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Pre-operative Trans-thoracic Doppler Ultrasonography Evaluation and Intra-operative Manual Evaluation of the Left Internal Thoracic Artery in Patients with Type 2 Diabetes with Coronary Artery Disease

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Patients with coronary artery disease, with (*n* = 25) and without (*n* = 59) type 2 diabetes, who were scheduled to undergo coronary artery bypass grafting were enrolled in this prospective study. The left internal thoracic artery (LITA) was assessed for graft suitability before surgery by trans-thoracic Doppler ultrasonography and during surgery by manual measurement. Significant differences were seen between pre-operative and intra-operative LITA blood flow rates and LITA diameters, and the values of each at the two time points showed significant correlation, suggesting that pre-operative measurements largely related to intra-operative conditions. The pre-operative and intra-operative LITA blood flow rates and LITA diameters were not significantly different between patients with and without type 2 diabetes. Pre-operative LITA blood flow was monophasic in three patients without diabetes and the LITA grafts of these patients were deemed unsuitable for implantation during surgery. It is concluded that type 2 diabetes does not seem to have a negative effect on the suitability of LITA grafts. In addition, trans-thoracic Doppler ultrasonography is an easy, cost-effective, reproducible and non-invasive examination method, which may help in the evaluation of LIMA function and contribute to graft selection.

KEY WORDS: Trans-thoracic Doppler ultrasonography; Internal thoracic artery; Diabetes mellitus, Coronary artery bypass graft; Coronary artery disease

Introduction

Diabetes mellitus is a major independent risk factor for development of coronary artery disease (CAD).[1] It accounts for approximately 25% of the coronary revascularization procedures performed each

year and the outcomes of these procedures are worse in patients with diabetes than in those without diabetes.[2] CAD in diabetes patients frequently involves multiple coronary vessels and rapidly progresses to atherosclerotic disease and severe compromise of left-ventricular function, all of which can contribute to unfavourable outcomes after myocardial revascularization.[2–4]

The choice of coronary artery bypass graft (CABG) surgery conduit can play a critical part in the outcome of surgical revascularization. The left internal thoracic artery (LITA) is generally preferred to vein grafts because vessel patency and survival are longer.[5–7] The usefulness of trans-thoracic colour-duplex Doppler ultra-sonography for pre-operative evaluation of the native LITA and for the post-operative detection of graft patency has been reported.[8,9]

The aim of this study was to compare LITA blood flow rates and diameters, using trans-thoracic Doppler ultrasonography before CABG and manually during surgery, in CAD patients with and without type 2 diabetes, and to evaluate whether any correlation exists between the pre-operative and intra-operative measurements.

Patients and methods

STUDY DESIGN AND PATIENTS

This prospective study was conducted between March and September 2008, in the Department of Cardiovascular Surgery and Department of Radiology at Turgut Ozal Medical Centre, Malatya, Turkey according to the principles of the 2002 Helsinki Declaration. Ethics approval was received from Inonu University Medical School Ethics Committee (protocol No. 2008/24, dated 18 March 2008). Written informed consent was obtained from all participants before the study was initiated.

Eligible patients were those with CAD, with or without type 2 diabetes, scheduled to undergo isolated CABG surgery. The exclusion criteria were poor general condition, the need for emergency surgery or re-operation, or the presence of arrhythmia.

PRE-OPERATIVE AND INTRA-OPERATIVE ASSESSMENTS

Glycosylated haemoglobin (HbA_{1c}), C peptide and insulin were all measured before surgery. Haemodynamic stability of the LITA before and during surgery was assessed by measurement of systolic and diastolic blood pressures and pulse rates.

Pre-operative assessments of LITA diameter, blood flow, end-diastolic velocity, peak systolic velocity and resistive index were done with trans-thoracic Doppler ultrasonography of the LITA, performed by one radiologist (A.S.) with the ATL HDI 3500 and 5000 devices (Philips Medical Systems, Bothell, WA, USA) and a 4 – 7 MHz linear probe. Filter and gain settings of the device were adjusted to obtain detailed information without artefacts. Ultrasound images of the arterial lumen, plaque and vessel wall structure were recorded in greyscale. During Doppler investigation, care was taken not to include the vascular wall and the Doppler angle was set to < 60°. Measurements were made at the fifth–sixth intercostal space. For each feature, three measurements were obtained and the mean was calculated. The effect of heart rate on the assessment of the LITA was removed from the sampling area.

Intra-operative LITA diameter and flow measurements were performed manually by the surgeon. Immediately before cardiopulmonary bypass was started, flow rate in the LITA graft was assessed by measurement of the volume of blood that flowed in 60 s under controlled

haemodynamic conditions from the distal cut end of the vessel into a graduated cylinder. The graft lumen diameter was measured with probes in the cut sections from the levels of the fifth–sixth intercostal space.

SURGICAL PROCEDURE

All operations were performed by the same surgical team, with patients under general anaesthesia. As standard, the LITA pedicle graft was prepared with a no-touch technique by low-voltage bipolar electrocauterization at the point where it originated from the subclavian artery and branched into the superior epigastric and musculophrenic arteries and clamping of the branches. Around 3 – 5 min after intravenous systemic heparinization with 300 IU/kg, the LITA was divided at the level of bifurcation.

At the time of LITA anastomosis, the part of the LITA proximal to the fifth and sixth left ribs was stored in gauze impregnated with warm serum, verapamil (a calcium channel blocker) and nitroglycerine to prevent spasm.

STATISTICAL ANALYSIS

Statistical analysis was performed with SPSS® version 15.0 for Windows (Chicago, IL, USA). Continuous (measured) data were expressed as mean ± SD and categorical data were expressed as numbers and percentages. The distribution of continuous (measured) variables (age, ejection fraction, etc.) was assessed with the Shapiro–Wilk normality test and comparisons of significance of the differences between two mean values was determined with the unpaired *t*-test. The relationship between continuous (measured) variables was evaluated with Pearson correlation analysis. Categorical variables were assessed with Pearson χ^2 analysis and Fisher's exact χ^2 test. A P-value < 0.05 was deemed statistically significant.

Results

The study sample comprised 84 patients scheduled to undergo isolated CABG surgery. Their characteristics did not differ significantly between those with and those without diabetes except for the ratio of men being higher in the non-diabetic group than in the diabetic group ($P = 0.001$; Table 1). The mean ± SD age of onset of type 2 diabetes was 6.9 ± 1.67 years (range 2 – 23 years), and the mean ± SD pre-operative blood concentration of HbA_{1c} was 8.04 ± 1.67%, of C peptide was 3.54 ± 2.91 ng/ml and of insulin was 24.01 ± 24.45 IU/ml.

Continuous (measured) variables all had normal distributions. The pre-operative LITA blood flow rates and diameters measured with ultrasonography differed significantly from the manual measurements taken intra-operatively ($P = 0.0001$ for both; Table 2). In addition, the values for each showed a statistically significant correlation between the pre-operative and intra-operative levels (blood flow rate $r = 0.31$, $P = 0.006$; LITA diameter $r = 0.66$, $P = 0.0001$). Blood flow rates and LITA diameters did not, however, differ significantly between the two study groups and there were also no statistically significant differences between the two groups for pre-operative LITA resistive index and end-diastolic blood velocity. Pre-operative systolic blood velocity in diabetic patients was, however, significantly higher than in non-diabetic patients ($P = 0.001$; Table 3).

None of the patients with diabetes had monophasic blood flow, as assessed by measuring Doppler blood flow velocity in the LITA, whereas three (5%) non-diabetic patients had monophasic flow patterns. The LITA grafts prepared during surgery for these

TABLE 1:
Baseline characteristics of patients in the diabetic and non-diabetic groups scheduled for coronary artery bypass graft surgery

Characteristic	Diabetics (n = 25)	Non-diabetics (n = 59)	Statistical significance
Men	11 (44)	50 (85)	P = 0.001
Age, mean ± SD (years)	61.8 ± 10.2	60.2 ± 12.7	NS
COPD	3 (12)	10 (17)	NS
Hypertension	15 (60)	25 (41)	NS
Hyperlipidaemia	21 (84)	42 (71)	NS
Smoking	12 (48)	41 (70)	NS
Obesity	8 (32)	16 (27)	NS
Family history of CAD	10 (40)	19 (32)	NS
Renal failure	1 (4)	1 (2)	NS
PAD	1 (4)	3 (5)	NS
Prior MI	15 (60)	38 (64)	NS
Left-ventricular EF, mean ± SD (%)	49.5 ± 10.6	47.8 ± 9.5	NS
PTCA	5 (20)	6 (10)	NS
Carotid stenosis	5 (20)	4 (7)	NS
LMCA involved	0	1 (2)	NS
One vessel involved	5 (20)	10 (17)	NS
Two vessels involved	10 (40)	30 (51)	NS
Three vessels involved	10 (40)	19 (32)	NS

Data presented as n (%) unless stated otherwise.
CAD, coronary artery disease; COPD, chronic obstructive pulmonary disease; EF, ejection fraction; LMCA, left main coronary artery; MI, myocardial infarction; PAD, peripheral arterial disease; PTCA, percutanous transluminal coronary angioplasty.
NS, not statistically significant ($P > 0.05$).

TABLE 2:
Comparison of pre-operative and intra-operative left internal thoracic artery (LITA) blood flow and diameter measured with Doppler ultrasonography and manually, respectively

Characteristic	Pre-operative (n = 84)	Intra-operative (n = 84)	Statistical significance
Blood flow (ml/min)	44.9 ± 16.9	66.6 ± 30.1	P = 0.0001
LITA diameter (mm)	1.88 ± 0.2	1.77 ± 0.4	P = 0.0001

Data presented as mean ± SD.

three non-diabetic patients could not be used owing to poor blood flow rate and thin vascular structure. Haemodynamic stability (heart rate and blood pressure) was within normal limits for all patients and there was no statistically significant difference between pre-operative and intra-operative values (Table 4).

Discussion

The treatment of CAD involves balloon angioplasty or stent insertion by CABG in selected patients, particularly in those with extensive lesions.[2] The LITA is the conduit of choice for revascularization of coronary arteries and LITA grafts are being used increasingly in minimally invasive coronary

TABLE 3:
Comparison of pre-operative and intra-operative left internal thoracic artery (LITA) characteristics in patients with and without type 2 diabetes

Characteristic	Diabetics (n = 25)	Non-diabetics (n = 59)	Statistical significance
Pre-operative			
Blood flow (ml/min)	48.3 ± 13.9	43.4 ± 17.9	NS
LITA diameter (mm)	1.92 ± 0.24	1.86 ± 0.23	NS
Resistive index	0.85 ± 0.04	0.85 ± 0.34	NS
Systolic blood velocity (cm/s)	78.6 ± 15.6	66.5 ± 13.7	P = 0.001
End-diastolic blood velocity (cm/s)	10.6 ± 2.1	10.9 ± 8.3	NS
Intra-operative			
Blood flow (ml/min)	70.8 ± 27.7	64.1 ± 31.3	NS
LITA diameter (mm)	1.82 ± 0.37	1.74 ± 0.36	NS

Data presented as mean ± SD.
NS, not statistically significant ($P > 0.05$).

TABLE 4:
Comparison of pre-operative and intra-operative haemodynamic stability in the left internal thoracic artery

Characteristics	Pre-operative (n = 84)	Intra-operative (n = 84)	Statistical significance
Heart rate (beats/min)	78.6 ± 9.5	79.3 ± 8.5	NS
Systolic blood pressure (mmHg)	113.6 ± 11.8	111.2 ± 15.2	NS
Diastolic blood pressure (mmHg)	74.6 ± 11.6	71.8 ± 9.7	NS

Data presented as mean ± SD.
NS, not statistically significant ($P > 0.05$).

surgery.[7] Long-term post-operative follow-up has shown superior patency and survival, and reduced incidence of recurrent angina with LITA grafts than with saphenous vein grafts.[10] The rate of dysfunction in LITA grafts is about 10% within 10 – 15 years of revascularization.[11] Unadjusted angiographic data gathered over 20 years showed graft failure of 5% over that period of follow-up.[12]

Trans-thoracic Doppler ultrasonography has been frequently and successfully used post-operatively to detect quantitative changes in LITA graft blood flow and other characteristics in order to reveal early graft dysfunction.[13 – 15] The method does, however, have some limitations. For example, measurement of the degree of graft stenosis might not be accurate, which might lead to the need for coronary angiography.[16] In different series, the success rate for graft assessment with ultrasonography has ranged from 78.3% to 98.6%.[9]

Pre-operative assessment of native LITA by transthoracic imaging has been recommended.[14] In the present study, intra-operative LITA evaluation by ultrasonography was not done because of the fact that the LITA has a single trunk and this increases the risk of injury with this method.[17] Intra-operative LITA diameter and blood flow measurements were, therefore, performed manually by the surgeon. The

LITA diameters measured intra-operatively were significantly lower than those measured pre-operatively, but this difference is attributed to vasospasm. Despite the smaller intra-operative diameter, blood flow rate was significantly higher intra-operatively than pre-operatively. This is perhaps because the LITA was dissected at the level of the fifth–sixth rib at which proximal subclavian arteries branch off the LITA and blood flows to the distal part without any vascular connections. During measurement, therefore, blood flow from the subclavian artery does not encounter any resistance except when spasm occurs in the LITA. In addition, warm and vasodilating agents were applied to the LITA pedicle during the procedure, which might have raised intra-operative blood flow compared with pre-operative values. Nevertheless, a significant and strong correlation was found between the pre-operative and intra-operative LITA diameter and blood flow rates, which shows that pre-operative measurements largely related to intra-operative measurements.

A monophasic flow pattern was observed pre-operatively in three patients without type 2 diabetes and intra-operative evaluation showed the LITA grafts harvested from these patients were not suitable for CABG. This suggests that pre-operative measurements provide important evidence about the status of the LITA. Gümüş *et al.*[13] used Doppler ultrasonography to assess graft suitability pre-operatively, as well as outcomes in the early post-operative period (days 7 – 10) and late post-operative period (3 months). They saw a triphasic flow pattern pre-operatively in the native LITA that changed into a biphasic (systole–diastolic) pattern in the early post-operative period. In the present study, 78 patients had a pre-operative triphasic flow pattern and three patients had a biphasic flow pattern. Flow pattern was not measured post-operatively in the present study, however all the grafts harvested from these 81 patients were suitable for CABG and no early or late complications were encountered.

Controversial results have been previously reported for the use of arterial grafts in patients with diabetes.[2,18] Pathology studies have indicated that atherosclerotic changes occur more commonly in the radial artery than in the LITA. In a histological study of grafts from these two vessels, significant atherosclerotic changes were noted in patients with diabetes.[19] In other studies, vasoconstriction was suggested to occur more easily and frequently in arterial grafts implanted in patients with diabetes.[2,6] No differences in LITA luminal diameter and graft patency rates have, however, been reported between patients with and without diabetes in the early post-operative period.[13,15] The present study showed that the difference in LITA blood flow between the diabetic and non-diabetic groups was not significant, even taking into account the three patients with monophasic flow patterns.

The pre-operative LITA resistive index and end-diastolic blood velocities were similar in the two study groups. Systolic blood velocity, however, was significantly higher in the patients with diabetes than in those without. We believe, though, that this difference is not clinically important.

In patients scheduled for CABG, pre-operative assessment with trans-thoracic Doppler ultrasonography of the native LITA seems to be an easy, non-invasive, cost-effective and practical method for graft assessment. Furthermore, type 2 diabetes does not seem to have a negative effect on intra-operative outcomes using the LITA.

Conflicts of interest

The authors had no conflicts of interest to declare in relation to this article.

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