Cite this article as: Bonacchi M, Prifti E, Bugetti M, Cabrucci F, Cresci M, Lucá F et al. In situ skeletonized bilateral thoracic artery for left coronary circulation: a 20year experience. Eur J Cardiothorac Surg 2019; doi:10.1093/ejcts/ezz138.

In situ skeletonized bilateral thoracic artery for left coronary circulation: a 20-year experience

Massimo Bonacchi () ^{a,*}, Edvin Prifti^b, Marco Bugetti^a, Francesco Cabrucci^a, Michael Cresci^a, Fabiana Lucá^c, Orlando Parise^c, Francesco Matteucci^c, Guido Sani^d, Daniel M. Johnson () ^{c,e} and Sandro Gelsomino () ^c

^a Cardiac Surgery Unit, Department of Experimental and Clinical Medicine, University of Florence, Firenze, Italy

^b Division of Cardiac Surgery, University Hospital Center of Tirana, Tirana, Albania

^c Cardiovascular Research Institute Maastricht - CARIM, Maastricht University Medical Centre, Maastricht, Netherlands

- ^d Cardiac Surgery, Department of Medical Biotechnologies, University of Siena, Siena, Italy
- ^e Institute of Cardiovascular Sciences, University of Birmingham, Birmingham, UK
- * Corresponding author. Unit of Cardiac Surgery, Department of Experimental and Clinical Medicine, University of Florence, Largo Brambilla, 3, 50144 Firenze, Italy. Tel: +393389855782; e-mail: massimo.bonacchi@unifi.it (M. Bonacchi).

Received 4 October 2018; received in revised form 8 March 2019; accepted 25 March 2019



Abstract

OBJECTIVES: Our goal was to analyse the outcomes in a patient population using a standardized technique for coronary artery bypass grafting (CABG) consisting of total arterial myocardial revascularization utilizing the *in situ* skeletonized bilateral thoracic artery for left coronary circulation. We also explored potential predictors of long-time unfavourable outcomes.

METHODS: Patients undergoing total arterial myocardial revascularization using *in situ* skeletonized bilateral thoracic artery for left coronary circulation between January 1997 and May 2017 were included prospectively in this study. The median follow-up (100% complete) was 103 months (interquartile range 61–189 months) and ranged from 1 to 245 months.

RESULTS: A total of 1325 consecutive patients were recruited. During the follow-up period, there were 131 deaths (9.8%), 146 repeat revascularizations (11.0%) and 229 major adverse cardiac events (17.2%). The 18-year freedom from major adverse cardiac events was $62.6 \pm 9.3\%$, $62.5 \pm 6.3\%$ and $53.9 \pm 11.0\%$, respectively. Multivariable models showed that a left ventricular ejection fraction $\leq 35\%$, chronic obstructive pulmonary disease, peripheral vascular disease (P < 0.001), chronic kidney disease and age ≥ 80 years (P = 0.002) were independent predictors of diminished long-term survival. Moreover, peripheral vascular disease and off-pump coronary artery bypass (both, P < 0.001) predicted repeat revascularization. Finally, age ≥ 80 years, peripheral vascular disease, left ventricular ejection fraction $\leq 35\%$, off-pump coronary artery bypass and chronic pulmonary obstructive disease were independent predictors of major adverse cardiac events during the long-term follow-up period (all, P < 0.001).

CONCLUSIONS: Coronary artery bypass using the *in situ* skeletonized bilateral thoracic artery for left coronary circulation configuration for total arterial myocardial revascularization resulted in satisfactory long-term results with a low incidence of death and late events and may represent a technique of choice in selected patients having CABG. Larger and long-term prospective studies are, however, warranted.

Keywords: Internal thoracic artery • Arterial myocardial revascularization • Coronary artery bypass

INTRODUCTION

The use of the left internal thoracic artery (LITA) to revascularize the left anterior descending artery (LAD) has been acknowledged as the gold standard for coronary artery bypass grafting (CABG) [1]. Moreover, the additional benefits of the use of the right internal thoracic artery (RITA) in a bilateral configuration, employing both internal thoracic arteries (BITA) has previously been reported [2–5]. A major issue with BITA use, however, is the risk of sternal complications [6]. Furthermore, many surgeons claim there is not enough evidence to support the use of BITA, mainly due to the conflicting results reported from heterogeneous studies [6–8].

In the most recent surgical revascularization guidelines (2018 European Society of Cardiology/European Association for Cardiothoracic Surgery), arterial grafting of the ITA to the LAD system is recommended (class I-B); BITA grafting should be considered in patients who do not have a high risk of sternal wound infection (class II-B); and skeletonization of the ITAs is recommended (class I-B) to improve outcomes in patients with a high risk of infection. Furthermore, use of the radial artery (RA) rather than the saphenous vein is recommended in patients with high-grade coronary artery stenosis (I-B) [9].

Since 1997 we have used a standardized CABG configuration for total arterial revascularization. It consists of the *in situ* skeletonized BITA for left coronary circulation grafting with, if necessary, an RA on the right coronary circulation for a total arterial myocardial revascularization (TAMR) configuration.

The goal was to report our experience over 20 years with this approach and we hypothesized that the use of the *in situ* skeletonized BITA for left coronary circulation grafting for TAMR configuration leads to positive long-term (>20 years) outcomes in terms of survival, repeat revascularization and major adverse cardiac events (MACE). We also explored potential predictors of these events.

METHODS

Approval was granted by the institutional ethics committee due to the prospective analysis of the study according to our national laws (Italian law nr.11960, released on 13 July 2004). Written consent was obtained from patients who had the surgical procedure to use their data for scientific purposes.

Patients were recruited for this study between January 1997 and December 2017. Data were collected prospectively in a dedicated database used for this study. All centres involved in this study used the same study protocol and patient selection process. Study practices were homogeneous, and outcome assessments were centralized. During the same period, the total number of patients undergoing various TAMR techniques was 15 124. Patients receiving RITA on the LAD, RITA on a right coronary branch, free or Y grafts, or a venous graft were excluded.

At the follow-up examination, both instrumental and clinical data were prospectively recorded in the database: hospital records, physician or outpatient records and telephone interviews with the patients themselves or family members were collected.

Definitions and study end points

Primary end points of this study were (i) late death; (ii) repeat coronary revascularization (percutaneous coronary intervention or repeat CABG); and (iii) MACE, including cardiac death, non-fatal myocardial infarction (MI) or angina, target vessel revascula-rization, stroke and heart failure.

Postoperative MI was diagnosed by troponin and electrocardiographic criteria [8]. The diagnosis and classification of diabetes mellitus (DM) were based on criteria suggested by the American Diabetes Association [10], and all patients with DM underwent strict glycemic control with preoperative continuous insulin infusion, insulin infusions during cardiopulmonary bypass and postoperative (24–48 h) maintenance of blood glucose at <10 mmol/l. Obesity was classified [11] as class I in patients with a body mass index (BMI) between 30 and 34.9 kg/m^2 ; as class II for those with a BMI between 35 and 39.9 kg/m^2 ; and class III for those with a BMI \geq 40 kg/m². Stroke was defined as a new onset of focal or global neurological deficit lasting more than 24 h. Definitions of chronic kidney disease and chronic obstructive pulmonary disease (COPD) were consistent with those of the Society of Thoracic Surgeons database.

Surgical technique

Surgery was carried out as previously reported [12, 13]. Indications and contraindications for BITA were the same as those we recently reported [13]: In summary, patients with a reasonable life expectancy (>1 year), those requiring minimization of aortic manipulation and those with at least 2 angiographically visible branches of the left coronary circulatory system that were graftable were included. Contraindications were poorly

Table 1: Patient characteristics (n = 1325)

Women	284 (21.4)
Mean age (years)	65.7 ± 12.3
Range	28-87
Diabetes	329 (24.8)
Hypertension	946 (65.3)
Smoking	414 (71.4)
Dyslipidaemia	564 (42.6)
CKD	
Creatinine 120-250	69 (5.2)
Creatinine >250	38 (2.8)
Dialysis	16 (1.2)
Previous CVD	42 (3.2)
PVD	111 (8.4)
COPD	
Mild: FEV ₁ ≥80% predicted	79 (5.9)
Moderate: FEV ₁ = 50–79% predicted	43 (3.2)
Moderate: FEV ₁ <50% predicted	5 (0.3)
NYHA	1.7 ± 0.9
CCS	3.2 ± 0.8
Stable angina	759 (57.3)
Unstable angina	566 (42.7)
Prior myocardial infarction	712 (53.7)
Prior coronary angioplasty	428 (32.3)
Preoperative IABP	168 (12.6)
Heavily calcified aorta ^a	123 (9.3)
Coronary angiography data	
3-Vessel disease	925 (69.8)
2-Vessel disease	329 (24.8)
Left main coronary artery stenosis	441 (33.3)
LVEF	51.6 ± 9.3
LVEF <u><</u> 35%	301 (22.7)
EuroSCORE II	2.9 ± 0.8
STS score	3.6 ± 2.7

Data are shown as mean \pm SD or n (%).

^aAorta with the ascending portion circumferentially calcified, detected with a thoracic Rx or a thoracic computed tomography scan or detected manually via surgical inspection during the operation.

CCS: Canadian Cardiovascular Society; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; CVD: cerebrovascular disease; FEV₁: forced expiratory volume in 1 s; IABP: intra-aortic balloon pump; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association; PVD: peripheral vascular disease; SD: standard deviation; STS: Society of Thoracic Surgeons.

controlled diabetes (defined as an uninterrupted HbA1c >8.0% for \geq 1 year despite standard care) [14], class III obesity and evolving or acute (6 h-7 days) MI.

The target for skeletonized *in situ* LITA was the LAD and its branches. All patients had RITA on a left-sided target: in patients in whom 2 graftable branches were available, the branch with the larger perfusion area was selected; if both branches had identical perfusion areas, the distal branch was selected for RITA grafting, whereas the other vessel was revascularized with composite, sequential ITA grafts or other available conduits if required. In patients with a heavily calcified aorta, off-pump coronary artery bypass (OPCAB) with the BITA was the procedure of choice to reduce the operative risk.

Care was taken throughout the operation to keep the pleurae closed, to preserve the pericardiacophrenic artery branches and to spare the communicating bifurcation of the ITAs to the wall of the chest. In cases where a radial graft was planned, the artery was harvested from the non-dominant arm after a preoperative assessment of the palmar arch with the Allen test. Digital plethysmography was carried out if required.

All interventions were carried out by 4 senior surgeons (M.B., E.P., G.S. and S.G.).

Postoperatively, the glycemic values were carefully controlled by using continuous insulin infusion, with particular consideration given to the high risk of deep sternal wound infection (DSWI) with BITA [13].

Statistical analyses

To address missing values (range 0.002–0.005), we used the fully conditional specification multiple imputation method (1000 replications).

The normality of the data was assessed using the Kolmogorov-Smirnov test. Continuous data were summarized as the mean (standard deviation) or the median (25th-75th percentiles) in case of skewed distributions. Categorical variables were reported as counts and percentages, and comparisons were carried out using the Fisher's exact test. Forty-two parameters (Supplementary Material, Table S1) were considered in the initial model. To enhance the accuracy of the model, the number of variables was reduced using variable clustering. All variables showing *P*-value <0.2 at univariable analysis were introduced into multivariable analyses.

The Kaplan-Meier method and the log-rank test were used for survival analysis. A Cox regression model was used to estimate predictors of death. The proportional hazard assumption was confirmed by use of Schoenfeld residuals. A competing risk analysis was used to avoid overestimation of the incidence of repeated revascularization and MACE. R, release 3.2.3 (R Foundation for Statistical Computing, Vienna, Austria) software and 'survival', 'cmprsk' and 'forestplot' packages were utilized. Significance for hypothesis testing was set at the 0.05 two-tailed level.

RESULTS

In total, 1325 patients who underwent CABG by the *in situ* skeletonized bilateral thoracic artery for left coronary circulation technique for TAMR during the period of study were included. During the same period, the total number of patients undergoing various TAMR techniques was 15 124. Preoperative characteristics are summarized in Table 1.

A total of 962 patients underwent on-pump arrested heart CABG and 363 patients had off-pump CABG. In the group undergoing on-pump CABG, various types of myocardial protection strategies were used in 355 patients. In the early stages of the study, St. Thomas' crystalloid cardioplegia was used whereas after 2009, Custodiol was utilized. Also, cold blood cardioplegia was used in 607 patients.

Early results

The early mortality rate was 1.4% (n = 19); the causes are shown in Supplementary Material, Table S2, along with other early outcomes. Surgical data are shown in Table 2. The RITA was routed via the transverse sinus in 873 patients (66%) and behind the superior caval vein in 452 (34%). The number of distal anastomoses in patients undergoing the off-pump procedure was 2.5 ± 0.8 vs 2.6 ± 0.9 in the on-pump group (P = 0.06).

Thirty-three patients (2.5%) had sternal wound infections; 12 (0.9%) of them required surgical treatment. Fifteen of these

patients had diabetes, whereas 18 did not (P > 0.05). Diabetes significantly increased the mortality rate in patients with wound infection [9/15 (60%) vs 0/18 (0%); P < 0.0001].

Main outcomes

There were 131 (9.8%) deaths during the follow-up period. Cumulative actuarial survival at 1, 5, 10, 15 and 18 years was $99.4 \pm 0.2\%$, $97.5 \pm 2.3\%$, $93.1 \pm 5.7\%$, $85.7 \pm 7.8\%$ and $62.6 \pm 9.3\%$,

Table 2:	Operative data	(n = 1325)
----------	----------------	------------

Urgent/emergency	379 (28.6)
Redo operation	77 (5.8)
Cardiopulmonary bypass time (min)	83.7 ± 21.3
Aortic cross-clamp time (min)	64.6 ± 16.4
Off-pump coronary artery bypass grafting	363 (27.4)
Number of distal anastomoses per patient	2.6 ± 0.7
Coronary artery endarterectomy	104 (7.8)
Sequential anastomoses in situ LITA-LAD-DA	365 (27.5)
Sequential anastomoses in situ LITA-DA-LAD	257 (19.4)
RITA grafted to the IA	238 (18)
RITA grafted to the OM	822 (62)
RITA grafted to the PL	265 (20)
Sequential anastomoses in situ RITA	19 (1.4)
Radial artery on the RCA or one of its branches	410 (30.9)

Data are shown as mean ± SD or n (%).

DA: diagonal branch of left descending artery; IA: intermediate artery; LAD: left anterior descending artery; LITA: left internal thoracic artery; OM: obtuse marginal artery; PL: posterolateral branch of the circumflex artery; RCA: right coronary artery; RITA: right internal thoracic artery; SD: standard deviation. respectively (Fig. 1A). When survival rates were further analysed (Fig. 1B–E), patients with left ventricular ejection fraction (LVEF) \leq 35%, peripheral vascular disease (PVD), COPD (all; *P* < 0.0001), \geq 80 years (*P* = 0.0002) and chronic kidney disease (*P* = 0.0001) all showed lower survival rates.

One hundred forty-six patients (11.0%) underwent repeat revascularization for graft failure: 16 (10.9%) had redo CABG whereas 130 (89%) underwent percutaneous coronary intervention. Also, in 57 of these patients, revascularization occurred on another non-previously revascularized vessel. Eighty-five patients experienced RA failure (20.7% of RA); 39 had RITA failure (2.9% of RITA); and 22 had LITA failure (1.6% of LITA). The cumulative incidence of repeat revascularization at 1, 5, 10, 15 and 18 years (Fig. 2A) was $2.3 \pm 0.4\%$, $4.2 \pm 0.6\%$, $8.4 \pm 1.1\%$, $18.3 \pm 3.8\%$ and $20.4 \pm 5.5\%$, respectively. Values were significantly higher in patients who had OPCAB (Supplementary Material, Table S3) and PVD (Fig. 2B and C).

The median follow-up (100% complete) period was 103 months (interquartile range 61–189 months) and ranged from 1 to 245 months. Cumulative follow-up was 156 424 patient-years.

Two hundred twenty-nine patients (17.2%) had MACE during the follow-up period. The cumulative incidence of MACE was 2.6 ± 0.4%, 5.1 ± 0.7%, 11.3 ± 2.1%, 26.3 ± 6.4% and 32.4 ± 8.0% at 1, 5, 10, 15 and 18 years, respectively (Fig. 3A). The cumulative incidence (Fig. 3B–F) was higher in patients ≥80 years, with PVD, LVEF <35%, undergoing off-pump surgery or with COPD. LVEF ≤35%, COPD, PVD (all; P < 0.0001), chronic kidney disease and age ≥80 years (P = 0.002) were independent predictors of diminished long-term survival (Table 3). Competing risk analysis of PVD and OPCAB (both, P < 0.001) predicted repeat revascularization whereas a number of factors were independent predictors of MACE [age ≥80 years, PVD, LVEF ≤ 35%, presence of OPCAB and COPD (all, P < 0.001)].



Figure 1: Overall survival (**A**) and survival in subgroups of patients. (**B**) by LVEF; (**C**) by PVD; (**D**) by COPD; (**E**) by Patient's Age; (**F**) by CKD. The Kaplan-Meier curves are plotted from 70% to 100% survival probability in (**A**) and from 10% to 100% survival probability in (**E**). All other curves are plotted from 0% to 100% survival probability. CI: confidence interval; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; LVEF: left ventricular ejection fraction; PVD: peripheral vascular disease.



Figure 2: Total cumulative incidence of repeat revascularization (A) and stratification by groups (B) by CABF; (C) by PVD. OPCAB: off-pump coronary (artery) bypass; PVD: peripheral vascular disease.

DISCUSSION

The routine use of BITA has been hampered by a number of factors despite the reported benefits of a second ITA [3-6]. The majority of published studies are biased by significant differences including techniques, anastomosis target and graft type.

We present a prospective 20-year experience in a relatively homogeneous population using a standard TAMR technique

including *in situ* skeletonized BITA for revascularization of left coronary branches and, when necessary, RA grafting for right coronary revascularization.

In our population, the incidence of long-term postoperative adverse outcomes was relatively low [6, 15], especially when one considers the duration of the follow-up. We believe these results are likely linked to 3 technical factors: (i) the TAMR graft configuration; (ii) the in situ BITA arrangement (no Y free grafts) with a relatively small number of sequential anastomoses to ensure, in most patients, the entire arterial flow to the main targeted vessel; (iii) the anastomosis of both thoracic arteries to the left circulation, with LAD targeted by LITA and RITA never crossing the posterior sternum. Total arterial revascularization using BITA has previously been shown to be advantageous in terms of long-term survival, incidence of cardiovascular events, reoperation and the need for angioplasty [2, 16]. The influence of TAMR on outcomes is presumably linked to the higher patency rate of arterial grafts over time and the avoidance of vein graft atherosclerosis as well as the less extensive manipulation of the ascending aorta. It remains to be established whether, and how much, the positive influence of TAMR in our study is dependent on the skeletonized technique graft design. Calafiore's group [17] previously reported that the long-term patency rate of skeletonized and pedicled ITA grafts was similar whereas other studies [18, 19] have shown that skeletonization of the ITA can improve conduit flow with larger vessel diameter. The recent Arterial Revascularization Trial (ART) [6, 20] demonstrated the absence of any mid-term (5-year and 10-year) benefit from BITA and that skeletonized harvesting did not add any further benefit compared to pedicled ITAs. However, only 48% of their patients received a skeletonized ITA with different configurations and, perhaps more importantly, follow-up was short. These factors could, at least in part, account for the differences seen with our study, because a recent study demonstrated that the differences between BITA and the use of the single internal thoracic artery only start to become evident after 5 years [15]. At this time point, results are also influenced by the progressive reduction in the patency of vein grafts not used in our study.

In situ RITA has previously been shown to have patency rates that are similar to those of in situ LITA [21, 22]; hence, this configuration has the potential advantage that coronary bypass flow is dependent on both ITAs simultaneously, resulting in a lower risk of left ventricular hypoperfusion. Other BITA configurations have significant drawbacks. The in situ RITA to the LAD plus the in situ LITA to another left ventricular coronary artery leads to a high risk of damage during resternotomy [23]. When used as a free graft, the RITA has been shown to have a low patency rate when it is connected proximally to the aorta [24]. In contrast, attachment of the free RITA to the in situ LITA (T or Y graft) has previously been observed to improve patency [17]. This arrangement does not, however, apply to the principle that LV revascularization occurs from 2 different sources, which could represent a key issue for optimal revascularization. The in situ LITA to LAD and the in situ RITA to the other left coronary target vessel avoid the difficulties of anastomosing a thin-wall vessel (e.g. the free RITA) to a thick-wall vessel (e.g. the aorta). Furthermore, it decreases the risk of injury in cases of mediastinal revision or reoperation because both ITAs lie in a safe position, requiring a lower number of anastomoses to be performed and, finally, offering the possibility to easily apply the 'non-touch' principle, by using different graft configurations [3].

Accumulating evidence suggests that the LAD and circumflex territory revascularization should take priority over the right



Figure 3: Total cumulative incidence of MACE (A) and by subgroups (B) by Patient's Age; (C) by PVD; (D) by LVEF; (E) by OPCAB; (F) by COPD. COPD: chronic obstructive pulmonary disease; LVEF: left ventricular ejection fraction; MACE: major adverse cardiac events; OPCAB: off-pump coronary (artery) bypass; PVD: peripheral vascular disease.

	HR	95% CI	P-value
Death			
LVEF <35%	11.71	5.65-24.27	< 0.001
COPD	4.27	2.37-7.67	< 0.001
PVD	14.84	6.70-32.89	< 0.001
CKD	3.40	1.82-6.37	< 0.001
Age ≥80 years	2.79	1.64-4.75	< 0.001
DM	2.53	0.79-17.52	0.089
IDDM	3.28	0.90-31.86	0.069
3-Vessel disease	2.76	0.61-18.83	0.093
	HR	95% CI	P-value
Repeat revascularization	า		
OPCAB	17.42	6.35-47.32	< 0.001
PVD	8.78	4.23-19.34	< 0.001
MACE			
Age ≥80 years	2.45	1.75-3.94	< 0.001
PVD	8.55	4.23-14.88	< 0.001
LVEF <35%	14.21	6.47-30.54	< 0.001
OPCAB	2.12	1.07-3.54	< 0.001
COPD	1.89	1.13-3.41	< 0.001
Female gender	2.05	0.67-7.77	0.069
CVD	3.04	0.75-25.05	0.064
CKD	4.55	0.67-10.85	0.078

 Table 3:
 Predictors of main outcomes

CI: confidence interval; CKD: chronic kidney disease; COPD: chronic obstructive pulmonary disease; CVD: cerebrovascular disease; DM: diabetes mellitus; HR: hazard ratio; IDDM: insulin-dependent diabetes mellitus; LVEF: left ventricular ejection fraction; MACE: major adverse cardiovascular events; OPCAB: off-pump coronary artery bypass; PVD: peripheral vascular disease.

coronary artery (in the majority of cases), because this vessel is not the clinical equivalent of the left-sided coronary branches [25, 26]. Nevertheless, a recent report (5) failed to identify differences in survival, repeat revascularization or combined outcomes between patients receiving RITA on the left or coronary circulation in accordance with previous patient cohorts [26, 27] that had shown no differences in long-term outcomes when the RITA was anastomosed to the right or left coronary circulation. In contrast with these findings, other reports have suggested that grafting RITA to the right coronary artery system may be less beneficial than grafting it to the left coronaries [20, 28].

Additionally, OPCAB was associated with an increased risk of repeated coronary revascularization and MACE. According to our experience, OPCAB has to be taken into consideration in terms of risk of events during the follow-up period. This observation confirms previous data showing reduced graft patency, increased risk of cardiac reintervention and death in patients who have undergone CABG [29]. We can presume that, among low-risk patients, adverse events related to cardiopulmonary bypass are rare and that 'technical adverse events', such as incomplete revascularization, diminished graft patency or reduced accuracy of anastomosis related to the technical challenge of OPCAB, may be responsible for the negative outcome. On the other hand, among higher-risk patients, cardiopulmonary bypass- and aortic manipulation-related events are more common and may outweigh technical adverse events. These types of events may not be increased in higher-risk patients, because most patient comorbidities do not mean that OPCAB is more difficult to perform. Our findings must, however, be interpreted with caution, taking into consideration that the poorer outcome in OPCAB might be a result of higher disease burden. Furthermore, OPCAB techniques and facilitating devices have evolved over time; hence our results may also be affected by our learning curve. Even taking this into account, the present findings suggest that a 'balanced' patient-centric approach should be utilized, as has been advocated even by the 2018 European Society of Cardiology/ European Association for Cardiothoracic Surgery Guidelines [9], with the balance shifted more towards OPCAB in patients with a high risk of stroke, renal dysfunction, blood transfusion, respiratory failure and development of atrial fibrillation, as was also



Figure 4: Graphical comparison demonstrating the benefit obtained with bilateral internal thoracic artery versus monolateral internal thoracic artery: our long-term survival curve is related to that from the ART study [6] and the thoracic long-term survival curves from another 2 studies [5, 30]. The Kaplan-Meier curves are plotted from 75% to 100% probability of survival. ART: Arterial Revascularization Trial.

suggested by the International Society for Minimally Invasive Cardiothoracic Surgery Consensus Conference [29].

Finally, the link between diabetes and DSWI has been studied extensively. The prevalence of diabetes has been found to be 3 times higher among patients with DSWI than in those without [2, 4, 6, 20], despite the fact that this patient population may have the most to gain from BITA grafting. Our data show that, with the skeletonized harvesting technique, patients with diabetes did not have a significantly higher associated risk of DSWI, although the mortality rate was significantly increased when patients presented with diabetes (60%; P < 0.0001). This finding is in accordance with those of other studies [3, 4] and could be explained by the aggressive treatment received by our patients with wellestablished DM who are referred for CABG surgery (intravenous insulin infusion). An alternative hypothesis, however, could be that this is related to the accurate ITAs skeletonized harvesting technique whereby collateral blood flow to the sternum is preserved.

In Fig. 4, we represent visually the advantage of the present surgical strategy in terms of patient survival: In this graph we compare long-term survival with that of the ART [6] and of 2 other recent large studies [5, 30] with long-term follow-up using only 1 thoracic artery and 1 saphenous vein for myocardial revascularization.

Limitations

A number of limitations need to be acknowledged, however. First, the homogeneous population (representing one of the main strengths of the paper) is also a drawback because it may introduce a selection bias (i.e. exclusion of patients with RITA on right coronary artery because of the ungraftable, highly diseased circumflex artery, patients with a second ITA with additional saphenous vein grafts). Hence, we cannot exclude the fact that this may contribute to the positive outcomes in this study, although the main risk factors of our patients in whom BITA were used are comparable to those reported in previous studies [20].

Second, the study was underpowered by the low event rate. To overcome this limitation and increase the power of the study, we used a variable reduction method in our analysis. Third, a direct comparison between a single and a double ITA as well as a skeletonized versus a non-skeletonized technique was not carried out nor did we examine the true influence of the skeletonized technique on the long-term outcomes. Although these are all important points, they are points that are beyond the main aim(s) of the present study. Fourth, the target vessels were determined mainly by the perfusion area of the recipient artery and were not selected randomly, which may have introduced bias. Finally, postoperative angiography was not routinely obtained, meaning graft patency was unknown.

CONCLUSIONS

Coronary artery bypass using the *in situ* skeletonized bilateral thoracic artery for left coronary circulation for TAMR resulted in satisfactory long-term results with low incidences of death and late events. Although our data do not provide a final answer regarding the potential benefits of using this approach in all patients, our findings encourage the use of this technique in selected patients having CABG.

SUPPLEMENTARY MATERIAL

Supplementary material is available at EJCTS online.

Conflict of interest: none declared.

REFERENCES

- 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] Lytle BW, Blackstone EH, Loop FD, Houghtaling PL, Arnold JH, Akhrass R et al. Two internal thoracic artery grafts are better than one. J Thorac Cardiovasc Surg 1999;117:855–72.
- [3] Dorman MJ, Kurlansky PA, Traad EA, Galbut DL, Zucker M, Ebra G. Bilateral internal mammary artery grafting enhances survival in diabetic patients: a 30-year follow-up of propensity score-matched cohorts. Circulation 2012;126:2935-42.
- [4] Stevens LM, Carrier M, Perrault LP, Hébert Y, Cartier R, Bouchard D et al. Influence of diabetes and bilateral internal thoracic artery grafts on long-term outcome for multivessel coronary artery bypass grafting. Eur J Cardiothorac Surg 2005;27:281–8.
- [5] Buttar SN, Yan TD, Taggart DP, Tian DH. Long-term and short-term outcomes of using bilateral internal mammary artery grafting versus left internal mammary artery grafting: a meta-analysis. Heart 2017;103: 1419-26.
- [6] Taggart DP, Benedetto U, Gerry S, Altman DG, Gray AM, Lees B et al. Bilateral versus single internal-thoracic-artery grafts at 10 years. N Engl J Med 2019;380:437-46.
- [7] Mohr FW, Morice M-C, Kappetein AP, Feldman TE, Ståhle E, Colombo A et al. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. Lancet 2013;381:629–38.
- [8] Thygesen K, Alpert JS, White HD, Jaffe AS, Apple FS, Galvani M et al. Universal definition of myocardial infarction. Circulation 2007;116: 2634-53.
- [9] Sousa-Uva M, Neumann F-J, Ahlsson A, Alfonso F, Banning AP, Benedetto U *et al.* 2018 ESC/EACTS Guidelines on myocardial revascularization. Eur J Cardiothorac Surg 2019;55:4–90.
- [10] American Diabetes Association. Diagnosis and classification of diabetes mellitus. Diabetes Care 2012;35(Suppl 1):S64-71.
- [11] Pi-Sunyer EX, Becker DM, Bouchard C, Clarleton RA, Colditz GA, Dietz WH et al. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults-the evidence report. National Institutes of Health. Obes Res 1998;6(Suppl 2):515-2095.
- [12] Bonacchi M, Battaglia F, Prifti E, Leacche M, Nathan NS, Sani G et al. Early and late outcome of skeletonised bilateral internal mammary arteries anastomosed to the left coronary system. Heart 2005;91:195–202.
- [13] Bonacchi M, Prifti E, Bugetti M, Parise O, Sani G, Johnson DM *et al*. Deep sternal infections after in situ bilateral internal thoracic artery grafting for left ventricular myocardial revascularization: predictors and influence on 20-year outcomes. J Thorac Dis 2018;10:5208–21.
- [14] Crowley MJ, Holleman R, Klamerus ML, Bosworth HB, Edelman D, Heisler M. Factors associated with persistent poorly controlled diabetes mellitus: clues to improving management in patients with resistant poor control. Chronic Illn 2014;10:291–302.
- [15] Iribarne A, Schmoker JD, Malenka DJ, Leavitt BJ, McCullough JN, Weldner PW et al. Does use of bilateral internal mammary artery

grafting reduce long-term risk of repeat coronary revascularization? A multicenter analysis. Circulation 2017;136:1676-85.

- [16] Bisleri G, Di Bacco L, Turturiello D, Mazzoletti A, Giroletti L, Repossini A et al. Improved outcomes of total arterial myocardial revascularization in elderly patients at long-term follow-up: a propensity-matched analysis. Ann Thorac Surg 2017;103:517–25.
- [17] Calafiore AM, Contini M, Vitolla G, Di Mauro M, Mazzei V, Teodori G et al. Bilateral internal thoracic artery grafting: long-term clinical and angiographic results of in situ versus Y grafts. J Thorac Cardiovasc Surg 2000;120:990-6.
- [18] Takami Y, Ina H. Effects of skeletonization on intraoperative flow and anastomosis diameter of internal thoracic arteries in coronary artery bypass grafting. Ann Thorac Surg 2002;73:1441–5.
- [19] Wendler O, Tscholl D, Huang Q, Schäfers HJ. Free flow capacity of skeletonized versus pedicled internal thoracic artery grafts in coronary artery bypass grafts. Eur J Cardiothorac Surg 1999;15:247–50.
- [20] Benedetto U, Altman DG, Gerry S, Gray A, Lees B, Pawlaczyk R et al. 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.
- [21] Buxton BF, Ruengsakulrach P, Fuller J, Rosalion A, Reid CM, Tatoulis J. The right internal thoracic artery graft-benefits of grafting the left coronary system and native vessels with a high grade stenosis. Eur J Cardiothorac Surg 2000;18:255-61.
- [22] Dion R, Glineur D, Derouck D, Verhelst R, Noirhomme P, El KG et al. Long-term clinical and angiographic follow-up of sequential internal thoracic artery grafting. Eur J Cardiothorac Surg 2000;17:407-14.
- [23] Joyce FS, McCarthy PM, Taylor PC, Cosgrove DM, Lytle BW. Cardiac reoperation in patients with bilateral internal thoracic artery grafts. Ann Thorac Surg 1994;58:80-5.
- [24] Fiore AC, Naunheim KS, Dean P, Kaiser GC, Pennington G, Willman VL et al. Results of internal thoracic artery grafting over 15 years: single versus double grafts. Ann Thorac Surg 1990;49:202-8; discussion 208-9.
- [25] Buxton BF, Komeda M, Fuller JA, Gordon I. Bilateral internal thoracic artery grafting may improve outcome of coronary artery surgery. Riskadjusted survival. Circulation 1998;98:II1-6.
- [26] Kurlansky PA, Traad EA, Dorman MJ, Galbut DL, Zucker M, Ebra G. Location of the second internal mammary artery graft does not influence outcome of coronary artery bypass grafting. Ann Thorac Surg 2011;91:1378-83; discussion 1383-4.
- [27] Sabik JF, Stockins A, Nowicki ER, Blackstone EH, Houghtaling PL, Lytle BW et al. Does location of the second internal thoracic artery graft influence outcome of coronary artery bypass grafting? Circulation 2008;118: S210-15.
- [28] Carrel T, Horber P, Turina MI. Operation for two-vessel coronary artery disease: midterm results of bilateral ITA grafting versus unilateral ITA and saphenous vein grafting. Ann Thorac Surg 1996;62:1289–94.
- [29] Puskas JD, Martin J, Cheng DCH, Benussi S, Bonatti JO, Diegeler A et al. ISMICS consensus conference and statements of randomized controlled trials of off-pump versus conventional coronary artery bypass surgery. Innovations (Phila) 2015;10:219–29.
- [30] DeSimone JP, Malenka DJ, Weldner PW, Iribarne A, Leavitt BJ, McCullough JN *et al.* Coronary revascularization with single versus bilateral mammary arteries: is it time to change? Ann Thorac Surg 2018;106: 466-72.