

Total Arterial Revascularization: A Superior Strategy for Diabetic Patients Who Require Coronary Surgery

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Background. Recent large randomized trials and meta-analyses have shown that, for patients with diabetes mellitus and advanced coronary artery disease, coronary artery bypass graft surgery (CABG) was superior to percutaneous intervention. We investigated whether total arterial revascularization (TAR) conferred an additional survival advantage for diabetic patients having CABG.

Methods. We reviewed 63,592 cases from an audited, collaborative Australian cardiac surgical database. A total of 34,181 patients undergoing first time isolated CABG from 2001 to 2012 were identified. Of the 34,181, 11,642 (34.1%) were diabetic patients, and TAR was performed in 12,271 of 34,181 (35.9%). Of the 11,642 diabetic patients, TAR was performed in 3,795 (32.6%) and non-TAR in 7,847 (67.4%). Propensity matching resulted in 6,232 matched pairs of patients who did and patients who did not have TAR. Data were linked to the National Death Index.

Results. In the propensity matched sample, of 6,232 diabetic patients, 2,017 (32.4%) underwent TAR and 1,967 (31.6%) did not ($p = 0.337$). Mean follow-up was 4.9 years. Perioperative mortality, including 30-day mortality, was similar: 1.2% (24 of 2,017) for TAR and 1.4% (28 of 1,967) for non-TAR ($p = 0.506$). Late mortality was less among diabetic patients who underwent TAR, 10.2% (205 of 2,017), than no TAR, 12.2% (240 of 1,967; $p = 0.041$). Kaplan-Meier survival for the diabetic TAR group at 1, 5, and 10 years was 96.2%, 88.9%, and 82.2%, respectively, versus 95.4%, 87.5%, and 78.3% for the diabetic non-TAR group (log rank, $p = 0.036$).

Conclusions. In a large propensity matched cohort of patients having CABG, TAR demonstrated further long-term prognostic benefit for diabetic patients, in the context of equivalent perioperative mortality.

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The incidence of diabetes mellitus, in concert with obesity, is increasing steadily in both Western and developing countries, with an associated increased burden of cardiovascular pathology and death [1]. Recent large, well-conducted randomized trials and exhaustive meta-analyses have clearly shown superior long-term survival for diabetic patients revascularized by coronary artery bypass graft surgery (CABG) by comparison with percutaneous coronary intervention [2, 3]. For diabetic patients having CABG, there is emerging evidence that those having multiple arterial grafts may have even greater long-term prognostic benefits (with similar perioperative mortality and morbidity) over those having conventional CABG with a left internal thoracic artery (LITA) graft and saphenous vein graft (SVG) [4–6]. The objective of this multicenter study was to examine the

effect of total arterial revascularization (TAR) by comparison to non-TAR, on the long-term survival of diabetic patients undergoing CABG, and to determine any impact on perioperative mortality and morbidity, especially on deep sternal wound infection (DSWI).

Patients and Methods

A post hoc subgroup analysis of diabetic patients was undertaken on data from the Australian and New Zealand Society of Cardiothoracic Surgeons (ANZSCTS) Database, from which a propensity-matched cohort was derived. The description has been previously published [7]. Ethics approval was by Melbourne Health (#QA2013097) and the ANZCTS Database Research Subcommittee.

Contributors to this collaborative database since its inception in 2001 are six Victorian state (five in Melbourne) university teaching hospitals, whose participation is mandatory. Since 2009, contributors have increased to 24 hospitals throughout Australia. The data are centrally submitted, collated, and audited by an independent data institute. Mandatory follow-up within

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Abbreviations and Acronyms

CABG	= coronary artery bypass graft surgery
DSWI	= deep sternal wound infection
ITA	= internal thoracic artery
LITA	= left internal thoracic artery
RA	= radial artery
RITA	= right internal thoracic artery
SVG	= saphenous vein graft
TAR	= total arterial revascularization

30 days of surgery is undertaken. Data were linked to the National Death Index registry that records all deaths within Australia and New Zealand to monitor long-term mortality. The censoring date was January 31, 2013.

Sample

We reviewed 63,592 cases from this audited collaborative cardiac surgical database, and identified 34,181 patients undergoing first time isolated CABG from 2001 to 2012. There were 11,642 diabetic patients (34.1%). Total arterial revascularization was performed in 12,271 patients (35.9%); 3,795 (30.9%) with diabetes versus 8,476 (69.1%) without diabetes. Propensity matching of the entire first time CABG cohort ($n = 34,181$) resulted in 6,232 matched pairs who did or did not have TAR. Within the propensity matched cohort, there were 3,984 diabetic patients (32%); of those, 2,017 (32.4%) had TAR and 1,967 (31.6%) did not. These patients form the basis of this analysis.

Endpoints

The primary endpoint was all-cause late mortality (any death occurring more than 30 days after surgery). Secondary endpoints were 30-day mortality, DSWI, postoperative myocardial infarction, low cardiac output, stroke, return to the operating room for bleeding, new onset renal failure requiring hemofiltration, and septicemia.

Surgical Technique

Although there was some site-specific variability, standard surgical techniques involved the following. All patients underwent median sternotomy and internal thoracic arteries (ITA) were harvested in a skeletonized or semiskeletonized manner. Radial artery (RA) conduits were harvested with an open atraumatic technique with sharp dissection, scissor division of branches between vascular clips, supplemented by low power cautery or harmonic scalpel. Where SVG were used in the non-TAR group, the vein was usually harvested from the lower leg, by open technique and scissor division of branches between clips. Thigh vein was generally avoided. All patients received prophylactic antibiotics and tight glucose control (<10 mmol/L). Anastomoses were performed during one period of cross clamping on cardiopulmonary bypass at 34° to 35° C. Myocardial protection was with combined antegrade and retrograde blood

cardioplegia (20° C). Off-pump surgery was used in 8.4% of cases, predominantly for ascending aorta atheroma.

Arterial Graft Spasm Prophylaxis

Topical papaverine was always used, and RAs were stored in papaverine-heparinized arterial blood until use. In addition, intravenous nitroglycerine or milrinone was given for 24 hours, and calcium-channel blocker empirically for 6 months for RA spasm prophylaxis. Details of conduit harvest and spasm prophylaxis have been published previously [8, 9].

Graft Deployment in Total Diabetes Cohort

In the TAR group ($n = 3,795$), there were 3,734 left internal thoracic arteries (LITA), 597 right internal thoracic arteries (RITA), 3,207 RA, and 784 T/Y grafts (20.7%), for a total of 11,077 distal anastomoses. In the non-TAR group ($n = 7,847$), there were 7,398 LITA, 299 RITA, 2,854 RA, and 330 T/Y grafts (4.2%), for a total of 27,126 distal anastomoses. The RITA anastomoses were almost exclusively to the circumflex, and RA predominantly to the posterior descending artery.

Statistical Analysis

Preoperative, operative, and postoperative data were compared for diabetic patients in unmatched ($n = 11,642$) then matched ($n = 3,984$) TAR and non-TAR groups. We set out to examine the effect of TAR on outcome specifically for the diabetic patient subgroup. Examining diabetic patients as a subgroup of the matched cohort enabled us to ensure the distribution of baseline measures was similar for all diabetic patients irrespective of TAR or non-TAR. We could then determine whether TAR itself conferred an additional survival advantage. Demographic and clinical data are presented as frequency distributions and proportions. Continuous variables are expressed as mean \pm SD. Univariate analysis of categorical variables was accomplished using χ^2 or two-tailed Fisher's exact tests, with the appropriate degrees of freedom to test for equality of proportions. Independent samples t tests (two-tailed) were used to test the equality of means of continuous variables. An optimal matching strategy, described elsewhere [7], was used to examine the effect of TAR versus other grafting strategies using propensity balancing according to recommendations provided by Blackstone [10]. Propensity score distribution among TAR and Non-TAR groups was significantly different before matching (0.461 versus 0.301) and comparable after matching (0.403 versus 0.404). Standardized differences were calculated to review balance in baseline variables before and after matching. In the matched cohort a high degree of balance was indicated by all standardized differences being less than 10%. Comparisons in the matched cohort were undertaken using paired samples t -tests or McNemar tests for binary variables and Kaplan-Meier survival curves were stratified and calculated as recommended by Austin [11, 12].

Propensity score between TAR (0.388) and non-TAR patients (0.387) within the diabetes subgroup did not differ ($p = 0.834$). To address the primary aim of the study,

χ^2 analyses were used to test independent proportions, and Cox proportional hazards regression was used to identify hazards for all-cause late mortality in the diabetes subgroup. Regression coefficients and hazard ratios with 95% confidence intervals were calculated to determine the relative influence of each covariate on survivor function. Actuarial analysis was conducted according to the method of Kaplan and Meier, and stratified survival distributions were tested with the log rank algorithm. All statistical tests were two sided, and a value of 0.05 was considered significant. Data were analyzed using IBM SPSS Statistics (version 22.0; IBM Corp, Armonk, NY).

Results

A total of 11,642 of 31,181 diabetic patients had CABG, 3,795 TAR and 7,847 non-TAR (Table 1).

Perioperative and Hospital Outcomes for All Diabetic Patients, Unmatched

Operative and 30-day mortality was 1.1% (43 of 3,795) for TAR and 2.1% (163 of 7,847) for non-TAR ($p < 0.001$). Major morbidity was also low; and DSWI was 0.9% for TAR and 1.1% for non-TAR ($p = 0.378$). Stroke and myocardial infarction were each 1% or less for TAR and for non-TAR. Details of the major complications are given in Table 1.

Late Outcomes, Unmatched

Kaplan-Meier survival for diabetic TAR patients ($n = 3,795$) undergoing first time isolated CABG in the unmatched (diabetes only) cohort at 1, 5, and 10 years was 96.6%, 90.3%, and 83.3%, respectively, versus non-TAR diabetic patients ($n = 7,847$), which was 94.6%, 86.4%, and 76.8%, respectively (log rank, $p < 0.001$; Fig 1).

Propensity Score Matched Outcomes

In the TAR propensity matched cohort ($n = 12,464$), there were 3,984 diabetic patients; of those, 2,017 had TAR and 1,967 did not. The demographic, intraoperative, and perioperative data are presented in Table 2. Patients were well matched for preoperative variables. The TAR diabetic group had 3.05 ± 1.05 distal arterial anastomoses, whereas the non-TAR diabetic group had 1.65 ± 0.14 ; and 47.8% of non-TAR patients had more than one arterial graft.

Perioperative and Hospital Outcomes

Perioperative mortality was 1.2% (24 of 2,017) for TAR versus 1.4% (28 of 1,967) for non-TAR ($p = 0.506$). Perioperative major morbidity was low, and similar in both groups. Stroke, myocardial infarction, and multiorgan failure were each less than 1%, and septicemia was 1.1% (Table 2). Importantly, DSWI was low, and similar: 0.8% for TAR and 1.2% for non-TAR ($p = 0.301$).

Long-Term Survival

The mean follow-up in the matched cohort was 4.5 ± 3.1 years. Late mortality was lower among diabetic patients who underwent TAR, 10.2% (205 of 2,017), versus 12.2%

(240 of 1,967) for non-TAR ($p = 0.041$). Kaplan-Meier survival for the matched diabetes groups at 1, 5, and 10 years was 96.2%, 88.9%, and 82.2%, respectively, for the diabetes TAR group; and 95.4%, 87.5%, and 78.3%, respectively, for the diabetes non-TAR group (log rank, $p = 0.036$; Fig 2). The non-TAR diabetes group had a greater risk of all-cause mortality (hazard ratio 1.22, 95% CI: 1.01 to 1.47, $p = 0.039$). A Cox proportional hazards model stratified for TAR showed additional hazards for death in this diabetes subgroup (Table 3). Among these, the most powerful were postoperative cardiac arrest, myocardial infarction, stroke, and multisystem organ failure.

Comment

Contemporary large randomized trials and metaanalyses have indicated that CABG is superior to percutaneous coronary intervention in diabetic patients [2, 3]. Recent reports have suggested that there may be additional benefit for diabetic patients undergoing CABG when more than one arterial graft is used [4–6].

In this study of diabetic patients undergoing CABG, there were two major findings: that TAR confers a significant survival benefit for diabetic patients who did not have TAR; and that the long-term benefits from TAR did not compromise perioperative outcomes, especially 30-day mortality and DSWI. Diabetic patients having TAR had low and similar 30-day mortality and low and similar perioperative major morbidity, including stroke, myocardial infarction, septicemia, and reoperation for bleeding, compared with diabetic patients who did not have TAR but, rather, more conventional CABG.

An important finding was that DSWI among diabetic patients was extremely low and similar, 0.8% for TAR and 1.2% for non-TAR, emphasizing that TAR can be achieved, even for diabetic patients, without compromising sternal integrity. Our strategies to achieve this have been alcohol-based skin preparations, preoperative, intraoperative, and postoperative (24 hours) antibiotics starting 1 hour before the skin incision, avoiding bone wax, vancomycin “paste” to the sternal edges before closing, tight perioperative glucose management, and routine use of skeletonized ITA. Numerous institutions have shown the value of skeletonized ITA harvest [5, 7, 13]. There is less chest wall trauma, the endothoracic fascia, which is partly vascular, covers the ITA bed, and the small branches between the ITAs and the intercostal arteries are divided in a manner that preserves the terminal intercostals and vascular supply to the sternum [13]. In addition, the skeletonized ITAs are longer, more dilated, and more versatile [7, 13].

We found aortic cross-clamp time and cardiopulmonary bypass time were comparable, indeed shorter, for TAR as opposed to non-TAR and in keeping with the number of anastomoses performed by a single cross-clamp technique; and that a mean of 3.1 arterial grafts could be placed expeditiously in the TAR diabetes group by a wide range of surgeons at several teaching institutions. Hence, coronary artery grafting may not be

Table 1. Preoperative, Intraoperative, and Early Postoperative Outcomes in Unmatched Diabetic Patients (n = 11,642)

Variables	TAR		Non-TAR		<i>p</i> Value
Preoperative variables					
Patients	3,795	32.6	7,847	67.4	...
Age, years	64.7	9.9	66.7	9.7	<0.001
Body mass index, kg/m ²	30.3	7.4	29.9	9.5	0.039
Female	952	25.1	1,877	23.9	0.169
Coronary risk factors					
Smoking History	2527	66.6	5165	65.8	0.413
Current smoker	533	14.0	1,112	14.2	0.855
Family history CAD	1,514	39.9	2,667	34.0	<0.001
Hypertension	3,281	86.5	6,934	88.4	0.003
Hypercholesterolemia	3,282	86.5	6,782	86.4	0.936
Preoperative risk factors					
Preoperative Creatinine	100.9	70.8	116.4	114.8	<0.001
Preoperative dialysis	46	1.2	267	3.4	<0.001
CBVD	422	11.1	1,064	13.6	<0.001
Peripheral vascular disease	590	15.5	1,344	17.1	0.032
Lung disease	473	12.5	1,006	12.8	0.588
Acute MI	1,962	51.7	4,581	58.4	<0.001
Angina	2,998	79.0	5,957	75.9	<0.001
Unstable angina	1,718	45.3	3,414	43.5	0.073
History of CHF	674	17.8	1,547	19.7	0.012
Current CHF	210	5.5	768	9.8	<0.001
NYHA class >1	2,479	65.3	4,703	59.9	<0.001
Ejection fraction < 60%	1,924	50.7	4,359	55.5	<0.001
Previous PCI	612	16.1	1,082	13.8	0.001
Nonelective status	1,269	33.4	3,234	41.2	<0.001
Left main disease	795	20.9	2,029	25.9	<0.001
Number diseased vessels	2.54	0.6	2.82	0.4	<0.001
Perioperative characteristics					
Cross-clamp time, minutes	57.4	36.1	66.5	32.3	<0.001
Perfusion time, minutes	76.1	44.4	94.2	38.2	<0.001
No. distal anastomoses	2.92	1.1	3.46	0.9	<0.001
No. arterial distal anastomoses	2.92	1.1	1.53	0.10	<0.001
No. ITA grafts	1.38	0.64	1.10	0.48	<0.001
No. radial distal anastomoses	1.54	0.98	0.43	0.69	<0.001
>1 distal arterial anastomoses	3,446	90.8	3,593	45.8	<0.001
ITA	3,734	98.4	7,398	94.3	<0.001
BITA	597	15.0	299	3.7	<0.001
RAC	3,207	84.5	2,854	32.6	<0.001
Early outcomes					
Deep sternal infection	34	0.9	84	1.1	0.378
Reoperation for bleeding	68	1.8	197	2.5	0.015
RBC transfusion	1,310	34.5	3,688	47.0	<0.001
Non-RBC transfusion	583	15.4	1,828	23.3	<0.001
Stroke	34	0.9	77	1.0	0.657
Hemofiltration	52	1.4	162	2.1	0.009
Perioperative MI	18	0.5	61	0.8	0.062

(Continued)

Table 1. Continued

Variables	TAR		Non-TAR		p Value
Septicemia	37	1.0	94	1.2	0.285
Cardiogenic shock	91	2.4	160	2.0	0.211
LOS >10 days	631	16.6	1,749	22.3	<0.001
30-day mortality	43	1.1	163	2.1	<0.001

Figures in the first and third columns represent number (n) for absolute numbers, and mean values for measurements. Figures in the second and fourth columns represent percentage (%) for absolute numbers, or standard deviation of mean values.

BITA = bilateral internal thoracic artery; CAD = coronary artery disease; CBVD = cerebrovascular disease; CHF = congestive heart failure; ITA = internal thoracic artery; LOS = length of stay; MI = myocardial infarction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; RAG = radial artery graft; RBC = red blood cells; SD = standard deviation; TAR = total arterial revascularization.

as difficult a technical challenge as previously considered. Arteriotomies were placed between plaques or distally. Endarterectomies were avoided. In general, operative times for TAR were 30 minutes longer, relating to additional conduit harvest, especially when bilateral ITA or bilateral RA were used, not to the actual grafting procedure.

Another concern with TAR is perioperative bleeding. We found reoperation rates for postoperative bleeding to be similar and low (1.7% to 2.5%), favoring TAR, reinforced by less red blood cell transfusion and coagulation factor requirement. That may be the result of a more precise ITA harvest and a smaller "raw" ITA bed that is covered by the remaining fascia and parietal pleura. These unexpected findings are a great positive for diabetic patients.

It is intuitive that the use of multiple arterial grafts will result in greater long-term benefits as arterial grafts have been shown to have higher late patency rates. Patency of

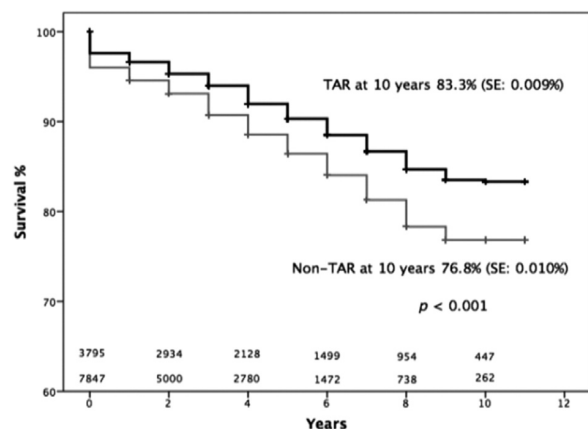


Fig 1. Comparison of Kaplan-Meier survival for unmatched diabetic total arterial revascularization (TAR) patients (black line) versus non-TAR patients (gray line [log rank, $p < 0.001$]).

Table 2. Preoperative, Intraoperative, and Early Postoperative Outcomes of Diabetic Propensity Matched Total Arterial Revascularization Patients (n = 3,984)

Preoperative Variables	TAR		Non-TAR		p Value
Patients	2,017	50.6	1,967	49.4	...
Age, years	64.8	9.6	64.5	9.8	0.339
Body mass index	30.2	6.3	30.4	11.5	0.520
Female	497	24.6	493	25.1	0.757
Coronary risk factors					
Smoking history	1,341	66.5	1,304	66.3	0.898
Current smoker	296	14.7	287	14.6	0.940
Family history CAD	814	40.4	787	40.0	0.823
Hypertension	1,756	87.1	1,707	86.8	0.795
Hypercholesterolemia	1,752	86.9	1,697	86.3	0.586
Preoperative risk factors					
Preoperative creatinine	99.9	1.5	97.4	1.1	0.211
Preoperative dialysis	15	0.7	9	0.5	0.243
CBVD	237	11.8	230	11.7	0.955
Peripheral vascular disease	310	15.4	340	17.3	0.102
Lung disease	240	11.9	231	11.7	0.880
Acute MI	1,043	51.7	1,028	52.3	0.727
Angina	1,608	79.7	1,579	80.3	0.663
Unstable angina	904	44.8	884	44.9	0.938
History of CHF	353	17.5	328	16.7	0.489
Current CHF	103	5.1	88	4.5	0.350
NYHA >1	1,320	65.4	1,236	62.8	0.086
Ejection fraction < 60%	1,025	50.8	984	50.0	0.617
Previous PCI	301	14.9	321	16.3	0.225
Nonelective status	648	32.1	670	34.1	0.194
Left main disease	67	3.3	29	1.5	<0.001
No. diseased vessels	2.66	0.54	2.67	0.54	0.463
Perioperative characteristics					
Cross-clamp time, minutes	61.5	34.8	66.4	33.6	<0.001
Perfusion time, minutes	80.9	42.6	93.0	43.1	<0.001
No. distal anastomoses	3.05	1.05	3.37	0.99	<0.001
No. distal arterial anastomoses	3.05	1.05	1.65	0.14	<0.001
No. ITA grafts	1.37	0.64	1.13	0.50	<0.001
No. radial distal anastomoses	1.68	0.95	0.53	0.74	<0.001
>1 distal arterial anastomosis	1,902	94.3	940	47.8	<0.001
ITA	1,985	98.4	1,868	95.0	<0.001
BITA	306	15.2	100	5.1	<0.001
RAC	1,787	88.6	777	39.5	<0.001
Early outcomes					
Deep sternal infection	17	0.8	23	1.2	0.301
Reoperation for bleeding	35	1.7	50	2.5	0.078
RBC transfusion	715	35.4	836	42.5	<0.001
Non-RBC transfusion	291	14.4	395	20.1	<0.001
Stroke	19	0.9	18	0.9	0.929
Hemofiltration	23	1.1	27	1.4	0.510
Perioperative MI	9	0.4	12	0.6	0.475

(Continued)

Table 2. Continued

Preoperative Variables	TAR		Non-TAR		p Value
Septicemia	23	1.1	22	1.1	0.948
Cardiogenic shock	42	1.2	13	0.7	<0.001
LOS >10 days	353	17.5	333	16.9	0.037
30-day mortality	24	1.2	28	1.4	0.506
Late mortality	205	10.2	240	12.2	0.041

Figures in the first and third columns represent number (n) for absolute numbers, and mean values for measurements. Figures in the second and fourth columns represent percentage (%) for absolute numbers, or standard deviation of mean values.

BITA = bilateral internal thoracic artery; CAD = coronary artery disease; CBVD = cerebrovascular disease; CHF = congestive heart failure; ITA = internal thoracic artery; LOS = length of stay; MI = myocardial infarction; NYHA = New York Heart Association; PCI = percutaneous coronary intervention; RAG = radial artery graft; RBC = red blood cells; SD = standard deviation; TAR = total arterial revascularization.

the LITA has consistently been shown to be more than 90% at 10 years, and in very long term reports, more than 90% at 20 years [9, 14]. The RITA is biologically identical to the LITA, with identical patencies when placed to the same vessel. Possibly for technical, and other reasons (competitive flow), patency rates to the circumflex and the right coronary artery are less favorable than for the left anterior descending artery, but nevertheless excellent and far superior to that of SVG [9].

A number of reports on RA patencies are now indicating patency rates of 90% or more (similar to the RITA) at 10 years, particularly when competitive flow situations are avoided [8, 15]. Conversely, SVG have progressive deterioration; initially fibromuscular hyperplasia (3- to 5-year time frame) then atherosclerosis, so that by 10 years only 60% are patent, and those patent have significant atheromatous disease. Ongoing deterioration and

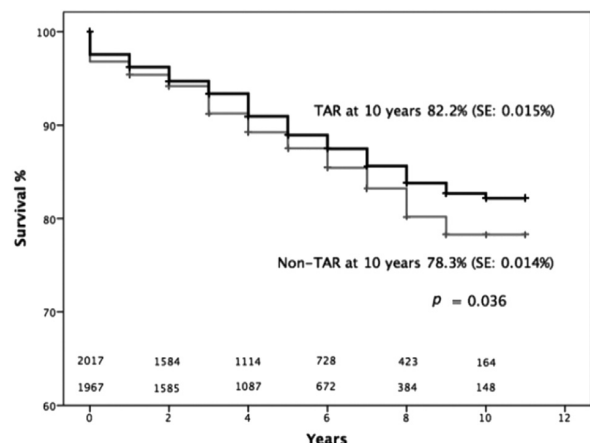


Fig 2. Comparison of Kaplan-Meier survival for matched diabetic total arterial revascularization (TAR) patients (black line) versus non-TAR patients (gray line) [log rank, $p < 0.036$].

Table 3. Hazards for All-Cause Late Mortality in Diabetes Subgroup

Predictor	β Estimate	SE	HR	(95% CI)	p Value
Age, per additional year	0.058	0.006	1.060	(1.05–1.07)	<0.001
Female	0.277	0.114	1.319	(1.05–1.65)	0.015
Smoking history	0.392	0.116	1.480	(1.18–1.86)	0.001
Preoperative creatinine	0.002	0.001	1.002	(1.01–1.03)	<0.001
Preoperative stroke	0.426	0.156	1.531	(1.12–2.07)	0.006
Peripheral vascular disease	0.467	0.107	1.600	(1.29–1.97)	<0.001
Lung disease	0.325	0.123	1.385	(1.09–1.76)	0.008
Congestive heart failure	0.471	0.105	1.602	(1.30–1.97)	<0.001
Ejection fraction < 60%	0.408	0.103	1.503	(1.23–1.84)	<0.001
Left main disease	0.377	0.106	1.458	(1.18–1.79)	<0.001
Number of diseased vessels	0.330	0.117	1.391	(1.10–1.75)	0.005
Postoperative MI	1.137	0.460	3.118	(1.26–7.68)	0.013
Postoperative cardiac arrest	1.142	0.212	3.133	(2.07–4.74)	<0.001
Postoperative stroke	0.747	0.300	2.110	(1.17–3.80)	0.013
Red blood cell use	0.215	0.102	1.240	(1.02–1.51)	0.034
GIT complication	0.736	0.297	2.087	(1.17–3.73)	0.013
Multisystem organ failure	1.673	0.281	5.328	(3.07–9.25)	<0.001

CI = confidence interval; GIT = gastrointestinal tract; HR = hazard ratio; MI = myocardial infarction; SE = standard error.

occlusion further reduces SVG patency at 15 years to approximately 30% [9, 14, 15]. Disappointingly recent, large SVG patency studies have shown that as many as 12% of SVGs may be occluded by 1 week postoperatively, and 20% to 25% occluded at 1 year [16].

Diabetic patients have a greater incidence of coronary risk factors—such as obesity, hypercholesterolemia, and hypertension—that further affect the development of atherosclerosis within the SVG and diffuse distal disease in the coronary artery, further compromising SVG patency and leading to poorer outcomes for diabetic patients compared with nondiabetic patients [1, 5, 6]. Hence, TAR and avoiding the SVG specifically address graft patency and long-term survival of diabetic patients in several ways. Arterial grafts, especially the ITA, are resistant to developing atheroma, even in diabetic patients, despite the greater prevalence of comorbid risk factors. The quality of SVG in diabetic patients may be compromised by chronic or recurrent lower limb infections. With diabetes, coronary arteries often have diffuse distal disease and poor runoff, which may also negatively impact SVG patency. Conversely, arterial graft endothelium produces nitric oxide, prostacyclin, and other favorable vasoactive factors that may be protective and help ameliorate progression of the distal coronary disease so prevalent among diabetic patients [17]. There is a better size match, and size discrepancy—especially between thigh SVG and coronary artery—is avoided. The use of SVG presents additional problems for diabetic patients. For example, SVG harvest from the leg may result in infection or poor healing. Conversely, endoscopic harvest of thigh SVG avoids lower limb wound problems, but is associated with poorer patency rates [16]; TAR avoids these problems and allows earlier mobilization.

Diabetic patients requiring CABG present a challenge: a poor prognosis if inadequately treated, diffuse coronary disease, and numerous comorbidities, including obesity, poor wound healing, and the possibility of DSWI. Although TAR results in better long-term survival, the modes of achieving this can and should be tailored to the patient. If bilateral ITA is not appropriate, for example, for morbid obesity or severe lung disease, then LITA plus bilateral RA can be used. The 10-year survival of TAR diabetic patients was excellent at 82.2%. That is similar to, or better than, survival for routine cohorts of patients having CABG by conventional LITA/SVG, for whom 10-year survival rates are usually reported as 75% [14, 15, 18]. Given that the non-TAR diabetic group had a mean of 1.65 arterial grafts per patient and 48% of patients in this group had at least two arterial grafts, the results for TAR are even more powerful when potentially compared with conventional LITA/SVG.

The strengths of this study include the large sample size, from a number of teaching hospitals, as well as that the surgery was performed by both senior residents and attending surgeons. Sequential, nonselective, prospective data collection used for this study is mandated by the government and audited. Mortality through the National Death Index ensures an unambiguous endpoint and complete follow-up.

Study Limitations

This study was retrospective, the non-TAR group was heterogeneous, the study does not capture interval events such as rehospitalizations, infarcts, and reinterventions, and it also assumes that both TAR and non-TAR groups had similar, standard postoperative secondary prevention with aspirin, statins, beta-blockers, and so forth.

Importance and Implications

The incidence of obesity and diabetes is increasing in both Western and developing countries. Moreover, general primary health care advances have increased longevity so that a 65-year-old (mean age in this study) person in many countries can expect to live to 86, another 21 years [7]. Therefore, the type of revascularization in diabetic patients will assume progressive importance.

We and others have previously shown that TAR enhances the prognosis of patients in general who require CABG [7, 14, 15, 18]. That finding can now be extended to diabetic patients. When TAR is used for diabetic patients, 4 additional patients per 100 operated on will be alive in 10 years, with, it is hoped, fewer intercurrent events. Apart from longer conduit harvest times (which did not translate into any clinical events), we could not document drawbacks by using TAR in diabetic patients. Diabetic patients undergoing CABG do less well than nondiabetic patients. We have been able to show that by the use of TAR/CABG for diabetic patients, one can upwardly adjust long-term survival so that it at least matches or may even surpass that for nondiabetic patients and general cohorts of patients undergoing revascularization by conventional LITA/SVG.

Conclusion

Total arterial revascularization in large numbers of diabetic patients is achievable, by senior trainees and attending surgeons in many institutions, with low peri-operative mortality and morbidity, including DSWI, identical to conventional CABG but resulting in superior long-term survival. These findings will gain increasing importance with the progressive longevity of the population and the increasing proportion of diabetic patients who may require CABG.

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DISCUSSION

DR BRETT C. SHERIDAN (Chapel Hill, NC): I have a technical question, Dr Tatoulis. Do you use the right internal thoracic artery as a free graft?

DR TATOULIS: About 50% of the time we use it as an in situ graft through the transverse sinus or anterior to the aorta to the high circumflex system. The other 50% of the time we use it either directly from the aorta or as a Y-graft—18% were Y-grafts.

DR JOHN W. HAMMON (Winston-Salem, NC): Very good, Jim. We really appreciate you Down Under folks pushing total arterial grafting. One of the things that we noticed at our institution was that in harvesting the radial artery in diabetic patients, we unfortunately found that at least 10% to 15% had significant atherosclerosis. So did you go ahead and use those, or what was your strategy in that situation?

DR TATOULIS: Thank you. Approximately 5% or 6% of radials cannot be used because of calcification and some degree of localized atheroma, and that is a higher level in diabetic patients, as you point out. In this series, 85% of patients had a radial and sometimes two radials. So we did not use the radial in 15% of patients. We do ultrasounds of the radial artery to look at the size and to see if there is calcification and then make a judgment. If there is just a small amount of medial wall calcification, we would use it, or sometimes discard the most distal 2 or 3 cm where the bulk of the calcification is. So we make a value judgment on the quality of the radial artery before it is harvested. I did not mention it previously, but in 22% of these patients, we used bilateral radial arteries as well.

DR NUNO GUERRA (Lisbon, Portugal): Do you feel that the insulin-dependent diabetes patients benefit more or less from double mammary artery grafting when compared with the oral antidiabetes patients?

DR TATOULIS: I am afraid I cannot answer that question, although this study included both insulin-dependent and oral medication treatment diabetic patients. In our country, we are using more and more insulin as a first-line treatment for diabetes. So it is difficult to differentiate the diabetic groups in the ways that we used to do. Oral diabetic agents are becoming obsolete in Australia, so I really cannot answer your question. But we do have exclusions. If people had huge body mass index, greater than 45, or had severe pulmonary disease, then we would not use a bilateral mammary strategy.

DR GEORGE LETSOU (Houston, TX): There must be some patients in your series who might have three arterial conduits and then a fourth vein graft or patients might have two arterial grafts and you choose to put a vein to a vessel that is not a very good vessel. I was wondering how you thought that might confound your data or how that might affect the data.

DR TATOULIS: It is absolutely true. The 2,000-odd in the total arterial matched group only had arterial grafts. The other group was heterogenous, exactly as you describe. So in the other group that did not do as well, some of those may well have had two arterial grafts and a vein graft. The study was not a comparison between the conventional usual operation of a left internal thoracic artery plus vein grafts and total arterial revascularization. So that may well have confounded and perhaps improved the outcomes of the second (non-TAR) group.

DR LETSOU: When you have a fourth graft, do you push to put a fourth arterial conduit?

DR TATOULIS: It really depends on how the native coronaries are and lie. If we think that we can revascularize them all with arterial grafts, we will certainly do so. Conversely, if you have an older patient and they need a fourth or fifth graft and you do not have adequate length or a sufficient arterial conduit, and particularly if the distal right is blocked, then we would certainly not hesitate to place a saphenous vein graft distally in an occluded right coronary system. So we are not totally wedded to the concept, and we tailor the surgery to the patient. As you saw, about 30% of these patients had total arterial revascularization, although it covers a number of institutions and a 10-year time period.

DR LIOR SASSON (Holson, Israel): In cases that you could not use the radial artery to the posterior descending artery, did you find any difference between the ones that you used radial artery or the ones you used venous graft to the right coronary artery?

DR TATOULIS: I really cannot answer that question specifically out of this study. If the right coronary stenosis is only moderate in a young patient, we may leave that alone and perhaps treat that with a stent if there is an indication in the future. If it is an older patient with an inferior infarct, with a totally occluded right coronary, we would not hesitate to use a saphenous vein if the radial artery was not of sufficiently good quality or length, or if it was not available for whatever reason.

DR SASSON: But do you think that the radial artery has an advantage on the right coronary artery over saphenous?

DR TATOULIS: I do. When you have saphenous vein grafts to the right coronary system, they are more likely to fail, and if they do fail, then a reoperation with a diseased right coronary graft is much more hazardous than one with a radial artery graft in that area. Radials to the posterior descending artery are less likely to fail, providing there is no competitive flow, but if they did fail, reoperation is safer with an arterial conduit to the posterior descending than a diseased vein graft.

DR SASSON: And one last question. Did you find any difference doing arterial grafts to the left system with a radial artery as opposed to a right internal mammary artery?

DR TATOULIS: We have looked at that in other studies, although we have not used the radial arteries as long. We have used the right mammary since 1982 and the radials only since 1996, but within those limitations, we found the patencies to be very similar between the right internal thoracic artery and the radial artery. Ten-year patency results will come out in the RAPCO (Radial Artery Patency and Clinical Outcomes) study to be presented later on this year at the American Association for Thoracic Surgery meeting.

DR SASSON: Thank you.

DR FRANK W. SELLKE (Providence, RI): Your study was very large and involved many of the hospitals in Melbourne. Was the distribution of total arterial revascularization versus nontotal revascularization similar for the different hospitals or did some hospitals, like your own, do 90% total arterial revascularization and others did 10%?

DR TATOULIS: There are some variations, obviously, over the 12-year time span. Most of the units in Melbourne have been influenced by Brian Buxton and myself, so most of us would do a very high proportion of multiple arterial grafts or total arterial revascularization.

DR SELLKE: How do you know that the gifted surgeons who do more of the total arterial revascularizations are not just better surgeons? I am just being devil's advocate here.

DR TATOULIS: That is the point I'm trying to make. I am not a gifted surgeon; I am a very average surgeon. I tried to make the point that if one can do a left internal thoracic artery to the left anterior descending artery, which hopefully all of us do, then doing a right internal thoracic artery is no different. It is bigger, it is easier to take down. It is just a matter of devoting the time. And if a resident or a physician assistant can take out a saphenous vein, they can take out a radial artery just as well. It is just a matter of taking the time. The radial artery is as robust and as long and as easy to use as a saphenous vein graft.

DR SELLKE: Your group has certainly been pioneers in this area, and we appreciate your presentation this year. Thank you.