ADULT

Incidence and clinical implications of intraoperative bilateral internal thoracic artery graft conversion: Insights from the Arterial Revascularization Trial

Check for updates

Umberto Benedetto, MD, PhD,[a] Douglas G. Altman, DSc,[b] Marcus Flather, MD,[c] Stephen Gerry, MSc,[b] Alastair Gray, PhD,[d] Belinda Lees, BSc, PhD,[a] and David P. Taggart, MD, PhD,[e] on behalf of the Arterial Revascularization Trial Investigators

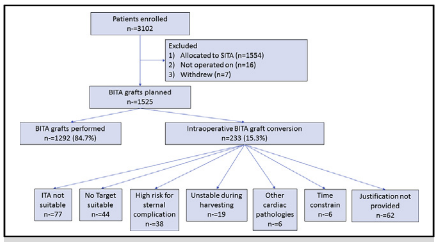
ABSTRACT

Background: The Arterial Revascularization Trial has been designed to answer the question whether the use of bilateral internal thoracic arteries can improve 10-year outcomes when compared with single internal thoracic arteries. In the Arterial Revascularization Trial, a significant proportion of patients initially allocated to bilateral internal thoracic arteries received other conduit strategies. We sought to investigate the incidence and clinical implication of bilateral internal thoracic artery graft conversion in the Arterial Revascularization Trial.

Methods: Among patients enrolled in the Arterial Revascularization Trial (n = 3102), we excluded those allocated to single internal thoracic arteries (n = 1554), those who did not undergo surgery (n = 16), and those who underwent operation but withdrew after randomization (n = 7). Propensity score matching was used to compare converted versus nonconverted bilateral internal thoracic artery groups.

Results: A total of 1525 patients were operated with the intention to receive bilateral internal thoracic artery grafting. Of those, 233 (15.3%) were converted to other conduit selection strategies. Incidence of conversion largely varied across 131 participating surgeons (from 0% to 100%). The most common reason for bilateral internal thoracic artery graft conversion was the evidence of at least 1 internal thoracic artery that was not suitable, which was reported in 77 cases. Patients with intraoperative bilateral internal thoracic artery graft conversion received a lower number of grafts (2.95 ± 0.84 vs 3.21 ± 0.74; $P < .001$). However, the hospital mortality rate was comparable to that of those who did not require bilateral internal thoracic artery graft conversion (0% vs 1.6%; $P = .1$), as well as the incidence of major complications. At 5 years, we found a nonsignificant excess of deaths (11.9% vs 8.4%; $P = .1$) and major adverse events (17.1% 13.2%; $P = .1$) mainly driven by an excess of revascularization in patients requiring conversion.

Conclusions: The incidence of intraoperative bilateral internal thoracic artery graft conversion is not infrequent. Bilateral internal thoracic artery graft conversion is not associated with increased operative morbidity, but its effect on late outcomes remains uncertain. (J Thorac Cardiovasc Surg 2018;155:2346-55)



BITA graft allocation and conversion in the ART.

Central Message

The incidence of intraoperative BITA graft conversion in the ART was not infrequent despite that participating surgeons were requested to have expertise in BITA grafts.

Perspective

Reasons for BITA graft underuse remain unclear. In the ART, participating surgeons were requested to have expertise in BITA grafts. We found that the incidence of intraoperative BITA graft conversion was not infrequent in the ART, thus supporting that BITA grafts may represent a challenge for experienced surgeons.

See Editorial Commentary page 2356.

From the [a]Bristol Heart Institute, University of Bristol, School of Clinical Sciences, United Kingdom; [b]Centre for Statistics in Medicine, Nuffield Department of Orthopaedics, Rheumatology & Musculoskeletal Sciences, and [d]Nuffield Department of Population Health, Health Economics Research Centre, University of Oxford, Oxford, United Kingdom; [c]Norwich Medical School, University of East Anglia and Norfolk and Norwich University Hospitals NHS Foundation Trust, Norwich, United Kingdom; and [e]Nuffield Department of Surgical Sciences, University of Oxford, John Radcliffe Hospital, Oxford, United Kingdom.

Supported by grants from the British Heart Foundation (SP/03/001), the UK Medical Research Council (G0200390), and the National Institute of Health Research Efficacy and Mechanism Evaluation Programme (09/800/29).

Received for publication Sept 29, 2017; revisions received Jan 10, 2018; accepted for publication Feb 7, 2018; available ahead of print March 17, 2018.

Address for reprints: Umberto Benedetto, MD, PhD, Bristol Heart Institute, University of Bristol, Senate House, Tyndall Ave, Bristol, BS8 1TH, United Kingdom (E-mail: Umberto.benedetto@bristol.ac.uk).

0022-5223/$36.00

https://doi.org/10.1016/j.jtcvs.2018.02.012

Abbreviations and Acronyms

ART	= Arterial Revascularization Trial
BITA	= bilateral internal thoracic artery
CABG	= coronary artery bypass grafting
CVA	= cerebrovascular accident
IABP	= intra-aortic balloon pump
ITA	= internal thoracic artery
LVEF	= left ventricular ejection fraction
MACCE	= major cardiac and cerebrovascular events
MI	= myocardial infarction
PS	= propensity score
SITA	= single internal thoracic artery
SVG	= saphenous vein graft

Scanning this QR code will take you to the supplemental video and tables for the article.

Although large observational studies have consistently suggested that the use of bilateral internal thoracic artery (BITA) grafting improves long-term survival when compared with single internal thoracic artery (SITA) grafting in coronary artery bypass grafting (CABG),[1,2] the use of BITA grafting remains particularly low. BITA grafting represents only 4% to 12% of all CABG procedures over the more traditional use of the SITA with additional saphenous vein grafts (SVGs).[3] The reasons for BITA underuse are multifactorial. Most surgeons do not perform BITA grafting because of the increased risk of sternal wound complications and technical complexity.[4,5] However, some patients initially intended to receive BITA grafts require intraoperative conversion to other conduit strategies. The incidence and causes of intraoperative BITA graft conversion and its clinical implication have never been investigated.

The Arterial Revascularization Trial (ART) has been designed to answer the question whether the use of BITAs can improve 10-year outcomes when compared with SITAs in CABG.[6] Interim 5-year results have shown similar clinical outcomes between the 2 groups.[7] In the ART, only surgeons with experience of 50 or more BITA operations were able to undertake BITA procedures in the trial.[6] We sought to investigate the reasons for intraoperative BITA graft conversion and its clinical implication by performing a post hoc analysis of the ART.

MATERIALS AND METHODS

A post hoc analysis of 5-year outcomes of the ART 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), those who did not undergo surgery (n = 16), and those who underwent operation but withdrew after randomization (n = 7).

Trial Design

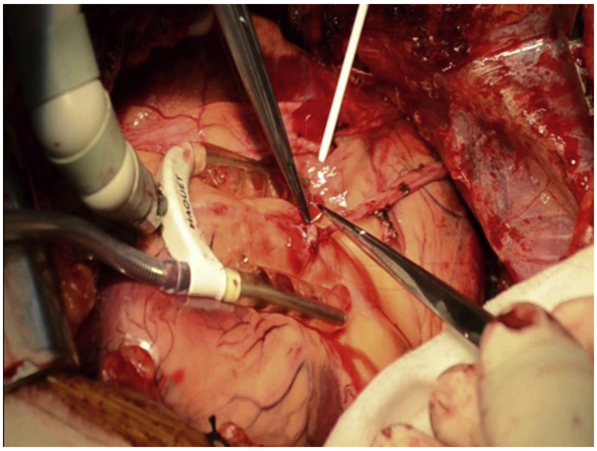
The ART was approved by the institutional review board of all participating centers, and informed consent was obtained from each participant. The protocol for the ART has been published.[6] Briefly, the ART is a 2-arm, randomized multicenter trial conducted in 28 hospitals in 7 countries (Appendix 1), with patients being randomized equally to SITA or BITA grafts. Eligible patients were those with multivessel coronary artery disease undergoing CABG. BITA graft configuration (y graft vs in situ graft vs free graft) was left at the discretion of the surgeon (Video 1). Patients requiring single grafts or redo CABG were excluded. Patients with evolving myocardial infarction (MI) (defined as the increase and decrease of a biomarker together with one of a longer list of criteria comprising ischemic symptoms, the development of pathologic Q waves, ischemic electrocardiographic 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 mail every year after surgery. No clinic visits were planned apart from the routine clinical 6-week postoperative visit. Participants were sent stamped addressed envelopes to improve the return rates of postal questionnaires. Study coordinators 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 reexploration for bleeding, intra-aortic balloon pump (IABP) insertion, MI, cerebrovascular accident (CVA), postoperative atrial fibrillation, sternal complications



VIDEO 1. Skeletonized left internal thoracic artery during off-pump surgery. Video available at: http://www.jtcvsonline.org/article/S0022-5223(18)30365-9/fulltext.

revascularization, and hospital mortality. Late outcomes were 5-year all-cause mortality and cumulative incidence of major cardiac and cerebrovascular events (MACCE), including cardiovascular death, CVA, MI, and repeat revascularization.

Outcome Definitions

Death was classified into cardiovascular and noncardiovascular, where possible, using autopsy reports and death certificates. Congestive heart failure, arrhythmia, MI, pulmonary embolus, and dissection were considered cardiovascular causes of death.

MI was diagnosed when 2 of the following 3 criteria were present: (1) unequivocal electrocardiogram changes; (2) elevation of cardiac enzyme(s) above twice the upper limit of normal or diagnostic troponin increases; or (3) chest pain typical for acute MI that lasted more than 20 minutes. CVA was defined as a new neurologic deficit evidenced by clinical signs of paresis, plegia, or new cognitive dysfunction including any mental status alteration lasting more than 24 hours or evidence on computed tomography or MRI scan of recent brain infarct (<6 months). Repeat revascularization was defined as coronary bypass surgery or percutaneous coronary intervention performed after the trial procedure. Sternal complications included sternal wound infection requiring antibiotics, vacuum-assisted closure 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

TABLE 1. Baseline characteristics

	Requiring conversion	Not converted before PSM	SMD before PSM	Not converted matched	SMD after PSM
N	233	1292		699	
Age, y (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 hyperlipemia	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
Preoperative 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

PSM, Propensity score matching; *SMD*, standardized mean difference; *SD*, standard deviation; *BMI*, body mass index; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *NYHA*, New York Heart Association; *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.

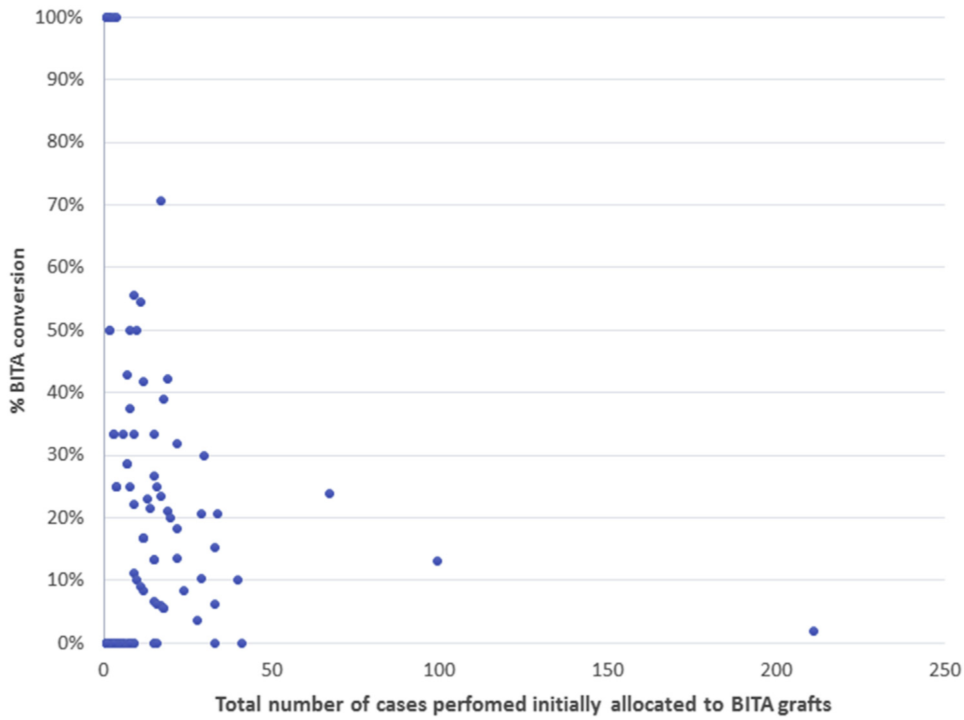


FIGURE 1. Scatter plot showing total number of cases initially allocated to BITA grafts performed by individual surgeons and relative rate of BITA conversion. *BITA*, Bilateral internal thoracic artery.

(Amelia R package). Because of the lack of randomization with regard to BITA conversion, a propensity score (PS) was generated for each patient from a multivariable logistic regression model (C-statistics 0.64) based on a prespecified set of covariates (as listed in Table 1) with requiring conversion versus nonconverted as a binary dependent variable.[9] Pairs of patients were derived using greedy 1:3 matching with a caliper 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 pretreatment variables in PS-matched patients using the standardized mean difference, with an absolute standardized difference of greater than 10% taken to represent meaningful covariate imbalance.[9] McNemar's test and paired *t* test were 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. A risk-competing framework was used to estimate the treatment effect on MACCE individual components (survival R package and riskRegression R package).

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 Table E1). The most common reason for BITA grafts conversion was the evidence of at least 1 internal thoracic artery (ITA) that was not suitable, which was reported in 77 cases (33.0%). This was due to damage 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 (ie, 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 cases (2.6%), and time constraint in 6 cases (2.6%). In 43 cases (18.5%), surgeons decided to not perform BITA grafts without providing a justification (Central Image).

Baseline characteristics in the 2 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, and left ventricular ejection fraction (LVEF) less than 0.5. Intraoperative data breakdown according to causes of BITA conversion showed that increased body mass index and diabetes were more common among those converted as perceived at higher risk for risk infection, that female gender was more common among those with poor targets, and that reduced LVEF was more common among those with those with hemodynamic instability during ITA harvesting (Table E2). After matching, the 2 groups were comparable for all baseline risk factors (all standardized mean difference <0.10) (Figure 2).

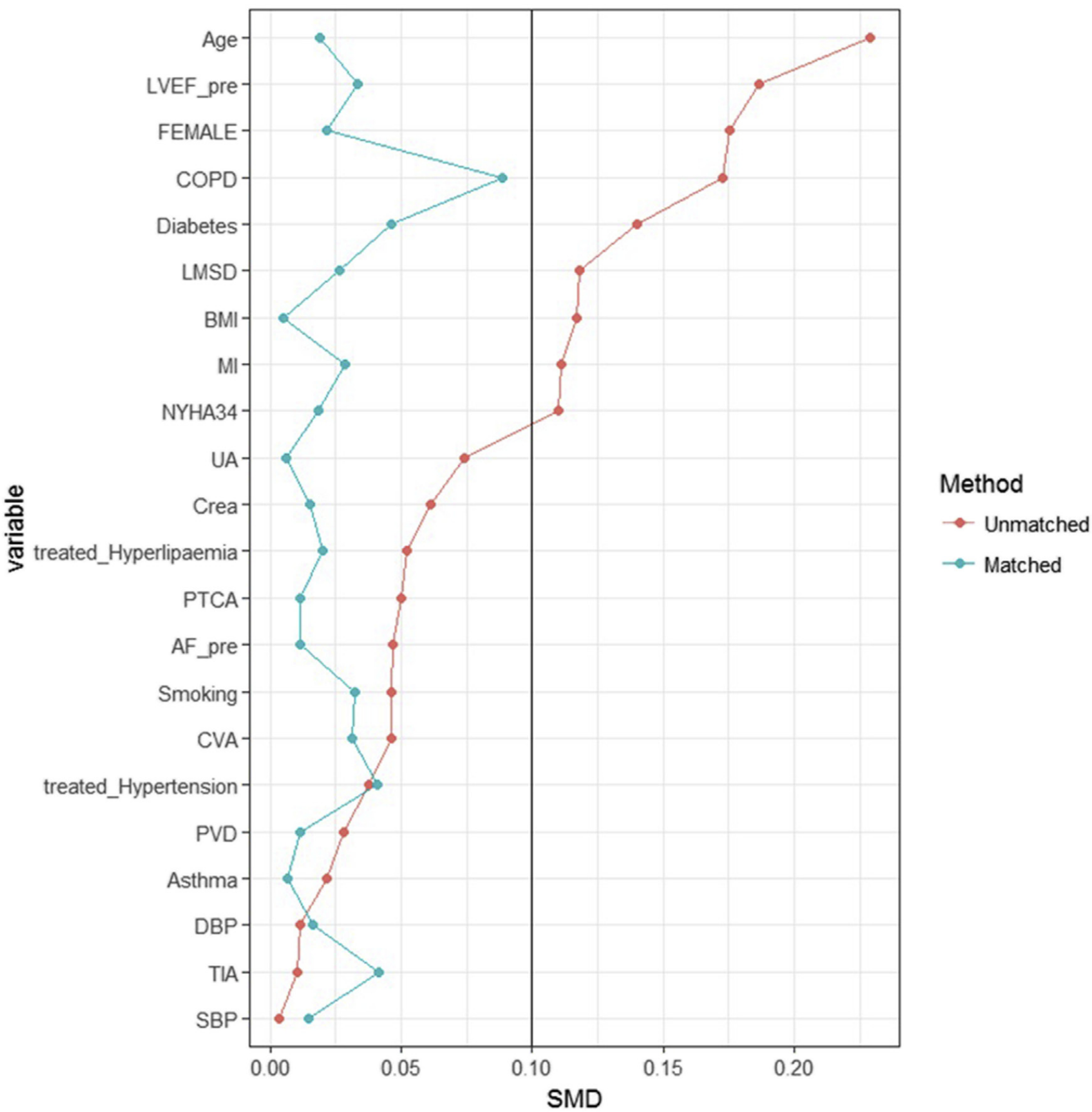


FIGURE 2. Changes in standardized mean after matching. *LVEF*, Left ventricular ejection fraction; *COPD*, chronic obstructive pulmonary disease; *LMSD*, left main stem disease; *BMI*, body mass index; *MI*, myocardial infarction; *NYHA*, New York Heart Association; *UA*, unstable angina; *PTCA*, percutaneous transcatheter coronary angioplasty; *AF*, atrial fibrillation; *CVA*, cerebrovascular accident; *PVD*, peripheral vascular disease; *DBP*, diastolic blood pressure; *TIA*, transient ischemic attack; *SBP*, systolic blood pressure; *SMD*, standardized mean difference.

Intraoperative 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 left anterior descending (95.3% vs 99.1%) and circumflex (82% vs 95.9%) territories being more likely to remain ungrafted. In the BITA conversion group, 19 patients (8.2%) 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 ITAs (18.2%) or hemodynamic instability during harvesting (15.8%) (Table E3).

Outcomes

Hospital outcomes are summarized in Table 3. Overall, patients requiring BITA graft conversion were 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 IABP and need for repeat revascularization were comparable between the 2 groups. Hospital breakdown

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)	<.001	294 (42.1)	<.001
LAD n (%)	222 (95.3)	1278 (98.9)	<.001	693 (99.1)	<.001
Circumflex n (%)	191 (82.0)	1231 (95.3)	<.001	670 (95.9)	<.001
RCA n (%)	157 (67.4)	890 (68.9)	.705	488 (69.8)	.539
Diagonal branches n (%)	64 (27.5)	395 (30.6)	.382	206 (29.5)	.617
N grafts (mean, SD)	2.95 (0.84)	3.21 (0.77)	<.001	3.21 (0.74)	<.001
Conduits (%)			<.001		<.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 + SVG		44 (3.4)		23 (3.3)	
BITA + SVG		761 (58.9)		422 (60.4)	
LITA	7 (3.0)				
LITA + RA	22 (9.4)				
LITA + RA + SVG	12 (5.2)				
LITA + SVG	156 (67.0)				
RA	1 (0.4)				
RA + SVG	2 (0.9)				
RITA	3 (1.3)				
RITA + RA	2 (0.9)				
RITA + RA + SVG	1 (0.4)				
RITA + SVG	8 (3.4)				
SVG	19 (8.2)				

PSM, Propensity score matching; *LAD*, left anterior descending artery; *RCA*, right coronary artery; *SD*, standard deviation; *BITA*, bilateral internal thoracic artery; *RA*, radial artery; *LITA*, left internal thoracic artery; *RITA*, right internal thoracic artery; *SVG*, saphenous vein graft.

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 (Table E4).

Five-year outcomes are summarized in Table 4 and Figure 3. In patients requiring conversion, we found a nonsignificant excess of deaths (11.9% vs 8.4%; *P* = .1) and MACCE (17.1% 13.2%; *P* = .1), mainly driven by an excess of revascularization (Figure 4). Those who

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	
Reexploration for bleeding n (%)	10 (4.3)	47 (3.6)	.8	20 (2.9)	.4
IABP insertion n (%)	12 (5.2)	55 (4.3)	.7	36 (5.2)	1
Renal replacement therapy n (%)	6 (2.6)	85 (6.6)	.03	52 (7.4)	.01
Sternal complications n (%)	13 (5.6)	64 (5.0)	.8	36 (5.2)	.9
Death n (%)	0 (0.0)	17 (1.3)	.2	11 (1.6)	.1
MI n (%)	7 (3.0)	18 (1.4)	.1	12 (1.7)	.4
CVA n (%)	5 (2.1)	13 (1.0)	.2	9 (1.3)	.5
Revascularization n (%)	1 (0.4)	9 (0.7)	1	5 (0.7)	1
POAF n (%)	69 (29.6)	329 (25.5)	.2	208 (29.8)	1

PSM, Propensity score matching; *IABP*, intra-aortic balloon pump; *MI*, 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 y	27 (11.9)	104 (8.2)	.08	58 (8.4)	.1
MACCE at 5 y	39 (17.1)	155 (12.4)	.03	90 (13.2)	.1
Cardiovascular death	8 (3.5)	44 (3.5)	1	29 (4.2)	.7
MI	9 (3.9)	42 (3.3)	.6	24 (3.5)	.7
CVA	7 (3.0)	31 (2.4)	.6	19 (2.7)	.8
Revascularization	12 (8.2)	81 (6.4)	.2	43 (6.2)	.2

PSM, Propensity score matching; *MACCE*, major adverse cardiac and cerebrovascular events; *MI*, myocardial infarction; *CVA*, cerebrovascular accident.

required conversion for hemodynamic instability during ITA harvesting and found to have a poor target or unsuitable ITA tended to have a higher rate of mortality and MACCE (Table E4).

Conduit Selection in Patients Initially Allocated to Single Internal Thoracic Artery

For descriptive purpose, we also reported conduit selection in those initially allocated to SITA grafting. Among

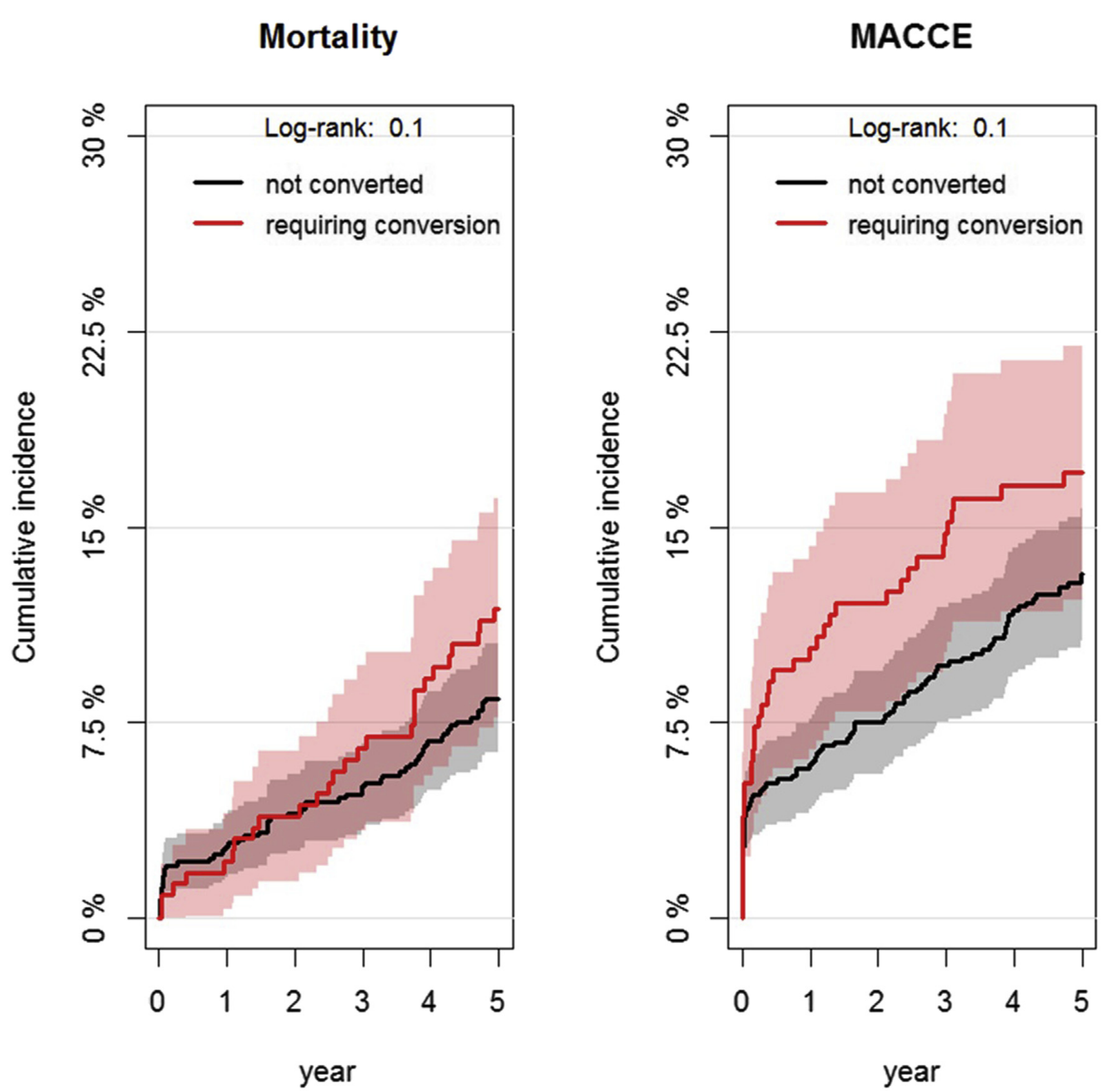


FIGURE 3. Cumulative incidence of mortality and MACCE in the matched sample. *MACCE*, Major adverse cardiac and cerebrovascular events.

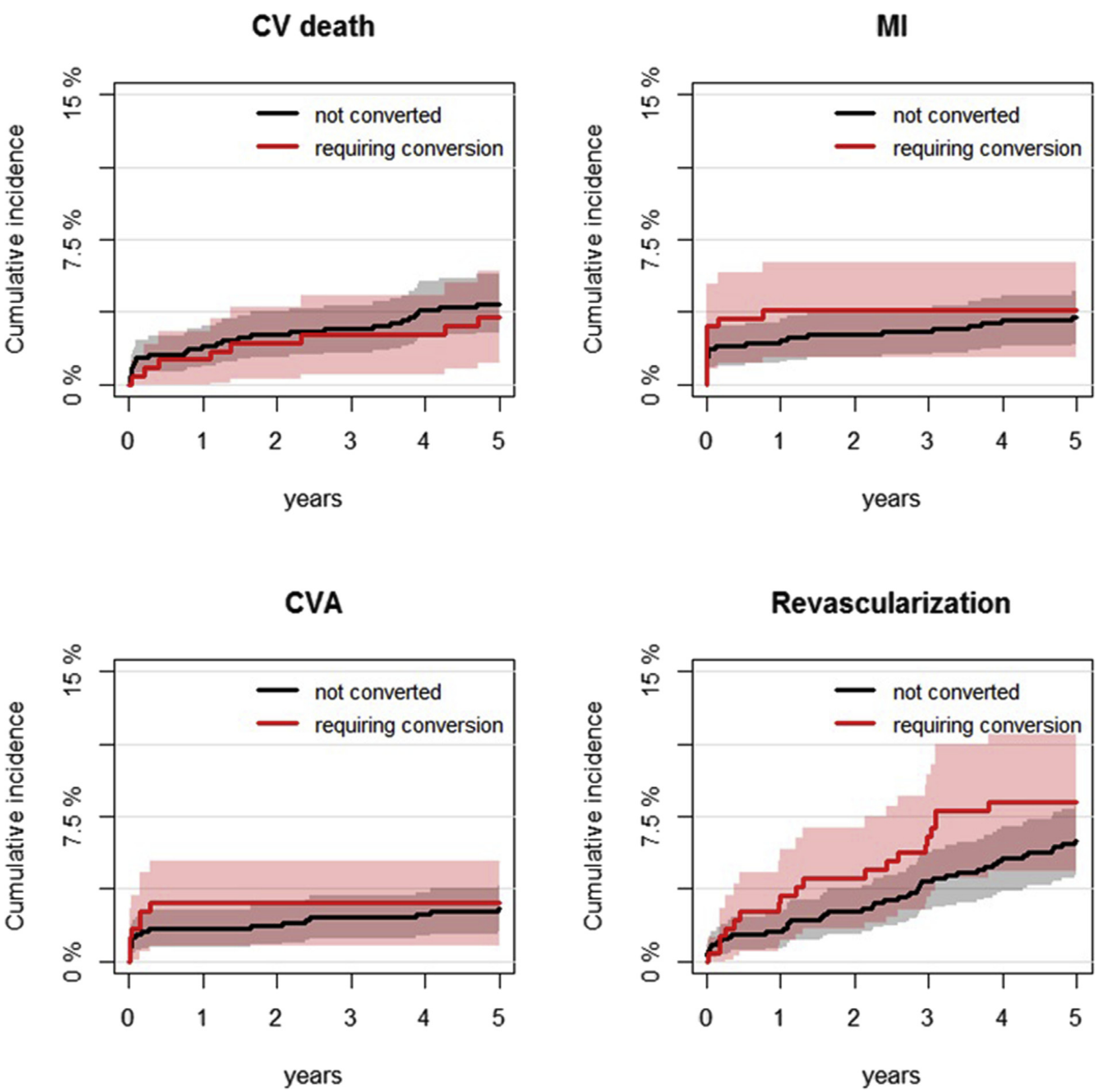


FIGURE 4. Cumulative incidence of CV death, MI, CVA, and revascularization in the matched sample. *CV*, Cerebrovascular; *MI*, myocardial infarction; *CVA*, cerebrovascular accident.

1554 patients initially allocated to SITA, 8 did not undergo operation (1 death, 4 withdrew, 3 cases with no reason reported), and the remaining 1546 underwent surgery. Of those, 1494 received SITA grafting (96.7%) and 38 received BITA grafting (2.5%) for the following reasons: no other suitable conduit available (n = 21, 1.4%), withdrew (n = 2, 0.1%), and reason not reported (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%), and need for unplanned surgery (n = 1, 0.5%).

DISCUSSION

Reasons for the underuse of BITA grafting are 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 graft 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 in view of the current intense professional and public scrutiny of cardiac surgeons.

The ART represents a unique opportunity to investigate the incidence and causes of intraoperative BITA graft conversion.[7] Of note, although participating surgeons were anticipated to be expert in BITA grafts, the rate of intraoperative conversion was not infrequent. 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 large variation in BITA grafting conversion across surgeons, which supports the central role for individual surgeon experience. Of note, an unsuitable ITA was reported as the main reason (33%) for intraoperative BITA graft conversion to other conduit strategies, and it was mainly related to injury during harvesting. Of note, the rate of an unsuitable ITA in those allocated to SITA grafts was only 0.6%, suggesting that harvesting 2 ITAs is more demanding and can influence a surgeon's precision. In 44 patients, BITA was not performed because of a poor target. Among those patients, only 7 required only 1 graft. In all other cases, the SVG and radial artery were used in addition to SITA grafts, suggesting the 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 the chest retractor during ITA harvesting may not always be tolerated, especially in the 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 (ie, osteoporotic sternum). In case of intraoperative conversion, SITA plus SVG was the most commonly used strategy, followed by SITA plus radial artery. Of note, 19 patients (8.2%) received SVG only.

In contrast to other clinical scenarios where intraoperative conversion significantly increases operative morbidity and mortality, such as off-pump to on-pump conversion,[11] BITA graft conversion was not associated with a 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 nonsignificant trend toward an excess of death and MACCE in patients requiring intraoperative conversion, in particular among those with perioperative hemodynamic instability, a poor target, and unsuitable ITA. We can speculate that perioperative myocardial injury, a lower number of grafts, and excess of an SVG only strategy in these 3 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, particularly 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.

Study Limitations

There are 2 main limitations in the present analysis. This is a retrospective analysis of the ART, and we cannot exclude residual confounding factors between the 2 groups despite PS 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 the skeletonized or pedicled technique.

CONCLUSIONS

The incidence of intraoperative BITA graft conversion is not infrequent among experienced surgeons participating in the ART. Although intraoperative BITA graft conversion does not increase the risk of operative mortality and major complications, BITA conversion might be associated with poorer outcomes on long-term follow-up. This requires further investigation.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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;130:539-45.
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. Rubin DB. *Multiple Imputation for Nonresponse in Surveys*. New York: John Wiley & Sons; 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;46:119-51.
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;152:270-6.
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;128:655-61.

Key Words: bilateral internal thoracic artery, outcomes, randomized controlled trial

APPENDIX 1.

Contributors: Ratnatunga C, Westaby S, Cook J, Wallis C, Wos S, Jasinski M, Widenka K, Blach A, Gocol R, Hudziak D, Zurek P, Deja M, Bachowski R, Mrozek R, Kargul T, Domarardzki W, Frackiewicz J, Zamvar V, Ezakadan D, Buxton B, Seevanayagam S, Matalanis G, Rosalion A, Negri J, Moten S, Atkinson V, Newcomb A, Polidano P, Pana R, Gerbo S, O'Keefe P, von Oppell U, Mehta D, Azzu A, Szafranek A, Kulatilake E, Evans J, Martin N, Banner D, Trivedi U, Forsyth A, Hyde J, Cohen A, Lewis M, Gardner E, MacKenzie A, Cooter N, Joyce E, Parker J, Champney F, Clark S, Dark J, Tocewicz K, Pillay T, Rowling S, Adams-Hall J, Bochenek A, Cisowski M, Bolkowski M, Morawski W, Guc M, Krejca M, Wilczynski M, Duralek A, Gerber W, Skarysz J, Shrestha R, Swiech W, Szmagala P, Krzych L, Pawlak A, Kepa K, Hasan R, Keenan D, Prendergast B, Odom N, McLaughlin K, Cummings-Fosong G, Mathew C, Iles-Smith H, Oomen A, Desai J, El-Gamel A, John L, Wendler O, Andrews M, Rance K, Williams R, Hogervorst V, Gregory J, Jessup J, Knighton A, Hoare A, Ritchie A, Choong C, Nair S, Jenkins D, Large S, Sudarshan C, Barman M, Dhital K, Routledge T, Rosengard B, Munday H, Rintoul K, Jarrett E, Lao-Sirieix S, Wilkinson A, Garner L, Osmond J, Holcombe H, Cale A, Griffin S, Dickson J, Spyt T, Hickey M, Sosnowski A, Peek G, Szostek J, Hadjinikalaou L, Logtens E, Oakley M, Leji S, Gaer J, Amrani M, Dreyfus G, Bahrami T, de Robertis F, Baig K, Asimakopoulos G, Vohra H, Pai V, Tadjkarimi S, Soleimani B, Stavri G, Bull G, Collappen H, Sadowksi J, Gaweda B, Rudzinski P, Stolinski J, Konstanty-Kalandyk J, Moraes F, Moraes C, Wanderley J, Pepper J, De Souza A, Petrou M, Trimlett R, Morgan T, Gavino J, Wang SF, Chandrasekaran V, Kanagasaby R, Sarsam M, Ryan H, Billings L, Ruddick L, Achampong A, Forster E, Pawlaczyk R, Siondalski P, Rogowski J, Roszak K, Jarmoszewicz K, Jagielak D, Gafka S, Mannam G, Naguboyin G, Rao Sajja L, Dandu B, Briffa N, Braidley P, Cooper G, Allen K, Sangha G, Bridge C, McMellon H, Casabona R, Actis Dato G, Bardi G, Del Ponte S, Forsennati P, Parisi F, Punta G, Flocco R, Sansone F, Zingarelli E, Dihmis W, Kuduvali M, Prince C, Rogers H, McQuade L, Anisimowicz L, Bokszanski M, Pawliszak W, Kolakowski J, Lau G, Ogorzeja W, Gumanska I, Kulinski P, Podesser B, Trescher K, Bernecker O, Holzinger C, Binder K, Schor I, Bergmann P, Kassal H, Motovova B, Trehan N, Meharwal Z, Malhotra R, Goel M, Kumer B, Bazaz S, Bake N, Singh A, Mishka Y, Gupta R, Basumatary S, Zembala M, Szafron B, Pacholewicz J, Krason M, Farmas A, Wojarski J, Zych B, Szymanik I, Kolwca M, Mazur W, Kurowicki A, Zurek S, Stacel T, Jaworska I, Sleight P, Channon K, Farrell B, Stables R, Vermes G, Pearson J, Pitman M, Yusuf S, Pocock S, Julian D, Treasure T, Von Oppel U, Kanagasabay R, Collinson J, Bakhai A, O'Hanlon R, Kotecha D, Qureshi K, Geisler T, Manzano-Espinosa L.

TABLE E1. Number of cases performed initially allocated to bilateral internal thoracic artery grafts and bilateral internal thoracic artery conversion rate

Surgeon	Total no. of cases performed initially allocated to BITA grafts	% BITA graft conversion
Unknown	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%

(Continued)

TABLE E1. Continued

Surgeon	Total no. of cases performed initially allocated to BITA grafts	% BITA graft conversion
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%

(Continued)

TABLE E1. Continued

Surgeon	Total no. of cases performed initially allocated to BITA grafts	% BITA graft conversion
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%

(Continued)

TABLE E1. Continued

Surgeon	Total no. of cases performed initially allocated to BITA grafts	% BITA graft conversion
127	3	0.0%
128	1	0.0%
129	33	15.2%
130	99	13.1%
131	3	33.3%

BITA, Bilateral internal thoracic artery.

TABLE E2. Baseline characteristics according to cause of bilateral internal thoracic artery graft conversion

	High risk for sternal complication	At least 1 ITA not suitable	Target not suitable	Other cardiac pathologies	Justification not provided	Time constraint	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 hyperlipemia	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)
Preoperative 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; *SD*, standard deviation; *BMI*, body mass index; *SBP*, systolic blood pressure; *DBP*, diastolic blood pressure; *NYHA*, New York Heart Association; *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 E3. Operative data according to cause of bilateral internal thoracic artery graft conversion

	High risk for sternal complication	At least 1 ITA not suitable	Target not suitable	Other cardiac pathologies	Justification not provided	Time constraint	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 + SVR	5 (13.2)	1 (1.3)	1 (2.3)	0 (0.0)	4 (9.3)	0 (0.0)	1 (5.3)
LITA + SVR	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 + SVR	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 + SVR	0 (0.0)	1 (1.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
RITA + SVR	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; *SD*, standard deviation; *LITA*, left internal thoracic artery; *RA*, radial artery; *RITA*, right internal thoracic artery; *SVG*, saphenous vein graft.

TABLE E4. Hospital outcomes and 5-year mortality and major adverse cardiac and cerebrovascular events according to cause of bilateral internal thoracic artery graft conversion

	High risk for sternal complication	ITA not suitable	Target not suitable	Other cardiac pathologies	Justification not provided	Time constraint	Unstable during harvesting
N	38	77	44	6	43	6	19
Reexploration 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 y	4 (10.5)	9 (11.9)	6 (13.8)	0 (0)	6 (14.1)	0 (0)	2 (10.8)
MACCE at 5 y	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; *MI*, myocardial infarction; *CVA*, cerebrovascular accident; *POAF*, postoperative atrial fibrillation; *MACCE*, major adverse cardiac and cerebrovascular events.