Analysis of Y-graft blood flow and flow reserve in conditions of increased myocardial oxygen consumption

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Background. **It is not well established whether early following surgery the blood flow of arterial composite Y-grafts may efficiently meet the flow demand of the coronary system. The aim of this study was to evaluate whether early after surgery arterial composite Y-grafts may increase the blood flow in response to an increase in myocardial oxygen consumption (MVO_2).**

Methods. **Twenty-seven patients who received complete arterial myocardial revascularization using the left internal thoracic artery (LITA) and the radial artery (RA) as composite Y-graft gave their consent to a pre-discharge coronary angiography and intravascular flow velocity measurements using a Doppler guidewire. Flow measurements were performed in the LITA main stem, the distal LITA and the RA, both at rest and during atrial pacing at 85% of the patient age-predicted maximum heart rate. The heart rate-systolic blood pressure product was considered as an indirect index of MVO_2. Hyperemic flow was determined after injection of adenosine. The flow reserve was defined as the ratio of blood flow during maximal hyperemia (Qmax) to baseline flow (Qbasal).**

Results. **Atrial pacing significantly increased MVO_2 ($p < 0.000$). None of the patients developed ischemic ST-segment modifications or complained of chest pain. Qbasal increased significantly in the LITA main stem ($p = 0.001$), distal LITA ($p = 0.041$) and RA ($p = 0.004$) while Qmax did not change significantly. As a consequence the flow reserve decreased in the LITA main stem ($p = 0.002$), distal LITA ($p = 0.000$) and RA ($p = 0.000$) but was not completely exhausted.**

Conclusions. **Early after surgery arterial composite Y-grafts may significantly increase blood flow in response to conditions of increased MVO_2 and maintain a normal myocardial oxygen supply-to-demand ratio.**

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Introduction

In order to increase the number of distal anastomoses using only two arterial grafts as much as possible the radial artery (RA) may be proximally placed on the left internal thoracic artery (LITA) as a Y-graft. Using this technique, described for the first time by Mills[1] in 1982 with both internal thoracic arteries, the RA flow is completely dependent on the flow of the LITA.

It has been shown that the flow reserve of the LITA used as a Y-graft is adequate at rest in the perioperative period and that it increases 6 months following surgery[2].

In the present study, we sought to determine whether the LITA used as a Y-graft with the RA may efficiently adapt to an increase in flow demand soon after the operation, particularly in patients whose myocardial revascularization was completely dependent on the LITA blood flow.

Methods

Study patients and selection criteria. Since February 1999, a program of myocardial revascularization using either the right internal thoracic artery or the RA in addition to the LITA has been started in our Department. Patient selection criteria for the different types of arterial grafting as well as the operative technique and definitions of postoperative complications have been previously described[3]. Up to February 2002, 453 patients received both the LITA and the RA. In 125 (27.5%) of these patients arterial myocardial revascularization was obtained using the two arteries as a Y-graft. Since March 2001, all the patients receiving a Y-graft were asked to undergo pre-discharge cardiac catheterization comprising angiography and intravascular flow velocity measurements. Up to February 2002, 40 patients gave their consent to the study protocol. Complete and reliable data were available only for 27 (67.5%) of these patients, who are the object of the present paper. In 13 (32.5%) patients, intravascular flow velocity measurements could not be perfectly recorded or were incomplete because of atrial pacing wire failure. The clinical characteristics of the study population are reported in table I.

This study was carried out in accordance with the recommendations of the World Medical Association Declaration of Helsinki[4] and was approved by the Research Committee of our Hospital. Written informed consent for the research protocol was obtained from each patient before cardiac catheterization.

Cardiac catheterization and angiography. The participants were brought to the cardiac catheterization laboratory in a fasting state. All cardioactive medications were continued as clinically indicated. All the patients received midazolam (5 to 10 mg i.v.) as precatheterization medication. Coronary angiography was performed using the standard femoral approach. Selective injection of the native coronary arteries and grafts was performed using diagnostic 6F catheters. After injection of a single bolus of 5000 IU of heparin, selective angiography of the coronary arteries was performed first, followed by Y-graft angiography. Evidence of a good angiographic result was the prerequisite to start the study protocol.

Intravascular flow velocity measurements. The intravascular flow velocity was measured using a 175 cm-long, flexible steerable Doppler guidewire (FloWire, Cardiometrics, Inc., Mountain View, CA, USA) with a diameter of 0.014" (0.036 cm) and forming part of a system coupled to a real-time spectrum analyzer, PAL videocassette recorder and video image printer. Simultaneous electrocardiographic, arterial blood pressure and central venous pressure signals were also continuously recorded on a multichannel recorder. The tip of the Doppler guidewire was advanced into the LITA until 2 to 3 cm distal to the site of branching of this vessel from the left subclavian artery. Being the Doppler signal dependent on the wire position relative to the flow stream within the vessel, the wire was manipulated until the best high quality phasic signal of blood flow velocity was obtained. Having measured the baseline resting LITA blood flow velocity, maximal resting hyperemic blood flow velocity was induced by injection of 30 µg of adenosine through the guiding catheter into the LITA. The resultant increase in coronary blood flow velocity was recorded. To confirm that the dose of adenosine produced maximal hyperemia (Qmax), the blood flow velocity was recorded after administration of an additional dose of 60 µg of adenosine. Following each adenosine injection, the Doppler signal was recorded for at least 60 s. Between successive doses of adenosine, the flow velocity was allowed to return to baseline.

Right atrial pacing was then started to evaluate the influence of increased myocardial oxygen consumption (MVO_2) induced by changes in heart rate on the LITA blood flow velocity. The heart rate-systolic blood pressure product was considered as an indirect index of MVO_2. Maintaining the Doppler guidewire in the same position, an external pulse generator was connected to the pacing wires placed on the right atrium during surgery. Atrial pacing was started at a value of 10 b/min above the patient's spontaneous sinus rhythm and progressively increased up to 85% of the patient's maximum predicted heart rate, considering that the maximum heart rate may be calculated using the formula 220-age (years), with a standard deviation of 10 to 12 b/min[5]. Atrial pacing was suspended in case of chest pain, atrioventricular block or ST-segment depression > 1 mm. After 3 min of atrial pacing at the maximum of the predicted heart rate, the baseline blood flow velocity was recorded. Qmax velocity was then induced by administration of 30 and 60 µg of adenosine through the guiding catheter as detailed before. Atrial pacing was then progressively reduced until the restoration of spontaneous sinus rhythm. Three minutes following the restoration of spontaneous sinus rhythm, intravascular flow measurements were repeated as detailed above within the distal LITA and RA and 2 to 3 cm distal to the Y anastomosis, both during sinus rhythm and atrial pacing.

Table I. Preoperative characteristics of the study population (27 patients).

Age (years)	55 ± 10
Gender (M/F)	27/0
Left main disease	4 (14.81%)
LVEF (%)	53 ± 9
Recent MI	12 (44.44%)
Diabetes mellitus	5 (18.51%)
Chronic renal failure	2 (7.4%)
COPD	1 (3.7%)
Multivessel disease	3 (11.1%)
Hypertension	15 (55.55%)

COPD = chronic obstructive pulmonary disease; LVEF = left ventricular ejection fraction; MI = myocardial infarction.

Quantitative biplane angiographic assessment. The segments of the LITA and RA investigated using the Doppler guidewire were analyzed and the vessel diameter was measured at end diastole by biplane quantitative coronary arteriography in two orthogonal views, usually but not exclusively the 30° right anterior oblique and 60° left anterior oblique projections, using electronic digital calipers (Thoshiba Corporation, Shimoishigami, Otawara-Shi, Tochigi-Ken, Japan) with the 6F guiding catheter as a known reference diameter. The graft cross-sectional area was computed assuming that the vessel was elliptical.

Flow velocity data analysis. Frequency analysis of the Doppler signal was carried out in real time using a velocimeter by fast Fourier transformation (FlowMap, Cardiometrics, Inc.). The systolic peak velocity, diastolic peak velocity and the time-average peak velocity were determined using the phasic coronary blood flow recordings. Quantitative estimation of the flow volume in the LITA main stem, distal LITA and RA was computed according to Doucette et al.[6] and considering the cross-sectional area and the time-average peak velocity. The flow reserve into the main stem of the LITA, distal LITA and RA was defined as the ratio of the estimates of blood flow during Qmax to the estimates of baseline flow (Qbasal), both at rest and during atrial pacing.

Statistical analysis. All statistical analyses were performed using the SPSS® 11.0 software (SPSS Inc., Chicago, IL, USA). Continuous data are presented as mean ± SD. Normal distribution was tested using both the Kolmogorov-Smirnov statistics with a Lilliefors significance level and the Shapiro-Wilk statistics. The paired Student's t-test was used after evidence of normality. A p value < 0.05 was considered as statistically significant.

Results

Clinical results. All the 27 patients underwent elective surgery using a pedicled Y-graft without concomitant procedures. All the operations were performed in conditions of extracorporeal circulation. The mean cardiopulmonary bypass time and aortic cross-clamping time were 92 ± 21 and 69 ± 23 min respectively. The anastomosis between the LITA and the RA was always performed after coronary anastomoses and during the ischemic time. The mean number of distal anastomoses was 3.59 ± 0.69 (range 2 to 5) (Table II). The difference between the average number of LITA and RA distal anastomoses was significant (1.37 ± 0.49 vs 2.22 ± 0.42, p < 0.000). The mean intensive care unit stay was 29 ± 13 hours. There were neither deaths nor perioperative myocardial infarctions. None of the patients developed major postoperative complications. Implantation of an intra-aortic balloon pump was never necessary. The mean hospital stay was 7 ± 1 days.

All the patients underwent postoperative angiography and intravascular flow velocity measurements before hospital discharge, after a mean of 5 ± 1 days following surgery. The average hemoglobin level at the time of the study was 9.49 ± 1.22 g/dl. No significant change in the mean arterial blood pressure, central venous pressure and heart rate was observed after adenosine injection. During atrial pacing, no significant change in the mean arterial blood pressure or any episode of atrioventricular block was recorded. The heart rate-systolic blood pressure product increased significantly during atrial pacing (9897 ± 1558 vs 15 128 ± 2145, p < 0.000). None of the patients developed ischemic ST-segment modifications or complained of chest pain.

The average length of stay in the catheterization laboratory for the 27 patients who completed the study was 75 ± 23 min.

Table II. Coronary anastomoses performed in the study population.

Graft type	Target coronary artery	No. patients	No. coronary anastomoses
LITA	LAD	17	17
	D-LAD	10	20
RA	OM	1	1
	OM1-OM2	3	6
	OM-PD	16	32
	OM1-OM2-PD	6	18
	D-OM1-OM2	1	3
Total		27	97

D = diagonal branch; LAD = left anterior descending coronary artery; LITA = left internal thoracic artery; OM = obtuse marginal branch; PD = posterior descending coronary artery; RA = radial artery.

Quantitative angiographic data. The patency rate was 100% both for the LITA and RA. During sinus rhythm, the cross-sectional area was slightly greater in the RA than in the LITA main stem (6.24 ± 1.88 vs 5.70 ± 1.28 mm^2, p = 0.25) and significantly greater in the LITA main stem than in the distal LITA (5.70 ± 1.28 vs 3.52 ± 1.10 mm^2, p < 0.000) and in the RA than in the distal LITA (6.24 ± 1.88 vs 3.52 ± 1.10 mm^2, p < 0.000). During atrial pacing, the cross-sectional area increased, but not significantly, in the LITA main stem (5.70 ± 1.28 vs 5.85 ± 1.39 mm^2, p = 0.55) and in the RA (6.24 ± 1.88 vs 6.28 ± 1.88 mm^2, p = 0.17) while it increased significantly in the distal LITA (3.52 ± 1.10 vs 3.66 ± 1.11 mm^2, p = 0.022).

Flow measurement data (Table III). During atrial pacing Qbasal increased significantly in each of the three main segments of the composite Y-grafts (LITA main stem, distal LITA and RA) while Qmax slightly changed from the values calculated during sinus rhythm. Qbasal and Qmax in the distal LITA and in the RA were not significantly different both during sinus rhythm and atrial pacing.

Consequently, atrial pacing caused a significant reduction in the flow reserve, taken as the ratio between Qmax and Qbasal. The flow reserve was significantly greater in the distal LITA than in the RA both during sinus rhythm and atrial pacing.

Discussion

The concept of anastomosing another bypass graft to an attached LITA was introduced by Mills[1] to avoid

Table III. Flow measurements.

	Qbasal			Qmax			Flow reserve		
	SR*	AP**	p	SR*	AP**	p	SR	AP	p
LITA (ms)	57.2 ± 23.3	75.1 ± 36.2	0.001	96 ± 34.4	101.9 ± 42.9	0.31	1.7 ± 0.5	1.4 ± 0.2	0.002
LITA (d)	30 ± 18.7[§]	37 ± 19.1[§§]	0.041	50.8 ± 26.5[†]	51.7 ± 24.8[††]	0.70	1.7 ± 0.3[‡]	1.4 ± 0.3[‡‡]	0.000
RA	34.2 ± 15.1[§]	40.2 ± 22.6[§§]	0.004	51.7 ± 24.5[†]	51.8 ± 27.5[††]	0.97	1.5 ± 0.2[‡]	1.3 ± 0.1[‡‡]	0.000

AP = atrial pacing; LITA (d) = left internal thoracic artery (distal); LITA (ms) = left internal thoracic artery (main stem); Qbasal = baseline flow (ml/min); Qmax = maximal hyperemia (ml/min); RA = radial artery; SR = sinus rhythm. * p = 0.000 for LITA (ms), LITA (d) and RA; ** p = 0.000 for LITA (ms), LITA (d) and RA; [§] p = 0.41; [§§] p = 0.85; [†] p = 0.57; [††] p = 0.98; [‡] p = 0.012; [‡‡] p = 0.012.

placing vein grafts into a severely atherosclerotic ascending aorta. A few years later, Tector et al.[7] reported the first series of patients who received both internal thoracic arteries using the T-graft technique. More recently, the RA has been widely used with the LITA as a composite Y-graft with excellent results[8].

The supporters of this technique maintain that composite grafts may be used to achieve total arterial and pedicled arterial revascularization in patients with multivessel disease with no increase in complications, while the skeptical are concerned about the possible inability of Y-grafts to fully respond to the left coronary system flow demand particularly early following surgery[9].

Many authors have measured the blood flow through composite grafts with different techniques. In 1999, Royse et al.[8] evaluated the intraoperative LITA performance by measuring both the free-flow of blood and the blood flow by transit-time Doppler technique, showing that the LITA may provide a 2.3-fold flow reserve to the coronary bed. In the same year, Wendler et al.[2], using a Doppler guidewire, showed that 1 week following surgery the flow reserve in the LITA main stem is adequate at rest for multiple coronary anastomoses and that it significantly increases, always at rest, 6 months later. More recently, Sakaguchi et al.[9], using positron emission tomography, found that 2 weeks following surgery the LITA used as a composite graft improves myocardial blood flow at rest but that it is not as effective as an independent graft for improving the flow reserve.

We have evaluated, in the perioperative period, the LITA flow reserve both at rest and in conditions of increased MVO_2 achieved by increasing heart rate by atrial pacing. Atrial pacing is an oxygen supply demand-stress associated with an increased coronary blood flow and a decreased diastolic time[10,11]. Experimental studies have shown that pacing-induced tachycardia adversely affects the myocardial tissue supplied by a stenosed coronary artery, particularly in the subendocardium, and increases the severity of ischemia as measured by ST-segment elevation[12]. In our study protocol, the patient heart rate was increased up to 85% of the patient age-predicted maximum, increasing significantly the MVO_2. During the period of atrial pacing none of the patients complained of chest pain or developed ischemic ST-segment modifications in spite of the unfavorable conditions of the perioperative period characterized, due to the recent surgical trauma, both by moderate anemia and a certain degree of coronary microvascular dysfunction[13]. Both these factors reduce the flow reserve in the early postoperative period. Nevertheless, the LITA main stem could maintain a normal oxygen supply-to-demand ratio in case of a maximal increase in MVO_2 because Qbasal increased significantly during atrial pacing. In this circumstance, the oxygen supply-to-demand ratio is maintained by decreasing the resistance at the coronary arteriolar level, thus increasing myocardial perfusion. Therefore, the LITA flow increased while the flow reserve decreased because Qbasal rose significantly while Qmax did not.

Qmax in sinus rhythm was significantly greater than Qbasal during atrial pacing in the LITA main stem, distal LITA and RA. These data confirm previous experimental results showing that the entire coronary reserve is not used during peak muscular exercise[14]. Therefore, the vasodilation induced by physiological stimuli does not appear to be as complete as that induced by pharmacological stimuli.

We also addressed the flow distribution between the two arms of the Y-grafts, represented in our patients by the distal LITA and RA. Qbasal and Qmax did not significantly differ between the distal LITA and RA both during sinus rhythm and atrial pacing, in spite of the significantly greater number of coronary anastomoses performed with the RA. As previously noticed by Royse et al.[8], half of the flow in the LITA main stem is likely to be delivered to the distal LITA and half to the RA. Interestingly, we noticed that while the flow reserve decreased significantly during atrial pacing both in the distal LITA and in the RA, it was significantly greater in the distal LITA than in the RA, both during sinus rhythm and atrial pacing. We could infer that the distal LITA is more efficient than the RA in adapting its size to the flow demand. This assumption is supported by the results of our angiographic assessment. We have noticed that during atrial pacing the cross-sectional area increased significantly in the distal LITA but not in the RA. This result is in contrast with the experience of Gurne et al.[15] who however studied a series of 28 patients with the LITA anastomosed on the left anterior descending coronary artery but not as a Y-graft.

Limitations of the study. There are several possible methodological limitations in the present study:
• the quality of the signal and the value of the peak velocity recorded are dependent on consistent and careful positioning of the wire. Operator-dependent measurement errors are possible. Such errors have been minimized but not excluded by analyzing only curves of good quality. In our experience, many data were cast off because they were considered as inappropriate and this resulted in the exclusion of 13 patients from the study;
• inaccuracies in the determination of the vessel cross-sectional area may contribute to the variability of the flow calculations. The vessel diameter was measured at end diastole by biplane quantitative coronary arteriography in two orthogonal views and the graft cross-sectional area was computed assuming that the vessel was elliptical. Although these measurements should be more appropriate than considering the vessel as having a circular cross section[2], inaccuracies in our estimation of the cross-sectional area may have occurred, limiting the reliability of clinical measurements;
• the elevation in heart rate was brief in duration (3 min). More sustained alterations could produce different effects on the flow reserve;
• cardioactive medications were continued as clinically indicated throughout the study. These drugs could have influenced the reliability of the flow measurements. However, all the patients who received a RA had diltiazem prescribed to minimize the risk of arterial spasm and it has been shown that this drug does not invalidate the measurements of the coronary flow reserve[16];
• this study is limited by the relatively small number of patients. This is due to the complexity of the protocol which markedly reduces patient compliance.

In conclusion a few days following surgery, the LITA main stem may maintain a normal oxygen supply-to-demand ratio in conditions of a maximal increase in MVO_2 induced by atrial pacing. As a consequence, the flow reserve decreases significantly because of a significant increase in Qbasal, while Qmax does not change. The entire flow reserve of the LITA is not used during the stress induced by atrial pacing. The flow distribution between the two arms of the Y-grafts seems to be the same, independently of the number of coronary anastomoses. The distal LITA shows a greater flow reserve with respect to the RA, probably because it more adapts its size to the flow demand more efficiently than the RA.

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