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Effect of Bilateral Internal Mammary Artery Grafts on Long-Term Survival A Meta-Analysis Approach

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Background—Although the potential survival benefit of bilateral internal mammary artery (BIMA) grafting in comparison with single internal mammary artery (SIMA) grafting has been emphasized by many investigators, the use of BIMA is still low in clinical practice in the absence of randomized trials and long-term results. In the current study, we aimed to assess if there is a long-term survival benefit of BIMA up to 10 years after coronary bypass surgery.

Methods and Results—We selected published articles comparing survival between SIMA and BIMA patients with follow-up duration of more than a mean of 9 years. We evaluated the log hazard ratio with 95% confidence interval for included studies by using a random-effects meta-analysis. Nine eligible observational studies provided 15 583 patients (8270 SIMA and 7313 BIMA) for meta-analysis. Five studies used propensity score methods for statistical adjustment, 2 with a propensity score-based patient-matching method and 3 with quintile-based stratification. A significant reduction in mortality by using BIMA was observed (hazard ratio, 0.79; 95% confidence interval, 0.75–0.84); no study showed any significantly harmful effect of BIMA on survival. Subgroups of studies using different statistical approaches—unmatched, quintile-based propensity score analysis, and propensity score-based exact patient matching—all showed the survival benefit of BIMA grafting.

Conclusions—BIMA grafting appears to have better survival with up to 10 years follow-up in comparison with SIMA grafting. Long-term survival benefit of BIMA seems to continue in the second decade after surgery. An ongoing randomized trial comparing SIMA and BIMA groups will add evidence on this issue. (*Circulation*. 2014;130:539-545.)

Key Words: coronary artery bypass ■ coronary disease ■ internal mammary arteries ■ meta-analysis ■ survival

The survival benefit of internal mammary artery (IMA) grafting in coronary artery bypass grafting (CABG) surgery was described over a quarter of a century ago.¹ Since then, the potential benefits of bilateral internal mammary artery (BIMA) grafting over single internal mammary artery (SIMA) grafting on survival and cardiac-related events have been emphasized by many investigators.^{2–11} In 2001, our group published a systematic review including a meta-analysis with 15 962 patients with the BIMA group showing a significant reduction in mortality (hazard ratio, 0.81; 95% confidence interval [CI], 0.70–0.94) after a median of 4 years of follow-up with no study showing significantly harmful effect of BIMA grafts.² This benefit is likely to be a consequence of documented patency rates of $\geq 90\%$ for BIMA grafts into the third decade of follow-up in contrast to vein grafts of which three-quarters are occluded or severely diseased by 10 years of follow-up.^{12,13}

However, BIMA grafting is still not widely accepted by cardiac surgeons, and, currently, $<10\%$ of European and $<5\%$ of North American patients receive BIMA grafts.^{14,15} Increasing use of BIMA grafting may in due course be influenced by the outcome of an ongoing multicenter, randomized trial comparing survival between SIMA and BIMA grafting, the Arterial Revascularisation Trial (ART), which has enrolled 3102 patients. Interim 1-year outcomes have been reported, but the primary end point of 10-year survival will not be reported until 2018.¹⁶ In this current systematic review and meta-analysis, we aimed to assess whether the use of BIMA grafting has a long-term survival benefit into the second decade after CABG.

Methods

Search Strategy and Selection Criteria

We searched MEDLINE, PubMed, Google Scholar databases from January 1990 to March 2012 by using Internet-based search engines.

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Table 1. Quality Assessment of Nonrandomized Studies*

Cohort selection was assessed on the answers to 3 questions	
1.	Were details of criteria for assignment of patients to treatments provided? (We awarded 1 star for relevant details).
2.	How representative was the exposed cohort? (One star if representative of typical patient undergoing CABG; no star if groups of patients were selected or selection of group was not described).
3.	How was the nonexposed cohort selected? (One star if drawn from the same community as the exposed cohort; no star if drawn from a different source, or selection of group not described).
Cohort comparability was assessed on the basis of study design or analysis of cohort differences	
4.	No differences between the 2 groups, or differences controlled for, in particular with reference to age, sex, ventricular function, or diabetic status (2 stars). One star was assigned if 1 of these 4 characteristics was not reported, even if there were no other differences between the groups, and other characteristics had been controlled for. No star was assigned if the 2 groups differed.
Outcome was assessed by 2 criteria	
5.	Assessment of outcome (1 star for information ascertained by record linkage or interview; no star if this information was not reported or ascertained in some other way).
6.	Adequacy of cohort follow-up (1 star if no patient or <20% of patients were lost to follow-up; no star if > 20% of patients were lost to follow-up, or if the researchers did not provide relevant information).

CABG indicates coronary artery bypass grafting.

*Same as in the previous review article by the same work group.²

The words used for search included “internal mammary (internal thoracic),” “single,” “unilateral,” “multiple,” “bilateral,” “artery,” and their combinations using the term “AND.” In addition, we searched reference lists of relevant studies, review articles, and meeting abstracts. We included published articles satisfying the following criteria: (1) survival comparison of single and bilateral IMA grafting; (2) long-term results with more than a mean of 9 years of follow-up; and (3) minimum 100 patients in each group. If any institution reported ≥ 2 reports on this issue, the latest one was included. Studies were excluded unless the comparability of patient characteristics was controlled either by design or analysis, at least for age, sex, ventricular function, and diabetes mellitus. Only articles published in English were included.

All data were extracted independently by 2 reviewers (G.Y. and D.T.). If there were any discrepancies, they were resolved by consensus meeting. In studies where hazard ratios were not given directly, we calculated them by using a spreadsheet method for extracting data from published literature provided by Tierney and colleagues.¹⁷ The primary outcome measurement was death from any cause.

Quality Assessment of Selected Studies

For the quality assessment of studies, we used the same criteria as in our previous meta-analysis.² The assessment scheme was based on the Ottawa-Newcastle system and classified into 3 parts: cohort selection, cohort comparability, and outcome (Table 1).¹⁸

Statistical Analysis

Meta-analysis was performed with the studies in which either the baseline patient characteristics were comparable or differences were adjusted by appropriate statistical methods. We evaluated the log hazard ratio with 95% CI for included studies and calculated combined hazard ratio and 95% CI by using a random-effects meta-analysis suggested by DerSimonian and Laird.¹⁹ For data analysis, we used R (version 2.15.2) running under Mac OS 10.7.²⁰ To prepare figures comparing hazard ratios, we used procedure forest plot in package rmeta.

Results

After our initial search of >800 potentially relevant references, 312 studies comparing SIMA and BIMA were assessed for the inclusion criteria of meta-analysis (Figure 1). A total of 9 studies (n=15583) were selected for meta-analysis (Table 2).^{3–11} Pair matching was used in 3 studies to create comparable patient groups.^{3–5} Five studies used propensity score methods to provide comparable samples, 2 using propensity score–based patient matching and 3 using quintile-based stratification.^{6,7,9–11}

Table 3 shows the quality assessment of selected studies. None of the studies was randomized or included a description of unbiased treatment assignment. Five articles reported information about treatment assignment.^{5–8,10} Although Rankin and colleagues⁸ showed a clear principle of patient allocation, with patients allocated prospectively to 2 faculty surgeons with different preferences, the treatment choices were at the discretion of the attending surgeon in the other 4 studies.^{5–7,10} Four studies had no information on losses to follow-up.^{6,8,10,11}

Three studies had >1000 patients in both the SIMA and BIMA groups.^{6,7,9} Lytle and colleagues⁶ included 1152 patients in each group after propensity score–based patient matching. The studies of Kurlansky and Stevens, each with >4000 patients, used the propensity score quintile stratification method for analysis.^{7,9} Regarding follow-up, 3 studies by Lytle, Glineur, and Rankin had the longest follow-up duration.^{6,8,11} The studies of Lytle and Glineur had >15 years of mean follow-up in both the SIMA and BIMA groups.^{6,11} The study by Rankin and colleagues⁸ had a median follow-up duration of 20 years. Although most studies included patients operated on before 2000, the study by Grau and colleagues¹⁰ included patients who had received surgery between 1994 and 2010, reflecting more recent clinical practice.

A meta-analysis of relative survival was performed with 9 studies containing 15583 patients (8270 SIMA and 7313 BIMA). A significant reduction in mortality by using BIMA was observed by meta-analysis (hazard ratio, 0.79; 95% CI, 0.75–0.84; Figure 2). A subgroup analysis considered studies using different statistical approaches: statistically unmatched,^{3–5,8} quintile-based propensity score analysis,^{7,9,11} and propensity score–based exact patient matching.^{6,10} All 3 subgroups showed a survival benefit of BIMA grafting with hazard ratios of 0.81 (95% CI, 0.69–0.94) in the statistically unmatched group, 0.81 (95% CI, 0.75–0.87) in the quintile-based propensity score analysis group, and 0.75 (95% CI, 0.65–0.85) in the propensity score–based exact matching group. The test for heterogeneity of results was not significant.

Other cardiac-related outcomes such as myocardial infarction, redo surgery, and percutaneous coronary intervention were reported in 6 studies, although they were not considered for meta-analysis because of different reporting patterns (Table 4). Six studies reported myocardial infarction as their secondary outcome, 5 of which showed lower incidences of new onset of myocardial infarction in the BIMA group during follow-up.^{3–5,7,8} Four studies investigated the incidence of redo surgery, 2 of which reported the benefit of BIMA grafting.^{7,8}

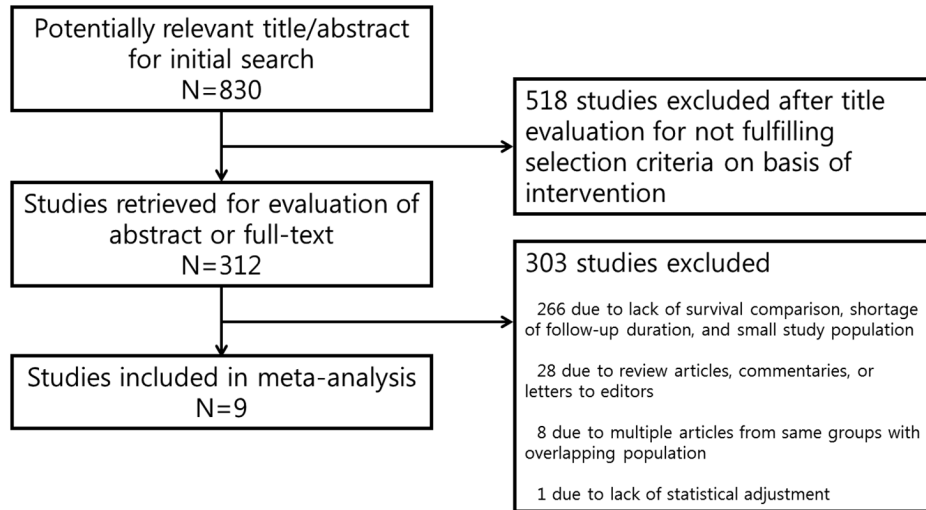


Figure 1. Search strategy for meta-analysis.

The incidence of percutaneous coronary intervention was presented in 4 studies with no study showing a difference between the 2 groups.^{3,7-9}

Early outcomes were reported in 4 studies (Table 5).^{3,7,9,10} Hospital mortality ranged from 0.6% to 4.6% in the SIMA group and from 0% to 2.6% in the BIMA group. Although 2 studies showed a higher rate of early mortality in the SIMA group, SIMA grafting was not identified as an independent predictor for hospital mortality after adjusted multivariate analysis in both studies.^{7,9} The incidence of sternal infection was presented in 4 studies with no study showing a difference between the 2 groups.^{3,7,9,10}

Discussion

This updated systematic review and meta-analysis makes 2 major advances in comparison with our previous report.² First, the number of patients in the BIMA group has increased considerably (from 4693 to 7313), now making it more comparable to the SIMA group (n=8270). Second, the duration of follow-up has been extended from a minimum of 4 years to a minimum of 9 years. Our key finding is that BIMA grafting appears to confer a long-term survival benefit in comparison with SIMA grafting after a mean of 9 years of follow-up (hazard ratio, 0.79; 95% CI, 0.75–0.84), and, of note, no studies showed worse outcome in the BIMA grafting.

Our findings are consistent with our previous systematic review that reported a significant reduction in mortality (hazard ratio, 0.81; 95% CI, 0.70–0.94) after a median of 4 years of follow-up with BIMA grafting and with no study showing significantly harmful effect of BIMA grafts.² Another meta-analysis from over a decade ago including 16362 patients from 9 studies also showed a similar survival benefit in the BIMA group (hazard ratio, 0.79; 95% CI, 0.66–0.91).²¹ However, our current results are likely to be much more robust and reliable, because that study did not require matching for baseline characteristics, had no minimal follow-up period, and does not include 6 further publications addressing this issue that have appeared over

the past decade.⁶⁻¹¹ The current meta-analysis tried to elongate the follow-up duration by maintaining the previous study's inclusion criteria on patient number and risk factor adjustment.

Long-term follow-up is essential to evaluate the true potential beneficial impact of BIMA grafting. Although studies with relatively short follow-up reported no survival benefit with BIMA grafting,²² several studies have reported that the survival benefit of BIMA grafting appears to continue to grow through the second decade of follow-up.^{3-11,23} In particular, Lytle and colleagues^{6,23} reported that the survival advantage of BIMA rather than SIMA grafting continued to diverge out to 20 years after surgery (at 7, 10, 15, and 20 years, respectively, 89% versus 87%, 81% versus 78%, 67% versus 58%, and 50% versus 37%; $P<0.0001$) and that SIMA grafting was an independent risk factor for mortality in constant- and late-hazard phases but not in the early phase. Likewise, Grau and colleagues¹⁰ reported a 5% survival advantage of BIMA patients at 5 years (96% versus 91%), 10% at 10 years (89% versus 79%), and 18% at 15 years (79% versus 61%). Kurlansky and colleagues²⁴⁻²⁶ also reported favorable results of BIMA use in elderly patients and women and superior long-term survival of BIMA grafting without an increase in operative mortality or morbidity in patients with both normal and reduced cardiac function. Although overall survival was the primary focus of our present study, 6 studies reported secondary outcomes such as myocardial infarction, reoperation, percutaneous coronary intervention, and angina with most suggesting an additional benefit of BIMA grafting on long-term cardiac-related secondary outcomes without evidence of harmful effects.^{3-5,7-9}

Intuitively, any long-term survival benefit of BIMA grafts is most likely explained by the dramatically superior patency of IMA grafts, as previously discussed,¹² and also by the protective effect that IMA grafts have on atherosclerosis by the increased synthesis of vasodilators such as nitric oxide and the decreased release of vasoconstrictors.²⁷ In the largest angiographic investigation of right IMA graft patency, Tatoulis and colleagues¹² reported patency rates of 90% in 991 angiograms at a mean of

Table 2. Studies Included for Meta-analysis

Study (Published Year)	Number of Patients		Follow-Up, Mean, y			Number of Deaths			Propensity Score Used	Age, Mean, y	
	SIMA	BIMA	SIMA	BIMA	Total	SIMA	BIMA	SIMA		BIMA	
Naunheim (1992) ³	100	100	14.3	14.4	14.4	36	19	No	51	50	
Pick (1997) ⁴	160	160	—	—	9.8	51	30	No	62	60	
Berrekouw (2001) ⁵	233	249	9.6	10	—	40	32	No	56	54	
Lytle (2004) ⁶	1152	1152	16.3	16.2	—	433*	349*	Yes†	58	58	
Stevens (2004) ⁷	2547	1835	12	8	11.3	366*	140*	Yes‡	63	57	
Rankin (2007) ⁸	490	377	—	—	20§	236*	165*	No	61	62	
Kurlansky (2010) ⁹	2369	2215	11.1	12.7	—	1312*	1534*	Yes‡	68	63	
Grau (2012) ¹⁰	928	928	—	—	9.0	131*	212*	Yes†	62	61	
Glineur (2012) ¹¹	291	297	15.1	16.3	16.1	—	—	Yes‡	61	57	

BIMA indicates bilateral internal mammary artery; IMA, internal mammary artery; LVD, left ventricular dysfunction; LVEDP, left ventricular end-diastolic pressure; LVEF, left ventricular ejection fraction; and SIMA, single internal mammary artery.

*Estimated number from individual report.

†Propensity score–based patient matching.

‡Propensity score–based quintile stratification.

§Median follow-up duration.

100 months follow-up. Furthermore, there was no evidence of atheromatous change in the right IMA, and its patencies at 10 years were equivalent to the left IMA for identical coronary territories and always better than those of radial artery or saphenous vein.

Accumulating evidence regarding the advantage of BIMA grafting has influenced the most recent guideline recommendations on surgical revascularization both in Europe (class IA) and the United States (IIaB).^{28,29} Despite such recommendations, however, the use of BIMA grafting in contemporary practice remains disappointingly low. According to the Society of Thoracic Surgeons adult cardiac surgery database in North America, between 1999 and 2009, although the use of a SIMA graft to the left anterior descending coronary artery increased from 87.7% in 2000 to 94.7% in 2009, the use of BIMA grafting increased from 3.5% to only 4.1%.¹⁴ In the United Kingdom and Australia, likewise, only 10% of CABG

patients receive 2 arterial grafts (and this may include a radial artery rather than a second IMA graft).¹⁵

Although overall survival was the primary concern in our present study, 6 studies reported secondary outcomes such as myocardial infarction, reoperation, percutaneous coronary intervention, and angina.^{3-5,7-9} Six studies reported myocardial infarction as a secondary outcome, 5 of which showed an advantage in the BIMA group. None of the studies with secondary outcomes showed inferior results in the BIMA group, with most reporting benefit of BIMA use. Although not conclusively, we can postulate that most evidence suggests that BIMA grafting appears to have an advantage over SIMA grafting on the long-term cardiac–related secondary outcomes with at least no harmful effects.

The location of the second IMA is indeed an important issue during BIMA grafting. In our series, 4 studies included information about the right IMA locations and other 4 studies had reported the target vessel of the right IMA in their previous reports. In Pick's study, 93% of right IMAs were bypassed to the left coronary artery territory.⁴ In other 4 studies, right IMAs were bypassed preferably to the left coronary system.^{5,6,9,11} Only 1 study by Naunheim and colleagues³ used the right IMA for the right coronary artery in all cases. Rankin and colleagues⁸ described their graft strategy most clearly. They used 2 IMAs for the 2 largest coronary arteries, which were the left anterior descending artery and left circumflex artery in 62% of patients. As reviewed from our selected articles, the majority of institutions used right IMA for the left coronary territory. Although it has been a prevailing belief that longevity is improved by placing both IMA grafts to the left coronary system, more recently published long-term data also support secondary IMA grafting to the right coronary system. Accordingly, the recently revised US guidelines for CABG included the use of second IMA grafting to the left circumflex artery or right coronary artery (when critically stenosed and

Table 3. Quality Assessment for Included Studies*

Study (Published Year)	Selection			Comparability	Outcome	
	1	2	3	4	5	6
Naunheim (1992) ³	–	★	★	★★	★	★
Pick (1997) ⁴	–	★	★	★★	★	★
Berrekouw (2001) ⁵	★	★	★	★★	★	★
Lytle (2004) ⁶	★	★	★	★★	★	–
Stevens(2004) ⁷	★	★	★	★★	★	★
Rankin (2007) ⁸	★	★	★	★★	★	–
Kurlansky (2010) ⁹	–	★	★	★★	★	★
Grau (2012) ¹⁰	★	★	★	★★	★	–
Glineur (2012) ¹¹	–	★	★	★★	★	–

*Criteria for stars are described in Table 1.

Sex (Female), %		Ventricular Function, Mean or %			Diabetes Mellitus, %		Anastomosis Number, Mean		Second IMA Position
SIMA	BIMA	Classification	SIMA	BIMA	SIMA	BIMA	SIMA	BIMA	
15	24	LVEDP	8.3	8.5	3	4	2.3	2.4	Right coronary artery in all cases
20	18	LVEF	57	58	27	18	3.3	3.4	Left coronary artery in 93%
16	10	LVEDP	12.5	12.9	7	6	3.2	3.3	Preferably to left coronary artery
14	12	No LVD	37	35	12	12	—	—	Preferably to left coronary artery
		Mild LVD	27	27					
		Moderate LVD	13	14					
		Severe LVD	23	24					
25	12	LVEF<40%	1.5	1.1	18	12	3.2	3.4	Left circumflex of right coronary artery
21	18	LVEF	49	50	16	22	—	—	Both IMAs to left coronary artery in 62%
26	15	LVEF<30%	6	4	27	21	3.1	3.3	Preferably to left coronary artery
11	11	LVEF	51	52	11	11	3.4	3.6	No data
32	22	LVEF	53	56	27	16	4	4.1	Preferably to left coronary artery

perfusing left ventricular myocardium) as a class IIa indication with level of evidence B.²⁹

Surgeons avoid the use BIMA grafts for various reasons, including increased risk of wound complications, a longer operation time, increased technical demands, lack of

randomized trials, and few long-term follow-up studies.³⁰ In an effort to obtain more reliable evidence, the ART trial randomly assigned 3102 patients to SIMA or BIMA grafting in 27 centers in 8 countries with a primary outcome of 10-year survival. In its interim analyses, 30-day mortality was just

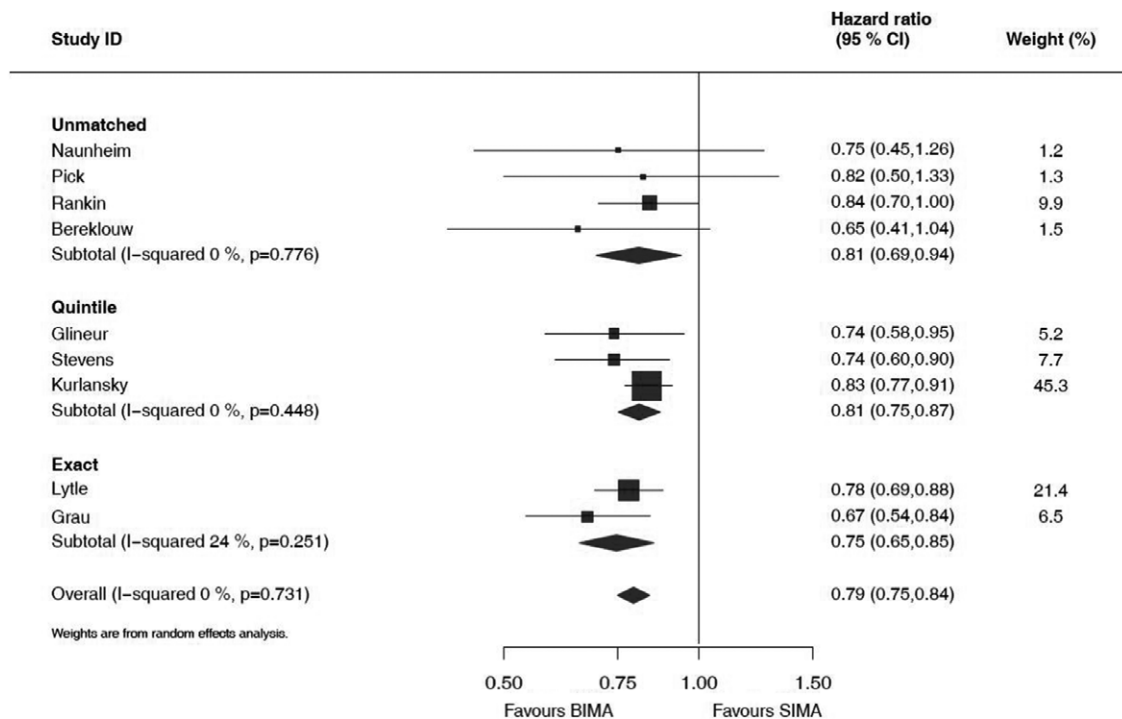


Figure 2. Effects of bilateral internal mammary artery grafting on long-term survival. Random-effects meta-analysis from 9 studies. Horizontal lines indicate 95% confidence interval. Unmatched group included studies with no statistical matching method. Quintile group included studies using quintile-based stratification method with propensity score. Exact group included studies with propensity score-based exact (1:1) matching method. The reference numbers of the studies are as follows: Naunheim et al³; Pick et al⁴; Rankin et al⁵; Berreklouw et al⁶; Glineur et al¹¹; Stevens et al⁷; Kurlansky et al⁸; Lytle et al⁶; and Grau et al¹⁰. BIMA indicates bilateral internal mammary artery; and SIMA, single internal mammary artery.

Table 4. Effect of Bilateral Internal Mammary Artery on Cardiac-Related Events

Study (year)	Cardiac-Related Events			
	MI	Reoperation	PCI	Angina
Naunheim (1992) ³	○	X	X	○
Pick (1997) ⁴	○	NA	NA	○
Berrekouw (2001) ⁵	○	X*		○
Stevens (2004) ⁷	○	○	X	NA
Rankin (2007) ⁸	○	○	X	NA
Kurlansky (2010) ⁹	X	X	X	NA

BIMA indicates bilateral internal mammary artery; IMA, internal mammary artery; MI, myocardial infarction; NA, no available data; PCI, percutaneous coronary intervention; ○, significantly favors BIMA group; and X, comparable between single and bilateral IMA group.

*Any coronary reintervention including reoperation and PCI.

>1% in both groups and 2.3% and 2.5% for SIMA and BIMA groups, respectively, at 1 year.¹⁶ The rates of stroke, myocardial infarction, and repeat revascularization (ie, safety end points) were similar at ≈2%, suggesting that the contemporary use of BIMA grafting by appropriately trained surgeons does not increase short-term mortality. Furthermore, the use of a second IMA graft only added 23 minutes to an operation already lasting almost 4 hours.

A potentially higher risk of sternal infection or dehiscence is probably the most important potential limitation to BIMA grafting. In the ART trial, the incidence of sternal reconstruction was higher in the BIMA group (SIMA 0.6% versus BIMA 1.9%). The ART trial reflected that the prevalence of diabetes mellitus in the real clinical practice was 24% in both the SIMA and BIMA groups. Diabetes mellitus is one of the strongest predictors of sternal dehiscence, and it is also noteworthy that diabetes mellitus was present in almost 50% of patients with sternal dehiscence.¹⁶ The avoidance of BIMA use in patients with diabetes mellitus (and other recognized risk factors, as well, such as obesity and pulmonary disease) allied to a skeletonization technique during IMA harvesting may significantly reduce the incidence of sternal wound complications.^{31,32}

This meta-analysis contained no randomized trials and is subject to the limitations and potential confounding and biases of all observational studies. Of particular relevance, it is known that some surgeons prefer BIMA grafting in lower-risk patients with a

greater chance of long-term benefit from CABG.²³ Accordingly, although statistical adjustments attempted to minimize biases in treatment assignment, undefined confounding factors may still exist. Our study has several other limitations. Various perioperative factors that might be related with postoperative patients survival such as ethnicity, pulmonary disease, renal disease, and postoperative complications including mediastinitis were not considered for analysis. Although 4 studies clearly showed that they only included first-time CABG patients, other studies did not clearly demonstrate whether they only included first-time surgery or not. The relatively lower incidence of diabetic patients in our series is another potential bias. Although the inclusion criteria regarding follow-up duration was more than a mean of 9 years for the whole study population, 3 studies showed >1 year difference of follow-up duration between the SIMA and the BIMA groups,^{7,9,11} which may add another potential bias to our study. Finally, publication bias may have had an influence on the combined results of observational studies.

Nevertheless, the available data in our meta-analysis appears to consistently suggest that BIMA grafting improves long-term survival after CABG in comparison with SIMA grafting; no study showed a detrimental effect. Along with the early results of the ART trial, this meta-analysis supports a much more liberal use of BIMA grafting.

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Dr Taggart thought of the idea for the study. Drs Yi, Rehman, Altman, and Taggart participated in the design of the study. Drs Yi and Taggart extracted most of the data, and Dr Yi made the initial draft. Drs Shine and Altman analyzed the data. All authors contributed to the final version of the article.

Disclosures

None.

References

1. Loop FD, Lytle BW, Cosgrove DM, Stewart RW, Goormastic M, Williams GW, Golding LA, Gill CC, Taylor PC, Sheldon WC. Influence of the internal-mammary-artery graft on 10-year survival and other cardiac events. *N Engl J Med*. 1986;314:1–6.
2. Taggart DP, D'Amico R, Altman DG. Effect of arterial revascularisation on survival: a systematic review of studies comparing bilateral and single internal mammary arteries. *Lancet*. 2001;358:870–875.
3. Naunheim KS, Barner HB, Fiore AC. 1990: Results of internal thoracic artery grafting over 15 years: single versus double grafts. 1992 update. *Ann Thorac Surg*. 1992;53:716–718.

Table 5. Effect of Bilateral Internal Mammary Artery Grafting on Early Outcomes

Study (Year)	Patient Number		Hospital Mortality, %			Reoperation for Bleeding, %			Sternal Infection, %			Length of Stay, Day		
	SIMA	BIMA	SIMA	BIMA	P Value	SIMA	BIMA	P Value	SIMA	BIMA	P Value	SIMA	BIMA	P Value
Pick (1997) ⁴	160	160	0.6	0	NS	2.5	5.0	NS	2.5	2	NS	NA	NA	NA
Stevens (2004) ⁷	2547	1835	2.6	1.3	0.003	5	4	NS	1.4	1.2	NS	8	8	NS
Kurlansky (2010) ⁹	2369	2215	4.6	2.6	0.001	3.2	1.8	0.003	1.1	1.4	NS	15.5	12.6	0.001
Grau (2012) ¹⁰	928	928	1.1*	0.8*	NS	1.7	1.1	NS	0.3	0.3	NS	6.9	6.9	NS
ART ¹⁶	1554	1548	1.2†	1.2†	NS	3.5	4.3	NS	0.6	1.9	3.24 (1.54–6.83) ‡	7.5	8.0	NA

BIMA indicates bilateral internal mammary artery; NA, no data available; NS, no significance; and SIMA, single internal mammary artery.

*In-hospital to 30 days mortality data.

†30-day mortality data.

‡ Hazard ratio with 95% CI.

4. Pick AW, Orszulak TA, Anderson BJ, Schaff HV. Single versus bilateral internal mammary artery grafts: 10-year outcome analysis. *Ann Thorac Surg.* 1997;64:599–605.
5. Berreklouw E, Rademakers PP, Koster JM, van Leur L, van der Wielen BJ, Westers P. Better ischemic event-free survival after two internal thoracic artery grafts: 13 years of follow-up. *Ann Thorac Surg.* 2001;72:1535–1541.
6. 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;78:2005–2014.
7. Stevens LM, Carrier M, Perrault LP, Hébert Y, Cartier R, Bouchard D, Fortier A, El-Hamamsy I, Pellerin M. 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;127:1408–1415.
8. Rankin JS, Tuttle RH, Wechsler AS, Teichmann TL, Glower DD, Califf RM. Techniques and benefits of multiple internal mammary artery bypass at 20 years of follow-up. *Ann Thorac Surg.* 2007;83:1008–1015.
9. 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;90:101–108.
10. Grau JB, Ferrari G, Mak AW, Shaw RE, Brizzio ME, Mindich BP, Strobeck J, Zapolanski A. Propensity matched analysis of bilateral internal mammary artery versus single internal mammary artery grafting at 17-year follow-up: validation of a contemporary surgical experience. *Eur J Cardiothorac Surg.* 2012;41:770–775.
11. Glineur D, D'hoore W, Price J, Dorméus S, de Kerchove L, Dion R, Noirhomme P, El Khoury G. Survival benefit of multiple arterial grafting in a 25-year single-institutional experience: the importance of the third arterial graft. *Eur J Cardiothorac Surg.* 2012;42:284–290.
12. Tatoulis J, Buxton BF, Fuller JA. The right internal thoracic artery: the forgotten conduit-5,766 patients and 991 angiograms. *Ann Thorac Surg.* 2011;92:9–17.
13. Nwasoka ON. Coronary artery bypass graft disease. *Ann Intern Med.* 1995;123:528–545.
14. ElBardissi AW, Aranki SF, Sheng S, O'Brien SM, Greenberg CC, Gammie JS. Trends in isolated coronary artery bypass grafting: an analysis of the Society of Thoracic Surgeons adult cardiac surgery database. *J Thorac Cardiovasc Surg.* 2012;143:273–281.
15. Bridgewater B, Keogh B, Kinsman R, Walton PK, on behalf of the Society for Cardiothoracic Surgery in Great Britain and Ireland. Sixth National Adult Cardiac Surgical Database Report 2008. London, UK: Dendrite Clinical Systems Limited; 2009.
16. Taggart DP, Altman DG, Gray AM, Lees B, Nygara F, Yu LM, Campbell H, Flather M, on behalf of ART Investigators. Randomized trial to compare bilateral vs. single internal mammary coronary artery bypass grafting: 1-year results of the Arterial Revascularisation Trial (ART). *Eur Heart J.* 2010;31:2470–2481.
17. Tierney JF, Stewart LA, Ghersi D, Burdett S, Sydes MR. Practical methods for incorporating summary time-to-event data into meta-analysis. *Trials.* 2007;8:16.
18. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed October 11, 2012.
19. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials.* 1986;7:177–188.
20. R Development Core Team. R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing; 2012. <http://www.R-project.org>. Accessed August 10, 2012.
21. Rizzoli G, Schiavon L, Bellini P. Does the use of bilateral internal mammary artery (IMA) grafts provide incremental benefit relative to the use of a single IMA graft? A meta-analysis approach. *Eur J Cardiothorac Surg.* 2002;22:781–786.
22. Sergeant P, Blackstone E, Meyns B. Validation and interdependence with patient-variables of the influence of procedural variables on early and late survival after CABG. K.U. Leuven Coronary Surgery Program. *Eur J Cardiothorac Surg.* 1997;12:1–19.
23. Lytle BW, Blackstone EH, Loop FD, Houghtaling PL, Arnold JH, Akhrass R, McCarthy PM, Cosgrove DM. Two internal thoracic artery grafts are better than one. *J Thorac Cardiovasc Surg.* 1999;117:855–872.
24. Galbut DL, Traad EA, Dorman MJ, DeWitt PL, Larsen PB, Kurlansky PA, Carrillo RG, Gentsch TO, Ebra G. Coronary bypass grafting in the elderly. Single versus bilateral internal mammary artery grafts. *J Thorac Cardiovasc Surg.* 1993;106:128–135.
25. Kurlansky PA, Traad EA, Galbut DL, Singer S, Zucker M, Ebra G. Coronary bypass surgery in women: a long-term comparative study of quality of life after bilateral internal mammary artery grafting in men and women. *Ann Thorac Surg.* 2002;74:1517–1525.
26. Galbut DL, Kurlansky PA, Traad EA, Dorman MJ, Zucker M, Ebra G. Bilateral internal thoracic artery grafting improves long-term survival in patients with reduced ejection fraction: a propensity-matched study with 30-year follow-up. *J Thorac Cardiovasc Surg.* 2012;143:844–853.e4.
27. 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;17:235–242.
28. Wijns W, Kolh P, Danchin N, Di Mario C, Falk V, Folliguet T, Garg S, Huber K, James S, Knuuti J, Lopez-Sendon J, Marco J, Menicanti L, Ostojic M, Piepoli MF, Pirllet C, Pomar JL, Reifart N, Ribichini FL, Schalij MJ, Sergeant P, Serruys PW, Silber S, Sousa Uva M, Taggart D. Guidelines on myocardial revascularization. The Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS). *Eur Heart J.* 2010;31:2501–2555.
29. Hillis LD, Smith PK, Anderson JL, Bittl JA, Bridges CR, Byrne JG, Cigarroa JE, Disesa VJ, Hiratzka LF, Hutter AM Jr, Jessen ME, Keeley EC, Lahey SJ, Lange RA, London MJ, Mack MJ, Patel MR, Puskas JD, Sabik JF, Selnes O, Shahian DM, Trost JC, Winniford MD. 2011 ACCF/AHA Guideline for Coronary Artery Bypass Graft Surgery: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation.* 2011;124:e652–e735.
30. Ioannidis JP, Galanos O, Katritsis D, Connery CP, Drossos GE, Swistel DG, Anagnostopoulos CE. Early mortality and morbidity of bilateral versus single internal thoracic artery revascularization: propensity and risk modeling. *J Am Coll Cardiol.* 2001;37:521–528.
31. De Paulis R, de Notaris S, Scaffa R, Nardella S, Zeitani J, Del Giudice C, De Peppo AP, Tomai F, Chiariello L. The effect of bilateral internal thoracic artery harvesting on superficial and deep sternal infection: The role of skeletonization. *J Thorac Cardiovasc Surg.* 2005;129:536–543.
32. 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;126:1314–1319.

CLINICAL PERSPECTIVE

The clinical benefit of single internal mammary artery in reducing 10-year mortality, myocardial infarction, recurrent angina, and the need for repeat intervention was established almost 3 decades ago. Since then, a considerable body of evidence has demonstrated the marked angiographic superiority of both internal mammary arteries in comparison with vein grafts at up to 2 decades of follow-up. Similarly, several individual studies have reported superior long-term survival with bilateral internal mammary arteries in comparison with a single mammary artery. The present meta-analysis, of almost 16 000 patients with a median follow-up of >9 years, provides additional support for a significant survival advantage of 2 internal mammary arteries at up to a decade of follow-up. However, currently <5% of patients in the United States and <10% of patients in Europe undergoing coronary artery bypass grafting receive 2 internal mammary arteries. The present study strongly implies that there should be far wider routine use of 2 internal mammary arteries in patients undergoing surgical revascularization.