# Serial Evaluation of Flow in Single or Arterial Y-Grafts to the Left Coronary Artery

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*Background.* It is unclear whether composite Y-grafts can withstand the flow demand of the coronary system at rest and under stress. This study compared the graft flow and flow reserve of the left internal mammary artery (LIMA) intraoperatively and over a 2-year follow-up in single or composite Y-graft configurations using the radial artery (RA).

*Methods.* One hundred patients who underwent offpump myocardial revascularization with a composite Ygraft (group 2) were compared with a homogeneous group of 100 patients treated with a single independent LIMA graft on the left anterior descending artery (LAD) (group 1). Intraoperative baseline flow and flow after adenosine infusion into the left ventricle were analyzed. Over a 2-year follow-up, noninvasive longitudinal evaluation of flow was carried out at rest and during maximal hyperemic response by transthoracic Doppler ultrasonography. Final functional evaluation was obtained through a 2-day stress/rest 99mTcsestamibi myocardial perfusion single-photon emission computed tomographic scan.

The radial artery (RA) has emerged in recent years as the main secondary arterial conduit option for myocardial revascularization procedures. Among different configurations of the RA, the Y-graft with the left internal mammary artery (LIMA) has gained wide popularity because it allows sufficient length and maximal arterial graft economy while avoiding unnecessary aortic manipulation [1–7]. Nevertheless concerns have arisen concerning its appropriateness in meeting adequate blood supply when challenged by maximal requirements.

This prospective study sought to investigate the functional and hemodynamic results in off-pump myocardial revascularization of the LIMA conduit in composite Ygraft configurations with the RA compared with independent single LIMA grafts.

Conduit flow and coronary flow reserve were investigated intraoperatively and over 2-year follow-up by noninvasive methods. Two-day stress/rest 99mTc-sestamibi myocardial perfusion single-photon emission computed *Results.* The proximal LIMA in a Y-graft configuration showed adaptability to flow dynamics. It had a greater average peak velocity (p = 0.02), flow volume (p < 0.01), and diameter (p < 0.01) than independent single LIMA grafts. Distal flow at rest and during adenosine recruitment was similar between groups both intraoperatively and at all time points of the follow-up. No steal phenomenon occurred at rest, nor was it induced by adenosine in the Y-graft group. Exercise nuclear scintigraphy showed satisfactory exercise tolerance and no inducible significant perfusion defects in both groups.

*Conclusions.* Left internal mammary artery Y-grafting with the RA is adequate for flow requirements of distal branches at rest and during maximal hyperemia and is able to adapt its dimension to flow demand. Optimal results for RA anastomoses are possible only in arteries with critical stenosis and of good size and quality.

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tomography (SPECT) was later used for functional assessment.

# Material and Methods

# Study Design and Patient Population

From May 2004 to June 2008, 200 patients underwent primary off-pump myocardial coronary artery revascularization. One hundred consecutive patients who received at least an independent LIMA graft on the left anterior descending (LAD) artery (group 1) were compared with 100 consecutive patients who had indications for LIMA/RA conduits as composite Y-grafts (group 2). Exclusion criteria were age greater than 80 years, allergy to contrast media, chronic atrial fibrillation, low ventricular function (ejection fraction < 30%), additional cardiac or surgical procedures, severe systemic comorbidities (dialysis, hepatic failure), impediments to the exercise test (neurologic or osteoarticular), contraindications to receiving adenosine (heart block or reactive respiratory disease), and contraindications for off-pump procedures. Anatomic selection criteria for off-pump operations were vessel size (< 1.2 mm) and freedom from diffuse coronary calcifications. Clinical selection criteria included the ab-

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| Table 1. Main Demographic and Clinical Characteristics |  |                      |         |  |  |  |
|--|--|----------------------|---------|--|--|--|
| Characteristics  |  | Group 2<br>(n = 100) | p Value |  |  |  |

| Age   | $67 \pm 15$                      | $66 \pm 12$                      | 0.6 |
|---|----------------------------------|----------------------------------|-----|
| 0   |                                  |                                  |     |
| Sex (male)  | 71                               | 77                               | 0.4 |
| Body mass index (kg/m <sup>2</sup> )                            | $\textbf{28.8} \pm \textbf{5.3}$ | $\textbf{27.2} \pm \textbf{5.8}$ | 0.4 |
| Diabetes  | 24                               | 22                               | 0.8 |
| Hypertension  | 39                               | 41                               | 0.8 |
| Dyslipidemia  | 44                               | 47                               | 0.7 |
| High-density lipoprotein<br>(mg/dL)                             | $79\pm15$                        | $72\pm17$                        | 0.3 |
| Creatinine (mg/dL)  | $0.8\pm0.7$                      | $\textbf{0.8} \pm \textbf{0.5}$  | 1   |
| Left main stem disease  | 13                               | 15                               | 0.8 |
| Left ventricular hypertrophy<br>(ILVM > 125 mg/m <sup>2</sup> ) | 24                               | 21                               | 0.7 |
| Preoperative LVEF < 40%   | 25                               | 22                               | 0.7 |
| Left anterior descending<br>CTFC                                | $26.5\pm8.8$                     | 29.2 ± 7.3                       | 0.2 |
| Peripheral vascular disease                                     | 7                                | 5                                | 0.7 |

Group 1 = independent LIMA graft; group 2 = composite Y-graft. Values are mean  $\pm$  SD or numbers.

CTFC = corrected thrombolysis in myocardial infarction (TIMI) frame count; ILVM = indexed left ventricular mass; LVEF = left ventricular ejection fraction.

sence of mechanical and electrical instability in the operating theater. Surgical indications were assessed as a greater than or equal to 70% diameter stenosis. Coronary stenoses were evaluated by the Quantitative Coronary Angiography Data System (Centricity Carddas Xi2, GE Healthcare, Burlington, VT). The number of coronary lesions was defined as the total number of stenoses greater than or equal to 70%. Coronary blood flow was assessed by means of the thrombolysis in myocardial infarction (TIMI) frame-counting method with a frame counter on the cineviewer. Corrected TIMI frame count was derived for a longer left LAD [8]. The 2 groups of patients were homogeneous with minimal demographic and clinical differences (Table 1).

The study was approved by the institutional research ethics committee, and all patients provided written consent.

### Surgical Procedure

The LIMA was harvested as a skeletonized graft. Before cutting the distal part of the LIMA, heparin was given at a dose of 300 IU/kg to achieve a target activated clotting time longer than 400 seconds. Diluted papaverine (100 mg/100 mL Ringer's solution) was sprayed on the artery and it was then wrapped in papaverine-soaked gauze.

The RA was harvested from the nondominant arm by means of an Ultracision Harmonic scalpel (Ethicon Endo-Surgery, Cincinnati, OH), distended to a moderate supraphysiologic pressure (about 180 to 200 mm Hg) with diluted papaverine (100 mg/100 mL Ringer's solution), and placed in a warm diluted diltiazem solution (25 mg/20 mL Ringer's solution). All patients in both groups underwent off-pump myocardial revascularization and

the LIMA was always grafted onto the LAD. In group 2 the RA was anastomosed to the left coronary artery. The RA in the composite Y-graft configuration with the LIMA was used in addition to an independent right internal mammary artery (RIMA) or as an alternative to the RIMA when there were contraindications to bilateral internal mammary artery use. Proximal critical stenosis (greater than or equal to 85% to 90%) and size of at least 1.5 mm and freedom from calcification or extensive atherosclerotic disease (or both) of the target vessel at preoperative cineangiography were mandatory indications for RA anastomosis [9, 10]. Diltiazem (0.5 to 1.0 mg/kg) was infused intraoperatively and during the first 24 hours after operation and was thereafter prescribed orally (100 to 200 mg/day) for at least 3 months. Ticlopidine was started 48 hours after operation at a dose of 250 mg/day in both groups.

### Intraoperative Flow Measurement

A transit-time flow meter (HT 323-CS; Transonic Systems Inc, Ithaca, NY) was used for graft flow measurements as previously described [11]. Each limb of the Y-graft was evaluated after the Y-anastomosis was completed. The final transit-time flow meter measurement was obtained in both groups after all distal anastomoses were completed. All data were interpreted as suggested by D'Ancona and colleagues [12]. The graft flow reserve (GFR) was evaluated after hyperemic maximal flow induced with adenosine infused into the left ventricle through a needle at a concentration of  $24 \,\mu g \cdot kg^{-1} \cdot min^{-1}$ . All baseline measurements were obtained under stable

Table 2. Early Postoperative Outcome

|  | Group 1<br>(n = 100)              | Group 2<br>(n = 100)            | p Value |
|--|-----------------------------------|---------------------------------|---------|
| Hospital death                               |                                   | 1                               | 1       |
| Number of<br>anastomoses/patient             | $\textbf{2.9} \pm \textbf{1.5}$   | $\textbf{2.8} \pm \textbf{1.7}$ | 0.6     |
| Completeness index                           | 0.99                              | 0.95                            | 1       |
| Ventilation time (hours)                     | $5.3\pm4.1$                       | $5.6\pm4.5$                     | 0.6     |
| Intensive care unit stay<br>(days)           | 2.3 ± 2.1                         | $\textbf{2.7} \pm \textbf{2.4}$ | 0.2     |
| Hospital stay (days)                         | $\textbf{7.4} \pm \textbf{2.3}$   | $7.5\pm2.5$                     | 0.7     |
| Chest tube drainage in 24 hours (mL)         | $370\pm160$                       | $350\pm130$                     | 0.3     |
| Revision for bleeding                        | 2                                 | 2                               | 1       |
| Perioperative acute<br>myocardial infarction | 2                                 | 4                               | 0.6     |
| Troponin I > 0.5 ng/mL                       | 42                                | 46                              | 0.6     |
| Mean troponin I peak<br>values (ng/mL)       | $\textbf{0.49} \pm \textbf{0.25}$ | $0.52\pm0.31$                   | 0.4     |
| Low-output syndrome                          | 1                                 | 2                               | 1       |
| Transient renal failure                      |                                   | 2                               | 0.4     |
| Inotropic support                            | 31                                | 37                              | 0.4     |
| Sternal wound infection                      | 0                                 | 0                               |         |

Group 1 = independent LIMA graft; group 2 = composite Y-graft. Values are mean  $\pm$  SD or numbers. LIMA = left internal mammary artery.

|                    | Group 1 (n = 100)               | Gr             |              |                                 |                      |
|--------------------|---------------------------------|----------------|--------------|---------------------------------|----------------------|
|                    | LIMA                            | LIMA main stem | LIMA distal  | RA                              | p Value <sup>a</sup> |
| Free flow (mL/min) |                                 |                |              |                                 |                      |
| After papaverine   | $63 \pm 31$                     | $149\pm38$     | $60\pm28$    | $75\pm28$                       | 0.5                  |
| After anastomosis  |                                 |                |              |                                 |                      |
| Maximum flow       | $55\pm15$                       | $123 \pm 25$   | $57\pm16$    | $65\pm18$                       | 0.3                  |
| Mean flow          | $30\pm13$                       | $60\pm16$      | $29\pm16$    | $33\pm14$                       | 0.6                  |
| Minimum flow       | $2.3\pm0.8$                     | $5.8\pm1.5$    | $2.1\pm0.7$  | $\textbf{3.1} \pm \textbf{0.9}$ | 0.06                 |
| Pulsatility index  | $1.85\pm0.7$                    |                | $1.89\pm0.8$ | $1.82\pm0.7$                    | 0.7                  |
| After adenosine    |                                 |                |              |                                 |                      |
| Mean flow          | $60 \pm 15$                     | $130\pm23$     | $59\pm15$    | $69\pm18$                       | 0.6                  |
| Pulsatility index  | $\textbf{2.1} \pm \textbf{1.1}$ |                | $2.3\pm1.2$  | $\textbf{2.4} \pm \textbf{1.5}$ | 0.2                  |
| Graft flow reserve | $2.3 \pm 1.0$                   | <b>2.1</b> ± 1 | $2.2\pm0.9$  | $2.1 \pm 1.1$                   | 0.4                  |

 Table 3. Transient Time Flow Results in Group 1 Versus Group 2

 $^{\mathrm{a}}$  p value for the comparison of distal independent LIMA and distal LIMA in composite Y-graft.

Group 1 = independent LIMA graft; group 2 = composite Y-graft; values are mean  $\pm$  SD

LIMA = left internal mammary artery; RA = radial artery.

conditions with a mean arterial pressure of 80 mm Hg (mean 79  $\pm$  13) and a heart rate between 70 and 87 beats/minute (mean 79  $\pm$  14).

#### Transthoracic Doppler Ultrasonography and Graft Flow Reserve Evaluation

Noninvasive graft flow evaluation was scheduled at 7 days after operation and every 9 months thereafter. The LIMA was imaged by a small multihertz transducer connected to an ultrasonography system (GE Vivid 7; GE Healthcare). The proximal LIMA was detected in both groups by placing the transducer on the left supraclavicular area. The distal LIMA was identified through the parasternal window. The LIMA flow velocities were assessed by pulsed Doppler ultrasonography under a color-coding guide. Systolic and diastolic peak and mean velocities were measured and diastolic-systolic peak velocity ratio, diastolic velocity time integral, fraction diastolic velocity time integral divided by the diastolic plus the systolic velocity time integral, and time-average peak velocity were derived. The diameter of the LIMA was calculated from the B-mode recording. Quantitative estimation of the flow volume in the proximal and distal LIMA of both groups was computed as proposed by Doucette and coworkers [13]. Because of the unsatisfactory ultrasonographic visualization of the RA, its flow was deduced from the proximal and distal LIMA flow in the Y-graft configuration. Graft flow evaluations were assessed at baseline and after maximal hyperemic response as reported previously [11]. Four patients in group 2 and 1 patient in group 1 had contraindications to adenosine (heart block) and were considered ineligible for GFR evaluation.

### Exercise Nuclear Scintigraphy

Patients were scheduled for nuclear stress scintigraphy 24 months after operation. The bicycle exercise test was conducted starting from a workload of 25 W and increased by

25 W at 2-minute intervals. A 12-lead electrocardiogram was recorded continuously. The test was considered positive when horizontal or downsloping ST depression of at least 0.1 mV was recorded by 2 adjacent leads 80 milliseconds after the J-point, accompanied by chest pain or not. The reference workload for healthy individuals was 2.5 W/kg in women and 3.0 W/kg in men between 21 and 30 years, minus 10% for each decade. The achieved maximum workload was registered as percentage of age, sex, and weight-predicted maximum exercise capacity. At peak exercise, 14 mCi (500 MBq) of Tc99m-sestamibi was administered. Exercise was maintained for 1 more minute, and SPECT imaging was performed. After 24 hours, 14 mCi (500 MBq) of Tc99m-sestamibi was injected again, and images at rest were obtained. The scintigram was considered positive if reversible filling defects were visible between the stress and resting images. Two experienced readers, unaware of the other study data, evaluated all SPECT images by reaching a consensus.

### Perioperative Data

Echocardiographic evaluation was performed preoperatively, 24 hours and 48 hours after surgery, and at discharge. Left ventricular ejection fraction, wall motion score index, and indexed left ventricular mass were calculated. An indexed left ventricular mass of greater than 125 g/m<sup>2</sup> was considered a marker of left ventricular hypertrophy.

Postoperative acute myocardial infarction was diagnosed when the 3 criteria indicated by the Joint European Society of Cardiology/American College of Cardiology guidelines were fulfilled [14].

### Statistical Analysis

Continuous variables were expressed as means  $\pm$  standard deviation and categorical data were expressed as percentages. The paired-sample *t* test was used to evaluate differences in continuous variables between groups

|                                |         | 7 Days                            | 3 Months                          | 12 Months                         | 21 Months                         | Between Groups | Within Groups | Interaction |
|--------------------------------|---------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|----------------|---------------|-------------|
| Proximal LIMA<br>diameter (mm) | Group 1 | 2.1 ± 0.3                         | 2.2 ± 0.3                         | 2.2 ± 0.6                         | 2.3 ± 0.7                         | 0.008          | 0.05          | 0.01        |
|                                | Group 2 | $\textbf{2.3} \pm \textbf{0.3}$   | $2.5\pm0.6$                       | $\textbf{2.8} \pm \textbf{0.6}$   | $\textbf{3.2}\pm\textbf{0.8}$     |                | 0.01          |             |
| Baseline                       |         |                                   |                                   |                                   |                                   |                |               |             |
| APV (m/sec)                    | Group 1 | $\textbf{0.24} \pm \textbf{0.12}$ | $\textbf{0.22} \pm \textbf{0.11}$ | $\textbf{0.25} \pm \textbf{0.14}$ | $\textbf{0.24} \pm \textbf{0.11}$ | 0.02           | 0.08          | 0.04        |
|                                | Group 2 | $\textbf{0.36} \pm \textbf{0.16}$ | $0.30\pm0.15$                     | $\textbf{0.27} \pm \textbf{0.11}$ | $\textbf{0.22} \pm \textbf{0.09}$ |                | 0.03          |             |
| Flow (mL/min)                  | Group 1 | $40 \pm 15$                       | $41\pm16$                         | $47\pm13$                         | $49\pm15$                         | 0.001          | 0.01          | 0.001       |
|                                | Group 2 | $67\pm21$                         | $76\pm24$                         | $79\pm23$                         | $82\pm28$                         |                | 0.001         |             |
| DSPV                           | Group 1 | $\textbf{0.34} \pm \textbf{0.1}$  | $0.31\pm0.07$                     | $0.33\pm0.06$                     | $0.34 \pm 0.07$                   | 0.07           | 0.1           | 0.08        |
|                                | Group 2 | $\textbf{0.38} \pm \textbf{0.08}$ | $0.33 \pm 0.09$                   | $0.36\pm0.05$                     | $0.36\pm0.06$                     |                | 0.08          |             |
| DVTI/DVTI+SVI                  | Group 1 | $0.42\pm0.07$                     | $0.41 \pm 0.1$                    | $0.42\pm0.06$                     | $0.42\pm0.08$                     | 0.08           | 0.07          | 0.05        |
|                                | Group 2 | $0.41 \pm 0.09$                   | $\textbf{0.40} \pm \textbf{0.11}$ | $\textbf{0.40} \pm \textbf{0.11}$ | $0.38\pm0.09$                     |                | 0.03          |             |
| Adenosine                      |         |                                   |                                   |                                   |                                   |                |               |             |
| APV (m/sec)                    | Group 1 | $0.51 \pm 0.19$                   | $0.48 \pm 0.17$                   | $0.54 \pm 0.21$                   | $0.53 \pm 0.22$                   | 0.08           | 0.06          | 0.06        |
|                                | Group 2 | $\textbf{0.68} \pm \textbf{0.26}$ | $0.64 \pm 0.22$                   | $0.58\pm0.19$                     | $0.45\pm0.16$                     |                | 0.03          |             |
| Flow (mL/min)                  | Group 1 | $84\pm21$                         | $87\pm19$                         | $100\pm22$                        | $108\pm21$                        | 0.001          | 0.003         | 0.001       |
|                                | Group 2 | $139\pm35$                        | $159\pm36$                        | $173\pm33$                        | $180\pm36$                        |                | 0.001         |             |
| DSPV                           | Group 1 | $\textbf{0.81} \pm \textbf{0.4}$  | $0.84 \pm 0.3$                    | $\textbf{0.89} \pm \textbf{0.3}$  | $0.9\pm0.4$                       | 0.04           | 0.02          | 0.05        |
|                                | Group 2 | $0.94 \pm 0.2$                    | $0.92\pm0.3$                      | $0.93 \pm 0.4$                    | $0.95\pm0.4$                      |                | 0.07          |             |
| DVTI/DVTI +<br>SVI             | Group 1 | $0.46\pm0.11$                     | $0.46\pm0.15$                     | $\textbf{0.48} \pm \textbf{0.17}$ | $0.46\pm0.13$                     | 0.08           | 0.07          | 0.07        |
|                                | Group 2 | $0.51\pm0.09$                     | $0.50\pm0.15$                     | $0.47\pm0.11$                     | $0.44\pm0.12$                     |                | 0.01          |             |
| GFR <sup>a</sup>               | Group 1 | $\textbf{2.1} \pm \textbf{0.1}$   | <b>2.19</b> ± 0.11                | $\textbf{2.18} \pm \textbf{0.3}$  | $\textbf{2.22}\pm\textbf{0.3}$    | 0.08           | 0.07          | 0.06        |
|                                | Group 2 | $\textbf{2.08} \pm \textbf{0.13}$ | $\textbf{2.11} \pm \textbf{0.15}$ | $\textbf{2.18} \pm \textbf{0.21}$ | $\textbf{2.21} \pm \textbf{0.2}$  |                | 0.06          |             |

Table 4. Proximal LIMA: Flow Measurement at Baseline and After Adenosine Infusion

<sup>a</sup> Ratio of hyperemic to baseline flow

Group 1 = independent LIMA graft; group 2 = composite Y-graft.

APV = average peak velocity; DSPV = diastolic-systolic peak velocity ratio; DVTI/DVTI + SVI = diastolic fraction of velocity-time integral; GFR = graft flow reserve; LIMA = left internal mammary artery.

for normally distributed values. The Mann-Whitney *U* test was used for variables not normally distributed (transit-time flow meter and GFR values) and categorical variables were analyzed with the  $\chi^2$  test or Fisher's exact test when appropriate. Analysis of factors influencing graft flow and GFR values was performed calculating hazard ratio (HR) with 95% confidential intervals (CIs). Multivariate analysis of variance with correction for serial measurements was performed for Doppler ultrasonography and flow data. All variables with *p* values less than 0.05 were considered significant and were analyzed in a multivariate logistic regression model to assess the impact of each on the results. Statistical analysis was performed with SPSS, version 13.0 for Windows (SPSS Inc, Chicago, IL).

# Results

One patient from group 2 died in the early postoperative period from low-output syndrome. Successful implantation of intraaortic balloon assistance was performed in 1 patient in group 1 and in 2 patients in group 2. Troponin I leakage in the upper limit of normal was similar in both groups. No sternal wound infections were registered (Table 2).

### Intraoperative Flow Evaluations

Intraoperative flow evaluations at baseline and during maximal stimulation are reported in Table 3.

On the basis of a univariate model for all patients from both groups, significant predictors of GFR less than 2.0 included age greater than 65 years, female sex, presence of diabetes, preoperative history of peripheral vascular disease, corrected TIMI frame count greater than 30, indexed left ventricular mass greater than 150 g/m<sup>2</sup>, and composite Y-graft. Multivariate analysis confirmed only preoperative history of peripheral vascular disease (odds ratio, 2.5; 95% CI, 1.5 to 5.4; p < 0.001), corrected TIMI frame count greater than 30 (HR 4.6; 95% CI, 3.3 to 6.8; p < 0.001), indexed left ventricular mass greater than 150 g/m<sup>2</sup> (HR 4.1; 95% CI, 2.8 to 8.1; p < 0.001), and composite Y-graft (HR, 3.8; 95% CI, 2.1 to 7.5; p < 0.001) as independent predictors of GFR less than 2.0.

#### Transthoracic Doppler Ultrasonography and Graft Flow Reserve Evaluation

Two patients had no adequate postoperative transthoracic window. One patient in group 2, who had a myocardial infarction 13 months after operation for occlusion of both the LIMA and RA, and 1 patient in group 1, who

#### Table 5. Distal LIMA: Flow Measurement at Baseline and After Adenosine Infusion

|                           |                    | 7 Days                            | 3 Months                         | 12 Months                         | 21 Months                         | Between<br>Groups | Within<br>Groups | Interaction |
|---------------------------|--------------------|-----------------------------------|----------------------------------|-----------------------------------|-----------------------------------|-------------------|------------------|-------------|
| Distal LIMA diameter (mm) | Group 1            | $2.0 \pm 0.2$                     | $2.1 \pm 0.3$                    | $2.1 \pm 0.5$                     | $2.1 \pm 0.5$                     | 0.2               | 0.08             | 0.1         |
| Distai LiwA diameter (mm) | Group 1<br>Group 2 | $2.0 \pm 0.2$<br>$1.9 \pm 0.3$    | $2.1 \pm 0.3$<br>$2.1 \pm 0.4$   | $2.1 \pm 0.3$<br>$2.1 \pm 0.4$    | $2.1 \pm 0.5$<br>$2.1 \pm 0.6$    | 0.2               | 0.08             | 0.1         |
| Baseline                  | Gloup 2            | 1.9 - 0.3                         | $2.1 \pm 0.4$                    | $2.1 \pm 0.4$                     | $2.1 \pm 0.0$                     |                   | 0.07             |             |
| APV (m/sec)               | Group 1            | $0.26 \pm 0.11$                   | $0.25 \pm 0.14$                  | $0.28\pm0.11$                     | $0.32 \pm 0.14$                   | 0.08              | 0.02             | 0.02        |
|                           | Group 2            | $0.23 \pm 0.13$                   | $0.24 \pm 0.12$                  | $0.26 \pm 0.13$                   | $0.30 \pm 0.18$                   |                   | 0.04             |             |
| Flow (mL/min)             | Group 1            | $40 \pm 18$                       | $41 \pm 19$                      | $46 \pm 18$                       | $48 \pm 19$                       | 0.09              | 0.01             | 0.01        |
|                           | Group 2            | $37\pm17$                         | $41\pm18$                        | $45\pm21$                         | $46 \pm 17$                       |                   | 0.03             |             |
| DSPV                      | Group 1            | $1.58\pm0.21$                     | $1.56\pm0.28$                    | $1.9\pm0.21$                      | $2.2\pm0.23$                      | 0.07              | 0.01             | 0.02        |
|                           | Group 2            | $1.56\pm0.19$                     | $1.65\pm0.25$                    | $1.89\pm0.23$                     | $\textbf{2.3} \pm \textbf{0.26}$  |                   | 0.02             |             |
| DVTI/DVTI + SVI           | Group 1            | $0.72\pm0.1$                      | $0.72\pm0.1$                     | $0.83\pm0.23$                     | $0.88\pm0.19$                     | 0.06              | 0.01             | 0.03        |
|                           | Group 2            | $0.69\pm0.2$                      | $0.71\pm0.12$                    | $0.83\pm0.25$                     | $0.88\pm0.15$                     |                   | 0.03             |             |
| Adenosine                 | -                  |                                   |                                  |                                   |                                   |                   |                  |             |
| APV (m/sec)               | Group 1            | $0.45\pm0.16$                     | $0.51\pm0.18$                    | $0.61\pm0.15$                     | $\textbf{0.64} \pm \textbf{0.19}$ | 0.07              | 0.02             | 0.03        |
|                           | Group 2            | $0.45\pm0.18$                     | $0.49 \pm 0.22$                  | $0.59\pm0.17$                     | $\textbf{0.61} \pm \textbf{0.18}$ |                   | 0.03             |             |
| Flow (mL/min)             | Group 1            | $81\pm21$                         | $85\pm22$                        | $103\pm27$                        | $108\pm31$                        | 0.1               | 0.003            | 0.05        |
|                           | Group 2            | $83\pm18$                         | $86\pm19$                        | $101\pm21$                        | $105\pm27$                        |                   | 0.01             |             |
| DSPV                      | Group 1            | $\textbf{2.2} \pm \textbf{0.27}$  | $\textbf{2.6} \pm \textbf{0.4}$  | $\textbf{3.0} \pm \textbf{0.54}$  | $\textbf{3.0} \pm \textbf{0.41}$  | 0.08              | 0.06             | 0.04        |
|                           | Group 2            | $\textbf{2.1} \pm \textbf{0.22}$  | $\textbf{2.7} \pm \textbf{0.31}$ | $\textbf{2.9} \pm \textbf{0.38}$  | $\textbf{2.9} \pm \textbf{0.29}$  |                   | 0.08             |             |
| DVTI/DVTI + SVI           | Group 1            | $\textbf{0.72} \pm \textbf{0.11}$ | $0.73 \pm 0.12$                  | $\textbf{0.81} \pm \textbf{0.17}$ | $\textbf{0.91} \pm \textbf{0.16}$ | 0.06              | 0.06             | 0.06        |
|                           | Group 2            | $\textbf{0.69} \pm \textbf{0.09}$ | $0.72\pm0.15$                    | $0.81 \pm 0.21$                   | $0.86 \pm 0.21$                   |                   | 0.07             |             |
| GFR <sup>a</sup>          | Group 1            | $2\pm0.1$                         | $\textbf{2.1} \pm \textbf{0.11}$ | $\textbf{2.2} \pm \textbf{0.32}$  | $\textbf{2.3} \pm \textbf{0.31}$  | 0.2               | 0.05             | 0.08        |
|                           | Group 2            | $\textbf{2.1} \pm \textbf{0.14}$  | $\textbf{2.1} \pm \textbf{0.18}$ | $\textbf{2.2} \pm \textbf{0.28}$  | $\textbf{2.2} \pm \textbf{0.26}$  |                   | 0.06             |             |

<sup>a</sup> Ratio of hyperemic to baseline flow.

Group 1 = independent LIMA graft; group II = composite Y-graft.

DSPV = diastolic-systolic peak velocity ratio; DVTI/DVTI + SVI = diastolic fraction of velocity-time integral;

had LIMA flow indexes suggestive of a new LAD pathologic condition later confirmed by angiography, were not evaluated further. Distal detection of the LIMA was successful in 192 (98%) patients. Two patients in group 2 had unreliable signals in the main LIMA stem because of underestimation of the true velocity. The heart rate and the systolic or diastolic blood pressure were similar in both groups at baseline and during hyperemic response. Maximal increase in coronary flow velocity was obtained within 60 seconds of drug infusion, and flow returned to baseline within 30 seconds of discontinuing the drug. No major adverse reactions occurred during or after adenosine infusion.

Compared with an independent LIMA graft, LIMA flow in a composite Y-graft was adequate at rest and during maximal hyperemia at all time points of follow-up (Tables 4 and 5).

#### Exercise Nuclear Scintigraphy Evaluation

Stress evaluation showed satisfactory exercise tolerance in both groups. Patients in group 1 achieved 79%  $\pm$  11% predicted exercise capacity versus 77%  $\pm$  15% in patients in group 2 (p = 0.2). The rate of patients achieving greater than 80% predicted exercise capacity was high in both groups: 87.6% (85/97) in group 1 versus 86.1% (80/93) in group 2 (odds ratio, 0.8; 95% CI, 0.3 to 2.1; p = 0.9). Five patients (3 from group 1 and 2 from group 2) had minimal

scintigraphic evidence of induced ischemia. Three of these patients had diseased diagonal or anterolateral branches that were not grafted at operation because of the poor quality or small diameter, or both. All other patients had no inducible significant perfusion defect.

#### Comment

This study provides evidence that the LIMA limb of a composite Y-graft has intraoperative free flow and completion diastolic, systolic, mean flow, and pulsatility index comparable to that of the independent LIMA graft both at rest and during maximal, adenosine-induced hyperemic response. The RA limb of the composite Y-graft shows excellent intraoperative flow without any evidence of steal phenomenon even during maximal flow demand. Hence the main stem of the Y-graft is able to provide an adequate blood supply to both limbs of the graft at baseline and during hyperemia. These results have also been confirmed at all time points of the follow-up.

Our data are in agreement with those of Royse and associates [15], who reported an intraoperative 2.3-fold reserve of composite mammary and RA grafts, and with those of Afflek and colleagues [3], who found a flow reserve of 1.6, computed as the ratio of free flow over completion flow, which was considered adequate for flow

requirements in the early postoperative period. Lemma and coworkers [4] reported that composite Y-grafts can efficiently adapt to increased flow demand induced by atrial pacing early after operation. Conversely, Sakaguchi and colleagues [16] found that composite Y-grafts were not as effective as independent LIMA grafts for improving flow reserve soon after operation. The major limitations of these studies, however, were the relatively small numbers of patients, the approximate methods used to induce the maximal flow, and the lack of an adequate control group and of a significant follow-up necessary to avoid any time-linked variability.

Our results provide evidence of an active increase of proximal LIMA diameter in Y-graft configuration. This process of adaptation, which begins soon after operation, enables the higher flow requirements of the Y-graft system [3, 5]. The mechanisms by which the LIMA graft is able to adapt its diameter are largely unclear; however the release of endothelial vasoactive mediators may be involved [17].

Conversely, the independent LIMA graft displays a specific pattern of phasic flow with a transition from systolicpredominant to diastolic-predominant peak flow velocity shifting from the subclavian to the coronary end. This pattern was not confirmed in the Y-graft, in which we detected a diastolic-predominant peak flow velocity in the subclavian end. This peculiar flow pattern is probably related to the reduced vascular resistance of the parallel vascular circuit represented by the Y-graft configuration. Conversely, an impaired diastolic-predominant peak flow velocity in the proximal LIMA may presumably be the expression of high resistance in the RA limb of the Y-graft configuration.

Interestingly, the results from multivariate logistic regression analysis of GFR less than 2.0 in the whole study population study revealed that low GFR was strictly linked to corrected TIMI frame count greater than 30, indexed left ventricular mass greater than 150 g/m<sup>2</sup>, preoperative history of peripheral vascular disease, and the use of composite Y-grafts. These patients showed more or less blunted diastolic peak flow velocity in the proximal LIMA when challenged by adenosine. Therefore the use of a LIMA/RA Y-graft should be avoided in patients with a history of peripheral vascular disease, poor coronary artery run-off, and left ventricular hypertrophy. In the present study, these findings are not followed by any superior midterm clinical benefits or by advantages in morbidity and cardiac function. However it should be considered that our population was strictly selected, had low surgical risk, and underwent uncomplicated surgical procedures.

The TIMI flow grading system is a widely used method of grading coronary flow [8]. It allowed us to precisely assess the objective evaluation of preoperative coronary flow for each target coronary vessel for the LIMA and RA.

The functional evaluation by means of 2-day stress/rest 99mTc-sestamibi myocardial perfusion SPECT, which is considered the gold standard for noninvasive detection of myocardial ischemia, showed that the Dopplerderived flow profile had a significant correlation with the results of nuclear exercise testing. Only a few patients, who had untreated diagonal or anterolateral branches, experienced ischemic S-T segment modification or a positive scintigram, or both.

Finally, we chose transthoracic Doppler ultrasonography as a totally noninvasive and easily repeatable method for postoperative evaluations, allowing us to perform morphologic and functional assessment of both the proximal and distal LIMA conduit [11,18–20]. The principal limitation of the study was the unsatisfactory direct assessment of the RA limb flow in the Y-graft, which was deduced with reasonable approximation from the proximal and distal LIMA flow.

In conclusion the LIMA main stem was adequate to meet the flow requirements of both distal branches either at rest or during maximal hyperemia and was able to adapt its dimension to flow demand. To avoid the effects of competitive flow, the RA graft should be anastomosed to the most severely diseased coronary targets (greater than or equal to 85% stenosis).

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