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Original Article / *Özgün Makale*

Comparison of vasodilatation responses of arterial grafts harvested with and without electrocautery: *in vitro* study results

Elektrokoter ile veya elektrokotersiz hazırlanan arter greftlerinin vazodilatasyon yanıtlarının karşılaştırılması: İn vitro çalışma sonuçları

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ABSTRACT

Background: In this study, we aimed to compare vasodilatation responses of arterial grafts harvested by electrocautery and without electrocautery by using the tissue bath system.

Methods: Between May 2013 and June 2014, 30 patients (19 males, 11 females, mean age 60.0±8.2 years; range 47 to 77 years) who underwent elective coronary artery bypass grafting (CABG) surgery were enrolled in the study. Sixteen samples from internal thoracic artery and radial artery grafts in each group were collected. The grafts were divided into two groups: grafts harvested by electrocautery (group 1) and grafts harvested without electrocautery (group 2).

Results: The vasodilatation responses of internal thoracic artery grafts were significantly reduced in group 1, compared to group 2. Although the vasodilatation responses of radial artery grafts in group 1 were lesser than in group 2, the difference was not statistically significant.

Conclusion: Vessel harvesting by electrocautery may cause serious endothelial injury particularly in internal thoracic artery grafts, rather than radial artery grafts. The procedure without electrocautery may be more advantageous during the harvesting of arterial grafts in terms of preventing early graft failure.

Keywords: Coronary bypass; internal thoracic artery; radial artery; vasodilatation.

ÖZ

Amaç: Bu çalışmada, elektrokoterli ve elektrokotersiz tekniklerle hazırlanan arter greftlerinin vazodilatasyon yanıtları organ banyosu düzeneği kullanılarak karşılaştırıldı.

Çalışma planı: Mayıs 2013 - Haziran 2014 tarihleri arasında elektif koroner arter baypas greft (KABG) cerrahisi uygulanan 30 hasta (19 erkek, 11 kadın, ort. yaş 60.0±8.2 yıl; dağılım 47-77 yıl) çalışmaya alındı. Her gruptan 16'şar internal torasik arter ve radial arter örneği alındı. Greftler iki gruba ayrıldı: elektrokoter kullanılarak hazırlanan greftler (grup 1) ve elektrokotersiz hazırlanan greftler (grup 2).

Bulgular: İnternal torasik arter greftlerinin vazodilatasyon yanıtları, grup 2'ye kıyasla, grup 1'de anlamlı olarak azaldı. Radial arter greftlerinin vazodilatasyon yanıtları grup 1'de grup 2'den düşük olmasına rağmen, fark istatistiksel olarak anlamlı değildi.

Sonuç: Elektrokoter ile damar preparasyonu, radial arter greftlerinden ziyade, internal torasik arter greftlerinde ciddi endotel hasarına neden olur. Erken greft yetmezliğinin önlenmesi açısından, arter greftlerinin hazırlanması esnasında elektrokotersiz işlem daha avantajlı olabilir.

Anahtar sözcükler: Koroner baypas; internal torasik arter; radial arter; vazodilatasyon.

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The interest in arterial grafts has gradually increased by the experimental study conducted by Murray et al.[1] in 1953 which demonstrated efficacy of the arterial grafts for coronary circulation. Internal thoracic artery (ITA) graft usage has increased steadily after the results of Green's study.[2] Recent studies have shown that ITA grafts have better long-term graft patency rates than standard vein grafts after coronary artery bypass grafting (CABG) surgery.[3,4] The first use of radial artery (RA) as a bypass graft was performed by carpentier in 1973; however, it was abandoned in a short time due to its poor patency rates.[5-7] Its usage was increased after Acar et al.[8] reported long-term patency rates for RA. Currently, RA is the second choice arterial graft after ITA in arterial revascularization.[9]

Arterial grafts are more prone to injury during preparation due to their structural characteristics. Internal thoracic artery is likely to tend to mechanical and thermal injury than RA during harvesting due to its thin intimal layer.[9] However, an excessive muscular thickness of radial artery may lead to spasm. Early graft failure and occlusion are, therefore, thought to be related to vasospasm mechanisms and trauma, eventually leading to endothelial injury during harvesting.[10] Minimally traumatic harvesting techniques, no-touch technique, and anti-spasmodic treatment protocols have been developed to prevent early graft failure.

In this study, we aimed to compare vasodilatation responses of arterial grafts harvested by electrocautery or without electrocautery by using the tissue bath system with ITA and RA grafts.

PATIENTS AND METHODS

Between May 2013 - June 2014, 30 patients (19 males, 11 females, mean age 60.0±8.2 years; range 47 to 77 years) who underwent elective CABG surgery were included in the study. According to the harvesting technique used, the patients were divided into two groups. In group 1, RA and ITA grafts were harvested by electrocautery, while the grafts were harvested without electrocautery in group 2. As a result, 16 samples were studied from ITA and RA grafts in each group. In totally, 64 samples were studied in the tissue bath system. The exclusion criteria were ≥80 years of age, serum creatinine level of ≥2 mg/dL, refusal to give an informed consent, the presence of peripheral arterial disease, diabetes mellitus (DM) or arteriovenous fistula, end-stage chronic renal failure requiring hemodialysis and abnormal Allen's test results. The study protocol was approved by the local ethics committee (No: 2013/54/05/03) and a written informed consent was obtained from each patient.

For harvesting ITA, exposure was achieved through a table mounted retractor which allowed the best exposure by elevating the sternal leaf. Sternal fracture, brachial plexus injury, or costochondral separation were the potential risks caused by excessively sternal elevation. Then, ITA grafts were collected with the pedicle containing adjacent veins, fascia, and adipose tissue. In each group, ITA was dissected until the bifurcation of musculophrenic artery was achieved and the superior epigastric artery and distal segments of ITA were *in vitro* studied after heparinization. Grasping the artery with forceps or retracting too much was avoided to prevent possible ITA injuries in both groups during harvesting. In group 1, a low power (20-30 watts) was used to avoid thermal injury. A proximal clip and distal cautery division were preferred in group 1, whereas two clips were placed and cut with scissors in group 2.

The Allen's test was routinely performed to identify the sufficiency of the ulnar circulation of non-dominant arm. If the capillary re-filling of the palm and digits took more than 10 seconds, a modified Allen's test was performed to confirm the results. Oxygen saturation of the thumb was measured through a oximetry. The patients with a positive Allen's or modified Allen's test results were excluded. In addition to these two tests, an 'intraoperative Allen's test' was also used.[11] After totally mobilization, RA was clamped for 20 seconds and color of the hand was visualized to assess the ulnar artery collateral circulation. An intra-arterial cannula was inserted to the other hand to monitor the blood pressure.

A curvilinear sharp incision was performed from 3 cm distal to the elbow crease following the rounded belly of the brachioradialis muscle, down to 1-2 cm above the wrist. From this point, the RA pedicle was dissected with sharp dissection including satellite veins and the branches were divided with scissors in group 2. Low-energy electrocautery (Valleylab Force FX monopolar 300W-300 Ohm, Bipolar 70W-100 Ohm, Tyco Healthcare, USA) was used to harvest the RA in group 1. The collateral branches were occluded with a hemostatic clip proximally to the RA and divided by electrocautery distally.

In both techniques, the distal part of the RA was ligated and divided as well. Metal probes or dilatators were not used to prevent an intimal injury. Distal segments of the RA grafts were studied in tissue bath system. The grafts were not exposed to any vasodilator drug. All grafts were prepared by two different surgeons.

The graft samples of the ITA and RA were transferred to the vascular laboratory in +4 °C Krebs solution (Composition: 122 mmol/L sodium chloride (NaCl), 5 mmol/L potassium chloride (KCl), 1.25 mmol/L calcium chloride ($CaCl_2$), 25 mmol/L sodium hydrogen carbonate ($NaHCO_3$), 1.2 mmol/L magnesium sulphate ($MgSO_4$), 1.0 mmol/L monopotassium phosphate (KH_2PO_4), and 11.5 mmol/L glucose). The reservoirs in the tissue bath system were filled with 20 mL of 37 °C Krebs solution which was continuously oxygenated with Carbogene gas of 95% O_2 and 5% CO_2 and changed in every 20 minutes to keep the tissues alive. After removal of the adjacent fatty tissues and adventitia, the grafts were sliced into 3 mm wide vascular rings and were suspended into the tissue bath system via steel hooks. The upper ends were attached to the transducer, while the lower ends were kept stable. The vascular rings were entrained by 2-3 g of active tension for 60 minutes by potassium chloride. To measure the vasodilation responses, samples were initially exposed to phenylephrine (Sigma-Aldrich, St. Louis, MO, USA) to induce submaximal vasoconstriction and Charbachol (Sigma-Aldrich, St. Louis, MO, USA) was, then, used to induce nitric oxide (NO)-mediated vasodilatation. Subsequently, charbachol was added to the tissue bath system cumulatively starting from a concentration of 10^{-10}M in two minutes intervals and the dose was augmented half logarithmically until a concentration of 10^{-4}M was achieved. All data was transferred to the computer with the help of the Transducer Acquisition System (MAY IOBS 99, FDT 05 Commat, Iletisim Co, Ankara-Turkey) and stored with MAY-MASTER MP36 analysis software (Commat, Iletisim Co, Ankara-Turkey). The vasodilation response curves were obtained and recorded, as previously described.

Statistical analysis

The demographic variables were analyzed by IBM SPSS version 20.0 for Mac (IBM Corporation, Armonk, NY, USA). The statistical analysis of the data obtained from the tissue bath system was performed by Graphpad Prism 4 Version (Graphpad Software, La Jolla, California, USA). The concentration-response curves were also constructed by this program. Non-linear regression analysis (variable slopes) and one way analysis of variance (ANOVA) were applied to the graphics. A p value of <0.05 was considered statistically significant.

RESULTS

The demographic data of the patients are summarized in Table 1.

After submaximal vasoconstriction of the graft samples from group 1 and group 2 by phenilephrine, vasodilatation responses induced by augmenting doses of charbachol were recorded. The data on percent vasodilatation and log EC50 (logarithmic half maximal effective concentration) values of different graft types are listed in Table 2.

In the comparison of the samples from ITA and RA grafts in terms of the amount of vasodilatation response to charbachol, vasodilatation responses with charbachol in group 1 were 27.9±2.1% for ITA

Table 1. Preoperative characteristics and operative data of patients

	Group 1 (electrocautery)			Group 2 (without electrocautery)			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Age			60.8±10.4			58.3±8.3	>0.05
EuroSCORE			2.9±1.0			3.1±2.3	>0.05
Body mass index			26.6±4.7			26.5±3.1	>0.05
Hypertension	4	26.66		3	20		>0.05
Preoperative ejection fraction			58.5±8.1			57.5±8.0	>0.05
Chronic obstructive pulmonary disease	5	33.33		6	40		>0.05
No. of grafts			2.7±0.8			3.0±0.6	>0.05
Cardiopulmonary bypass time (min)			70.5±18.6			72.4±17.4	>0.05
Cross-clamp time (min)			42.8±10.7			44.7±12.0	>0.05
Intesive care unit stay (day)			2.9±1.1			2.3±1.6	>0.05
Hospital stay (day)			7.7±2.7			8±3.4	>0.05

SD: Standard deviation; EuroSCORE: European System for Cardiac Operative Risk Evaluation.

Table 2. Vasodilatation responses of arterial grafts

	Group 1 (electrocautery)		Group 2 (without electrocautery)		
	%VD		%VD		
	Mean±SD	logEC50	Mean±SD	logEC50	*p*
Internal thoracic artery	27.9±2.1	-1.963	65.5±5.0	-5.132	0.0490
Radial artery	36.6±3.2	-3.185	55.8±7.0	-4.747	0.5317

%VD: Percent vasodilatation; SD: Standard deviation.

and 36.6±3.2% for RA. The log EC values in group 1 were -1.963 for ITA and -3.185 for RA. In addition, vasodilatation responses with charbachol for group 2 were 65.5±5.0% for ITA and 55.8±7.0% for RA. The log EC values in group 2 were -5.132 for ITA and -4.747 for RA.

The vasodilation responses of phenylephrine pre-treated ITA grafts in group 1 and group 2 were 27.9±2.1% and 65.5±5.0%, respectively (Figure 1). The vasodilation response of ITA grafts showed a statistically significant difference (p=0.0490) among the samples.

The vasodilation responses of phenylephrine pre-treated RA grafts in group 1 and group 2 were 36.6±3.2% and 55.8±7.0%, respectively (Figure 2). The vasodilation response was lesser in group 1 than in group 2; however, there was no statistically significant difference between the groups (p=0.5317).

DISCUSSION

There is a large number and variety of grafts which can be used during CABG surgery. The most commonly used ones are ITA and saphenous vein (SV). In several studies, ITA grafts have been proposed thanks to their more resistant nature to atherosclerosis and higher long-term patency rates than SV grafts.[3,4,12] Currently, the second most commonly used arterial graft is RA.[13]

One of the factors which affect CABG patency is vascular trauma during harvesting.[10] In particular, ITA is more sensitive to trauma than other arterial grafts. In addition, the vein grafts response well to the vasodilator agents against spasm, while arterial grafts are more resistant. The RA grafts are more prone to spasm than other arterial grafts. In case of exposure to the mechanical stimulation, spasm is inevitable due to the thick muscular layer of the RA. It can be attributed to the low patency rates of RA grafts due to skeletonized harvesting and dilatation with metallic probes. Therefore, RA is suggested to harvest with adjacent veins and vasodilator agents were used to prevent vasospasm.[8,14] During harvesting, the most common causes of graft damage are surgical techniques and thermal damage resulting from the improper use of electrocautery. During graft harvesting, use of the electrocautery may bring advantages of hemostasis and harvesting time; however, we believe that it may cause endothelial injury more than with the use of conventional technique with scissors.

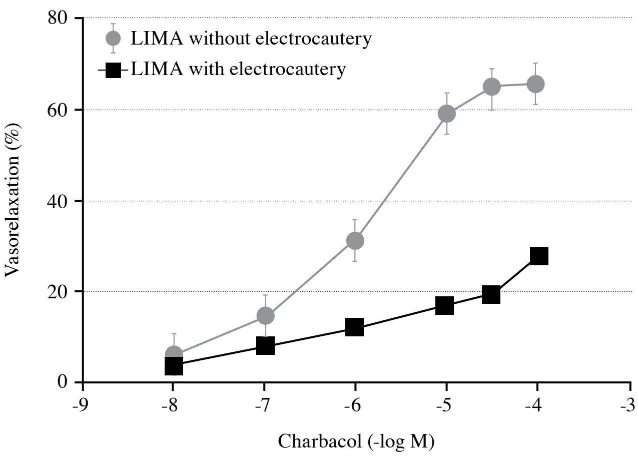

Figure 1. Comparison of concentration-vasodilatation response curves of internal thoracic artery grafts. LIMA: Left internal mammary artery.

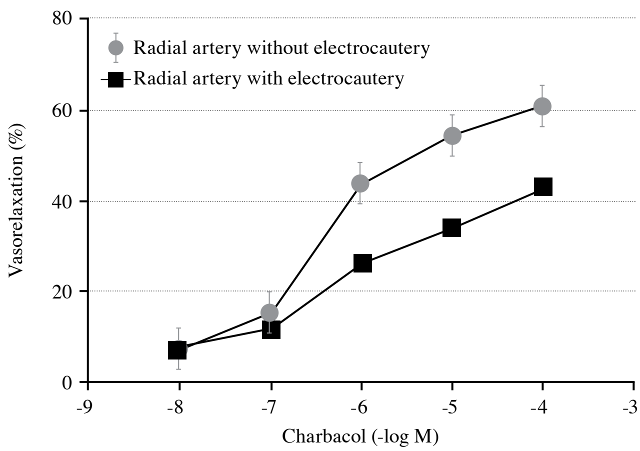

Figure 2. Comparison of concentration-vasodilatation response curves of radial artery grafts.

Coagulation and incision are made by protein degradation with contacting electrocautery directly to the tissue. During this process, it may consist more than 300 °C temperatures on the tissue. Lethola et al.[15] reported that endothelial changes may occur, if the tip of electrocautery touches the metallic clips. These changes can induce early- and late-term graft failures. In our study, we dissected RA and ITA grafts with and without electrocautery and examined endothelium-derived NO dependent relaxation. Despite using low voltage cautery in both arteries, we found less relaxation responses in the cautery group. In particular, there was significant decrease in the ITA's relaxation responses. It also suggest that ITA has a higher degree of endothelial injury.

According to the He's functional classification system, ITA is defined as type 1 and RA as type 3. type 1, somatic arteries such as ITA secrete more endothelium-derived NO than type 3 extremity arteries like RA.[9] He and Liu[16] and He et al.[17] demonstrated that ITA's endothelium secreted more NO and had much more eNOS activity than RA's endothelium. In this study, we considered that ITA grafts relaxation response decreased significantly due to higher degree of endothelial injury. Low relaxation response in the RA graft can be explained by thermal endothelial injury, as it had thicker media layer and tight myocyte conjunctions than elastic arteries like ITA. Even if electrocautery is used in low voltage, it can damage the endothelium. In contrast, when low-voltage energy is used for a short time period, it may cause lesser thermal damage.[18] In recent studies, in addition to 'no-touch' technique, an ultrasonic cautery harvesting method has been used by many surgeons to avoid thermal endothelial injury.[10,18-21] In the majority of these studies, ultrasonic dissection of the grafts has been reported to be superior than electrocautery dissection on endothelial injury. Furthermore, it has been suggested that the use of ultrasonic cautery is safer and can reduce the amount of dissection time, and metallic clips. However, further studies are required to show endothelial injury by ultrastructural and immunohistochemical imagining.

In conclusion, although harvesting ITA and RA by electrocautery seems to be useful to control hemorrhage and reduce operation time compared to the procedures without electrocautery, it may result in serious endothelial injury in the ITA graft, in particular. Therefore, electrocautery usage should be reduced during arterial graft harvesting and it should be cautiously used with the possible lowest voltage, where applicable.

Declaration of conflicting interests

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