Off-Pump Bilateral Versus Single Skeletonized Internal Thoracic Artery Grafting in High-Risk Patients

Takeshi Kinoshita, MD; Tohru Asai, MD, PhD; Tomoaki Suzuki, MD, PhD; Atsushi Kambara, MD; Keiji Matsubayashi, MD, PhD

Background—We compared the outcomes in propensity score-matched high-risk patients (European System for Cardiac Operative Risk Evaluation [EuroSCORE] ≥5) undergoing off-pump coronary artery bypass graft surgery using bilateral or single skeletonized internal thoracic artery (ITA).

Methods and Results—Of 794 consecutive patients undergoing isolated coronary artery bypass graft surgery (788 by the off-pump technique without emergent conversion to cardiopulmonary bypass), the 536 who had a EuroSCORE ≥5 and underwent off-pump skeletonized single (n=236) or bilateral (n=300) ITA were retrospectively analyzed after excluding the 6 who were transferred to our hospital after receiving percutaneous cardiopulmonary support, the 45 who had only 1 target in the left-side coronary area, and the 207 with EuroSCORE <5. A total of 235 pairs were matched using propensity scores calculated from 7 preoperative factors (C statistic, 0.65). The rate of postoperative complications was similar between the groups. The mean observation period was 3.2 years. The 5-year estimated survival rate free from overall death and cardiac event in patients receiving bilateral versus single ITA grafting was 85.8±5.5% versus 74.8±4.9% (P=0.002) and 87.4±4.6% versus 66.1±5.7% (P=0.001), respectively. In multivariate Cox proportional hazard models, bilateral ITA grafting was significantly associated with a lower risk of overall death (hazard ratio, 0.56; 95% CI, 0.32 to 0.87; P=0.009) and cardiac event (hazard ratio, 0.40; 95% CI, 0.24 to 0.69; P=0.001).

Conclusions—In high-risk patients, off-pump skeletonized left-sided bilateral in situ ITA grafting is associated with lower risk of overall death and cardiac event than single ITA grafting without increased operative risk. (Circulation. 2011; 124(suppl 1):S130–S134.)

Key Words: coronary artery bypass grafting ■ off-pump coronary artery bypass ■ propensity score

Bilateral internal thoracic artery (BITA) grafting has been reported to provide better long-term outcomes than single internal thoracic artery (SITA) grafting.1–3 However, little is known about its significance for high-risk patients when using the off-pump technique. The purpose of the present study was to compare postoperative outcomes in propensity score-matched high-risk patients undergoing isolated off-pump BITA or SITA grafting and to quantify any benefit of BITA grafting for this subset.

Methods
All patients had previously granted permission for use of their medical records for research purposes. The study was approved by the Institutional Review Board. Between January 2002 and December 2009, 794 consecutive patients underwent isolated coronary artery bypass graft (CABG) surgery at our institution. Of these patients, 6 underwent emergent percutaneous cardiopulmonary support at other hospitals during cardiopulmonary resuscitation for cardiac arrest caused by acute myocardial infarction and were then transferred to our hospital where they underwent emergent coronary bypass surgery with percutaneous cardiopulmonary support. The remaining 788 patients underwent off-pump CABG without emergent conversion to cardiopulmonary bypass during surgery. Of this cohort, the 536 patients who had logistic European System for Cardiac Operative Risk Evaluation (EuroSCORE) ≥5 and underwent off-pump CABG surgery using SITA (n=236) or BITA (n=300) with complementary saphenous vein (SV), gastroepiploic artery (GEA), or both were retrospectively analyzed after excluding the 6 patients who were transferred to our hospital after receiving percutaneous cardiopulmonary support, the 45 patients who had only 1 target vessel in the left-side coronary area, and the 207 patients with logistic EuroSCORE <5.

Propensity Score Matching
Propensity scores were created to quantify the likelihood that a given patient would receive BITA grafting. Bivariate analyses were performed to examine differences in baseline characteristics between patients who received SITA grafting and those who received BITA grafting (Table 1). Propensity scores were then calculated using a multivariate logistic regression model based on the following 7 preoperative characteristics with a significance level of <0.05 in univariate analyses: age, female sex, body mass index, smoking, previous myocardial infarction, circumflex coronary artery >75% stenosis, and right coronary artery >75% stenosis.4,5 The area under the receiver operating characteristic curve was 0.65 (95% CI, 0.61 to 0.70; P=0.001). The Hosmer-Lemeshow goodness-of-fit χ² for this model was 8.35 (P=0.400). Patients who received BITA grafting had a significantly higher mean propensity score than those who...
received SITA grafting (95% CI of mean, 0.568 to 0.597 versus 0.521 to 0.555; \( P = 0.001 \)). There was considerable overlap in the propensity scores of patients who received BITA grafting (minimum, 0.210; maximum, 0.880) and those who received SITA grafting (minimum, 0.218; maximum, 0.820). Each patient who received BITA grafting was matched with the patient who received SITA grafting with the closest propensity score (within 0.030 on a scale of 0 to 1). By propensity score, 235 pairs were successfully matched in a 1:1 manner (ie, BITA group, \( n = 235 \); SITA group, \( n = 235 \)).

End Points and Definition
The end points were overall death and cardiac event (cardiac death, myocardial infarction, repeat revascularization). Cardiac death included deaths caused by myocardial infarction or heart failure and sudden death. Deep sternal infection was defined as any chest wound infection involving the sternum or mediastinal tissues during the follow-up period. This definition included infections with exposure of the deep fascia or sternum.

Surgical Technique
The off-pump technique was used for all patients. The ITA and GEA were harvested with an ultrasonic scalpel using the skeletonization technique (Harmonic Scalpel; Ethicon Endo-Surgery; Cincinnati, OH).10–12 During anastomosis, a suction-type mechanical stabilizer (Octopus 4.3; Medtronic; Minneapolis, MN) was used to immobilize the target site of the coronary artery. Distal myocardial perfusion was maintained using an intracoronary shunt tube (Anastath; Edwards Lifescience; Irvine, CA). Vein-to-aorta proximal anastomosis was performed using partial clamping or an anastomotic device. To prevent complications related to manipulation of the ascending aorta, we routinely performed CT scan and epiatomic ultrasonography and assessed the severity and location of atherosclerosis of the aorta. When the surgeon judged that partial clamping of the ascending aorta would increase the risk of embolism, a proximal anastomotic device was used, for instance the Novare Enclose device (Novare Surgical Systems; Cupertino, CA), the HEARTSTRING Proximal Seal System (Guidant Corporation; Santa Clara, CA), or the Symmetry Aortic Connector System (St Jude Medical; St Paul, MN). To assess the graft functioning, a recording of the transit time flow trace was made routinely after each graft had been completed and immediately before chest closure.

Graft Arrangement
The basic strategy for myocardial revascularization was in situ grafting of the ITA to the left anterior descending coronary artery (LAD). The second ITA and SV were grafted to the circumflex branches, diagonal branches, or both. The inferior wall was revascularized using the SV, the in situ GEA, or both. Use of the GEA required stenosis of >90% of the target vessels. In the majority of patients who received BITA grafting, the in situ right-side ITA was tunneled through a right-sided pericardial incision and routed anterior to the aorta across the midline for grafting to the LAD, and the in situ left-side ITA was used for the diagonal branches, circumflex branches, or both. To prevent complications related to resternotomy, at the end of the procedures, the right-side ITA was covered with loosely approximated mediastinal tissue before the sternum was reaproximated with wires. On the rare occasions when the in situ right-side ITA was too short for grafting to the LAD, it was grafted to the circumflex branches through the transverse sinus, and the in situ left-side ITA was grafted to the LAD. When the right-side ITA was injured at its proximal portion or too short for grafting to the LAD and circumflex branches, a composite graft was constructed. In these cases, the in situ left-side ITA was anastomosed to the LAD, the free graft of the right-side ITA was anastomosed to the in situ left-side ITA in an end-to-side fashion, and its distal end was connected to the circumflex branches. Complete revascularization was accomplished when at least 1 bypass graft was placed distal to a >75% narrowing in each diseased territory. Left main trunk stenosis would require bypass grafting to both the LAD and the circumflex territory to be considered complete.

Statistical Analysis
Comparison of clinical characteristics between 2 groups were performed using Pearson \( \chi^2 \) test for categorical variables, unpaired \( t \) test for normally distributed variables, and Mann-Whitney \( U \) test for skewed variables. The estimated survival rates were calculated using the Kaplan-Meier method and compared using the log-rank test. The hazard ratios and 95% CIs for the association between BITA grafting and overall death or cardiac event were estimated using the Cox proportional hazard models. The proportional hazards assumption was checked by inspecting the log-log survival curves. No violation of the assumption was detected. All statistical testing was 2 sided. Results were considered statistically significant at \( P < 0.05 \).
analyses were performed with the SPSS version 11.0 (SPSS Inc; Chicago, IL) statistical software.

**Results**

In the original cohort, patients who received BITA grafting were significantly younger, more often men with high body mass index, and more likely to have a smoking history. They also had higher prevalence of previous myocardial infarction and more often had critical stenoses in the circumflex and right coronary arteries (Table 1). After propensity score matching, the 2 matched groups had similar baseline characteristics (Table 2).

**Operative Data**

Operation time was significantly longer in the BITA group than in the SITA group (269 ± 54 versus 251 ± 65 min, Operation time was significantly longer in the BITA group than in the SITA group (269 ± 54 versus 251 ± 65 min, *P* = 0.001). Sequential grafting tended to be used more often in the SITA group (69.4% versus 61.3%, *P* = 0.067). No significant difference was found between the BITA group and the SITA group in the number of distal anastomoses (3.5 ± 1.0 versus 3.4 ± 0.9, *P* = 0.204) and the rate of complete revascularization (100.0% versus 98.7%, *P* = 0.248). Table 3 summarizes ITA arrangements and graft combinations. In both groups, the LAD was revascularized using the in situ ITA. In the BITA group, the second ITA was anastomosed to the circumflex coronary artery, the diagonal branch, or both as an in situ graft in 229 (97.4%) patients and as a free graft in 6 (2.6%) patients. The GEA was used as an in situ graft in 106 (45.1%) patients in the BITA group and 83 (35.3%) patients in the SITA group (*P* = 0.001). Partial clamping was used in 49 of 66 (74.2%) patients in the BITA group and 161 of 212 (75.9%) in the SITA group (*P* = 0.67).

**In-Hospital and Postoperative Outcomes**

There was no significant difference between the 2 groups in the occurrence of postoperative complications (Table 4). The blood glucose levels of the BITA and SITA groups on postoperative days 0, 1, and 2 were 148 ± 37 and 150 ± 35 mg/dL (*P* = 0.476), 177 ± 40 and 176 ± 35 mg/dL (*P* = 0.389), and 152 ± 34 and 147 ± 28 mg/dL (*P* = 0.301), respectively. The follow-up rate of the patients was almost complete (99.3%). The mean duration of the observation period was 3.2 ± 1.6 years. The 5-year estimated rate of survival free
from overall death and cardiac event in the BITA group versus the SITA group was 85.8 ± 5.5% versus 74.8 ± 4.9% (Figure 1) and 87.4 ± 4.6% versus 66.1 ± 5.7% (Figure 2), respectively. BITA grafting was independently associated with both overall death and cardiac event in a multivariate Cox proportional hazards model based on the following variables: age, female sex, body mass index, diabetes mellitus, long-term hemodialysis, smoking, peripheral arterial disease, previous myocardial infarction, and ejection fraction <40% (Table 5).

### Discussion

The present study enrolled 470 propensity-matched patients with logistic EuroSCORE ≥5 and at least 2 target vessels in the left-side coronary area who underwent isolated off-pump CABG surgery using in situ skeletonized SITA or BITA with complementary SV or GEA. The major finding of the study was that patients who received in situ BITA grafting to the LAD and the next most important left-sided coronary arteries were independently at lower risk of overall death and cardiac event than those who received in situ SITA grafting to the LAD plus SV or GEA graft to other coronary arteries.

In the present study, the survival benefit of BITA grafting over SITA grafting was seen as early as 2 to 3 years. This finding does not concur with the many reports in which the survival benefit of BITA grafting is seen only after longer follow-up.1–7 Possible explanations are that a nonfatal event for low-risk patients might easily cause a fatal outcome in high-risk patients and that the ITA is more likely to be patent than the SV when grafted to the left-side coronary area at all times after surgery.13 Lytle and coworkers7 compared the outcome in 1152 propensity score-matched pairs receiving BITA or SITA grafting with a mean follow-up of 16.5 years and demonstrated that advanced age, abnormal left ventricular function, and noncardiac risk factors reduced overall survival but that the incremental benefit of BITA grafting began relatively early after surgery and persisted during follow-up in such high-risk patients. Patients enrolled in the present study had multiple risk factors, including a mean age of 73.2 years, diabetes in 51.7%, chronic kidney disease in 60.8%, hypertension in 68.3%, peripheral arterial disease in 22.6%, and <40% ejection fraction in 29.5%. Our findings indicate that BITA grafting to the left-side coronary area is a good surgical strategy for high-risk patients to further improve outcomes after CABG surgery.

There is no gold standard for how to use the right-side ITA. It is easier to use the right-side ITA as a free graft to make a composite graft than as an in situ graft, but reduced early graft patency has been reported in recent publications.14–16 Complete skeletonization makes the in situ right-side ITA long enough to reach the left-side coronary area, including the distal LAD. Right-side ITA grafting to the right coronary artery has been shown to fail more frequently than grafting to the left-side coronary territories.13,17 We have used the

### Table 4. Postoperative Complications

<table>
<thead>
<tr>
<th></th>
<th>SITA (n=235)</th>
<th>BITA (n=235)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Deep sternal infection</td>
<td>2 (0.9)</td>
<td>3 (1.3)</td>
<td>0.686</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>55 (23.4)</td>
<td>50 (21.3)</td>
<td>0.580</td>
</tr>
<tr>
<td>Perioperative myocardial infarction</td>
<td>2 (0.9)</td>
<td>2 (0.9)</td>
<td>0.999</td>
</tr>
<tr>
<td>Stroke</td>
<td>4 (1.7)</td>
<td>1 (0.4)</td>
<td>0.372</td>
</tr>
<tr>
<td>30-d mortality</td>
<td>5 (2.1)</td>
<td>4 (1.7)</td>
<td>0.736</td>
</tr>
</tbody>
</table>

Data are presented as n (%). Abbreviations as in Table 1.

### Table 5. Multivariate Cox Proportional Hazard Models

<table>
<thead>
<tr>
<th></th>
<th>HR (95% CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall death</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BITA grafting</td>
<td>0.56 (0.32–0.87)</td>
<td>0.009</td>
</tr>
<tr>
<td>Age*</td>
<td>2.40 (1.54–3.45)</td>
<td>0.010</td>
</tr>
<tr>
<td>Long-term hemodialysis</td>
<td>2.98 (1.45–4.88)</td>
<td>0.016</td>
</tr>
<tr>
<td>Peripheral arterial disease</td>
<td>2.50 (1.50–4.03)</td>
<td>0.020</td>
</tr>
<tr>
<td>Ejection fraction &lt;40%</td>
<td>2.60 (1.54–4.30)</td>
<td>0.014</td>
</tr>
<tr>
<td>Cardiac event</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BITA grafting</td>
<td>0.40 (0.24–0.69)</td>
<td>0.001</td>
</tr>
<tr>
<td>Long-term hemodialysis</td>
<td>2.90 (1.43–4.80)</td>
<td>0.017</td>
</tr>
<tr>
<td>Ejection fraction &lt;40%</td>
<td>3.34 (1.68–5.15)</td>
<td>0.016</td>
</tr>
</tbody>
</table>

Overall death (sample size, 470; patients with events, 55; no. censored, 415). Cardiac event (sample size, 470; patients with events, 65; no. censored, 405). HR indicates hazard ratio. Other abbreviations as in Table 1.

*HR per 10-y increase.
skeletonized in situ right-side ITA to revascularize the LAD in 88.5% (208/235) and the circumflex and diagonal branches in 8.9% (21/235) in the BITA group. Our findings suggest that skeletonized in situ right-side ITA grafting to the LAD is a feasible and reliable strategy.

Sternal infection is a rare, but life-threatening complication after surgery. Although the use of the BITA has been considered a risk factor for sternal infection, especially in patients with diabetes, reduction of wound complications has been reported when the skeletonization technique is properly applied\textsuperscript{18–21} and serum glucose is well managed.\textsuperscript{22} In the present study, all ITAs were skeletonized, and postoperative serum glucose was well controlled. Sternal infection occurred in 3 (1.3%) patients in the BITA group and 2 (0.9%) patients in the SITA group \( (P=0.686) \). We believe that with strict serum glucose control, diabetes no longer is a contraindication for the use of the skeletonized BITA.

The present study has a number of potential limitations. First, even with propensity matching, a completely fair comparison between BITA and SITA grafting cannot be performed. Although the propensity score can adjust for confounding by indication and selection bias, residual unobserved confounding cannot be eliminated. Second, all enrolled subjects were Japanese patients who underwent revascularization using the off-pump technique at a single center, which limits the generalizability of the findings. Third, the heterogeneous distribution of GEA and SV use between the groups also made fair comparison difficult. Finally, the lack of available coronary angiographic data did not allow us to evaluate whether the survival benefit of BITA grafting is related to graft patency.

In conclusion, off-pump skeletonized left-sided BITA grafting is independently associated with a lower risk of overall death and cardiac event without increased incidence of deep sternal infection in high-risk patients. The benefit of BITA grafting begins early after operation.

Disclosures

None.

References

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