# Single versus bilateral internal thoracic artery grafting in patients with low ejection fraction

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# Abstract

Coronary artery bypass grafting (CABG) is the standard of care for the treatment of complex coronary artery disease. However, the optimal surgical treatment for patients with reduced left ventricular function with low ejection fraction (EF) is inconclusive. In our center, left-sided coronary grafting with bilateral internal thoracic artery (BITA) is generally the preferred method for surgical revascularization, also for patients with low EF. We compared early and long-term outcomes between BITA grafting and single internal thoracic artery (SITA) grafting in patients with low EF.

We evaluated short- and long-term outcomes of all patients who underwent surgical revascularization in our center during 1996 to 2011, according to EF  $\geq$ 30% and <30%. Univariate and multivariate analyses were performed. In addition, patients who underwent BITA and SITA grafting were matched using propensity score matching.

In total, 5337 patients with multivessel disease underwent surgical revascularization during the study period. Of them, 394 had low EF. Among these, 188 underwent SITA revascularization and 206 BITA grafting. Those who underwent SITA were more likely to have comorbidities such as chronic obstructive pulmonary disease, diabetes, congestive heart failure, chronic renal failure, and a critical preoperative condition including preoperative intra-aortic balloon pump insertion.

Statistically significant differences were not observed between the SITA and BITA groups in 30-day mortality (8.5% vs 6.8%, P=.55), sternal wound infection (2.7% vs 1.0%, P=.27), stroke (3.7% vs 6.3%, P=.24), and perioperative myocardial infarction (5.9% vs 2.9%, P=.15). Long-term survival (median follow up of 14 years, interquartile range, 11.2–18.9) was also similar between the groups. Property score matching (129 matched pairs) yielded similar early and long-term outcomes for the groups.

This study did not demonstrate any clinical benefit for BITA compared with SITA revascularization in individuals with low EF.

**Abbreviations:** BITA = bilateral internal thoracic artery, CABG = coronary artery bypass graft, CVD = cardiovascular disease, CHF = congestive heart failure, COPD = chronic obstructive pulmonary disease, CRF = chronic renal failure, CVD = cerebrovascular disease, EF = ejection fraction, IABP = intra-aortic balloon pump, IDDM = insulin dependent diabetes mellitus, IQR = interquartile range, ITA = internal thoracic artery, LV = left ventricular, MI = myocardial infarction, ND = neurological dysfunction, NIDDM = non-insulin dependent diabetes mellitus, PVD = peripheral vascular disease, SITA = single internal thoracic artery, SVG = saphenous vein grafts, SWI = sternal wound infection.

Keywords: bilateral mammary artery, bilateral internal thoracic artery, coronary artery bypass grafting, coronary artery bypass surgery, ejection fraction, low ejection fraction, single mammary artery, single internal thoracic artery

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# 1. Introduction

The standard revascularization approach was once considered a coronary artery bypass grafting (CABG) procedure, employing the left internal thoracic artery connected to the left anterior descending artery, together with saphenous vein grafts (SVGs) connected to other coronary targets.<sup>[1]</sup> This approach showed superior patency compared with surgical revascularization procedures that employed only SVGs. The employment of additional arterial grafts, mainly bilateral internal thoracic artery (BITA), has since demonstrated superior survival<sup>[1–4]</sup> and a decreased need for repeat coronary revascularization, compared with revascularization with a single internal thoracic artery (SITA).<sup>[5,6]</sup>

Medicine

Despite the advancement in revascularization techniques, the surgical treatment of patients with reduced left ventricular (LV) function has remained a challenge. A few studies have demonstrated a negative effect of low ejection fraction (EF) on early and long-term survival after CABG.<sup>[7–10]</sup> Still, the eminent role of CABG in patients with low EF was confirmed by the data of the STICH Extension Study. There, surgical revascularization (mainly SITA) yielded long-term survival benefit in the treatment

of ischemic cardiomyopathy, compared with optimal medical therapy.<sup>[11]</sup>

The adoption rate of BITA has been relatively low in many centers, despite the continual demonstration of improved outcomes. In our center, left-sided coronary grafting with BITA is the preferred method for surgical revascularization for the majority of patients undergoing isolated CABG, including those with low LV EF.<sup>[12]</sup> In this report, we compared outcomes of BITA and SITA grafting in patients with low EF.

# 2. Patients and methods

Data were accessed from electronic medical records. The study was approved by the Institutional Review Board of the Tel Aviv Sourasky Medical Center. Between 1996 and 2011, 5337 primary CABG procedures for multivessel disease were performed at our institution. Of these, 3096 consecutive patients (58.5% of all patients) underwent BITA grafting. The remaining 2242 patients underwent SITA grafting, mostly accompanied by SVGs. We compared demographic data, clinical characteristics, and procedural outcomes of patients with low EF ( $\leq$ 30%) operated in our center, between those who underwent BITA and SITA. Of the 394 (7.4%) patients with low EF during the study period, 206 (52.2%) underwent BITA and 188 (47.8%) underwent SITA revascularization.

Index hospitalization data including surgical technique, comorbidities and short term outcomes were available from patient medical records, while long term survival information was obtained by accessing data from the Israeli National Registry database. In our institution, the practice is to operate only after having complete data. Therefore, complete data were available for presurgery parameters, as well as postsurgery outcomes and long-term survival.

During the study period, the decision to perform either BITA or SITA grafting was made mainly according to the surgeon's discretion. Our group has a tendency not to use BITA grafting in patients with an increased risk for sternal wound complications such as very elderly patients, patients with chronic obstructive pulmonary disease (COPD), and women with obesity and diabetes mellitus (DM).<sup>[12,13]</sup> Evidently, our surgeons also preferred performing a quicker and more straightforward SITA rather than BITA revascularization for patients with a presumable lower life expectancy and more comorbidities such as chronic renal failure, peripheral vascular disease, previous myocardial infarction (MI) and a critical preoperative state, or in need of emergent procedures or with other preoperative comorbidities. Nonetheless, patients with these comorbidities were not ruled out of receiving the BITA revascularization strategy. In both BITA and SITA grafting, revascularization of the right coronary system was performed almost exclusively with SVGs.

All internal thoracic arteries (ITAs) were harvested as skeletonized vessels.<sup>[13]</sup> Additional technical aspects of these BITA procedures are detailed in previous publications of our group.<sup>[14]</sup>

#### 3. Definitions and data collection

Patient data were analyzed according to EuroSCORE clinical data standards.<sup>[15]</sup> Diabetes was classified as non-insulin dependent diabetes mellitus (NIDDM) and as insulin dependent (and treated) diabetes (IDDM). A perioperative MI was defined

as the postoperative appearance of new Q waves or ST segment elevation of >2 mm on an electrocardiograph, accompanied by a creatine phosphokinase-myocardial band >50 mU/mL, with or without a regional wall motion abnormality.<sup>[16]</sup> A cerebrovascular accident was defined as a new permanent neurological deficit and computed tomographic evidence of cerebral infarction. Deep sternal wound infection (SWI) was defined as the presence of a deep infection in combination with late dehiscence requiring a major surgical intervention (full or partial sternectomy, muscle or omental flapping, deep wound debridement, etc.). Our definition of "emergency operation" was based on the EuroSCORE and includes patients operated within 24 hours of cardiac catheterization<sup>[15]</sup>; or those with ongoing angina, acute evolving MI or pulmonary edema, or in cardiogenic shock.<sup>[16]</sup>

# 4. Statistical analysis

Sample size was calculated using a significance level of 5% and a power of 80%. We assumed that the overall survival during the study period was 50% in the BITA group and 35% in the SITA group. We also assumed that the same number of patients underwent SITA and BITA. Using these assumptions, 163 patients were needed in each group.

Categorical variables were reported as frequencies and percentages. Continuous variables were expressed as medians and interquartile ranges (IQRs). The Chi-square test and Mann–Whitney U test were used to compare respectively categorical and continuous characteristics of patients who underwent BITA and SITA. The Chi-square test and Fisher exact test were used to compare short term outcomes between groups. The reverse censoring method was used to calculate the median follow-up time. Kaplan-Meier curves were used to estimate median survival times, and thus to describe mortality during the follow-up period. The log rank test was used to compare mortality between groups. Multivariate Cox regression was used to investigate the association between grafting technique and mortality while controlling for potential confounders. The regression included 4 blocks. In the first block, grafting technique, age, and sex were forced into the regression. In the second block, preprocedure parameters (NIDDM, IDDM, DM with end organ dysfunction, COPD, chronic renal failure [CRF], a recent MI, an old MI, unstable angina, intra-aortic balloon pump [IABP] insertion, a critical preoperative state, an emergency procedure, redo surgery, peripheral vascular disease [PVD], cardiovascular disease [CVD], neurological dysfunction [ND], number of vessel disease, left main disease, and prior percutaneous intervention) were entered into the regression and then considered for removal using the backward method (the Wald test was used as the criterion, P > .1 was used as the cutoff value for removal). In the third block, procedure parameters ( $\geq 3$  bypass grafts, the number of sequential grafts, the number of SVGs, radial artery grafts, right gastroepiploic artery grafts, revascularization to the right coronary system, and off pump procedures) were entered and then considered for removal using the backward method as in the previous block. In the last block, the study period (before or after the year 2000) was entered into the regression. Propensity score was calculated as a patient's probability of undergoing BITA grafting. Propensity score was calculated using logistic regression. Age, sex, NIDDM, IDDM, COPD, congestive heart failure (CHF), CRF, old MI, recent MI,

# Table 1

# Demographic and clinical data for the unmatched and matched cohorts according to bilateral internal thoracic artery (BITA) versus single internal thoracic artery (SITA) grafting.

		Pre-match		Post-ma	atch (univariate analysis)	
	SITA (N = 188)	BITA (N=206)	Р	SITA (N = 129)	BITA (N=129)	Р
Age, y	67.5 (60-76)	67.5 (58–73)	.284	68 (IQR 60-76)	68 (IQR 58–76)	.941
Sex						
Male	146 (77.7%)	175 (85.0%)	.063	106 (82.2%)	103 (79.8%)	.743
Female	42 (22.3%)	31 (15.0%)		23 (17.8%)	26 (20.2%)	
NIDDM	83 (44.1%)	75 (36.4%)	.117	55 (42.6%)	56 (43.4%)	>.999
IDDM	14 (7.4%)	3 (1.5%)	.003	2 (1.6%)	3 (2.3%)	>.999
COPD	31 (16.5%)	14 (6.8%)	.003	14 (10.9%)	11 (8.5%)	.664
CHF	128 (68.1%)	116 (56.3%)	.016	84 (%65.1%)	77 (59.7%)	.443
CRF	37 (19.7%)	22 (10.7%)	.012	21 (16.3%)	16 (12.4%)	.473
IABP	57 (30.3%)	28 (13.6%)	<.001	30 (23.3%)	25 (19.4%)	.487
Redo	12 (6.4%)	6 (2.9%)	.099	5 (3.9%)	6 (4.7%)	>.999
PVD	42 (22.3%)	54 (26.2%)	.371	25 (19.4%)	31 (24%)	.418
CVD	27 (14.4%)	24 (11.7%)	.423	13 (10.1%)	15 (11.6%)	.839
LM	51 (27.1%)	56 (27.2%)	.99	37 (28.7%)	34 (26.4%)	.784
Triple vessel disease	144 (76.6%)	168 (81.6%)	.22	100 (77.5%)	101 (78.3%)	.99
ND	18 (9.6%)	7 (3.4%)	.012	6 (4.7%)	7 (5.4%)	>.999
Recent MI	100 (53.2%)	96 (46.6%)	.191	60 (46.5%)	60 (46.5%)	>.999
Old MI	118 (62.8%)	96 (44.6%)	.671	77 (59.7%)	77 (59.7%)	>.999
Acute MI	74 (39.4%)	67 (32.5%)	.157	47 (36.4%)	41 (31.8%)	.526
UAP	116 (61.7%)	111 (53.9%)	.117	71 (55%)	70 (54.3%)	>.999
Critical	62 (33%)	32 (15.5%)	<.001	34 (26.4%)	27 (20.9%)	.349
Emergency	62 (33%)	49 (23.8%)	.043	41 (31.8%)	34 (26.4%)	.392
Euro-SCORE, median	12 (9–14)	9 (7–11)	<.001	10 (8–13)	10 (7–12)	.085

CHF = congestive heart failure, COPD = chronic obstructive pulmonary disease, CRF = chronic renal failure, CVD = cerebrovascular disease, IABP = intra-aortic balloon pump, IDDM = insulin dependent diabetes mellitus, MI = myocardial infarction, ND = neurological dysfunction, NIDDM = non-insulin dependent diabetes mellitus, PVD = peripheral vascular disease.

unstable angina, IABP, redo procedure, PVD, CVD, ND, number of vessel disease, left main disease, and prior percutaneous intervention were used to calculate the propensity score. An absolute difference of up to 5% in the propensity score was considered as eligible for matching. Categorical variables including pre-procedure, surgical parameters, and short-term outcomes were compared between the matched groups using the McNemar test and continuous variables using the Wilcoxon signed ranks test. Univariate and multivariate stratified Cox regressions were used to study the association between grafting technique and mortality during the follow-up period. Variables were entered into the multivariate regression as described earlier for the unmatched cohort. All statistical tests were two tailed and P < .05 was considered as statistically significant. SPSS software was used for all statistical analyses (IBM SPSS Statistics for Windows, version 25, IBM corp., Armonk, NY, 2017).

#### 5. Results

# 5.1. Baseline characteristics of the unmatched cohort

Preoperative patient characteristics were significantly different between the SITA and the BITA groups. Patients treated with SITA grafting were more likely to have comorbidities such as DM, COPD, CHF, and CRF, and were more likely to be in a preoperative critical condition with higher rates of emergency procedures and perioperative IABP insertion (Table 1). The median Euro-SCORE was significantly higher in the SITA than the BITA group.

In the SITA compared with the BITA group, the usage of vein grafts, radial artery, and grafts to the right system was higher, the rate of operations performed without extracorporeal circulations was higher, and the use of the right gastroepiploic artery was lower (Table 2).

# Table 2

Intraoperative characteristics of the unmatched and matched cohorts according to bilateral internal thoracic artery (BITA) versus single internal thoracic artery (SITA) grafting.

	Pre-match			Post-match (univariate analysis)			
	SITA (N=188)	BITA (N=206)	Р	SITA (N=129)	BITA (N=129)	Р	
SVG number	146 (77.7%)	55 (26.7)	<.001	102 (79.1%)	35 (27.1%)	<.001	
Radial artery ARTERY	36 (19.1%)	5 (2.4%)	<.001	26 (20.2%)	3 (2.3%)	<.001	
GEA	13 (6.9%)	33 (16.0%)	.005	6 (4.7%)	24 (18.6%)	.001	
More than 3 bypass grafts	114 (60.6%)	151 (73.3%)	.007	88 (68.2%)	91 (70.5%)	.798	
ОРСАВ	50 (26.6%)	32 (15.5%)	.007	32 (24.8%)	19 (14.7%)	.790	
Sequential grafting	80 (42.6%)	96 (46.6%)	.419	58 (45%)	56 (43.4%)	.899	
Right system grafting	134 (71.3%)	119 (57.8%)	.005	91 (70.5%)	75 (58.1%)	.056	

GEA = gastro epiploic artery, OPCAB = off pump coronary artery bypass surgery, SVG = saphenous vein grafts.

## Table 3

		Unmatched			Matched	
	SITA	BITA	Р	SITA	BITA	Р
Early mortality	16 (8.5%)	14 (6.8%)	.522	10 (7.8%)	9 (7.0%)	>.999
Deep infection	5 (2.7%)	2 (1%)	.266	2 (1.6%)	1 (0.8%)	>.999
Post op CVA	7 (3.7%)	13 (6.3%)	.243	5 (3.9%)	5 (3.9%)	>.999
Periop MI	11 (5.9%)	6 (2.9%)	.152	5 (3.9%)	3 (2.3%)	.727
RE exploration	7 (3.7%)	2 (1%)	.093	3 (2.3%)	2 (1.6%)	>.999

. Early outcomes – univariate analysis of the unmatched and the matched cohorts according to bilateral internal thoracic artery (BITA) versus single internal thoracic artery (SITA) grafting.

CVA = cerebrovascular event, MI = myocardial infarction.

# 5.2. Early outcomes including (30-day) mortality, the unmatched analysis

Between patients who underwent SITA and BITA grafting, significant differences were not observed in early mortality (8.5% vs 6.8%, P=.55), SWI (2.7% vs 1.0%, P=.27), stroke (3.7% vs 6.3%, P=.24), and perioperative myocardial infarction (5.9% vs 2.9%, P=.15) (Table 3).

## 5.3. Late outcomes of the unmatched group

The median follow-up was 13.9 years (IQR 11.2–18.9 years). Overall, during the study period, 61.1% of the SITA group and 66.5% of the BITA group died. Median long-term survival did not differ significantly between the SITA and BITA groups: 9.51 (standard error [SE] 1.05) and 9.93 (SE 0.65) years, respectively, P=.77 (Fig. 1 and Table 4).

In multivariate analysis, group assignment to SITA or BITA was not associated with better late survival (adjusted hazard ratios (HR) 1.002, 95% CI: 0.745–1.349), P=.988; while older age, DM, end organ damage, COPD, and PVD were associated with decreased survival (Table 5). In an attempt to evaluate any association between revascularization strategy (BITA or SITA) and outcomes in patients who were operated with or without cardiopulmonary bypass, we performed an additional analysis after stratifying the whole cohort according to the use of cardiopulmonary bypass. The results showed no statistically



Figure 1. Kaplan–Meier survival curves for the unmatched analysis of the bilateral internal thoracic artery (BITA) and single internal thoracic artery (SITA) groups.

significant difference in early outcomes and overall survival between the type of surgery (BITA or SITA) performed, with or without cardiopulmonary bypass. The only exception was the higher occurrence of early cerebrovascular event (CVA) in the off pump coronary artery bypass surgery patients: 4/32 events in the BITA group versus 0/50 in the SITA group. The low number of early CVAs, as well as other early outcomes, precluded the performance of a multivariate analysis and reaching any definite conclusion.

# 5.4. Outcomes according to the matched cohort

After performing propensity matching for the entire cohort of patients with low EF, 129 pairs of well-matched patients were created (Table 1). Between the matched groups who underwent BITA and SITA grafting, there were no statistically significant differences in early (30-day) mortality (7.8% vs 7.0%, P > .99), occurrences of early postoperative SWI (1.6% vs 0.8%, P = .99), perioperative MI (3.9% vs 2.3%, P = .727), and postoperative stroke (3.9% versus 3.9%, P = .99) (Table 3). Kaplan–Meier curves for long-term survival of the matched groups are presented in Fig. 2. There was no statistically significant difference in long term survival between the BITA and SITA groups (P = .36). In multivariate analysis of the matched groups of patients, the revascularization strategy, SITA or BITA, was likewise not associated with poor long-term survival (P = .21, Table 4).

# 6. Discussion

The main finding of this study is the comparable early and longterm outcomes of patients with low LV EF, who underwent BITA revascularization and those who underwent CABG with SITA only. In a median follow-up of 14 years, the survival of the BITA group was similar before and after propensity matching to that of the SITA group (unmatched: median survival 9.93 [SE 0.65] vs

#### Table 4

Long-term survival of the unmatched and the matched cohorts according to bilateral internal thoracic artery (BITA) versus single internal thoracic artery (SITA) grafting.

	ι	Inmatched			Matched	
Years	SITA	BITA	Р	SITA	BITA	Р
1	82.10%	88%	.77	84.10%	86.50%	.36
3	75.00%	78.20%		76.70%	75.90%	
5	64.50%	72.50%		66.10%	69.40%	
10	46.80%	46.80%		45.80%	46.50%	

overall survival of the annatoried and matched conorts according to a multivariate analysis	Overall	survival	of the	unmatched	and	matched	cohorts	according	to a	a multivariate	analysis.
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-		Unmatched			Matched	
	Adj HR	CI for HR	Р	Adj HR	CI for HR	Р
BITA	1.002	(0.745-1.349)	.988	0.710	(0.414-1.217)	.213
Male	1.065	(0.772-1.469)	.7	0.470	(0.183-1.209)	.117
Age	1.042	(1.028-1.056)	<.001	1.043	(1.007-1.080)	.020
DM EOD	1.644	(1.112-2.431)	.013	3.033	(1.384-6.647)	.006
COPD	1.898	(1.302-2.766)	.001	20.881	(3.522-123.786)	.001
IABP	1.356	(0.992-1.854)	.056	8.710	(2.058-36.861)	.003
PVD	1.425	(1.068-1.902)	.016			
Yr 2000	0.791	(0.586-1.067)	.125	0.923	(0.437-1.952)	.835
CRF				2.083	(0.723-6.003)	.174
GEA				4.938	(1.395–17.484)	.013

COPD = chronic obstructive pulmonary disease, CRF = chronic renal failure, IABP = intra-aortic balloon pump, PVD = peripheral vascular disease.

9.51 [SE 1.05] years, *P*=.77; matched: 9.58 [SE 0.79] vs 8.98 (SE 1.27), *P*=.36).

A few studies showed improved long-term survival among patients with multivessel disease who underwent BITA revascularization strategy compared with CABG utilizing SITA and SVGs<sup>[17–20]</sup> or RA.<sup>[21]</sup> Those retrospective observational reports designated the use of 2 ITAs according to patients' life expectancy. Therefore, those undergoing BITA revascularization were mostly young, more frequently men and without comorbidities such as low EF, diabetes mellitus, recent MI, PVD, COPD, and CRF. Further, emergency cases were rarely offered the option of BITA grafting.<sup>[17,18]</sup>

In the prospective randomized ARTS trial, Taggart et al<sup>[22]</sup> reported no difference in outcomes 10 years after surgery for either the SITA or BITA revascularization strategy. A sensitivity analysis was carried out with adjustment for EF (<50% vs  $\geq 50\%$ ) and other factors such as age, sex, and diabetes. Interestingly in the subgroup analysis for death from any cause, patients with an EF >50% had a slightly better outcome than those with an EF <50%, but with no statistical significance.

Increased operative mortality<sup>[22-28]</sup> and reduced long-term survival<sup>[26,27,29,30]</sup> were demonstrated in various studies of



patients with low EF who underwent surgical coronary revascularization compared with those with normal LV EF.

Ten-year results from the STICH trial<sup>[31]</sup> showed lower cardiovascular mortality, 40.5% versus 49.3% (P=.006) among individuals with low EF randomly assigned to receive CABG (610 patients) compared with medical therapy (602 patients). Indeed, this landmark study reestablished the important role of CABG surgery in treating patients with multivessel disease and low ventricular EF. Nonetheless, some questions remain with regard to the appropriate surgical strategy for these patients.

In a report by Galbut et al,<sup>[32]</sup> 4537 consecutive patients with known EF underwent CABG between 1972 and 1994, either by SITA or BITA grafting. The patients were categorized according to revascularization mode and their EF was classified as <30%. 30-50%, and above 50%. After propensity score matching, there were 87 low EF matched pairs of BITA versus SITA grafting, 448 matched pairs in the intermediate EF group, and 1137 pairs with normal EF. Although no significant difference in early outcome was found in all the groups for either revascularization modality, BITA revascularization provided better 10- and 20-year survival for good and intermediate LV function. Interestingly, there were no differences in the rates of early mortality, early complication, or long-term (7–7.9 years) survival between the SITA and BITA groups among the 87 matched pairs with EF < 30%. BITA grafting was found to be an independent predictor for late survival for patients with good or intermediate LV function but not for those with poor EF. This led authors to speculate whether the findings may have been due to the relatively small sample size and short follow for this group of patients.

Another report by Mohammadi et al<sup>[33]</sup> on 3701 CABG procedures evaluated 111 propensity matched pairs with relatively reduced LV function (EF <40%). Notably, when harvested as a pedicle graft, almost 70% of right ITAs were used to revascularize the right coronary system. Some surgeons had performed only 3 previous BITA procedures, and no surgeon within the group had performed >33 BITA cases. No T grafts were performed in the entire cohort. After a mean follow up of 8 years, there was no difference in early mortality or complication between the groups. Long-term survival was also similar between the matched groups. After performing the Cox multivariate proportional hazard model, BITA versus SITA revascularization was found to be an insignificant predictor for decreased survival (P = .3).

The advantage of ITA revascularization over SVG is attributed to the accelerated attrition rate in vein grafts 5 to 10 years after surgery.<sup>[34,35]</sup> This phenomenon of intimal hyperplasia, ballooning, and accelerated atherosclerosis that occurs in veins exposed to arterial circulation is time dependent and may attenuate the benefit of multiple arterial grafts to years after the procedure. Possibly, the high-risk patients who a priority had diminished ventricular function did not survive to benefit from the seemingly advantageous revascularization.

In the current study, we compared the early and long-term outcomes of 394 patients operated with either SITA or BITA revascularization between 1996 and 2011. All ITAs were skeletonized and all ITAs were used to revascularize the left coronary system with either an in situ or a composite T graft configuration. Our group did not arbitrarily preselect patients for BITA revascularization according to their life expectancy and comorbidities. Rather, the inclination was to perform routine left-sided arterial revascularization using BITA for most patients. Surgeons in our group were generally highly experienced in ITA skeletonization, insitu BITA, and composite T grafting, as described in previous studies from our group.<sup>[12-14,36]</sup> Additionally, the number of matched patients presented in the current study is larger and the mean follow up duration is longer than presented in previous reports. Nonetheless, our results do not support the routine use of BITA revascularization for persons with reduced LV function. It is possible that a more carefully structured patient selection process could have vielded different outcomes; for example, had selection been directed by variates that have been found to be associated with poor long-term outcome such as older age and the presence of COPD, PVD, and NIDDM affecting end organs, rather than the determination of BITA or SITA according to the discretion of the surgeon. Selection of BITA according to more stringently defined criteria might un-mask the benefits of BITA in persons with poor LV.

## 6.1. Limitations of the study

This is a single-center observational retrospective analysis, and thus, the findings may not be generalizable to other centers. The use of BITA or SITA revascularization was determined by each surgeon, with no prespecified criteria directing the use of either revascularization strategy. This raises the possibility of unobservable covariates that cannot be accounted for in the Cox models, and that may cause bias and modify results even though matching was performed.

Moreover, supplemental pre-procedural evaluation of myocardial viability by various imaging techniques, and exact echocardiographic data on LVEDD and valvular function other than crude EF evaluation were unavailable. These could have more accurately distinguished hibernated or scarred myocardium and the exact advancement level, and other contributing factors to the failing left ventricle. In addition, post-procedural angiographic data that could have supported the clinical observations were not available. Neither were there data or distinctions between the types and severity of the coronary lesions and target vessel diameter. Additionally, complete follow-up of major adverse cardiac events or cardiac-related mortality after the index hospitalization were not available for all patients and thus remained unevaluated. Revealing and analyzing such occurrences could have unmasked potential advantages of SITA versus BITA revascularization. Although this study was underpowered to demonstrate small differences in early outcome, the incidence of early adverse events was similar between the groups. Finally, due to the long period of follow-up, a calendar bias cannot be ruled out.

# 7. Conclusion

This study could not demonstrate short or long-term benefit derived by the use of BITA grafting for myocardial revascularization in persons with low EF. A large-scale randomized trial may further illuminate the ideal revascularization strategy for this population.

#### Author contributions

Conceptualization: Ariel Farkash, Yanai Ben-Gal. Data curation: Rephael Mohr. Formal analysis: Tomer Ziv-Baran. Investigation: Ariel Farkash. Methodology: Dmitri Pevni, Tomer Ziv-Baran.

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