Total Arterial Myocardial Revascularization With Composite Grafts Improves Results of Coronary Surgery in Elderly: A Prospective Randomized Comparison With Conventional Coronary Artery Bypass Surgery

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Background—Total arterial myocardial revascularization with composite grafts proved to enhance the long-term benefits of coronary surgery. We assessed the hypothesis that full arterial revascularization (FAR) may improve clinical outcome even in elderly and at short term.

Methods and Results—A prospective randomized study was designed to compare FAR with conventional coronary artery bypass grafting (CABG) surgery [left interval thoracic artery (LITA) on left anterior descending (LAD) plus additional saphenous vein grafts] with the following end points: early and late death, graft occlusion, reintervention, angina recurrence, and acute myocardial infarction (AMI). We enrolled 200 consecutive patients >70 years of age; population was equally divided at random in Group 1 (G1, FAR) and Group 2 (G2, Conventional). The groups resulted comparable with respect to all preoperative continuous and discrete variables and risk factors (Euroscore: G1 = 8.1 versus G2 = 8.1). No differences between G1 versus G2 were observed in terms of postoperative complications (perioperative AMI: 2% versus 3%), mean intensive care unit (ICU) (hours: 39 ± 11 versus 40 ± 9) and hospital stay (days: 6 ± 2 versus 7 ± 3) nor were there any differences in hospital mortality (G1 = 5% versus G2 = 4%). At the mean follow-up of 14 ± 5 months the incidence of angina recurrence was 3% in G1 versus 12% in G2. Angiographic controls of grafts showed a superior graft patency rate of all the arterial grafts when compared with saphenous vein grafts. Conventional CABG surgery was identified as incremental risk factor for angina recurrence and as predictor for graft occlusion.

Conclusions—Total arterial myocardial revascularization improved clinical outcome of patients undergoing coronary surgery in the elderly, whereas saphenous vein grafts negatively affected patient prognosis in terms of graft patency and freedom from late cardiac events. (Circulation. 2003;108[suppl II]:II-29-II-33.)

Key Words: aging ■ arteries ■ coronary disease ■ revascularization ■ surgery

Progressive advances in surgical techniques and perioperative care led to an increasing number of patients >70 years of age undergoing coronary surgery during the past decade.1,2 Despite the proven benefits of internal thoracic arteries (ITAs) on long-term outcome,3-4 the saphenous vein graft has been widely accepted as the conduit of choice for myocardial revascularization in the elderly, as a consequence of the reduced life expectancy of the elderly population and to concerns about excessive surgical invasiveness in this subset of patients when arterial grafts were used.5 In addition, patients >70 years of age hold a higher risk for postoperative morbidity and mortality, which is related not only to the aging process “per se” but also to the presence of several associated comorbidities.6

Many authors demonstrated that total arterial revascularization improved the clinical outcome of patients undergoing coronary artery bypass surgery when compared with the conventional technique (LITA on LAD plus additional saphenous vein grafts).3,4,7,8 However, none of the previous studies analyzed in a prospective and randomized study the advantages of total arterial grafting in elderly patients. Therefore, in the present study we evaluated at short- and mid-term the safety and usefulness of total arterial revascularization with composite grafts in patients aging >70 years.

Methods

Patient Selection Criteria

Two hundred consecutive patients undergoing coronary surgery and >70 years of age were assigned at random to Group 1 (G1: 100 pts., receiving total arterial myocardial revascularization with composite grafts) or to Group 2 (G2: 100 pts., receiving conventional CABG surgery, ie, LITA on LAD plus additional saphenous vein grafts). We excluded from this study patients with left ventricular ejection fraction <25%, single vessels disease, emergency operations and high-risk patients with Euroscore >10. After undersigning informed consent...
Surgical Strategy
All of the patients underwent on-pump coronary artery bypass surgery through a standard sternotomy approach. Both of the ITAs were harvested as pedicled conduits; in patients undergoing Radial artery (RA) harvesting, we carried out a preoperative evaluation of the nondominant arm (Allen Test, oximetric plethysmography) in order to assess the adequacy of collateral flow from the ulnar artery. The RA was harvested preserving its satellite veins and surrounding connective tissue to minimize wall damage and risk of spasm. After systemic heparinization, both the ITAs and the RA were divided distally, and a solution of papaverine hydrochloride was applied topically (on the ITAs) or injected intraluminally (in the RA). When the RA was used as a free graft, it was maintained in situ until the related coronary anastomosis had to be performed in order to avoid arterial damage because of unnecessary storage.

Composite arterial grafts were realized always before cardiopulmonary bypass by an end-to-side anastomosis (with a 8/0 polypropylene running suture) of the right internal thoracic artery (RITA) and/or RA in a Y/T graft configuration to the fascial side of the in situ LITA.

We realized the composite arterial grafts according to three different configurations: type 1 configuration was used in case of a dominant, not occluded right coronary artery; in this geometry the RITA is anastomosed as a Y graft to the in situ LITA, and multiple sequential anastomoses are carried out in presence of multivessel disease; this configuration was used in presence of borderline stenosis of the obtuse marginal, occluded right coronary artery and in presence of low runoff of the target coronary vessels.

Type 3 configuration was mainly used when planned configuration type 1 or 2 could not be performed because of atheromatous lesions of the ascending aorta (switch from type 1 to type 3) or unfavourable anatomy of the posterolateral vessels (switch from type 2 to type 3): in this geometry 2 segments of RA or/plus RITA are anastomosed end-to-side to the LITA, in order to obtain a double Y graft.

Standard extracorporeal circulation was then instituted, under mild hypothermia with a mean arterial blood pressure >50 mmHg. Distal anastomoses were performed end-to-side or side-to-side (diamond-shaped for sequential anastomoses) with a 8/0 polypropylene running suture. We performed proximal anastomoses under aortic side clamping with a 6/0 (for saphenous vein grafts) or a 7/0 (for arterial conduits) polypropylene running suture, during rewarming. The proximal anastomosis of the RA (free graft) on the ascending aorta was performed in most cases on a saphenous vein patch sewn on the ascending aorta, whereas we avoided the use of the RITA as a free graft on the ascending aorta.

In patients receiving RA grafts, Diltiazem was administered i.v. at a mean dose of 0.5–1.5 μg/Kg/min, and it was continued for the first 48 hours after surgery. Thereafter we administered Diltiazem (≥120 mg/day) orally for at least 6 months.

Follow-Up
Patient follow-up consisted of periodical 3-months visits up to at least 12 months. Patient information was also collected from the cardiologist of the patient and home physicians, and by telephone interview. We considered as end-points of the study: early and late death, graft occlusion, reintervention, recurrence of angina (ie, chest pain of Canadian cardiovascular score (CCVS) class II or higher; clinical symptoms were then confirmed by means of exercise test and myocardial perfusion imaging with Thallium-201/Technetium-99m), and incidence of early and late myocardial infarction.

### TABLE 1. Preoperative Characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>G 1</th>
<th>G 2</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (female)</td>
<td>46%</td>
<td>44%</td>
<td>0.88</td>
</tr>
<tr>
<td>Age (*)</td>
<td>76.9±4.1</td>
<td>77±3.8</td>
<td>0.85</td>
</tr>
<tr>
<td>Diabetes</td>
<td>40%</td>
<td>38%</td>
<td>0.88</td>
</tr>
<tr>
<td>Hypertension</td>
<td>69%</td>
<td>67%</td>
<td>0.88</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>38%</td>
<td>36%</td>
<td>0.88</td>
</tr>
<tr>
<td>Obesity</td>
<td>15%</td>
<td>12%</td>
<td>0.67</td>
</tr>
<tr>
<td>COPD</td>
<td>30%</td>
<td>32%</td>
<td>0.87</td>
</tr>
<tr>
<td>Creatinine clearance &lt;50 ml min</td>
<td>19%</td>
<td>20%</td>
<td>1</td>
</tr>
<tr>
<td>Venous vascular disease</td>
<td>7%</td>
<td>7%</td>
<td>0.78</td>
</tr>
<tr>
<td>Unstable angina</td>
<td>32%</td>
<td>31%</td>
<td>0.88</td>
</tr>
<tr>
<td>Recent MI (&lt;90 days)</td>
<td>47%</td>
<td>44%</td>
<td>0.77</td>
</tr>
<tr>
<td>Infarates pre-op</td>
<td>6%</td>
<td>7%</td>
<td>1</td>
</tr>
<tr>
<td>Ejection fraction</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30–50%</td>
<td>35%</td>
<td>40%</td>
<td>0.55</td>
</tr>
<tr>
<td>&lt;30%</td>
<td>15%</td>
<td>12%</td>
<td>0.67</td>
</tr>
<tr>
<td>Redo surgery</td>
<td>6%</td>
<td>5%</td>
<td>1</td>
</tr>
<tr>
<td>Euroscore (*)</td>
<td>8.4±2.5</td>
<td>8.1±2.3</td>
<td>0.37</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>G 1: Total Arterial Revascularization—G 2: Conventional Revascularization</th>
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<tbody>
<tr>
<td></td>
<td>COPD: Chronic Obstructive Pulmonary Disease; MI: Myocardial Infarction. (*) value expressed as mean±SD.</td>
</tr>
</tbody>
</table>

Statistical Analysis
Comparisons of variables between the patient groups were assessed using the χ² test with Yates correction for discrete variables and the unpaired t test for continuous variables. Data for continuous variables are expressed as mean ± SD. A probability value <0.05 was considered statistically significant.

Multivariate logistic regression analysis was used to assess the independent predictors of graft occlusion. Finally, to identify the independent predictors of event-free survival, multivariate analysis was carried out with the Cox proportional hazard regression model using the variables significant at the P<0.1 level at univariate analysis.

The statistical analysis was calculated with the StatSoft (Version 5.1, ‘97 Edition, StatSoft Italia S.r.l.).

Results
Preoperative Data
Patient preoperative characteristics are shown in Table 1. The 2 groups resulted similar at univariate analysis for all of the continuous and discrete variables; in particular, no significant differences were observed in terms of operative high-risk profile, as assessed by the Euroscore system (mean: G1: 8.4±2.5 versus G2: 8.1±2.3, P=0.37).

Intraoperative Data and Early Outcome
No differences between the groups were observed with regards to aortic cross clamping time (G1: 33.8±10 minutes versus G2: 32.6±7.2 minutes), whereas the cardiopulmonary bypass time was greater in patients receiving conventional coronary surgery (G1: 58.2±16 minutes versus G2: 77.5±9.7 minutes, P<0.001), as a consequence of the additional time required to perform the proximal anastomoses of the venous grafts. We were able to achieve a similar completeness of revascularization in the 2 groups (mean number of anasto-
moses: G1: 2.44±0.8 versus G2: 2.46±0.6); the mean target vessel diameters were 1.5±0.3 mm and 1.6±0.2 mm in Group 1 and Group 2, respectively.

The 3 different configurations of composite arterial grafts were used in 5% of patients for type 1 configuration (this geometry was restricted to few cases without atheromalous disease of the ascending aorta) and in 60% and 35% of patients for type 2 and 3 geometries, respectively.

Additional intraoperative data are shown in Table 2. We did not observe any differences with regards to mechanical ventilation time (G1: 31±5 hours versus G2: 32±4 hours, \( P=0.12 \)) and ICU stay (G1: 39±11 hours versus G2: 40±9 hours, \( P=0.48 \)) nor with respect to the incidence of major postoperative complications, as shown in Figure 1.

There were no significant differences in terms of hospital mortality between the groups (G1: 5 pts. versus G2: 4 pts.), and also the causes of death were similar in the 2 groups: sepsis (G1: 2 pts. versus G2: 1 pt.), multiple organ failure (G1: 2 pts. versus G2: 2 pts.), and abdominal ischemia (G1: 1 pt. versus G2: 1 pt.). Cerebrovascular complications occurred more frequently in patients undergoing conventional coronary surgery, but this difference failed to reach a significant probability value (G1: 1 pt. versus G2: 5 pts., \( P=0.21 \)); all of the patients who developed cerebrovascular accidents had ascending aorta manipulation for proximal graft anastomosis.

Moreover, 9 patients of Group 2 developed a specific group-related complication (ie, leg wound complication) related to saphenous vein graft harvesting; most of these patients had diabetes (7/9 pts., 77.7%). Conversely, no arm wound complication was observed in relation to RA harvesting. Moreover, the incidence of sternal wound complications was identical in both groups (G1=1% versus G2=1%), despite the use of double mammary harvesting in 31% of pts. in Group 1.

### Mid-Term Results

We evaluated all of the the hospital survivors (G1: 95 pts. versus G2=96 pts.) at 2, 6, and 12 months postoperatively (mean follow-up, 15±4 months) by means of clinical examination and cycloergometric test. Angiograms were carried out at random and in patients with a positive or doubtful cycloergometric test. At follow-up, the incidence of cardiac-related events was higher in patients receiving conventional coronary surgery, as shown in Figure 2. Coronary angiography (mean follow-up period: 18±2 months) was performed on 91 pts. in Group 1 and 89 pts. in Group 2 (95.7% and
92.7% of hospital survivors, respectively). In Group 1 evaluation was carried out on 91 LITAs (all anastomosed on 91 LADs, plus 7 sequential anastomoses on diagonal branches), 55 RAs (anastomosed either termino-laterally or sequentially on 8 diagonal branches, 38 obtuse marginal branches, and on 26 right coronary arteries), and 21 RITAs (anastomosed either termino-laterally or sequentially on 8 diagonal branches, 24 obtuse marginal branches, and on 20 right coronary arteries); in Group 2 89 LITAs (anastomosed on 89 LADs and sequentially on 6 diagonal branches) and 116 saphenous vein grafts (anastomosed either termino-laterally or sequentially on 3 diagonal branches, 65 obtuse marginal branches, and 55 right coronary arteries). Angiograms revealed the following graft patency rates: in Group 1 grafts patency was 99% for LITA (1 occluded graft on LAD), 100% for RITA, and 96.7% for RA (2 occluded grafts on the circumflex system); in Group 2 grafts patency was 100% for LITAs and 84% for saphenous vein grafts (2 occluded grafts on diagonal branches, 10 on obtuse marginal branches, and 8 on right coronary arteries).

When we used the Kaplan-Meier analysis to evaluate the survival-free from recurrent angina or myocardial infarction, we observed a significantly improved outcome in patients undergoing total arterial myocardial revascularization; in addition, diabetes and hyperlipidemia had a negative impact on clinical outcome especially of patients receiving saphenous vein grafts. (Figure 3B)

The only variables significantly associated with graft occlusion both at univariate and multivariate stepwise regression analysis were the presence of diabetes, hyperlipidemia, and conventional coronary surgery (diabetes: odds ratio [OR] = 1.17, 95% confidence interval [CI] = 1.10–1.24, P < 0.0001; hyperlipidemia: OR = 1.10, 95% CI = 1.02–1.18, P = 0.022; conventional surgery: OR = 1.16, 95% CI = 1.08–1.23); moreover, at the Cox proportional hazard model, late cardiac related events were also significantly affected by the presence of saphenous vein grafts, hyperlipidemia, and diabetes (saphenous grafts: hazards ratio [HR] = 2.29, 95% CI = 1.49–3.08, P = 0.041; hyperlipidemia: HR = 2.10, 95% CI = 1.32–2.89, P = 0.062; diabetes: HR = 2.87, 95% CI = 2.05–3.69, P = 0.011).

Discussion

The percentage of patients undergoing coronary surgery >70 years of age has been steadily increasing during the past 10 years, mainly as a consequence of the progressive advances in medical care. Several authors reported about the safety and usefulness of cardiac surgical procedures in the treatment of the elderly population, which is progressively representing the largest fraction of patients undergoing coronary artery bypass surgery. Coronary surgery has been associated with an higher risk of perioperative morbidity and mortality in the elderly, when compared with younger populations;
however, the greater operative risk in elderly patients seems to be not only because of age, per se, but mostly related to the presence of several associated comorbidities.\textsuperscript{14–17}

Despite the demonstrated advantages of myocardial revascularization with arterial grafts,\textsuperscript{3–4} the majority of surgeons preferred the use of saphenous vein grafts in an attempt to reduce surgical invasiveness and the operative risks in the elderly population; conversely, Morris et al\textsuperscript{5} reported their experience in the use of LITA on LAD in octogenarians, showing an improved mid- and long-term outcome when compared with saphenous vein grafts and, therefore, suggesting to extend the already proven benefits of arterial revascularization even in the elderly.

Our study was designed to evaluate the safety and the advantages of total arterial myocardial revascularization in comparison with the conventional technique (LITA on LAD plus additional saphenous vein grafts) in elderly patients scheduled for isolated coronary surgery. This study was designed as a prospective randomized evaluation in order to allow a comparison of 2 different surgical techniques in a similar group of patients, avoiding selection bias. We adopted only few exclusion criteria (left ventricular ejection fraction \(<25\%\), emergency CABG, single vessel disease, and patients with an Euroscore \(>10\)) in an attempt to avoid an unpredictable distribution of high-risk patients in the 2 groups, thus affecting the reliability of the study. Consistently with previous studies,\textsuperscript{2,3,5,7} also our patients had an higher prevalence of renal dysfunction, cerebrovascular disease, chronic obstructive pulmonary disease, and diabetes when compared with the younger CABG population. With the exception of diabetes, whose prevalence was higher in our study group, compared with other studies, the prevalence of concomitant diseases was similar to that reported in previous studies.\textsuperscript{2,5}

Primarily our results demonstrate the safety of total arterial myocardial revascularization in the elderly population, because the early results in Group 1 were similar to those of Group 2 in terms of completeness of myocardial revascularization, postoperative morbidity, and hospital mortality; moreover, patients receiving total arterial myocardial revascularization with composite grafts had a significant shorter cardiopulmonary bypass time (as a consequence of the absence of proximal anastomoses) and less cerebrovascular accidents (because ascending aorta manipulation is minimized), even if the difference between the groups did not reach a statistical significance.

Moreover, the mid-term outcome of patients in Group 1 was significantly better than Group 2 in terms of recurrence of angina/myocardial infarction, graft occlusion, and percutaneous transluminal coronary angioplasty reintervention, therefore showing a superior actuarial freedom from late cardiac events at Kaplan-Meier analysis.

Finally, when we evaluated the impact of associated comorbidities on the outcome of elderly patients, we observed that saphenous vein grafts (conventional technique), diabetes, and hyperlipidemia were able to affect outcome only of patients belonging to Group 2; in fact, multivariate analysis identified diabetes, saphenous vein grafts, and hyperlipidemia as independent predictors for graft occlusion and the same variables were also found to be independent risk factors for angina recurrence and myocardial infarction using the Cox regression model. At any time interval of the follow-up there was evidence that patients receiving total arterial grafts had a lower incidence of late cardiac events when compared with patients receiving saphenous vein grafts.

In conclusion, this study demonstrates the favorable results of total arterial myocardial revascularization in the elderly, in terms of clinical outcome, when compared with the conventional technique, particularly in presence of associated comorbidities as diabetes and hyperlipidemia, which are very common in this subset of patients.

Moreover, extremely diseased coronary arteries and poor quality saphenous veins are more likely to be found in elderly patients and, therefore, the conventional technique may be less suitable for a safe and effective myocardial revascularization than total arterial revascularization.

References

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