JAMA Cardiology | Original Investigation

Long-term Outcomes Associated With Total Arterial Revascularization vs Non–Total Arterial Revascularization

Rodolfo V. Rocha, MD; Derrick Y. Tam, MD; Reena Karkhanis, MBBS; Xuesong Wang, MSc; Peter C. Austin, PhD; Dennis T. Ko, MD, MSc; Mario Gaudino, MD; Alistair Royse, MD; Stephen E. Fremes, MSc, MD, FRCSC

IMPORTANCE The optimal conduits for coronary artery bypass grafting (CABG) remain controversial in multivessel coronary artery disease.

OBJECTIVE To compare the long-term clinical outcomes of total arterial revascularization (TAR) vs non-TAR (CABG with at least 1 arterial and 1 saphenous vein graft) in a multicenter population-based study.

DESIGN, SETTING, AND PARTICIPANTS This multicenter population-based cohort study using propensity score matching took place from October 2008 to March 2017 in Ontario, Canada, with a mean and maximum follow-up of 4.6 and 9.0 years, respectively. Individuals with primary isolated CABG were identified, with at least 1 arterial graft. Exclusion criteria were individuals from out of province and younger than 18 years. Patients undergoing a cardiac reoperation or those in cardiogenic shock were also excluded because these conditions would potentially bias the surgeon toward not performing TAR. Analysis began April 2019.

EXPOSURES Total arterial revascularization.

MAIN OUTCOMES AND MEASURES Primary outcome was time to first event of a composite of death, myocardial infarction, stroke, or repeated revascularization (major adverse cardiac and cerebrovascular events). Secondary outcomes included the individual components of the primary outcome.

RESULTS Of 49 404 individuals with primary isolated CABG, 2433 (4.9%) received TAR, with the total number of bypasses being 2, 3, and 4 or more vessels in 1521 (62.5%), 865 (35.6%), and 47 individuals (1.9%), respectively. The mean (SD) age was 61.2 (10.4) years and 1983 (81.5%) were men. After propensity score matching, 2132 patient pairs were formed, with equal total number of bypasses (mean [SD], 2.4 [0.5]) but with more arterial grafts in the TAR group (mean [SD], 2.4 [0.5] vs 1.2 [0.4]; $P < .01$). In-hospital death (15 [0.7%] vs 21 [1.0%]; $P = .32$) did not differ between TAR vs non-TAR groups after propensity score matching. Throughout 8 years, TAR was associated with improved freedom from major adverse cardiac and cerebrovascular events (hazard ratio, 0.78; 95% CI, 0.68-0.89), death (hazard ratio, 0.80; 95% CI, 0.66-0.97), and myocardial infarction (hazard ratio, 0.69; 95% CI, 0.51-0.92). There was no difference in stroke and repeated revascularization.

CONCLUSIONS AND RELEVANCE Total arterial revascularization was associated with improved long-term freedom from major adverse cardiac and cerebrovascular events, death, and myocardial infarction and may be the procedure of choice for patients with reasonable life expectancy requiring CABG.

JAMA Cardiol. doi:10.1001/jamacardio.2019.6104
Published online February 19, 2020.

Supplemental content

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Stephen E. Fremes, MSc, MD, FRCSC, Schulich Heart Centre, Sunnybrook Health Sciences Centre, 2075 Bayview Ave, Room H4 05, Toronto, ON M4N 3M5, Canada (stephen.fremes@sunnybrook.ca).

Coronary artery bypass grafting (CABG) is the preferred revascularization strategy in patients with multivessel disease.[1] Graft selection has been shown to influence the outcomes following CABG. The use of the left internal mammary artery (LIMA) to bypass a stenotic left anterior descending artery provides improved outcomes compared with saphenous venous grafts (SVG) and is considered standard of care.[2] The incremental benefit of a second arterial graft has also been described in multiple studies, using both the right internal mammary artery[3] and radial artery[4] postulated to the related more durable patency compared with SVGs.[5,6]

One strategy to address the inferior SVG patency rates is to perform CABG with total arterial revascularization (TAR). By avoiding SVGs, the rates of graft occlusion and severe stenosis would be lower, potentially decreasing the late incidence of myocardial infarction (MI), repeated revascularization, and death.[7]

Few studies have compared TAR with CABG using at least 1 SVG (non-TAR). Two randomized clinical trials were limited to 1-year follow-up.[8,9] Most large observational studies have only described in-hospital outcomes.[10,11] Moreover, studies reporting the long-term outcomes of TAR have been limited to survival[12,13] or involved a small number of patients.[14,15] In 2018, our group completed a large, population-level study showing a long-term improvement in major adverse cardiac and cerebrovascular events (MACCE) of multi-arterial vs single arterial revascularization after isolated CABG.[16] Using a similar approach, we sought to compare TAR and non-TAR revascularization in terms of long-term freedom from MACCE in this study. We hypothesized that TAR would be associated with better freedom from MACCE.

Key Points

Question What are the short-term and long-term outcomes of total arterial revascularization at a population-based level?

Findings In this cohort study of 49 404 patients, compared with the coronary artery bypass with at least 1 arterial and 1 saphenous venous graft, total arterial revascularization was associated with improved long-term freedom from major adverse cardiac and cerebrovascular events, death, and myocardial infarction.

Meaning Total arterial revascularization may be the procedure of choice for patients with reasonable life expectancy requiring coronary artery bypass grafting.

Methods

Study Design

All primary isolated CABGs from the 11 institutions that perform CABG in Ontario, Canada, from October 2008 to March 2017, were identified through the CorHealth Ontario Cardiac Registry. Patients were then linked to 4 additional administrative databases (eTable 1 in the Supplement). These data sets were linked using unique encoded identifiers and analyzed at ICES (formerly, Institute for Clinical Evaluative Sciences). Patients undergoing a cardiac reoperation or those in cardiogenic shock were also excluded. eFigure 1 in the Supplement presents the case selection algorithm for our study.

ICES is an independent, nonprofit research institute whose legal status under Ontario's health information privacy law allows it to collect and analyze health care and demographic data, without consent, for health care system evaluation and improvement. The use of data in this project was authorized under section 45 of Ontario's Personal Health Information Protection Act, which does not require review by a research ethics board. Patient consent was also waived for this reason.

Outcomes

The primary outcome for this study was the time to first event of a composite of death, MI, stroke, or repeated revascularization (MACCE). Secondary outcomes included the individual components of the primary outcome and sternal reconstruction, reported as time-to-event outcomes. Tertiary outcomes included the following in-hospital events: death, stroke, MI, kidney dysfunction requiring dialysis, red blood cell transfusion, and hospital length of stay.

The strategy to identify total number of grafts and number of arterial grafts was based on the Ontario Health Insurance Plan coding claims.[16] All individuals with CABG with 2, 3, or 4 or more bypasses and at least 1 arterial graft were identified. If the total number of bypasses was equal to the total number of arterial grafts and there was no Canadian Classification of Health Interventions code of saphenous vein harvesting, patients were considered to have undergone TAR. If the total number of bypasses was greater than the total number of arterial grafts and the Canadian Classification of Health Interventions code of saphenous venous harvesting was present, patients were considered to have undergone non-TAR. In the non-TAR group, all cases were required to have at least 1 arterial graft (presumably to bypass the left anterior descending artery) and at least 1 SVG.

Preoperative frailty was determined using the Hospital Frailty Risk Score algorithm.[17] To identify long-term outcomes, we used validated diagnostic codes based on the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* and Canadian Classification of Health Interventions.[18] eTable 2 in the Supplement presents all administrative database codes used.

Statistical Analysis

Analysis began April 2019. Continuous variables are reported as the mean (SD) or median (interquartile range). Categorical variables are reported as frequencies and percentages. A 2-tailed *P* value less than .05 was considered statistically significant. All statistical analyses were conducted using SAS, version 9.4.5. (SAS Institute). Per ICES policy, all cells with fewer than 6 events were presented as ≤5 to avoid potential patient identification.

Prior to matching, baseline demographics were compared using unpaired *t* test or Mann-Whitney rank sum test (continuous data) or χ^2 (categorical data). Propensity score matching (PSM) was used to adjust for prespecified clinically relevant baseline characteristics that were potentially confounding variables. We first calculated propensity scores using

Table 1. Demographic Characteristics of TAR vs Non-TAR Groups Post-PSM

Variable	Post-PSM, No. (%)		SMD
	TAR (n = 2132)	Non-TAR (n = 2132)	
Age, mean (SD), y	61.9 (9.8)	62.0 (9.8)	<.01
BMI, mean (SD)	29.1 (5.5)	29.4 (5.3)	.05
Creatinine, mean (SD), mg/dL	1.01 (0.50)	1.01 (0.62)	<.01
Charlson Comorbidity Index, mean (SD)	1.2 (1.3)	1.2 (1.2)	.01
Frailty score, mean (SD)[a]	2.0 (3.1)	2.0 (3.0)	.02
Male	1770 (83.0)	1770 (83.0)	<.01
Income quintile			
1	371 (17.4)	446 (20.9)	.09
2	429 (20.1)	436 (20.5)	.01
3	409 (19.2)	413 (19.4)	<.01
4	472 (22.1)	423 (19.8)	.06
5	451 (21.2)	414 (19.4)	.04
Residence in rural area	412 (19.3)	404 (18.9)	.01
LVEF, %			
<20	22 (1.0)	24 (1.1)	.01
20-34	121 (5.7)	121 (5.7)	.00
35-49	456 (21.4)	465 (21.8)	.01
≥50	1430 (67.1)	1423 (66.7)	.01
Missing	103 (4.8)	99 (4.6)	.01
Hypertension	1453 (68.2)	1401 (65.7)	.05
Diabetes	627 (29.4)	639 (30.0)	.01
Smoker			
Current	571 (26.8)	714 (33.5)	.15
Former	649 (30.4)	613 (28.8)	.04
History of MI	403 (18.9)	455 (21.3)	.06
Recent MI (<30 d)	595 (27.9)	600 (28.1)	.01
CVA	138 (6.5)	144 (6.8)	.01
COPD	141 (6.6)	169 (7.9)	.05
Dialysis	6 (0.3)	15 (0.7)	.06
Hyperlipidemia	1534 (72.0)	1558 (73.1)	.03
PVD	221 (10.4)	227 (10.6)	.01
Previous PCI	422 (19.8)	495 (23.2)	.08
NYHA			
1	1057 (49.6)	1109 (52.0)	.05
2	179 (8.4)	190 (8.9)	.02
3	91 (4.3)	71 (3.3)	.05
4	24 (1.1)	22 (1.0)	.01
Missing	781 (36.6)	740 (34.7)	.04
2-Vessel disease	562 (26.4)	562 (26.4)	<.01
3-Vessel disease	1174 (55.1)	1174 (55.1)	<.01
Left main disease	614 (28.8)	613 (28.8)	<.01
Off-pump CABG	556 (26.1)	478 (22.4)	.09

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); CABG, coronary artery bypass grafting; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; LVEF, left ventricle ejection fraction; MI, myocardial infarction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; PSM, propensity score matching; PVD, peripheral vascular disease; SMD, standardized mean differences; TAR, total arterial revascularization.

SI conversion factor: To convert creatinine to μmol/L, multiply by 88.4.

[a] Frailty score calculated based on the validated algorithm.[17]

hierarchical logistic regression models that accounted for patient-specific demographics, socioeconomic status, extent of coronary artery disease (all variables from **Table 1**), as well as accounting for the clustering of patients within the same hospital through the inclusion of hospital-specific random effects. Patients undergoing TAR were matched 1:1 to patients undergoing non-TAR, using the propensity score with a caliper of 0.2 of the standard deviation of the legit of the propensity score without replacement.[19] We performed a hard match for total number of bypasses (ie, 2-vessel CABG TAR could only be matched to 2-vessel non-TAR), and on- vs off-pump surgery was also included in the PSM calculations. Standardized mean differences (SMD) were determined to compare baseline characteristics of all patients; an SMD less than 0.1 was considered as an indicator of good balance between groups.[20]

Additional PSM analysis, using similar methodology, was performed to evaluate the use of TAR compared with non-TAR in the 3 specific patient subgroups: (1) CABG with 2 bypasses

Table 2. Operative and Postoperative In-Hospital Outcomes of the Post-PSM TAR vs Non-TAR Groups

Outcome	Post-PSM, No. (%)		*P* Value
	TAR (n = 2132)	Non-TAR (n = 2132)	
Total No. of bypasses, mean (SD)	2.4 (0.5)	2.4 (0.5)	NA
Total No. of arterial bypasses, mean (SD)	2.4 (0.5)	1.2 (0.4)	<.01
Radial artery graft	1527 (71.6)	302 (14.2)	<.01
MI	7 (0.3)	10 (0.5)	.47
Stroke	9 (0.4)	12 (0.6)	.49
Kidney dysfunction requiring dialysis	11 (0.5)	8 (0.4)	.49
RBC transfusion	883 (41.4)	865 (40.6)	.56
Length of stay, median (IQR), d	6 (5-7)	6 (5-7)	.16
In-hospital death	15 (0.7)	21 (1.0)	.32

Abbreviations: IQR, interquartile range; MI, myocardial infarction; NA, not applicable; PSM, propensity score matched; RBC, red blood cell; TAR, total arterial revascularization.

(TAR with 2 arterial bypasses vs non-TAR with 1 artery and 1 vein); (2) CABG with 3 bypasses (TAR with 3 arterial bypasses vs non-TAR with 1 artery and 2 veins); and (3) CABG with 3 bypasses (TAR with 3 arterial bypasses vs non-TAR with 2 arteries and 1 vein). We were not able to analyze the specific group of patients undergoing CABG with 4 bypasses (TAR vs non-TAR) owing to the small number of patients in the TAR group.

Time-to-event analyses were performed using Cox proportional hazards models to compare MACCE and survival. Acute MI, stroke, and repeated revascularization were compared using a cause-specific hazards model accounting for death as a competing risk.[21] Hazard ratios (HR) were determined up to 30 days, and 1, 5, and 8 years after surgery with robust sandwich-type variance estimators to account for clustering in the matched pairs.[22] Major adverse cardiac and cerebrovascular events and survival were depicted using the Kaplan-Meier survival functions.[23] Cumulative incidence functions were generated for MI, stroke, and repeated revascularization.[21] Tertiary in-hospital outcomes were compared between the propensity matched cohorts using the McNemar test for categorical outcomes and parametric (paired *t* tests) or nonparametric (Wilcoxon signed rank test) tests for continuous outcomes.

Results

Study Population

Overall, 49 404 individuals of primary isolated CABG were identified, with 2, 3, or 4 or more total number of bypasses and at least 1 arterial graft. A total of 2433 individuals (4.9%) with TAR were identified, with 1521 (62.5%) of them having 2 bypasses, 865 (35.6%) having 3 bypasses, and 47 (1.9%) having 4 or more bypasses. Prior to matching, patients from the TAR group were younger (mean [SD] age, 61.2 [10.4] vs 66.0 [9.8] years; $t_{2432} = 289.52$; $P < .01$), had a higher proportion of patients with left ventricle ejection fraction 50% or more (1657 [68.1%] vs 1423 [60.3%]; $\chi^2_4 = 130.544$; $P < .01$), and less comorbidities (eTable 3 in the Supplement). After PSM, 2132 patient pairs were formed, with a mean (SD) age of 62.0 (9.8) years vs 61.9 (9.8) years (SMD < 0.01) for TAR and non-TAR, respectively (Table 1). The baseline SMDs were all less than 0.1 after matching, with the exception of current smoking status (TAR, 571 [26.8%] vs non-TAR, 714 [33.5%]; SMD = 0.15).

In-Hospital Outcomes

The operative and postoperative outcomes of the unadjusted cohorts are presented in eTable 4 in the Supplement. In-hospital outcomes for the PSM cohorts are presented in **Table 2**. In the PSM cohorts, the total number of bypasses were equal (mean [SD], 2.4 [0.5]), and the number of arterial grafts were higher in the TAR group (mean [SD], 2.4 [0.5] vs 1.2 [0.4]; $P < .01$; relative risk [RR], 1.31 [95% CI, 1.09-1.56]). There were more radial grafts in the TAR group (1527 [71.6%] vs 302 [14.2%]; $P < .01$; RR, 5.06 [95% CI, 4.56-5.61]). In-hospital death (15 [0.7%] vs 21 [1.0%]; $P = .32$; RR, 0.71 [95% CI, 0.37-1.39]), MI (7 [0.3%] vs 10 [0.5%]; $P = .47$; RR, 0.70 [95% CI, 0.27-1.94]), stroke (9 [0.4%] vs 12 [0.6%]; $P = .49$; RR, 0.75 [95% CI, 0.33-1.71]), kidney dysfunction requiring dialysis (11 [0.5%] vs 8 [0.4%]; $P = .49$; RR, 1.38 [95% CI, 0.55-3.42]), blood transfusion (883 [41.4%] vs 865 [40.6%]; $P = .56$; RR, 1.02 [95% CI, 0.95-1.09]), and length of stay (median [interquartile range], 6 [5-7] vs 6 [5-7] days; $P = .16$; mean difference, −0.31; $t_{2131} = -1.42$) did not differ between TAR vs non-TAR groups after PSM, respectively.

Primary Outcome: MACCE

The primary study outcome in the PSM cohorts is presented in **Table 3**, and **Figure 1** outlines the freedom from MACCE. The mean and maximum follow-up was 4.6 and 9.0 years, respectively. Fewer patients with TAR experienced MACCE throughout the follow-up. Up to 8 years, freedom from MACCE for TAR was 73.5% (95% CI, 70.7%-76.1%) vs 68.9% (95% CI, 66.0%-71.5%) for non-TAR (HR, 0.78; 95% CI, 0.68-0.89; $P < .01$).

Secondary Outcomes

Death

Long-term death in the PSM cohorts is presented in Table 3, and 8-year survival is presented in **Figure 2**. Up to 8 years, survival for TAR was 85.9% (95% CI, 83.6%-87.9%) vs 83.6% (95% CI, 81.2%-85.7%) for non-TAR (HR, 0.80; 95% CI, 0.66-0.97; $P = .02$).

Myocardial Infarction

Total arterial revascularization was associated with a lower incidence of MI after CABG at 1-, 5-, or at 8-year follow-up (Table 3). The cumulative incidence of MI accounting for death as a competing risk at 8-year follow-up for TAR vs non-TAR was 6.0% (95% CI, 4.7%-7.5%) and 8.0% (95% CI, 6.5%-9.6%),

Table 3. Follow-up Outcomes of PSM TAR vs Non-TAR Groups

Outcome	Estimated Probability, % (95% CI)		HR (95% CI)	*P* Value
	TAR (n = 2132)	Non-TAR (n = 2132)		
Freedom from MACCE[a]				
30 d	98.2 (97.5-98.7)	97.3 (96.5-97.9)	0.67 (0.45-1.00)	.03
1 y	94.8 (93.8-95.7)	92.6 (91.4-93.6)	0.69 (0.55-0.88)	<.01
5 y	84.0 (82.2-85.7)	78.8 (76.7-80.7)	0.73 (0.63-0.85)	<.01
8 y	73.5 (70.7-76.1)	68.9 (66.0-71.5)	0.78 (0.68-0.89)	<.01
Survival				
30 d	99.2 (98.7-99.5)	99.0 (98.5-99.4)	0.81 (0.43-1.54)	.52
1 y	98.0 (97.3-98.5)	97.6 (96.9-98.2)	0.82 (0.55-1.24)	.30
5 y	92.8 (91.4-93.9)	90.6 (89.1-91.9)	0.74 (0.59-0.94)	.02
8 y	85.9 (83.6-87.9)	83.6 (81.2-85.7)	0.80 (0.66-0.97)	.02
Cumulative Incidence				
MI				
30 d	0.4 (0.2-0.7)	0.5 (0.2-0.8)	0.80 (0.32-2.03)	.64
1 y	1.0 (0.7-1.5)	1.8 (1.3-2.4)	0.58 (0.34-0.98)	.04
5 y	3.5 (2.7-4.4)	5.3 (4.3-6.5)	0.63 (0.45-0.87)	<.01
8 y	6.0 (4.7-7.5)	8.0 (6.5-9.6)	0.69 (0.51-0.92)	.01
Stroke				
30 d	≤5[b]	≤5[b]	0.40 (0.08-2.06)	.27
1 y	≤5[b]	≤5[b]	0.45 (0.16-1.31)	.14
5 y	2.2 (1.5-3.0)	2.2 (1.6-3.0)	0.94 (0.60-1.50)	.81
8 y	3.2 (2.3-4.3)	3.1 (2.2-4.2)	0.97 (0.64-1.47)	.88
Revascularization				
30 d	≤5[b]	≤5[b]	0.22 (0.05-1.03)	.05
1 y	2.1 (1.5-2.7)	3.0 (2.3-3.7)	0.69 (0.47-1.01)	.05
5 y	6.4 (5.3-7.6)	7.8 (6.6-9.2)	0.80 (0.62-1.01)	.06
8 y	9.5 (7.9-11.2)	11.1 (9.4-12.9)	0.82 (0.66-1.02)	.08

Abbreviations: HR, hazard ratio; MACCE, major adverse cardiac and cerebrovascular event; MI, myocardial infarction; PSM, propensity score matched; TAR, total arterial revascularization.

[a] MACCE: Composite of death, MI, stroke, or repeated revascularization.

[b] Per ICES policy, all cells with fewer than 6 events were presented as ≤5 to avoid potential patient identification.

respectively (HR, 0.69; 95% CI, 0.51-0.92; *P* = .01) (eFigure 2 in the Supplement).

Stroke

The cumulative incidence of stroke accounting for death as a competing risk was not significantly different throughout follow-up for the 2 cohorts (Table 3). Up to 8 years, the stroke incidence was 3.2% (95% CI, 2.3%-4.3%) in the TAR group compared with 3.1% (95% CI, 2.2%-4.2%) in the non-TAR group (HR, 0.97; 95% CI, 0.64-1.47; *P* = .88) (eFigure 3 in the Supplement).

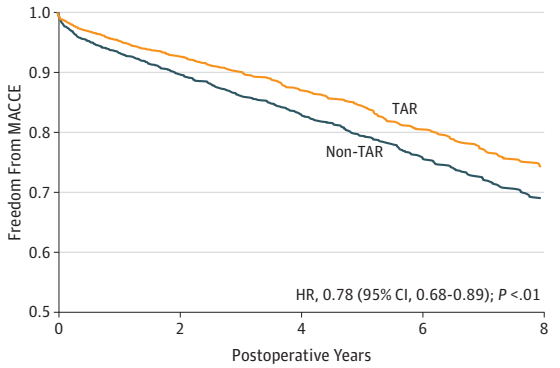
Repeated Revascularization and Sternal Reconstruction

Total arterial revascularization was associated with less repeated revascularization after CABG up to 30-day, 1-year, and 5-year follow-up (Table 3). The cumulative incidence of repeated revascularization up to 8 years for TAR vs non-TAR was 9.5% (95% CI, 7.9%-11.2%) vs 11.1% (95% CI, 9.4%-12.9%), respectively (HR, 0.82; 95% CI, 0.66-1.02; *P* = .08) (eFigure 4 in the Supplement). Total arterial revascularization was associated with an increased cumulative incidence of sternal reconstruction up to 1 year (HR, 2.78; 95% CI, 1.30-5.98; *P* = .01) in the post-PSM study population.

Surgeons Volume

After PSM, 75 surgeons performed non-TAR CABG and 72 performed TAR. The median (interquartile range) number of isolated CABGs performed by the surgeons who performed TAR was 94 per year (42-121), while for the surgeons who performed non-TAR, the median (interquartile range) annual volume was 92 (36-120) (*P* = .78).

Figure 1. Freedom From MACCE Curves for Propensity Score–Matched TAR vs Non-TAR Groups Up to 8-Year Follow-up

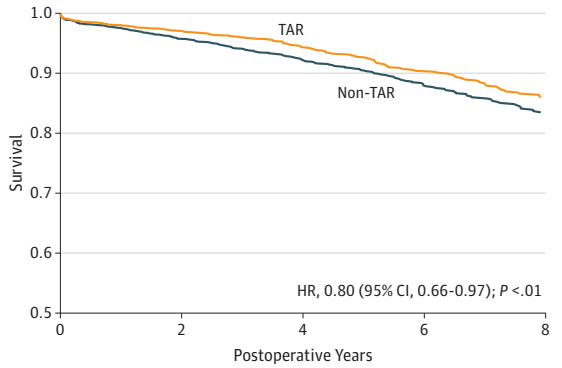


No. at risk

Non-TAR	2132	1712	1145	700	317
TAR	2132	1688	1200	751	324

HR indicates hazard ratio; MACCE, major adverse cardiac and cerebrovascular event; TAR, total arterial revascularization.

Figure 2. Survival Curves for 8-Year All-Cause Survival for Propensity Score–Matched TAR vs Non-TAR Groups



No. at risk

Non-TAR	2132	1818	1262	809	370
TAR	2132	1766	1299	837	372

HR indicates hazard ratio; TAR, total arterial revascularization.

Sensitivity Analysis

We examined the association of the ratio of arterial vs SVGs with the primary outcome of MACCE as a sensitivity analysis. In patients undergoing CABG restricted to 3 bypasses (TAR with 3 arterial bypasses vs non-TAR with 1 artery and 2 veins [67% SVG]), 790 well-matched pairs were formed. Freedom from MACCE was statistically lower for TAR (76.5%; 95% CI, 72.0%-80.4%) vs non-TAR (71.0%; 95% CI, 66.1%-75.4%) (HR, 0.76; 95% CI, 0.60-0.97; $P = .02$), but there were no statistically significant differences in the individual components of the primary outcome (eFigure 5 in the Supplement). There were no statistical differences in MACCE (HR, 0.91; 95% CI, 0.72-1.15; $P = .44$) or the components of MACCE when comparing TAR with 3 arterial grafts vs non-TAR using 2 arterial grafts and 1 vein (33% SVG, 814 pairs). Furthermore, there were no statistical differences in MACCE (HR, 0.86; 95% CI, 0.73-1.02; $P = .08$) or the components of MACCE when comparing TAR with 2 arterial grafts vs non-TAR with 1 arterial graft and 1 vein (50% SVG, 1328 pairs).

Discussion

In this large, population-based, multicenter study evaluating the long-term outcomes of TAR vs non-TAR, we observed (1) the overall prevalence of TAR in the province of Ontario in Canada was low (2433 [4.9%]); (2) patients undergoing TAR were younger and healthier compared with non-TAR patients; (3) after PSM, in-hospital outcomes were excellent and equivalent between techniques; (4) TAR was associated with improved long-term freedom from MACCE, survival, and cumulative incidence of MI; and (5) the TAR benefit was more prominent as the number of SVGs increased in the non-TAR group.

The search for the best graft selection has led to multiple observational studies and 1 major randomized clinical trial, the Arterial Revascularization Trial (ART) trial.[16,24,25] Currently, there are 2 main hypotheses: the first relates to the incremental benefit of arterial grafting. Pu et al,[24] in a population study of multiple arterial graft vs single arterial graft in the province of British Columbia in Canada, observed an association of multiple arterial graft with reduced mortality (HR, 0.79; 95% CI, 0.72-0.87) and repeated revascularization (HR, 0.74; 95% CI, 0.66-0.84) during 15-year follow-up. The ART trial, which compared bilateral internal mammary arteries vs single internal mammary artery, showed at 10 years, that there was no statistical difference in the risk of death (HR, 0.96; 95% CI, 0.82-1.12) or MACCE (HR, 0.90; 95% CI, 0.79-1.03).[25] The study was criticized by the large number of radial arterial grafts in the single internal mammary artery group and high incidence of intraoperative crossover from bilateral internal mammary arteries to single internal mammary artery.[26] A second contemporary hypothesis relates to the incremental harm associated with having any SVGs given that the mode of failure for vein grafts is accelerated atherothrombosis compared with string sign from noncompetitive flow for arterial grafts; the former is thought to lead to worse outcomes. Our study investigates this second line of thought, with a multicenter population-level study of MACCE and its components using a moderately large sample size over 8 years of follow-up.

One postulated advantage of CABG is the protection against flow-limiting lesions, occlusion, and/or acute thrombosis of non–flow-limiting plaques.[27] Nonetheless, this advantage is only present if the graft remains patent. In a patient-level meta-analysis from 6 trials, the use of radial artery grafts compared with an SVG was associated with reduced graft occlusion (HR, 0.44; 95% CI, 0.28-0.70) along with a lower incidence of MI (HR, 0.72; 95% CI, 0.53-0.99) and repeated revascularization (HR, 0.50; 95% CI, 0.40-0.63).[4] Although our study provides no data on graft patency, cases using SVGs were associated with worse outcomes (MACCE, survival, and cumulative incidence of MI) despite extensive adjustment.

The long-term survival benefit of TAR compared with non-TAR observed in our study is consistent with previous retrospective studies. Royse et al[12] reported a 22% relative survival advantage for TAR in an Australian analysis of 28 710 PSM patients compared with non-TAR. A further subanalysis comparing TAR vs multiarterial grafting with only 1 SVG in 26 632 PSM patients also resulted in a 22% relative survival advantage. Likewise, in a recent meta-analysis that pooled 12 small matched/adjusted observational studies in 33 597 patients, TAR was associated with an HR of 0.85 (95% CI, 0.81-0.89) for all-cause mortality compared with non-TAR.[28]

There are 2 randomized clinical trials comparing TAR vs non-TAR, to our knowledge. Muneretto et al[9] randomized 200 patients (100 in TAR vs 100 non-TAR). At 1 year, survival was similar, but the non-TAR group had more recurrent angina ($P < .01$), MI ($P = .03$), repeated revascularization ($P = .01$), and occluded grafts ($P = .01$). In addition, more than 95% of arterial grafts (right/left internal mammary and radial arteries) were patent at 1 year compared with only 84% patent SVGs. In the CARRPO trial, 331 patients (TAR vs non-TAR) were followed up to 1 year.[8] Again, survival was not different. Mean patency index was 87% in the TAR group vs 88% in the non-TAR group ($P = .52$). Nonetheless, the authors attributed the patency index similarity to the higher than normal rate of failure for the

right internal mammary, likely a consequence of the 12% of grafts anastomosed to moderately rather than critically stenosed right coronary arteries.

The data from observational studies are confounded by the surgeons' subjective decision as to which technique to perform.[29] In the ART trial,[25] the as-treated analysis revealed similar results as seen in observational studies, ie, associating bilateral internal mammary arteries with superior outcomes. However, the as-treated analysis is also confounded by indication. A second large trial with a target sample size of 4300 patients comparing multiple arterial graft with single arterial graft, the Randomization of Single vs Multiple Arterial Grafts (ROMA) trial (NCT03217006) is ongoing and will hopefully provide a definitive answer as to whether using more arterial grafts will lead to better survival and lower number of adverse events in the long term (S.E.F. and M.G. are ROMA principal investigators).[30]

One of the additional advantages of performing an all-arterial graft CABG is the potential to minimize aortic manipulation and decrease the rate of postoperative stroke.[31,32] We did not observe a difference in the early or late incidence of stroke in TAR vs non-TAR. This might be associated with the similar number of cases performed on-pump (still requiring aortic cannulation and crossclamping) in each group and that in off-pump cases, aortic manipulation during proximal anastomosis might have occurred using side biting clamp.

In our sensitivity analysis, we studied patients who had 2 or 3 CABG. There appeared to be a more prominent relative benefit observed as the ratio of SVGs increased in the non-TAR group. While hypothesis generating given the potential for type II error associated with a small sample size when creating subgroups in a sensitivity analysis and the different nature of the subgroups (extent of coronary disease), we found that as the number of SVGs increased according to the ratio of arterial grafts to SVGs, there was an increased signal toward improved outcomes in the TAR group. These findings are consistent with the study by Royse et al[12] that showed a detrimental long-term effect of using more than 1 SVG.

Strengths and Limitations

While this analysis is the largest multicenter study comparing the outcomes of TAR vs non-TAR, to our knowledge, it has the usual limitations associated with administrative database research such as data granularity and the retrospective nature of the analysis. Nonetheless, we limited the analysis to a contemporary timeframe using a set of previously validated codes for both CorHealth Ontario and the other linked data sets.[18] To account for imbalances in baseline characteristics, PSM with an extensive number of baseline covariates was performed, including factors such as income quintile and distance to health care provider, which might affect the health status of an individual. Nevertheless, any matching procedure cannot adjust for unmeasured confounders.[29] To adjust for surgeon factors, we matched on off-pump surgery and used a hierarchical model to adjust for institution. That said, we could not adjust for surgeon expertise, which might be higher among TAR proponents. Our databases do not include information regarding prior surgeon volume or experience (years in practice) at the time they performed their first case included in our analysis. Another limitation is the lack of information regarding the use of sequential grafts, target vessel bypassed, vessel size, or completeness of revascularization. We also did not adjust the *P* value for multiple testing of secondary outcomes.

Conclusions

In this large, population-based, multicenter study evaluating the long-term outcomes of TAR vs non-TAR, in-hospital outcomes were excellent and similar between groups. However, at late follow-up, TAR was associated with improved long-term freedom from MACCE, survival, and cumulative incidence of MI. Large randomized clinical trials are needed to confirm the superiority of TAR in the long-term outcomes of a young CABG population.

ARTICLE INFORMATION

Accepted for Publication: December 12, 2019.

Published Online: February 19, 2020. doi:10.1001/jamacardio.2019.6104

Author Affiliations: Schulich Heart Centre, Sunnybrook Health Sciences Centre, Division of Cardiac Surgery, Department of Surgery, University of Toronto, Toronto, Ontario, Canada (Rocha, Tam, Karkhanis, Fremes); Institute of Health Policy, Management and Evaluation, University of Toronto, Toronto, Ontario, Canada (Tam, Karkhanis, Austin, Fremes); Cardiovascular Program, ICES, Toronto, Ontario, Canada (Wang, Austin, Ko); Schulich Heart Centre, Sunnybrook Health Sciences Centre, Division of Cardiology, Department of Medicine, University of Toronto, Toronto, Ontario, Canada (Ko); Department of Cardio-Thoracic Surgery, Weill Cornell Medicine, New York, New York (Gaudino); Division of Cardiac Surgery, Royal Melbourne Hospital, Parkville, Victoria, Australia (Royse); Department of Surgery, The University of Melbourne, Melbourne, Victoria, Australia (Royse).

Author Contributions: Dr Rocha and Ms Wang had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Rocha, Tam, Gaudino, Royse, Fremes.
Acquisition, analysis, or interpretation of data: Rocha, Karkhanis, Wang, Austin, Ko, Fremes.
Drafting of the manuscript: Rocha, Tam, Wang, Royse.
Critical revision of the manuscript for important intellectual content: Rocha, Tam, Karkhanis, Austin, Ko, Gaudino, Royse, Fremes.
Statistical analysis: Wang.
Obtained funding: Rocha.
Administrative, technical, or material support: Karkhanis.
Supervision: Gaudino, Fremes.

Conflict of Interest Disclosures: Dr Tam is supported by the Ontario Ministry of Health Clinician Investigator's Program. Drs Austin and Ko are supported by a Mid-Career Award from the Heart and Stroke Foundation. Dr Fremes reports grants from Randomization of Single vs Multiple Arterial Grafts (ROMA) trial and serves as the Bernard S. Goldman Chair in Cardiovascular Surgery outside the submitted work. No other disclosures were reported.

Funding/Support: This study was supported by the Bernard S. Goldman Grant for Cardiovascular Surgery and ICES, which is funded by an annual grant from the Ontario Ministry of Health and Long-Term Care.

Role of the Funder/Sponsor: The funders had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: The analyses, conclusions, opinions and statements expressed herein are solely those of the authors and do not reflect those of the funding or data sources; no endorsement is intended or should be inferred.

Additional Information: Parts of this material are based on data and information compiled and provided by the Ontario Ministry of Health and

Long-Term Care (MOHLTC), CorHealth, and Canadian Institute for Health Information. The authors acknowledge that the clinical registry data used in this publication is from participating hospitals through the CorHealth Ontario Cardiac Registry of Ontario, which serves as an advisory body to the MOHLTC, is funded by the MOHLTC.

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