Incidence and clinical implications of intraoperative BITA grafts conversion. Insights from the Arterial Revascularization Trial.

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ABBREVIATIONS

ART: Arterial revascularization trial

BITA: Bilateral internal thoracic arteries

BMI: Body mass index

CABG: coronary artery bypass grafting

CVA: cerebrovascular accident

COPD: chronic obstructive pulmonary disease

ITA: internal thoracic artery

LVEF: left ventricular ejection fraction

MACCE: major cardiac and cerebrovascular events

MI: myocardial infarction

PCI: percutaneous coronary intervention

POAF: postoperative atrial fibrillation

PS: propensity score

SITA: Single internal thoracic artery

SVG: saphenous vein grafts

SMD: standardized mean difference

Central Message: The incidence of intraoperative bilateral internal thoracic artery (BITA) graft conversion in the ART was not irrelevant despite participating surgeons were requested to have expertise in BITA grafts.

Prospective statement: Reasons beyond bilateral internal thoracic artery (BITA) grafts underutilization remain unclear. In the ART participating surgeons were requested to have expertise in BITA grafts. We found that in the ART the incidence of intraoperative BITA graft conversion was not irrelevant thus supporting that BITA grafts may represent a challenge also for experienced surgeons.

Abstract

Background: The arterial revascularization trial (ART) has been designed to answer the question whether the use of bilateral internal thoracic arteries (BITA) can improve 10-year outcomes when compared to single internal thoracic artery (SITA). In the ART, a significant proportion of patients initially allocated to BITA received other conduit strategies. We sought to investigate the incidence and clinical implication of BITA grafts conversion in the ART.

Methods: Among patients enrolled in the ART (n=3102), we excluded those allocated to SITA (n=1554), those who did not undergo surgery (n=16) and those operated on but withdrew after randomization (n=7). Propensity score matching was used to compare converted vs non-converted BITA groups.

Results: A total of 1525 patients were operated with intention to receive BITA grafting. Of those, 233 (15.3%) were converted to other conduit selection strategies. Incidence of conversion largely varied across 28 centres involved (from 0% to 42.9%). The most common reason for BITA grafts conversion was the evidence of at least one internal thoracic artery not suitable which was reported in 77 cases. Patients with intraoperative BITA graft conversion received a lower number of grafts (2.95±0.84 vs 3.21±0.74; $P<0.001$). However, hospital mortality rate was comparable to those who did not require BITA graft conversion (0 vs 1.6%; $P=0.1$) as well as the incidence of major complications. At 5 years we found a non-significant excess of deaths (11.9% vs 8.4%; $P=0.1$) and major adverse events (17.1% 13.2%; $P=0.1$) mainly driven by an excess of revascularization in patients requiring conversion.

Conclusions: The incidence of intraoperative BITA graft conversion is not irrelevant . BITA graft conversion is not associated with increased operative morbidity but its effect on late outcomes remain uncertain.

Keywords: bilateral internal thoracic artery; randomised controlled trial; outcomes

Despite evidence from large observational studies have consistently suggested that the use of bilateral internal thoracic artery (BITA) graft improves long term survival when compared to single internal thoracic artery (SITA) graft in coronary artery bypass graft (CABG) surgery [1,2], the use of BITA graft remains particularly low. As a matter of fact, BITA grafting represents only 4–12% of all CABG procedures over the more traditional use of the SITA with additional saphenous vein grafts (SVG) [3]. Reasons for BITA underutilization are multifactorial. Most of surgeons just do not perform BITA grafting based on the increased risk of sternal wound complications and technical complexity [4,5]. However, same patients initially intended to receive BITA grafts requires intraoperative conversion to other conduits strategies. Incidence and causes of intraoperative BITA grafts conversion and its clinical implication has never been investigated.

The arterial revascularization trial (ART) has been designed to answer the question whether the use of bilateral internal thoracic arteries (BITA) can improve 10-year outcomes when compared to single internal thoracic artery (SITA) in coronary artery bypass grafting (CABG) [6]. Interim 5-year results have shown similar clinical outcomes between the two groups [7]. In ART only surgeons with experience of ≥50 BITA operations were able to undertake BITA procedures in the trial [6]. We sought to investigate reasons for intraoperative BITA grafts conversion and its clinical implication by performing a post-hoc analysis of the ART.

Methods

A post-hoc analysis of 5-year outcomes of the ART trial was conducted. This research adheres to the principles set forth in the Declaration of Helsinki (http://www.wma.net/en/30publications/10policies/b3/index.html). Among patients enrolled in the ART (n=3102) from 2004 to 2007, we excluded those allocated to SITA (n=1554) and those who did not undergo surgery (n=16) and those operated on but withdrew after randomization (n=7).

Trial design

The ART was approved by the institutional review board of all participating centers, and informed consent was obtained from each participant. The protocol for the ART has been published [6]. Briefly, the ART is a 2-arm, randomized multicenter trial conducted in 28 hospitals in 7 countries, with patients being randomized equally to SITA or BITA grafts. Eligible patients were those with multivessel coronary artery disease undergoing CABG. BITA grafts configuration (y graft vs. in-situ graft vs. free graft) was left at discretion of the surgeon (video). Patients requiring single grafts or redo CABG were excluded. Patients with evolving MI (defined as the rise and fall of a biomarker together with one of a longer list of criteria comprising ischaemic symptoms, the development of pathologic Q waves, ischaemic ECG changes, and a coronary artery intervention) were also excluded. However, patients with unstable angina defined as pain on any activity or rest pain were included.

Follow-up

Questionnaires were sent to study participants by post every year after surgery. No clinic visits were planned apart from the routine clinical 6-week post-operative visit. Participants were sent stamped addressed envelopes to improve the return rates of postal questionnaires. Study co-ordinators contacted participants by telephone to alert them to the questionnaire's arrival and to ask them about medications, adverse events and health services resource use. Five-year follow-up was completed for all patients included in the present analysis.

Study outcomes

Hospital outcomes investigated were re-exploration for bleeding, intra-aortic balloon pump (IABP) insertion, myocardial infarction (MI), cerebrovascular accident (CVA), postoperative atrial fibrillation (POAF), sternal complications revascularization and hospital mortality. Late outcomes were 5-year all-cause mortality and cumulative incidence of major cardiac and cerebrovascular events (MACCE) including cardiovascular (CV) death, CVA, MI and repeat revascularization.

Outcomes definitions

Death was classified into cardiovascular and non-cardiovascular, where possible, using autopsy reports and death certificates. Congestive heart failure, arrhythmia or myocardial infarction, pulmonary embolus and dissection were considered cardiovascular causes of death.

MI was diagnosed when two of the following three criteria were present: 1. Unequivocal ECG changes; 2. Elevation of cardiac enzyme(s) above twice the upper limit of normal or diagnostic troponin rises; 3. Chest pain typical for acute MI which lasted more than 20 minutes. CVA was defined as new neurological deficit evidenced by clinical signs of paresis, plegia or new cognitive dysfunction including any mental status alteration lasting more than 24 hours and/or evidence on CT or MRI scan of recent brain infarct (less than 6 months). Repeat revascularization was defined as coronary bypass surgery or percutaneous coronary intervention (PCI) performed after trial procedure. Sternal complications included sternal wound infection requiring antibiotics, VAC therapy, debridement or reconstruction.

Statistical analysis

Multiple imputation (m=3) was used to address missing data. Rubin's method [8] was used to combine results from each of the imputed data sets (Amelia R package). Due to lack of randomization with regards to BITA conversion, a propensity score (PS) was generated for each patient from a multivariable logistic regression model (C-statistics 0.64) based on pre-specified set of covariates (as listed in Table 1) with requiring conversion vs non-converted as a binary dependent variable [9]. Pairs of patients were derived using greedy 1:3 matching with a calliper of width of 0.2 standard deviation of the logit of the PS (nonrandom R package). The quality of the match was assessed by comparing selected pre-treatment variables in propensity score–matched patients using the standardized mean difference (SMD), with an absolute standardized difference of greater than 10% taken to represent meaningful covariate imbalance. [9]. McNemar's test and paired t-test was used to assess the statistical significance of the risk difference for hospital outcomes and stratified log-rank was used to assess the statistical significance of the risk difference for mortality and MACCE at 5 years. Risk competing framework was used to estimate the treatment effect on MACCE individual components (survival R package and riskRegression R package). All p-values <0.05 were considered to indicate statistical significance.

Results

Study population

A total of 1525 patients were operated with intention to receive BITA grafting. Of those, 233 (15.3%) were converted to other conduit selection strategies. Incidence of conversion largely varied across 131 participating surgeons (Figure 1 and Supplementary Table 1). The most common reason for BITA grafts conversion was the evidence of at least one internal thoracic artery (ITA) not suitable which was reported in 77 (33.0%) cases. This was due to during harvesting (n=41), poor flow without apparent injury (n=23) and conduit too short for grafting (n=13). The second most common reasons for BITA conversion were poor target not suitable for BITA grafts in 44 cases (18.9%) and perceived increased risk for sternum complication (i.e. osteoporosis) in 38 cases (16.3%). Other causes were hemodynamic instability which occurred during BITA harvesting in 19 cases (8.1%), intraoperative evidence of other cardiac pathologies requiring intervention in 6 (2.6%) cases and time constrain in 6 (2.6%) cases. In 43 cases (18.5%), surgeons decided to not perform BITA grafts without providing a justification (Central Picture).

Baseline characteristics in the two groups are reported in Table 1. Overall subjects with intraoperative BITA graft conversion presented a higher risk profile. In particular they were more likely to be older and female and were more likely to have diabetes, chronic obstructive pulmonary disease (COPD) and left ventricular ejection fraction (LVEF)<0.5. Intraoperative data breakdown according to causes of BITA conversion showed that increased body mass index (BMI) and diabetes was more common among those converted as perceived at higher risk for risk infection, female gender was more common among those with poor targets and reduced LVEF was more common among those with those with hemodynamic instability during ITA harvesting (Supplementary Table 3). After matching the two groups were comparable for all baseline risk factors (all SMD<0.10; Figure 2).

Intra-operative data

Intraoperative data are summarized in Table 2. Patients who had BITA graft conversion were more likely to be undergo on-pump surgery (23.2% vs. 42.1%) and to receive a lower number of grafts (2.95±0.84 vs 3.21±0.74), with LAD (95.3% vs 99.1%) and circumflex (82% vs 95.9%) territories being more likely to remain ungrafted. In the BITA conversion group, 19 (8.2%) patients received SVG only. Intraoperative data breakdown according to causes of BITA conversion showed that the number of grafts was lower among those found to have poor targets (2.52±0.90), and the rate of patients receiving SVG only was higher among those with unsuitable ITA (18.2%) or hemodynamic instability during harvesting (15.8%) (Supplementary Table 4).

Outcomes

Hospital outcomes are summarised in Table 3. Overall patients requiring BITA graft conversion was not associated with a higher incidence of hospital morbidity or mortality. In particular, no patient requiring BITA graft conversion experienced hospital death and the need for intra-aortic balloon pump and need for repeat revascularization was comparable between the two groups. Hospital breakdown according to causes of BITA conversion showed that those requiring conversion for hemodynamic instability during ITA harvesting presented the highest rate of IABP insertion, renal replacement therapy and postoperative MI (Supplementary Table 5).

Five-year outcomes are summarised in Table 4 and Figure 3. In patients requiring conversion we found a non-significant excess of deaths (11.9% vs 8.4%; P=0.1) and MACCE (17.1% 13.2%; P=0.1) mainly driven by an excess of revascularization (Figure 4). Those who required conversion for hemodynamic instability during ITA harvesting and found to have poor target or unsuitable ITA tended to have a higher rate of mortality and MACCE. (Supplementary Table 5).

Conduit selection in patients initially allocated to SITA

For descriptive purpose, we also reported conduits selection in those initially allocated to SITA graft. Among 1554 patients initially allocated to SITA, eight were not operated on (1 death, 4 withdrew, 3 cases with no reason reported) and the remaining 1546 underwent surgery. Of those, 1494 received SITA graft (96.7%) and 38 received BITA grafts (2.5%) for the following reasons: no other suitable conduit available (n=21, 1.4%), withdrew (n=2, 0.1%) and reason not report (n=15, 1.0%). Only 14 patients received neither SITA nor BITA (0.9%) for the following reasons: ITA unsuitable (n=10, 0.6%), unsuitable target (n=2, 0.1%), hemodynamic instability (n=1, 0.5%), need for unplanned surgery (n=1, 0.5%).

Discussion

Reasons beyond underutilization of the BITA graft remains uncertain [4,5]. Many surgeons just do not perform BITA grafts in view of the increased risk of sternal wound [10] and technical complexity [4]. However, the incidence of intraoperative BITA grafts conversion to other graft strategies in patients initially intended to receive BITA grafts remains unknown [7]. The perceived increased risk of operative morbidity related to intraoperative conversion can partially contribute to the reluctance of many surgeons to perform BITA grafts also in view of the current intense professional and public scrutiny of cardiac surgeons'.

The ART trial represents a unique opportunity to investigate the incidence and causes of intraoperative BITA graft conversion [7]. Interestingly, despite participating surgeons were anticipated to be expert in BITA grafts, the rate of intraoperative conversion was not irrelevant. In fact 15.3% of patients initially intended to received BITA grafts required intraoperative conversion to other conduit strategies. However, we noticed that there was a very large variation in BITA grafting conversion across centres and surgeons which supports the central role for individual surgeon experience. Interestingly, unsuitable ITA was reported as the main reason (33%) for intraoperative BITA grafts conversion to other conduit strategies and it was mainly related to injury during harvesting. Of notice, the rate of unsuitable ITA in those allocated to SITA graft was only 0.6% suggesting that harvesting two ITAs is more demanding and can influence surgeon's precisions. In addition, in 44 patients, BITA was not performed because of poor target. Among those patients, only 7 patients requited 1 grafts only. In all other cases, SVG and/or RA were used in addition to SITA grafts, suggesting that technical difficulty of performing BITA grafts rather than the absence of graftable targets. We also found that 19 patients become unstable during BITA harvesting and we can hypothesis that prolonged heart compression secondary to the use of chest retractor during ITA harvesting may not be always tolerated especially in presence of reduced LVEF. On the other hand, a main reason for conversion not related to complication or technical complexity was the perception of increased risk of sternal wound complication after chest opening (i.e. osteoporotic sternum). In case of intraoperative conversion, SITA plus SVG was the most commonly opted strategy followed by SITA plus RA. Of note, 19 patients (8.2%) received SVG only.

In contrast to other clinical scenarios when intraoperative conversion significantly increases operative morbidity and mortality such as off-pump to on-pump conversion [11], BITA grafts conversion was not associated with significantly higher rate of operative complications although those requiring conversion for hemodynamic instability during ITA harvesting presented a numerically higher rate of IABP insertion, renal replacement therapy and postoperative MI. At 5 years, we found a non-significant trend towards an excess of death and MACCE in patients requiring intraoperative conversion in particular among those with perioperative hemodynamic instability, poor target and unsuitable ITA. We can speculate that perioperative myocardial injury, lower number of grafts and excess of SVG only strategy in these three groups respectively might have partially contributed to this trend.

The unique technical challenges of BITA grafts fuels the perception that adoption of this myocardial revascularization strategy may increase operative morbidity in particular when intraoperative conversion to other conduit strategies is required. The present results support the hypothesis that BITA conversion does not significantly increase operative morbidity. However, the large variation in BITA conversion and its potential implication on late outcomes highlight the importance of negotiating the learning curve with appropriate patient selection, individualized grafting strategy, peer-to-peer training of the entire team, and graded clinical experience.

There are two main limitations in the present analysis. This is a retrospective analysis of the ART and we cannot exclude residual confounding factors between the two groups despite propensity score adjustment. The number of patients requiring conversion was relatively small and there was a relatively low incidence of adverse events. Therefore, the analysis was likely to be underpowered to detect significant difference between groups for comparisons. Finally, we had no information whether BITA injury during harvesting occurred with skeletonised or pedicled technique.

In conclusion, the incidence of intraoperative BITA graft conversion is not irrelevant also among experienced surgeons participating in ART. While intraoperative BITA grafts conversion does not increase the risk of operative mortality and major complications, BITA conversion might be associated with poorer outcomes at long term follow-up. However, the latter conclusions require further investigations.

Appendix. Contributors:

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References

1. 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;149:841-7
2. 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 Aug 12;130(7):539-45.
3. Head SJ, Börgermann J, Osnabrugge RL, Kieser TM, Falk V, Taggart DP, et al. Coronary artery bypass grafting: Part 2--optimizing outcomes and future prospects. Eur Heart J. 2013; 34:2873-86.
4. 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
5. Mastrobuoni S, Gawad N, Price J, Chan V, Ruel M, Mesana TG, et al. Use of bilateral internal thoracic artery during coronary artery bypass graft surgery in Canada: The bilateral internal thoracic artery survey. J Thorac Cardiovasc Surg. 2012; 144:874-9.
6. 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 [ISRCTN46552265]. Trials. 2006;7:7
7. Taggart DP, Altman DG, Gray AM, Lees B, Gerry S, Benedetto U, et al; ART Investigators. Randomized Trial of Bilateral versus Single Internal-Thoracic-Artery Grafts. N Engl J Med. 2016;375:2540-9

8. D.B. Rubin. Multiple Imputation for Nonresponse in Surveys. J Wiley & Sons, New York (1987)
9. Austin PC. A tutorial and case study in propensity score analysis: an application to estimate the effect of in-hospital smoking cessation counseling on mortality. Multivariate Behav Res, 2011;46:119–151.
10. Benedetto U, Altman DG, Gerry S, Gray A, Lees B, Pawlaczyk R, et al; Arterial Revascularization Trial investigators. Pedicled and skeletonized single and bilateral internal thoracic artery grafts and the incidence of sternal wound complications: Insights from the Arterial Revascularization Trial. J Thorac Cardiovasc Surg. 2016 Jul;152(1):270-6.
11. Patel NC, Patel NU, Loulmet DF, McCabe JC, Subramanian VA. Emergency conversion to cardiopulmonary bypass during attempted off-pump revascularization results in increased morbidity and mortality. J Thorac Cardiovasc Surg. 2004 Nov;128(5):655-61.

Table 1. Baseline characteristics

	Requiring Conversion	Not Converted Before PSM	SMD before PSM	Not converted matched	SMD after PSM
N	233	1292		699	
Age (mean (sd))	65 (9)	63 (9)	0.229	65 (8)	0.019
Female = 1 (\%)	47 (20.2)	176 (13.6)	0.175	135 (19.3)	0.022
BMI (mean (sd))	29 (4)	28 (4)	0.117	29 (4)	0.005
SBP (mean (sd))	132 (18)	132 (18)	0.003	132 (18)	0.015
DBP (mean (sd))	75 (11)	75 (11)	0.011	75 (11)	0.016
Creatinine (mmol/L)	95 (21)	97 (21.5)	0.061	96 (21)	0.015
NYHA III/IV n(%)	42 (18.0)	290 (22.4)	0.110	131 (18.7)	0.018
Unstable angina n(%)	14 (6.0)	102 (7.9)	0.074	43 (6.2)	0.006
Treated Hypertension	177 (76.0)	1002 (77.6)	0.038	543 (77.7)	0.041
Treated Hyperlipaemia	222 (95.3)	1216 (94.1)	0.052	663 (94.8)	0.020
Diabetes n(%)			0.140		0.046
No	165 (70.8)	994 (76.9)		508 (72.7)	
On insulin	17 (7.3)	76 (5.9)		51 (7.3)	
Oral	51 (21.9)	222 (17.2)		140 (20.0)	
Smoking n(%)			0.046		0.032
Current	32 (13.7)	198 (15.3)		92 (13.2)	
Ex	129 (55.4)	696 (53.9)		381 (54.5)	
Never	72 (30.9)	398 (30.8)		226 (32.3)	
COPD n(%)	13 (5.6)	29 (2.2)	0.173	26 (3.7)	0.088
Asthma n(%)	11 (4.7)	67 (5.2)	0.021	32 (4.6)	0.007
PVD n(%)	17 (7.3)	85 (6.6)	0.028	49 (7.0)	0.011
TIA n(%)	8 (3.4)	42 (3.3)	0.010	19 (2.7)	0.041
CVA n(%)	5 (2.1)	37 (2.9)	0.046	12 (1.7)	0.031
MI n(%)	104 (44.6)	506 (39.2)	0.111	322 (46.1)	0.029
PCI n(%)	40 (17.2)	198 (15.3)	0.050	117 (16.7)	0.011
Preop AF pre n(%)	4 (1.7)	15 (1.2)	0.047	11 (1.6)	0.011
LVEF_pre (\%)			0.187		0.033
≥ 50% (good)	161 (69.1)	994 (76.9)		473 (67.7)	
31-49% (moderate)	67 (28.8)	268 (20.7)		209 (29.9)	
≤ 30% (poor)	5 (2.1)	30 (2.3)		17 (2.4)	
LMD n(%)	40 (17.2)	282 (21.8)	0.118	127 (18.2)	0.026

SMD: standardized mean difference; PSM: propensity score matching; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; COPD: chronic obstructive pulmonary disease; PVD: peripheral vascular disease; TIA: transient ischemic attack; CVA: cerebrovascular accident; MI: myocardial infarction; PCI: percutaneous coronary intervention; AF: atrial fibrillation; LVEF: left ventricular ejection fraction; LMD: left main disease.

Table 2. Intraoperative data

	Requiring Conversion	Not Converted Before PSM	P-value Before PSM	Not converted matched	P-value After PSM
n	233	1292		699	
Off-pump n(%)	54 (23.2)	584 (45.2)	<0.001	294 (42.1)	<0.001
LAD n(%)	222 (95.3)	1278 (98.9)	<0.001	693 (99.1)	<0.001
Circumflex n(%)	191 (82.0)	1231 (95.3)	<0.001	670 (95.9)	<0.001
RCA n(%)	157 (67.4)	890 (68.9)	0.705	488 (69.8)	0.539
Diagonal branches n(%)	64 (27.5)	395 (30.6)	0.382	206 (29.5)	0.617
N grafts (mean (sd))	2.95 (0.84)	3.21 (0.77)	<0.001	3.21 (0.74)	<0.001
Conduits (%)			<0.001		<0.001
Unknown	0 (0.0)	2 (0.2)		0 (0.0)	
BITA		270 (20.9)		139 (19.9)	
BITA+RA		215 (16.6)		115 (16.5)	
BITA+RA+SV		44 (3.4)		23 (3.3)	
BITA+SV		761 (58.9)		422 (60.4)	
LITA	7 (3.0)				
LITA+RA	22 (9.4)				
LITA+RA+SV	12 (5.2)				
LITA+SV	156 (67.0)				
RA	1 (0.4)				
RA+SV	2 (0.9)				
RITA	3 (1.3)				
RITA+RA	2 (0.9)				
RITA+RA+SV	1 (0.4)				
RITA+SV	8 (3.4)				
SVG	19 (8.2)				

PSM: propensity score matching; LAD: left anterior descending artery; RCA: right coronary artery; BITA; bilateral internal thoracic arteries; RA: radial artery; SVG: saphenous vein graft

Table 3. Hospital outcomes

	Requiring Conversion	Not Converted Before PSM	P-value Before PSM	Not converted matched	P-value After PSM
N	233	1292		699	
Re-exploration for bleeding n(%)	10 (4.3)	47 (3.6)	0.8	20 (2.9)	0.4
IABP insertion n(%)	12 (5.2)	55 (4.3)	0.7	36 (5.2)	1
Renal replacement therapy n(%)	6 (2.6)	85 (6.6)	0.03	52 (7.4)	0.01
Sternal complications n(%)	13 (5.6)	64 (5.0)	0.8	36 (5.2)	0.9
Death n(%)	0 (0.0)	17 (1.3)	0.2	11 (1.6)	0.1
MI n(%)	7 (3.0)	18 (1.4)	0.1	12 (1.7)	0.4
CVA n(%)	5 (2.1)	13 (1.0)	0.2	9 (1.3)	0.5
Revascularization n(%)	1 (0.4)	9 (0.7)	1	5 (0.7)	1
POAF n(%)	69 (29.6)	329 (25.5)	0.2	208 (29.8)	1

PSM: propensity score matching; IABP: intra-aortic balloon pump; Myocardial infarction; CVA: cerebrovascular accident; POAF: postoperative atrial fibrillation

Table 4. Five-year outcomes

	Converted	Not Converted Before PSM	P-value Before PSM	Not converted matched	P-value
N	233	1292		699	
Mortality at 5 years	27(11.9)	104(8.2)	0.08	58(8.4)	0.1
MACCE at 5 years	39(17.1)	155(12.4)	0.03	90(13.2)	0.1
cardiovascular death	8(3.5)	44(3.5)	1	29(4.2)	0.7
MI	9(3.9)	42(3.3)	0.6	24(3.5)	0.7
CVA	7(3.0)	31(2.4)	0.6	19(2.7)	0.8
Revascularization	12(8.2)	81(6.4)	0.2	43(6.2)	0.2

PSM: propensity score matching; MACCE: major adverse cardiac and cerebrovascular events; MI: myocardial infarction; CVA: cerebrovascular accident

Figure Legend

Central Picture: BITA grafts allocation and conversion in the ART (BITA: bilateral interval thoracic artery; SITA: single internal thoracic artery; ITA: internal thoracic artery)

Figure 1. Scatter plot showing total number of cases initially allocated to BITA grafts performed by individual surgeons and relative rate of BITA conversion.

Figure 2. Changes in standardized mean after matching (SMD: standardized mean difference; PSM: propensity score matching; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; COPD: chronic obstructive pulmonary disease; PVD: peripheral vascular disease; TIA: transient ischemic attack; CVA: cerebrovascular accident; MI: myocardial infarction; PCI: percutaneous coronary intervention; AF: atrial fibrillation; LVEF: left ventricular ejection fraction; LMD: left main disease).

Figure 3. Cumulative incidence of mortality and major adverse cardiac and cerebrovascular events (MACCE) in the matched sample

Figure 4. Cumulative incidence of cardiovascular (CV) death, myocardial infarction (MI), cerebrovascular accident (CVA) and revascularization in the matched sample

Video. Skeletonised left internal thoracic artery during off-pump surgery

Supplementary Table 1. Number of cases performed initially allocated to bilateral interval thoracic artery (BITA) grafts and BITA conversion rate.

#Surgeon	Total number of cases performed initially allocated to BITA grafts	%BITA grafts conversion
Unknow	67	23.9%
1	1	0.0%
2	1	100.0%
3	1	0.0%
4	1	0.0%
5	1	100.0%
6	15	0.0%
7	9	22.2%
8	6	0.0%
9	1	100.0%
10	9	33.3%
11	1	0.0%
12	1	100.0%
13	2	100.0%
14	1	0.0%
15	1	0.0%
16	15	6.7%
17	5	0.0%
18	8	0.0%
19	18	5.6%
20	17	5.9%
21	15	13.3%
22	6	33.3%
23	20	20.0%
24	9	11.1%
25	15	0.0%
26	7	28.6%
27	30	30.0%
28	5	0.0%
29	6	0.0%
30	8	50.0%
31	4	0.0%
32	9	0.0%
33	15	13.3%

34	7	0.0%
35	40	10.0%
36	1	0.0%
37	4	25.0%
38	10	50.0%
39	13	23.1%
40	7	28.6%
41	1	0.0%
42	2	0.0%
43	12	16.7%
44	1	0.0%
45	12	41.7%
46	2	0.0%
47	2	0.0%
48	1	0.0%
49	34	20.6%
50	9	55.6%
51	24	8.3%
52	15	26.7%
53	17	70.6%
54	1	0.0%
55	5	0.0%
56	1	0.0%
57	29	20.7%
58	8	25.0%
59	1	0.0%
60	4	25.0%
61	7	42.9%
62	3	0.0%
63	1	0.0%
64	5	0.0%
65	8	37.5%
66	12	16.7%
67	2	50.0%
68	17	23.5%
69	28	3.6%
70	14	21.4%
71	1	100.0%
72	4	0.0%
73	2	0.0%
74	29	10.3%

75	41	0.0%
76	18	38.9%
77	22	31.8%
78	4	25.0%
79	3	100.0%
80	1	0.0%
81	33	6.1%
82	4	0.0%
83	1	0.0%
84	9	0.0%
85	1	0.0%
86	16	0.0%
87	1	0.0%
88	1	0.0%
89	2	50.0%
90	16	6.3%
91	11	54.5%
92	19	21.1%
93	3	33.3%
94	19	42.1%
95	1	100.0%
96	4	0.0%
97	1	100.0%
98	1	0.0%
99	18	5.6%
100	22	13.6%
101	2	0.0%
102	2	0.0%
103	8	0.0%
104	33	0.0%
105	1	0.0%
106	12	16.7%
107	12	8.3%
108	3	0.0%
109	4	100.0%
110	1	0.0%
111	2	100.0%
112	22	18.2%
113	4	0.0%
114	10	10.0%
115	2	0.0%

116	2	0.0%
117	1	0.0%
118	211	1.9%
119	1	0.0%
120	16	25.0%
121	1	0.0%
122	15	33.3%
123	8	0.0%
124	3	0.0%
125	1	100.0%
126	11	9.1%
127	3	0.0%
128	1	0.0%
129	33	15.2%
130	99	13.1%
131	3	33.3%

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Supplementary Table 2. Baseline characteristics according to cause of bilateral interval thoracic artery (BITA) grafts conversion

	High risk for sternal complication	At least 1 ITA not suitable	Target not suitable	Other cardiac pathologies	Justification not provided	Time constrain	Unstable during ITA harvesting
N	38	77	44	6	43	6	19
Age (mean (sd))	65.01 (8.87)	65.59 (8.19)	65.64 (9.39)	68.88 (8.63)	64.43 (8.63)	64.44 (8.29)	65.76 (8.68)
Female n(%)	7 (18.4)	16 (20.8)	12 (27.3)	0 (0.0)	10 (23.3)	0 (0.0)	2 (10.5)
BMI (mean (sd))	30.21 (4.28)	27.51 (3.25)	28.82 (3.11)	27.91 (2.60)	29.53 (4.01)	29.10 (2.85)	28.54 (4.61)
SBP (mean (sd))	132 (15)	131 (20)	134 (19)	129 (15)	130 (16)	140 (12)	131 (17)
DBP (mean (sd))	78 (10)	74 (10)	75 (10)	81 (11)	74 (13)	80 (15)	74 (10)
Creatinine (mmol/L)	97.49 (23.50)	94.27 (18.31)	99.48 (25.05)	100.08 (25.67)	92.51 (18.37)	89.00 (11.47)	93.85 (20.55)
NYHA III/IV n(%)	4 (10.5)	17 (22.1)	6 (13.6)	2 (33.3)	8 (18.6)	2 (33.3)	3 (15.8)
Unstable angina n(%)	1 (2.6)	6 (7.8)	3 (6.8)	1 (16.7)	1 (2.3)	0 (0.0)	2 (10.5)
Treated Hypertension	29 (76.3)	53 (68.8)	33 (75.0)	6 (100.0)	32 (74.4)	6 (100.0)	18 (94.7)
Treated Hyperlipaemia	38 (100.0)	73 (94.8)	42 (95.5)	6 (100.0)	39 (90.7)	6 (100.0)	18 (94.7)
Diabetes n(%)							
No	24 (63.2)	56 (72.7)	30 (68.2)	4 (66.7)	29 (67.4)	4 (66.7)	18 (94.7)
On insulin	3 (7.9)	9 (11.7)	2 (4.5)	0 (0.0)	3 (7.0)	0 (0.0)	0 (0.0)
Oral	11 (28.9)	12 (15.6)	12 (27.3)	2 (33.3)	11 (25.6)	2 (33.3)	1 (5.3)
Smoking n(%)							
Current	6 (15.8)	7 (9.1)	7 (15.9)	1 (16.7)	7 (16.3)	1 (16.7)	3 (15.8)
Ex	18 (47.4)	46 (59.7)	24 (54.5)	2 (33.3)	22 (51.2)	4 (66.7)	13 (68.4)
Never	14 (36.8)	24 (31.2)	13 (29.5)	3 (50.0)	14 (32.6)	1 (16.7)	3 (15.8)
COPD n(%)	3 (7.9)	4 (5.2)	1 (2.3)	0 (0.0)	4 (9.3)	0 (0.0)	1 (5.3)
Asthma n(%)	3 (7.9)	1 (1.3)	0 (0.0)	1 (16.7)	6 (14.0)	0 (0.0)	0 (0.0)
PVD n(%)	4 (10.5)	5 (6.5)	1 (2.3)	1 (16.7)	4 (9.3)	0 (0.0)	2 (10.5)

TIA n(%)	2 (5.3)	3 (3.9)	3 (6.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
CVA n(%)	1 (2.6)	1 (1.3)	1 (2.3)	1 (16.7)	0 (0.0)	0 (0.0)	1 (5.3)
MI n(%)	13 (34.2)	38 (49.4)	21 (47.7)	2 (33.3)	21 (48.8)	2 (33.3)	7 (36.8)
PCI n(%)	14 (36.8)	10 (13.0)	9 (20.5)	1 (16.7)	2 (4.7)	0 (0.0)	4 (21.1)
Preop AF pre n(%)	2 (5.3)	1 (1.3)	0 (0.0)	0 (0.0)	1 (2.3)	0 (0.0)	0 (0.0)
LVEF_pre (\%)							
≥ 50% (good)	31 (81.6)	52 (67.5)	30 (68.2)	3 (50.0)	31 (72.1)	4 (66.7)	10 (52.6)
31-49% (moderate)	6 (15.8)	24 (31.2)	12 (27.3)	3 (50.0)	12 (27.9)	2 (33.3)	8 (42.1)
≤ 30% (poor)	1 (2.6)	1 (1.3)	2 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)	1 (5.3)
LMD n(%)	7 (18.4)	14 (18.2)	7 (15.9)	1 (16.7)	5 (11.6)	3 (50.0)	3 (15.8)

ITA: internal thoracic artery; BMI: body mass index; SBP: systolic blood pressure; DBP: diastolic blood pressure; COPD: chronic obstructive pulmonary disease; PVD: peripheral vascular disease; TIA: transient ischemic attack; CVA: cerebrovascular accident; MI: myocardial infarction; PCI: percutaneous coronary intervention; AF: atrial fibrillation; LVEF: left ventricular ejection fraction; LMD: left main disease.

Supplementary Table 3. Operative data according to cause of bilateral interval thoracic artery (BITA) grafts conversion.

	High risk for sternal complication	At least 1 ITA not suitable	Target not suitable	Other cardiac pathologies	Justification not provided	Time constrain	Unstable during ITA harvesting
n	38	77	44	6	43	6	19
Off-pump n(%)	4 (10.5)	23 (29.9)	15 (34.1)	1 (16.7)	9 (20.9)	0 (0.0)	2 (10.5)
LAD n(%)	37 (97.4)	76 (98.7)	37 (84.1)	5 (83.3)	43 (100.0)	6 (100.0)	18 (94.7)
Circumflex n(%)	37 (97.4)	70 (90.9)	25 (56.8)	5 (83.3)	33 (76.7)	6 (100.0)	15 (78.9)
RCA n(%)	24 (63.2)	52 (67.5)	31 (70.5)	3 (50.0)	26 (60.5)	6 (100.0)	15 (78.9)
Diagonal branches n(%)	12 (31.6)	22 (28.6)	7 (15.9)	1 (16.7)	14 (32.6)	2 (33.3)	6 (31.6)
N grafts (mean (sd))	3.03 (0.79)	3.04 (0.77)	2.52 (0.90)	2.83 (1.47)	3.00 (0.82)	3.50 (0.55)	3.16 (0.76)
Conduits (%)							
LITA	0 (0.0)	0 (0.0)	4 (9.1)	1 (16.7)	2 (4.7)	0 (0.0)	0 (0.0)
LITA+RA	2 (5.3)	3 (3.9)	4 (9.1)	0 (0.0)	13 (30.2)	0 (0.0)	0 (0.0)
LITA+RA+SV	5 (13.2)	1 (1.3)	1 (2.3)	0 (0.0)	4 (9.3)	0 (0.0)	1 (5.3)
LITA+SV	30 (78.9)	48 (62.3)	32 (72.7)	5 (83.3)	21 (48.8)	5 (83.3)	15 (78.9)
RA	0 (0.0)	0 (0.0)	1 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
RA+SV	0 (0.0)	2 (2.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
RITA	0 (0.0)	1 (1.3)	2 (4.5)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
RITA+RA	0 (0.0)	1 (1.3)	0 (0.0)	0 (0.0)	1 (2.3)	0 (0.0)	0 (0.0)
RITA+RA+SV	0 (0.0)	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
RITA+SV	0 (0.0)	6 (7.8)	0 (0.0)	0 (0.0)	1 (2.3)	1 (16.7)	0 (0.0)
SVG	1 (2.6)	14 (18.2)	0 (0.0)	0 (0.0)	1 (2.3)	0 (0.0)	3 (15.8)

ITA: internal thoracic artery; LAD: left anterior descending artery; RCA: right coronary artery; BITA; bilateral internal thoracic arteries; RA: radial artery; SVG: saphenous vein graft

Supplementary Table 4. Hospital outcomes and 5-year mortality and major adverse cardiac and cerebrovascular events (MACCE) according to cause of bilateral interval thoracic artery (BITA) grafts conversion

	High risk for sternal complication	ITA not suitable	Target not suitable	Other cardiac pathologies	Justification not provided	Time constrain	Unstable during harvesting
N	38	77	44	6	43	6	19
Re-exploration for bleeding n(%)	0 (0.0)	2 (2.6)	2 (4.5)	0 (0.0)	6 (14.0)	0 (0.0)	0 (0.0)
IABP insertion n(%)	3 (7.9)	3 (3.9)	1 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)	5 (26.3)
Renal replacement therapy n(%)	1 (2.6)	1 (1.3)	1 (2.3)	0 (0.0)	1 (2.3)	1 (16.7)	1 (5.3)
Sternal complications n(%)	3 (7.9)	2 (2.6)	2 (4.5)	1 (16.7)	4 (9.3)	0 (0.0)	1 (5.3)
Death n(%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
MI n(%)	0 (0.0)	4 (5.2)	1 (2.3)	0 (0.0)	0 (0.0)	0 (0.0)	2 (10.5)
CVA n(%)	1 (2.6)	3 (3.9)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)
Revascularization n(%)	0 (0.0)	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
POAF n(%)	12 (31.6)	21 (27.3)	13 (29.5)	4 (66.7)	10 (23.3)	2 (33.3)	7 (36.8)
Mortality at 5 years	4 (10.5)	9(11.9)	6(13.8)	0(0)	6(14.1)	0(0)	2(10.8)
MACCE at 5 years	3(8)	18(24)	8(18.3)	1(16.7)	4(9.7)	1(16.7)	4(21.1)

ITA: internal thoracic artery; IABP: intra-aortic balloon pump; Myocardial infarction; CVA: cerebrovascular accident; POAF: postoperative atrial fibrillation; MACCE: major adverse cardiac and cerebrovascular events