String-Sign in Left Internal Thoracic Artery Is Associated With Regression in Left Main Trunk Stenosis After Coronary Artery Bypass

Ken Yokoyama,1 MD, Katsumi Miyauchi,1 MD, Masaki Kawamura,1 MD, Kan Kajimoto,2 MD, Tomotaka Dohi,1 MD, Shinichiro Yamagami,1 MD, Tatsuzi Kano,1 MD, Atsushi Amano,2 MD, Yasuyuki Hosoda,2 MD, and Hiroyuki Daida,1 MD

SUMMARY

The left internal thoracic artery (LITA) is the conduit of choice for coronary artery bypass (CABG) due to favorable long-term patency. Uncommonly, diffuse narrowing like a string without significant stenosis of an anastomosis is observed in the LITA graft (called “string sign”). Isolated left main trunk (LMT) diseases were reported to regress in some cases. However, the relationship between “string sign” and the regression of solitary LMT disease remains unknown.

We retrospectively studied 40 consecutive patients with isolated LMT stenosis who underwent CABG using LITA and who underwent angiography before and after operation (31 males, 9 females, mean age, 65.0 years). The patients were divided into 2 groups according to the postoperative angiographic outcomes of the LITA graft: one group included patients with “string sign” (6 patients), the other group consisted of patients with a patent LITA graft (34 patients).

There were no significant differences in clinical backgrounds between the two groups. The 2 groups showed similar quantitative % coronary artery stenosis of the LMT before operation (77.5% versus 76.8%) and the observation period was similar in both groups. Coronary angiography after CABG revealed that % stenosis of the LMT in patients with “string sign” was significantly less than that in patients with a patent LITA graft (41.7 ± 26% versus 82.5 ± 11%, P < 0.001). Regression in LMT was significantly more frequently observed in the “string sign group”. Furthermore, ostial stenosis was more frequent in patients with “string sign”.

“String phenomenon” of the LITA graft is one of the signs related to the regression of LMT stenosis, and especially in ostial stenosis of the LMT. (Int Heart J 2011; 52: 84-87)

Key words: Left internal thoracic artery, Bypass surgery, String sign, Isolated left main trunk diseases, Regression

The left internal thoracic artery (LITA) is the conduit of choice for coronary artery bypass (CAB) because of high long term patency rates and improved survival.1 Despite overall excellent patency rates, several studies have shown that diffuse or distal narrowing of LITA grafts led to graft failure, the so-called “string sign”.2–7 Various causes for this entity have been suggested, including damage during harvesting and mobilization, spasm, inflammation as part of a post-pericardiotomy syndrome,2–3 steal phenomenon arising from a large undivided proximal branch of the LITA,4 or competitive flow in only mildly stenosed native coronary arteries.4,6,7 In addition, isolated left main trunk (LMT) diseases were reported to regress in some cases.9,10 However, the relationship between “string sign” and the regression of solitary LMT disease is unknown. For this reason, we assessed all cases of “string sign” in patients with solitary LMT stenosis who underwent CABG using LITA.

METHODS

Patient selection and data collection: Of 1100 patients who underwent CABG by a cardiovascular surgeon at Juntendo University Hospital between September 1990 and December 2000, 282 patients underwent CABG using LITA. Of these 282 patients, 50 patients who presented with symptomatic LMT disease or documented myocardial ischemia and angiographic evidence of > 50% diameter stenosis of the LMT suitable for LITA graft were selected. Patients were not eligible for enrollment if they underwent repeat CABG, off-pump CABG, or CABG with valve or other significant surgery. Elective CABG was performed according to international established techniques. LITA was anastomosed to the LAD and reversed saphenous vein grafts (SVG) were connected to the proximal segment of the CX. After surgery, all patients were scheduled for coronary angiography at 1 year follow-up. Patients who declined to undergo the coronary angiography were excluded. Consequently, 40 patients were analyzed in this study.

From the Departments of 1 Cardiovascular Medicine and 2 Cardiovascular Surgery, Juntendo University, Tokyo, and 3 Division of Cardiology, Internal Medicine, Urayasu Juntendo University, Chiba, Japan.
Address for correspondence: Katsumi Miyauchi, MD, Department of Cardiovascular Medicine, Juntendo University, 2-1-1 Hongo, Bunkyo-ku, Tokyo, Japan.
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Data on the following variables were collected: age, gender, angina class (Canadian Cardiovascular Society classification) before CABG, coronary risk factors (hypertension, diabetes, dyslipidemia, current smoking, family history), and LITA flow velocity of the LITA immediately after CABG, and angiographic findings.

**Cardiac catheterization:** Selective coronary angiography was performed before and after CABG. Selective graftography of the LITA was also performed after CABG. To exclude the possibility of catheter induced spasm, we routinely administered intracoronary and/or intragraft nitroglycerin, and performed an angiogram 1 minute later. The patients were divided into 2 groups according to the angiographic lesion morphology: one group included patients with “string sign”, the other group patients with patent grafts. String sign was defined as distal segmental narrowing of the LITA graft with significant reduction of flow, but no significant stenosis at anastomosis of the LITA to the LAD was observed. Angiographic measurements were made with validated quantitative coronary angiographic software (CAAS II for Windows, version 4.1.1; Pie Medical Imaging BV, Maastricht, Netherlands) before the operation and at follow-up angiography by experienced cardiologists blinded to the baseline characteristics and clinical outcomes of the patients. Percent diameter stenosis of LMT before and after an operation was measured separately. Regression was defined as reduced %stenosis with less than 50% stenosis in the LMT lesion at follow-up CAG compared to pre-CAG.

**Statistical analysis:** Continuous variables are expressed as the mean ± standard deviation (SD), and were compared using one-way ANOVA with Dunnett’s test. Categorical data are tabulated as frequencies and ratios, and were compared using the chi-square test.

A $P$ value of less than 0.05 was considered statistically significant, unless indicated otherwise. All data were analyzed using SPSS version 11.0 for Windows.

### RESULTS

The postoperative course was uneventful. The angiographic lesion morphology observed in postoperative angiography showed that 6 patients (15%) had the “string sign” in the LITA. The 34 other patients (85%) had a patent LITA graft after CABG.

**Clinical and angiographical findings:** The baseline clinical characteristics are summarized in Table I. The mean age of all study patients was 65.0 years. Eight patients (20%) had severe symptoms of CCS angina class III-IV. Thirty-five patients (87%) had one or more coronary risk factors, the most common of which were hypertension in 22 patients (55%), hypercholesterolemia in 20 patients (50%), diabetes mellitus in 16 patients (40%), and current smoking in 15 patients (38%). One patient (2.5%) had end-stage renal disease with hemodialysis. The mean diameter stenosis of the LMT was 82%, and the mean LVEF by left ventriculography was 59.8%.

Table II presents the clinical and angiographical findings before and after CABG in patients with “string phenomenon” and with a patent graft. There were no significant differences in age, angina class, prior cardiovascular history, or coronary risk factors between the two groups. Female gender was slightly more common in the string group compared to the patent group, although the difference was not statistically significant. In addition, the free flow velocity of LITA graft during the operation was similar between the two groups. Preoperative angiographical findings also showed no differences in the diameter stenosis of LMT (77.5 ± 4.1% versus 76.8 ± 1.7; $P = 0.77$), and

<table>
<thead>
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<th>Parameter</th>
<th>String Sign (+)</th>
<th>String Sign (-)</th>
<th>$P$</th>
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<tbody>
<tr>
<td>Age (years)</td>
<td>65.0 ± 5.6</td>
<td>65.1 ± 5.8</td>
<td>0.7</td>
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<tr>
<td>Gender (Female) (%)</td>
<td>50.0</td>
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<td>Diabetes (%)</td>
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<td>Dyslipidemia (%)</td>
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<td>50.0</td>
<td>1.0</td>
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<tr>
<td>Current smoker (%)</td>
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<td>41.2</td>
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<td>Family history (%)</td>
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<td>17.7</td>
<td>1.0</td>
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<td>60.3 ± 15.2</td>
<td>56.9 ± 15.2</td>
<td>0.6</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td>61.7 ± 7.1</td>
<td>59.5 ± 7.0</td>
<td>0.5</td>
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<tr>
<td>Ostium lesion (%)</td>
<td>83.3</td>
<td>14.7</td>
<td>0.0008</td>
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<tr>
<td>Observation period (days)</td>
<td>364.5 ± 60.0</td>
<td>344.5 ± 59.3</td>
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</table>

**Figure 1.** Degree of stenosis in left main trunk before and after bypass surgery. Coronary angiography after CABG revealed that % stenosis of LMT in patients with “string sign” was significantly less than that in patients with a patent LITA graft (41.7 ± 26% versus 82.5 ± 11%, $P < 0.001$).
left ventriculography showed no significant differences in LVEF (61.7±2.9 versus 59.5±11.2; P = 0.5). However, the postoperative angiographical findings showed a smaller diameter stenosis of LMT in patients with “string sign” than in those with a patent graft (41.7±4.7 versus 82.0±2.0; P < 0.0001) as shown in Figure 1. Significant regression in LMT lesions was more frequently observed in the string group than in those with patent LITA grafts (Figure 2). In addition, ostial stenosis of the LMT was more frequent in patients with “string phenomenon” than in those with a patent graft (83.3% versus 14.7%; P = 0.008). There was no significant difference in the observation period between the 2 groups.

**Discussion**

This study showed that “string sign” was associated with regression of LMT stenosis in patients with isolated LMT disease, especially in ostial stenosis. Significant stenosis in the left main trunk is a class I indication for CABG. Many patients were due to undergo urgent CABG, but isolated LMT disease had regressed in some patients.

The longitudinal thinning of LITA grafts was described by Barner in 1974. He referred to this as “diffuse atrophy” because the native coronary arteries to which the LITA were anastomosed appeared to be patent and to have good flow. Since that time, several reports of this phenomenon have been published. Geha, et al described the “distal thread phenomenon” in 2% of LITA grafts at 13 months post CABG. They correlated this with anastomosis of the graft to a marginally stenotic recipient coronary artery. Collectively, these variants have come to be known as the “string sign”. Various other causes for this phenomenon have been suggested. Damage during harvesting, mobilization, and anastomosis can cause occlusion and focal distal narrowing, but does not fully explain the more common diffuse appearance of the “string sign”. Spasm and inflammation of the LITA graft from a post-pericardiotomy syndrome have also been suggested. The notable lack of the “string sign” on the contralateral ITA in cases with bilateral grafts, however, strongly argues against this. Another possibility is failure to ligate proximal branches.

Perhaps the most likely cause is competitive flow. Siebenmann, et al described 10 cases of LITA “string sign”; stenosis of the vessel bypassed was 50% or less in all cases. In the cases with bilateral ITA grafts, the contralateral ITA, which was grafted to a severely stenotic vessel, was widely patent. Hashimoto, et al followed 30 LITA and 23 gastroepiploic artery grafts for a mean of 24 months. Stenosis of the recipient artery was significantly more severe in functioning grafts than in nonfunctioning ones. Kawasui, et al performed follow-up on 100 cases with LITA grafts to the LAD and found the “string sign” in only 3 of 14 patients who had an LITA grafted to competitive flow conditions. They concluded that IMA grafting was acceptable for a moderate stenotic artery. Villareal, et al prospectively reviewed 288 cases of LITA angiography and reported that there was evidence of competitive flow in 81% (22 of 27) of patients whose internal mammary grafts had developed the “string sign”.

Our study supports the hypothesis that competitive flow predisposes LITA grafts to the “string sign” as already reported. Postoperative angiography demonstrated that no significant stenosis in the LMT was observed in the “string group”. In addition, 5 (86.3%) of them had ostial stenosis of the LMT (Table II). However, three causes for the absence of severe stenosis at reangiography can be considered. One may be due to overstimulation at preoperative angiography, as reported in nonoperated patients. Another cause may be due to regression of LMT stenosis, and the final one may be associated with coronary vasospasm. These considerations suggest that we must ascertain the presence or absence of competitive flow at preoperative angiography, and predict regression of LMT stenosis. However, we cannot comment on the competitive flow or the frequency of graft failure in patients with stenosis of the LMT, especially ostial stenosis, because this study had only a small number of patients and the design was retrospective. We believe that a prospective and large population study with elective pre- and postoperative angiography using a flow wire or Doppler wire will be needed in order to clarify this suggestion and to further characterize this phenomenon.

Several essential drugs such as statins were used less frequently in this cohort as compared to patients in a recent clinical study, and intensive lipid-lowering therapy with a statin has been shown to be related to plaque regression. Therefore, statins were not directly correlated to the LMT regression in the current study. In addition, balloon angioplasty or bare-metal stent was the sole PCI for all patients in the study period. Therefore, we had no choice but to select PCI as the method of revascularization instead of CABG in this study period. The use of drug-eluting stents and the recent advances in operative skills for PCI could improve the clinical outcomes in LMT lesions. Therefore, LMT is a potentially attractive target PCI and we select DES in some cases of LMT disease. From this point of view, this study should not be applied to the current clinical setting.

The present study represents a retrospective analysis of a consecutive series of patients undergoing A-C bypass with LMT lesion at a single center, except for those patients who underwent emergency surgery.

In conclusion, “string phenomenon” of LITA grafts is one
of the signs related to the regression of LMT stenosis, especially in ostial stenosis of the LMT.

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REFERENCES