Late results of first myocardial revascularization in multiple vessel disease: single versus bilateral internal mammary artery with or without saphenous vein grafts

Antonio Maria Calafiore a, *, Gabriele Di Giammarco b, Giovanni Teodori a, Michele Di Mauro b, Angela Lorena Iaco b, Antonio Bivona b, Marco Contini b, Giuseppe Vitolla b

aDivision of Cardiac Surgery, University Hospital, Torino, Italy
bDepartment of Cardiology and Cardiac Surgery, ‘G D’Annunzio’ University, Chieti, Italy

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Abstract

Objective(s): We evaluated our experience to investigate if the use of bilateral internal mammary artery (BIMA) grafting, with or without complementary saphenous vein grafts (SVGs), if compared to the use of single IMA and SVG(s), increases the quality of the results of coronary bypass grafting in patients younger than 75 years who undergo first myocardial revascularization.

Methods: From September 1986 to December 1999, 1602 patients younger than 75 years underwent first myocardial revascularization using left internal mammary (LIMA) to left anterior descending (LAD) and SVG(s) (n = 576) or BIMA (one IMA on the LAD) with or without SVG(s) (n = 1026). Propensity score analysis was used to select 1140 patients with the same preoperative and operative characteristics. Thirty day outcome was evaluated as well as 10-year freedom from death by any cause, cardiac death, acute myocardial infarction (AMI), AMI in a grafted area (GA), redo/PTCA, redo/PTCA in a GA, target cardiac events (death from cardiac cause, AMI in a GA, redo/PTCA in a GA), and any event. Follow-up ranged from 3.5 to 16.8 years (mean 7.3 ± 4.8 years).

Results: Thirty day mortality was 2.8% in Group LIMA and 2.1% in Group BIMA, P n.s.; incidence of major complications was, respectively, 7.0 versus 5.4%, P n.s. Group BIMA showed better 10-year freedom from cardiac death (96.5 ± 0.8 versus 91.3 ± 1.4, P = 0.0288), AMI (98.0 ± 0.6 versus 94.3 ± 1.2, P = 0.0180), AMI in a GA (98.4 ± 0.6 versus 94.7 ± 1.1, P = 0.0057) and target cardiac events (93.9 ± 1.1 versus 86.3 ± 1.8, P = 0.0388). Cox analysis confirmed that LIMA + SVG was an independent risk factor from lower freedom from cardiac death, AMI, AMI in a GA and cardiac events. Conclusions: As freedom from cardiac events is a main target of any revascularization procedure, we think that, when a patient undergoes a first coronary surgery and is younger than 75 years, BIMA grafting should not be denied, especially if his life expectancy is higher than 10 years.

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Keywords: Bilateral internal mammary artery; Single mammary artery; Saphenous vein

1. Introduction

The superiority of the left internal mammary (LIMA) versus the saphenous vein graft (SVG) when the target vessel is the left anterior descending (LAD) artery was clearly demonstrated with many papers that, even if retrospective and non-randomised, showed incontrovertible findings [1–3]. The possibility that the use of the second mammary artery could increase the benefit of the LIMA grafting was investigated for many years, without reaching definitive conclusions [4–8].

However, during the last years, many reports pointed out on the superior outcome when bilateral internal mammary artery (BIMA) grafting was compared to the single IMA. Many of these studies reported patients operated on during the first years of coronary surgery, completely different from the patients operated on later, when the mean age is increased and the diffusion of interventional cardiology started to change the scenario of coronary surgery [9–11].

We evaluated our experience to investigate if the use of BIMA grafting, with or without complementary
SVG(s), if compared to the use of single IMA and SVG(s), increases the quality of the results of coronary bypass grafting in patients younger than 75 years who undergo first myocardial revascularization.

2. Material and methods

From September 1986 to December 1999, 1602 patients younger than 75 years underwent first myocardial revascularization using LIMA to LAD and SVG(s) (n = 576) or BIMA (one IMA on the LAD) with or without SVG(s) (n = 1026). Propensity score analysis was used to select 1140 patients (71.2%), matching each LIMA + SVG(s) with a BIMA ± SVG(s) with the nearest propensity score. Two groups of patients (Group LIMA and Group BIMA), 570 each, were obtained (goodness-of-fit $R^2 = 4.4$, df = 8, $P = 0.82$). Table 1 shows the preoperative characteristics of the patients included in the study.

Patient selection. All the patients included in the study were suitable for single LIMA or BIMA grafting. In the first part of our experience, use of BIMA grafting was limited to patients with morbid obesity, diabetes and chronic obstructive pulmonary disease. When IMA skeletonization started, in 1994, BIMA grafting was also used in these patients. Single or bilateral IMA grafting was mainly decided according to surgeon’s practice or experience. Allocation to off-pump surgery depends on the basis of the expertise of the surgeon responsible for the operation.

Surgical technique. Cardiopulmonary bypass (CPB) was used in 817 patients (71.7%), whereas 323 (28.3%) were operated on without CPB. In every case, a median sternotomy was used. CPB was instituted by cannulation of ascending aorta and right atrium. Myocardial protection was cold crystalloid in 183 cases, intermittent antegrade cold blood in 97 cases and intermittent antegrade warm blood in the remaining 537 [12]. Proximal SVG anastomoses were performed using a side clamp in 263 cases during a single cross clamping time in the remaining 300.

Off-pump. The method of exposure of the target coronary vessel and of stabilization was already reported [13]. In the most recent years, an apical suction was used to expose in particular the lateral and the inferior wall (Xpose™, Guidant Corporation, Cupertino, CA, US). When the coronary artery was exposed, stabilization was achieved with a pressure (Acces Ultima™, Guidant Corporation, Cupertino, CA, USA) or suction (Axius Vacuum 2™ System, Guidant Corporation, Cupertino, CA, USA) stabilizer. The target vessel was occluded with a 4/0 Prolene, passed on a small piece of silicone tubing and then gently snared.

Clinical data collection, monitoring and definition. A set of perioperative data were collected prospectively for all patients undergoing CABG at our institution. The following were recorded and defined.

Mortality included death by cause. Cardiac mortality included any death by cardiac causes and sudden deaths. Cerebrovascular accident (CVA) was defined as global or focal neurological deficit, diagnosed by a neurologist and confirmed by a brain CT scan. Acute myocardial infarction (AMI) was defined as enzymatic elevation, EKG sign of necrosis, new akinetic segment(s) at echocardiogram, ventricular arrhythmias non-K+ related. During the follow-up, the possibility that AMI occurred in the grafted area (GA) was considered. Early major events (EME) were defined as the sum of death by any cause, CVA, AMI, low output syndrome (need of IABP and or inotropic drugs for more than 12 h), need of mechanical ventilation for more than 24 h, acute renal failure (postoperative blood creatinine ≥2.0 mg%, if the preoperative value was normal (≥1.5), or 1 mg higher if pathologic), gastrointestinal complications. Early negative primary end points (ENPEP) were defined as the sum of death by any cause, AMI and CVA. Redo/PTCA was defined as any intervention in any territory or in the GA; target cardiac events as cardiac deaths, AMI in a GA and redo/PTCA in a GA. any event as death by any cause, AMI any territory, redo/PTCA any territory.

Follow-up. All the patients were followed up in our outpatients clinic 3, 6 and 12 months after surgery and thereafter at yearly intervals. The more recent information was obtained calling the patient or the referring cardiologist. Follow-up was 100% complete; dead line was fixed on August 31, 2003.

Statistical analysis. Results are expressed as mean value ± standard deviation. Statistical analysis comparing two groups was performed with unpaired two-tailed t testing for the means or $\chi^2$ test for categorical variables. Stepwise logistic regression (SLR) was used to realize a model to calculate saturated propensity score (the probability to be
selected for LIMA + SVG given a set of preoperative risk factors already reported [14]). The goodness of model was evaluated using the Hosmer and Lemeshow goodness-of-fit statistic and residual analysis. Each LIMA + SVG(s) patient was matched with the BIMA ± SVG(s) patient with the closest propensity score. Variables at the basis of the model are shown in Appendix A. SLR was used to select the independent variables that could predict the end points of this study and included all the univariate variable with a $P$ value $\leq 0.2$. In the final regression model independent variables were expressed as odds ratio with the 95% confidence limit (CL); the related $P$ value was also reported. SLR was used to identify the independent predictors of early events. Actuarial curves were obtained with the Kaplan–Meier method. The statistical significance was calculated with the log-rank test. Cox analysis was used to evaluate the independent risk factors for reduced late events. In the Cox analysis model, independent variables were expressed as hazard ratio (HR) with the 95% CL; the related $P$ value was also reported. The SPSS software (Chicago, IL, USA) was used. $P$ values $\leq 0.05$ were considered significant.

### 3. Results

Table 2 shows the operative details. In Group LIMA, the internal mammary artery was anastomosed always with the LAD, in 66 cases sequentially with the diagonal. In Group BIMA, an internal mammary artery (the left in 317 cases, 55.6%, and the right in 253 cases, 44.4%) was always anastomosed to the LAD, whereas the diagonal grafted in a sequential way in 76 cases (13.3%). The remaining IMA was anastomosed to the LAD, whereas the diagonal grafted in a Y fashion in 128 cases (22.5%); in 383 cases (67.2%) no veins were considered significant.

Table 3 shows the postoperative results. There was no difference between groups except the length in Intensive Care Unit and postoperative in hospital stay. SLR showed that the quality of revascularization was not a risk factor for any death cause, cardiac death, AMI, CVA, ENPEP or EMEs.

Mean follow-up of the survivors was $7.3 \pm 4.8$ years ($3.5–16.8$), $7.5 \pm 4.7$ for Group LIMA and $7.1 \pm 5.0$ for Group BIMA ($P$, n.s.).

After a mean of $4.0 \pm 4.3$ years, 96 patients died, 60 in Group LIMA versus 36 in Group BIMA, 58 for cardiac causes (39 versus 19). Twenty-one patients had AMI (15 versus 6), 19 in the GA (14 versus 5); 42 patients had a redo or PTCA (23 versus 19), 26 in the GA (15 versus 11); 78 patients had a TCE (49 versus 29) and 132 had any event (79 versus 53). Table 4 shows the 10-year actuarial results of the events investigated. Cox analysis showed that use of LIMA and SVG(s) was an independent predictor for lower freedom from cardiac death ($HR = 1.9, 95\% \, CL = 1.1–3.9, \, P = 0.0282$), AMI ($HR = 2.3, 95\% \, CL = 1.1–5.5, \, P = 0.0263$), AMI in a GA ($HR = 2.8, 95\% \, CL = 1.1–7.0, \, P = 0.0102$) and from target cardiac events ($HR = 1.5, 95\% \, CL = 1.1–2.2, \, P = 0.0476$). Fig. 1 shows the curves related to these events.

### 4. Discussion

Superiority of LIMA on SVG, if grafted on LAD, was clearly demonstrated during the 1980s when different
papers showed a superior survival, when patients had a LIMA on LAD and a superior better patency rate of LIMA versus SVG [1–3].

The possibility that increasing the number of arterial anastomoses long-term results could be even better was then explored. The first arterial conduit that could be added to the LIMA was the RIMA that, of course, presented characteristics similar to the LIMA [15–18]. However, some drawbacks limited the widespread utilization of BIMA grafting: (a) the increase of deep sternal wound problems, especially in diabetic patients; (b) the reduced length of RIMA that limited its utilization as an in situ graft; (c) the low patency rate (similar to the SVG one) if grafted to the RCA, the nearest target coronary vessel; (d) the longer operative time. Moreover, during the past decade, many reports failed to show any advantage of BIMA over LIMA grafting [4–8].

Recently there was an increasing evidence of improved results when BIMA grafting was used. Pick et al. showed, in two groups of patients who had LIMA on LAD and a RIMA, or SVG, on the lateral wall, no difference in survival, but lower incidence of cardiac deaths, AMI and angina return [9]. On the contrary, Lytle et al. [10] reported better survival after 5, 10 and 15 years if BIMA was used, independently from the anastomotic site of the RIMA. The same authors found less incidence of repeat revascularization. Berreklouw et al. [11] and Endo et al. [19] found no advantage in survival, whereas both reported lower

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**Fig. 1.** (A) Five-year freedom from cardiac death. Group BIMA (—) and Group SIMA (---). (B) Five-year freedom from acute myocardial infarction. Group BIMA (—) and Group SIMA (---). (C) Five-year freedom from acute myocardial infarction in a grafted area. Group BIMA (—) and Group SIMA (---). (D) Five-year freedom from target cardiac events. Group BIMA (—) and Group SIMA (---).
incidence of repeat revascularization in case of BIMA grafting. Berreklouw also showed higher freedom from angina return, AMI and, globally, from ischemic events.

BIMA grafting in diabetic patients, one of the most important limitations to this strategy, was recently demonstrated not to be a major problem [20,21], especially when BIMA is harvested as a skeletonized conduit [22]. Many studies showed that the most important target for the RIMA is not the RCA system, but the lateral wall [8,9,18,23]. How to use the two IMAs (in situ, as a Y or T graft, pedicled or skeletonized) is still controversial, but data from the literature seem to show good results with all these strategies [10,21,24,25].

Our study shows that, in a propensity score analysis that includes patients with age lower than 75 years who undergo first myocardial revascularization, BIMA grafting is related, 10 years after surgery, to significantly higher freedom from cardiac events, both at univariate and multivariate analysis, if compared to single LIMA with SVG(s). Moreover, there is a strong trend toward a better survival and a better event-free survival. As there is some evidence that using the RIMA on the right coronary system does not provide better results than using SVGs, we use the RIMA directly to the RCA only when this vessel is more important than the circumflex artery and has a normal wall; the posterior descending artery can be used as target coronary vessel using the Y graft configuration. Preserving the integrity, as much as possible, of the left ventricle very likely can provide superior results than grafting the left anterior descending artery and the RCA, except when this latter is better represented than the circumflex artery.

Interestingly, freedom from redo/PTCA was not different in the two groups. Myocardial infarction due to occlusion of a graft or progression of disease in the native territory seems to be more likely to happen than progressive caliber reduction of a conduit or grafted or ungrafted coronary vessels with subsequent angina.

As freedom from cardiac events is a main target of any revascularization procedure, we think that, when a patient undergoes a first coronary surgery and is younger than 75
years, BIMA grafting is not to be denied, especially if his life expectancy is higher than 10 years.

References


Appendix A. Variables included in the propensity score model

<table>
<thead>
<tr>
<th>Variables</th>
<th>B-value</th>
<th>P-value</th>
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<tr>
<td>COPD</td>
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<tr>
<td>No. of anastomoses</td>
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<td>Diabetes</td>
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</tr>
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<td>ECV</td>
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<td>EF (\leq 35%)</td>
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<td>Urgency</td>
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<tr>
<td>Ventricular arrhitmias</td>
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COPD, chronic obstructive pulmonary disease; ECV, extracardiac vasculopathy; EF, ejection fraction; CHF, chronic heart failure; CRF, chronic renal failure; AMI, acute myocardial infarction.
Appendix B. Conference discussion

Dr C. Alhan (Istanbul, Turkey): I just want to ask, do you have any strict contraindications for the use of BIMA?

Dr Calafiore: The standard complications really were not different in the two groups, because in the great majority of the patients who had both internal mammary arteries the conduits were harvested skeletonized. Skeletonizing the internal mammary arteries protects the sternal vascularization and reduces the incidence of deep sternal wound problems. We can use the two mammary arteries in diabetic patients, for instance, without a higher incidence of sternal wound problem. This aspect was not a problem.

Dr A. Schachner (Holon, Israel): You stress that a dominant right coronary artery is suitable for a reimplantation. Is it your observation? Because if you have a very nice developed right coronary artery, I think the patency rate of the right internal mammary can be very good.

Dr Calafiore: We are doing a study with the long-term patency rate of the arterial conduits five years after surgery. We found that, if the right coronary artery is of good quality, the use of the right internal mammary artery on it gives an excellent patency rate. The problem is the extension of the use of the right internal mammary artery to all the right coronary arteries. If we have a right coronary artery more important of the circumflex artery, if the coronary wall is satisfying, the right internal mammary artery can be used. The concept cannot be generalized, but I think it can be a good strategy.