Intraoperative and Laboratory Evaluation of Skeletonized Versus Pedicled Internal Thoracic Artery

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Background. The skeletonization of internal thoracic artery is postulated to improve graft length, early blood flow, sternal blood supply, and postoperative respiratory function. Concern exists that skeletonization may injure internal thoracic artery, precluding good results of surgery. Reports on endothelial function of skeletonized internal thoracic artery are lacking.

Methods. A prospective assessment of early clinical outcomes of 357 consecutive patients undergoing coronary artery bypass grafting was performed: 287 patients with nonskeletonized and 70 with skeletonized left internal thoracic artery (LITA). The lengths of LITA and of its discarded distal segment, as well as free LITA blood flow, were measured. The dose-effect relationship for relaxation to acetylcholine was studied in the organ bath.

Results. Apart from a higher incidence of breaching the pleura with nonskeletonized LITA the clinical outcomes were comparable. The length of skeletonized LITA was 17.8 ± 1.14 cm versus 20.3 ± 0.52 cm skeletonized (p = 0.11). The length of discarded LITA was shorter in nonskeletonized artery (0.8 ± 0.28 cm versus 2.6 ± 0.49 cm; p = 0.022). The free LITA blood flow was 66.3 ± 7.42 mL/min in nonskeletonized vessel versus 100.3 ± 14.84 mL/min in skeletonized (p = 0.048). The acetylcholine-induced relaxation was similar in both groups (maximal relaxation, 80.7% ± 5.95% in nonskeletonized versus 72.9% ± 9.11% in skeletonized; not significant; negative logarithm of half-maximal effect, 7.43 ± 0.18 versus 7.1 ± 0.10, respectively; p = 0.063).

Conclusions. Skeletonization does not damage the endothelial function of the LITA. Higher free blood flow and available LITA length should encourage the use of skeletonized LITA in clinical practice.


Internal thoracic artery (ITA) is the conduit of choice in the surgical treatment of coronary artery disease. According to the Coronary Artery Surgery Study results, grafting of the left anterior descending (LAD) coronary artery with the left internal thoracic artery (LITA) has been the independent predictor of survival after coronary artery bypass grafting [1]. Left ITA grafts when compared with saphenous vein grafts remain patent and free from arteriosclerosis for a longer time [2]. Paracrine endothelial function is considered one of the crucial factors responsible for the observed differences in the fate of arterial and venous coronary artery grafts. The level of nitric oxide production by the endothelium of ITA is very high when compared with the low and variable amount produced by the endothelium of the saphenous vein [3]. Since the first microsurgical anastomosis of the LITA with coronary arteries by Kolesov [4] and the first systematic usage of this graft by Green [5], the ITA had been harvested as a pedicle together with concomitant veins, lymphatics, sympathetic plexus, and internal thoracic fascia. The skeletonization was described first by Keeley [6] in 1987. He postulated that this technique allowed for longer available graft length, hence opportunity for more distal coronary artery anastomoses and easier sequential grafting. The higher early blood flow through the skeletonized LITA has also been implied to be a factor decreasing the risk of hypoperfusion syndrome [7]. Advocates of this technique claim that the injury to the chest wall is minimized, hence sternal blood supply is better preserved, which may be even more important when both ITAs are used [8]. Better postoperative respiratory function has also been reported [9]. In some cardiac surgical centers, skeletonization has been the routine method of ITA harvesting [10]. Most surgeons harvest the LITA as a pedicle, being afraid of injury to the LITA, including its endothelium, thus precluding good early and late results of surgery [11, 12]. Indeed, the reports on endothelial function of skeletonized ITA are lacking.

The aim of our work was to assess the early clinical results of coronary artery bypass grafting using skeletonized LITA to assess the intraoperative parameters of skeletonized and nonskeletonized LITA and to assess the in vitro endothelial function of segments of skeletonized versus nonskeletonized LITA.

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Patients and Methods
We have analyzed early clinical outcomes of 357 consecutive patients who underwent coronary artery bypass grafting with the use of LITA-LAD graft in our institution. Patients with LITA-LAD graft, who apart from coronary artery bypass grafting underwent concomitant valve replacement or left ventricular aneurysctomy, those in whom both ITAs or radial artery were used, and those operated on off cardiopulmonary bypass were not included in the analysis. Nonskeletonized LITA was used in 287 (group 1) and skeletonized LITA in 70 patients (group 2). There were 49 women in group 1 (17.1%) and 9 women in group 2 (12.8%; not significant [NS]). The mean age of patients in group 1 was 54.2 ± 9.21 years, and in group 2, 56.4 ± 7.87 years (NS). Both groups were comparable according to their angina level: mean Canadian Cardiovascular Society class was 2.8 ± 1.07 in group 1 versus 2.7 ± 0.87 in group 2 (NS). There were 48 (16.7%) diabetic patients in group 1 and 15 (21.4%) diabetic patients in group 2 (NS). Of these 11 (3.8%) and 3 (4.3%), respectively, were insulin-dependent (NS).

In addition to LITA-LAD anastomosis, a mean of 2.6 ± 0.76 venous grafts were performed per patient in group 1 (range, 0 to 4) and 2.3 ± 0.68 venous grafts per patient in group 2 (range, 0 to 3; NS).

Analysis of Clinical Results
The following parameters were taken into account in the assessment of early clinical outcomes of surgical treatment: 30-day mortality; the peak postoperative creatine kinase and aspartate transaminase levels; incidence of perioperative infarction, confirmed electrocardiographically and enzymatically, and low cardiac output state requiring intraaortic balloon pump; incidence of regrafting of LAD because of left ventricular hyperperfusion syndrome; breaching the pleura; and sternum healing complications requiring sternal resuturing.

Postoperative enzymes levels were presented as mean ± standard error of the mean (SEM) and compared using Student’s t test for independent data. Nonparametric outcomes were analyzed using Fisher’s exact test.

Intraoperative Assessment
In group 1, LITA was harvested as a pedicle. The internal thoracic fascia was incised with the electrocautery along both sides of the LITA approximately 0.5 cm away from concomitant veins. Next, the flap of fascia, muscle, and fat tissue containing the LITA and concomitant veins was dissected with the electrocautery, working from its distal to proximal ends, and ligating the major LITA branches with Ligaclips (Ethicon, Somerville, NJ). After heparin was administered, the LITA was divided distally, the end was closed with the Ligaclip, and it was wrapped in a swab soaked with 0.2% papaverine solution.

In group 2, the left pleura was dissected laterally so that the LITA and its concomitant veins could be seen along their course. The internal thoracic fascia was incised just medial to the LITA in the first intercostal space, where it is less adherent to the chest wall. The skeletonization of the LITA was performed from this point distally leaving both concomitant veins at the chest wall. Apart from cutting the fascia, most of the dissection was blunt. The tributaries were ligated tangential to the vessel wall and distally and were divided with scissors to avoid heat injury. After the LITA had been harvested to its bifurcation level, the concomitant vein was divided at the first intercostal space, and the skeletonization was performed proximally up to the subclavian artery. Care was taken to avoid phrenic nerve injury. As in group 1, after heparin was administered, the LITA was divided distally, the end was closed with the Ligaclip, and it was wrapped in a swab soaked with 0.2% papaverine solution.

In Vitro Assessment
Local ethics committee approval for in vitro experiments was obtained. The distal segments of LITA not used for grafting were evaluated in organ baths as described previously [13]. Segments from 10 patients from each group were used.

Three-millimeter-long LITA segments were mounted on stainless steel hooks in organ bath chambers. Krebs-Henseleit solution of the following composition was used (in mol/L): NaCl, 118.0; KCl, 4.70; CaCl₂, 2.52; MgSO₄, 1.64; NaHCO₃, 24.88; KH₂PO₄, 1.18; glucose, 5.55; sodium pyruvate, 2.0 (pH 7.4). The bath was oxygenated with carbogen (95% O₂, 5% CO₂), and the temperature was maintained at 37°C. After the arterial segments had been stretched to a resting tension of 4.0 g, they were incubated for 1 hour, during which time they were thoroughly washed.

Experiments were performed using the Hugo-Sachs Elektronik (March-Hugstetten, Germany) isolated organ set. Vascular wall tension was measured with F30 isometric force transducer with bridge amplifier 336 (Hugo-Sachs Elektronik) and recorded with the Grahtec WR 3310 linear recorder (Hugo-Sachs Elektronik). At the beginning of the experiment, the arterial segment was exposed repeatedly to 120 mol/L potassium chloride, causing contraction with subsequent thorough washout and relaxation. This was performed until two subsequent responses were identical within 10% error limit, which assured that the preparation was stable. In the next step, the arterial segment was contracted with 10⁻⁵ mol/L norepinephrine. After this, acetylcholine was applied in increasing concentrations, starting with 10⁻⁶ mol/L and going in negative logarithm half molar cumulative steps.
up to $10^{-4}$ mol/L to establish the dose-effect relationship for the relaxation response.

Acetylcholine causes relaxation by means of nitric oxide release from the endothelium. Relaxation response to acetylcholine has been regarded in many laboratories as a measure of the presence of functioning endothelium in the examined arterial segment [3, 13].

The following substances were used: (-)-arterenol bitartrate and acetylcholine chloride (Sigma Chemical Co, St. Louis, MO).

The artery contraction was measured as an increase in the vessel wall tension above the resting tension. The relaxation was assessed as the decrease in the wall tension from the precontracted level and expressed as a percentage of the contraction obtained with norepinephrine.

The relaxation responses at each dose level are presented as a mean ± SEM and compared using the Mann-Whitney test. The dose-effect relationships were obtained from a regression analysis to the general logistic equation of Michaelis and Menten (1913):

$$E = \frac{E_{\text{max}} \cdot D^n}{D^n + K_D^n}$$

where $E$ is effect, $E_{\text{max}}$ is maximal effect, $D$ is dose, $K_D$ is drug-receptor complex dissociation constant equal to the dose causing half-maximal effect ($ED_{50}$), and $n$ is the Hill coefficient. From the above, the mean $ED_{50}$ and Hill coefficient, ± SEM, were estimated. Calculated $ED_{50}$ and corresponding pD$_2$ ($-\log ED_{50}$), as well as Hill coefficients, were compared using Student’s $t$ test for independent data.

In all instances of statistical analysis, $p$ less than 0.05 was considered significant.

### Results

The clinical outcomes are summarized in Table 1. Apart from the incidence of breaching the left pleura, outcomes were similar in both groups.

The mean available LITA length was $17.8 \pm 1.14$ cm in group 1 versus $20.3 \pm 0.52$ cm in group 2 ($p = 0.11$). The distal segment of LITA that was discarded after trimming it to the length necessary for LAD grafting was significantly shorter in group 1, measuring on average $0.8 \pm 0.28$ cm and $2.6 \pm 0.49$ cm in group 2 ($p = 0.022$) (Fig 1). The mean LITA free blood flow was $66.3 \pm 7.42$ mL/min in group 1 versus $100.3 \pm 14.84$ mL/min in group 2 ($p = 0.048$) (Fig 2).

The dose-effect curves for acetylcholine-induced endothelium-dependent relaxation after precontraction with a dose of norepinephrine producing 80% maximal effect were plotted for LITA segments from both groups (Fig 3). Maximal relaxation was similar in both groups (80.7% ± 5.95% in group 1 versus 72.9% ± 9.11% in group 2; NS). Skeletonized LITA, however, appeared somewhat more sensitive to acetylcholine: $ED_{50} 8.55 \times 10^{-8}$ ± $1.83 \times 10^{-8}$ mol/L in group 1 versus $4.02 \times 10^{-8}$ ± $1.39 \times 10^{-8}$ mol/L in group 2, with corresponding pD$_2$ of 7.43 ± 0.18 versus 7.1 ± 0.10, respectively ($p = 0.063$). Hill coefficients equaled 0.9 ± 0.22 versus 0.6 ± 0.06, respectively (NS).

### Table 1. Early Clinical Outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group 1 (n = 287)</th>
<th>Group 2 (n = 70)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>5 (1.4%)</td>
<td>1 (1.4%)</td>
<td>NS</td>
</tr>
<tr>
<td>Perioperative myocardial infarction</td>
<td>24 (8.4%)</td>
<td>5 (7.1%)</td>
<td>NS</td>
</tr>
<tr>
<td>Maximal postoperative creatine kinase</td>
<td>545 ± 72.7 IU</td>
<td>498 ± 112.2 IU</td>
<td>NS</td>
</tr>
<tr>
<td>Maximal postoperative aspartate transaminase</td>
<td>36.0 ± 3.23 IU</td>
<td>31.4 ± 4.91 IU</td>
<td>NS</td>
</tr>
<tr>
<td>Intraaortic balloon pump</td>
<td>13 (4.5%)</td>
<td>2 (4.3%)</td>
<td>NS</td>
</tr>
<tr>
<td>LAD regrafted (LV hypoperfusion)</td>
<td>2 (0.7%)</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Sternal dehiscence</td>
<td>5 (1.4%)</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Left pleura opened</td>
<td>231 (80.5%)</td>
<td>8 (11.4%)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

LAD = left anterior descending coronary artery; LITA = left internal thoracic artery; LV = left ventricular; NS = not significant.
Comment

The early clinical results of coronary artery bypass grafting using the skeletonized LITA were presented to illustrate the cohort of patients rather than to draw conclusions about outcomes. We observed neither increased mortality nor increased frequency of perioperative myocardial infarction, nor higher indicator enzyme levels in patients in whom the skeletonized LITA was used. The number of patients requiring intraaortic counterpulsation was similar in both groups. It indeed appears that skeletonization does not increase the operative risk.

As we expected, there were less sternal healing problems after mammary skeletonization, although a statistically significant difference could not be proven. The left pleura was opened significantly less frequently when LITA was skeletonized. We believe that skeletonization makes preservation of the pleura easier. This may contribute toward better postoperative respiratory function as has been reported previously [9].

In spite of the subjective feeling of the operating surgeons, the skeletonized LITA did not appear to be significantly longer than the one harvested as a pedicle, when measured from its origin to bifurcation. In practice, however, possibly because the broad flap of fascial and fatty tissue is absent, we found the skeletonized LITA more pliable, lying more medially in its proximal course and therefore easily reaching the distal LAD or even distal branches of the circumflex artery. Indeed, the discarded segments were significantly longer for skeletonized LITA. This may be of value as the most distal muscular segment of LITA is no longer used, and the more proximal, elastic, and bigger in diameter artery is used for anastomosis construction.

The free blood flow from the skeletonized LITA was almost twice as high as that from the nonskeletonized one. A possible explanation of this phenomenon is the local sympathectomy, which probably occurs with skeletonization. However, one must remember that the skeletonized LITA was transected at a higher level, at which the diameter of the artery is greater than in more distal segments. Additionally, the action of 0.2% papaverine on the naked arterial wall may have a more-direct effect than on one buried inside the pedicle. Whatever the mechanism is, higher free blood flow through the bypass conduit is likely to be beneficial for early postoperative left ventricular perfusion, regardless of capacity of the coronary vascular bed.

We consider the results of the in vitro assessment very important inasmuch as the main argument against LITA skeletonization is the fear that it may be detrimental to its function as a bypass conduit. It has been shown that gentle skeletonization preserves thoracic artery morphologic integrity [14]. Our results demonstrate very well preserved endothelium-dependent relaxation, reflected by the response of skeletonized LITA to acetylcholine. This seems to confirm that the paracrine function of LITA endothelium, so important for graft function, is not affected by careful skeletonization. Moreover, our results suggest that skeletonized LITA may be somewhat more sensitive to acetylcholine than nonskeletonized vessel. We cannot explain this effect. It may depend on the damage to the sympathetic plexus. Whatever the nature of this phenomenon, better relaxation function of skeletonized LITA may be clinically advantageous.

In conclusion, skeletonization does not damage the endothelial function of the LITA. Higher early blood flow and available LITA length, together with smaller chest wall injury and better expected healing of the sternum, should encourage the use of skeletonized LITA in clinical practice.

References

The Society of Thoracic Surgeons: Thirty-sixth Annual Meeting

Mark your calendars for the Thirty-sixth Annual Meeting of The Society of Thoracic Surgeons, which will be held at the Greater Fort Lauderdale Broward County Convention Center in Fort Lauderdale, Florida, January 31–February 2, 2000. The Postgraduate Course will provide in-depth coverage of thoracic surgical topics selected to enhance and broaden the knowledge of practicing thoracic and cardiac surgeons.

Advance registration forms, hotel reservation forms, and details regarding transportation arrangements, as well as the complete meeting program, will be mailed to Society members. Also, complete meeting information is available on The Society’s Web site located at http://www.sts.org. Nonmembers wishing to receive information on attending the meeting may contact the Society’s Secretary, Peter C. Pairolero.

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