Patency rate of the internal thoracic artery to the left anterior descending artery bypass is reduced by competitive flow from the concomitant saphenous vein graft in the left coronary artery

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Received 20 January 2008; received in revised form 30 June 2008; accepted 11 July 2008; Available online 23 August 2008

Abstract

Objective: In coronary artery bypass grafting (CABG), insufficient bypass flow can be a cause of occlusion or string sign of the internal thoracic artery (ITA) graft. A patent saphenous vein (SV) graft from the ascending aorta can reduce the blood flow through the ITA graft, and may affect its long-term patency. In the present study, we examined the impact of the patent SV graft to the left coronary artery on the long-term patency of the ITA to left anterior descending (LAD) artery bypass.

Methods: We reviewed the coronary angiograms of 313 patients who had two bypasses to the left coronary artery including 1 in situ ITA to LAD graft between March 1986 and December 2006. Patients who had occlusion of either bypass grafts to the left coronary artery in the early angiography, were excluded. In 64 patients (20.4%), bilateral ITAs were individually anastomosed to the LAD and the second target branch in the left coronary artery (BITA group), while 249 patients (79.6%) had the ITA to LAD bypass and the SV graft to the second target branch in the left coronary artery (ITA/SV group). The mean follow-up period was 6.8 years.

Results: The cumulative patency rate of ITA-LAD bypasses at 10 years was 100% in the BITA group and 81.4% in the ITA/SV group. The ITA to LAD bypass was occluded in 14 (5.6%) patients of the ITA/SV group. In the ITA/SV group, the cumulative graft patency rate of the ITA to LAD bypass in patients who had severe (≥76%) native coronary stenosis between the two anastomotic sites was 98.6% at 5 years, and was significantly higher than that of 82.3% in patients without severe stenosis (p < 0.0001).

Conclusions: Long-term patency of the ITA-LAD bypass was affected by the presence of the patent SV graft to the left coronary artery, particularly when the native coronary stenosis between the two anastomotic sites was not severe. Competitive flow from SV graft could play an important role in occlusion of the in-situ arterial graft.

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Keywords: Coronary artery bypass grafting; Internal thoracic artery; Saphenous vein graft; Competitive flow; Graft arrangement

1. Introduction

The utilization of an internal thoracic artery (ITA) in coronary artery bypass grafting (CABG) has decreased the operative mortality without increasing the operative complications [1,2]. The ITA to the left anterior descending artery (LAD) in coronary revascularization has been proven to have a superior long-term patency rate [3], and it improves the long-term mortality and morbidity in patients with coronary artery disease [4–8] as compared to use of vein grafts to the LAD.

On the other hand, a current issue regarding the ITA graft is that competitive flow in the ITA graft causes graft occlusion or ‘string sign’, which represents the narrowing of the artery along its whole length [9]. In previous reports, competitive flow usually arose when native coronary stenosis was not severe, and the patency rate of the ITA graft inversely correlated with severity of native stenosis [10–12].

Recently, various grafts such as ITA, radial artery, gastroepiploic artery, and saphenous vein (SV) graft are applied and designed in various configurations. There are several reports investigating the hemodynamic features of bypass grafts. Kawasuji and colleagues compared the flow capacities of arterial grafts and SV graft and demonstrated that the flow capacity of the in situ ITA graft which represented diastolic blood pressure, was less than that of SV graft, whose proximal anastomosis was placed on the ascending aorta [13]. When the in situ ITA and the SV graft were connected to the same coronary artery system, the patent SV graft may affect the in situ ITA graft. Such
interactions between the SV graft and arterial bypass grafts have not yet been delineated.

The purposes of this study are to examine the effects of the graft material, for the circumflex or diagonal branch on the long-term patency of the ITA to LAD graft, and to delineate the interactive effect between the bypass grafts aiming at establishing appropriate usage of the SV graft and strategy for optimal graft arrangement in CABG.

2. Materials and methods

We reviewed the coronary angiograms of 313 patients who underwent CABG with two bypasses to the left coronary artery including one in situ ITA to LAD graft and early postoperative angiography between March 1986 and December 2006. Of these, 263 were male and 50 female with a mean age of 60.9 ± 8.9 years and a mean follow-up period of 6.8 ± 4.9 years. In our institution, early postoperative coronary and graft angiography was routinely performed about 2 weeks after surgery, except for patients with renal insufficiency, severe atherosclerosis in the aorta or aged more than 80 years. Late coronary angiography was done when patients suffered from chest pain or recurrence of angina pectoris was suspected by electrocardiogram or other clinical symptoms. Late coronary angiograms were carried out on 133 patients in this series (42.5%; 133/313). All coronary angiograms were independently evaluated by cardiologists for coronary artery stenosis and graft patency. Stenoses were grouped as 51—75% and 76—100% by a precise measurement of the minimal luminal diameter and labeled as 'moderate' and 'severe', respectively in the present study.

The in situ ITA graft or the SV graft as an aorto-coronary bypass was exclusively used in an individual fashion for these patients. The patients who did not undergo early postoperative angiography, who had graft occlusion in either of two bypass grafts to the left coronary artery in the early angiography, and who had a gastroepiploic artery, radial artery, sequential or composite graft, were excluded from this study. Patients whose bypass graft to the right coronary artery was occluded, but both bypass grafts to the left coronary artery were patent in early angiography, were included. Ninety-three patients had two bypass grafts to the left coronary artery, and 220 patients had two bypass grafts in the left coronary artery and 1 in the right coronary artery. The second target site in the left coronary artery was the left circumflex artery (LCX) in 270 patients and the diagonal branch (Dx) in 220 patients. The patients who did not undergo early postoperative angiography between March 1986 and December 2006. Of these, 263 were male and 50 female with a mean age of 60.9 ± 8.9 years and a mean follow-up period of 6.8 ± 4.9 years. In our institution, early postoperative coronary and graft angiography was routinely performed about 2 weeks after surgery, except for patients with renal insufficiency, severe atherosclerosis in the aorta or aged more than 80 years. Late coronary angiography was done when patients suffered from chest pain or recurrence of angina pectoris was suspected by electrocardiogram or other clinical symptoms. Late coronary angiograms were carried out on 133 patients in this series (42.5%; 133/313). All coronary angiograms were independently evaluated by cardiologists for coronary artery stenosis and graft patency. Stenoses were grouped as 51—75% and 76—100% by a precise measurement of the minimal luminal diameter and labeled as 'moderate' and 'severe', respectively in the present study.

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Patients were divided into two groups based on the graft selection for the second target site in the left coronary artery. The BITA group comprised 64 patients in whom the bilateral in situ ITAs were individually anastomosed to the LAD and the second target site (Fig. 1). In the ITA/SV group, 249 patients had a single in situ ITA to LAD and the SV graft to the second target site in the left coronary artery (Fig. 2). Characteristics of both groups are shown in Table 1. In addition, the ITA/SV group was divided into two subgroups based on the severity of native left coronary stenosis between two distal anastomotic sites, which was referred from preoperative coronary angiography (Fig. 3). The subgroup S comprised 189 patients who had severe (76—100%) stenosis between two anastomotic sites, while the subgroup M consisted of 60 patients who had moderate (51—75%) or less stenosis between two anastomotic sites. For example, the subgroup S included patients who had severe stenosis at the origin of LAD or circumflex, and the subgroup M included patients with the stenotic lesion localized in the left main trunk.

3. Operative technique

Our current operative technique has been described previously [14]. In brief, our standard technique since 2000 was off-pump CABG without aortic manipulation. Additionally, we preferably use the bilateral in situ ITAs when we place two bypass grafts to relatively large branches in the left coronary artery region in patients without considerable operative risk, such as chronic obstructive pulmonary disease or an advanced age of more than 75 years. A suction-type stabilizer and an apical heart positioner were used for off-pump CABG. The surgical field was maintained by a CO2 blower and an intracoronary shunt.

Before introduction of an off-pump operation, conventional CABG was performed with ascending aortic and bicaval cannulations. The core temperature was maintained between

![Image](https://academic.oup.com/ejcts/article-abstract/34/4/833/498307/834)
32 °C and 34 °C. Intermittent tepid blood cardioplegia was infused antegrade and retrograde.

The ITA was harvested in either conventional (combined with vein and fascia), semiskelletalized (partially combined with vein) or skeletonized fashion [14]. All distal portions of ITA grafts were greater than 1.5 mm in diameter assessed by insertion of a 1.5-mm flexible probe.

4. Long-term patency rate of the ITA to LAD bypass

We analyzed the long-term patency of the ITA to LAD bypass and examined the effects of graft materials anastomosed to the second target site in the left coronary artery and severity of the native coronary stenosis between two distal anastomotic sites.

5. Statistical analysis

The continuous variables are expressed as mean values ± standard deviations and compared between the two groups by using Wilcoxon rank-sum test. The data of two independent groups were compared using Fisher's exact probability test. The Kaplan–Meier method was used to determine the cumulative graft patency rate and log–rank test was used to compare two groups. The differences in the outcomes were considered statistically significant at a probability value of <0.05.

6. Results

The baseline rate of off-pump CABG in the BITA group was significantly higher than that in the ITA/SV group. Male and hypertensive patients were included in the BITA group with a significantly higher rate as compared to the ITA/SV group. On the other hand, the population of CABG with three distal anastomoses was significantly higher in the ITA/SV group than in the BITA group.

In the ITA/SV group, 14 bypass grafts were occluded during the follow-up period (5.6%; 14/249), whereas, all the ITA-LAD bypasses remained patent in the BITA group. The cumulative patency rate of the ITA-LAD bypass in the ITA/SV group was 94.9% at 5 years and 81.4% at 10 years (Fig. 4).

Table 1

Baseline characteristics in both groups

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>BITA</th>
<th>ITA/SV</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>64</td>
<td>249</td>
<td>0.30</td>
</tr>
<tr>
<td>Age</td>
<td>59.8 ± 8.7</td>
<td>61.2 ± 8.9</td>
<td>0.05</td>
</tr>
<tr>
<td>Follow-up period (years)</td>
<td>4.6 ± 4.4</td>
<td>7.3 ± 4.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Male/female</td>
<td>59 (92%)/5 (8%)</td>
<td>204 (82%)/45 (18%)</td>
<td>0.046</td>
</tr>
<tr>
<td>Hypertension</td>
<td>40 (63%)</td>
<td>117 (47%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>38 (59%)</td>
<td>126 (52%)</td>
<td>0.34</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>30 (47%)</td>
<td>109 (44%)</td>
<td>0.66</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>50.4 ± 12.2</td>
<td>52.8 ± 13.5</td>
<td>0.26</td>
</tr>
<tr>
<td>Operative procedure</td>
<td>On-pump/off-pump</td>
<td>29 (45%)/35 (55%)</td>
<td>248 (99.6%)/1 (0.4%)</td>
</tr>
<tr>
<td>Second target branch in the left coronary artery</td>
<td>Dx/LCX</td>
<td>6 (9%)/58 (91%)</td>
<td>37 (15%)/212 (85%)</td>
</tr>
<tr>
<td>+ Bypass graft to RCA</td>
<td>19 (30%)</td>
<td>201 (81%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Mean ± standard deviation. LVEF: left ventricular ejection fraction; CABG: coronary artery bypass grafting; LAD: left anterior descending artery; Dx: diagonal branch; LCX: left circumflex artery; ITA: internal thoracic artery; RCA: right coronary artery; SV: saphenous vein.

Fig. 3. Patients in the ITA/SV group were divided into two subgroups in regard to severity of the native coronary stenosis between two anastomotic sites (solid line: ITA; dash line: SV graft). ITA: internal thoracic artery; SV: saphenous vein; LMT: left main trunk.

Fig. 4. The cumulative patency rate of the ITA to LAD bypass grafts. The cumulative patency rates at 10 years were 100% in the BITA group and 81.4% in the ITA/SV group. Number at risk is described below the x-axis.
In a comparison of two subgroups of the ITA/SV group, the ITA to LAD bypass graft was occluded in five patients of the subgroup S (2.6%; 5/189) and in nine patients of the subgroup M (15%; 9/60). The cumulative patency rate of the ITA to LAD bypass in the subgroup S were 98.6% at 5 years and 91.2% at 10 years, whereas those in the subgroup M were 82.3% at 5 years and 45.6% at 10 years \( (p < 0.0001) \) (Fig. 5).

The early and late coronary angiograms of 14 patients with occlusions of the ITA to LAD bypass were carefully reviewed. In 4 out of 14 patients, there were no stenoses of the ITA-LAD bypasses in the early angiograms. However, through SV graft injection of the late angiograms, strong bypass flow from SV graft opacified not only the left circumflex artery but also LAD. In addition, the ITA grafts were visualized by retrograde flow and exhibited ‘string sign’ (Fig. 6).

7. Discussion

Significant differences in hemodynamic characteristics between the ITA graft and the SV graft have been reported.

The SV graft as the aorto-coronary bypass has higher flow capacity than the in situ ITA graft [13] owing to higher blood pressure directly from the ascending aorta and its greater diameter of the SV graft, as compared with those of the in situ ITA graft. Therefore, we presumed that if the patent SV graft to the left coronary artery was present, it might decrease the blood flow in the in situ ITA graft, and diminish its advantage as arterial materials.

In the present study, we attempted to prove the interactive effect between the individual bypass grafts with the different blood source, investigating from a viewpoint of blood flow and patency of arterial grafts. To minimize a bias associated with the bypass grafts and coronary arteries, only patients who had a simple graft arrangement and coronary artery lesions were included. In particular, to eliminate procedural differences, such as on-pump versus off-pump and technical failure, which would be one of the most fundamental biases, patients who had early occlusion of the bypass graft to the left coronary artery were entirely excluded. We focused on the patency of the ITA to LAD bypass, because it is clinically important for survival after CABG.

The results of this study demonstrated that the presence of the patent SV graft anastomosed to the second target site in the left coronary artery reduced the patency rate of the ITA to LAD graft, particularly when the native coronary stenosis between the two distal anastomoses in the left coronary artery was not severe. It was suspected that a mechanism of occlusion of the ITA-LAD bypass was associated with competitive flow from the SV graft by our careful observation of the late coronary angiogram about string of the ITA-LAD bypass.

We previously investigated competitive and reversal flow in sequential and composite arterial grafts, and identified that some specific situations, which were related to two or more coronary branches and arrangement of bypass grafts, significantly increased the incidence of competitive and reversal flow [15]. Moreover, we reported that the graft arrangement with maximized antegrade bypass flow in the arterial grafts played an important role in achieving the advantages of arterial materials and minimizing the incidence of cardiac events after CABG [16]. Since arterial graft occlusion due to insufficient bypass flow mostly occurs within 1 or 2 years [10,16], the long-term prognosis could be jeopardized. We believe that this interactive effect from the SV graft should be avoided as far as possible to achieve the advantage of the arterial graft.

Schmidt and colleagues recommended the use of arterial graft to the second target branch in the left coronary artery because of the superior survival rate [17]. Importance of the circumflex artery over the right coronary artery and inferior patency of the venous graft [18] are considered as primary reasons for the superiority. Results of our study may suggest that interactions of the SV graft on the in situ ITA may be another possible explanation for the superiority of arterial grafting to the second target site in the left coronary artery. We suppose that the use of the SV graft in the right coronary artery region hardly affects the bypass flow in the ITA to LAD graft.

Implications of this study are as follows: patency rate of the ITA to LAD bypass had been believed similar, irrespective
of graft arrangement for the second target branch in the left coronary artery. However, the results of this study strongly suggested that the in situ ITA to LAD bypass only, bilateral ITA grafting, sequential grafting and the composite Y graft to the LAD and the second target branch will provide the higher patency rate of the ITA to LAD bypass than the use of the SV graft to the circumflex or diagonal branch, when the stenosis between the two anastomotic sites in the native left coronary artery is moderate or less. Even in patients unsuitable for bilateral ITA harvest, the avoidance of the SV graft from ascending aorta should be considered.

We suggest that, on the contrary, the in situ ITA to LAD bypass concomitant with the aorto-coronary bypass is suitable when the left coronary and circumflex artery is remarkably large or a large mount of bypass flow is required. The isolated ITA to LAD can be a reasonable option of choice in patients with a localized lesion in the left main trunk. For the concomitant diagonal branch, Dion and colleagues reported excellent long-term patency of sequential grafting with the in situ ITA [19]. According to our previous study, when the circumflex artery is almost occluded and the stenosis in LAD is moderate, the composite Y graft is not recommended, because of the high incidence of competitive flow in the ITA to LAD bypass graft [15]. The severity and location of stenoses in the native coronary artery, the size of the target branch, the distance between and positional relationship of the two target sites, quality of the ITA graft, anticipated flow demand and atherosclerosis of the aorta, etc., should be taken into account for decision of strategy for the second target branch in the left coronary artery.

Limitations of the present study are as follows: first, because this study was retrospective and non-randomized, some differences regarding the characteristics of the BITA and ITA/SV groups were noted. Furthermore, the sample size was considered relatively small. However, the influence of these differences on the late angiographic results could be minimized, because early angiography confirmed that all 313 patients had patent grafts to the left coronary artery, and 133 (42.5%) patients underwent late angiography. Since more than 85% of patients after CABG underwent early angiography in our institution between 1986 and 2006, we considered that the selection bias for angiography was not so significant. Second, although the follow-up period was not enough for development of vein graft disease and ischemia in the left coronary artery region, it would be sufficient for examining correlations between the insufficient flow and arterial graft occlusion, as compared with previous studies [10,16]. In addition, progression of native coronary artery disease during the follow-up period, the length and the location of the stenotic lesion, the size of the circumflex coronary artery could not be taken into account. Moreover, peripheral vascular resistance in the myocardial tissue, and flow demands could also have important roles in the coronary perfusion. However, these factors could not be quantified by reliable methods. The effects of diabetes, hypertension, hyperlipidemia, aspirin and statin medical therapy may be the next concern in the future.

It may be controversial in management of ‘string sign’, which differs from graft occlusion. Several previous reports documented that the ITA graft with string sign could recover its own lumen when the native coronary artery disease became severe [20,21]. In the statistical analyses of this study, graft occlusion probably associated with string sign was not separated from the other graft occlusion. The reasons for this were as following: (1) contrast medium from the ITA injection did not reach LAD, (2) reversibility is not guaranteed for all ITA grafts presenting string sign, (3) the purpose of this study is to delineate the effect of the abundant blood flow from the SV graft, and (4) it is generally accepted that both graft occlusion and string sign are commonly associated with the abundant native coronary flow.

When we use the combination of the in situ arterial and in situ aorta-coronary venous grafts, it would be necessary to pay attention not to place influence on the patency of the important bypass especially created with the in situ ITA graft. This study is not conclusive in nature and is hypothesis generating only. Further investigations for interactive effects and considerations for the appropriate usage of the SV graft are necessary to establish the strategy for graft arrangement.

References


