Effects of ultrasonic skeletonization on internal thoracic and gastroepiploic arteries for coronary artery bypass grafting

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Received 24 February 2006; received in revised form 14 July 2006; accepted 24 July 2006

Abstract

Objective: There are few data available on the effect of ultrasonic skeletonization with the harmonic scalpel on internal thoracic artery (ITA) and gastroepiploic artery (GEA) vessel function.

Methods: Rings of segments of the skeletonized ITA, pedicled ITA, skeletonized GEA, and pedicled GEA were studied. Arterial segments were treated with high KCl and norepinephrine (NE) to obtain smooth muscle contractions. Endothelium-dependent and independent vasorelaxant potencies in \(10^{-6}\) mol/l NE-pre-constricted arteries were assessed by acetylcholine (ACh), and isosorbide dinitrate (ISDN) and diltiazem, respectively.

Results: There were no differences in contractile potencies induced by high KCl and NE between the rings cut from skeletonized and pedicled grafts. The rings from skeletonized and pedicled vessels also showed equal sensitivity to ISDN and diltiazem. However, the rings from pedicled grafts showed greater relaxation responses to ACh than rings from skeletonized grafts.

Conclusion: Ultrasonic complete skeletonization with the harmonic scalpel may retain smooth muscle function of skeletonized grafts, whereas endothelial function of ultrasonic skeletonized grafts may be significantly compromised.

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Keywords: Ultrasonic scalpel; Skeletonization; Vascular function; Internal thoracic artery; Gastroepiploic artery

1. Introduction

The usefulness of the skeletonized internal thoracic artery (ITA) and gastroepiploic artery (GEA) for coronary artery bypass grafting (CABG) has been well established [1—4]. Although several benefits have been indicated, some surgeons remain concerned that skeletonization can cause vasospasm and mechanical irritation of the grafts [5]. However, Higami et al. [6—8] developed a new ultrasonic complete skeletonization technique in which an ultrasonic scalpel is used. The ultrasonic activated scalpel uses ultrasonic energy to denature tissue protein into sticky coagulum through high frequency vibration of the blade and cavitational fragmentation that disrupts low-density tissues such as fat and parenchyma [6—8]. Although the ultrasonic scalpel has been reported to be safe and less invasive than conventional cautery knives [6—8], few data are available on the vascular functions of the arterial grafts harvested with this device. The main purpose of this study was to characterize the in vitro vasomotor activities of arterial rings cut from ultrasonically skeletonized ITA and GEA grafts in comparison with those from the pedicled grafts. These grafts were obtained directly from patients undergoing CABG, and thus, the results may reflect the functional status of any grafts that were inserted in the body.

2. Materials and methods

Approval from the human ethics committee of the Kagoshima University School of Medicine was obtained for this study. Discarded distal segments of skeletonized ITA (n = 50), pedicled ITA (n = 30), skeletonized GEA (n = 50), and pedicled GEA (n = 30) were collected from a total of 112 patients undergoing CABG. All patients were <75 years old (mean 69.9 years old; range 61—74 years old), and patients on dialysis were not included in the study. Four surgeons, using a standardized technique, performed dissections of the ITA and GEA grafts during each procedure.

2.1. Surgical procedure

For ultrasonically skeletonized grafts harvesting, GEA and ITA grafts were harvested using the harmonic scalpel (Harmonic Scalpel, Ethicon Endo Surgery, OH, USA) [6—8].

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For skeletonized ITA harvesting, fatty and satellite veins around the arteries were removed by lightly sweeping it away by the ‘quick touch’ method as the ultrasonic scalpel was moved along the length of the vessel to expose the adventitia of the arteries. Each artery was divided with the ultrasonic scalpel 0.1–0.2 cm away from the adventitia. Major branches were ligated with clips. The harvest time was 20–25 min, approximately the same time required for pedicled dissection. For skeletonized GEA harvesting, the GEA was encircled with vessel loops at every 10 cm distance. While gently pulling up the vessel loops, the greater omentum was divided 0.1–0.2 cm away from the GEA trunk throughout the necessary graft length using the ultrasonic scalpel with coagulating shears. The harvest time was 15–20 min, approximately the same time required for pedicled dissection. For pedicled ITA harvesting, graft segments were harvested by an electrocautery approximately 1–2 cm away from both sides of the arteries. For pedicled GEA harvesting, the omentum was incised with ultrasonic scissors along both sides of the GEA approximately 1–2 cm away from the GEA. The major arterial branches were ligated with clips.

2.2. Organ-chamber experiments

The discarded distal end of each arterial graft was immediately stored in a chamber filled with cold (4 °C) Krebs solution composed of Na⁺, 144 mmol/l; K⁺, 5.9 mmol/l; Ca²⁺, 2.5 mmol/l; Mg²⁺, 1.2 mmol/l; Cl⁻, 128.7 mmol/l; HCO₃⁻, 25 mmol/l; SO₄²⁻, 1.2 mmol/l; H₂PO₄⁻, 1.2 mmol/l; and glucose, 11 mmol/l. Both the pedicled and harvested graft were dissected free of surrounding satellite veins, fatty and connective tissue in a dissecting chamber and were cut into 2–3 mm wide rings. Vessel rings were mounted on wire hooks with one end connected to an isometric force-displacement transducer (UL-100GR, Minebea, Tokyo, Japan) and then suspended in 37 °C Krebs solution in water-jacketed organ baths. All solutions were bubbled with 95% O₂:5% CO₂ throughout the organ-chamber experiments, and the pH was adjusted to 7.3–7.4 (37 °C). The force transducer was linked to a bridge amplifier (GE Medical, Tokyo, Japan) and a pen recorder (Panasonic, Tokyo, Japan) to allow the continuous recording of tension in the vessel segment. Every effort was made to avoid damage to the endothelium while dissecting and mounting the vascular rings. Vascular segments were progressively stretched (20 mN) and allowed to equilibrate for 120 min.

In an initial series of experiments, control contractile responses were induced by adding high KCl (100 mmol/l) to the Krebs solution for 7 min, every 30 min. When a stable level of contraction to the high KCl solution was obtained, the dose-dependent contractile response to norepinephrine (NE) was determined as the maximum amplitude of the phasic response. To determine the vasodilative responses in the rings from skeletonized and pedicled ITA and GEA grafts, the endothelium-dependent relaxations were assessed by the addition of acetylcholine (ACh; Sigma), and the endothelium-independent relaxations were assessed by isosorbide dinitrate (ISDN, Eisai, Tokyo, Japan), and diltiazem (Tanabe, Tokyo, Japan) in 10⁻⁶ mol/l NE-precontracted arteries. In all experiments, rings cut from a single graft artery were not used in duplicate in the same experimental protocol. In addition, only one concentration-response relationship was studied in a given ring.

2.3. Statistical analysis

The results are expressed as mean ± SD (n: number of isolated vessels). Statistical analysis was performed by a two-factor analysis of variance for repeated measures, followed by Scheffé’s test (for multiple comparisons) or a two-tailed, unpaired Student’s t-test (for comparison between the values of each groups). A chi-square test for independence was used for a cross-tabs table (Table 1). Probability values <0.05 were considered significant.

### Table 1

<table>
<thead>
<tr>
<th></th>
<th>Skeletonized</th>
<th>Pedicled</th>
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<tbody>
<tr>
<td>ITA</td>
<td>20.9 (9/43)</td>
<td>3.4 (1/29)</td>
</tr>
<tr>
<td>GEA</td>
<td>10.0 (5/50)</td>
<td>0 (0/30)</td>
</tr>
</tbody>
</table>

* p < 0.05, skeletonized versus pedicled. (a/b): numbers of unresponsive vessels/total tested vessels. Statistical analysis was performed using a chi-square test for independence.

![Fig. 1](https://academic.oup.com/ejcts/article-abstract/30/4/592/507061)  
**Fig. 1.** Maximal tension with 100 mmol/l KCl. ITA, internal thoracic artery; GEA, gastroepiploic artery (n: number of isolated vessels).
arteries without response to the KCl solution also demonstrated no reactions to NE, these arteries were excluded from NE-trials. There was no significant difference (two-factor factorial analysis of variance) between the skeletonized and the pedicled ITA contractions and between the skeletonized and the pedicled GEA contractions in response to NE (Fig. 2).

Relaxation was expressed as the percent relaxation of the precontraction induced by norepinephrine (10^{-6} mol/l). In endothelium-dependent relaxation in the ITA and GEA grafts (Fig. 3), pedicled vessels showed greater relaxation responses to ACh than did skeletonized vessels (p < 0.05 or p < 0.01, unpaired Student’s t-test). Moreover, the percentages of the complete loss of ACh-mediated vasodilation was significantly (p < 0.05, chi-square test for independence) greater in the skeletonized ITA compared with those in the pedicled rings, although there was no significant difference between the skeletonized and pedicled arteries cut from the GEA grafts (Table 1).

Our results show that there was no significant difference between skeletonized and pedicled vessels with regard to the endothelium-independent relaxation induced by ISDN and diltiazem (Fig. 4).

4. Discussion

This report focused on the direct vascular reactions of human ITA and GEA used as pedicled or skeletonized grafts. Herein, we firstly clarified that ultrasonic skeletonization with the harmonic scalpel retained the smooth muscle function of harvested arteries, whereas the endothelial function of the vessel was evidently reduced in comparison with the pedicled harvesting technique. These results emphasize the risk of ultrasonic skeletonization for endothelial damage in the arteries supplying grafts for coronary bypass surgery, resulting in the diminution of the endothelium-dependent vasorelaxing response and the acceleration of local thrombosis and platelet aggregation.

Recently, skeletonization has been increasingly used for the dissection of ITA and GEA grafts during revascularization procedures and an ultrasonic scalpel has been reported to be useful for the dissection [6—8]. The clinical advantages of the skeletonized ITA include an increased effective length of ITA, an increased vessel diameter leading to improved free flow through the ITA, and a decreased incidence of sternal infection. Most importantly, skeletonization of the bilateral ITA allows for an increase in the number of sites where graft
material can be anastomosed. However, the main disadvantage of this technique is that it is more traumatic to the arterial wall than conventional pedicled preparations, although some studies have refuted this idea [4,9—12]. Therefore, the question still arises as to whether or not skeletonization with this device results in damage to the vascular functions of the grafts.

In our experiments, the smooth muscle contractive function was equally preserved in both ultrasonically skeletonized and pedicled vessels, as reflected by the response of the vessels to high KCl and NE. With regard to endothelium-independent relaxation, ISDN produced equal relaxation in both ultrasonically skeletonized and pedicled vessels. These results suggest that the bypass vessels examined appear to preserve the contractile and relaxing functions despite ultrasonic skeletonization. These results are consistent with previous in vivo observations by Guadino et al. [3] where the reactivity of skeletonized and pedicled ITA had no significant difference in ITA responses to ISDN injected intraluminally and to methylergometrine injected intravenously. Moreover, the use of specific immunohistological and electron microscope techniques to assess even minimal changes in the ultrasonically skeletonized vessel wall argue in favor of our observations [9,13,14].

The most important finding of this study is that ultrasonic skeletonization may affect the endothelial function in arterial grafts used for myocardial revascularization. In our experiments, arterial rings from pedicled grafts showed greater relaxation responses to ACh than rings from ultrasonically skeletonized grafts, suggesting that ultrasonic skeletonization may damage the endothelial function in the grafts. Moreover, the percentages of the complete loss of ACh-reactions, which indicates the severe damage of the endothelial cells, was also significantly greater in skeletonized rings than in pedicled rings. It is well known that ACh induces an endothelium-dependent release of NO to mediate vasorelaxation and inhibit platelet aggregation in the vessels [15]. Therefore, our results using the most common type of endothelium-dependent vasodilator, clearly confirm that the ultrasonically skeletonized vessel may suffer functional injury of the endothelium in comparison with the pedicled grafts.

To our knowledge, only limited information is available concerning the endothelial functions of the skeletonized grafts for surgical revascularization. A recent histological study performed using a scanning electron microscope showed that skeletonizing the radial artery with an ultrasonic scalpel is associated with a higher risk of endothelial damage than those harvested as a pedicle [10]. On the other hand, Deja et al. [11] have suggested that, during in vitro skeletonization with scissors, the sensitivities to endothelium-dependent vasodilators, such as ACh and bradykinin, did not differ significantly between skeletonized and pedicled ITA. These results suggest that gentle skeletonization without an ultrasonic scalpel might preserve endothelial function.

The harmonic scalpel can dissect perivascular tissues, and coagulate and cut vascular branches as a result of mechanical incision by vibration, cavitational fragmentation and protein coagulation [7]. This results in a low level of damage to the vessel due to a low temperature in comparison with an electric cautery [14]. However, Kinoshita and Omura [12] investigated the relationship between the tissue temperature surrounding a shear type blade edge and the duration of action, and reported that the relatively high temperature remained at 80 °C for 8 s, and then increased rapidly to 150 °C. Generally, in comparison with vascular smooth muscles, endothelial cells consist of one thin layer and are easily damaged by stress, such as shear and heat stress [16,17]. Therefore, one might expect that the heat and ultrasonic vibration produced by this device could result in some damage to the endothelium of the skeletonized arterial grafts. However, it has been recently suggested that, in the nine ultrasonically skeletonized ITA, the excellent preservation of the structural and ultrastructural integrity of the vessel walls, with particular regard to the endothelium, has been demonstrated [18]. These results suggested that ultrasonic ITA skeletonization is not detrimental to vessel wall structures, although the lack of a sensitive method to detect endothelial damage limits the conclusions that can be drawn from these experimental models. In contrast, our in vitro isometric tension measurements may more exactly reflect the vasomotor functions found in clinical practice after CABG than the figures of the structural integrity of the
vessels. Therefore, the question arises whether ultrasonic skeletonization mediates minimal mechanical damage, which cannot be detected by electron microscopy, or unusual functional devastation of the signal transduction system in the endothelial cells. Further pharmacological and biochemical studies are necessary to clarify the situation.

In conclusion, our results coincidentally provide valuable additional information regarding the functional status in ultrasonically skeletonized grafts. We provide the first pharmacological evidence that ultrasonic skeletonization with the harmonic scalpel is definitely more traumatic for endothelium function than the conventional pedicled harvesting technique. Although skeletonization with the ultrasonic scalpel is believed to dissect grafts more safely than an electric cautery, careful surgical manipulation is required during its utilization. Considering the application of our results to clinical trials, an improvement of blood flow in the skeletonized grafts after the application of endothelium-independent vasodilators such as ISDN and/or diltiazem may be expected to increase the safety of arterial revascularization by reducing the risk of graft hypoperfusion syndrome.

References


