Total arterial revascularization with internal thoracic and radial artery grafts in triple-vessel coronary artery disease is associated with improved survival

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Objectives: We sought to evaluate our experience with total arterial revascularization and compare it with the traditional approach of a single internal thoracic artery supplemented by saphenous veins.

Methods: From 1995 to 2010, 6059 patients with triple-vessel coronary artery disease underwent primary isolated coronary artery bypass grafting at 8 centers. A study cohort of 3774 patients was formed, with 2988 (79%) undergoing total arterial revascularization and 786 (21%) receiving only saphenous veins to supplement a single in situ internal thoracic artery. In the total arterial revascularization group, bilateral internal thoracic arteries were used in 1079 patients (36%) and at least 1 radial artery was used in 2916 patients (97%). Propensity score matching was used for risk adjustment.

Results: Patients undergoing total arterial revascularization were younger (65.0 ± 10.4 years vs 71.3 ± 7.9 years, $P < .001$) and less likely to have diabetes, cerebrovascular disease, recent myocardial infarction, and severe left ventricular impairment. At 15 years, patients who underwent total arterial revascularization experienced superior unadjusted survival (62% ± 1.1% vs 35% ± 1.9%, $P < .001$). Multivariable Cox regression in the entire study cohort showed the total arterial group had improved survival with a hazard ratio of 0.79 (95% confidence interval, 0.70-0.90; $P < .001$). After propensity score matching yielded 384 patient pairs, patients who underwent total arterial revascularization showed improved survival at 15 years than patients who underwent single arterial revascularization (54% ± 3.3% vs 41% ± 3.0%, $P = .0004$).

Conclusions: This large multicenter study suggests that a strategy of total arterial revascularization is associated with improved long-term survival compared with the use of only a single arterial and saphenous vein grafts. Total arterial revascularization should be encouraged in patients with a reasonable life expectancy. (J Thorac Cardiovasc Surg 2014;148:1238-44)

Despite percutaneous coronary interventions becoming a feasible modality for coronary revascularization, coronary artery bypass grafting (CABG) remains the standard of care for patients with 3-vessel coronary disease. Although use of the left internal thoracic artery (LITA) has been shown to enhance survival, the impact of using arterial grafts exclusively on long-term survival is still debated.

In the past decade, there have been a number of studies showing the safety and feasibility of the right internal thoracic artery (RITA) and radial arteries (RAs) when used to supplement the LITA.[1-7] The patency of these conduits is at least equivalent to, if not superior to, that of the saphenous vein (SV).[3,5,6]

Given the patency and biology of arterial conduits, there is speculation that their extensive use may translate to improved long-term survival. As such, we sought to evaluate our experience with total arterial revascularization (TAR) using internal thoracic arteries (ITAs) and RAs and compare it with the traditional approach of just a single internal thoracic artery (SITA) supplemented by SVs (SITA + SV) in patients with 3-vessel coronary artery disease.

METHODS

We reviewed a multicenter database containing a total of 23,343 adult coronary artery procedures performed from March 1, 1977, to December 31, 2010, across 8 centers affiliated with the University of Melbourne, Australia. These were Austin, Cabrini, Epworth Richmond, Epworth Eastern, Knox, Royal Melbourne, St Vincent's Melbourne, and Warringal Hospitals.

The database records detailed patient demography, preoperative risk factors, operative technique, postoperative hospital course, and clinical outcome including in-hospital morbidity and 30-day mortality. Data were collected prospectively. Survival status of patients was obtained from the Australian National Death Index, which records all deaths within Australia, the censoring date for which was April 30, 2013.[8]

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Abbreviations and Acronyms

BITA = bilateral internal thoracic artery
CABG = coronary artery bypass grafting
ITA = internal thoracic artery
LAD = left anterior descending
LITA = left internal thoracic artery
RA = radial artery
RITA = right internal thoracic artery
SITA = single internal thoracic artery
SV = saphenous vein
TAR = total arterial revascularization

Study Sample

Patients were included for analysis if they had 3-vessel coronary disease, underwent primary isolated nonemergency CABG, and received at least 1 in situ ITA. Patients were excluded if they received any other conduits, such as the gastroepiploic artery, ulnar artery, or cephalic vein, because these conduits have never been incorporated into routine clinical use during the time period.

Three-vessel disease was defined as 3 coronary systems each with greater than or equal to 60% stenosis in any angiographic view (left main stenosis >60% was counted as 2 systems, the left anterior descending [LAD] and circumflex, such that left main and right coronary disease was considered 3-vessel disease). Stenosis was graded as 0% to 19%, 20% to 39%, 40% to 59%, 60% to 79%, 80% to 99%, or total occlusion. This meant the traditional cutoff of 50% for left main-stem disease could not be applied.

We selected patients undergoing surgery since January 1995, because this coincided with the introduction of the RA conduits into routine clinical practice, permitting TAR to be achieved in combination with the LITA and RITA.

Within these data, we identified the subgroup undergoing TAR, whereby patients received at least 1 in situ ITA supplemented by an additional in situ or free ITA or RAs. The SITA and SV group (SITA + SV) was identified as those receiving 1 in situ ITA supplemented by SVs only. Patients who received a mixture of both arterial and venous conduits to supplement a SITA (ie, LITA + RA + SV, bilateral internal thoracic artery [BITA] + SV configurations) were excluded.

A total of 6059 patients underwent operation for 3-vessel coronary artery disease during the study period. Of these, 2285 received a mixture of both arterial and venous conduits to supplement a SITA and thus were excluded. As such, 3774 patients were ultimately included for analysis, with 2988 (79%) in the TAR group and 786 (21%) in the SITA + SV group.

Study End Points

We examined early outcomes, which included 30-day mortality, deep sternal wound infection, conduit harvest site infection, postoperative myocardial infarction, postoperative stroke, return to the operating room for bleeding, acute renal impairment (± requirement for dialysis), and a composite end point of ''any adverse event'' that encompasses the events listed. Furthermore, we examined long-term survival using data from the National Death Index.[8]

Surgical Technique

All patients underwent median sternotomy. The ITAs were harvested as a pedicle or in a skeletonized fashion, the latter being performed after the year 2000. ITAs and RAs were prepared with a solution of Ringer's Lactate and papaverine 1 mmol/L (40 mg/100 mL). Most procedures were performed with a standard cardiopulmonary bypass using a combination of antegrade and retrograde cardioplegia.

In the TAR cohort, a number of different graft configurations were used. In certain patients, the use of sequential anastomoses permitted more than 1 distal anastomosis to be achieved for a given conduit. Composite ''Y'' grafts were used to enhance flexibility and were recorded in the database as 2 separate conduits creating 2 distal anastomoses.

When a LITA was used (n = 2978), it was grafted to the LAD territory in 2621 patients (88%) and the circumflex system in the remaining 357 patients (12%). A sequential anastomosis to the diagonal territory using the LITA was performed in 619 patients (21%) as part of a LITA-diagonal-LAD configuration, making a total of 3597 distal anastomoses using the LITA.

A RITA was used in 1089 cases. It was used as an in situ conduit in 554 patients (51%) and as a free graft in the remainder. In 10 patients, a RITA was used instead of a LITA. Altogether, 1079 patients received the RITA as part of a BITA strategy. By taking into account 42 sequential anastomoses, a total of 1131 distal anastomoses were performed with the RITA. These were performed to the LAD artery in 235 patients (22%), the diagonal artery in 136 patients (12%), the circumflex artery in 371 patients (34%), and the right coronary artery in 389 patients (36%).

At least 1 RA was used in 2916 patients (98%). A single RA was used in 1507 patients, whereas bilateral RAs were used in 1409 patients such that a total of 4325 RA conduits were used. Preference was given to the proximal anastomosis of the RA with the aorta rather than the LITA because of a potential size mismatch with and for protection of the LITA to LAD graft. By taking into account 533 sequential anastomoses, a total of 4858 distal anastomoses were performed with the RA. Of these, 646 (13%) were to the diagonal artery, 2017 (42%) were to the circumflex artery, and 2195 (45%) were to the right coronary artery.

Statistical Analysis

Preoperative demographic and investigative data, operative variables, postoperative (30-day) mortality, morbidity, and 15-year survival were compared between the TAR and SITA + SV groups.

Categoric variables were expressed as frequencies and compared using the Fisher exact and chi-square tests. Continuous variables were expressed as mean ± standard deviation and compared using the unpaired *t* test. The Kaplan–Meier method was used to analyze survival. Multivariable logistic regression and Cox regression, both performed in a backward elimination fashion, were used to identify independent predictors of early and late outcomes, respectively. The backward elimination method was used to include all potential predictors of end points in the initial models and subsequently eliminate covariates in an iterative process to create a final model. Inclusion of all potentially important variables in the initial model allows their joint predictive behavior to be initially evaluated, which is important given that a set of variables may exhibit predictive capability even if a subset does not.

Propensity score matching was performed to correct for the bias associated with the use of TAR. A propensity score was generated for each patient in the standard fashion by performing a logistic regression with the grafting strategy as the dependent variable. Baseline clinical and investigative variables that are expected to influence cardiac surgery patient outcomes were included. These are shown in Table 1. The c-statistic was calculated for the propensity model. Once this was generated, patients were matched 1 to 1 on their propensity score without replacement using the ''greedy'' matching method with a fixed caliper width of 0.05. A caliper width of 0.05 was selected to ensure a close match with respect to covariates while also minimizing the number of subjects excluded from matching.

After matching, standardized differences were used to assess the degree of baseline variable balance in the manner described by Austin.[9] A high degree of balance is reflected by a standardized difference of 10% or less. Standardized differences were calculated for the entire nonmatched population and to aid reader identification of imbalanced baseline variables.