Comparison of Bilateral Internal Thoracic Artery Revascularization Using In Situ or Y Graft Configurations

A Prospective Randomized Clinical, Functional, and Angiographic Midterm Evaluation

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Background—Bilateral internal thoracic arteries (BITA) demonstrated superiority over other grafts to the left coronary system in terms of patency and survival benefit. Several BITA configurations are proposed for left-sided myocardial revascularization, but the ideal BITA assemblage is still unidentified.

Methods and Results—From 03/2003 to 08/2006, 1297 consecutive patients underwent isolated bypass surgery in our institution. 481 patients met the inclusion criteria for randomization, and 304 (64%) were randomized. Patients were allocated to BITA in situ grafting (n = 147) or Y configuration (n = 152) then evaluated for clinical, functional, and angiographic outcome after 6 months and 3 years. Patient telephone interviews were conducted every 3 months and a stress test performed twice yearly under the referring cardiologist’s supervision. Angiographic follow-up was performed 6 months after surgery. The primary and secondary end points were, respectively, major adverse cerebrocardiovascular events (MACCE) and the proportion of ITA grafts that were completely occluded at follow-up angiography. More arterial anastomoses were performed in patients randomized to the Y than the in situ configuration (3.2 versus 2.4; P < 0.001). No significant difference between the 2 groups in terms of hospital mortality or morbidity was found. At follow-up, there was no significant difference in any MACCE rate between the 2 groups. 450 out of 464 anastomosis (97%) in the BITA Y group and 287 of 295 (97%) in the BITA in situ group were controlled patent (P = 0.99).

Conclusion—Excellent patency rates were achieved using both BITA configurations with no significant differences in terms of MACCE up to 19 months postoperatively, but longer-term results remain to be established. (Circulation. 2008; 118[suppl 1]:S216–S221.)

Key Words: surgery • bypass • coronary disease • internal thoracic artery

The ideal bypass conduit for each targeted diseased coronary vessel remains a subject of intense controversy. For the left coronary system, bilateral internal thoracic arteries (BITA) have clearly demonstrated long term superiority over all other types of grafts (either venous or arterial) in terms of patency, freedom from arteriosclerosis, and survival benefit.1,2

Several configurations of BITA have been proposed to achieve complete left-sided myocardial revascularization. There are 3 commonly accepted techniques. Two are BITA in situ grafting: (1) left ITA (LITA) to the left anterior descending artery (LAD) and right ITA (RITA) in the transverse sinus to the circumflex artery (LCX) or (2) RITA anterior to the aorta to the LAD and LITA to the LCX. The third configuration is the composite T or Y graft configuration: using free RITA graft anastomosed proximally to the LITA.3

Concerns were raised for each of these configurations. With the “in situ” BITA with the RITA crossing the mid line anteriorly, there is a risk of ITA damage in case of a redo operation. In situ BITA with the RIMA in the transverse sinus can only reach and revascularize the proximal LCX branches. Composite Y or T grafting with BITA brought back concern of a potential “steal phenomenon” of the LITA by the RITA. Because the ideal BITA assemblage has not yet been identified, we prospectively randomized patients to one of two types of BITA configurations with a first evaluation at 6 months and then a follow up at 3 years to assess the clinical, functional, and...
Table 1. Inclusion and Exclusion Criteria

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>Exclusion Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Angiographic evidence of severe coronary obstruction (&gt;70% by visual estimate)</td>
<td>Diabetes with a HbA1c &gt;7.5.</td>
</tr>
<tr>
<td>Elective procedure</td>
<td>FEV1 &lt;60% predicted value.</td>
</tr>
<tr>
<td>Isolated CABG</td>
<td>Body mass index &gt;35</td>
</tr>
<tr>
<td>Age &lt;75 years and life expectancy &gt;5 years</td>
<td>Reoperation</td>
</tr>
<tr>
<td>Other configuration then LIMA → LAD territory; RIMA → LCX territory.</td>
<td></td>
</tr>
</tbody>
</table>

CABG indicates coronary artery bypass surgery; FEV1, forced expiratory volume in the first second; HbA1c, Hemoglobin A1C; LIMA, left internal mammary artery; RIMA, right internal mammary artery; LAD, left anterior descending artery; LCX, circumflex artery.

angiographic results. This manuscript reports the midterm evaluation 6 months after randomization.

Patients and Methods

Study Design

All patients referred for isolated surgical coronary revascularization from April 2003 to July 2006 were screened according to the inclusion criteria (Table 1). Patients were randomly assigned to undergo one of two alternative surgical strategies: BITA in situ (LITA to the LAD and RITA to the marginal branches into the transverse sinus) or BITA Y (LITA to the LAD and RITA to the marginal branches but anastomosed proximally to the LITA in a Y configuration as described by Barra JA et al3). Randomization was performed the day before the operation after the patient’s record was reviewed without knowledge of the preoperative angiogram. Complementary grafting was performed with either a saphenous vein graft or a pedicled right gastroepiploic artery depending on the location and quality of the targeted coronary vessel, but also depending on the surgeon’s choice. All patients were scheduled for a systematic angiography at 6 and 36 months after surgery. All patients gave written informed consent at the time of bypass surgery and before the angiographic investigation. The study protocol was approved by the Ethics Committee at our institution.

Patients

From 2003 to 2006, 1297 consecutive patients underwent isolated bypass surgery at our institution. Of these, 481 patients (37%) met the inclusion criteria for enrolment in the study (Figure 1). Three hundred four of 481 patients (63%) were actually randomized. The remaining 177 patients were not randomized because of (1) refusal of systematic angiographic control (85%) and (2) logistic incapacity to randomize patients (15%). BITA grafting was performed with an in situ configuration in 147 patients and with a Y configuration in 152. Five patients initially allocated to the BITA in situ group were excluded for protocol violations. In these cases, the surgeon decided to deviate from the assigned revascularization strategy in favor of a BITA Y configuration. Patient’s demographics and clinical characteristics are shown in Table 2. The BITA were harvested and grafted as previously described.4-5 Operative characteristics are detailed in Table 3.

Postoperative Management and Follow-Up

Patients received prophylactic low dose fractionated heparin postoperatively, and 160 mg of aspirin daily starting on postoperative day 2. Patients were interviewed by telephone at 3 and 6 months and then twice yearly thereafter. If the patient had been hospitalized between interviews, inpatient records were obtained. Patients had a systematic stress test on a cycloergometer twice a year performed under the supervision of their referring cardiologist.

Follow-up angiography was scheduled at both 6 months and 3 years after surgery. Nitroglycerin (2 mg) was injected into each graft before filming. At least two orthogonal views of each ITA graft were obtained, with continued exposure as required to visualize distal runoff and the size of the target coronary bed.

Data Analysis

The clinical end point was occurrence of MACCE defined as a combined end point including: death from any cause; perioperative myocardial infarction (occurring between 0 and 30 days); late myocardial infarction (occurring between 31 days and 6 years); additional cardiac surgery; coronary angioplasty; and stroke. Myocardial infarction was defined as the apparition of a new Q wave, a rise of more than 10 ng/ml of troponin in the early postoperative period or any episode of chest pain with typical rise and fall of cardiac enzymes thereafter.

The angiographic end point was the proportion of ITA grafts that were completely occluded at follow-up angiography. Complete

Table 2. Baseline Demographic and Clinical Characteristics

<table>
<thead>
<tr>
<th></th>
<th>BITA Y n=152 (%)</th>
<th>BITA In Situ n=152 (%)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>138 (91)</td>
<td>127 (86)</td>
<td>0.23</td>
</tr>
<tr>
<td>Age, y</td>
<td>62 ± 7</td>
<td>62 ± 8</td>
<td>0.55</td>
</tr>
<tr>
<td>Hypertension</td>
<td>107 (70)</td>
<td>105 (69)</td>
<td>0.84</td>
</tr>
<tr>
<td>Smokers</td>
<td>57 (37)</td>
<td>65 (42)</td>
<td>0.37</td>
</tr>
<tr>
<td>Diabetic</td>
<td>31 (20)</td>
<td>29 (19)</td>
<td>0.88</td>
</tr>
<tr>
<td>High cholesterol</td>
<td>109 (71)</td>
<td>109 (71)</td>
<td>0.93</td>
</tr>
<tr>
<td>Previous infarction</td>
<td>56 (37)</td>
<td>42 (28)</td>
<td>0.16</td>
</tr>
<tr>
<td>Obesity (BMI &gt;30)</td>
<td>69 (45)</td>
<td>53 (35)</td>
<td>0.1</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>11 (7)</td>
<td>19 (12)</td>
<td>0.14</td>
</tr>
<tr>
<td>Euroscore (additive)</td>
<td>0.6±1.9 (2.3)</td>
<td>2.9±2.0 (2.7)</td>
<td>0.19</td>
</tr>
<tr>
<td>Left ejection fraction &lt;30%</td>
<td>5 (3)</td>
<td>5 (3)</td>
<td>0.78</td>
</tr>
<tr>
<td>No. of 3 vessels disease</td>
<td>119 (78)</td>
<td>114 (75)</td>
<td>0.48</td>
</tr>
</tbody>
</table>

BITA indicates bilateral internal thoracic artery; BMI, body mass index.
Statistical Analysis
We calculated that the enrolment of at least 152 patients per group would provide the study with 80% power to detect a relative reduction of 8% in the rate of graft occlusion, from an estimated 10% with BITA Y grafting to 2% with BITA in situ grafting, assuming a 20% within-patient correlation for graft occlusion, a 2-tailed test, and an alpha value of 0.05. Data are expressed as the mean ±1 SD. In bivariate analyses, the association of independent variables with each outcome variable was tested with Chi square test for independent samples (binary variables).

All probability values are 2-tailed. The Statistical Analysis Software (SAS, 9.1 releases, SAS Institute Inc) was used in the statistical analysis.

Results
The total number of graft anastomosis performed in each patient was similar in both groups (Table 3). However, the BITA Y configuration allowed the right ITA to reach more distal marginal branches and, in some cases, the PLA or the PDA; consequently, the number of graft anastomoses performed with ITA was significantly larger in the BITA Y group than in the BITA in situ group. As a consequence, a larger number of complementary grafts, particularly saphenous vein grafts, were used in the BITA in situ group.

In-Hospital Events
Three patients died during hospitalization (Table 4) (2 in the BITA in situ group and one in the BITA Y group, P=0.97). In the BITA in situ group, one patient had to be reoperated because of ischemia that occurred 4 hours after admission to the ICU. All mammary grafts were doubled with a saphenous vein graft, and a left ventricular assist device was implanted. The patient died of multiple organ failure (MOF) at day 8. Another patient had to be reoperated for mediastinitis at day 8 and died of MOF after multiple abdominal operations for necrotico-hemorrhagic pancreatitis. In the BITA Y group, one patient died of sudden death on day 5 while on the ward.

There were no significant differences in the rate of stroke or infarction between the two groups.

Clinical and Functional Follow-Up
Clinical
Clinical follow-up is 100% complete with a mean follow-up of 19.8 ±11.7 months in the BITA Y group and 18.8 ±11.6 months in the BITA in situ group (P=0.93; Figure 2). No deaths occurred from hospital discharge to the follow-up time. Four patients in the BITA in situ group and 2 in the BITA Y group suffered from a recurrence of angina during follow-up (P=0.64). All these patients had positive stress tests and underwent a repeated catheterization. Of these 6 patients, 2 patients had an occlusion of the graft and 4 had a progression of the disease.

In the BITA in situ group, the 4 patients with angina recurrence underwent percutaneous coronary intervention (PCI) of (1) a marginal branch (6 months postoperatively) because of a RITA occlusion in one patient, (2) the right coronary because of disease progression in 2 patients (12 and 14 months, respectively, postoperatively), (3) the PDA just after the anastomosis of the saphenous vein graft in one patient (6 months postoperatively).
In the BITA Y group, 2 patients with recurrence of angina underwent PCI. In the first patient, the PDA was stented after the occlusion of a saphenous vein graft (26 months postoperatively); in the second patient, the LAD was treated because of disease progression 1 cm distal to the LITA anastomosis (20 months postoperatively).

No patient underwent a redo cardiac surgery between hospital discharge and the 6-month follow-up.

One patient in the BITA in situ group suffered a stroke 14 months postoperatively.

Functional follow-up is 100% complete with a mean follow-up of 16\(\pm\)10.7 months in the BITA Y group and 15.9\(\pm\)11.2 months in the BITA in situ group (\(P=0.67\)). Stress tests were positive for ischemia in every symptomatic patient (4 in the BITA in situ, and 2 in the BITA Y; \(P=0.64\)). All other patients had negative stress tests. Mean exercise duration and maximal workloads were similar in the BITA in situ in comparison with the BITA Y group (145\(\pm\)30 Watts versus 150\(\pm\)32 Watts; \(P=0.87\)).

Angiographic Follow-Up
Angiographic follow-up was obtained in 146 patients (96%) in the BITA Y group and in 126 patients (82%) in the BITA in situ group with a mean follow-up of 6.1\(\pm\)0.6 months and 6.2\(\pm\)0.7 months, respectively (\(P=0.87\); Table 5). Withdrawal of consent by 32 patients was the main reason for the incomplete 6-month angiography control. The observed ITA anastomotic patency rate was 97% in both groups (\(P=0.99\)).

One asymptomatic patient in the BITA in situ group had an occlusion of the RGEA grafted on a dominant right coronary at the angiographic follow-up, which was dilated during the systematic control procedure.

The evolution of left ventricular ejection fractions from the preoperative measurement to the 6-month control did not show a significant difference between the two groups (60.9\(\pm\)11.5% to 62.1\(\pm\)12% in the BITA Y group versus 61.2\(\pm\)10% to 62\(\pm\)11.5% in the BITA in situ group; \(P=0.69\)).

**Discussion**
In this large, prospective, randomized, single-center clinical trial, we found no significant difference in clinical status or any difference in graft patency rates between the BITA in situ and BITA Y configurations at midterm follow-up. The only significant difference is the larger number of arterial anastomoses allowed by the BITA Y configuration.

The ITA is currently the conduit of choice in CABG surgery for the left coronary system because of its superior graft patency. Although the RITA and the LITA are comparable in size, flow capacity, and patency, the in situ RITA used through the transverse sinus is less useful because its length is not always sufficient to reach all the targeted anastomotic sites on the left side. Therefore, several configurations have been proposed to achieve left-side coronary revascularization.

Some authors have proposed the use of the in situ RITA over the aorta to revascularize the LAD and the LITA to the lateral wall to the marginals.\(^8\) We rarely use this configuration because the RITA crossing the mid line anterior to the aorta is a risk factor for ITA damage and myocardial ischemia in case of a redo operation.\(^9\) A solution proposed by other authors is to implant the RITA into the aorta. Studies on the patency rate of ITA as a free graft attached to the aorta have shown significantly lower rates compared to in situ grafts.\(^10\)

The Y-graft configuration was first described by Barra JA in 1991.\(^3\) This group proposed a BITA assemblage in which
the RITA is attached to the in situ LITA and directed to the lateral and posterior wall of the left ventricle, whereas the LITA is directed to the anterior surface of the heart. Complete arterial revascularization of the left coronary system was achieved with such a configuration. As mentioned earlier, Calafiore et al.\textsuperscript{10} demonstrated a better patency rate for free RITA as part of composite grafts from the in situ LITA when compared with those attached to the aorta. The authors postulated that the lower patency rates of free arterial grafts arising from the aorta were related to exposure of these grafts to turbulence and its associated risk of intimal damage.

However, concerns have arisen about the flow capacity of this BITA Y configuration, particularly in the main stem of the left ITA, and over the theoretical possibility of a steal phenomenon resulting in a fall of perfusion pressure in one of the branches during a period of maximal myocardial blood flow demand. Although intraoperative flow measurements have suggested that the flow capacity is sufficient to meet myocardial flow requirements in the perioperative period,\textsuperscript{11} postoperative measurements of flow reserve in the proximal ITA by Doppler techniques,\textsuperscript{12} and in the reperfused myocardium by positron emission tomography,\textsuperscript{13} have produced conflicting results. In a recently reported study measuring the fractional flow resistance in both branches of the BITA Y, we did not find evidence of a steal phenomenon of the RITA from the LITA.\textsuperscript{14}

The present study is the first large, prospective, randomized trial comparing 2 types of BITA configurations to revascularize the left coronary system with systematic angiographic control. Indeed, only a few authors have reported the comparison between the 2 types of BITA assemblages, and these studies were all retrospective. Calafiore and al.\textsuperscript{15} reported a series of 1818 patients who received BITA (76% BITA in situ versus 24% BITA Y) with a mean clinical follow-up of 33 months. An angiographic control was available in only 5% of the patients at a mean follow-up time of 17 months. The authors concluded that there were no differences between the 2 groups. Lev-Ran and colleagues\textsuperscript{16} also concluded that there was no difference between the 2 BITA configurations based on a series of 1000 patients who received BITA (35% BITA in situ versus 65% BITA Y). Their clinical follow-up ranged from 2 to 56 months. Late angiographic control was obtained in only 6% of the patients and was driven by symptoms in all cases.

A potentially relevant question raised by the present study is the difference in the number of ITA anastomoses between the 2 groups (3.2 in the BITA Y versus 2.4 in the BITA in situ, \( P < 0.01 \)), even if the total number of anastomosis per patients was similar. As of today, there are no series reporting the long-term clinical benefit of such increases of anastomoses with the use of the BITA Y configuration. In a recent study, Rankin and al.\textsuperscript{17} found excellent 20-year survival with in situ BITA grafting. The cumulative percent of repeat revascularization at 20 years is 40.7% (PTCA 35.7% and redo 5%). Considering the higher attrition rate of venous graft compared with ITA graft, and the larger use of venous anastomoses in the BITA in situ group, we could speculate that the adjunction of this significant number of ITA anastomosis could, at long term, decrease the number of late reinterventions in the BITA Y group. The ongoing 3-year clinical and angiographic follow-up of this population will help to address the validity of this hypothesis.

**Conclusion**

Excellent patency rates were achieved in both groups with no significant difference in terms of MACCE or ITA patency.

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**Table 5. 6 Months Systematic Angiographic Control**

<table>
<thead>
<tr>
<th>ITA anastomosis angiographic patency control</th>
<th>BITA Y n=146</th>
<th>BITA In Situ n=126</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>LIMA</strong></td>
<td>190/197 (96%)</td>
<td>166/169 (98%)</td>
<td>0.96</td>
</tr>
<tr>
<td>Diagonal</td>
<td>49/51</td>
<td>43/43</td>
<td>0.55</td>
</tr>
<tr>
<td><strong>LAD</strong></td>
<td>141/146</td>
<td>123/126</td>
<td>0.88</td>
</tr>
<tr>
<td><strong>RIMA</strong></td>
<td>260/267 (97%)</td>
<td>121/126 (96%)</td>
<td>0.69</td>
</tr>
<tr>
<td>Intermediate</td>
<td>10/10</td>
<td>1/1</td>
<td></td>
</tr>
<tr>
<td><strong>OM1</strong></td>
<td>135/137</td>
<td>120/125</td>
<td>0.37</td>
</tr>
<tr>
<td><strong>OM2</strong></td>
<td>81/84</td>
<td>66/69</td>
<td></td>
</tr>
<tr>
<td><strong>PLA</strong></td>
<td>17/19</td>
<td>13/13</td>
<td></td>
</tr>
<tr>
<td><strong>PDA</strong></td>
<td>17/17</td>
<td>12/12</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>450/464 (97%)</td>
<td>287/295 (97%)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Complementary graft anastomosis patency control</th>
<th>BITA Y n=146</th>
<th>BITA In Situ n=126</th>
<th>( P ) Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RGEA</strong></td>
<td>27/30 (90%)</td>
<td>32/38 (84%)</td>
<td>0.73</td>
</tr>
<tr>
<td><strong>SVG</strong></td>
<td>57/59 (97%)</td>
<td>71/76 (93%)</td>
<td>0.66</td>
</tr>
</tbody>
</table>

BITA indicates bilateral internal thoracic artery; ITA, internal thoracic artery; LIMA, left internal mammary artery; RIMA, right internal mammary artery; RGEA, right gastroepiploic artery; SVG, saphenous vein graft; LAD, left anterior descending artery; OM1, obtuse marginal 1; OM2, obtuse marginal 2; PLA, posterolateral artery; PDA, posterodescending artery.
Long-term follow-up will help determine whether the larger number of ITA distal anastomosis allowed by the use of the Y graft configuration translates into a superior late clinical outcome.

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Disclosures
None.

References
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