Effectiveness of radial artery–based multiarterial coronary artery bypass grafting: Role of body habitus

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ABSTRACT

Background: The multiarterial grafting survival advantage noted in the overall population undergoing coronary artery bypass grafting is not well defined in the obese. We investigated the early to late survival effects of the radial artery in left internal thoracic artery–based multiarterial bypass grafting (radial artery–multiarterial bypass grafting) versus single arterial bypass grafting (left internal thoracic artery–single arterial bypass grafting) in obese patients.

Methods: We analyzed 15-year Kaplan–Meier survival in 6102 patients receiving primary, left internal thoracic artery–based coronary artery bypass grafting with 2 or more grafts divided into body mass index groups: nonobese (<30 kg/m²) and all-obese, comprised of mildly obese (30–35 kg/m²) and morbidly obese (>35 kg/m²). Risk-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) of radial artery–multiarterial bypass grafting versus left internal thoracic artery–single arterial bypass grafting were derived via Cox regression and applied separately for early (<0.5 years), intermediate (0.5–5 years), and late (5–15 years) follow-up in each body mass index cohort. Propensity score matching between radial artery–multiarterial bypass grafting and left internal thoracic artery–single arterial bypass grafting cohorts within the body mass index groups was performed as a corroborating analysis.

Results: Radial artery–multiarterial bypass grafting was more frequently used in obese patients who were younger (62 ± 10 years; mild/morbid: 45.4%/54.4% radial artery–multiarterial bypass grafting) compared with nonobese patients (66 ± 10 years; 37.4% radial artery–multiarterial bypass grafting). Unadjusted 15-year survival was significantly better for radial artery–multiarterial bypass grafting in all body mass index groups. Multivariate analysis showed a survival benefit of radial artery–multiarterial bypass grafting over the entire 0- to 15-year study period in the all-obese cohort (HR, 0.85; 95% CI, 0.74–0.98) and was more pronounced in the mildly obese (HR, 0.79; 95% CI, 0.66–0.96) versus morbidly obese (HR, 0.88; 95% CI, 0.69–1.13). The radial artery–multiarterial bypass grafting survival benefit was realized between 0.5 and 5 years postoperatively and was comparable for all-obese (HR, 0.69; 95% CI, 0.51–0.94) and non-obese (HR, 0.68; 95% CI, 0.52–0.88) groups. Propensity score matching was confirmatory.

Conclusions: Radial artery–multiarterial bypass grafting confers a long-term survival advantage in both obese and nonobese patients. (J Thorac Cardiovasc Surg 2018;156:43–51)

The 15-year survival in propensity-matched obese patients receiving MABG (red) versus SABG (blue).

Central Message

RA-MABG improves long-term outcomes in obese patients compared with LITA-SABG and thus should be strongly considered as the grafting strategy of choice by the Heart Team in obese patients.

Perspective

In light of the worldwide obesity epidemic, the obese patient undergoing CABG is an increasingly common challenge for the cardiac surgeon. Whether the multiarterial survival advantage is also found in obese patients is not well defined and warrants further analysis.

See Editorial Commentary page 52.

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Abbreviations and Acronyms

BITA	= bilateral internal thoracic artery
BMI	= body mass index
CABG	= coronary artery bypass grafting
CI	= confidence interval
HR	= hazard ratio
LITA	= left internal thoracic artery
MABG	= multiarterial bypass grafting
NNT	= number needed to treat
RA	= radial artery
RI	= revascularization index
SABG	= single arterial bypass grafting
SVG	= saphenous vein graft

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Obesity has reached epidemic proportions. The World Health Organization estimates that obesity doubled within the last 3 decades, with approximately 70% of American adults being overweight or obese compared with less than 25% 40 years ago.¹⁻³ Obesity is a well-known risk factor for coronary atherosclerosis and other cardiovascular conditions, such as hypertension, heart failure, peripheral vascular disease, and atrial fibrillation.^{4,5} Obesity is also an independent predictor of long-term morbidity and mortality driven by its well-established association with the cardiometabolic syndrome and likely through yet unrecognized mechanisms.⁶ Not surprisingly, obesity is increasingly common among patients undergoing coronary artery bypass grafting (CABG) with 39% to 51% of patients undergoing CABG who are in the 2004-2014 Society of Thoracic Surgeons Database being obese.⁷

The existing data on the impact of obesity on CABG outcomes are conflicting with some investigators reporting improved, equivalent, or worse outcomes in obese patients⁸⁻¹³ compared with nonobese patients. These studies overwhelmingly focus on patients undergoing left internal thoracic artery (LITA)-based single arterial bypass grafting (SABG), and there is a paucity of data on whether multiarterial bypass grafting (MABG) is associated with a similar survival advantage that has been repeatedly described in the overall CABG population.¹⁴⁻¹⁹ Because postoperative survival is linked to coronary arterial graft durability, the enhanced inflammatory and prothrombotic states characteristic of the obese⁶ could more negatively affect arterial versus venous graft

durability and thus mitigate the survival benefit of MABG. Benedetto and colleagues²⁰ noted improved survival only among obese patients undergoing bilateral internal thoracic artery (BITA) grafting but reported equivalent survival when the radial artery (RA) was used as the second arterial graft in conjunction with the LITA.²¹

Within this context, we compared the long-term survival of obese and nonobese patients undergoing RA-MABG and traditional LITA-SABG in an attempt to define the superior grafting strategy in the increasingly commonly encountered obese patients undergoing CABG.

MATERIALS AND METHODS

This investigation is a retrospective analysis of prospective cardiac surgery experiences at 2 Ohio centers (1994-2007). Data were collected in accordance with the Society of Thoracic Surgeons National Adult Cardiac Surgery Database standards. Study data were restricted to those available in the database with no additional review of hospital records or patient contact. This study received institutional review board approval from both participating institutions, and the need for informed consent was waived.

Patients and Study Groups

The study group consisted of patients receiving isolated, primary LITA-CABG with 2 or more grafts between 1994 and 2007. Patients were excluded in case of concomitant surgery, single graft, no LITA, BITA grafting, salvage surgery, preoperative renal failure, and reoperations. Patients with preoperative renal failure were excluded because of poor prognosis and their ineligibility for RA-MABG because of the need for RA-based dialysis access. Patients were stratified into body habitus groups based on body mass index (BMI): nonobese (BMI <30 kg/m²) and all-obese (BMI ≥30 kg/m²), which comprised the mildly obese (BMI 30-35 kg/m²) and the morbidly obese (BMI >35 kg/m²). Each group was divided according to the specific grafting strategy used: RA-MABG (LITA/RA ± saphenous vein graft [SVG]) or LITA-SABG (LITA/SVG). The operative technique and perioperative management have been described.^{15,19,22} Cardiopulmonary bypass (97%) and aortocoronary grafting (99%) were used in the majority of patients.

Surgery and Follow-up

The primary outcome measure was all-cause mortality across the BMI groups for RA-MABG versus LITA-SABG with secondary analysis focusing on the time frame of the mortality comparison. Mortality data were secured from recurrent (semiannual) queries of the US Social Security Death Index database (<http://ssdi.genealogy.rootsweb.com>; last checked November 2011). Mortality data were obtained from the 1994-2013 Ohio death index for verification and exclusively for determining mortality after November 2011.

Statistical Analysis

Continuous variables were expressed as mean ± standard deviation and compared using the independent *t* test or Mann-Whitney *U* test based on normality. Categorical variables were expressed as counts (percentages) and compared by the chi-square test. Fifteen-year survival, based on all-cause mortality (inclusive of acute perioperative mortality), was derived via Kaplan-Meier analysis and compared for RA-MABG versus LITA-SABG cohorts across the BMI groups (log rank test) and was performed on all patients (unadjusted) as well for within each BMI group and MABG and SABG propensity-matched subcohorts. Comparisons were also done for mild and morbid obese patients combined, which comprised the obese group.

Comparative outcomes in grafting subcohorts and body habitus groups were confounded by significant demographic and risk factor differences (Table 1). Our primary risk adjustment to reduce such confounding was

TABLE 1. Demographic, comorbidity, and operative data in patients receiving single arterial bypass graft versus multiarterial bypass graft stratified to nonobese, mild obese, and morbid obese

Patient factors	Nonobese (N = 3566)			Mild obese (N = 1591)			Morbid obese (N = 945)		
	SABG (N = 2232)	MABG (N = 1334)	% Diff	SABG (N = 869)	MABG (N = 722)	% Diff	SABG (N = 431)	MABG (N = 514)	% Diff
	Mean $\pm$ SD	Mean $\pm$ SD		Mean $\pm$ SD	Mean $\pm$ SD		Mean $\pm$ SD	Mean $\pm$ SD	
Continuous									
Age (y)	67.3 $\pm$ 10.2	63.2 $\pm$ 10.4	40.2	64.8 $\pm$ 9.6	61.0 $\pm$ 9.7	39.3	61.4 $\pm$ 9.8	58.7 $\pm$ 9.3	23.1
BSA (m ²)	1.89 $\pm$ 0.20	1.95 $\pm$ 0.19	30.8	2.10 $\pm$ 0.19	2.20 $\pm$ 0.18	31.2	2.27 $\pm$ 0.20	2.34 $\pm$ 0.20	22.4
Ejection fraction	49.0 $\pm$ 11.4	49.3 $\pm$ 10.3	2.7	49.3 $\pm$ 11.3	49.2 $\pm$ 10.6	1.4	49.2 $\pm$ 11.5	49.0 $\pm$ 10.1	1.1
Perfusion time (min)	79 $\pm$ 33	82 $\pm$ 31	9.6	81 $\pm$ 30	84 $\pm$ 32	10.8	81 $\pm$ 36	88 $\pm$ 30	16.6
Crossclamp time (min)	47 $\pm$ 20	53 $\pm$ 22	24.3	48 $\pm$ 20	53 $\pm$ 22	21.3	49 $\pm$ 23	56 $\pm$ 22	24.8
RI	0.53 $\pm$ 0.71	0.80 $\pm$ 0.73	37.8	0.52 $\pm$ 0.72	0.78 $\pm$ 0.76	34.8	0.51 $\pm$ 0.70	0.80 $\pm$ 0.80	31.9
No. of grafts	3.23 $\pm$ 0.82	3.62 $\pm$ 0.89	40.0	3.26 $\pm$ 0.85	3.62 $\pm$ 0.95	39.9	3.23 $\pm$ 0.90	3.65 $\pm$ 0.90	39.2
No. of distal arterial anastomoses	1 $\pm$ 0	2.26 $\pm$ 0.54	332.6	1 $\pm$ 0	2.27 $\pm$ 0.54	331.0	1 $\pm$ 0	2.30 $\pm$ 0.60	321.2
No. of distal vein anastomoses	2.28 $\pm$ 0.82	1.36 $\pm$ 0.86	108.9	2.26 $\pm$ 0.85	1.34 $\pm$ 0.91	103.9	2.23 $\pm$ 0.90	1.35 $\pm$ 0.90	82.3
Year of surgery (1-14)	5.89 $\pm$ 3.64	8.65 $\pm$ 2.91	83.8	5.99 $\pm$ 3.75	8.45 $\pm$ 2.97	73.0	6.57 $\pm$ 3.76	8.98 $\pm$ 2.89	71.9
Categoric	Counts (%)	Counts (%)	% Diff	Counts (%)	Counts (%)	% Diff	Counts (%)	Counts (%)	% Diff
Male	1510 (67.7)	1050 (78.7)	25.2	564 (64.9)	558 (77.3)	26.9	227 (52.7)	317 (61.7)	17.3
Smoking	1447 (64.8)	935 (70.1)	11.2	559 (64.3)	477 (66.1)	3.6	287 (66.6)	328 (63.8)	5.6
Diabetes	641 (28.7)	348 (26.1)	5.9	381 (43.8)	294 (40.7)	6.0	220 (51.0)	282 (54.9)	7.2
Insulin dependence	216 (9.7)	89 (6.7)	11.0	133 (15.3)	76 (10.5)	15.0	88 (20.4)	94 (18.3)	5.5
Hypercholesterolemia	1425 (63.8)	981 (73.5)	21.0	604 (69.5)	554 (76.7)	15.9	313 (72.6)	403 (78.4)	13.3
Hypertension	1745 (78.2)	1043 (78.2)	0.0	752 (86.5)	597 (82.7)	11.2	372 (86.3)	447 (87.0)	2.0
Peripheral vascular disease	411 (18.4)	160 (12.0)	18.0	149 (17.1)	68 (9.4)	23.7	67 (15.5)	49 (9.5)	19.0
Cerebrovascular disease	685 (30.7)	224 (16.8)	33.1	249 (28.7)	116 (16.1)	30.2	105 (24.4)	73 (14.2)	26.1
Cerebrovascular accident	197 (8.8)	77 (5.8)	11.8	76 (8.7)	41 (5.7)	12.8	31 (7.2)	26 (5.1)	9.9
Chronic lung disease	491 (22.0)	223 (16.7)	13.4	158 (18.2)	107 (14.8)	9.3	89 (20.6)	106 (20.6)	0.1
Myocardial infarction	1292 (57.9)	715 (53.6)	8.6	504 (58.0)	381 (52.8)	9.9	257 (59.6)	250 (48.6)	21.0
Congestive heart failure	259 (11.6)	75 (5.6)	21.4	109 (12.5)	61 (8.4)	14.4	65 (15.1)	65 (12.6)	7.4
2-vessel disease	459 (20.6)	237 (17.8)	7.1	207 (23.8)	129 (17.9)	14.6	105 (24.4)	87 (16.9)	18.5
3-vessel disease	1713 (76.7)	1078 (80.8)	9.9	648 (74.6)	586 (81.2)	15.9	314 (72.9)	423 (82.3)	22.6
Multivessel disease	2172 (97.3)	1315 (98.6)	8.9	855 (98.4)	715 (99.0)	6.4	419 (97.2)	510 (99.2)	16.5
Left main disease	526 (23.6)	312 (23.4)	0.4	178 (20.5)	157 (21.7)	3.0	76 (17.6)	103 (20.0)	6.3
PCI									
Balloon angioplasty	184 (8.2)	93 (7.0)	4.8	87 (10.0)	48 (6.6)	13.3	50 (11.6)	24 (4.7)	26.9
Stent	188 (8.4)	169 (12.7)	13.9	90 (10.4)	93 (12.9)	8.6	49 (11.4)	67 (13.0)	5.5
Arrhythmia	283 (12.7)	76 (5.7)	24.3	110 (12.7)	29 (4.0)	33.0	36 (8.4)	39 (7.6)	3.1
Unstable angina	779 (34.9)	392 (29.4)	11.8	283 (32.6)	239 (33.1)	1.1	156 (36.2)	166 (32.3)	7.9
Emergency	146 (6.5)	69 (5.2)	5.8	55 (6.3)	34 (4.7)	8.0	35 (8.1)	21 (4.1)	18.3
CABG + other surgery	232 (10.4)	116 (8.7)	5.8	81 (9.3)	72 (10.0)	2.5	42 (9.7)	39 (7.6)	8.3
NYHA class									
1	86 (3.9)	113 (8.5)	19.3	43 (4.9)	58 (8.0)	14.9	15 (3.5)	32 (6.2)	16.1
2	311 (13.9)	288 (21.6)	20.1	93 (10.7)	156 (21.6)	32.2	54 (12.5)	99 (19.3)	19.6
3	1048 (47.0)	557 (41.8)	10.5	394 (45.3)	312 (43.2)	4.1	185 (42.9)	216 (42.0)	1.7
4	787 (35.3)	376 (28.2)	15.2	339 (39)	196 (27.1)	24.6	177 (41.1)	167 (32.5)	17.1
Any transfusion	853 (38.2)	470 (35.2)	5.9	257 (29.6)	181 (25.1)	9.9	136 (31.6)	174 (33.9)	4.7

Year of surgery: 1 (1994) to 14 (2007). RI = number of grafts minus number of diseased coronary vessels. SABG, Single arterial bypass graft; MABG, multiarterial bypass graft; SD, standard deviation; BSA, body surface area; RI, revascularization index; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; NYHA, New York Heart Association.

based on comprehensive multivariate risk adjustment using Cox regression using all covariates in Table 1, including the revascularization index (RI), regardless of their level of statistical significance. The RI was defined as the difference between the number of grafts and the number of diseased coronary systems. To confirm our findings, we next derived separate propensity score models using nonparsimonious logistic regression for each BMI group with RA-MABG considered as treatment. These models resulted in distinctly different propensity scores for the respective RA-MABG versus LITA-SABG subcohorts showing good discrimination in all BMI groups. Separate 1-to-1 (greedy), propensity-matched grafting method patient pairs were obtained within each BMI group. Patients receiving RA-MABG were always matched to the closest propensity score LITA-SABG counterparts ($\pm 2\%$ difference). Adequacy of matching was confirmed by calculating the standardized percent difference.²³

RA-MABG versus LITA-SABG treatment effects were first quantified as the 0- to 15-year hazard ratios (HRs $\pm 95\%$ confidence intervals [CIs]) using Cox proportional hazard regression models applied to all patients without adjustment (unadjusted HR), in all patients with comprehensive risk adjustment (covariate adjusted HR) for all factors in Table 1, and in propensity-matched patients (match-adjusted HR). To relax the proportional hazard assumption in the Cox regression, adjusted HRs were also calculated for multiple time segments (years) (early: 0-0.5; intermediate: 0.5-5; and late: 5-15) both for all patients and for matched-only patients. The propensity-matched survival comparison data were also used to quantify RA-MABG versus LITA-SABG treatments effects estimated as (1) the number needed to treat (NNT) to result in 1 life saved (lost) calculated at 5, 10, and 15 years postoperatively, and (2) added years of survival at the 50%, 75%, and 90% survival levels. Statistical analysis was conducted with SPSS version 22.0 software (SPSS Inc, Chicago, Ill).

RESULTS

The study population was composed of 6102 patients, with 2536 (41.6%) all-obese, 1591 (26.1%) mildly obese, and 945 (15.5%) morbidly obese. Nonobese patients (N = 3566, 58.4%) were predominantly overweight (BMI = 25-30 kg/m²; N = 2547 [71.4%]) versus normal

(BMI <25 kg/m²; N = 1019 [28.6%]). Among the nonobese cohort, 561 (15.7%) had small body habitus (body surface area <1.7 m²).

RA-MABG was used in 2570 patients overall (42.1%) and was more frequent (48.7%) in the all-obese group (mildly obese: 45.4%, morbidly obese: 54.4%), who were younger (62 ± 10 years) compared with the nonobese group, who were older (66 ± 10 years; 37.4% RA-MABG). Patient characteristics differed substantially between RA-MABG and LITA-SABG counterparts irrespective of BMI (Table 1). Briefly, for all BMI groups, the RA-MABG group tended to be younger, to have a greater RI, and to have more male subjects. Also, the frequency of RA-MABG increased substantially over the study period from approximately 20% in the 1990s to 60% to 70% by the mid-2000s, as is reflected in the year of surgery variable (Table 1).

Early, Intermediate, and Late Survival

Overall perioperative (30-day) mortality was 1.2% (74/6102), and this was similar in the nonobese (1.3%) and all-obese (1.1%) (0.9%, mildly, and 1.3%, morbidly). Overall, the all-obese had a slightly and nonsignificantly ($P = .095$) better long-term survival compared with the nonobese (Figure 1). The RA-MABG cohort was 4.2 years younger than the LITA-SABG cohort and showed substantially superior survival ($P < .001$, all) at 5 years (90.0% vs 83.7%), 10 years (70.9% vs 61.1%), and 15 years (47.3% vs 40.3%) (Figure 1). Kaplan-Meier analysis showed superior unadjusted 0- to 15-year RA-MABG survival compared with LITA-SABG across all BMI groups (Figure 2; all significant). Unadjusted RA-MABG versus LITA-SABG

FIGURE 1. Unadjusted 15-year cumulative survival after primary CABG surgery: (left) all obese (grey line; mean age: 61.9 ± 9.9 years) versus all non-obese (black line; 65.8 ± 10.5 years) cohorts; and (right) MABG (red line; 61.7 ± 10.2 years) versus SABG (blue line; 66.0 ± 10.2 years) surgery cohorts. Error bars = ± 1 standard error estimates. Percentages shown correspond to survival (%) for each comparison group at 5, 10, and 15 years. Survival comparisons were based on log-rank test. CABG, Coronary artery bypass grafting; MABG, multiarterial bypass grafting; SABG, single arterial bypass grafting.

FIGURE 2. Comparison of unadjusted 15-year cumulative survival for MABG (red) versus SABG (blue) surgery cases after stratification to BMI groups: (A) nonobese, (B) all-obese, (C) mild obese, and (D) morbid obese. Error bars = ± 1 standard error estimates. Percentages shown correspond to survival (%) for each comparison group at 5, 10, and 15 years. All pairwise comparisons were significant (log rank). CABG, Coronary artery bypass grafting; MABG, multiarterial bypass grafting; SABG, single arterial bypass grafting.

mortality HRs are summarized for each BMI group (Figure 3) and separately for early, intermediate, and late time-segments in a Forest plot in Figure 3.

Risk-Adjusted Multiarterial Bypass Grafting Effects (Cox Regression)

Comprehensive risk adjustment using Cox regression modeling was applied in all patients for each BMI group comparison to derive RA-MABG to LITA-SABG treatment effect. The covariate adjusted treatment effect results

are summarized in Figure 3. In the entire 0- to 15-year period, RA-MABG compared with LITA-SABG was associated with improved survival in the nonobese cohort (HR, 0.91; 95% CI, 0.80-1.03) and in the all-obese cohort (HR, 0.85; 95% CI, 0.74-0.98). This RA-MABG survival benefit in obese patients was more pronounced in the mildly obese (HR, 0.79; 95% CI, 0.66-0.96) than in the morbidly obese (HR, 0.88; 95% CI, 0.69-1.13) (Figure 3).

Time-segmented, covariate-adjusted mortality HRs showed that the RA-MABG survival benefit is

FIGURE 3. Top: Forest plot showing the time-segmented MABG versus SABG HRs (95% CI) for all body habitus subcohorts: unadjusted (left), covariate-adjusted (middle), and propensity-matched (right) patients. Bottom: Overall and time-segmented MABG versus SABG HRs across all body habitus groups: unadjusted, covariate-adjusted, and propensity-matched results. SABG/MABG = LITA-SABG/RA-MABG; early (0-0.5 years); intermediate (0.5-5 years); late (5-15 years). *Reported HRs also adjusted. CI, Confidence interval; MABG, multiarterial bypass grafting; SABG, single arterial bypass grafting.

predominantly realized in the intermediate postoperative period (0.5-5 years) in both the all-obese (HR, 0.69; 95% CI, 0.51-0.94) and nonobese (HR, 0.68; 95% CI, 0.52-0.88). Here too, the RA-MABG survival advantage was greater for the mildly obese (HR, 0.54; 95% CI, 0.36-0.81) than in the morbidly obese (HR, 0.88; 95% CI, 0.55-1.43).

Propensity matching resulted in 1013, 490, and 267 well-matched RA-MABG and LITA-SABG pairs in the nonobese, mildly obese, and morbidly obese cohorts, respectively (Table E1). The corresponding Kaplan–Meier survival curves are shown in Figure E1. The RA-MABG versus LITA-SABG treatment effects from the propensity-matched comparisons for the overall and the time-segmented follow-up are summarized in Figure 3. The propensity-matched comparisons confirmed the results of primary covariate-adjusted analysis.

Last, for the matched pairs, we calculated the NNT with RA-MABG to save a single life at the 5-, 10- and 15-year follow-ups in each BMI category. The NNT ranged from

10 to 26 patients in the mildly obese group and from 19 to 35 patients in the morbidly obese group, whereas the effect among nonobese patients was more modest (40-67). By using the 50% survival threshold, all-obese patients were estimated to have 1.9 added years of survival (Δt) with RA-MABG, whereas in nonobese patients the RA-MABG added years effect was 0.3 years of additional survival. The added years benefit was more pronounced in the mildly obese ($\Delta t = 2.1$ years) compared with the morbidly obese ($\Delta t = 1.2$ years) (Figure 4).

DISCUSSION

Our data indicate that RA-MABG improves long-term survival in obese patients compared with traditional LITA-SABG. This is principally driven by enhanced survival among the mildly obese in the intermediate postoperative (0.5-5 years) period. This analysis further adds to the growing body of evidence of the effectiveness and versatility of RA-MABG and so should allay reservations about using the RA as the second artery in obese patients.

No. needed to Treat (NNT)	Non-Obese			Obese			Mild Obese			Morbid Obese		
	S_{MABG}	S_{SABG}	NNT	S_{MABG}	S_{SABG}	NNT	S_{MABG}	S_{SABG}	NNT	S_{MABG}	S_{SABG}	NNT
5 year	88.2%	85.7%	40	88.4%	83.9%	22	89.0%	85.1%	26	86.9%	81.4%	18
10 year	66.8%	64.7%	48	67.3%	62.2%	20	70.7%	64.2%	15	60.6%	57.8%	35
15 year	43.1%	41.6%	67	46.3%	37.9%	12	49.4%	39.6%	10	40.5%	35.2%	19
Added Years (Δt)	Non-Obese			Obese			Mild Obese			Morbid Obese		
	T_{MABG}	T_{SABG}	ΔT	T_{MABG}	T_{SABG}	ΔT	T_{MABG}	T_{SABG}	ΔT	T_{MABG}	T_{SABG}	ΔT
50% survival	13.7	13.4	0.3	13.7	11.8	1.9	14.6	12.5	2.1	12.4	11.2	1.2
75% survival	8.5	7.8	0.7	8.1	7.5	0.6	9	7.7	1.3	7.4	7	0.4
90% survival	4.1	3.1	1	4.3	3.1	1.2	4.3	3.1	1.2	3.8	2.9	0.9

FIGURE 4. Estimated benefit of multiarterial bypass grafting versus single arterial bypass grafting in propensity-matched patients across body mass index categories: Numbers needed to treat to save 1 life and added years of life. NNT, Number needed to treat.

Obesity is not simply a clinical challenge stemming from patients' increased size, although this in and of itself poses significant hurdles to postoperative mobility and nursing care and its incident complications. Obesity is increasingly recognized as a complex condition with significant metabolic, hemodynamic, and structural cardiovascular aberrations. Obese patients are characterized by endothelial dysfunction, increased circulating blood volume, decreased arterial resistance, pulmonary hypertension, biventricular hypertrophy, diastolic dysfunction, and increased stroke volume and sympathetic activation.²⁴ The adipocyte, in addition to being the storage unit for excessive fat, is also an active endocrine organ secreting a variety of bioactive substances with diverse physiologic effects.⁶ Circulating levels of angiotensin II, C-reactive protein, fibrinogen, tumor necrosis factor- α , and plasminogen activator inhibitor-1 are proportional to BMI. C-reactive protein, a well-known marker of chronic inflammation, has been implicated in triggering acute coronary syndromes.⁶ Although the specific impact of the obese milieu on radial arterial coronary grafts has not been characterized, obesity has been linked to increased RA vasoreactivity, calcification, atherogenesis, and myointimal hyperplasia when the RA is used in dialysis access.²²⁻²⁷ This pathogenic nature of obesity is reflected in our obese patients' higher incidence of multiple comorbidities, such as diabetes, hypertension, and hyperlipidemia (Table 1) despite being younger than the nonobese, a finding also noted by others.^{9,10,21} Given these offsetting effects on survival, the younger higher-risk obese patients had similar unadjusted survival as the older, lower-risk nonobese patients (Figure 1). RA-MABG was associated with improved unadjusted long-term survival in the overall study population (Figure 1) as well as in all BMI-based subcohorts (Figure 2). This overall RA-MABG survival advantage was driven by improved survival in the 0.5- to 5-year postoperative period (Figure 3).

As in another report,²¹ RA-MABG was used more frequently among all-obese patients (48.7%) compared with nonobese patients (37.4%), a finding driven by our commitment to maximizing the number of arterial given the relatively young age of the obese in an effort to improve their long-term survival. Additional contributing elements to the aggressive use of RA-MABG among the obese were easier technical aspects of the typically larger RA found in the obese, avoidance of a large size mismatch between the typically large SVG of the obese and their coronary arteries, and preventing wound healing complications by minimizing dissection of the lower extremity inherent in SVG harvesting in the obese. The perioperative mortality in the all-obese was equivalent to the nonobese, a finding that was also noted by others¹⁰⁻¹² and was equivalent across all BMI subcohorts. Given such equivalent and low

perioperative mortality, CABG should not be avoided in obese patients.

Given the distinctly different pathophysiology of obese patients, the conflicting reports of the impact of obesity on operative outcomes in principally LITA-SABG⁹⁻¹³ and considering the diminished long-term survival of obese patients,⁸ the question of whether the multiarterial survival advantage seen in the general CABG population is also noted among obese patients needs further clarification. The existing data on the impact of obesity on CABG outcomes are modest and contradictory because of various methodological issues. Even less data are available on the impact of multiarterial grafting in obese patients receiving CABG. In a study of 229 obese propensity-matched BITA-MABG versus LITA-SABG study groups, Benedetto and colleagues²⁰ reported a long-term survival advantage with the BITA grafting during a median follow-up period of 4.5 years. The BITA-MABG obese cohort showed no increased perioperative complications except for a nonstatistically significant trend for increased risk of deep sternal wound infections. In another study of 2007 obese patients, Benedetto and colleagues,²¹ in contrast to our findings, noted equivalent 7.5-year postoperative survival between RA-MABG and LITA-SABG groups (HR, 1.05; 95% CI, 0.80-1.38). This was true regardless of their diabetes status. In nonobese patients, a statistically significant RA-MABG associated survival advantage was noted (HR, 0.78; 95% CI, 0.65-0.94). The time course of these effects was not evaluated. There are a number of possible methodological differences between our study and that of Benedetto and colleagues²¹ that may account for the alternative conclusions. Although both studies involved a relatively large number of patients, our study cohort had a higher prevalence of female patients (21%-47% vs 13%), diabetes (26%-55% vs 18%), smoking (64%-70% vs 16%), chronic obstructive pulmonary disease (9% vs 19%), and peripheral vascular disease (9%-19% vs 7%). Furthermore, our RA-MABG use was less selective, with 37.4% of the nonobese, 45.4% of the mildly obese, and 54.4% of the morbidly obese patients receiving an RA graft compared with 15% of nonobese and 20% of obese patients in Benedetto and colleagues' study. In addition, our overall RA-MABG group received 2.3 arterial grafts, whereas this number is unspecified in the other study. Finally, our propensity matching between RA-MABG and LITA-SABG cases was accomplished within each BMI group, whereas Benedetto and colleagues²¹ propensity-matched patients from the 2 grafting groups within the entire patient cohort (both obese and nonobese) and then used a second-order interaction between the grafting strategy and BMI, which was forced into the Cox models. The differences in the follow-up periods between the studies unlikely affected the diverse findings because the bulk of our RA-MABG survival advantage was realized in the

intermediate postoperative time period that was well within Benedetto and colleagues' follow-up period.

Our RA-MABG survival advantage in the all-obese cohort during the overall 0 to 15-year follow-up period (HR, 0.85; 95% CI, 0.74-0.98) was principally driven by a statistically significant decreased mortality HR among the mildly obese (HR, 0.79; 95% CI, 0.66-0.96) with only a nonsignificant trend toward lower mortality among the morbidly obese (HR, 0.88; 95% CI, 0.69-1.13) (Figure 3 and Figure E1). In light of the reported diminished 5-year survival among the morbidly obese,^{8,10,12,13} it is possible that this group may not live long enough to realize the RA-MABG-associated survival advantage, an effect that is most prominent within this same 5-year period. The same reasoning might hold true for underweight patients (body surface area <1.7 m²), who we have also shown to have a decreased 5-year survival⁸ and thus likewise may not benefit from the RA-MABG survival benefit. Because these patients comprised 15.7% of the nonobese cohort, it is possible that the borderline statistically significant RA-MABG survival advantage noted in the nonobese (HR, 0.91; 95% CI, 0.80-1.03) may be due to the lack of appreciable RA-MABG impact on survival among the underweight, although we did not specifically analyze this in the current study.

We are unaware of other studies focusing on the time course of any form of MABG survival advantage in the obese. Risk-adjusted, time-segmented HRs document a similar chronological pattern of the RA-MABG survival advantage in the all-obese and nonobese groups, with most of the benefit being realized in the 0.5- to 5-year postoperative time frame (Figure 3), a pattern similar to that within the general CABG population.¹⁹ Because the survival advantage of RA-MABG versus LITA-SABG is likely driven by improved graft durability, expectedly there was no survival advantage within the first 6 months postoperatively because the SVG and RA patencies have been reported to be equivalent up to 1 year postoperatively²⁸ and only begin to diverge thereafter.²⁹ We hypothesize that the reason behind the mortality HR of RA-MABG versus LITA-SABG in the obese trending to unity after 5 years postoperatively may be due to the higher mortality risk, in which case these patients may die with their coronary grafts rather than because of their coronary grafts. Alternatively, the hyperinflammatory obese milieu may adversely affect arterial graft durability and thus negate any survival benefit. Graft-specific failure rates and the specific cause of death are unavailable to us, but may be helpful in clarifying the cause of this observation. The relatively early (0.5-5 year) RA-MABG survival advantage documented in this article and among the general CABG population¹⁹ appears earlier than what has been reported with BITA-MABG.^{16,19} Because RA-MABG does not increase the risk of sternal wound complications, the observed improved long-term survival advantage was accomplished without any increased risk of sternal wound infections

inherent with BITA use,³⁰ an observation particularly important in this cohort as obesity is a known risk factor for sternal infections.^{8,10}

We also calculated the number of patients needed to be treated (NNT) to save 1 life by preferentially adopting the RA-MBAG over the LITA-SABG strategy, as well as the number of additional survival years conferred by this strategy. Although it has been estimated that a wide adoption of MABG would result in an additional 64,000 person-life years over the course of a decade,³¹ we are unaware of these 2 specific metrics being previously applied to obese CABG patients. These metrics corroborate the multivariate and propensity-matched analyses showing that obese patients benefit more from RA-MABG than the nonobese patients (Figure 4). This observation supports the existence of an "obesity paradox" within the RA-MABG population, which has also been reported by others⁹ and warrants further analysis.

Study Strengths and Limitations

The strength of our study stems from the large size of our study group and the robust adjustments for confounding factors associated with obesity by using both propensity-matching techniques and Cox regression, with both techniques yielding corroborating results. In addition, our analysis defines the time-varying course of the RA-MABG-mediated survival advantage. Finally, as an additional guide to cardiac surgeons for the optimal grafting strategy in the obese, we provide the number of patients needed to treat to save 1 life and the number of additional years of survival associated with the RA-MABG grafting strategy, both of which are supportive of more aggressive use of RA-MABG in the obese patient.

Conversely, there are a number of weaknesses in our study. First, our study reflects a single practice experience and is retrospective in nature, and thus its conclusions may be subject to potential patient selection bias and make generalization to other settings difficult. Further, we are unable to define the cause of death, and thus we are unable to assess whether the survival advantage is due to decreased cardiovascular mortality stemming from the presumed enhanced arterial graft durability or other non-graft-related factors. Finally, we did not separately compare RA-MABG with LITA-SABG in patients with a small body habitus or in those patients who were overweight but not obese (BMI 25-30 kg/m²).

CONCLUSIONS

Our analysis supports the aggressive use of the RA as a second arterial conduit in LITA-based CABG in the obese. Compared with the traditional LITA-SABG, this grafting strategy is associated with an improved long-term survival that is principally realized within 0.5 to 5 years postoperatively. Our results suggest that RA-MAB should be

seriously considered by the Heart Team as the superior grafting strategy in the obese.

Conflict of Interest Statement

Authors have nothing to disclose with regard to commercial support.

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Key Words: multiarterial CABG, obesity, body mass index

FIGURE E1. Comparison of 15-year cumulative survival shown for propensity-matched MABG (red) versus SABG (blue) surgery cases within each BMI group: A, Nonobese (1013 pairs). B, All-obese (757 pairs). C, Mild obese (490 pairs). D, Morbid obese (267 pairs). Error bars = ± 1 standard error estimate. CABG, Coronary artery bypass grafting; MABG, multiarterial bypass grafting; SABG, single arterial bypass grafting.

TABLE E1. Demographic, comorbidity, and operative data in propensity-matched single arterial bypass graft versus multiarterial bypass graft cases stratified to nonobese, mild obese, and morbid obese

Continuous variables	Nonobese (N = 1013 pairs)			Mild obese (N = 490 pairs)			Morbid obese (N = 267 pairs)		
	SABG	MABG	% Diff	SABG	MABG	% Diff	SABG	MABG	% Diff
	(N = 1013)	(N = 1013)		(N = 490)	(N = 490)		(N = 267)	(N = 267)	
	Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD	
Age (y)	64.3 ± 10.5	64.4 ± 10.2	1.6	62.2 ± 9.5	62.5 ± 9.7	2.9	60.3 ± 9.5	59.9 ± 9.4	4.7
BSA (m ²)	1.93 ± 0.19	1.93 ± 0.19	1.2	2.13 ± 0.18	2.13 ± 0.18	4.1	2.30 ± 0.23	2.30 ± 0.23	1.0
Ejection fraction	49.3 ± 11.3	49.4 ± 10.4	1.1	48.7 ± 11.5	49.6 ± 10.5	7.8	49.3 ± 10.9	49.3 ± 9.2	0.1
Perfusion time (min)	81.0 ± 31.0	81.0 ± 31.0	1.6	85 ± 30	82 ± 33	10.1	82 ± 34	82 ± 28	1.6
Crossclamp time (min)	51.0 ± 21.0	51.0 ± 22.0	0.4	51 ± 20	50 ± 21	8.3	51 ± 23	51 ± 20	3.4
RI	0.66 ± 0.74	0.69 ± 0.70	4.7	0.65 ± 0.72	0.64 ± 0.72	1.4	0.58 ± 0.74	0.55 ± 0.77	3.5
No. of grafts	3.46 ± 0.85	3.48 ± 0.83	2.9	3.46 ± 0.86	3.42 ± 0.87	5.2	3.37 ± 0.9	3.35 ± 0.86	2.6
No. of distal arterial anastomoses	1 ± 0	2.23 ± 0.50	345.2	1 ± 0	2.22 ± 0.48	360.0	1 ± 0	2.19 ± 0.47	362.2
No. of distal vein anastomoses	2.46 ± 0.85	1.25 ± 0.82	143.6	2.46 ± 0.86	1.19 ± 0.86	147.5	2.37 ± 0.9	1.15 ± 0.87	137.5
Year of surgery (1-14) ^a	6.44 ± 3.9	8.48 ± 2.98	58.8	6.19 ± 3.88	8.16 ± 3.03	56.6	6.71 ± 3.86	8.67 ± 3.07	56.0
Categoric variables	Counts (%)	Counts (%)	% Diff	Counts (%)	Counts (%)	% Diff	Counts (%)	Counts (%)	% Diff
Male	765 (75.5)	763 (75.3)	0.5	353 (72.0)	352 (71.8)	0.4	155 (58.0)	149 (55.8)	4.3
Smoking	705 (69.6)	695 (68.6)	2.1	315 (64.30)	320 (65.3)	2.0	176 (65.9)	175 (65.5)	0.8
Diabetes	260 (25.7)	277 (27.3)	3.7	200 (40.8)	205 (41.8)	2.0	138 (51.7)	145 (54.3)	5.0
Insulin dependence	75 (7.4)	78 (7.7)	1.3	52 (10.6)	54 (11.0)	1.4	53 (19.9)	53 (19.9)	0.0
Hypercholesterolemia	719 (71.0)	713 (70.4)	1.3	360 (73.5)	357 (72.9)	1.4	201 (75.3)	203 (76.0)	1.7
Hypertension	785 (77.5)	785 (77.5)	0.0	408 (83.3)	408 (83.3)	0.0	231 (86.5)	229 (85.8)	2.3
Peripheral vascular disease	137 (13.5)	135 (13.3)	0.6	54 (11.0)	54 (11.0)	0.0	32 (12.0)	33 (12.4)	1.2
Cerebrovascular disease	213 (21.0)	204 (20.1)	2.2	96 (19.6)	104 (21.2)	4.1	46 (17.2)	54 (20.2)	7.9
Cerebrovascular accident	74 (7.3)	73 (7.2)	0.4	25 (5.1)	34 (7.0)	9.1	13 (4.9)	17 (6.4)	7.7
Chronic lung disease	197 (19.5)	191 (18.9)	1.5	86 (17.6)	74 (15.1)	6.8	56 (21.0)	57 (21.4)	0.9
Myocardial infarction	551 (54.4)	545 (53.8)	1.1	270 (55.1)	260 (53.1)	3.9	141 (52.8)	149 (55.8)	5.7
Congestive heart failure	82 (8.1)	71 (7.0)	4.5	53 (10.8)	50 (10.2)	2.2	39 (14.6)	33 (12.4)	6.9
2-vessel disease	184 (18.2)	191 (18.9)	1.8	87 (17.8)	104 (21.2)	8.9	55 (20.6)	50 (18.7)	4.8
3-vessel disease	810 (80.0)	804 (79.4)	1.5	397 (81.0)	380 (77.6)	8.7	209 (78.3)	213 (79.8)	3.7
Multivessel disease	994 (98.1)	995 (98.2)	0.9	484 (98.8)	484 (98.8)	0.0	264 (98.9)	263 (98.5)	4.4
Left main disease	250 (24.7)	239 (23.6)	2.5	103 (21.0)	102 (20.8)	0.5	47 (17.6)	47 (17.6)	0.0
PCI									
Balloon angioplasty	74 (7.3)	79 (7.8)	2.1	37 (7.6)	35 (7.1)	1.7	22 (8.2)	19 (7.1)	4.7
Stent	114 (11.3)	102 (10.1)	4.1	58 (11.8)	60 (12.2)	1.3	28 (10.5)	33 (12.4)	6.4
Arrhythmia	71 (7.0)	70 (6.9)	0.4	38 (7.8)	28 (5.7)	9.0	21 (7.9)	15 (5.6)	9.9
Unstable	309 (30.5)	312 (30.8)	0.6	164 (33.5)	165 (33.7)	0.4	92 (34.5)	88 (33.0)	3.0
Emergency	60 (5.9)	61 (6.0)	0.5	25 (5.1)	28 (5.7)	3.2	12 (4.5)	14 (5.2)	4.1
CABG + other surgery	89 (8.8)	84 (8.3)	1.9	48 (9.8)	50 (10.2)	1.5	18 (6.7)	24 (9.0)	9.6
NYHA class									
1	71 (7.0)	66 (6.5)	2.2	32 (6.5)	33 (6.7)	0.9	9 (3.4)	9 (3.4)	0.0
2	195 (19.3)	193 (19.1)	0.5	72 (14.7)	71 (14.5)	0.6	40 (15.0)	40 (15.0)	0.0
3	430 (42.5)	432 (42.7)	0.4	221 (45.1)	234 (47.8)	5.0	119 (44.6)	119 (45.0)	0.0
4	317 (31.3)	322 (31.8)	1.0	165 (33.7)	152 (31.0)	5.5	99 (37.1)	99 (37)	0.0
Any transfusion	367 (36.2)	356 (35.1)	2.2	127 (25.9)	132 (26.9)	2.3	83 (31.1)	86 (32.0)	2.3

Year of surgery: 1 (1994) to 14 (2007). RI = number of grafts minus number of diseased vessels. SABG, Single arterial bypass graft; MABG, multiarterial bypass graft; SD, standard deviation; BSA, body surface area; RI, revascularization index; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; NYHA, New York Heart Association.