Arterial revascularization in primary coronary artery bypass grafting: Direct comparison of 4 strategies—Results of the Stand-in-Y Mammary Study

Giuseppe Nasso, MD,[a] Roberto Coppola, MD,[b] Raffaele Bonifazi, MD,[a] Felice Piancone, MD,[a] Giuseppe Bozzetti, MD,[a] and Giuseppe Speziale, MD[a]

Objective: It is unclear (1) whether the use of 2 arterial conduits rather than a single conduit in multivessel coronary artery bypass grafting significantly improves results despite the concomitant use of saphenous vein grafts and (2) whether any among different configurations of composite grafts (left/right thoracic arteries and radial artery) offers an advantage over the others.

Methods: Eight hundred fifteen patients were randomized to one of 3 different strategies of revascularization by using the left thoracic artery plus the right thoracic artery or using the left thoracic artery plus the radial artery. Venous grafts were used for the remaining targets. Patients randomized to receive 1 arterial graft served as control subjects. Operative mortality and morbidity were comparable among groups.

Results: The rate of cerebrovascular complications was not statistically lower among patients receiving 2 arterial grafts. At 2 years, overall survival was not significantly different among groups ($P = .59$). Cardiac event–free survival was significantly better in patients receiving 2 arterial grafts versus control subjects ($P < .0001$), even among elderly patients ($P = .022$). The 3 investigated strategies using 2 arterial conduits were similar concerning early and midterm results.

Conclusions: Revascularization with 2 arterial conduits offers better midterm event-free survival than a single arterial graft, irrespective of which second-choice arterial conduit is used (radial artery or right thoracic artery), the simultaneous use of saphenous vein grafts, and the patient's age.

The proved superiority of internal thoracic arteries (ITAs) over great saphenous vein (GSV) grafts in terms of long-term outcome, which is particularly evident when the left anterior descending coronary artery (LAD) is involved,[1-3] has pushed surgeons to explore the potentials of total arterial revascularization.

Even the use of 1 additional arterial graft has been indicated to improve the results of coronary artery bypass grafting (CABG). Bilateral ITA grafting in conjunction with GSV grafts has ameliorated the survival and reduced the risk of reoperation compared with single ITA grafting plus GSV grafting to the remaining coronary targets.[4-6] Such benefits might be evident, even with the use of composite grafts[7] and in elderly patients at midterm follow-up.[8] Nonetheless, recent data suggest that the gap between the results of free arterial grafts and GSV grafts might be reducing in the contemporary era.[9]

Composite grafts are among the technical improvements proposed to allow arterial revascularization with reduced conduit use and preserved left internal thoracic artery (LITA)–LAD grafting. The Y-side configuration of a free right internal thoracic artery (RITA) anastomosed end-to-side to a pedicled LITA is effective to obtain an adequate revascularization of the whole left coronary system,[10] but there are no studies analyzing the results of such graft configuration versus other strategies of revascularization with more than 1 arterial conduit, either free or in the Y configuration. Controversies exist about whether the use of more than 1 arterial conduit significantly ameliorates the patient's outcome, even though GSV grafts are simultaneously used to complete the operation, in comparison with the established strategy of using LITA–LAD grafts plus GSV grafts. A specific subpopulation of patients (ie, the elderly, who are increasingly frequent in practice) are a major subject in these debates. The Stand-in-Y Mammary Study has been designed with the purpose to contribute to the knowledge base on these issues.

From the Division of Cardiac Surgery,[a] Anthea Hospital, Bari, Italy; and the Division of Cardiac Surgery,[b] Villa Azzurra Hospital, Rapallo, Italy.

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Address for reprints: Giuseppe Nasso, MD, Division of Cardiac Surgery, Anthea Hospital, Via C. Rosalba, 35-37, 70124 Bari, Italy (E-mail: gnasso@libero.it).

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MATERIALS AND METHODS

Aim

We sought to compare in a prospective randomized investigation 3 different strategies of myocardial revascularization with the use of 2 arterial conduits in a contemporary (2003–2006) cardiac surgical experience.

Inclusion of Patients

The present study was prospectively started in January 2003. Each patient scheduled for coronary surgery was evaluated at the time of

Abbreviations and Acronyms

CABG = coronary artery bypass grafting
CI = confidence interval
CPB = cardiopulmonary bypass
GSV = great saphenous vein
ITA = internal thoracic artery
LAD = left anterior descending coronary artery
LITA = left internal thoracic artery
OR = odds ratio
RA = radial artery
RITA = right internal thoracic artery

admission to the cardiac surgery unit. Patients were considered suitable to enter the Stand-in-Y Mammary Study on the basis of the following criteria:

- primary elective isolated myocardial revascularization for multivessel coronary disease with involvement of the LAD artery, according to the current guidelines, scheduled[11];
- use of full cardiopulmonary bypass (CPB) planned; and
- availability of conduits (GSV; possibility to harvest the radial artery [RA] from the nondominant arm and to harvest the RITA).

By using historical data, a sample size calculation was performed, with a 0.8 statistical power, a 95% CI, and a .05 α level. The outcome end point for sample size calculation was the expected rate of graft failure in the arterial revascularization groups versus the traditional revascularization group. Taking into calculation a 0.33 rate of control to case patients, a 0.14 expected event rate among case patients and a 0.07 expected event rate among control subjects yielded a sample size of 636 cases. Sample size calculation was performed with PS Software version 2.1.30 for Windows.

Before randomization and according to institutional policy, all patients were subjected to echocardiographic Doppler evaluation of the ulnar compensation during RA compression in the nondominant arm, according to a previously described methodology.[12] Evidence of adequate compensation was required for eligibility of RA harvest and to enter the study. Similarly, patients carrying more than 1 of the described risk factors for deep sternal wound infection (diabetes and obesity [body mass index $\geq$30])[13] were not considered suitable for bilateral ITA harvest because of excessive risk of sternal wound infection; hence these individuals were excluded from the study before randomization. No modifications were included in the institutional protocols to comply with the study inclusion/exclusion criteria.

Additional exclusion criteria were as follows: redo procedure, planned use of any arterial graft other than thoracic arteries and the RA, any associated cardiac surgical procedure other than coronary surgery, and history of systemic inflammatory conditions, vasculitis, or thoracic/mediastinal radiation therapy. Decreased ejection fraction and advanced age were not among the exclusion criteria.

The local ethics committees provided formal approval to the protocol. Patients were asked to provide informed consent to enter the investigation. Enrolled patients were then randomized with the aid of a computerized algorithm to one of 4 groups corresponding to 4 different strategies of revascularization, as detailed below:

- *Group 1*. Y graft: in situ LITA graft to LAD artery and isolated RITA graft to secondary target with or without GSV graft(s) to revascularize the remaining target(s);
- *Group 2*. In situ RITA graft to the LAD plus in situ LITA graft with or without GSV graft(s) to revascularize the remaining target(s);
- *Group 3*. In situ LITA graft to the LAD plus free aortocoronary RA graft to the secondary target or Y graft: in situ LITA graft to the LAD and isolated RA segment to the secondary target with or without GSV graft(s) to revascularize the remaining target(s); and
- *Group 4*. In situ LITA graft to the LAD artery plus GSV graft(s) to revascularize all non-LAD targets.

Study groups are outlined in Figure 1. The RITA and the RA were managed as the second-choice conduit and were used to revascularize the secondary coronary target. The RA was always harvested from the nondominant arm. The RA was used either as a free graft in the aortocoronary configuration or in the Y configuration with the LITA; the latter was performed when the secondary target presented subocclusive stenosis. The RITA and RA grafts, irrespective to the configuration, were anastomosed to coronary targets with stenosis of 70% or greater.[14,15] Because our experience with the use of the gastroepiploic artery as a bypass conduit is limited, the use of this conduit was excluded from the present study to avoid bias. T grafts were never performed in the present series.

This trial was conducted under an intent-to-treat protocol. Reasons for incomplete fulfillment of the treatment assigned by randomization were as follows: intraoperative finding of coronary arteries unsuitable for grafting with the second-choice arterial conduit and intraoperative finding of first- or second-choice arterial graft unsuitable to perform a coronary graft. In consideration of the study inclusion criteria detailed above, 2 intraoperative conditions were defined to be determinants of exclusion from the study: (1) intraoperative conversion to off-pump CABG and (2) intraoperative finding of the LAD being unsuitable to receive grafts.

Study End Points

Study end points were in-hospital outcomes (mortality rate and morbidity), 2-year freedom from all-cause death, and adverse cardiac event–free survival (adverse cardiac events included cardiac death, acute myocardial infarction, recurrent angina, graft occlusion at coronary angiography, redo coronary surgery, or percutaneous transluminal coronary angioplasty).

Surgical Procedure

After a full median sternotomy and before opening the pericardium, the LITA and RITA (when applicable) were harvested in standard fashion before heparinization. Thoracic arteries were harvested skeletonized in all cases. When applicable, the RA was harvested before heparinization with a longitudinal forearm incision from the lateral edge of the biceps tendon up to a point between the radial styloid and the tendon of the flexor radialis muscle up to the wrist crease. Y grafts were constructed before establishment of CPB with end-to-side anastomosis of the RITA or RA segment to the LITA. After harvesting the conduits and after ascending aortic and right atrial cannulation, CPB was established, and the heart was arrested; myocardial protection was accomplished with antegrade and/or retrograde blood multidose cardioplegia according to the surgeon's preference. Arterial conduits were usually divided only after a clotting time of greater than 400 seconds to avoid intraluminal thrombosis. The conduits were then tested for 15 seconds to verify the adequacy of flow and were then carefully inspected to detect intraluminal thrombosis or luminal dissection. Manipulation was done gently as well. Immediately before performance of anastomosis, a papaverine solution was placed on arterial conduits to avoid vasospasm. For free grafts, the distal anastomosis usually preceded the proximal anastomosis. The latter was generally performed during aortic side clamping and with the heart beating. The distal anastomosis of free grafts usually preceded the distal anastomosis of in situ thoracic arteries. For sequential grafts, side-to-side anastomosis to the target coronary artery (diamond shaped) was performed. The order in which the anastomoses were performed remained under the discretion of the operating surgeon. The non-LAD, nonsecondary coronary targets, if present, received a GSV bypass graft in the aortocoronary configuration in all cases. After weaning from CPB, the adequacy of graft flow was assessed by using a Doppler probe after a systolic pressure of 80 mm Hg was obtained.