European Journal of Cardio-Thoracic Surgery 41 (2012) 770–776
doi:10.1093/ejcts/ezr213 Advance Access publication 20 January 2012

ORIGINAL ARTICLE

Propensity matched analysis of bilateral internal mammary artery versus single left internal mammary artery grafting at 17-year follow-up: validation of a contemporary surgical experience†

Juan B. Grau[a,b,*], Giovanni Ferrari[b], Andrew W.C. Mak[c], Richard E. Shaw[c], Mariano E. Brizzio[a], Bruce P. Mindich[a], John Strobeck[c] and Alex Zapolanski[a]

[a] The Valley Columbia Heart Center, Columbia University College of Physicians and Surgeons, Ridgewood, New Jersey, USA
[b] University of Pennsylvania School of Medicine, Philadelphia, PA, USA
[c] The Valley Columbia Heart Center, Ridgewood, NJ, USA

* Corresponding author. The Valley Columbia Heart Center, 223 North Van Dien Avenue, Ridgewood, NJ 07450, USA. Tel: +1-201-4478377; fax: +1-201-4478658; e-mail: jbg2136@columbia.edu (J.B. Grau).

Received 23 August 2011; received in revised form 17 October 2011; accepted 25 October 2011

Abstract

OBJECTIVES: Bilateral internal mammary arteries (BIMA) remains widely underutilized in coronary artery bypass grafting (CABG). Although prior research has demonstrated a long-term benefit of the use of BIMA over left internal mammary artery (LIMA)-only, validation of these results is lacking in a contemporary surgical experience. We compared complications and survival at 17-year follow-up in a large series of consecutive CABG patients from a single institution that underwent BIMA grafting with a propensity-matched group where LIMA only was used.

METHODS: Propensity scores representing the estimated probabilities of patients receiving either BIMA or LIMA alone were developed based on 22 observed baseline covariates in a logistic regression model with procedure group as the dependent variable. The nearest-neighbour-matching algorithm with Greedy 5-1 Digit Matching was used to produce two patient cohorts of 928 patients each balanced for baseline factors. We compared 30-day morbidity and mortality, as well as long-term survival at 5-year intervals up to 17-year follow-up.

RESULTS: In-hospital and 30-day mortality was 0.8% for the BIMA group and 1.1% for the LIMA-saphenous vein grafting (SVG). No significant difference was found in complications, mortality and/or length-of-stay between these two groups. Off-pump was done in 48.9% of BIMA cases and 51.3% of LIMA cases. Regardless of the types of grafts used, on-pump patients were more likely to have postoperative permanent strokes and longer postoperative lengths of stay. Use of the BIMA over LIMA-only had a statistically significant impact conferring a 10% survival advantage at 10-year and 18% at 15-year follow-up. The Kaplan–Meier survival curves comparing off-/on-pump BIMA and off-/on-pump LIMA-SVG patients demonstrated a 22% survival advantage for off-pump BIMA patients when compared with on-pump LIMA-SVG patients at 15-year follow-up.

CONCLUSIONS: Perioperative complications do not increase with the use of BIMAs. Long-term survival is optimized with off-pump CABG and BIMA grafting. The low morbidity and mortality rates in this series are likely due to the continuous evolution of technology and the adoption of less invasive options for CABG patients. A more widespread use of BIMAs in CABG patients would continue to improve the overall excellent short- and long-term results of this operation.

Keywords: Coronary artery bypass • Mammary arteries • Off-pump

INTRODUCTION

The use of bilateral internal mammary arteries (BIMA) grafting has been documented to be advantageous over left internal mammary artery (LIMA) grafting [1–5]. Although some surgeons still question its overall effectiveness in coronary artery bypass grafting (CABG) surgery, BIMA grafting has been shown to significantly improve clinical outcomes [1] and increase long-term survival, even in patients with chronic kidney disease [2] and diabetes [3] and those who are 70 years of age or less [4, 5]. In-hospital and 30-day mortality rates for LIMA patients have also been reported to be 1.5–2.7 times higher than that of BIMA patients [2, 4]. However, the increased risk of sternal wound infections (SWIs) that has been associated with BIMA grafting remains unresolved. Some studies cite no increase in the risk of SWIs with BIMA grafting [6, 7], while others report an increased incidence of SWIs particularly in diabetic patients [8, 9]. Despite the risks involved, BIMA grafting appears to be highly effective at

† Presented at the 25th Annual Meeting of the European Association for Cardio-Thoracic Surgery, Lisbon, Portugal, 1–5 October 2011.

improving short- and long-term survival. Unfortunately, BIMA grafting is used sparingly and remains widely underutilized, accounting for only 4% of CABG procedures in the USA [10].

The objective of this study was to compare the perioperative risks, complications, outcomes, in-hospital (up to 30 days) and long-term survival in a large series of consecutively isolated CABG patients who underwent BIMA grafting versus LIMA grafting between 1994 and 2010. Data from two propensity-matched groups of patients selected from this contemporary experience were analysed.

MATERIALS AND METHODS

Patient population

This study included patients who had isolated CABG procedures that utilized internal mammary artery (IMA) grafting performed at The Valley Heart and Vascular Institute between January 1994 and December 2010. Data were collected prospectively using standard elements and definitions from the Society of Thoracic Surgeons (STS) database. The database was approved by the local Institutional Review Board (IRB), and informed consent was waived for this study.

A total of 6313 patients with isolated CABG were available for inclusion in this study. Of these, 1459 procedures (23.1%) were performed using BIMA grafting and 4854 (76.9%) with LIMA-saphenous vein grafting (SVG). All available LIMA-SVG patients who had not undergone valvular or previous CABG surgeries were included. Patients undergoing procedures that involved the use of radial arteries as conduits and where bypass was performed on only one coronary artery were excluded. Preliminary comparisons of demographic and preoperative comorbidities are presented in Table 1.

Since the BIMA and LIMA-SVG groups were significantly different on a majority of the baseline characteristics, propensity-matching was used to provide a more balanced comparison between the groups. Baseline characteristics of the propensity-matched groups are presented in Table 2. The groups were well-balanced on all characteristics with the exception of age and body mass index (BMI), which were found to be significantly higher in the LIMA-SVG group (Table 2).

The overall goals of this study were to: (i) examine in-hospital and 30-day operative morbidity; and (ii) to compare long-term survival by assessing all-cause mortality. In-hospital and 30-day operative mortality outcomes were documented in the STS database and included in the analyses. Long-term mortality was ascertained by searching demographic information for each patient' in the social security death index (SSDI) database and matching it with death index records.

Surgical technique

Each patient underwent off-pump or on-pump CABG at the discretion of the surgeon, using either the BIMA or LIMA-SVG as the conduit(s) of choice. Mammary arteries were not skeletonized as it was not a routine practice at our institution. Of the total 928 propensity-matched BIMA patients, 454 (48.9%) procedures were performed without cardiopulmonary bypass (off-pump) and 474 (51.1%) with cardiopulmonary bypass (on-pump). Likewise, 476 (51.3%) LIMA-SVG patients underwent off-pump CABG, while 452 (48.7%) underwent on-pump CABG. Various factors factored in when deciding whether off-pump or on-pump CABG approach should be used, including difficulty level, characteristics of the aorta, target sizes, haemodynamic stability and tolerance to cardiac mobilization. The final decision was left entirely to the surgeon and evolved as more experience

Table 1: Baseline characteristics of all 6313 isolated coronary bypass graft surgery patients comparing use of BIMA and LIMA-SVG

	BIMA *N* (%), 1459 (23.1%)	LIMA-SVG *N* (%), 4854 (76.9%)	*P*-value
Age (mean ± SD)	58.6 ± 9	69.1 ± 10	<0.0001
BMI (mean ± SD)	27.8 ± 4	28.3 ± 5	<0.001
Gender (male)	1358 (93.1)	3306 (68.1)	<0.0001
History of smoking	922 (63.2)	3010 (62.0)	0.41
History of diabetes mellitus	100 (6.9)	1881 (38.8)	<0.0001
History of renal failure	14 (1.0)	316 (6.5)	<0.0001
Elevated cholesterol	996 (68.3)	3081 (63.5)	<0.01
History of hypertension	910 (62.4)	3667 (75.5)	<0.0001
Prior myocardial infarction	632 (43.3)	2446 (50.4)	<0.0001
Prior cerebrovascular accident	36 (2.5)	363 (7.5)	<0.0001
History of aardiovascular disease	44 (3.0)	482 (9.9)	<0.0001
History of peripheral vascular disease	102 (7.0)	712 (14.7)	<0.0001
Chronic lung disease	18 (1.2)	251 (5.2)	<0.0001
History of arrhythmias	80 (5.5)	536 (11.0)	<0.0001
Haematocrit	41.3 ± 4	38.5 ± 5	<0.0001
Left main disease	474 (32.5)	1659 (34.2)	0.23
Triple vessel disease	1240 (85.0)	3998 (82.4)	<0.001
Left ventricular ejection fraction	52 ± 11	49 ± 13	<0.0001

Table 2: Baseline characteristics of 928 propensity-matched isolated coronary artery bypass patients comparing use of BIMA and LIMA-SVG

	BIMA *N* (%), 928 (50.0%)	LIMA-SVG *N* (%), 928 (50.0%)	*P*-value
Age (mean ± SD)	60.9 ± 9	62.1 ± 9	<0.01
BMI (mean ± SD)	27.6 ± 4	28.9 ± 5	<0.001
Gender (male)	828 (89.2)	829 (89.3)	0.94
History of smoking	598 (64.4)	635 (68.4)	0.07
History of diabetes mellitus	100 (10.8)	101 (10.9)	0.94
History of renal failure	13 (1.4)	17 (1.8)	0.48
Elevated cholesterol	625 (67.3)	605 (65.2)	0.34
History of hypertension	631 (68.0)	641 (69.1)	0.62
Prior myocardial infarction	416 (44.8)	420 (45.3)	0.85
Prior cerebrovascular accident	35 (1.9)	23 (1.2)	0.11
History of cardiovascular disease	39 (2.1)	29 (1.6)	0.22
History of peripheral vascular disease	84 (4.5)	92 (5.0)	0.53
Chronic lung disease	17 (1.8)	20 (2.1)	0.96
History of arrhythmias	56 (3.0)	69 (3.7)	0.23
Haematocrit	41.1 ± 4	40.8 ± 5	0.74
Left main disease	304 (32.8)	295 (31.8)	0.66
Triple vessel disease	752 (81.0)	761 (82.0)	0.86
Left ventricular ejection fraction	52 ± 11	51 ± 12	0.09

was gathered with the off-pump platform. These data are not included in our analysis, since they were not documented for most of the patients in the series.

Off-pump cases were performed using a commercially available stabilizing device. Due to the fact that at least four different surgeons performed these procedures throughout the 17 years, there were some minor variations in surgical technique. There were nonuniform criteria for grafting sequences. Proximal anastomosis was performed using a partial occlusion clamp, and intracoronary shunts were used occasionally. For extremely calcified aortas, the 'no-touch technique' was applied.

Traditional cardiopulmonary bypass (on-pump) procedures were performed with the following standard techniques: central cannulation, roller pumps, membrane oxygenators, appropriate filters, antegrade and retrograde cardioplegia, and mild hypothermia at 30–34°C.

Data analysis

Data were prospectively collected and stored in a database certified by the Society of Thoracic Surgeons. Continuous data are displayed as means with standard deviation. Categorical data are expressed as proportions. Univariate statistical tests for continuous data included tests of mean differences using the Student's *t*-test. Categorical variables were analysed using the Chi-squared test. Survival was analysed using Kaplan–Meier survival curves. Multivariate analysis of long-term outcomes was analysed using Cox proportional hazards regression modelling, including in-hospital clinical and procedural variables as factors in the model. Propensity-matching was used to provide a more valid comparison between the groups. Propensity scores representing the estimated probabilities of patients receiving either BIMA or LIMA-SVG alone were developed based on 22 observed baseline covariates in a logistic regression model with procedure group as the dependent variable (All variables in Table 2 plus surgical acuity, pump status, arteries bypassed and use of intra-aortic balloon pump from Table 3 were used to construct the propensity model). The nearest-neighbour-matching algorithm with Greedy 5-1 Digit Matching was employed to find as many 1:1 matches between the surgical approaches based on the propensity scores to produce two balanced patient cohorts. A value of $P < 0.05$ was used to determine the statistical significance of all tests used. Analyses were performed using the SPSS statistical software package version 18.0 (IBM/SPSS Inc., Chicago, IL).

RESULTS

There was no statistically significant difference in terms of surgical acuity between the BIMA and LIMA-SVG patients; slightly more than half of each group underwent urgent CABG (Table 3). About half of the propensity-matched cases from each group (48.9% for BIMA and 51.3% for LIMA-SVG) were conducted off-pump, but there was no significant difference between the two groups. The only significant difference in surgery status between the two groups was in the number of arteries bypassed. The BIMA group had a slightly higher number of bypassed arteries when compared with the LIMA-SVG group (3.6 versus 3.4; $P < 0.0001$). STS-predicted mortality rates were similar for both the BIMA and LIMA-SVG groups (1.1 versus 1.2% respectively; $P = 0.14$).

Table 3: Surgical status and results comparing propensity-matched BIMA and LIMA-SVG patients

	BIMA *N* (%), 928 (50.0%)	LIMA-SVG *N* (%), 928 (50.0%)	*P*-value
Surgery acuity			
Elective	424 (45.7)	405 (43.6)	0.77
Urgent	482 (51.9)	498 (53.7)	
Emergent	21 (2.3)	23 (2.5)	
Emergent/salvage	1 (0.1)	2 (0.2)	
Arteries bypassed	3.6	3.4	<0.0001
Off-pump	454 (48.9)	476 (51.3)	0.31
Intra-aortic balloon pump used	89 (4.8)	96 (5.2)	0.59
STS-predicted mortality rate	1.1%	1.2%	0.14
Mortality (in-hospital to 30 Days)	7 (0.8)	10 (1.1)	0.47
Postoperative permanent stroke	5 (0.5)	5 (0.5)	1.00
Postoperative renal failure	6 (0.6)	7 (0.8)	0.78
Postoperative myocardial infarction	18 (1.0)	22 (2.4)	0.52
Reoperation for bleeding	10 (1.1)	16 (1.7)	0.24
Deep sternal wound infection	3 (0.3)	3 (0.3)	1.00
Sepsis	8 (0.9)	4 (0.4)	0.25
Postoperative atrial fibrillation	185 (19.9)	178 (19.2)	0.68
Required blood transfusion	332 (35.8)	292 (31.5)	<0.05
Post-surgery length of stay (days)	6.9 ± 4	6.9 ± 4	0.98

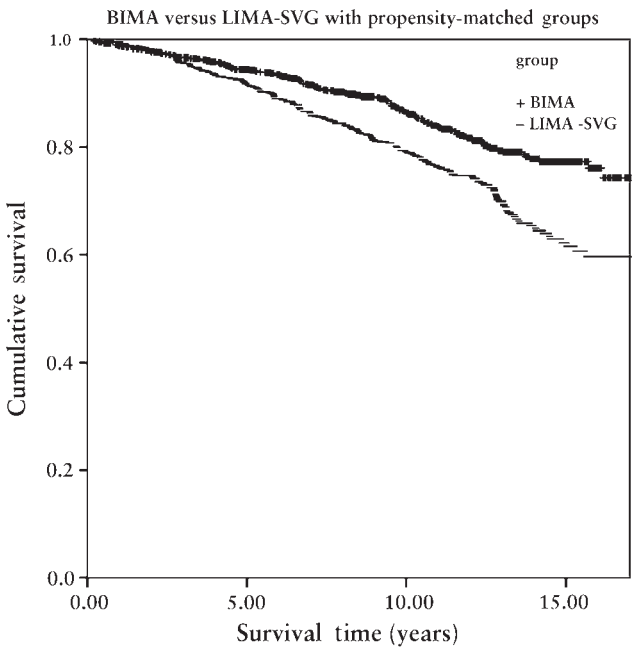

Figure 1: Kaplan–Meier survival curves comparing propensity-matched BIMA and LIMA-SVG patients ($P < 0.0001$).

In-hospital and 30-day mortality was similar between the BIMA and LIMA-SVG groups, 0.8 versus 1.1%, respectively; $P = 0.47$ (Table 3). Overall, there was no significant difference between perioperative complications and post-surgery length of stay. However, more BIMA patients required blood transfusions than LIMA-SVG patients (35.8 versus 31.5%; $P < 0.05$).

Average follow-up time for the cohorts was 9.0 ± 5 years. The use of the BIMA resulted in an overall long-term survival advantage for CABG patients when compared with those who had the LIMA-SVG utilized (Fig. 1). Initial long-term survival at 1 year for

both groups was very high (99%). Differences in survival were first observed at around 3 years, resulting in a 5% survival advantage for BIMA patients at 5 years (96 versus 91%). By 10 years, the long-term survival advantage increased to 10% (89 versus 79%) and was most pronounced at 15 years, conferring a survival advantage of 18% (79 versus 61%) for BIMA patients over LIMA-SVG patients.

Since age and BMI were statistically significantly different between BIMA and LIMA-SVG patients after propensity adjustment, a Cox proportional hazards regression analysis was used to determine the independent association of these factors with long-term survival. This analysis demonstrated that after controlling for the effects of patient age and BMI, patients receiving a LIMA-SVG procedure were almost one and a half times more likely to die compared with the BIMA patients (Hazard ratio (HR) = 1.485 [1.191–1.852, 95% confidence interval (CI)]; see Table 4).

Given the improved outcomes and mortality reported for patients undergoing CABG, the use of cardiopulmonary bypass (off pump versus on pump) was analysed. Observed in-hospital and 30-day mortality was not significantly different among off-/on-pump BIMA and off-/on-pump LIMA-SVG patients, although the STS-predicted mortality rate for on-pump LIMA-SVG patients was significantly higher than the other three subgroups (Table 5). However, on-pump patients had a higher prevalence of postoperative permanent stroke (1.1% for on-pump BIMA and 1.1% for on-pump LIMA-SVG; $P = 0.02$). On average, on-pump patients stayed in the hospital for almost 8 days, compared with 6 days for off-pump patients ($P < 0.0001$).

Table 4: COX proportional hazards regression model with adjusted hazard ratios (HR) and 95% confidence intervals (CI) for age and BMI to evaluate increased risk for late mortality in propensity-matched BIMA and LIMA-SVG patients

Factor	Adjusted HR	95% CI	*P*-value
Age	1.074	1.059–1.089	<0.0001
BMI	0.995	0.969–1.021	0.70
Use of LIMA-SVG versus BIMA	1.485	1.191–1.852	<0.0001

Long-term survival of off-pump versus on-pump BIMA and LIMA-SVG patients confirmed the superiority of BIMA over LIMA-SVG and off-pump over on-pump CABG (Table 6). First-year survival was identical for all the four subgroups of patients, while survival rates start to diverge at 3 years. By 15 years, the use of BIMA and off-pump techniques has bestowed a 22% survival advantage over their counterparts who underwent on-pump LIMA-SVG grafting (81 versus 59%). It appears that the advantageous effects of BIMA use override that of off-pump procedure use, which is indicated in the overall higher survival rates for on-pump BIMA patients when compared with off-pump LIMA-SVG patients.

Cox proportional hazards regression analysis was performed to determine the independent and unique association between baseline factors and risk of late mortality. This analysis demonstrated that increasing age, higher STS mortality risk score and the grouping of off-pump/on-pump status with BIMA/LIMA-SVG were significantly and independently associated with increased risk for late mortality (Table 7). Subgroup analysis of the pump status/IMA grouping showed that the patients having on-pump LIMA-SVG had nearly double the risk of late mortality compared with those patients who had off-pump BIMA (adjusted HR = 1.712 [1.203–2.438, 95% CI]; $P < 0.01$). This analysis confirms the independent increase in the risk of late mortality associated with patients having on-pump LIMA-SVG and the survival benefit from off-pump used with BIMA.

DISCUSSION

This retrospective study found that CABG patients who underwent BIMA grafting had significantly better long-term survival when compared with propensity-matched patients who underwent LIMA-SVG grafting. A significant survival advantage for BIMA patients was found throughout the 17-year follow-up period. This difference continued to diverge between the groups and became most pronounced at 15 years. Long-term survival rates at each time interval for these two patient groups were higher than those reported in other studies [2, 5, 10–12]. Thirty-day mortality rates for both groups were lower than STS-predicted rates and those cited in other similar studies [1, 4, 5, 10, 11]. Fewer in-hospital and 30-day deaths occurred in the BIMA group when compared with the LIMA-SVG.

Table 5: Surgical results comparing propensity-matched off-/on-pump BIMA and off-/on-pump LIMA-SVG patients

	BIMA off-pump *N* (%), 454 (48.9%)	BIMA on-pump *N* (%), 474 (51.1%)	LIMA-SVG off-pump *N* (%), 476 (51.3%)	LIMA-SVG on-pump *N* (%), 452 (48.7%)	*P*-value
Mortality (in-hospital to 30 Days)	5 (1.1)	2 (0.4)	5 (1.1)	5 (1.1)	0.63
Postoperative permanent stroke	0 (0.0)	5 (1.1)	0 (0.0)	5 (1.1)	<0.05
Postoperative renal failure	5 (1.1)	1 (0.2)	3 (0.6)	4 (0.9)	0.40
Postoperative myocardial infarction	6 (1.3)	12 (2.5)	15 (3.2)	7 (1.5)	0.18
Reoperation for bleeding	5 (1.1)	5 (1.1)	10 (2.1)	6 (1.3)	0.49
Deep sternal wound infection	0 (0.3)	3 (0.6)	0 (0.3)	3 (0.7)	0.11
Sepsis	2 (0.4)	6 (1.3)	2 (0.4)	2 (0.4)	0.28
Postoperative atrial fibrillation	83 (18.3)	102 (21.5)	81 (17.0)	97 (21.5)	0.20
Required blood transfusion	152 (33.5)	180 (38.0)	136 (28.6)	156 (34.5)	<0.05
Post-surgery length of stay (days)	6.3 ± 3	7.6 ± 4	6.1 ± 3	7.8 ± 6	<0.0001

Table 6: Kaplan–Meier results comparing BIMA/LIMA-SVG and pump status groups on long-term survival using log-rank test

Year(s) of follow-up	1 (%)	5 (%)	10 (%)	15 (%)
Off-pump BIMA	99	96	89	81
On-pump BIMA	99	95	88	78
Off-pump LIMA-SVG	99	92	80	61
On-pump LIMA-SVG	99	90	77	59

Off-pump BIMA versus on-pump LIMA-SVG $P < 0.001$.
On-pump BIMA versus on-pump LIMA-SVG $P < 0.01$.

Table 7: Cox proportional hazards regression model with adjusted hazard ratios (HR) and 95% confidence intervals (CI) for age, BMI, and STS mortality risk score to evaluate increased risk for late mortality in propensity-matched off-/on-pump BIMA and off-/on-pump LIMA-SVG patients

Factor	Adjusted HR	95% CI	*P*-value
Age	1.065	1.049–1.082	<0.0001
BMI	0.995	0.969–1.021	0.70
STS mortality risk	1.281	1.065–1.541	<0.01
Pump status with IMA Group[a]: off-pump BIMA versus on-pump LIMA-SVG	1.712	1.203–2.438	<0.01

[a]Overall group significantly associated with late mortality $P = 0.001$.

The number of arteries bypassed for both the LIMA and BIMA groups were higher than the national STS average, which can be explained by increased efforts of surgeons to achieve a more complete revascularization in the patients undergoing BIMA grafting, who are typically younger [13]. Interestingly, a higher number of BIMA patients needed blood transfusions than LIMA patients, which is in concordance with prior published reports [14, 15] and is likely related to a more extensive dissection necessary for the harvesting of both IMAs.

No increase in perioperative complications was found when BIMA grafting was used. This finding serves to assuage surgeons' concerns that BIMA grafting increases the risk for complications, such as SWIs, postoperative MIs, and postoperative stroke. In fact, BIMA grafting has been shown to yield similar or lower rates of SWIs when compared with other grafting procedures [6]. Additionally, skeletonization of the IMAs during harvesting has been shown to minimize the likelihood of SWIs [16], particularly in diabetic patients [17, 18]. In our study, we did not control for this variable as most surgeons involved in this study did not routinely skeletonize either mammary artery.

Although this is not the first retrospective study examining short- and long-term mortality and complications between BIMA and LIMA-SVG patients, our study represents one of the largest retrospective propensity-matched studies in terms of size of patient population and length of follow-up. It is, however, the largest study examining these differences in a contemporary series of patients. Similar studies analysed patients who underwent procedures from 1971 to 1995, whereas our experience extends from 1994 to 2010 [1, 10, 12]. Our contemporary series of patients underwent CABG procedures more recently, where technology, surgical techniques, and other procedural factors are likely more advanced and refined than they were in the 1970s and 1980s.

Our results demonstrated a significant interplay between conduit selection and pump status. The increased use of off-pump CABG procedures has been shown to result in overall lower stroke rates and stroke-related mortalities in the published literature [19, 20]. This finding has been confirmed in our series, in addition to lower postoperative lengths of stay. In addition, we found that the use of BIMA in conjunction with off-pump surgery resulted in a statistically significant improvement in long-term survival. This confirms that conduit selection and pump status provide an independent and unique additive benefit, which was confirmed by the multivariate Cox proportional hazards regression model comparing off-pump BIMA with on-pump LIMA-SVG. This fact was further supported by the Kaplan–Meier analysis comparing on-pump BIMA versus on-pump LIMA-SVG.

The differential survival advantage conferred by the use of BIMA over LIMA in our study, particularly at 15 years, was greater than that reported in other studies [1, 5, 10, 12]. Our findings add to the growing literature that asserts the superiority of BIMA over LIMA use, particularly in terms of improved short- and long-term mortality with no significant increase in perioperative complications for CABG patients, despite the increased operative time, technical skill and demands of the procedure.

It has been reported that IMAs have atheroprotective effects through increased synthesis of potent vasodilators like nitric oxide and decreased production of vasoconstrictors such as endothelin-1 and angiotensin-II [21]. Moreover, IMAs have also been found to transmit their atheroprotective properties and increase collateral circulation to recipient vessels thereby preserving myocardial viability and improving overall post-CABG outcomes [21]. These factors may have contributed to the survival advantage observed in our cohort that received BIMA.

Translational studies have also been conducted to analyse the different aspects between the IMAs and other conduits, such as the radial artery and saphenous vein. Differential gene expression, protein levels and histological features have been found that explain the superiority of IMA' as a CABG conduit, including decreased blood coagulation via increased tissue plasminogen activator and reduced tissue factor levels, anti-atherosclerotic properties via decreased LOX-1 receptor expression, and regulated cell growth via decreased platelet-derived growth factor (PDGF) and MAP Kinase levels [22–24].

Along with proven superior clinical outcomes in numerous large published series, the exceptional inherent biological features of IMA combined with new surgical approaches to coronary bypass grafting should help increase the overall use of BIMAs in coronary revascularization. Our study confirms that a more widespread use of both IMAs may provide superior outcomes and better long-term survival after coronary revascularization without an increase in immediate complications.

Limitations

Follow-up data were conducted using the social security death index (SSDI). Although mortality information for the majority of

patients was found using this database, there were a small number of patients with incorrect social security numbers or other erroneous information. It is possible that records in the SSDI have not yet been updated for patients who recently expired. However, given the relatively large sample size in this study, it is unlikely that these limitations would substantially alter the results, and any errors would most likely be equally distributed across the groups. Furthermore, cause of death was not reported as this information was not available in the SSDI.

With regard to the patients who had a stroke as a complication of CABG, we do not provide any information about the characteristics of the ascending aorta as the routine use of intraoperative transoesophageal echocardiogram (TEE) was not standardized throughout the study period and therefore this information is not available for all patients.

This retrospective study was conducted at a medium-sized, non-academic hospital that serves a rather large and affluent patient population. Due to its location in an affluent suburb outside of a major city, this hospital serves a generally wealthier group of patients who have the resources and knowledge to maintain healthier lifestyles. These attributes may have predisposed this institution to an overall different experience than that of a large academic or small community hospital. Nonetheless, the long follow-up time, large series of patients and statistical methods (e.g. propensity matching) included in this study were substantial enough to reduce sampling bias as much as possible without compromising the integrity of the study.

In conclusion, the low rates of morbidity and mortality in this series of patients are likely due to the constant evolution of technology and the adoption of less invasive options for CABG patients. A more widespread use of BIMAs for CABG would continue to improve the overall excellent short- and long-term results of this operation.

ACKNOWLEDGEMENT

We want to convey our special thanks to Kathleen B. Sayles RN BSN CCRP for her invaluable work gathering data to make this manuscript possible. Without her precious contribution and leadership we would have never been able to complete this project.

Conflict of interest: none declared.

REFERENCES

[1] Stevens LM, Carrier M, Perrault LP, Hébert Y, Cartier R, Bouchard D *et al*. Single versus bilateral internal thoracic artery grafts with concomitant saphenous vein grafts for multivessel coronary artery bypass grafting: effects on mortality and event-free survival. J Thorac Cardiovasc Surg 2004;127:1408–15.

[2] Kinoshita T, Asai T, Murakami Y, Hiramatsu N, Suzuki T, Kambara A *et al*. Efficacy of bilateral internal thoracic artery grafting in patients with chronic kidney disease. Ann Thorac Surg 2010;89:1106–11.

[3] Kinoshita T, Asai T, Nishimura O, Suzuki T, Kambara A, Matsubayashi K. Off-pump bilateral versus single skeletonized internal thoracic artery grafting in patients with diabetes. Ann Thorac Surg 2010;90:1173–9.

[4] Di Mauro M, Iacò AL, Contini M, Vitolla G, Weltert L, Di Giammarco G *et al*. First time myocardial revascularization in patients younger than 70 years. Single versus double internal mammary artery. Ital Heart J 2005;6: 390–5.

[5] Toumpoulis IK, Anagnostopoulos CE, Balaram S, Swistel DG, Ashton RC JrDeRose JJ Jr. Does bilateral internal thoracic artery grafting increase long-term survival of diabetic patients? Ann Thorac Surg 2006;81: 599–606.

[6] Deng Y, Byth K, Paterson HS. Semi-skeletonized internal mammary artery grafts and sternal wound complications. Asian Cardiovasc Thorac Ann 2004;12:227–32.

[7] Momin AU, Deshpande R, Potts J, El-Gamel A, Marrinan MT, Omigie J *et al*. Incidence of sternal infection in diabetic patients undergoing bilateral internal thoracic artery grafting. Ann Thorac Surg 2005;80: 1765–72.

[8] Nakano J, Okabayashi H, Hanyu M, Soga Y, Nomoto T, Arai Y *et al*. Risk factors for wound infection after off-pump coronary artery bypass grafting: should bilateral internal thoracic arteries be harvested in patients with diabetes? J Thorac Cardiovasc Surg 2008;135:540–5.

[9] Savage EB, Grab JD, O'Brien SM, Ali A, Okum EJ, Perez-Tamayo RA *et al*. Use of both internal thoracic arteries in diabetic patients increases deep sternal wound infection. Ann Thorac Surg 2007;83:1002–6.

[10] Kurlansky PA, Traad EA, Dorman MJ, Galbut DL, Zucker M, Ebra G. Thirty-year follow-up defines survival benefit for second internal mammary artery in propensity-matched groups. Ann Thorac Surg 2010; 90:101–8.

[11] Endo M, Nishida H, Tomizawa Y, Kasanuki H. Benefit of bilateral over single internal mammary artery grafts for multiple coronary artery bypass grafting. Circulation 2001;104:2164–70.

[12] Lytle BW, Blackstone EH, Sabik JF, Houghtaling P, Loop FD, Cosgrove DM. The effect of bilateral internal thoracic artery grafting on survival during 20 postoperative years. Ann Thorac Surg 2004;78:2005–14.

[13] Shahian DM, Edwards FH, Peterson ED. Data analyses of the Society of Thoracic Surgeons National Adult Cardiac Surgery Database. STS 2010 Harvest 3 Report 2010;CAB17-34.

[14] Kurlansky P. Thirty-year experience with bilateral internal thoracic artery grafting: where have we been and where are we going? World J Surg 2010;34:646–51.

[15] Berroeta C, Benbara A, Provenchère S, Ajzenberg N, Benessiano J, Depoix JP *et al*. A comparison of bilateral with single internal mammary artery grafts on postoperative mediastinal drainage and transfusion requirement. Anesth Analg 2006;103:1380–5.

[16] Boodhwani M, Nathan HJ, Lam BK, Rubens FD. The internal thoracic artery skeletonization study: a paired, within-patient comparison [NCT00265499]. Trials 2006;7:1.

[17] Saso S, James D, Vecht JA, Kidher E, Kokotsakis J, Malinovski V *et al*. Effect of skeletonization of the internal thoracic artery for coronary revascularization on the incidence of sternal wound infection. Ann Thorac Surg 2010;89:661–70.

[18] Peterson MD, Borger MA, Rao V, Peniston CM, Feindel CM. Skeletonization of bilateral internal thoracic artery grafts lowers the risk of sternal infection in patients with diabetes. J Thorac Cardiovasc Surg 2003;126:1314–9.

[19] El Diasty M, Gonzalez JA, Perez J, Cid F, Mosquera V, Cuenca J *et al*. Early results of off-pump coronary artery bypass graft surgery using bilateral internal thoracic artery grafts in octogenarian patients during ten years. Interact Cardiovasc Thorac Surg 2009;8:104–7.

[20] Brizzio ME, Zapolanski A, Shaw RE, Sperling JS, Mindich BP. Stroke-related mortality in coronary surgery is reduced by the off-pump approach. Ann Thorac Surg 2010;89:19–23.

[21] Jorapur V, Cano-Gomez A, Conde CA. Should saphenous vein grafts be the conduits of last resort for coronary artery bypass surgery? Cardiol Rev 2009;17:235–42.

[22] Payeli SK, Latini R, Gebhard C, Patrignani A, Wagner U, Lüscher TF *et al*. Prothombotic gene expression profile in vascular smooth muscle cells of human saphenous vein, but not internal mammary artery. Arterioscler Thromb Vasc Biol 2008;28:705–10.

[23] Li DY, Chen HJ, Staples ED, Ozaki K, Annex B, Singh BK *et al*. Oxidized low-density lipoprotein receptor LOX-1 and apoptosis in human atherosclerotic lesions. J Cardiovasc Pharmacol Ther 2002;7:147–53.

[24] Yang Z, Oemar BS, Carrel T, Kipfer B, Julmy F, Lüscher TF. Different proliferative properties of smooth muscle cells of human arterial and venous bypass vessels: role of PDGF receptors, mitogen-activated protein kinase, and cyclin-dependent kinase inhibitors. Circulation 1998; 97:181–7.

APPENDIX. CONFERENCE DISCUSSION

Dr D.P. Taggart *(Oxford, UK)*: If what you have shown us is correct, because this is one of the longest propensity-matched follow-ups that exists in the literature, then again, as Professor Buxton showed us, this is potentially very important.

But this is also the first time I have seen a paper on bilateral internal mammary arteries which showed no difference; there was absolutely no difference in deep sternal wound infection. There are two possibilities here, either you are doing something totally different from every other group who has ever achieved this, or, alternatively, in your propensity matching you must have excluded patients who did have deep sternal wound infections. So the obvious question I am going to ask you is, of the bilateral IMA grafts you have shown us here, what percentage is that of the total population who had bilateral IMA grafts?

Dr Grau: Of the total of 6,000 patients, around 1,800 of them had bilateral mammaries. From that total, we selected the group for propensity matching analysis. The overall risk of a sternal wound infection in that population was around 0.5%, so it was very low in the entire group even before our selection by propensity matching. This was shown in one of the first tables when I described the two populations; the risk of a sternal wound infection in the overall series of 6,000 cases was also very low.

But the truth of the matter is that there was no difference between bilateral mammaries and the use of a single mammary, understanding that the other 4,000 patients that were not included in the single mammary SVG were likely to be people who were sick or were older and who we couldn't match by propensity matching analysis to the BIMA group. There was nobody younger.

Dr Taggart: Do you use some different technique for harvesting your mammary arteries?

Dr Grau: Well, I have listened to some of the questions from the previous presentation, and I have to say that what we do is we do not overuse the Bovie to cauterise anything over the sternal side of the mammary bed. We use clip, clip and cut, so there is no diathermy injury to the arcade feeding the middle of the sternum. We do not skeletonise completely, as Dr. Buxton was showing in his slides. We leave the veins attached to the in-situ mammary. Basically these are the two things that we do. We do meticulous harvesting of the mammary.

Dr D. Pagano *(Birmingham, UK)*: How many surgeons were involved in this study?

Dr Grau: Four surgeons in total from 1994 to 2010.

Dr Pagano: And has the rate of use of double mammary changed over time?

Dr Grau: Yes, it did change. In the 1990s, I would say 1996-1997, one of the surgeons led in the use of bilateral mammaries and everybody kind of followed track after that.

Dr Pagano: So there are two methodological issues that I think you need to address and recognise the potential limitations of your outstanding results. First of all, if you do a propensity score matching within a single unit, you are really tied down by confounding by indication. The second thing is that if you have four surgeons, you will have some variability in the outcomes, and that variability may be significant, and you should consider using surgeons as a random effect to account for that.

Dr Grau: Point well taken.

European Journal of Cardio-Thoracic Surgery 41 (2012) 776–777
doi:10.1093/ejcts/ezs005 Advance Access publication 13 February 2012

EDITORIAL COMMENT

Bilateral internal mammary arteries: a very important missing trick for coronary artery bypass grafting

David P. Taggart*

Department of Cardiac Surgery, John Radcliffe Hospital, Oxford University Hospitals NHS Trust, Oxford, UK

* Corresponding author. Department of Cardiac Surgery, John Radcliffe Hospital, Oxford University Hospitals NHS Trust, Oxford OX3 9DU, UK. Tel: +44-1865-221121; fax: +44-1865-220244; e-mail: david.taggart@orh.nhs.uk (D.P. Taggart).

Received 5 December 2011; received in revised form 12 December 2011; accepted 30 December 2011

Keywords: Coronary artery bypass grafting • Bilateral • Internal mammary arteries

In the current issue of the journal, Grau *et al.* [1] described 17-year outcomes of a propensity-matched group of 928 patients with bilateral internal mammary arteries (BIMAs) and 928 with a left internal mammary artery (LIMA) and additional vein grafts as necessary. Their most important conclusion is a clinically important survival benefit with BIMAs at ∼10% at 10 years and 18% at 15 years and further enhanced if performed as an off-pump procedure. If correct, this should encourage a change in clinical practice because currently fewer than 10% of patients in Europe and fewer than 5% in the USA receive BIMA grafts. So, two fundamental questions are: (i) are the conclusions supported by the data and (ii) are the conclusions consistent with other existing evidence?

Before answering these questions, some relevant background information is useful. The IMA story began in earnest over a quarter of a century ago when Loop *et al.* [2] from the Cleveland Clinic published their seminal paper reporting that an IMA graft to the left anterior descending coronary artery, in comparison to a saphenous vein graft, over a 10-year period significantly improved the survival accompanied by a reduction in the incidence of myocardial infarction, recurrent angina and the need for repeat intervention. In 2001, our own group published the first systematic review of BIMA versus SIMA in almost 15 000 patients and reported a hazard ratio of death at 0.81 in favour of BIMA patients [3]. Such observations were entirely consistent with several angiographic studies reporting superior angiographic patency of both IMAs in comparison to saphenous vein grafts when placed to the left-sided coronary vessels both early [4] and late [5] after surgery.

Although such evidence in favour of BIMA has been available for over a decade, their routine use in clinical practice as