs 4.5%, $P = .873$; group III: 3.2% vs 2.0%, $P = .086$). SITA versus BITA was not a predictor of operative mortality on logistic regression analysis. There was no difference in freedom from any postoperative complication, including sternal wound infection, between matched SITA and BITA groups. Late survival was significantly enhanced with the use of BITA grafting in groups II and III (10- and 20-year survival, SITA vs BITA, in group II: 57.7% ± 0.3% and 19% ± 2.5% vs 62.0% ± 2.3% and 33.1% ± 3.4%, respectively, $P = .016$; and in group III: 67.1% ± 1.4% and 35.8% ± 1.7% vs 74.6% ± 1.3% and 38.1% ± 2.1%, respectively, $P = .012$). Likewise, choice of SITA versus BITA was a significant predictor of late mortality on Cox regression in both groups II ($P < .007$) and III ($P < .001$).

Conclusions: Broadly applied BITA compared with SITA grafting in propensity-matched patients provides enhanced long-term survival with no increase in operative mortality or morbidity for patients with normal and reduced EF. The expanded use of BITA grafting should be seriously considered. (J Thorac Cardiovasc Surg 2012;143:844-53)

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Twenty-five years ago, we reported a 12-year experience with 227 patients who underwent bilateral internal thoracic artery (BITA) grafting with low operative risk and excellent intermediate-term results.[1] Several subsequent retrospective studies have documented an advantage for BITA over single internal thoracic artery (SITA) grafting in reducing late mortality and cardiac events.[2-6]

Patients with reduced ejection fraction (EF) undergoing coronary artery bypass grafting (CABG) have an increased operative mortality (OM)[7-12] and reduced late survival[10,11,13-16] compared with patients with normal EF. Because of the reluctance to use BITA grafting in patients with increased risk, the impact of this surgical approach on perioperative and long-term survival in this high-risk group remains undefined. To determine the influence of BITA grafting in patients with left ventricular dysfunction, we report the clinical outcomes with a 30-year follow-up

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Abbreviations and Acronyms

BITA = bilateral internal thoracic artery
CABG = coronary artery bypass grafting
EF = ejection fraction
ITA = internal thoracic artery
LAD = left anterior descending
LITA = left internal thoracic artery
OM = operative mortality
RITA = right internal thoracic artery
SITA = single internal thoracic artery

from a consecutive cohort of patients in whom one third had impaired systolic function and approximately one half received BITA grafting.

MATERIALS AND METHODS

This report involves 4537 consecutive patients who underwent CABG between February 1972 and May 1994, 2340 of whom received SITA grafting and 2197 received BITA grafting. Waiver of informed consent was granted by the institutional review board. The study population consisted of 146 patients receiving SITA and 87 patients receiving BITA with an EF less than 0.30 (group I); 656 patients receiving SITA and 600 patients receiving BITA with an EF between 0.30 and 0.50 (group II); and 1538 patients receiving SITA and 1510 patients receiving BITA with an EF greater than 0.50 (group III). Appendix E1 shows a listing of clinical variables associated with unmatched patients. Excluded from this study were patients with concomitant cardiovascular procedures and those in whom only 1 distal graft was performed. The series includes all elective, urgent, emergency, and salvage cases.

To adjust for differences in patient risk factors, patients receiving SITA and BITA in groups I, II, and III were matched by propensity score as described in the "Statistical Analysis" section. Groups I, II, and III matched patients constitute the clinical material for this comparative analysis. The coronary and perioperative risk factors for propensity-matched patients are summarized in Table 1. Although patients receiving SITA and BITA had different risk profiles before matching, there were no significant differences in any of the risk factors in propensity-matched groups I, II, or III.

Patient preoperative anginal symptoms were defined by the Canadian Cardiovascular Society. Patients with unstable angina included patients with Canadian Cardiovascular Society class III or IV. In group I SITA, there were 4 patients (4.6%) in class I, 1 patient (1.1%) in class II, 27 patients (31.0%) in class III, and 55 patients (63.2%) in class IV. In group I BITA, there were 7 patients (8.0%) in class I, 3 patients (3.4%) in class II, 31 patients (35.6%) in class III, and 46 patients (52.9%) in class IV. The distribution of class III or IV symptoms was comparable for patients receiving SITA and BITA (94.2% vs 88.5%; $P = .280$).

In group II SITA, there were 9 patients (2.0%) in class I, 18 patients (4.0%) in class II, 191 patients (42.6%) in class III, and 230 patients (51.3%) in class IV. In group II BITA, there were 16 patients (3.6%) in class I, 23 patients (5.1%) in class II, 199 patients (46.9%) in class III, and 199 patients (44.4%) in class IV. There was no significant difference in the proportion of group II patients receiving SITA (93.9%) and BITA (91.3%) who had class III or IV symptoms ($P = .127$).

In group III SITA, there were 29 patients (2.6%) in class I, 62 patients (5.5%) in class II, 579 patients (50.9%) in class III, and 467 patients (41.1%) in class IV. In group III BITA, there were 38 patients (3.3%) in class I, 69 patients (6.1%) in class II, 542 patients (47.7%) in class III, and 488 patients (42.9%) in class IV. The distribution of class III or IV symptoms is similar for SITA and BITA in group III (92.0% vs 90.6%; $P = .234$).

Operative Data

The operation was performed in group I SITA electively in 27 cases (31.0%), urgently in 47 cases (54.0%), on an emergency basis in 10 cases (11.5%), and on a salvage basis in 3 cases (3.4%). In group I BITA, the operation was performed electively in 30 cases (34.5%), urgently in 53 cases (60.9%), on an emergency basis in 3 cases (3.4%), and on a salvage basis in 1 case (1.1%). A comparison of elective versus non-elective urgency revealed no significant difference ($P = .630$). Operations in 10 SITA (11.5%) and 9 BITA (10.3%) cases were repeat operations ($P = .808$).

In group II SITA, the operation was performed electively in 190 cases (42.4%), urgently in 217 cases (48.4%), on an emergency basis in 36 cases (8.0%), and on a salvage basis in 5 cases (1.1%). In group II BITA, the operation was performed electively in 201 cases (44.9%), urgently in 229 cases (51.1%), on an emergency basis in 18 cases (4.0%), and on a salvage basis in 0 cases (0.0%). The distribution of non-elective cases was similar for the 2 cohorts (57.6% vs 55.1%; $P = .459$).

In group III SITA, the operation was performed electively in 561 cases (49.3%), urgently in 477 cases (42.0%), on an emergency basis in 94 cases (8.3%), and on a salvage basis in 5 cases (0.4%). In group III BITA, the operation was performed electively in 565 cases (49.7%), urgently in 533 cases (46.9%), on an emergency basis in 38 cases (3.3%), and on a salvage basis in 1 case (0.1%). The distribution of nonelective cases was similar for the 2 cohorts (50.7% vs 50.3%; $P = .867$). Operations in 77 patients receiving SITA (6.8%) and 82 patients receiving BITA (7.2%) were repeats ($P = .681$).

Details of the operative technique used in the present series, including internal thoracic artery (ITA) mobilization, orientation, and reconstruction in BITA grafting, have been published.[1] The ITA is dissected from the chest wall in a skeletonized fashion 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 have been implemented to enhance myocardial protection during the operation. Cardiopulmonary bypass was used in all operations. The operative data for propensity-matched patients, by group, are shown in Appendix E2. Operative variables were mostly comparable between matched groups with the exception of the mean distal grafts ($P = .031$) and aortic crossclamp time ($P = .009$) in group I. In groups II and III, the aortic crossclamp time was, as expected, significantly greater for those receiving BITA than for those receiving SITA ($P < .001$).

Data Collection and Management

Perioperative data were obtained by prospective review of the patient's hospital record, catheterization reports, cineangiograms, and echocardiography. Follow-up information was obtained through comprehensive questionnaires and by telephone interview with surviving patients, family members, or the patient's personal physician. A Patient Registration Form and a Patient Follow-Up Form were completed for each patient in the study. Appendix E3 shows the definitions of terms.

Statistical Analysis

Demographic and clinical data are presented as frequency distributions and simple percentages. Values of continuous variables are expressed as mean ± standard deviation. Univariate analysis of selected preoperative and postoperative discrete variables was accomplished by chi-square, continuity-adjusted chi-square analysis, or 2-tailed Fisher exact test with the appropriate degrees of freedom to test for the equality of proportions in the case of categoric variables. Two-sample t tests (2-tailed) were used to test for the equality of means of continuous variables.