

# Full myocardial revascularization with bilateral internal mammary artery Y grafts

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**Background:** Bilateral internal mammary artery (BIMA) grafting in coronary artery surgery provides better long term outcomes than single internal mammary artery and saphenous vein grafting but the optimum configuration of BIMAs has not been established. This study analyzed perioperative and late outcomes of patients who underwent BIMA grafting with a composite Y configuration.

**Methods:** Patients (n=922) who underwent BIMA Y grafting were identified from a cardiac surgical database and then cross matched against hospital and cardiology databases and the state death register to identify episodes of repeat coronary angiography, cardiac surgical re-intervention and death. Analysis of repeat angiography was performed after retrieval of the angiogram reports.

**Results:** In 95% of patients, full myocardial revascularization was achieved with BIMAs alone, using a composite Y configuration with an average of 4.1 IMA to coronary artery anastomoses per patient. The perioperative mortality was 1.5% and the 5-, 10- and 15-year survival estimates were 95%, 87% and 77% respectively. Analysis of 166 symptom-driven post-discharge coronary angiograms showed grafts to the left anterior descending artery and increasing severity of coronary artery stenosis at preoperative angiography as predictors of anastomotic patency.

**Conclusions:** Full myocardial revascularization can be achieved with reasonable safety in most patients with triple vessel disease and good left ventricular function, and provides good late survival.

**Keywords:** Coronary artery bypass; internal mammary artery (IMA); myocardial revascularization



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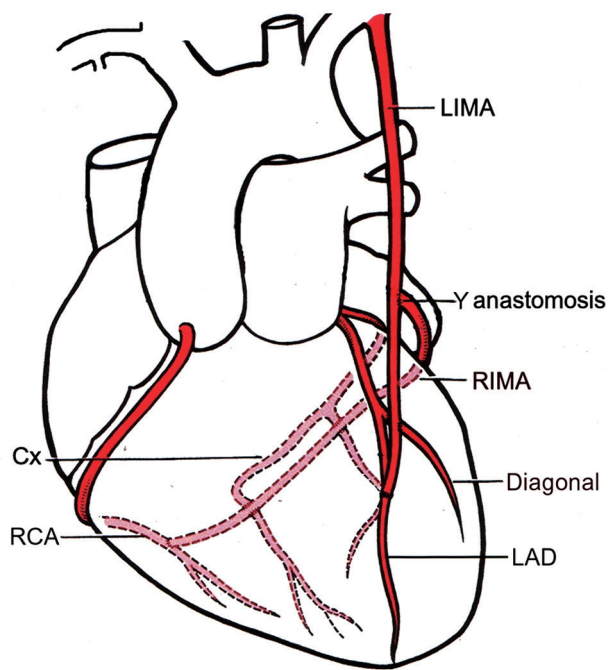
## Introduction

Bilateral internal mammary artery (BIMA) grafting in coronary artery surgery has been associated with improved long term survival and freedom from late cardiac events. Tector *et al.* popularized the BIMA Y configuration with a report of perioperative outcomes in 287 unselected patients in 1994 (1). A subsequent 8.5-year follow-up report of an unselected group of 897 patients who underwent full myocardial revascularization purely with BIMAs as composite grafts demonstrated the safety and mid-term benefit of the procedure (2). There have been numerous other reports of excellent perioperative outcomes in

smaller cohorts. Navia *et al.* reported excellent results in 1,447 patients in whom myocardial revascularization was performed off pump, purely with BIMA composite grafts (3). There have been no other reports of full myocardial revascularization purely with BIMA composite grafts in patient cohorts of that magnitude, with late follow up.

## Patients and methods

922 patients who underwent coronary artery graft surgery under the care of a single surgeon (HSP) using BIMAs in a Y graft configuration were identified from a cardiac surgical



**Figure 1** Bilateral internal mammary artery (BIMA) Y graft configuration for triple vessel disease

database of prospectively collected data from October 1994 to April 2007. The names were matched against hospital and cardiology databases in western Sydney and against the New South Wales Register of Births, Deaths and Marriages. This method of follow-up has been validated with greater than 99% accuracy (4).

### Patient selection

Patients undergoing coronary bypass surgery were selected for the BIMA Y configuration according to a protocol previously described (5). This included patients aged less than 66 years who had triple vessel disease and a left ventricular ejection fraction greater than 50%. Patients were excluded from selection by protocol if any of the following existed; systemic steroid therapy, a high take off posterior descending coronary artery requiring grafting, or acute coronary insufficiency. The protocol anticipated complete myocardial revascularization using the BIMA Y graft without additional conduit and without inappropriate hazard from the BIMA harvesting. Following the identification of a 4% incidence of right phrenic nerve injury associated with high right internal mammary artery (RIMA) harvesting (6), pulmonary dysfunction was

considered to be a relative contraindication, and in 2001 the protocol age was increased from 66 to 70 years. Other patients less than 70 years old underwent BIMA Y grafting in accordance with the principle that it was the preferred configuration when all grafts could be completed solely with the BIMAs using a Y configuration, or when there was insufficient alternative conduit in any patient.

### Operative technique

The operative technique has been described previously (5). Operations were performed through a median sternotomy with cardiopulmonary bypass and cardioplegic arrest with the exception that 3 patient underwent off pump surgery. The internal mammary arteries (IMA) were harvested using a semi-skeletonizing technique. The RIMA was harvested as a free graft with extended harvesting superiorly under the subclavian vein and inferiorly to just beyond the bifurcation. The RIMA beyond the bifurcation was not used. The first anastomosis was of the distal end of the RIMA end-to-side in parallel to its target vessel. The RIMA was then anastomosed sequentially with side-to-side perpendicular anastomoses to the left ventricular free wall vessels. It was then anastomosed end-to-side in parallel to the left IMA (LIMA). The LIMA was then anastomosed in parallel to the anterior wall vessels (*Figure 1*). Bypass grafts were performed to all graftable vessels with at least a 50% stenosis. For the purpose of data analysis, triple vessel disease was defined as a 50% or greater stenosis in the proximal half of the largest coronary artery in each of the three systems. Accordingly, bypass grafts were frequently performed to vessels in all three systems in patients with double vessel disease when smaller vessels had stenoses.

### Post-discharge angiography

Episodes of repeat angiography were performed at the discretion of the attending cardiologist, usually for symptoms or signs suggestive of recurrent myocardial ischemia. The episodes were identified from cardiology databases and the reports reviewed. Grafts were considered to be obstructed if a graft stenosis of at least 75% existed or if there was a string sign. For statistical analysis, these were considered to be anastomotic occlusions. For patients with multiple angiograms, the last angiogram prior to coronary intervention was used for the analysis of graft obstruction. Coronary graft anastomoses (n=7) that were not part of the BIMA Y configuration were excluded from the analysis of

**Table 1** Patient variables (Age: mean, 56.7 years; SD, 7.7 years; range, 29-85 years)

Preoperative	%	Operative	%	Postoperative	%
Female	14	Redo surgery	2	Perioperative death	1.5
Urgent	31	Concomitant procedure	8	Myocardial infarction	1.3
Symptom class 4	36	Cardiac	5	Stroke	1.2
Diabetes	25	Non cardiac	3	DSWI	2.4
LVEF <50%	12	Saphenous vein use	5	IABP	2.6
PVD	5	Free BIMA	1	Bleeding reopening	3.5
Pulmonary disease	4	BIMA Y + Ao to RCA	4	Right phrenic injury	4.3
Renal failure	4				
Prior stroke	1				
Double vessel disease	20				

PVD, peripheral vascular disease; LVEF, left ventricular ejection fraction; BIMA Y + Ao to RCA see *Figure 2*; DSWI, deep sternal wound infection; IABP, intra-aortic balloon pump

predictors of occlusion.

### Follow up

For the estimate of late survival, follow up data was collected to April 2013 (mean, 11.7 years; range, 0-18 years) and for the analysis post-discharge angiography and repeat surgical intervention data were collected to February 2008 (mean, 7.3 years; range, 0-13.3 years).

### Statistical analysis

The statistical software package SPSS Version 21 was used to analyze the data. Two-tailed tests with a significance level of 5% were used throughout. Multiple logistic regression analysis with backward stepwise variable selection was used to identify the independent predictors of perioperative death. The candidate variables for inclusion were those potential risk factors associated with perioperative death at the  $P < 0.1$  level on univariate analysis. Kaplan-Meier survival curves were used to illustrate the distribution of the time from operation until death. Cox proportional hazards models were used to assess the association between survival times and various risk factors of interest and to identify the independent predictors.

For the subset of 166 patients requiring re-catheterization, the data were considered at a per graft level within patients. Multiple logistic regression analysis was used to investigate the joint effects of (I) named coronary artery; (II) anastomosis type (end to end versus side to side); (III) percentage of stenosis in coronary arteries at preoperative angiography; (IV)

artery size and; (V) graded disease severity at surgery on the presence of occlusion in a graft.

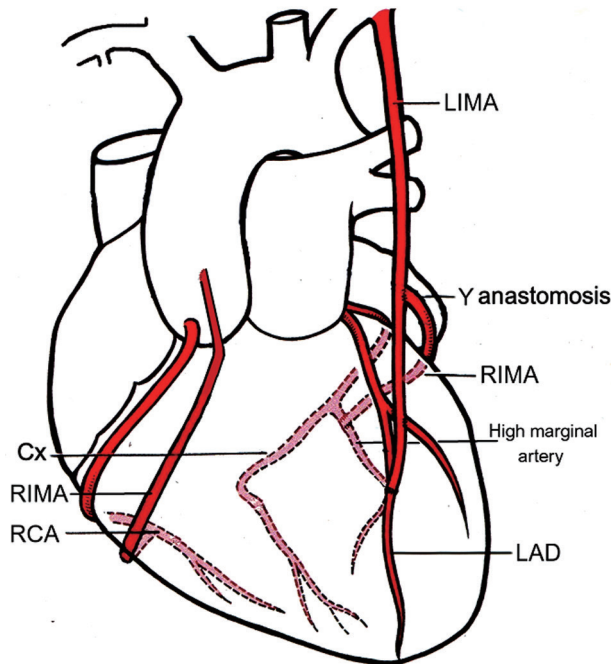
The study was approved by the Western Sydney Local Health District Human Research Ethics Committee.

### Results

The patient cohort consisted largely of young male patients with good left ventricular function and triple vessel coronary disease. The mean additive EuroSCORE was 1.8 (interquartile range, 0-3) and the perioperative mortality was 1.5%. The major demographic, operative and perioperative variables are listed in *Table 1*. The mean number of IMA to coronary anastomoses was 4.1 per patient (standard deviation, 1.0; range, 2-7). Additional conduits were used in 43 patients (5%), saphenous vein in 42 and radial artery in 1 patient. These patients were included in the analysis. A modified BIMA Y graft configuration was used in 4% of patients (*Figure 2*). The mean length of the harvested free RIMA grafts was 18.5 cm (SD, 1.9 cm). Twenty-six patients in the study underwent subsequent redo cardiac surgery at a mean of 4 years (range, 5 months-9 years). Of the total cohort, 86% fulfilled protocol selection criteria. Non-protocol patients were predominantly those with impaired left ventricular function. Thirty-eight patients (4%) who met the protocol for BIMA Y grafting received other configurations and were not included. BIMA grafts were used in 43% of all isolated coronary artery bypass operations during the same period, and of the BIMA grafts, 87% were used in a Y configuration. Trainee surgeons performed 23% of the procedures with no significant differences in

measured outcomes. The trainee operations increased from 17% to 29% after the publication of the Cleveland Clinic data on BIMA graft outcomes (7). Independent predictors

of perioperative mortality and late death are presented in *Table 2*.



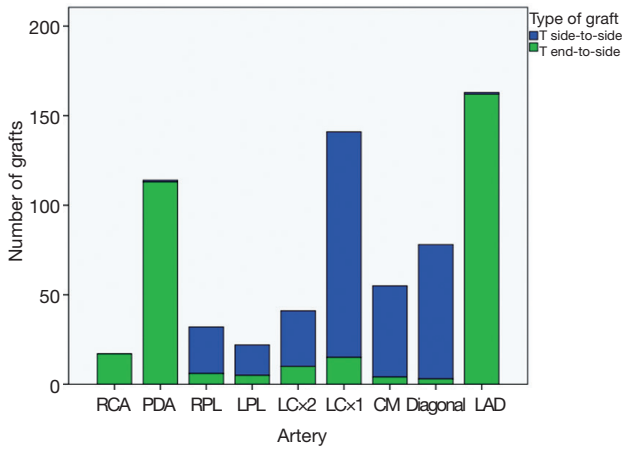
**Figure 2** Alternate bilateral internal mammary artery (BIMA) configuration for grafting a high marginal circumflex branch and the right coronary system with two separate segments of the free RIMA. Cx, circumflex artery; LAD, left anterior descending artery; LIMA, left internal mammary artery; RCA, right coronary artery; RIMA, right internal mammary artery

### Post-discharge angiography

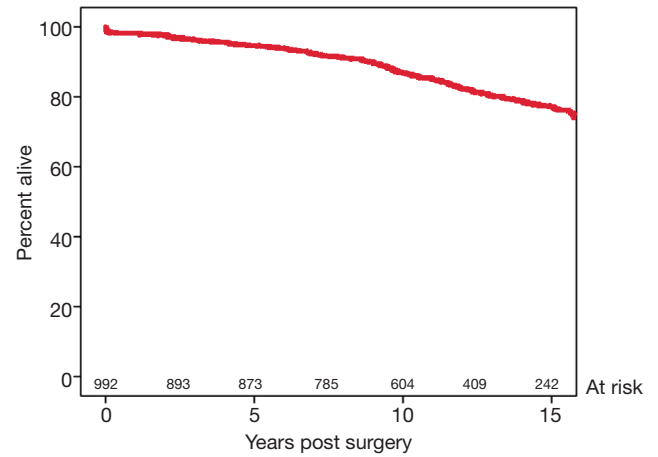
One hundred and sixty-six patients underwent post-discharge coronary angiography at a mean of 3.5 years (range, 2 weeks-13 years). In 77 patients (46%), all anastomoses were considered patent. In the 166 angiograms analyzed, the patency to the left anterior descending artery (LAD) was 91%, patency of the largest branch of the circumflex artery was 80%, and patency to that of the right coronary system was 64%. The distribution and types of grafts analyzed (end-to-side or side-to-side) are shown in *Figure 3*. The percentages of anastomotic occlusions for those arteries that received at least 5 of each type of anastomosis are shown in *Figure 4*. There was only a weak trend towards increased anastomotic occlusion for end to side anastomoses versus side to side anastomoses [odds ratio (OR), 1.7; 95% confidence interval (CI), 0.80-3.4;  $P=0.18$ ] by logistic regression analysis accounting for named artery, percent stenosis of native artery at preoperative angiography, subjective grading of severity and extent of disease in the native artery at surgery, and size of artery. The interaction between the type of anastomosis and the coronary stenosis in predicting anastomotic occlusion was not significant ( $P=0.46$ ) (*Figure 4*). Anastomoses to all named arteries except the diagonal artery had a significantly higher probability of occlusion than those to the LAD. The severity of coronary artery stenosis inversely predicted

**Table 2** Independent predictors of perioperative mortality and late death

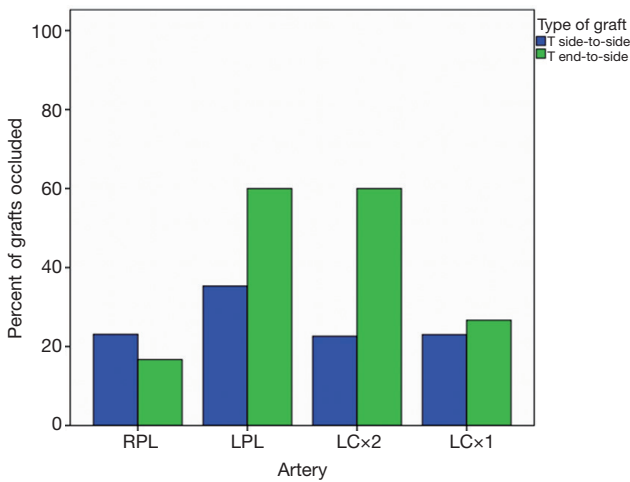
Independent predictor	Odds ratio	95% confidence interval	P-value
<b>Perioperative death</b>			
Age per decade	2.1	1.0-4.4	0.048
Peripheral vascular disease	5.9	1.6-22	0.009
Symptom class 4	4.9	1.4-17	0.013
Renal failure	15.0	4.4-51	<0.001
<b>Late death (follow-up: median, 13.2 years; 95% CI, 12.7-13.7; range, 0-18 years)</b>			
Age per decade	1.7	1.4-2.2	<0.001
Peripheral vascular disease	3.0	1.9-4.8	<0.001
<b>Left ventricular ejection fraction</b>			
<30% vs. >50%	8.5	3.9-18	<0.001
30-50% vs. >50%	1.8	1.2-2.7	0.009
Pulmonary disease	1.9	1.1-3.3	0.024
Prior stroke	2.7	1.1-6.6	0.031



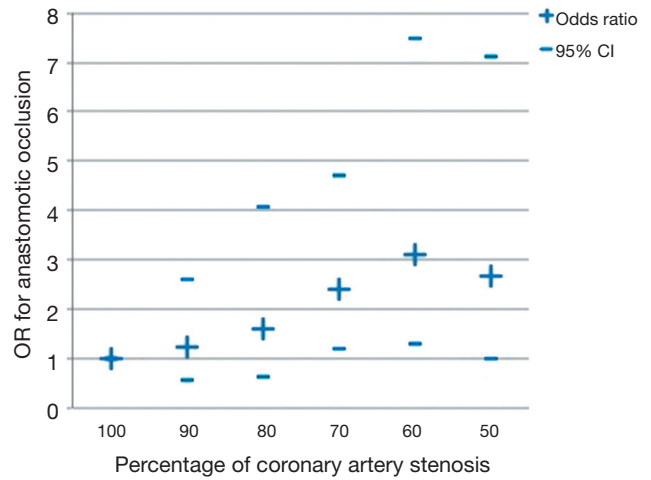
**Figure 3** Distribution of anastomoses according to named coronary arteries and side-to-side (blue) or end-to-side (green) anastomoses. RCA, right coronary artery; PDA, posterior descending artery; RPL, postero-lateral branch of RCA; LPL, postero-lateral branch of circumflex artery; LCx2, second lateral branch of circumflex artery; LCx1, first lateral branch; OM, intermediate or high marginal branch; Diagonal, diagonal branch of LAD; LAD, left anterior descending artery



**Figure 5** Kaplan-Meier survival curve. The 5-, 10- and 15-year overall survival estimates were 95%±0.7%, 87%±1.2% and 77%±1.7% respectively



**Figure 4** Percentage of anastomotic occlusions according to named coronary arteries and side-to-side (blue) or end-to-side (green) anastomoses showing those with a minimum of 5 of each type of anastomosis



**Figure 6** Odds ratio (OR) for anastomotic occlusion according to severity of coronary artery stenosis at preoperative angiography

anastomotic occlusion. For end-to-side anastomoses the occlusion probability per 10% increase in native coronary stenosis severity above 50% was OR=0.75 (95% CI, 0.61-0.92; P=0.005) and for side-to-side anastomoses it was OR=0.83 (95% CI, 0.67-1.0; P=0.088). Long-term survival is shown in *Figure 5*. *Figure 6* shows the relationship

between the preoperative coronary stenosis severity and risk of anastomotic occlusion.

**Discussion**

**LIMA versus BIMA or other**

Since the Cleveland Clinic data showed that “two internal thoracic arteries are better than one” (7) for patients undergoing coronary artery surgery, there have been numerous reports from other centers showing similar benefits (8). The proponents of conventional single IMA



and saphenous vein grafting rather than BIMA grafting require that the margin of benefit of BIMA surgery be sufficient to offset the cost of increased operating time and a higher rate of sternal wound complications. For surgeons who contemplate a change from conventional surgery, they not only face a learning curve associated with the change but also the dilemma of the choice between various arterial conduits and configurations.

The place of the radial artery as the second conduit is also debated. The RAPCO randomized trial comparing the radial artery to saphenous vein for the second conduit in patients aged over 70 years is not complete but has not shown any differences in clinical outcomes or graft patencies at 5 years (9). In that trial the radial artery was anastomosed to the ascending aorta. A similar randomized trial in the same age group comparing conventional bypass surgery against total arterial revascularization with composite RIMA or radial artery grafts from the LIMA showed a benefit for arterial grafting with improved graft patency and clinical outcomes (10). The Radial Artery Patency Study also showed improved radial artery patency relative to that of saphenous vein (11).

The other component of the RAPCO study compared the RIMA and the radial artery as the second conduit in patients aged less than 70 years (9). Again, both were anastomosed proximally to the ascending aorta and composite grafts were not used. At a mean follow up of 5.5 years, protocol angiography demonstrated similar patency between radial artery and free RIMA grafts ( $P=0.28$ ). Ruttman *et al.* used propensity matching to compare outcomes for the use of the RIMA against the radial artery as the second conduit and found that the RIMA provided benefit for both for clinical events and survival (12). Tatoulis *et al.* examined 1,408 symptom-driven postoperative angiograms for assessment of late IMA and radial artery graft patency. The RIMAs and radial arteries had equivalent patency rates for the circumflex and right coronary artery territories (13). For Australian surgeons, it is of note that the government remuneration is greater for a single IMA and radial artery grafting than for BIMA grafting.

### ***In situ* or free RIMA**

Detachment of the RIMA for use as a free graft allows it to provide more extensive myocardial revascularization. Shah *et al.* showed improved graft patency to the right coronary system for free RIMA grafts over *in situ* grafts (14) and, also from Melbourne, Tatoulis *et al.* reported excellent results in

5,766 patients who underwent BIMA grafting using almost equal numbers of free and *in situ* RIMAs. The analysis of 991 symptom-driven angiograms showed the patency for each was similar except for grafts to the right coronary artery where the free RIMA was superior (15).

A randomized trial with mid-term angiographic follow up comparing BIMAs in Y composite or *in situ* configurations showed no difference in clinical outcomes or graft patency but the composite configuration achieved more arterial anastomoses (16). Calafiore *et al.* reported similar findings with excellent results in over 1,800 BIMA graft patients (17). Fukui *et al.* performed angiographic follow up to compare the outcomes of *in situ* to free RIMA grafts in a variety of configurations and found no difference in clinical outcomes or graft patency except when the *in situ* RIMA was used as the inflow for other grafts, usually with an end to end anastomosis (18).

When the free RIMA graft is applied to the circumflex system it is commonly used as part of a composite graft from the LIMA. The reasons for this preference are multiple and include the following: the composite anastomosis is ideally matched and avoids the problems of IMA anastomoses to the left side of the aorta (19), the aortic “no touch” technique reduces the risk of stroke and is particularly useful in off pump surgery, and a greater length of RIMA is available for more extensive myocardial revascularization, perhaps avoiding the use of a third conduit.

### **The right coronary system revascularization**

Graft patency rates to the right coronary system are lower than those to the other systems and the impact of competitive flow appears greater. Few authors have compared the options for right coronary grafting in conjunction with BIMA Y grafting to the left system. Pevni *et al.* retrospectively analyzed the outcomes for the use of the right gastroepiploic artery, saphenous vein or the terminal segment of the RIMA from the composite graft for revascularization of the right system. There was a trend towards more perioperative complications in the terminal RIMA group but perioperative mortality and midterm survival and freedom from angina were similar (20). A randomized trial testing similar comparisons between the saphenous vein and the right gastroepiploic artery to the right coronary system incorporated a non-randomized group of terminal RIMA grafts from a BIMA Y configuration for analysis. There were no reported differences in clinical outcomes and at three-year protocol angiography the

saphenous vein graft patency was significantly greater than that of the right gastroepiploic artery and the terminal RIMA. There were 20 graft occlusions for the arterial grafts which were inversely related to the functional stenosis in the right coronary artery. No difference was found between the terminal RIMA patency and that of the right gastroepiploic artery (21).

### Competitive flow

This is a study of largely protocol driven BIMA Y grafting. All reasonable coronary arteries with stenosis  $\geq 50\%$  received a bypass graft. As the RIMA usually extended from the LIMA to the right coronary system, there was a low threshold for creating a side to side anastomosis to any reasonable free wall coronary artery. At the commencement of this protocol driven procedure in 1994, the effect of competitive flow on IMA graft patency was unrecognized and throughout the program there remained no evidence to suggest that the threshold for anastomoses should change despite the increasing evidence that graft patency was related inversely to competitive flow. The data from Cleveland Clinic confirmed the effect of competitive flow but not that the risk of graft occlusion was such that the use of IMAs should be withheld in such situations (22). The data showed that there was no particular threshold of coronary stenosis at which arterial graft occlusion probability rose steeply. The findings from this study are consistent with the above. There is much conflicting data on the sensitivity of various grafts and configurations to the effects of competitive flow. It is likely that the lower the patency rates of grafts to each of the coronary artery systems, the greater the measurable effect of competitive flow. It also seems that larger arteries provide more competitive flow for the same severity of stenosis such that adding the measurement of the residual lumen diameter will provide a more predictive functional stenosis (21). There is insufficient evidence to indicate that there is a difference in effect on *in situ* versus free IMA grafts or between composite, sequential or individual grafts. However, this study did demonstrate that there is little difference between the effects of competitive flow on end to side and side to side anastomoses.

If right coronary revascularization can be performed with the terminal portion of the free RIMA from the BIMA Y composite graft with outcomes equivalent to the use of an alternative conduit, that would be appropriate. However, in this study there was a 4.3% incidence of right phrenic nerve injury resulting

from the extended RIMA harvesting required to gain sufficient length for optimal revascularization of triple vessel disease. As previously reported, most of the phrenic neuropraxias are reversible (6) but the question remains, whether it would be better to harvest 900 additional coronary bypass conduits or accept 43 phrenic neuropraxias. The other factor that is difficult to evaluate is the increased risk of deep sternal wound infection. The incidence is higher after BIMA harvesting compared to single IMA harvesting and it is likely that extended RIMA harvesting is worse than limited RIMA harvesting (23). If only a short segment of free RIMA is required, only a short segment should be harvested. Diabetics have a higher incidence of wound infection than non-diabetics but it may be that the management of the diabetes in the perioperative period contributes to the risk of infection as much as the disease itself (24).

The long term survival of patients in this series closely matches that of a very similar demographic cohort of 5,766 patients reported by Tatoulis *et al.* using non-composite BIMA grafts (15). The analysis of the 991 symptom-driven angiograms showed the IMA graft patency rates to be higher than those in the current study. However, many of those angiograms identified saphenous vein graft deterioration as the cause of symptoms. There were very few vein grafts in this study and so those patients who presented for angiography due to graft dysfunction did so with IMA graft dysfunction.

### Study limitations

This is not a direct patient follow-up analysis. Data relating to the incidence of death, post-discharge angiography and late surgical re-intervention were obtained through databases. Although this method has routinely provided better than 98% accuracy when checked against direct patient follow up, there remains the potential to underestimate the incidence of late adverse events. The study cohort was largely selected by protocol and therefore no control group existed. It is difficult to compare the angiographic graft patencies in this study to those of other symptom-driven angiogram analyses due to the paucity of vein grafts in this study. Analysis of predictors of anastomotic patency did not account for within patient variables or time to angiography. The absolute numbers of side-to-side anastomoses to the LAD, diagonal, posterior descending and right coronary arteries were low and did not allow comparison of anastomotic types for these vessels.

In conclusion, the perioperative and late outcomes of full myocardial revascularization purely with BIMA Y composite grafts are similar to those using BIMAs and additional conduits in other configurations. Competitive flow in the native coronary artery reduces the anastomotic patency rate of arterial grafts but there is no clear threshold beyond which arterial grafts should not be used.

## Acknowledgements

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