Does Use of Bilateral Internal Mammary Artery Grafting Reduce Long-Term Risk of Repeat Coronary Revascularization?

A Multicenter Analysis

Editorial, see p 1686

BACKGROUND: Although previous studies have demonstrated that patients receiving bilateral internal mammary artery (BIMA) conduits during coronary artery bypass grafting have better long-term survival than those receiving a single internal mammary artery (SIMA), data on risk of repeat revascularization are more limited. In this analysis, we compare the timing, frequency, and type of repeat coronary revascularization among patients receiving BIMA and SIMA.

METHODS: We conducted a multicenter, retrospective analysis of 47 984 consecutive coronary artery bypass grafting surgeries performed from 1992 to 2014 among 7 medical centers reporting to a prospectively maintained clinical registry. Among the study population, 1482 coronary artery bypass grafting surgeries with BIMA were identified, and 1297 patients receiving BIMA were propensity-matched to 1297 patients receiving SIMA. The primary end point was freedom from repeat coronary revascularization.

RESULTS: The median duration of follow-up was 13.2 (IQR, 7.4–17.7) years. Patients were well matched by age, body mass index, major comorbidities, and cardiac function. There was a higher freedom from repeat revascularization among patients receiving BIMA than among patients receiving SIMA (hazard ratio [HR], 0.78 [95% CI, 0.65–0.94]; *P*=0.009). Among the matched cohort, 19.4% (n=252) of patients receiving SIMA underwent repeat revascularization, whereas this frequency was 15.1% (n=196) among patients receiving BIMA (*P*=0.004). The majority of repeat revascularization procedures were percutaneous coronary interventions (94.2%), and this did not differ between groups (*P*=0.274). Groups also did not differ in the ratio of native versus graft vessel percutaneous coronary intervention (*P*=0.899), or regarding percutaneous coronary intervention target vessels; the most common targets in both groups were the right coronary (*P*=0.133) and circumflex arteries (*P*=0.093). In comparison with SIMA, BIMA grafting was associated with a reduction in all-cause mortality at 12 years of follow-up (HR, 0.79 [95% CI, 0.69–0.91]; *P*=0.001), and there was no difference in in-hospital morbidity.

CONCLUSIONS: BIMA grafting was associated with a reduced risk of repeat revascularization and an improvement in long-term survival and should be considered more frequently during coronary artery bypass grafting.

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Clinical Perspective

What Is New?

- This is one of the first retrospective analyses of outcomes with bilateral internal mammary artery grafting to be conducted in a multicenter format with a specific focus on repeat revascularization.
- The analysis included 47 984 consecutive coronary artery bypass grafting surgeries performed from 1992 to 2014 among 7 medical centers and linked both coronary artery bypass grafting and percutaneous coronary intervention regional registries in Northern New England to provide data on both long-term survival and risk of repeat revascularization, as well.

What Are the Clinical Implications?

- Patient undergoing coronary artery bypass grafting with bilateral internal mammary artery grafting had a 22% greater freedom from repeat revascularization with a 13.2-year median revascularization follow-up.
- In addition, patients receiving a bilateral internal mammary artery had a 21% reduction in all-cause mortality with a 12-year median survival follow-up with no increase in postoperative morbidity.
- The survival benefit of bilateral internal mammary artery grafting was most pronounced after 5 years from surgery, which has important implications in the interpretation of randomized trial data on coronary revascularization techniques.

Coronary artery bypass grafting (CABG) remains the most commonly performed cardiac surgical procedure in the United States with 151 474 operations performed in 2015, which represents a 2% growth in volume from the year prior.[1] This growth has occurred in the setting of a continued evidence base for the superiority of CABG over percutaneous coronary intervention (PCI) among select patient subgroups such as those with complex, multivessel disease and those with diabetes mellitus.[2–5] With a national in-hospital mortality rate that has remained <2%, despite an increasingly higher risk group of patients presenting for surgery, the greatest challenge to CABG remains long-term saphenous vein graft patency.[6,7]

Although a variety of technological devices, harvesting methods, and storage techniques have been investigated for saphenous vein graft patency, one of the most significant advancements in conduit patency has been the use of a second arterial conduit.[8,9] Bilateral internal mammary artery (BIMA) grafting was first described by Suzuki and colleagues[10] in 1973, with the first large analysis of clinical outcomes reported by Lytle and colleagues[11] in 1983. Since this seminal publication, multiple meta-analyses of single-institution studies have demonstrated that BIMA grafting is associated with a significant reduction in mortality, with no studies demonstrating any adverse effects on survival.[12–15]

Despite many retrospective analyses showing improved survival with BIMA grafting, the overall adoption rate has been low both nationally and internationally, increasing from 3.5% in 1999 to only 4.1% in 2009 in the United States.[16,17] The popularity of BIMA use has been tempered by concerns over increased operative time, potentially higher rates of sternal wound complications, and, until recently, the lack of randomized trial data supporting the results of observational studies.[18–20] Most important, several large observational studies have failed to demonstrate a significant reduction in risk of future PCI, which raises the possibility that the observed survival benefit of BIMA grafting may be a reflection of patient selection unaccounted for in risk adjustment.[21–24]

In this analysis, we leverage the results of a large, multicenter, prospectively maintained clinical registry to specifically address whether CABG performed with BIMA grafting decreased the long-term risk of repeat coronary revascularization.

METHODS

Data Source

The Northern New England Cardiovascular Disease Study Group registry of cardiac surgery was queried for all consecutive patients who underwent first-time, isolated CABG from 1992 to 2014 (N=47 984). The study group is a voluntary regional consortium of 7 hospitals in New Hampshire, Vermont, and Maine that provide the majority of PCI and cardiac surgery in the region. The cardiac surgery and associated PCI registry was established in 1987 for quality improvement. Data on arterial grafting during CABG were first collected in 1992. The data within the registries are prospectively maintained and validated every 2 years against hospital administrative databases to ensure complete capture of all relevant procedures in the region, and to ensure that vital status at discharge has been accurately coded. The institutional review boards at 6 of the 7 centers have designated the registry as a quality improvement registry, and thus patient consent was waived. The remaining center has obtained patient consent. This is a multicenter study, and all authors had full access to data and take full responsibility for their integrity and analysis.

Patient Groups and Operative Details

Among the 47 984 patients who underwent first-time, isolated CABG during the study period, patients were divided into those who received CABG with a single internal mammary artery (SIMA) and those who received CABG with a BIMA

(n=1482). Patients were then propensity matched 1:1 for a total study cohort of 1297 patients receiving BIMA and 1297 patients receiving SIMA. The cardiac surgery registry does not collect data on arterial conduit proximal anastomosis (pedicle versus free graft to aorta) or arterial conduit distal anastomosis target location (lateral versus inferior wall). The collaborative's PCI registry does collect data on target vessel location.

Data Collection

Data were collected on patient demographics, baseline comorbidities, cardiac function, intraoperative times, number of distal anastomoses, postoperative morbidity, length of hospital stay, and in-hospital mortality. For long-term mortality data, registry data are linked to the Social Security Administration Master Death Index. To supplement death data from the Death Master Index, which is not complete as of 2011, we contacted the states of New Hampshire, Vermont, and Maine directly to obtain death data. All patients in these registries receive a unique patient identifier. We then used these unique patient identifiers to follow patients in the cardiac registry prospectively for repeat CABG, and used these same identifiers to link patients to the PCI registry to assess for subsequent percutaneous interventions.

Study End Points

The primary end point of this analysis was freedom from repeat coronary revascularization stratified by SIMA versus BIMA. In addition, data were collected on type of revascularization performed and target vessel revascularization. Secondary end points of the analysis included in-hospital morbidity (frequency of stroke and mediastinitis), in-hospital mortality, and long-term survival.

Statistical Analysis

Patients with SIMA and BIMA were compared by age, sex, body mass index, prior PCI, comorbid disease, ejection fraction, coronary anatomy, priority at surgery, year of procedure, and hospital. Differences in categorical variables were assessed by using the χ^2 test, and comparison of median values was performed by using the Wilcoxon rank sum test. To balance differences in patient and disease characteristics between groups, a treatment propensity match was used to create comparable groups for analysis. The propensity model included the following variables: age, sex, body mass index, prior PCI, peripheral vascular disease, diabetes mellitus, chronic obstructive pulmonary disease, congestive heart failure, prior dialysis or creatinine ≥2, ejection fraction, number of diseased vessels, left main artery stenosis ≥50%, left anterior descending artery disease ≥70%, circumflex artery disease ≥70%, right coronary artery disease ≥70%, recent myocardial infarction, priority at surgery, year of procedure, and hospital at which the index procedure was done. Crude and adjusted time-to-event curves showing time to a subsequent revascularization procedure, and long-term mortality, as well, were generated by the Kaplan-Meier method and compared by using a log-rank test. Cox proportional hazards regression was used to calculate hazard ratios (HRs) with 95% confidence intervals. Stata 14.1 statistical software (StataCorp LP) was used for all analyses.

RESULTS

Patient Characteristics

Among the 47 984 patients undergoing isolated CABG during the study period, 1482 patients received a BIMA and 46 502 patients received a SIMA. Among the unmatched cohort, patients receiving a BIMA were younger, were more often male, and had a lower rate of major comorbidities such as diabetes mellitus, peripheral vascular disease, chronic obstructive pulmonary disease, and congestive heart failure (Table 1). The predicted mortality risk for patients receiving a BIMA was approximately half that of patients receiving a SIMA (0.6% versus 1.1%, $P<0.001$). Patients receiving a BIMA also had less circumflex artery disease and less 3-vessel disease, and they were more likely to have their index procedure done in the 1990s rather than in the later years of the study in comparison with SIMA cases. Center rates of BIMA versus SIMA use varied.

A propensity match created 2 groups with equal risk of receiving a BIMA with 1297 patients in each group. The match was effective in eliminating differences in all major baseline characteristics with the exception of small differences remaining in ejection fraction, surgical priority, and hospital center; however, all hospitals had patients in both SIMA and BIMA groups (Table 1).

Intraoperative and Postoperative Data

Intra- and postoperative characteristics for each group in the matched data set are described in Table 2. The majority of procedures were performed on-pump and did not differ between groups. Mean cross-clamp time and cardiopulmonary bypass time were significantly longer among patients receiving BIMA versus patients receiving SIMA (cross-clamp time, 63.6 versus 53.3 minutes; cardiopulmonary bypass time, 93.3 versus 85.1 minutes; $P<0.001$ for both variables). The median number of anastomoses performed was also significantly different between groups (BIMA, 4, versus SIMA, 3; $P<0.001$). A ratio variable comparing the number of distal anastomoses with the number of diseased vessels was generated to serve as a proxy for completeness of revascularization. A ratio <1.0, for example, indicates that fewer anastomoses were done than the number of diseased vessels. Both patients with BIMA and SIMA showed very low rates of a ratio <1.0 (3.4% versus 3.5%). However, patients receiving a BIMA were more likely to have a ratio of ≥2.0 than patients receiving a SIMA (33.7% versus 27.3%, $P<0.001$).

Median hours to extubation, while statistically significant, was not clinically significantly different between groups. In addition, red blood cell transfusion, use of an intra- or postoperative intra-aortic balloon pump, and length of stay did not differ between groups.

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Repeat Revascularization

The median duration of follow-up was 13.2 (IQR, 7.4–17.7) years and did not differ between groups (13.1 y for SIMA; 13.2 y for BIMA). Patients receiving a BIMA had a lower frequency of repeat coronary revascularization in comparison with patients receiving a SIMA (BIMA 15.1% [n=196] versus SIMA 19.4% [n=252], *P*=0.004). There was a higher freedom from revascularization among patients receiving a BIMA than among patients receiving a SIMA (HR, 0.78 [95% CI, 0.65–0.94]; *P*=0.009) (Figure). To control for the potential effect of completeness of revascularization on the risk of repeat revascularization, a Cox proportional hazards model was created to adjust for the ratio of distal anastomoses to the number of diseased vessels. When controlling for completeness of revascularization, the use of a BIMA was still a significant predictor of freedom from repeat revascularization (HR, 0.77; *P*=0.008). Likewise, when controlling only for the number of distal anastomoses, BIMA remained a significant predictor of freedom from repeat revascularization (HR, 0.79; *P*=0.015).

The majority of revascularization procedures were PCIs (94.2%), and this did not differ between groups (*P*=0.274) (Table 3). Groups did not differ in the ratio of native versus graft vessel PCI (*P*=0.899) or the targets receiving PCI, with the most common PCI targets in both groups being the right coronary artery (*P*=0.133) and circumflex artery (*P*=0.093) (Table 4).

Morbidity and Mortality

Unadjusted rates of in-hospital mortality and stroke for patients receiving a BIMA were half those of patients receiving a SIMA (mortality, 0.9% versus 2.0%, *P*=0.005; stroke, 0.8% versus 1.5%, *P*=0.037) and median length of stay was shorter by 1 day for patients receiving a BIMA (*P*<0.001) (Table 5). After propensity matching, there was no significant difference between groups in any in-hospital outcomes including mortality, stroke, length of stay, or mediastinitis. The median duration of survival follow-up was 12 (IQR, 6.5–16.5) years. Unadjusted long-term survival was higher among the patients receiving a BIMA than among patients receiving a SIMA (HR, 0.50 [95% CI, 0.46–0.55]; *P*<0.001). After propensity matching, BIMA survival remained superior in comparison with SIMA (HR, 0.79 [95% CI, 0.69–0.91]; *P*=0.001). The survival difference between groups began to diverge beyond 5 years. At 1, 5, 10, and 15 years, the survival rate for SIMA was 97.5%, 91.7%, 79.8%, and 63.2%, respectively, whereas for BIMA the survival rates were 97.9%, 92.4%, 82.6%, and 71.6%, respectively.

DISCUSSION

In this longitudinal, multicenter analysis of patients undergoing CABG, we demonstrate that the use of a BIMA is associated with improved long-term freedom from repeat revascularization in comparison with the use of a SIMA. Moreover, we show that BIMA grafting was associated with improved long-term survival with no increase in postoperative morbidity in comparison with SIMA grafting.

There is a clear scientific basis for our observed findings in this analysis. Histological analyses of the internal mammary artery have demonstrated a nonfenestrated internal elastic lamina that can inhibit the intimal hyperplasia observed in saphenous vein grafts.[25] In addition, the internal mammary artery has been demonstrated to produce higher quantities of vasodilators like prostacyclin and nitric oxide in comparison with saphenous vein grafts.[26] Last, genomic transcriptional analyses of both left and right internal mammary arteries have shown that both conduits are associated with a downregulation of signaling pathways involved in atherosclerosis.[27] When clinical studies have specifically examined the patency rate of the right internal mammary artery through angiography, rates of ≥90% have been reported at 10 years.[28,29] Thus, intuitively, one would expect that 2 internal mammary arteries would be associated with superior long-term freedom from repeat revascularization in comparison with a single internal mammary artery with a saphenous vein graft.

The majority of single-institution analyses on BIMA grafting usually include mortality as the primary end point and data on risk of future revascularization (beyond simply reoperative CABG) is often not present. For example, in a recent meta-analysis analysis by Yi and colleagues[12] of 9 studies with a mean follow-up of ≥9 years that examined the effect of BIMA on survival, the incidence of PCI was reported in only 4 studies, and no study showed a difference between BIMA versus SIMA with regard to risk of future PCI. In our analysis, as in previous publications by other groups, patients receiving a BIMA were younger, in general, and had a lower operative risk.[30,31] Demonstrating an adjusted survival benefit of BIMA grafting is clearly significant, but also showing a concurrent advantage in risk of revascularization is important for supporting the argument for greater BIMA use.

Consistent with other studies in the literature, we demonstrate that BIMA grafting was associated with improved long-term survival. With a 12-year median duration of survival follow-up, patients receiving a BIMA had a 21% reduction in all-cause mortality that appeared most pronounced after 5 years from index CABG. It is important to note that this survival advantage was achieved with no increase in postoperative morbidity and only a 10-minute increase in aortic cross-clamp time. Our study is unique in that, in addition to demonstrating a survival benefit of BIMA grafting, we provide a highly detailed characterization of repeat revascularization that has not been well reported in the literature. In our analysis with a median

Table 1. Patient and Disease Characteristics for Unmatched vs. Matched Cases

	Unmatched			Matched		
	SIMA	BIMA		SIMA	BIMA	
Variable	(n=46 502), n (%)	(n=1482), n (%)	*P* Value*	(n=1297), n (%)	(n=1297), n (%)	*P* Value*
Age, y						
<60	14 146 (30.4)	860 (58.0)	<0.001	730 (56.3)	751 (58.0)	0.402
60–69	15 696 (33.8)	384 (25.9)		341 (26.3)	336 (25.9)	
70–79	13 703 (29.5)	202 (13.6)		200 (15.4)	176 (13.6)	
≥80	2932 (6.3)	36 (2.4)		26 (2.0)	34 (2.6)	
Female	12 034 (25.9)	276 (18.6)	<0.001	246 (19.0)	237 (18.3)	0.650
Body mass index						
<31	31 789 (68.6)	1078 (73.0)	<0.001	942 (72.6)	950 (73.3)	0.756
31–36	10 608 (22.9)	315 (21.3)		273 (21.1)	274 (21.1)	
≥37	3940 (8.5)	83 (5.6)		82 (6.3)	73 (5.6)	
Prior PCI	7884 (17.1)	273 (18.5)	0.161	251 (19.34)	234 (18.0)	0.392
Comorbid disease						
Vascular disease	9658 (20.8)	243 (16.4)	<0.001	219 (16.9)	208 (16.0)	0.560
Diabetes mellitus	15 840 (34.1)	238 (16.1)	<0.001	217 (16.7)	213 (16.4)	0.833
COPD	5418 (11.7)	122 (8.2)	<0.001	112 (8.6)	105 (8.1)	0.620
CHF	6386 (13.7)	100 (6.8)	<0.001	110 (8.5)	89 (6.9)	0.121
Dialysis/creatinine ≥2	1571 (3.4)	35 (2.4)	0.032	35 (2.7)	32 (2.5)	0.710
Ejection fraction						
<40	5691 (13.8)	105 (8.0)	<0.001	135 (10.4)	105 (8.1)	0.038
40–49	6486 (15.7)	209 (15.9)		201 (15.5)	204 (15.7)	
50–59	10 548 (25.5)	410 (31.1)		350 (27.0)	405 (31.2)	
≥60	18 612 (45.0)	595 (45.1)		611 (47.1)	583 (45.0)	
Coronary artery disease						
Left main stenosis ≥50%	13 841 (29.8)	411 (27.7)	0.092	388 (29.9)	367 (28.3)	0.364
LAD≥70%	37 959 (83.3)	1201 (82.6)	0.462	1091 (84.1)	1080 (83.3)	0.559
CX≥70%	28 109 (61.7)	775 (53.3)	<0.001	694 (53.5)	727 (56.1)	0.193
RCA≥70%	31 572 (69.3)	1048 (72.1)	0.024	931 (71.8)	940 (72.5)	0.693
No. diseased vessels						
1	5613 (12.3)	191 (13.1)	0.002	179 (13.8)	155 (12.0)	0.220
2	16 885 (37.0)	593 (40.8)		492 (37.9)	527 (40.6)	
3	23 126 (50.7)	670 (46.1)		626 (48.3)	615 (47.4)	
MI within 7 days	8922 (19.2)	239 (16.1)	0.003	214 (16.5)	218 (16.8)	0.833
Priority at surgery						
Elective	14 179 (30.5)	523 (35.3)	<0.001	501 (38.6)	455 (35.1)	0.005
Urgent	29 603 (63.7)	901 (60.8)		730 (56.3)	800 (61.7)	
Emergency	2681 (5.8)	58 (3.9)		66 (5.1)	42 (3.2)	
Time period						
1992–1997	14 334 (30.8)	629 (42.4)	<0.001	494 (38.1)	519 (40.0)	0.540
1998–2003	15 769 (33.9)	449 (30.3)		427 (32.9)	394 (30.4)	
2004–2009	9792 (21.1)	241 (16.3)		232 (17.9)	232 (17.9)	
2010–2014	6607 (14.2)	163 (11.0)		144 (11.1)	152 (11.7)	

(*Continued*)

Table 1. Continued

Variable	Unmatched			Matched		
	SIMA (n=46 502), n (%)	BIMA (n=1482), n (%)	*P* Value*	SIMA (n=1297), n (%)	BIMA (n=1297), n (%)	*P* Value*
Hospital						
1	5615 (12.1)	164 (11.1)	<0.001	149 (11.5)	150 (11.6)	<0.001
2	8158 (17.5)	76 (5.1)		213 (16.4)	52 (4.0)	
3	13 711 (29.5)	459 (31.0)		335 (25.8)	408 (31.5)	
4	8584 (18.5)	541 (36.5)		229 (17.7)	464 (35.8)	
5	7586 (16.3)	177 (11.9)		273 (21.1)	160 (12.3)	
6	1628 (3.5)	26 (1.8)		56 (4.3)	25 (1.9)	
7	1220 (2.6)	39 (2.6)		42 (3.2)	38 (2.9)	
Predicted mortality risk, median (IQR)	1.1 (0.6–2.2)	0.6 (0.4–1.2)	<0.001	0.3 (0.2–0.8)	0.3 (0.2–0.7)	0.521

CHF indicates congestive heart failure; COPD, chronic obstructive pulmonary disease; CX, circumflex; IQR, interquartile range; LAD, left anterior descending; MI, myocardial infarction; PCI, percutaneous coronary intervention; and RCA, right coronary artery.

**P* value for χ^2 test or Wilcoxon rank sum test.

revascularization follow-up time of 13 years, we demonstrate a 22% reduction in risk of future repeat revascularization when a BIMA is used during CABG. The risk of repeat revascularization between BIMA and SIMA groups is most pronounced beyond 5 years, which is consistent with the anticipated failure rate of saphenous vein grafts. As expected, the majority of repeat revascularization procedures involved PCI rather than reoperative CABG, and the target most commonly intervened on among patients receiving a BIMA was the right coronary artery. Although several previous studies have demonstrated an advantage of BIMA grafting with regard to the risk of repeat reoperation or future myocardial infarction, our analysis, which integrates CABG and PCI registries, represents one of the largest series to specifically demonstrate a reduction in risk of PCI associated with BIMA grafting.[32–35] It is important to note that the observed advantage conferred by BIMA grafting occurred with no increase in morbidity and a reduction in mortality that was consistent with previously published single-institution analyses and meta-analyses.[12,13] Moreover, even after controlling for completeness of revascularization, a potential confounder in many studies, the advantage of BIMA grafting persisted.

Despite the overwhelming evidence in favor of BIMA grafting, currently <5% of patients in the United States receive a BIMA during CABG.[16] In recognition of the advantages conferred by a BIMA, the Society of Thoracic Surgeons has recently issued new practice guidelines with a class IIa (level of evidence B) recommendation that a second arterial graft be considered during CABG.[36] Enthusiasm for broader use of a BIMA approach has been tempered by concerns over sternal wound complications and a lack of randomized control trial data. Although we did not demonstrate any difference between patients receiving BIMA and SIMA in rates of mediastinitis, analysis of this complication was limited to the index hospitalization.

ART (Arterial Revascularization Trial) is an ongoing trial that has randomly assigned >3000 patients to receive either SIMA or BIMA grafting during CABG.[37,38] The primary end point of the study is death from any cause at 10-year follow-up, with additional secondary

Table 2. Intraoperative and Postoperative Comparison of SIMA vs. BIMA

Variable	SIMA (n=1297)	BIMA (n=1297)	*P* Value*
Pump support, n (%)			
On pump	1172 (90.4)	1168 (90.1)	0.263
Off pump	124 (9.6)	124 (9.6)	
Converted to on pump	1 (0.1)	5 (0.4)	
Clamp time, min, mean (SD)	53.3 (25.3)	63.6 (28.2)	<0.001
Pump time, min, mean (SD)	85.1 (32.0)	93.3 (38.5)	<0.001
Number of distal anastomoses, median (IQR)	3 (3–4)	4 (3–4)	<0.001
Ratio of no. distals to no. diseased vessels, n (%)			
<1.0	44 (3.4)	45 (3.5)	<0.001
1.0–1.9	895 (69.3)	811 (62.8)	
2.0–2.9	256 (19.8)	278 (21.5)	
≥3.0	97 (7.5)	158 (12.2)	
Red blood cell transfusion,† n (%)	160 (28.6)	176 (29.7)	0.679
Intra- or postoperative IABP, n (%)	19 (1.6)	20 (1.6)	0.930
Time to initial extubation, h, median (IQR)	6 (4.0–10.1)	6.2 (4.0–11.3)	0.005
Total length of stay, days, median (IQR)	7 (5–10)	7 (5–9)	0.679
Postoperative length of stay, days, median (IQR)	5 (4–6)	5 (4–6)	0.706

BIMA indicates bilateral internal mammary artery; IQR, interquartile range; IABP, intra-aortic balloon pump; and SIMA, single internal mammary artery.

**P* value for χ^2 or Wilcoxon rank sum test.

†Red blood cell transfusion data available from 2000 through 2014.

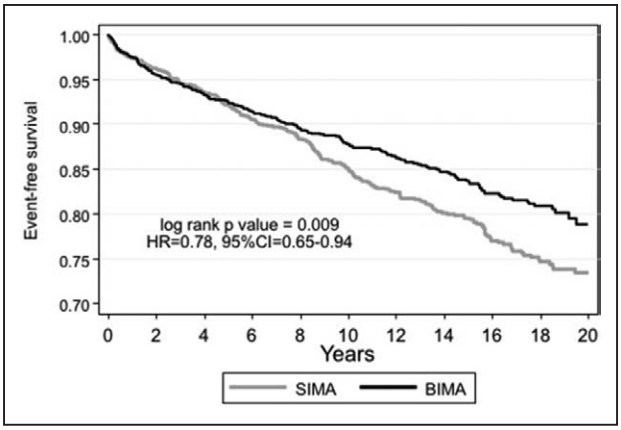

Figure. Years to repeat revascularization procedure for BIMA vs. SIMA for propensity-matched cohort.
BIMA indicates bilateral internal mammary artery; CI, confidence interval; HR, hazard ratio; and SIMA, single internal mammary artery.

outcome measures including a composite of death from any cause, stroke, or myocardial infarction; rate of repeat revascularization; safety; quality of life; and cost effectiveness. Recently, the 5-year interim analysis of ART was published and demonstrated no significant difference between groups with regard to the primary or secondary composite end point.[20] In addition, there was a significantly increased risk of sternal wound complications among those receiving a BIMA. Although the absence of an effect at 5 years is not unexpected given the projected patency rates of saphenous vein grafts (our analysis demonstrates a separation in risk of repeat revascularization beyond 5 years), the increased risk of sternal wound complications is an important consideration in patient selection.

Although our analysis has important clinical implications with regard to current management of patients with multivessel disease, there are broader implications for future clinical trials comparing CABG with PCI. Specifically, as newer-generation stents are developed and potential indications for PCI expand to areas such as the left main coronary artery, some may ask whether BIMA should now be the standard with which PCI is compared. For example, in the SYNTAX trial (Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery), <30% of patients in the 3-vessel disease subgroup received a BIMA.[39] Most pooled meta-analyses of BIMA grafting demonstrate a HR of 0.8 in comparison with survival with SIMA, and we demonstrate a HR of 0.78 for risk of repeat revascularization

Table 3. Repeat Procedure for Coronary Artery Disease, SIMA vs. BIMA

Procedure	SIMA	BIMA	*P* Value*
Subsequent procedure for CAD, n (%)	252 (19.4)	196 (15.1)	0.004
Procedure, n (%)			
Isolated CABG	10 (4.0)	9 (4.6)	0.274
CABG + valve	6 (2.4)	1 (0.5)	
PCI	236 (93.7)	186 (94.9)	

BIMA indicates bilateral internal mammary artery; CABG, coronary artery bypass grafting; CAD, coronary artery disease; PCI, percutaneous coronary intervention; and SIMA, single internal mammary artery.
**P* value for χ^2.

Table 4. Coronary Vessels Intervened in Among Those With Subsequent PCI

	SIMA (n=228), n (%)	BIMA (n=184), n (%)	*P* Value*
Coronary territory			
Left main	20 (8.8)	18 (9.8)	0.724
LAD	60 (26.3)	47 (25.5)	0.859
Circumflex	94 (41.2)	61 (33.2)	0.093
RCA	91 (39.9)	87 (47.3)	0.133
Intervention location			
Native vessel(s) only	167 (73.3)	131 (71.2)	0.899
Graft vessel(s) only	53 (23.3)	46 (25.0)	
Both native and graft vessels	8 (3.5)	7 (3.8)	

BIMA indicates bilateral internal mammary artery; LAD, left anterior descending; PCI, percutaneous coronary intervention; RCA, right coronary artery; and SIMA, single internal mammary artery.
**P* value for χ^2.

Table 5. Intra- and Postoperative Outcomes, Crude and Propensity-Adjusted: SIMA vs. BIMA

Variable	SIMA	BIMA	*P* Value*
Procedures, n			
Crude	46 502	1482	NA
Adjusted	1297	1297	NA
Mortality, n (%)			
Crude	913 (2.0)	14 (0.9)	0.005
Adjusted	15 (1.2)	10 (0.8)	0.315
Return to OR for bleeding, n (%)			
Crude	1093 (2.4)	39 (2.6)	0.484
Adjusted	28 (2.2)	36 (2.8)	0.311
Mediastinitis/sternal dehiscence, n (%)			
Crude	367 (0.8)	16 (1.1)	0.219
Adjusted	10 (0.8)	12 (0.9)	0.666
Stroke, n (%)			
Crude	682 (1.5)	12 (0.8)	0.037
Adjusted	9 (0.7)	9 (0.7)	1.000
Length of stay surgery to discharge, median d (IQR)			
Crude	6 (4–7)	5 (4–6)	<0.001
Adjusted	5 (4–6)	5 (4–6)	0.706

BIMA indicates bilateral internal mammary artery; IQR, interquartile range; NA, not applicable; OR, operating room; and SIMA, single internal mammary artery.
**P* value for χ^2 or Wilcoxon rank sum test.

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and a HR of 0.79 for survival. Therefore, one would anticipate that the observed benefit of CABG versus PCI would be significantly higher if BIMA was the comparator group. Recently, Habib and colleagues[40] tested such a hypothesis and demonstrated that multiarterial grafting compared with either bare metal stent PCI or drug-eluting stent PCI resulted in significantly improved survival and freedom from future reintervention. Moreover, the observed effect of multiarterial grafting was more pronounced than when PCI was compared with single-arterial grafting.

Study Limitations

There are several limitations to our analysis. First, although our study is based on a prospectively maintained, multicenter registry, the data were analyzed retrospectively with a propensity match. As described previously, unmatched patients receiving a BIMA were younger, had fewer comorbidities, had less circumflex disease, and had less 3-vessel disease. Therefore, there may be unaccounted-for selection bias that may influence treatment assignment and the observed findings. Second, our clinical registry does not contain data on proximal conduit configuration or distal targets. There are strong data, however, to suggest that conduit configuration does not influence the clinical benefit of BIMA grafting.[41–43] Third, we express the burden of coronary artery disease in this analysis as the number of diseased vessels because more advanced measurements for quantifying the degree of coronary disease, such as SYNTAX score, were not available as variables in our registry. Fourth, our registry does not contain the specific location (ie, proximal versus distal to the anastomosis) where repeat revascularization occurred in native vessels. Fifth, our analysis presents data on mediastinitis that occurred only during the index hospitalization. Longitudinal data on sternal complications were not available in our registry, and therefore, the rate of sternal complications may be higher than that presented in this analysis. Last, although migration rates within the Northern New England area are low, it is possible that some patients would be lost to follow-up if they sought repeat revascularization at an institution outside 1 of the 7 hospitals in our region. Although such events could potentially cause an underestimation of the risk of repeat revascularization, we do not expect that this effect would result in confounding, because migration would not be expected to affect patients receiving a BIMA at a different rate than patients receiving a SIMA.

Conclusions

In summary, we demonstrate that in a large, multicenter registry with 13 years of follow-up data, patients who undergo CABG with a BIMA have a reduced risk of future repeat revascularization events. This reduction in repeat revascularization risk is observed in the setting of an improvement in long-term survival and no increased risk of postoperative morbidity. Our findings have significant implications for clinical practice of achieving long-term patency of conduits in CABG and the design of future trials comparing CABG with PCI when repeat revascularization is considered as an end point.

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DISCLOSURES

None.

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FOOTNOTES

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