Original Research Article

Pedicled and skeletonized single and bilateral internal mammary artery grafts and the incidence of sternal wound complications: Insights from the Arterial Revascularization Trial (ART)

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Clinical trial registration: ISRCTN46552265

Disclosures: None

Study support: ART is funded jointly by a grant from the British Heart Foundation (SP/03/001) and a grant from the Medical Research Council (G0200390).

Word count:

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Abbreviation

ASMD: absolute standardised mean difference

ART: Arterial Revascularization trial.

ATE: average treatment effect on the population

BIMA bilateral internal mammary artery

CABG: coronary artery bypass grafting

ESS: Effective sample size

IMA: internal mammary artery

SIMA: single internal mammary artery

S: skeletonized

P: pedicled

Structured Abstract

Objective(s): The question of whether skeletonized internal mammary artery (IMA) harvesting reduces the incidence of sternal wound complications in comparison to the pedicled technique, in the context of single or bilateral IMAs, remains controversial. We studied the impact IMA harvesting strategy on sternal wound complication in the Arterial Revascularization trial (ART).

Methods: Patients enrolled in the ART (n=3103) were randomised to coronary artery bypass grafting with single or bilateral IMAs. Sternal wound complication rates were examined according to the harvesting technique that was documented in 2056 patients. The IMA harvesting technique, based on surgeon preference, resulted in 4 groups: pedicled single IMA (P-SIMA, n=607), pedicled bilateral IMA (P-BIMA, n=459), skeletonized single IMA (S-SIMA, n=512) and skeletonized bilateral IMA (S-BIMA, n=478). Propensity Scores weighting was used to estimate the impact of the harvesting technique on sternal wound complications.

Results: A total of 219 of 2056 patients (10.6%) experienced a sternal wound complication within 1 year from the index operation. Of those, only 25 (1.2%) patients required sternal wound reconstruction. P-BIMA (OR **1.80; 95%CI 1.23 to 2.63**) but not S-BIMA (**OR 1.00; 95%CI 0.65 to 1.53**) or S-SIMA (OR **0.89; 95%CI 0.57-1.38**) was associated with a significantly increased risk of any sternal wound complications compared to P-SIMA.

Conclusions: **The present ART sub-study suggests that, with a skeletonization technique, the risk of sternal wound complication with BIMA grafting is at a similar level to that after standard pedicled SIMA harvesting whilst skeletonized SIMA harvesting did not add any further benefit when compared to pedicled SIMA harvesting.**

Central picture: Incidence of sternal wound complications according to internal mammary artery harvesting strategies (P-SIMA: pedicled single internal mammary artery; P-BIMA: pedicled bilateral internal mammary arteries; S-SIMA: skeletonized SIMA; S-BIMA: skeletonized bilateral internal mammary arteries)

Central message

In the Arterial Revascularization trial, the risk of sternal wound complication with bilateral internal mammary arteries was comparable to that after single pedicled harvesting.

Perspective Statement

By using skeletonized harvesting technique, the risk of sternal wound complication with bilateral internal mammary artery (IMA) grafting is at a similar level to that after standard pedicled single IMA harvesting also in patients at higher risk such as insulin dependent diabetes, females and those with increased body mass index.

Bilateral IMAs should not be denied on basis of increased risk of sternal wound complication if sketetonized harvesting technique is used.

The long term patency of conduits is one of the most important determinants of long-term outcomes in coronary artery bypass grafting (CABG). The left internal mammary artery (IMA) is unanimously acknowledged as the best coronary conduit [1]. Although the right IMA has identical function and patency rates to the left IMA and despite accumulation of evidence on long term benefit by using bilateral IMAs (BIMA) over the past 20 years [2-4], the right IMA remains largely underutilized [5] mainly due to concerns over the potential for sternal wound complications [6].

There are two established techniques for harvesting the IMA: pedicled and skeletonized. Harvesting the IMA(s) in a pedicled fashion can potentially lead to significant sternal devascularisation [7,8]. As opposed to pedicled harvesting, minimization of tissue mobilization during skeletonized IMA harvesting has been shown to preserve substantial collateral flow to the sternum by sparing some of the sternal and intercostal branches that arise from the internal mammary artery as a common trunk [7,8]. This finding may have potential clinical significance with respect to reducing the risk of sternal wound complications by improving wound healing and, in particular, when both left and right IMAs are used [9].

However, the magnitude of the potential clinical benefit from skeletonized over pedicled IMA harvesting on sternal wound complications still remains to be determined [10,11]. Moreover, skeletonized IMA harvesting is a more technically demanding and time consuming technique and concerns remain over a perceived increased risk of injury to the IMAs during skeletonization that may affect early outcomes [12]. Consequently, in the absence of a general consensus, pedicled IMA harvesting, remains the generally preferred approach worldwide.

The Arterial Revascularization Trial (ART) is a randomized comparison of bilateral IMA (BIMA) versus single IMA (SIMA) grafting in CABG surgery [13] and is also one of the largest studies of contemporary CABG with a high proportion of patients undergoing skeletonized IMA harvesting. We studied the impact of IMA harvesting strategy on sternal wound complication by conducting an analysis of data collected prospectively in the Arterial Revascularization trial (ART).

Methods

This research adheres to the principles set forth in the Declaration of Helsinki (http://www.wma.net/en/30publications/10policies/b3/index.html). The ART has been approved by the institutional review board of all participating centers and informed consent was obtained from each participant. The protocol for ART has been published [14] Briefly, ART is a two-arm, randomized multicentre trial, conducted in 28 hospitals in seven countries, with patients being randomized equally to SIMA or BIMA grafts. Eligible patients were those with multivessel coronary artery disease (including urgent patients but not evolving myocardial infarction) undergoing CABG, whereas those requiring single grafts or redo CABG were excluded. Only surgeons with experience of ≥50 BIMA operations were able to participate in the trial; standard methods for anaesthesia and myocardial protection were used according to local practice. **For the purpose of the present analysis, patients were classified according to the "as treated" principle in the following groups: pedicled single IMA (P-SIMA), skeletonized single IMA (S-SIMA), pedicled bilateral IMA (P-BIMA) and skeletonized BIMA (S-BIMA).** IMA harvesting technique was based on surgeon preference. This information was not recorded from the outset of the trial. Thus only 2056 out of 3102 patients were included in the analyses; **among those 1022 and 1034 were initially allocated to BIMA and SIMA respectively. Crossover rate from**

BIMA to SIMA was 115/1022(11.2%) and from SIMA to BIMA was 30/1034(2.9%). Finally a total of 937 and 1119 patients received BIMA and SIMA respectively.

Outcomes definition

The primary end-point for these analyses was the incidence of any sternal wound complication within 1 year after the index procedure, which included a broad definition ranging from superficial sternal wound discharge to sternal wound reconstruction. We also investigated the impact of IMA harvesting strategy on the incidence of severe sternal wound complications, defined as sternal wound infection requiring antibiotics and/or sternal wound reconstruction. Adverse events including sternal wound complications were adjudicated blind by a member of the Clinical Event Review Committee.

Statistical analysis

For baseline characteristics, variables are summarised as mean for continuous variables and percentage for categorical variables. The chi squared test was used to test unadjusted association between treatment variable and outcomes. Multiple imputation (m=3) was used to address missing data (165 patients). Rubin's method [15] was used to combine results from each of *m* imputed data sets.

Inverse probability of treatment weighting for modelling causal effects was used to for multiple treatments comparison [16]. One of the advantages of this technique over standard pairwise propensity matching is the possibility of simultaneous comparisons between multiple treatments. Moreover, all the individuals in the study can be used for the outcomes evaluation whilst a large number of subjects may not be used in a propensity matching in particular when the sample size of treatment and control groups are similar. A generalised boosted model was implemented to estimate multinomial propensity scores (PS) adjusting for 14 pre-treatment covariates, and the propensity score was assumed as the probability that an individual with pre-treatment characteristics X receives treatment t (twang R package).The average treatment effect on the population (ATE) was used to answer the question of how, on average, the outcome of interest would change if everyone in the population of interest had been assigned to a particular treatment relative to if they had all received another single treatment. To estimate the ATE, we gave treated patients weight $w_i = 1/(1 – p(x_i))$, where p(xi) is the propensity score, and reference patients $w_i = 1/p(x_i)$. P-SIMA was considered as the reference group in all comparisons. The absolute standardised mean difference (ASMD) was used as a balance metric to summarize the difference between two univariate distributions of a single pre-treatment variable. A value ≥0.20 (20%) was considered as an indicator of imbalance [17]. Effective sample size (ESS) was calculated to account for the potential loss in precision from weighting [16]. We then estimated the treatment effect estimates with a weighted regression model that contained only a treatment indicator. In addition, a combination of propensity score weighting and covariate adjustment (double robust) was used to correct the effect of IMA harvesting technique for residual imbalance and to estimate the effect size of other covariates. Lastly, we estimated the treatment effect within subgroups according to the presence of diabetes on insulin, gender and body mass index ≥30. R version 3.1.2 (2014-10-31) was used for all statistical analysis.

Results

Study population

Among 2056 patients included in the present analysis, 1022 and 1034 were initially allocated to BIMA and SIMA respectively. Crossover rate from BIMA to

SIMA was 115/1022(11.2%) and from SIMA to BIMA was 30/1034(2.9%). Finally a total of 937 and 1119 patients received BIMA and SIMA respectively. IMA harvesting groups compared were: 607 P-SIMA, 459 P-BIMA, 512 S-SIMA and 478 S-BIMA. The second IMA was initially attempted to be harvested but not used in 15 BIMA to SIMA crossovers. Of those, 5 were skeletonized and 10 were pedicled. Reasons for the second IMA not to be used were: evidence of injury during harvesting (n=4, all pedicled), unsatisfactory flow (n=5, 3 skeletonized, 2 pedicled) or unsatisfactory length or size (n=6, 2 skeletonized, 4 pedicled). Overall, rate of injured/unsatisfactory second IMA was 5/483(1.0%) by using skeletonized technique and 10(2.1%) by using pedicled technique (P=0.22). Among those 15 cases, only 1 patient who received pedicled harvesting, experienced sternal wound complication.

Distribution of pre-treatment variables among IMA harvesting technique groups

Table 1 summarises the distribution of pre-treatment variables. Although the four groups were comparable for most of the pre-treatment variables, insulin dependent diabetes was more common in patients receiving S-BIMA than in patients receiving P-BIMA. In addition more women received either skeletonized SIMA or BIMA. Finally off-pump surgery was more frequently performed in S-SIMA and S-BIMA groups compared to pedicled groups.

After multinomial propensity score estimation balance check showed that the groups were sufficiently similar (ASMDs <0.20) to support causal estimation of the treatment effects, although subjects receiving P-BIMA continued to have a slightly lower prevalence of diabetes on insulin.

Incidence of sternal wound complications

A total of 219 out of 2056 patients (10.7%) experienced a sternal wound complication within 1 year from the index operation. Of those, 75 (3.6%) patients had severe sternal wound complications including 50 (2.4%) with sternal wound infection requiring antibiotic therapy but not reconstruction and 25 (1.2%) who needed sternal wound reconstruction. Most sternal wound complications including those requiring reconstruction occurred during the first three months (Figure 1).

Effect of harvesting technique on sternal wound complication

Table 2 and Figure 2 show the incidence of any sternal wound complications according to IMA harvesting groups. P-BIMA patients had a higher incidence of any sternal wound complication compared to the other groups. There were too few severe wound complications to detect differences among the treatment groups. Table 3 summarises the effect of IMA harvesting technique on the incidence of any sternal wound complications. PS weighted analysis showed that P-BIMA but not S-BIMA was associated with a significantly increased risk (~ 2 times) of any sternal wound complications when compared to P-SIMA. On the other hand, S-SIMA did not provide any benefit on the incidence of any sternal wound complication when compared to P-SIMA. When the analysis was restricted to severe sternal wound complications only we were unable to demonstrate any significant impact of P-BIMA **(OR 1.60; 95%CI 0.85-3.00), S-BIMA (OR 1.15;95%CI 0.58-2.28) and S-SIMA (OR 0.97; 95%CI 0.45-2.07)** when compared to P-SIMA.

Subgroup analysis

Subgroup analysis (Table 3) suggested that the detrimental effect of P-BIMA on the incidence of any sternal wound complication might be exaggerated in the presence of diabetes on insulin **(OR 4.05; 95%CI 0.86-19.21)** although this analysis was largely underpowered due to the very small number of patients on insulin (n=118). Of note, P-BIMA remained significantly associated with a higher risk of any sternal wound complication in patients not diabetic **(OR 1.84; 95%CI 1.18-2.85).** Moreover P-BIMA significantly increased the risk of any sternal wound complication in both obese and non-obese patients.

In the situation of a single IMA, skeletonized SIMA did not add any significant benefit in terms of sternal wound complication when compared to P-SIMA also among high risk subgroups.

Independent risk factors for sternal wound complication

In a double robust analysis **(Table 4 and Table 5),** P-BIMA but not S-BIMA remained independently associated with an increased risk of any sternal wound complication. Insulin dependent diabetes, female gender, and higher BMI were independent risk factors for **any and severe** sternal wound complications.

Mortality within 30 days and at 1 year

There were 31 (1.5%) deaths within 30 days and 55 (2.6%) deaths by 1 year follow-up. Mortality at 30 day and 1 year was comparable among IMA harvesting groups (Table 2). 30 day mortality among patients with and without sternal wound reconstruction was 0/25(0%) and 31/2031(1.5%). At 1 year, total deaths among patients with and without sternal wound reconstruction were 3/25(12%) and 52/2031 (2.7%).

Discussion

Despite increasing evidence from observational studies of the long term survival benefit of a second IMA [2,3], it remains largely underutilised being used in 4.1% of CABG in the USA [5], and around 10% in the UK and Australia [18]. Concern about sternal wound complication is one of the main reasons limiting the use of more than one IMA, as a severe sternal wound complication dramatically increases in-hospital mortality as well as the expense of hospital stay [6].

The present post hoc analysis of the ART demonstrates that in the modern era of CABG surgery sternal wound complications still affect about 10% of patients. In particular, severe sternal wound infection requiring antibiotic therapy or sternal wound reconstruction still affects nearly 2% and 1% of the surgical population respectively. The anticipated impact of sternal wound complication on resource consumption and patient outcomes represents an important consideration in the utilisation of BIMA grafting and an argument in favour of skeletonized IMA over pedicled IMA harvesting.

The main finding of the present analysis is that BIMA harvesting can be safely performed using the skeletonized technique without increasing the risk of sternal wound complications when compared to the standard approach using a pedicled SIMA. Furthermore, skeletonized BIMA harvesting does not seem to significantly increase the risk even in higher risk groups, such as diabetics on insulin, females and the obese (BMI≥30). On the other hand, pedicled BIMA was associated with a nearly 2 fold increased risk of any sternal wound complication. The detrimental effect of pedicled BIMA harvesting on sternal wound complication was relevant not only in high risk cases such as those who were obese or who had insulin dependent diabetes but also in the lowest risk CABG population who were not diabetic or obese, whilst skeletonized BIMA harvesting did not significantly increase the risk of sternal wound complications.

On the other hand, in the context of a single IMA graft, there was no evidence of the superiority of skeletonized SIMA harvesting over pedicled SIMA harvesting in reducing the risk of sternal wound complications.

Skeletonized harvesting has been proposed to minimise the risk of sternal wound complication by preserving sternal perfusion especially in the context of BIMA usage [6]. Kamiya et al. [7] showed better oxygen saturation and blood flow in the microcirculation of sternal tissue when using skeletonized rather than pedicled IMA. Similarly, Boodhwani et al. [8], using radionuclear perfusion scanning, demonstrated that sternal perfusion was greater after skeletonized rather than pedicled harvesting.

However, whether skeletonized IMA harvesting should be considered the standard approach with BIMA grafting and whether this approach also provides a significant benefit in SIMA grafting still needs to be determined. The potential clinical superiority of skeletonized over pedicled harvesting on sternal wound complications has been addressed only in a few studies with conflicting results reported [10-11]. Studies published to date are remarkably underpowered to detect any clinical benefit on low rate events such as sternal wound complications [11]. Moreover, skeletonized harvesting is more technically demanding and time consuming and, in the absence of general consensus, pedicled harvesting still remains the preferred approach worldwide.

ART is one of the largest studies of contemporary CABG with a high proportion of patients undergoing skeletonized IMA harvesting [13]. To our knowledge, the present study is the largest analysis on the impact of IMA harvesting performed to date. We found that **skeletonization while performing BIMA was safe as did not increase the risk of damage to harvested IMA. In fact, rate of injured/unsatisfactory**

second IMA was 1.0% by using skeletonized technique and 2.1% by using pedicled technique thus supporting previous reports [22]. Moreover, mortality rate at 30 days and 1 year was comparable among the two techniques. With regard to sternal wound complications, skeletonized BIMA harvesting did not increase its risk when compared to pedicled SIMA and subgroup analysis suggested a protective effect from skeletonized BIMA also among high risk subjects. On the other hand, pedicled BIMA grafts seemed to increase the risk of sternal wound complications also among low risk subgroups (ie not on insulin nor obese). We also found no evidence that skeletonized SIMA harvesting added any protective effect when compared to a pedicled SIMA.

Limitations

The present analysis has some limitations. Despite propensity score adjustment, the present analysis was unable to address hidden biases due to unobserved differences between treated and control patients before treatment. The present study was underpowered to detect differences in severe sternal wound complications among groups **and most of sternal complications were clinically less relevant.** Fortunately, the low incidence of severe sternal wound complications would have required a much larger number of patients for analysis. Nevertheless, the difference in the rate of severe wound problems between the 2 groups supports the intrinsic benefit of the skeletonized technique of artery harvesting in terms of severe sternal wound complications. **Sparing of the communicating bifurcation of internal mammary artery to the chest wall and preservation of pericardiacophrenic artery branch has been reported to minimize the risk of sternal wound complication in patients receiving pedicled BIMA [23]. In the present study we could not confirm**

this hypothesis as data on technical aspects of harvesting technique were not reported.

Conclusion

In conclusion, the present ART sub-study suggests that, with a skeletonization technique, the risk of sternal wound complication with BIMA grafting is at a similar level to that after standard pedicled SIMA harvesting whilst skeletonized SIMA harvesting did not add any further benefit when compared to pedicled SIMA harvesting. Skeletonized BIMA harvesting seems to provide a protective effect also in those at higher risk such as insulin dependent diabetes, females and those with increased BMI.

Disclosures

None

Acknowledgment

U.B. contribution was supported by the NIHR Bristol Cardiovascular Biomedical Research Unit

References

1. Loop FD, Lytle BW, Cosgrove DM, Stewart RW, Goormastic M, Williams GW et al. 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;358:870-5.
3. Yi G, Shine B, Rehman SM, Altman DG, Taggart DP. Effect of bilateral internal mammary artery grafts on long-term survival: a meta-analysis approach. Circulation. 2014;130:539-45.
4. Benedetto U, Raja SG, Albanese A, Amrani M, Biondi-Zoccai G, Frati G. Searching for the second best graft for coronary artery bypass surgery: a network meta-analysis of randomized controlled trials. Eur J Cardiothorac Surg. 2015;47:59-65
5. Tabata M, Grab JD, Khalpey Z, Edwards FH, O'Brien SM, Cohn LH et al Prevalence and variability of internal mammary artery graft use in contemporary multivessel coronary artery bypass graft surgery. Circulation 2009; 120:935–940.
6. Catarino PA, Black E, Taggart DP. Why do UK cardiac surgeons not perform their first choice operation for coronary artery bypass graft? Heart. 2002;88:643-4.
7. Kamiya H, Akhyari P, Martens A, Karck M, Haverich A, Lichtenberg A. Sternal microcirculation after skeletonized versus pedicled harvesting of the internal thoracic artery: a randomized study. J Thorac Cardiovasc Surg 2008;135:32–7.

8. Boodhwani M, Lam BK, Nathan HJ, Mesana TG, Ruel M, Zeng W et al. Skeletonized internal thoracic artery harvest reduces pain and dysesthesia and improves sternal perfusion after coronary artery bypass surgery: a randomized, double blind, within-patient comparison. Circulation 2006;114:766–73.
9. Sá MP, Cavalcanti PE, de Andrade Costa Santos HJ, Soares AF, Albuquerque Miranda RG, Araújo ML et al. Skeletonized versus pedicled bilateral internal mammary artery grafting: Outcomes and concerns analyzed through a meta-analytical approach. Int J Surg. 2015;16:146-152.
10. Sá MP, Ferraz PE, Escobar RR, Vasconcelos FP, Ferraz AA, Braile DM et al. Skeletonized versus pedicled internal thoracic artery and risk of sternal wound infection after coronary bypass surgery: meta-analysis and meta-regression of 4817 patients. Interact Cardiovasc Thorac Surg. 2013;16:849-57.
11. Onorati F, Esposito A, Pezzo F, di Virgilio A, Mastroroberto P, Renzulli A. Hospital outcome analysis after different techniques of left internal mammary grafts harvesting. Ann Thorac Surg. 2007;84:1912-9.
12. Raja SG, Dreyfus GD. Internal thoracic artery: to skeletonize or not to skeletonize? Ann Thorac Surg. 2005;79:1805-11.
13. Taggart DP, Altman DG, Gray AM, Lees B, Nugara F, Yu LM et al; 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;31:2470-81.
14. Taggart DP, Lees B, Gray A, Altman DG, Flather M, Channon K; ART Investigators. Protocol for the Arterial Revascularisation Trial (ART). A randomised trial to compare survival following bilateral versus single internal mammary grafting in coronary revascularisation. Trials. 2006;7:7.

15. Rubin, D.B. (1987) *Multiple Imputation for Nonresponse in Surveys*. J. Wiley & Sons, New York.
16. McCaffrey DF, Griffin BA, Almirall D, Slaughter ME, Ramchand R, Burgette LF. A tutorial on propensity score estimation for multiple treatments using generalized boosted models. Stat Med. 2013;32:3388-414
17. Cohen J. Statistical Power Analysis for the Behavioral Sciences. 2nd edn. Hillsdale, NJ: Lawrence Erlbaum Associates Publishers; 1988.
18. Bridgewater B, Keogh B, on behalf of the Society for Cardiothoracic Surgery in Great Britain and Ireland. Sixth National Adult Cardiac Surgical Database Report 2008.
19. Benedetto U, Montecalvo A, Kattach H, Amrani M, Raja SG; Harefield Cardiac Outcomes Research Group. Impact of the second internal thoracic artery on short- and long-term outcomes in obese patients: A propensity score matched analysis. J Thorac Cardiovasc Surg. 2015;149:841-847
20. Cho KR, Kim JS, Choi JS, Kim KB. Serial angiographic follow-up of grafts one year and five years after coronary artery bypass surgery. Eur J Cardiothorac Surg. 2006;29:511-6
21. Wee CC, Girotra S, Weinstein AR, Mittleman MA, Mukamal KJ. The relationship between obesity and atherosclerotic progression and prognosis among patients with coronary artery bypass grafts the effect of aggressive statin therapy. J Am Coll Cardiol. 2008;52:620-5.
22. **Athanasiou T, Crossman MC, Asimakopoulos G, Cherian A, Weerasinghe A, Glenville et al. Should the internal thoracic artery be skeletonized? Ann Thorac Surg. 2004;77:2238-46.**

23. Sajja LR, Mannam G, Dandu SB, Sompalli S. Reduction of sternal wound infections in diabetic patients undergoing off-pump coronary artery bypass surgery and using modified pedicle bilateral internal thoracic artery harvest technique. J Thorac Cardiovasc Surg. 2012;144:480-5.

Table 1. Distribution of pre-treatment variables (as mean or percentage) before (unweighted) and after (weighted) propensity score

	P-SIMA n=607	S-SIMA n=512	P-BIMA n=459	S-BIMA n=478	ASMD	P	P-SIMA **ESS=550**	S-SIMA **ESS =454**	P-BIMA **ESS =429**	S-BIMA **ESS =430**	ASMD	P
	Unweighted						Weighted					
Age, year (SD=9)	64	65	63	64	*0.23*	*<0.001*	64	64	64	64	*0.06*	*0.36*
Female	11%	19%	12%	14%	*0.22*	*<0.001*	12%	14%	13%	12%	*0.05*	*0.36*
BMI (SD=4)	28.29	28.17	28.30	28.38	*0.05*	*0.44*	28.24	28.28	28.31	28.24	*0.02*	*0.77*
Creatinine,mmol/l (SD=22)	97.91	100.00	98.23	98.30	*0.09*	*0.13*	97.83	98.97	98.36	98.43	*0.05*	*0.37*
NYHA III/IV	26%	19%	28%	22%	*0.20*	*<0.001*	24%	22%	24%	21%	*0.06*	*0.37*
Diabetes orally treated	**19%**	**19%**	**19%**	**19%**	***0.02***	***0.70***	**18%**	**19%**	**19%**	**19%**	***0.02***	***0.73***
Diabetes on insulin	5%	6%	3%	8%	*0.21*	*<0.001*	5%	6%	3%	6%	*0.13*	*0.02*
Smoker	12%	13%	14%	16%	*0.10*	*0.10*	13%	13%	13%	14%	*0.03*	*0.65*
COPD	7%	6%	9%	6%	*0.13*	*0.05*	7%	7%	7%	6%	*0.04*	*0.51*
PVD	9%	8%	7%	7%	*0.07*	*0.27*	7%	8%	7%	8%	*0.04*	*0.61*
Prior stroke	3%	4%	2%	3%	*0.09*	*0.16*	3%	3%	2%	3%	*0.09*	*0.10*
Prior MI	42%	44%	39%	35%	*0.19*	*<0.001*	41%	41%	42%	39%	*0.06*	*0.38*
LVEF <.50	28%	26%	23%	21%	*0.16*	*0.01*	26%	25%	25%	23%	*0.06*	*0.39*
Caucasian	91%	92%	88%	92%	*0.15*	*0.02*	91%	92%	91%	93%	*0.07*	*0.28*
On pump	56%	42%	52%	39%	*0.35*	*0.00*	49%	46%	48%	46%	*0.07*	*0.29*

ASMD: absolute standardised mean difference; SD= standard deviation for all patients; P-SIMA: pedicled single internal mammary artery; P-BIMA: pedicled bilateral internal mammary arteries; S-SIMA: skeletonized SIMA; S-BIMA: skeletonized bilateral internal mammary arteries; ESS: effective sample size; BMI: body mass index; NYHA: New York Heart Association; COPD: chronic obstructive pulmonary disease; PVD: peripheral vascular disease; MI: myocardial infarction; LVEF: left ventricular ejection fraction

Table 2. Outcomes among treatment groups.

	All SWC (n=219)	Severe SWC (n=150)			30 day mortality (n= 31)	1 year mortality (n=55)
		All (n=75)	SWC requiring antibiotics (n=50)	Sternal wound reconstruction (n=25)		
P-SIMA (n=607)	58 (9.5%)	20 (3.3 %)	14(2.3%)	6 (1.0%)	8 (1.3%)	13 (2.1%)
S-SIMA (n=512)	41(8.0%)	14 (2.7 %)	12(2.3%)	2(0.4%)	8 (1.6%)	15 (2.9%)
P-BIMA (n=459)	74 (16.1%)	24 (5.2 %)	17(3.7%)	7(1.5%)	7 (1.5%)	12 (2.6%)
S-BIMA (n=478)	46(9.6%)	17 (3.7 %)	7(1.5%)	10(2.1%)	8 (1.7%)	15 (3.1%)
χ^2 tests P **P-SIMA as reference**						
S-SIMA	**0.39**	**0.60**	**1**	**0.30**	**0.80**	**0.44**
P-BIMA	**0.0014**	**0.12**	**0.19**	**0.57**	**0.79**	**0.68**
S-BIMA	**1**	**0.86**	**0.37**	**0.20**	**0.62**	**0.33**

P-SIMA: pedicled single internal mammary artery; P-BIMA: pedicled bilateral internal mammary arteries; S-SIMA: skeletonized SIMA; S-BIMA: skeletonized bilateral internal mammary arteries; SWC: sternal wound complication

Table 3. Propensity Score weighted effect (OR[95%CI]) of internal mammary artery harvesting on sternal wound complication.

	Overall	Diabetes On insulin	Diabetes Orally treated	Not Diabetic	Female	Male	BMI≥30	BMI<30
Comparison P-SIMA as ref	N=2056	N=118	N=386	N=1552	N=283	N=1773	N=631	N=1425
P-BIMA	**1.80 [1.23-2.63]**	4.05 [0.86-19.21]	1.41 [0.58-3.45]	**1.84 [1.18-2.85]**	1.08 [0.41-2.83]	**1.96 [1.30-2.98]**	**2.07 [1.09-3.90]**	**1.67 [1.03-2.68]**
S-SIMA	0.89 [0.57-1.38]	1.35 [0.29-6.15]	1.25 [0.49-3.19]	0.75 [0.43-1.29]	0.72 [0.27-1.90]	0.91 [0.55-1.51]	1.46 [0.73-2.90]	1.09 [0.65-1.83]
S-BIMA	1.00 [0.65-1.53]	1.92 [0.48-7.73]	1.54 [0.64-3.73]	0.78 [0.46-1.34]	1.59 [0.65-3.91]	0.86 [0.52-1.42]	0.83 [0.39-1.80]	0.59 [0.32-1.09]

Bold: P<0.05; OR: Odds ratio; CI: confidence interval; P-SIMA: pedicled single internal mammary artery; P-BIMA: pedicled bilateral internal mammary arteries; S-SIMA: skeletonized SIMA; S-BIMA: skeletonized bilateral internal mammary arteries; BMI: Body Mass index

Table 4. Results of double robust Propensity Score-weighted analysis on the incidence of any sternal wound complication

	OR	95%CILL	95%CI UL	P
P-BIMA vs P-SIMA	**1.85**	**1.25**	**2.74**	**0.002**
S-SIMA vs P-SIMA	**0.98**	**0.64**	**1.52**	**0.94**
S-BIMA vs P-SIMA	**0.87**	**0.55**	**1.36**	**0.53**
Age†	**1.00**	**0.99**	**1.02**	**0.77**
Female	**1.58**	**1.07**	**2.34**	**0.02**
BMI†	**1.08**	**1.04**	**1.13**	**<0.001**
Creatinine†	**0.99**	**0.98**	**1.00**	**0.01**
NYHA III-IV	**1.01**	**0.70**	**1.45**	**0.96**
Diabetes orally treated	**1.20**	**0.82**	**1.74**	**0.34**
Diabetes on insulin	**2.17**	**1.29**	**3.66**	**0.003**
Smoking	**1.27**	**0.83**	**1.95**	**0.27**
COPD	**1.23**	**0.70**	**2.18**	**0.47**
PVD	**0.81**	**0.44**	**1.48**	**0.49**
Prior stroke	**1.67**	**0.80**	**3.50**	**0.17**
Prior MI	**0.94**	**0.68**	**1.30**	**0.70**
LVEF<.50	**1.02**	**0.71**	**1.46**	**0.91**
Caucasian	**1.09**	**0.79**	**1.50**	**0.59**

† *used as continuous variable; Odds ratio; LLCI: confidence interval lower limit; CI UL: confidence interval upper limit*

P-SIMA: pedicled single internal mammary artery; P-BIMA: pedicled bilateral internal mammary arteries; S-SIMA: skeletonized SIMA; S-BIMA: skeletonized bilateral internal mammary arteries; BMI: body mass index; NYHA: New York Heart Association; COPD: chronic obstructive pulmonary disease; PVD: peripheral vascular disease; MI: myocardial infarction; LVEF: left ventricular ejection fraction

Table 5. Results of double robust Propensity Score-weighted analysis on the **incidence of severe sternal wound complication**

	OR	95%CI LL	95%CI UL	P
P-BIMA vs P-SIMA	**1.61**	**0.85**	**3.07**	**0.15**
S-SIMA vs P-SIMA	**1.14**	**0.56**	**2.31**	**0.71**
S-BIMA vs P-SIMA	**0.92**	**0.43**	**1.98**	**0.82**
Age†	**1.00**	**0.97**	**1.03**	**0.79**
Female	**2.48**	**1.38**	**4.45**	**0.002**
BMI†	**1.11**	**1.04**	**1.18**	**0.001**
Creatinine†	**1.00**	**0.99**	**1.01**	**0.76**
NYHA III-IV	**0.83**	**0.42**	**1.61**	**0.57**
Diabetes orally treated	**1.78**	**1.00**	**3.16**	**0.049**
Diabetes on insulin	**2.72**	**1.25**	**5.92**	**0.01**
Smoking	**1.72**	**0.88**	**3.35**	**0.11**
COPD	**2.08**	**0.97**	**4.46**	**0.06**
PVD	**0.53**	**0.17**	**1.66**	**0.27**
Prior stroke	**1.74**	**0.62**	**4.90**	**0.29**
Prior MI	**0.92**	**0.54**	**1.59**	**0.77**
LVEF<.50	**1.03**	**0.56**	**1.87**	**0.93**
Caucasian	**1.26**	**0.73**	**2.18**	**0.40**

† *used as continuous variable; Odds ratio; LLCI: confidence interval lower limit; CI UL: confidence interval upper limit*

P-SIMA: pedicled single internal mammary artery; P-BIMA: pedicled bilateral internal mammary arteries; S-SIMA: skeletonized SIMA; S-BIMA: skeletonized bilateral internal mammary arteries; BMI: body mass index; NYHA: New York Heart Association; COPD: chronic obstructive pulmonary disease; PVD: peripheral vascular disease; MI: myocardial infarction; LVEF: left ventricular ejection fraction

Figure Legends

Figure 1. Time from index operation to any and severe sternal wound complication

Figure 2. Incidence of any sternal wound complication according to internal mammary artery harvesting strategies. (P-SIMA: pedicled single internal mammary artery; P-BIMA: pedicled bilateral internal mammary arteries; S-SIMA: skeletonized SIMA; S-BIMA: skeletonized bilateral internal mammary arteries)