

Bilateral Versus Single Internal Mammary Artery Use in Coronary Artery Bypass Grafting: A Propensity Matched Analysis



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Background

Bilateral internal mammary artery (BIMA) grafts have demonstrated superior long-term outcomes compared with single internal mammary artery (SIMA) grafts. Despite this, BIMA remains widely underutilised due to perceived technical challenges and concerns regarding wound healing. We sought to examine the morbidity and mortality associated with BIMA use in a propensity-matched cohort of patients.

Methods

From 2009 to 2016, 3,594 consecutive patients underwent coronary artery bypass surgery at three affiliated institutions. Thirty-day (30) mortality and morbidity data were collected prospectively. Propensity-score matched analyses were performed for BIMA versus SIMA use controlling for a number of preoperative characteristics.

Results

Overall, 29% of procedures were performed off pump, with a greater proportion in the BIMA group (43% vs. 21%, $p < 0.001$). In the propensity-score analysis consisting of 820 matched pairs, there were similar rates of 30-day mortality (1.3% BIMA vs. 0.9% SIMA, $p = 0.48$) and deep sternal wound infection (1.1% BIMA vs. 0.9% SIMA, $p = 0.84$). The rate of superficial sternal wound infection trended towards being higher in the BIMA group (2.6% vs. 1.3%, $p = 0.077$). The rates of red blood cell transfusions (27.4% vs. 27%, $p = 0.217$), other blood product transfusions (18% vs. 20%, $p = 0.217$), and reoperation for bleeding (2.9% vs. 2.1%, $p = 0.349$) were similar.

Conclusions

Bilateral internal mammary artery use was associated with similar rates of deep sternal wound infection compared to SIMA use, with a preponderance of superficial sternal wound infections that did not result in increased mortality or transfusion requirements. The use of BIMA should be more widely considered for coronary artery bypass surgery.

Keywords

Coronary artery bypass surgery • Arterial revascularisation • Deep sternal wound infection

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Introduction

The choice of the second conduit after the left internal mammary artery in coronary artery bypass grafting (CABG) remains an important topic of debate. Internal mammary arteries have demonstrated superior long-term patency rates compared to saphenous vein grafts, likely due to their relative resistance to atherosclerosis [1]. Although the final 10-year results of the randomised Arterial Revascularization Trial (ART) are awaited [2], bilateral internal mammary artery (BIMA) use has been repeatedly shown in large scale observational and meta-analyses to have superior long-term survival when compared to a single internal mammary artery (SIMA) use [3]. Despite these encouraging results, many surgeons are reluctant to adopt this technique due to perceived technical challenges associated with conduit harvesting, prolonged operative times, difficulties with obtaining adequate conduit length, and concerns regarding sternal wound healing particularly in obese and diabetic patients [4].

It has been suggested that, with experience, appropriate patient selection, and the use of a skeletonised harvesting technique to minimise chest wall trauma [5], these issues can be overcome. To assess this, a propensity-matched analysis was performed in all patients undergoing isolated CABG with BIMA versus SIMA use in a centre with considerable experience in this operation [6].

Methods

Between January 2009 and October 2016, 3594 consecutive patients underwent CABG at one of three affiliated institutions (Royal Prince Alfred Hospital, Strathfield Private Hospital or Macquarie University Hospital, Sydney, Australia). In total, 1,297 patients had BIMA use, and the remaining 2,297 had SIMA only. Data was prospectively collected for these patients including patient demographics, preoperative risk factors, operative technique, and 30-day postoperative mortality and morbidity. Approval for the study was granted by the local Human Ethics Review Committees.

All patients had full median sternotomy and those with minimally invasive incisions such as anterior thoracotomy or hemi-sternotomy were excluded. Deep sternal wound infection was defined as an infection involving muscle and bone, with or without mediastinal involvement as demonstrated by surgical exploration and one of either positive cultures or treatment with antibiotics. Superficial sternal wound infection was defined as either clinical or microbiological evidence of infection involving the subcutaneous presternal tissues only.

Operative Techniques

All patients were considered for BIMA harvest where the conduit was available and where there were no prohibitive comorbidities. These included morbid obesity, severe chronic obstructive pulmonary disease (COPD), poorly controlled diabetes, chest wall deformity, previous radiotherapy

or proximal inflow occlusion such as subclavian artery stenosis. Internal mammary arteries were meticulously dissected and skeletonised by ligating branches with ligaclips or with the aid of the Harmonic scalpel (Ethicon, Somerville, MA, USA). The skeletonised technique was used to minimise chest wall trauma and to maintain collateral inflow to the sternum as well as to maximise length of conduit. All conduits in our series were harvested with the skeletonised technique or occasionally in a “semi-skeletonised” fashion, whereby the artery was dissected out and branches ligated along with its venae comitantes but leaving the surrounding fascia, connective tissue and muscle intact. Heparin was then administered in the usual fashion prior to distal division of the artery. Topical papaverine was applied for spasm prophylaxis.

The graft configuration and surgical technique (on-pump versus off-pump) varied amongst surgeons. The left IMA (Internal Mammary Artery) was most commonly grafted to the left anterior descending artery, although where conduit length permitted, this was occasionally grafted with a right IMA. Amongst the surgeons who preferred off-pump surgery, the right IMA was kept as an in situ graft and extended end-to-end with a radial artery. This composite graft is then passed either across the front of the aorta or behind through the transverse sinus to reach around to the lateral wall and then posteriorly in a series of sequential anastomoses. This technique of total-arterial, anaortic, off-pump CABG has been described previously [7]. Amongst the surgeons who preferred on-pump CABG, the right IMA was either left in situ, or used as a free graft from the aorta or in a T-configuration from the left IMA. This was supplemented by radial and/or vein grafts.

In most cases, the sternum was closed with single or double sternal wires according to surgeon preference. In some patients who were considered suitable based on body weight and following intraoperative assessment of sternal bone quality, they were closed using a series of looped polydioxanone (PDS) sutures (Ethicon). The impact of the varied closure techniques is the subject of another analysis.

Statistical Methods

Propensity-score calculation and matching was used to adjust for confounding factors. These included 23 baseline characteristics: age, sex, body mass index (BMI), Euroscore I, the presence of pulmonary hypertension, operative status (elective vs. urgent), smoking history, current smoking status, diabetes in particular insulin dependent diabetes, respiratory disease, hypercholesterolaemia, hypertension, redo-sternotomy, previous cerebrovascular accident (CVA), peripheral vascular disease (PVD), New York Heart Association (NYHA) classifications 3 and 4 for heart failure, left main disease of 50% or more, number of diseased vessels, dialysis dependent renal failure, immunosuppressive therapy, and whether the surgery was performed on-pump or off-pump. Propensity scoring was performed using logistic regression to generate a

propensity score and patients were matched using nearest neighbour matching on a 1:1 basis without match replacement using a caliper width of 0.05.

Within the matched sample, paired t tests were used for continuous data, whereas the McNemar's test was used for categorical outcomes. Statistical significance was defined as $p < 0.05$. All analyses were performed with SPSS statistical software version 23 (IBM, Armonk, NY, USA).

Results

Patient Demographics

In the unmatched cohort (Table 1), there were a number of differences in baseline characteristics between the two groups. As might be expected, patients in the BIMA group were generally lower risk than those in the SIMA group; they were younger (mean age of 63.5 compared with 67 in the SIMA group, $p < 0.001$), more likely to be male (87% vs. 79%, $p < 0.001$) and a greater proportion of them underwent elective surgery (36% vs. 32.2%, $p < 0.023$). The BIMA group

also had a lower incidence of diabetes (30% vs. 39%, $p < 0.001$), respiratory disease (7.2% vs. 12.5%, $p < 0.001$), redo sternotomies (0.8 vs. 2.8%, $p = 0.005$), slightly lower BMI (28.5 vs. 28.9, $p = 0.007$), heart failure associated with NYHA class III or class IV symptoms (6.9% vs. 10% $p = 0.005$) and accordingly had lower Euroscores (4.3 vs. 5.8 $p < 0.001$) [8]. Conversely, those in the BIMA group had more diffuse coronary disease, with 2.7 diseased vessels per patient on average compared with 2.56 in the SIMA group ($p < 0.001$).

Over 40% of patients receiving BIMA had off-pump surgery, compared with just over 20% in the SIMA group ($p < 0.001$). This likely reflects differences in surgeon preference as the "off-pump" surgeons in our institution also favoured a technique of total arterial, anaortic coronary surgery which necessitated the use of bilateral mammary arteries.

Perioperative Outcomes

Propensity score matching yielded two well-matched groups of 820 patients each (Table 1). Although we

Table 1 Preoperative characteristics for unmatched and propensity-matched groups.

	Unmatched n = 3,594			Matched n = 1,640		
	BIMA (n = 1,297)	SIMA (n = 2,297)	P value	BIMA (n = 820)	SIMA (n = 820)	P value
Age (mean)	63.5	66.8	<0.001	64.1	64.3	0.552
Sex (male)	86.8%	79%	<0.001	85.2%	82.8%	0.192
BMI	28.5	28.9	0.007	28.6	28.7	0.513
Euroscore I	4.33	5.75	<0.001	4.72	5.31	0.053
Pulmonary hypertension	1.7%	1.9%	0.584	1.8%	2.2%	0.719
Operative status (elective)	36%	32.2%	0.023	35.1%	33%	0.404
Hypercholesterolaemia	60.8%	66.9%	<0.001	65.4%	67.4%	0.396
Hypertension	77%	80.9%	0.005	79.9%	81.2%	0.518
Smoker – previous	59.5%	60.3%	0.643	60%	63.3%	0.200
Smoker – current	15.5%	17.5%	0.126	18.5%	20%	0.487
Diabetes mellitus	30%	38.8%	<0.001	33.3%	36.8%	0.147
Diabetes mellitus (insulin)	10.2%	12%	0.155	8.3%	8.7%	0.754
Respiratory disease	7.2%	12.5%	<0.001	8.5%	10.1%	0.287
Redo sternotomy	0.8%	2%	0.005	0.9%	1.1%	0.791
CVA	3.5%	3.5%	0.977	3.9%	3.7%	0.896
PVD	9.4%	9.3%	0.906	11.2%	11.3%	1.00
LM disease $\geq 50\%$	30.7%	27.9%	0.068	30.2%	31.5%	0.629
No. diseased vessels	2.7	2.56	<0.001	2.68	2.70	0.341
Dialysis (renal failure)	1.5%	1.9%	0.365	2.1%	1.3%	0.345
Imm. Rx	0.5%	1.4%	0.014	0.6%	2.2%	0.011
LVEF (mod/sev)	14.2%	18.9%	<0.001	16.6%	20.2%	0.069
Off pump	43.3%	21.1%	<0.001	41.8%	37%	0.007
NYHA (III/IV)	6.9%	10.1%	0.005	7.2%	7.2%	1.00

Abbreviations: BMI, body mass index; CVA, cerebrovascular accident; PVD, peripheral vascular disease; LM disease $\geq 50\%$, left main disease greater than or equal to 50%; Imm. Rx, immunosuppressive therapy; LVEF (mod/sev), moderate or severely impaired left ventricular ejection fraction; NYHA (III/IV), class III or IV New York Heart Association functional classification

attempted to match for surgical technique, there remained a higher proportion of off-pump operations in the BIMA group (42% vs. 37%, $p = 0.007$) but with less discrepancy than in the unmatched cohort. Of the procedures that were performed on-pump, cardiopulmonary bypass and cross clamp times were similar between groups (80.8 mins compared with 80.2 mins and 59.7 mins versus 58.5 mins, $p = 0.75$ and $p = 0.39$ respectively). After matching for disease severity, both groups received a comparable number of grafts (3.17 for BIMA versus 3.15 for SIMA, $p = 0.76$). The number of arterial distal anastomoses was expectedly higher in the BIMA group (2.77 vs 1.87, $p < 0.001$).

Postoperative outcomes for both matched and unmatched groups are presented in Table 2. In the matched cohort, BIMA use trended towards an increased risk for superficial sternal wound infection (SSWI) (2.6% vs. 1.3%, $p = 0.077$) although this did not reach statistical significance (Table 2F). There were similar rates of deep sternalwound infection (DSWI) (1.1 vs. 0.9%, $p = 0.804$), sepsis (0.2% for each group), readmission for DSWI (0.6% versus 0.4%, $p = 0.73$) and 30-day mortality (1.3% vs. 0.9%, $p = 0.481$) (Table 2J,K).

Harvesting of bilateral mammary arteries was not associated with more bleeding complications. In fact, BIMA patients were transfused less packed red cells and other blood products than the SIMA patients; 0.98 units versus 1.45 units of packed cells, $p = 0.006$, 0.23 versus 0.37 units of platelets, $p = 0.007$ and 0.54 versus 0.97 units of fresh frozen plasma, $p = 0.001$. Take-back for bleeding was similar between groups (2.9% vs. 2.1%, $p = 0.349$).

A number of outcomes however, seemingly favoured SIMA use. These included requirement for inotropic support postoperatively (75% vs 53% for BIMA vs SIMA respectively, $p = 0.003$), new postoperative arrhythmia (21% vs 8%, $p < 0.001$) and respiratory failure requiring positive pressure ventilation (2.1% versus 0.9%, $p = 0.052$) (Table 2B,C). Other respiratory complications such as re-intubation, clinically significant pleural effusion and prolonged ventilation did not differ between groups.

Discussion

A substantial body of observational studies and meta-analyses suggests that the use of bilateral mammary arteries is associated with a significant reduction in overall mortality at 10 years [3,9–13]. The addition of a right internal mammary conduit to the graft configuration is also viewed by many contemporaneous surgeons as being crucial to achieving total arterial revascularisation [14]. Both the European and US guidelines recommend the use of BIMA in those under 70 years old (class IIA recommendation) [15,16]. In spite of this, most patients currently receive one mammary artery only with an estimated 4–12% receiving bilateral mammaries [13]. Barriers to the universal adoption of bilateral mammary artery use include surgical complexity and concerns over sternal wound complications [4].

Previous reports have suggested that the benefits of BIMA can be extended to higher risk subgroups of patients such as those with diabetes [17], renal failure [18], advanced age [19,20] and in females [21]. As such, the surgeons in our study institutions adopted a relatively liberal approach to use of bilateral mammary arteries, where more than one third of the cohort received BIMAs. Patients usually had to have reasons to not receive bilateral mammaries, rather than the converse. Using this approach, about a third of patients receiving bilateral mammaries had diabetes mellitus, 8% of these with insulin dependent diabetes, 8% with respiratory disease, 19% were smoking at the time of surgery and the average BMI was 28.6. Even with this significant risk burden, deep sternal wound infections occurred infrequently, at just over 1% in the BIMA group and there was no increase in rates of redo sternotomy for bleeding, transfusion requirements or 30 day in hospital mortality. Our study suggests that with meticulous dissection and careful skeletonisation of the mammary artery, acceptable and safe outcomes can be achieved even in those traditionally considered too high risk. Due to changing referral patterns and patient demographics, it may no longer be feasible or reasonable to limit the use of BIMA to patients with normoglycaemia, normal body habitus or without other risk factors.

A significant proportion of the cases in the present series were performed off pump, largely dependent on surgeon preference and familiarity rather than patient selection. More than 40% of cases in the BIMA group were performed on pump, which was slightly higher than the 37% in the SIMA group despite our best attempts to match the cohorts. The use of a bypass circuit has been associated with coagulopathy and systemic inflammatory response syndrome [22] which may have influenced transfusion and postoperative inotrope requirements. A detailed analysis of on pump versus off-pump surgery and the effect of various graft configurations is beyond the scope of this paper but it is important to note that BIMA grafting can be performed safely and with acceptable results both ways. The convention for the “off pump surgeons” in our institutions was to maintain patients on a low dose milrinone infusion (0.2 $\mu\text{g}/\text{kg}/\text{min}$) for up to 12 hours postoperatively as a systemic vasodilator when using all arterial conduits [7]. This explains the increased use of cardiac inotropes in our BIMA group and possibly increased rates of postoperative arrhythmias.

Despite the large volume of observational data conferring a survival advantage to use of bilateral mammaries, a contradiction exists between observational and randomised studies. To date, there have been four randomised controlled trials (RCTs) comparing outcomes of BIMA and SIMA [2,23–25]. All of these trials show similar survival following BIMA and SIMA grafting. In the most recently published and largest of these, the Arterial Revascularization Trial (ART) [2], mortality was 8.7% after BIMA grafting and 8.4% following SIMA grafting at 5 years, $p = 0.77$. Several reasons have been proposed to explain this discrepancy between observational and randomised data. Firstly, the rate of vein graft failure within 5 years may not be high enough to have an

Table 2 Intraoperative and postoperative outcomes for unmatched and propensity-matched groups.

	Unmatched n = 3,594			Matched n = 1,640		
	BIMA (n = 1,297)	SIMA (n = 2,297)	P value	BIMA (n = 820)	SIMA (n = 820)	P value
A) INTRAOPERATIVE						
CPB (mins)	78.7	82.5	0.002	80.8	80.2	0.754
Cross clamp (mins)	58	59	0.082	59.7	58.5	0.388
No. distals	3.15	2.98	<0.001	3.17	3.15	0.762
No. arterial distals	2.81	1.75	<0.001	2.77	1.87	<0.001
B) CARDIAC						
New arrhythmia	18.3%	18.5%	0.893	21%	8%	<0.001
Perioperative MI	0%	0%	–	0	0%	–
Pericardial effusion	0.7%	0.7%	0.990	0.7%	0.2%	0.289
Cardiac inotropes (> 4 hours post op)	69.4%	59.9%	<0.001	74.5%	53.2%	0.003
C) RESPIRATORY						
Post-op ventilation hours	15.9	22.6	0.001	16.8	20.2	0.088
Reintubation	2.5%	3.2%	0.247	3.4%	2.7%	0.480
Pneumonia	1.5%	1.8%	0.469	1.7%	1.1%	0.405
Pleural effusion	6.7%	10%	0.001	7.4%	7.1%	0.849
Pneumothorax	0.3%	0.9%	0.036	0.2%	0.7%	0.289
Prolonged air leak	0%	0.1%	0.287	0%	0%	–
Resp failure — CPAP	1.8%	1.4%	0.343	2.1%	0.9%	0.052
Prolonged ventilation >24 hrs	4.5%	7.6%	<0.001	5.7%	6.3%	0.682
DVT	0.6%	0.6%	0.850	0.7%	0.1%	0.063
PE	0.2%	0.2%	0.887	0.1%	0%	1.00
Pulmonary oedema	0%	0.2%	0.132	0%	0.2%	0.500
D) BLEEDING COMPLICATIONS						
Drain loss (4 hrs, mls)	297	279	0.047	307	327	0.231
Blood product requirement (pRBC)	24.9%	32.9%	<0.001	27.4%	27%	0.217
Blood product requirement (non-RBC)	16.5%	19.7%	0.018	17.6%	20.1%	0.217
pRBC (No. units)	0.95	1.48	<0.001	0.983	1.45	0.006
Platelets (No. units)	0.243	0.317	0.011	0.233	0.371	0.007
FFP (No. units)	0.537	0.755	0.002	0.539	0.968	0.001
FVII (units)	0.016	0.015	0.916	0.015	0.025	0.667
Cryoprecipitate (No. units)	0.435	0.585	0.125	0.394	0.598	0.183
E) REOPERATION						
Any cause	6.5%	6.3%	0.856	6.6%	4.1%	0.034
Graft failure	0.3%	0.3%	0.840	0.4%	0.1%	0.625
Bleeding	2.8%	2.5%	0.599	2.9%	2.1%	0.349
F) INFECTIOUS						
SSWI	3.1%	1.4%	0.001	2.6%	1.3%	0.077
DSWI	1.2%	0.8%	0.182	1.1%	0.9%	0.804
Sepsis	0.2%	0.5%	0.119	0.2%	0.2%	1.00
UTI	1.5%	1.8%	0.523	1.5%	0.9%	0.289
G) NEUROLOGICAL						
Stroke	0.5%	1.0%	0.143	0.7%	0.6%	0.791
TIA	0.2%	0.1%	0.857	0.2%	0.2%	1.00
H) RENAL						
ARF	2.8%	3.7%	0.156	3.5%	3.3%	0.890
ARF requiring dialysis	1.0%	2.4%	0.004	1.5%	2.8%	0.082

Table 2. (continued).

	Unmatched n = 3,594			Matched n = 1,640		
	BIMA (n = 1,297)	SIMA (n = 2,297)	P value	BIMA (n = 820)	SIMA (n = 820)	P value
I) GASTROINTESTINAL COMPLICATIONS						
Gastrointestinal bleeding	0.5%	0.8%	0.255	0.6%	0.4%	0.727
Ileus	0.6%	0.6%	0.981	0.7%	0.4%	0.508
Any complication	1.2%	1.0%	0.760	1.2%	0.9%	0.629
J) RE-ADMISSION						
30 day (any)	7.2%	6.6%	0.480	7.3%	5.5%	0.147
DSWI	0.6%	0.3%	0.249	0.6%	0.4%	0.727
K) OTHER						
MACCE	2.1%	2.7%	0.250	2.6%	1.7%	0.310
Multisystem failure	0.1%	0.1%	0.920	0.1%	0%	1.00
30 day mortality	1.1%	1.2%	0.791	1.3%	0.9%	0.481
Delayed mobilisation	7.2%	10.8%	0.001	9.4%	11.6%	0.162

Abbreviations: CPB, cardiopulmonary bypass; Perioperative MI, perioperative myocardial infarction; respiratory failure; CPAP, continuous positive pressure ventilation; DVT, deep vein thrombosis; PE, pulmonary embolus; pRBC, packed red blood cells; FFP, fresh frozen plasma; FVII, Factor VII concentrate; SSWI, superficial sternal wound infection; DSWI, deep sternal wound infection; UTI, urinary tract infection; TIA, transient ischaemic attack; ARF, acute renal failure; MACCE, major adverse cardiac and cerebrovascular events

adverse effect and the anticipated benefits of BIMA may become evident closer to the 10 year mark [26,27]. In the ART trial, there was also a high rate of crossover in the group allocated to BIMA (14%) and excellent compliance with optimal medical therapy, both of which can dilute the treatment effect. It is, of course, plausible that in non-randomised studies, unmeasured confounders rather than revascularisation strategy are responsible for the survival advantage seen in patients receiving BIMA [28]. Even if this were the case, there is still good evidence to show that use of multiple arterial grafts positively affects other cardiac endpoints such as myocardial infarction, symptom recurrence and need for repeat revascularisation [29,30]. Until longer follow-up data of the ART study and other randomised trials is available, the optimal revascularisation strategy still favours bilateral mammaries over that of a single mammary.

Almost half of the conduits in the ART trial were harvested in a pedicled fashion and this likely contributed to higher rates of sternal reconstruction in the bilateral mammary group at 1.9%. It has been suggested that by using a skeletonised technique, the risk of sternal wound complication with BIMA grafting is similar to that of a pedicled single mammary, whereas skeletonising a single internal mammary did not confer any additional benefit over that of a pedicled conduit [5]. In the present series, all of the conduits were routinely taken down in a skeletonised fashion with a resulting deep sternal wound infection rate of 1.1% in the bilateral mammary group and no significant increase in superficial sternal wound infections.

Several limitations of the current study must be acknowledged. It is a retrospective analysis of prospectively collected

data. Even though we adjusted for as many potential cofounders as possible in our propensity score matching, the effect of unknown or unobserved confounders cannot be eliminated. Less tangible factors such as patient frailty, graftability and location of the target vessels and familiarity and comfort of the surgeon all influence conduit selection. These considerations are difficult to quantify and are a common limitation of non-randomised data. There was also a substantial bias by two of the surgeons in our group towards use of bilateral mammary arteries to facilitate the anaortic off pump bypass strategy and again, the effect of using an off-pump technique and subsequent differences in conduit configuration on outcomes is difficult to measure. Finally, our analysis includes only 30-day and in-hospital outcomes and does not provide longer term clinical endpoints such as freedom from symptoms, mortality and redo revascularisation.

Conclusion

Bilateral internal mammary artery harvest is associated with low rates of bleeding, transfusion requirements and redo sternotomy with acceptable rates of sternal wound complications. It can be performed safely even in the higher risk cohort using the skeletonised technique and should be more widely considered and utilised.

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