Effects of heart rate on phasic Y-graft blood flow and flow reserve in patients with complete arterial myocardial revascularization: an intravascular Doppler catheter study

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Abstract

Objective: It is not well established whether the blood flow of arterial composite Y-grafts can efficiently respond to the flow demand of the coronary system early postoperatively. The aim of this study was to evaluate if soon after the operation, arterial composite Y-grafts can increase blood flow in response to an increase in myocardial oxygen consumption (MVO2).

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 guide wire. Flow measurements were performed in the LITA main stem, the distal LITA and the RA, both at rest and during atrial pacing at the 85% of the patient age-predicted maximum. The heart rate–systolic blood pressure product was considered as an indirect index of MVO2. Hyperemic flow was determined after injection of adenosine. The flow reserve (FR) was defined as the ratio of blood flow during maximal hyperemia (Qmax) to baseline flow (Qbasal).

Results: Atrial pacing increased MVO2 significantly (P<0.000). None of the patients developed ischemic S-T segment modifications or complained of chest pain. Qbasal increased significantly in the LITA main stem (P=0.001), distal LITA (P=0.002) and RA (P=0.004) while Qmax did not change significantly. As a consequence, the FR 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: Soon after the operation, arterial composite Y-grafts can significantly increase blood flow in response to conditions of increased MVO2, keeping normal the myocardial O2 supply-to-demand ratio.

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Keywords: Y-graft; Composite arterial graft; Left internal thoracic artery; Radial artery; Flow reserve; Atrial pacing

1. Introduction

In order to extend as much as possible the number of distal anastomoses using only two arterial grafts, the radial artery (RA) can be proximally placed on the left internal thoracic artery (LITA) as a composite Y-graft. Using this technique, the RA flow is completely dependent on the flow of LITA.

It has been shown that the flow reserve (FR) of the LITA used as a composite Y-graft is adequate in the perioperative period at rest and that it increases after 6 months from the operation [1]. Nothing has been described over whether the LITA used as a composite Y-graft can provide adequate flow supply at periods of peak myocardial demand in the perioperative period and some concerns still remain about the possibility of LITA to fully respond to the flow demand of the coronary system soon after myocardial revascularization [2].

In the present study, we sought to determine whether LITA used as a Y-graft with RA can 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.

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2. Material and methods

2.1. Study patients and selection criteria

Since February 1999, a program of myocardial revascularization using either the right internal thoracic artery (ITA) or RA in addition to LITA has been started in our department. Patient selection criteria for the different types of arterial grafting as well as operative technique and definitions of postoperative complications have been previously described [3]. Up to February 2002 in 453 patients both the LITA and the RA were used as arterial grafts. In 125 (27.5%) of these patients, arterial myocardial revascularization was obtained using the two arteries as a composite Y-graft. Since March 2001, all the patients receiving a composite 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 could be taken only in 27 (67.5%) of these patients, who are the subjects 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 wires failure. Clinical characteristics of the study population are reported in Table 1.

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.

2.2. Cardiac catheterization and angiography

Patients were brought to the cardiac catheterization laboratory in a fasting state. All cardio-active medications were continued as clinically indicated. All the patients received midazolam (5–10 mg i.v.) as pre-catheterization medication. Coronary angiography was performed by standard femoral approach. Selective injection of the native coronary arteries and grafts was performed by 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.

2.3. Intravascular flow velocity measurements

Intravascular blood flow velocity was measured using a 175-cm long, 0.014-inch (0.036 cm) diameter flexible steerable Doppler guide wire (FloWire, Cardiometrics, Inc., Mountain View, CA), part of a system coupled to a real-time spectrum analyzer, PAL videocassette recorder and video image printer. Simultaneous electrocardiogram, arterial blood pressure and central venous pressure signals were also continuously recorded on a multi-channel recorder. The tip of the Doppler guide wire was advanced into the LITA and stopped 2–3 cm after LITA take off from the left subclavian artery. The Doppler signal being 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. After the baseline resting, LITA blood flow velocity was measured, maximal resting hyperemic blood flow velocity was induced by injection of 30 μg of adenosine through the guiding catheter into the left ITA. The resultant increase in blood flow velocity was recorded. To confirm that the dose of adenosine produced maximal hyperemia, blood flow velocity was recorded after administration of an additional dose of 60 μg of adenosine. After every adenosine injection, the Doppler signal was recorded at least for 60 s. Flow velocity was allowed to return to baseline between doses of adenosine.

Right atrial pacing was then started to examine the influence of an increased myocardial oxygen consumption (MVO$_2$) induced by changes in heart rate (HR) on LITA blood flow velocity. The HR–systolic blood pressure product was considered as indirect index of MVO$_2$. Keeping the Doppler guide wire in the same position, an external pulse generator was connected to the pacing wires placed on the right atrium during the operation. Atrial pacing was started at a value of 10 beats per minute over the patient’s spontaneous sinus rhythm and progressively increased up to the 85% of the patient’s maximum predicted HR, considering that maximum HR can be calculated from the formula: 220–age (years), with a standard deviation of 10–12 beats per minute [5]. Atrial pacing was stopped if there was a presence of chest pain, atrioventricular block or S-T segment depression greater than 1 mm. After 3 min of atrial pacing, baseline blood flow velocity was recorded. Maximal hyperemic flow velocity was then induced by administration of 30 and 60 μg of adenosine through the guiding catheter and blood flow velocity was recorded. Atrial pacing was then progressively reduced up to the spontaneous sinus rhythm. Three minutes after restoration of the spontaneous

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Table 1
Properative characteristics of the study population (27 patients)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)$^a$</td>
<td>55 ± 10</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>27/0</td>
</tr>
<tr>
<td>Left main disease</td>
<td>4 (14.8%)</td>
</tr>
<tr>
<td>LVEF (%)$^a$</td>
<td>53 ± 9</td>
</tr>
<tr>
<td>Recent MI</td>
<td>12 (44.4%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>5 (18.5%)</td>
</tr>
<tr>
<td>CRF</td>
<td>2 (7.4%)</td>
</tr>
<tr>
<td>COPD</td>
<td>1 (3.7%)</td>
</tr>
<tr>
<td>Polyvascular disease</td>
<td>3 (11.1%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>15 (55.5%)</td>
</tr>
</tbody>
</table>

LVEF, left ventricular ejection fraction; MI, myocardial infarction; CRF, chronic renal failure; COPD, chronic obstructive pulmonary disease.

$^a$ Mean ± standard deviation.
sinus rhythm, intravascular flow velocity measurements were repeated as detailed above in distal LITA and RA, 2–3 cm after the Y anastomosis, both during sinus rhythm and atrial pacing.

2.4. Quantitative biplane angiographic assessment

The segments of LITA and RA investigated by the Doppler guide wire were analyzed and the vessel diameter was measured at end diastole by biplane quantitative coronary arteriography in two orthogonal views, usually but not exclusively 30° right anterior oblique and 60° left anterior oblique projection, using an 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 the vessel as elliptical.

2.5. Flow velocity data analysis

Frequency analysis of the Doppler signal was carried out in real time by fast Fourier transformation with the use of a velocimeter (FlowMap, Cardiometrics, Inc.). Systolic peak velocity, diastolic peak velocity and the time-average peak velocity were determined from phasic coronary blood flow recordings. Quantitative estimation of the flow volume in the LITA main stem, distal LITA and RA were computed considering the cross-sectional area and the time-average peak velocity, according to Doucette et al. [6]. The FR was defined as the ratio of the estimates of blood flow during maximal hyperemia ($Q_{\text{max}}$) to the estimates of baseline flow ($Q_{\text{basal}}$), both at rest and during atrial pacing.

2.6. Statistical analysis

All statistical analyses were performed using the SPSS® 11.0 software (SPSS Inc., Chicago, IL, USA). Continuous data are presented as mean ± standard deviation. Normal distribution was tested using both the Kolmogorov–Smirnov statistics with a Lilliefors’s significance level and the Shapiro–Wilk statistics. Paired Student’s t test was used after evidence of normality. A probability value less than 0.05 was considered statistically significant.

3. Results

3.1. Clinical results

All the 27 patients underwent elective operation using a pedicled composite Y-graft without concomitant procedures. All the operations were performed with normothermic extracorporeal circulation. Mean cardiopulmonary bypass time and aortic cross-clamp time were 92 ± 21 and 69 ± 23 min, respectively. The anastomosis between LITA and RA was always performed after coronary anastomoses and during the ischemic time. The mean number of distal anastomoses was 3.59 ± 0.69 (range 2–5) (Table 2). Mean intensive care unit stay was 29 ± 13 h. There were neither deaths nor perioperative myocardial infarctions and none of the patients had major postoperative complications. 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 from the operation. The average hemoglobin level at the time of the study was 9.49 ± 1.22 g/dl. Patency rate was 100% both for LITA and RA coronary anastomoses. During atrial pacing, the HR–systolic blood pressure product increased significantly (9897 ± 1558 vs. 15,128 ± 2145, $P < 0.000$). None of the patients developed ischemic S-T segment modifications or complained of chest pain during the procedure.

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

3.2. Flow measurement results

During atrial pacing, $Q_{\text{basal}}$ increased significantly in each of the three main segments of the composite Y-grafts (LITA main stem, distal LITA and RA) while $Q_{\text{max}}$ slightly changed from the values calculated during sinus rhythm (Table 3). As a consequence, atrial pacing caused a significant reduction of the FR, a value calculated as the ratio between $Q_{\text{max}}$ and $Q_{\text{basal}}$.

4. Discussion

The concept of anastomosing another bypass graft to an attached LITA was introduced by Mills [7] to avoid placing vein grafts into a severely atherosclerotic ascending aorta. A few years later, Tector et al. [8] reported the first series of

<table>
<thead>
<tr>
<th>Graft type</th>
<th>Target coronary artery</th>
<th>No. of patients</th>
<th>No. of coronary anastomoses</th>
</tr>
</thead>
<tbody>
<tr>
<td>LITA</td>
<td>LAD</td>
<td>17</td>
<td>17</td>
</tr>
<tr>
<td></td>
<td>d-LAD</td>
<td>10</td>
<td>20</td>
</tr>
<tr>
<td>RA</td>
<td>OM</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>OM1–OM2</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>OM–PD</td>
<td>16</td>
<td>32</td>
</tr>
<tr>
<td></td>
<td>OM1–OM2–PD</td>
<td>6</td>
<td>18</td>
</tr>
<tr>
<td></td>
<td>d-OM1–OM2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td></td>
<td>97</td>
</tr>
</tbody>
</table>

LITA, left internal thoracic artery; RA, radial artery; LAD, left anterior descending (coronary artery); D, diagonal (branch); OM, obtuse marginal (branch); PD, posterior descending (coronary artery).
patients who received both the 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 [9].

The supporters of this technique maintain that composite Y-grafts may be used to achieve total arterial and pedicled arterial revascularization in patients with multivessels disease with no increase in complications, while sceptics are concerned about the possible inefficiency of Y-graft to fully respond to the coronary system flow demand, particularly at short term after the operation.

Some authors have already measured blood flow in composite Y-grafts, with different techniques and in different conditions. In 1999, Royse et al. [9] valued the intraoperative LITA flow measuring both the free-flow and the blood flow by transit-time Doppler technique, showing that the LITA can provide a 2.3-fold FR to the coronary bed. In the same year, Wendler et al. [1], using a Doppler guide wire, showed that after 1 week from the operation, the FR in the LITA main stem is sufficient at rest for multiple coronary anastomoses and that it significantly increases, always at rest, after 6 months. More recently, Sakaguchi et al. [2], using positron emission tomography, found that after 2 weeks from the operation, LITA used as a composite Y-graft improves myocardial blood flow at rest but that it is unable to fully respond to the flow demand of the whole left coronary system early after the operation.

To the best of our knowledge, this is the first study that analyzes the performance of Y-grafts in the presence of increased MVO₂ soon after the operation. In our study, blood flow was measured by quantitative angiography combined with intravascular flow velocity measurements using a Doppler guide wire, as reported by Doucette et al. [6]. Our results show that after a few days from the operation in presence of an increased MVO₂ arterial Y-grafts can provide adequate blood flow to the coronary system. In the perioperative period, clinical conditions suggesting inadequate perfusion for single LITA grafts have been reported [10,11] and are attributed to a disproportionate relation between flow and myocardial demand. In our experience, during atrial pacing at the 85% of the maximum predicted HR, causing a significant increase of MVO₂, Qbasal increased significantly in each of the three main parts of Y-grafts (LITA main stem, distal LITA and RA) (Table 3). None of the patients developed ischemic S-T segment modification or complained of chest pain, showing that the increase of blood flow in composite arterial Y-grafts can keep a normal O₂ supply-to-demand ratio.

The FR depends on several factors [12] and is reduced early after the operation because patients are slightly anemic and some degree of stunning is still present after bypass surgery [13]. In our experience, FR was significantly reduced but not exhausted in Y-grafts during the period of atrial pacing. Qmax was studied by selective injection of adenosine in the Y-graft at a dosage sufficient to induce maximal vasodilatation. The vasodilatation induced by adenosine increased Qbasal significantly both during sinus rhythm and atrial pacing but the value of Qmax was almost the same in both conditions. As a consequence, FR was significantly reduced but not completely exhausted during atrial pacing, Qbasal being increased by the increased cardiac work (Table 3).

4.1. Limitation of the study

There are several possible methodologic limitations in the present study. (1) 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, minimized but not excluded by analyzing only curves of good quality. In our experience, many data were cast off as inappropriate excluding 13 patients from the study. (2) Inaccuracies in determination of the vessel cross-sectional area may contribute to the variability of the flow calculations. 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 the vessel as elliptical. Although these measurements should be more appropriate than considering the vessel having a circular cross-section [2], inaccuracies in our estimation of the cross-sectional area may have occurred, limiting the reliability of clinical measurements. (3) The elevation in HR was brief in duration (3 min). More sustained alterations could produce different effects on the FR. (4) Cardio-active medications were continued as clinically indicated throughout
the study. These drugs could affect the reliability of flow measurements. However, all the patients who received a RA had diltiazem prescribed to minimize the risk of arterial spasm and this drug has been shown not to invalidate the measurements of coronary flow [14]. (5) This study is limited by the relatively small number of patients, due both to the complexity of the protocol, that make its acceptance very low by the patient, and to the high cost of the whole procedure.

In conclusion, soon after the operation, LITA used as a Y-graft with RA can efficiently adapt to an increase in flow demand, keeping normal the O₂ supply-to-demand ratio. From a functional point of view, our study shows an excellent hemodynamic performance in the perioperative period of LITA and RA as composite arterial grafts. Clinically the use of these grafts can be recommended even for myocardial revascularization supplying a large territory, without unfavorable consequences.

References


Appendix A. Conference discussion

Dr P. Sergeant (Leuven, Belgium): On this very last line, would you then suggest that your favor would be that the second arterial graft would be the free RIMA and not the radial artery?

Dr Lemma: No, we didn’t try to evaluate the difference between the RIMA and the radial artery. This is one of our objects in an ongoing study.

Dr F. Mohr (Leipzig, Germany): Did you take the native coronary artery stenosis into account, especially at the site of the radial artery?

Dr Lemma: No, we didn’t. Usually we use the radial artery when the amount of the stenosis on the coronary artery is greater than 50%.

Dr Mohr: 50%?

Dr Lemma: 50.

Dr Mohr: This is not a high grade stenosis.

Dr Lemma: I know.

Dr Mohr: You didn’t see any problems there?

Dr Lemma: So far, no.

Dr P. Sergeant: The number 50 hits me a little bit. If it is less than 50% would you then still graft the vessel?

Dr Lemma: No, we wouldn’t. We graft the vessel only if the stenosis is greater than 50%, and we use the radial artery when the grade of the stenosis is greater of 50%.

Dr A. Moritz (Frankfurt, Germany): It is a bit puzzling because in the literature and I think in some of the papers you cited they describe very well kind of a steal phenomenon between the circumflex area and the LAD. Did you correlate the flow reserve also to the degree of the original coronary artery stenosis, because any additional flows through the native coronary system of course would add to the total flow.

And a second question, to a topic not addressed in the paper but maybe you have an experience, do you supply patients with a Y graft to left and the right system? Do you think by your flow measurements or do you have any experience that this might be a problem, because the two systems have very different resistance and flow patterns?

Dr Lemma: About the first question, we didn’t correlate the flow to the severity of the coronary stenosis but only to the number of distal anastomoses of each of the two branches of the Y-graft.

About the second question, all the distal anastomoses we made using the radial artery were on the left coronary artery system.

Dr Moritz: Have you any experience with other ones?

Dr Lemma: No we haven’t.

Dr G. D’Ancona (Quebec City, Canada): You put the catheter inside the artery, is that right?

Dr Lemma: Yes it is.

Dr D’Ancona: Why didn’t you use less invasive methods like intraoperative transit time flow measurement? It is even more accurate than Doppler. Doppler is not so precise in the measurement.

Dr Lemma: We studied our patients before discharge so it is not possible using transit time flow measurements. Anyhow, intravascular flow velocity measurements are very precise if you can have tracks of good quality.

Dr D’Ancona: Also, you didn’t exclude the native flow from the coronary, did you? I mean, there can be some stealing phenomena from the native coronary. You didn’t put snares proximally in, did you?

Dr Lemma: No we didn’t. As I told you before, our patients were studied about one week postoperatively.