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Long Term Follow-Up, Clinical Outcomes and Quality of Life after Total Arterial Revascularisation versus Conventional Coronary Surgery: A Retrospective Study

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***Abstract*—**Graft patency underpins long-term prognosis after coronary artery bypass grafting surgery (CABG). The benefits of the combined use of only the left internal mammary artery and radial artery, referred to as total arterial revascularisation (TAR), on long-term clinical outcomes and quality of life are relatively unknown. The aim of this study was to identify whether there were differences in long term clinical outcomes between recipients of TAR compared to a cohort of mostly arterial revascularization involving the left internal mammary, at least one radial artery and at least one saphenous vein graft. A retrospective analysis was performed on all patients who underwent TAR or were re-vascularized with supplementary saphenous vein graft from February 1996 to December 2004. Telephone surveys were conducted to obtain clinical outcome parameters including major adverse cardiac and cerebrovascular events (MACCE) and Short Form (SF-36v2) Health Survey responses. A total of 176 patients were successfully contacted to obtain postop follow up results. The mean follow-up length from time of surgery in our study was TAR 12.4±1.8 years and conventional 12.6±2.1. PCS score was TAR 45.9±8.8 vs LIMA/Rad/SVG 44.9±9.2 (p=0.468) and MCS score was TAR 52.0±8.9 vs LIMA/Rad/SVG 52.5±9.3 (p=0.723). There were no significant differences between groups for NYHA class 3+ TAR 9.4% vs. LIMA/Rad/SVG 6.6%; or CCS 3+ TAR 2.35% vs. LIMA/Rad/SVG 0%.

***Keywords*—**CABG, MACCEs, quality of life, total arterial revascularization.

I. Introduction

TREATMENT with CABG is the gold standard for complex and multi-vessel coronary disease. [1]. Furthermore, the beneficial effect of CABG especially for left main coronary disease is well known and it offers a survival advantage compared with medical treatment [2]. From the patient perspective, the health-related quality of life also improves markedly postoperatively [3], [4]. This is largely attributed to the improved oxygenation of the cardiac myocardium following revascularisation which relieves symptoms and may prolong life. Long-term morbidity and mortality as well as relief from angina with CABG is critically dependent on the long-term patency of the bypass grafts [5]-[7].

The grafts used in CABG may be arteries or veins. The left internal mammary artery (LIMA) is routinely anastomosed to the left anterior descending artery which supplies the largest amount of myocardium. The secondary conduits used together with the LIMA remain under intense discussion. The radial artery (RA) is a segment of artery harvested from the forearm after the brachial artery divides at the elbow and its use is associated with an extremely low incidence of hand and arm complications [8]. Both LIMA and RA have been exposed to arterial pressures and flows since birth, and therefore may behave in a similar manner in the long-term. Saphenous vein (SVG) is harvested from the leg and is first exposed to the high pressures and flows of the arterial system when used as a graft. The high pressures exposed to the vein lead to the development of atheroma at an accelerated rate with subsequent progressive graft failure. The average number of grafts is 3.4 per patient, worldwide [9]. Most patients receive one LIMA, and the remainder of the grafts is SVG, with the result that most grafts are veins rather than arteries.

The great saphenous vein features a limited long-term patency, with a relatively high failure rate within a decade [10]-[13]. Alternative grafts such as bilateral internal mammary artery or RA grafts are increasingly used especially in younger patients with suitable revascularisation targets [14], [15]. Whether the use of a TAR approach to CABG has an effect on long term outcomes including the health-related quality of life remains unclear. We analysed data for all consecutive patients at least 10 years or more post-coronary surgery at our institution between February 1996 and December 2004 to assess long term outcomes.

II. Methods

A. Trial Design

All patients of post-coronary surgery of 10 or more years were identified from clinical databases. Patients were divided into two groups: TAR (LIMA, and right IMA or RA or both) or conventional revascularisation (LIMA and a mixture of RA and SVGs). The primary outcome measures were angiographic graft patency at greater than or equal to 10 years, and the secondary outcomes were MACCE more than 10 years postoperatively, clinical outcomes and the health-related

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quality of life (HRQoL) measured by the generic questionnaire SF-36.

B. Patient Inclusion

All included patients were provided with written and oral informed consent. After the compilation of a list of patients who underwent CABG at our institution between February 1996 and December 2004, a random number sequence was applied to reorder patients. From the randomized sequence, patients were contacted in a sequential manner to obtain consent for participation in the study (asymptomatic patients only were included). This process was performed to reduce the risk of inclusion bias.

The Ethics Committee of the Royal Melbourne Hospital approved this study. 267 patients were included in the study after successful contact to obtain postoperative follow up results via phone or mail interviews. Hospital charts and medical records from general practitioners and cardiologists were reviewed.

C. Operative Technique and Postoperative Care

After a full median sternotomy, the LIMA was harvested by a no-touch technique with minimal trauma as either a pedicled or skeletonized graft and treated with papaverine solution. The RA was harvested in a similar fashion from the non-dominant arm where possible after confirming palmar perfusion via the ulnar artery with on-table assessment using pulse oximetry. A variety of techniques were used in the composition of grafts including conventional grafting and 'y' grafts of the LIMA and RA (usually performed prior to initiating cardiopulmonary bypass - CPB). The myocardium was protected using intermittent antegrade or retrograde cold-blood cardioplegia or crystalloid cardioplegia. Patients were heparinised prior to CPB and supplemented with heparin to maintain the activated clotting time above 450 s. This was fully reversed with protamine at the end of the procedure. Patients received intravenous nitro-glycerine infusions for the first 24h, if feasible.

D. Follow-Up

The standard postoperative medications for patients included aspirin, a beta blocker, and amlodipine for at least three months unless contra-indicated. Patients were contacted either by telephone interview or mail, and consent for the survey was obtained. Patient deaths were recorded, and, if possible, the reason for death obtained from relatives. Patient demographic, risk factor, drug profile, and self-reported symptoms of chest pain or shortness of breath and standardised scores (Canadian Cardiovascular Score (CCS) for pain, New York Heart Association Score (NYHA) for shortness of breath) were collected. All-cause death and post-operative MACCE were recorded. These included deaths from myocardial cause, myocardial infarction, and coronary revascularisation procedures either by percutaneous or surgical approaches. Quality of Life data were assessed using the SF36 form.

E. Short Form-36 Questionnaire

The HRQoL outcomes was evaluated using the SF-36 questionnaire which contains 36 questions covering eight different health dimensions. The questionnaire contains items assessing different health dimensions from the patient's perspective: physical functioning, physical role, bodily pain, general health perceptions, vitality, social functioning, emotional role, and mental health. For each dimension, scores are calculated and converted into a scale of 0 to 100, that is, from the worst to the best possible status. A physical component summary is calculated from the first four scales and a mental component summary from the last four [16].

III. Statistical Analysis

All statistical computation was performed by using STATA v13.1. Categorical variables were investigated with chi-squared or Fisher exact testing where appropriate. Continuous, normally-distributed variables were investigated with a t-test and are presented as means with standard deviations. The Mann-Whitney test was used for variables with non-normal distribution.

IV. Results

From February 1996 to December 2004, 2423 patients underwent CABG at our institution. A total of 176 patients were successfully contacted to obtain follow-up results.

A. Preoperative Characteristics

Mean age, in years, at the time of surgery was 64.5±8.2 in the TAR group and 64.8±8.8 in the conventional group (LIMA+RA+SVG). Baseline characteristics were comparably distributed between groups (Table I); except for smoking status (TAR 60% vs conventional 28.1%, $p<0.00$), ejection fraction ≤50% (TAR 38.8% vs conventional 62.2%, $p=0.015$), history of unstable angina (TAR 21.3% vs conventional 4.7%, $p = 0.004$), history of acute myocardial infarction (TAR 46.7% vs conventional 18.8%, $p=0.001$) and the use of nitrates TAR 12% vs conventional 32.8% ($p=0.003$).

B. Follow Up Clinical and Functional Status Data

The mean follow-up length from time of surgery in our study was TAR 12.4±1.8 years and conventional 12.6±2.1 years. There were no significant differences between groups in CCS class, NYHA status, medications, and MACE outcomes (MI since surgery, PCI since surgery, redo-CABG since surgery and stroke since surgery).

Overall this study cohort showed no significant differences in overall SF-36 scores for physical health TAR vs conventional (45.9±8.8 vs 44.9±9.2, $p=0.468$) and mental health domains TAR vs conventional (52.0±8.9 vs 52.5±9.3, $p=0.723$).

V. Discussion

It has been over half a century since the first CABG operation was performed [17]. There have been many changes to conduit selection for grafting since then. Whilst the use of

the saphenous vein as a secondary conduit has been slowly declining due to its limited long term patency rates ranging from 41-63% [10]-[13], it still remains the most frequently used graft in addition to the LIMA.

TABLE I
PREOPERATIVE AND ANGIOGRAPHIC STATUS

	Type of revascularisation				
	Total arterial (n=85)		LIMA+RA+SVG (n=91)		P value
Female sex	8	(10.7)	13	(20.3)	0.113
Age (yrs)	64.5	±8.2	64.8	±8.8	0.837
BMI	31.4	±28.3	29.7	±26.8	0.731
CCS class ≥3	43	(59.7)	33	(62.3)	0.774
NYHA ≥3	44	(59.5)	37	(58.7)	0.931
Smoker (current or ex)	45	(60)	18	(28.1)	0.000
Family history	34	(45.3)	33	(51.6)	0.464
Diabetes	22	(29.3)	11	(17.2)	0.093
Hypercholesterolaemia	66	(88.0)	49	(76.6)	0.075
Renal failure (CKD 3-4)	2	(2.7)	2	(3.1)	0.872
Hypertension	62	(82.7)	47	(73.4)	0.187
Previous PCI (PTCA or Stent)	5	(6.75)	2	(3.1)	0.341
Previous Surgery	4	(5.33)	0	(0)	0.061
Ejection Fraction ≤50%	26	(38.8)	28	(62.2)	0.015
LM stenosis >50%	12	(16.0)	4	(6.3)	0.073
Angina - unstable	16	(21.3)	3	(4.7)	0.004
AMI	35	(46.7)	12	(18.8)	0.001
Aspirin	60	(80.0)	46	(71.9)	0.262
Nitrate	9	(12.0)	21	(32.8)	0.003
Beta Blockers	46	(61.3)	33	(54.6)	0.246

Presented as number (%), mean ±SD. BMI: body mass index; CCS: Canadian Cardiovascular Society; NYHA: New York Heart Association; LM: Left main; AMI: Acute myocardial infarction.

It is well known that the LIMA has a much better graft patency rate than SVG. It is likely that other arteries when used as grafts will have overall graft survival and freedom from disease that approaches the success of the LIMA. The concept of TAR where arteries are used for all grafts may improve long-term wellness and improve length of life. The only practical approach to achieve TAR is to use the RA in addition to the LIMA. TAR is not used extensively worldwide because of a paucity of long-term graft survival and clinical outcomes data for the RA and TAR.

Long term results from several trials conducted recently show that the RA graft has superior patency rates over saphenous vein grafts [14], [15], [18]-[20]. These studies have confirmed excellent long-term graft patency and have reported superior long-term survival rates, even after propensity score matching [21]. Nonetheless, concerns exist about vasospasm and the development of atherosclerotic changes in radial grafts. The risk of vasospasm in radial grafts is attributed to the relatively thick media of smooth muscle cells [22]. Although significant atherosclerosis of radial grafts is rare, it is more common than in LIMA grafts (5.3 vs 0.7%) [23], [24].

This study helps to validate the use of RA and TAR with outcomes assessed at least 10 years following surgery. Our data confirm that TAR is comparable to a conventional approach to revascularisation with similar clinical outcomes and long-term MACCE results.

TABLE II
FOLLOW UP CLINICAL AND FUNCTIONAL STATUS

	Type of revascularisation				
	Total arterial (n=85)		LIMA+RA+SVG (n=91)		P value
Age at follow up	76.4	±8.4	77.7	±8.3	0.277
Current level of dependency: Independent	58	(68.2)	80	(87.9)	0.002
Years after surgery	12.4	±1.8	12.6	±2.1	0.547
Aspirin	69	(81.2)	65	(71.4)	0.130
Platelet inhibitors	9	(10.6)	12	(13.2)	0.595
Warfarin	9	(10.6)	17	(18.9)	0.123
Beta blockers	40	(47.1)	38	(41.8)	0.479
NYHA Class 3+	8	(9.4)	6	(6.6)	0.49
CCS Class 0	59	(69.4)	76	(83.5)	0.103
CCS Class 1	19	(22.4)	11	(12.1)	-
CCS Class 2	5	(5.9)	4	(4.4)	-
CCS Class 3	2	(2.35)	0	(0)	-
AMI since surgery	3	(3.5)	5	(5.5)	0.532
PCI since surgery	5	(5.9)	6	(6.6)	0.846
Redo CABG since surgery	0	(0)	1	(1.1)	0.332
Stroke since surgery	4	(4.71)	6	(6.6)	0.589
SF-36 PCS	45.9	±8.8	44.9	±9.2	0.468
SF-36 MCS	52.0	±8.9	52.5	±9.3	0.723

Presented as number (%), mean ±SD. CCS: Canadian Cardiovascular Society; NYHA: New York Heart Association; AMI: Acute myocardial infarction; PCI: percutaneous intervention; SF-36 PCS and MCS: correlated physical and mental health summary scores.

Our results show that compared to the conventional revascularisation, TAR can be performed safely with comparable overall HRQoL. For both types of revascularisation, there was no statistical difference in the overall correlated physical and mental health scores. This is likely due to the similarity between the two cohorts in relation to the method of revascularisation. Both cohorts received the gold standard CABG operation with LIMA grafts and while one group had a TAR, the conventional group also received at least a LIMA and RA graft in addition to the use of saphenous vein for other anastomoses.

The impact of a failed SVG graft may be less in this study than in other literature. In the all three-conduit group the usual procedure in this institution was to graft LIMA to the left anterior descending artery (which supplies most of the heart), RA to the second most threatened territory and SVG to the least threatened territory. Therefore, if saphenous vein grafts failed, the larger myocardial important territories may have still received adequate supply, which may minimize the symptoms of MACCE and suppress the decline in quality of life. It is once again important to realize that this all three-conduit group is a 'mostly arterial' population as the most threatened territories are generally re-vascularized with arteries.

It is likely that not every bypass failure leads to symptoms or cardiac complications as assessed in our study through the prospective collection of clinical data and HRQoL outcomes through the completion of SF-36 questionnaires. The SF-36 is

a structured questionnaire designed to measure a variety of physical, emotional and mental health related impairments that are not necessarily solely attributed to heart failure. We chose the SF-36 because it is a widely used instrument with well-documented validity, sensitivity, and reliability [25]-[26]. There are limited studies looking into the HRQoL outcomes in patients who underwent TAR, and our data address this gap by showing comparable overall SF-36 scores.

This study features all the limitations of a retrospective cross-sectional study. Data regarding preoperative or intraoperative decisions affecting conduit choices were not available. In addition, the homogeneous nature of our operative technique likely impacted the overall long-term clinical outcome data and MACCE outcomes.

This study is based on a large cohort of consecutive patients who underwent CABG where the RA has been used as the primary additional conduit in approximately 90% of cases [27]. The current rate of TAR at our institution is amongst the highest in the world. However, in the first two years of our sample, there was a greater proportion of patients who received a combination of LIMA, RA and SVG as this represented a transitional phase towards TAR. Therefore, this experience provides a very useful "window" to study the effects of the three different grafts within the same patient, thereby reducing the potential confounding bias of inter-patient variability. Secondly, this study uses prospectively collected data that included clinical outcomes, HRQoL questionnaire as well as the provision of coronary angiography for definitive assessment of the conduits.

VI. Conclusion

In conclusion, TAR using LIMA and RA proved to be safe and efficient over the long term in our patient cohort. The long term clinical outcomes and HRQoL measured by the SF-36 questionnaire more than 10 years in the post-operative period show similar results to the conventional revascularisation. Further follow-up in our trial with coronary angiography data will help to clarify if graft patency is superior after TAR and therefore associated with improved long term cardiac event-free survival and HRQoL outcomes.

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