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GLOBAL CARDIOLOGY
Global Cardiology 2024; **4**
Published online 30 December 2024 | **DOI**: 10.4081/cardio.2024.46

ARTICLE

Prognostic factors and outcome in patients submitted into coronary artery bypass surgery with total arterial myocardial revascularization (TAMR)

Elias Tassoulas,[1] Dimitrios Tasoulas,[2] Christos Papaconstantinou,[3] Ioannis Chlorogiannis[4]

[1]3 Manolaki Street, Arta; [2]2nd Cardiology Department, General Hospital of Nikea, Piraeus; [3]Emeritus Professor of Cardiac Surgery, AHEPA Hospital, Thessaloniki; [4]Consultant Cardiac Surgeon and Director of Cardiac Surgery Department in Athens Euroclinic Hospital, Athens, Greece

Abstract

Background: Coronary artery bypass grafting relieves symptoms and improves survival in patients with severe coronary artery disease. Large series and meta-analyses show that total arterial myocardial revascularization (TAMR) may offer additional survival benefit. The primary objective of this study was to investigate long-term (>5 years) survival of patients undergoing TAMR. The change in coronary artery disease risk factors during the follow-up period was also evaluated.
Methods: Forty patients undergoing coronary artery bypass grafting (CABG) with total arterial myocardial revascularization (TAMR) were studied. All patients were screened for coronary artery disease risk factors at entry and follow-up. Repeat coronary angiography at a 5-year follow-up was used to investigate the long-term patency of arterial grafts.
Results: Mean patient EuroSCORE was 1.42±1.1%. Mean follow-up time was 9.3±4.8 years (range: 1 month to 15.6 years). The 30-day mortality was 2.5% (1/40 patients), while the 12-month mortality was 7.5% (3/40 patients) with an actual survival of 92.5%. The 5-year and 10-year mortality was 15.8% (6/38 patients) and 33.3% (10/30 patients) respectively, while actual survival reached 84.2% and 66.7% at 5 and 10 years respectively. A total of 10/40 patients (25%) died during follow-up. Mean time-to-event was 3.5±2.7 years (range: one month to 7.1 years); 40% of deaths occurred during the first 2 years from the procedure, and 40% occurred during the period from 4.5 to 6.5 years post-surgery. The main cause of death was cerebrovascular disease in 30% of patients, while 20% died of cancer. 40% of fatalities were cardiac-related but not due to ischemic heart disease. The incidence of major adverse cardiac and cerebrovascular events (a composite outcome of cardiac-related death, myocardial infarction, need for revascularization and stroke) was 17.5% during follow-up. Total morbidity reached 30%. The use of the radial artery resulted in a similar survival to the use of bilateral internal mammary arteries exclusively. The numbers of grafts used were 39 Left internal mammary artery grafts (LIMA), 34 right internal mammary artery grafts (RIMA) and 24 right radial artery grafts (RAD). Repeat coronary angiography at a 5-year follow-up revealed that all arterial grafts were patent. Control of arterial hypertension (blood pressure <130/80 mm Hg) was achieved in 65% of patients postoperatively compared to 22.5% preoperatively (p=0.01).
Conclusions: TAMR is safe and effective with encouraging results in terms of long-term survival. This is the first reported study investigating long-term outcomes in patients undergoing total arterial revascularization in Greece.

Key words: total arterial myocardial revascularization; TAMR; coronary artery disease; coronary artery bypass grafting.

Received: 25 May 2024; Accepted: 13 October 2024.
**Correspondence to: Elias Tassoulas, 3 Manolaki Street, Arta 47132, Greece. E-mail: eltassou@otenet.gr*

Introduction

Coronary artery disease (CAD) is a major health problem. World Health Organisation (WHO) data demonstrate coronary artery disease causes 12.8% of all deaths and in industrialised countries this figure is 16%. In spite of the fact that coronary artery disease patients' survival has steadily improved, it still remains the leading cause of death in both men and women. CAD prevalence increases with age and is higher in males. Twenty-five % of males and 15% of females aged between 60-79 years of age suffer from CAD in the USA, and this percentage increases to 37% and 23% respectively for the age over 80 years. Despite improvement in prevention and treatment of CAD, mortality is expected to increase further in the coming years.

One percent of the patients seen by General Practitioners in the UK suffer from angina. It has been estimated that 2.7 million people have coronary artery disease symptoms. The annual mortality rate for patients with mild angina and stable symptoms ranges from 0.9-1.7%, but it is much higher for those with unstable angina. Approximately 10% of the patients annually with stable angina will develop worsening symptoms needing revascularization. Around 105,000 deaths in the UK annually are due to CAD and in addition another 32,000 deaths are due to other cardiac disease conditions. The total number of deaths due to cardiovascular disease (cerebral vascular accident included) is 216,000. CAD is consuming the largest expenditure in the health sector and the annual cost to the NHS is 7.9 billion GBP.

A patent coronary artery circulation ensures the balance between myocardial oxygen demand and supply. Imbalance between these two conditions causes myocardial ischemia, resulting in angina pectoris symptoms with or without ECG changes. There are four main clinical syndromes that may occur in patients suffering from chronic myocardial ischemia: i) stable angina; ii) unstable angina; ii) syndrome X (cardiac syndrome X); and iv) ischemic cardiomyopathy of which the main symptoms and signs are due to left ventricular dysfunction (LVD).

There is good evidence that use of the left internal mammary artery (LIMA) to bypass the Left anterior descending artery (LAD) has a prognostic benefit. However, there are less data on whether the use of multiple arterial grafts implanted on different vessel targets have a prognostic significance. There is minimal information on whether the use of the LIMA or even the RIMA as a pedicled graft makes a difference in comparison to the use of free arterial grafts such as the radial artery. Furthermore, the characteristics of these patients as well as the features of their disease that can predispose to graft failure have not been sufficiently investigated. There is minimal information in Greek Cardiology-Cardiac Surgery Centres about the outcome of patients, who have undergone coronary artery bypass grafting (CABG) with total arterial myocardial vascularization (TAMR) exclusively.

Methods

The primary purpose of this study is to investigate the long-term (>5 years) survival of patients who underwent CABG surgery using only arterial grafts (TAMR). A secondary aim of the study is to investigate the change in CAD risk factors during the follow-up period.

Study population

The population of the study consists of 40 patients, who underwent CABG surgery. The main characteristic of the study is the exclusive use of arterial grafts in all patients. The CABG surgeries were performed between 05/10/2000 and 07/11/2011 by the same cardiac surgical team.

Study protocol

The study protocol included basic demographics and risk factors are illustrated in Table 1. Information collected and databased included:

i) Anonymised patient identifiers (patient number and initials).
ii) Date of cardiac surgery.
iii) Age at the time of the operation.
iv) Sex.
v) Patient demographics.
vi) Family history.
vii) Smoking (packs per week).
viii) Dyslipidaemia (lipid values: total cholesterol, HDL cholesterol, LDL cholesterol and triglycerides in mg/dl).
ix) Diabetes mellitus (fasting serum glucose, glycosylated haemoglobin HBA1c, treatment with diabetic diet, hypoglycaemic tablets or insulin).
x) Arterial hypertension (systolic and diastolic blood pressure).
xi) History of previous cardiac surgery or percutaneous angioplasty (PCI).

All patients were screened for the existence of predisposing cardiovascular risk factors: Specifically, they were screened for: i) arterial hypertension; ii) diabetes mellitus; iii) dyslipidaemia; iv) positive family history for CAD; and v) smoking. Patients with a history of blood pressure greater than 130/80 mmHg were considered hypertensives. Patients who received hypoglycaemic tablets, insulin, as well as those who had a positive glucose tolerance test and followed a healthy diabetic diet were considered diabetics. Patients were considered dyslipidaemic, if they had total cholesterol levels higher than 190 mg/dL, LDL higher than 115 mg/dL, HDL lower than 45 mg/dL for men and 55 mg/dL for women, and triglycerides higher than 150 mg/dL or a combination of the above. Patients with a positive family history were considered those who had at least one first-degree relative with premature onset of coronary artery disease at an age younger than 55 years for men and 65 years for women. Smokers were considered those who smoked at least one pack per week.

Table 1. The protocol of the data set collected on all the patients.

Pt/Nr 27	Variables		Preoperative	Postoperative
Essential information	Initials		PP	PP
	Date of CABG		25/04/2006	
	Age		53	
	Sex		Man	
	Ethnic origin		Caucasian	
	Family history		Positive	
	Smoking		No	No
	Packets /week		0	
Lipid profile	Hyperlipidaemia		Yes	
	Total cholesterol		263 mg/dL	139 mg/dl
	HDL		35 m mg/dL	43 mg/dl
	LDL		185 mg/dL	76 mg/dL
	Triglycerides		170 mg/dL	102 mg/dL
	Number of lipid profile check postoperative			16
Diabetes mellitus	Diabetes mellitus		No	No
	Serum glucose		90 mg/dL	96 mg %
	HbA1C		0.0%	
	Diet			
	Tablets			
	Insulin			
	Number of glucose measurements postoperative			16
BP	Hypertension		Yes	
	Blood pressure average value		150/90 mmHg	120/80 mmHg
	Number of BP measurements postop			20
ETT protocol	Exercise tolerance test		No	
	Duration		Min 0 sec	
	Heart rate (increase)			
	BP (increase)			
	ETT			
	Arrhythmia			
Echocardiogram	LVD		4.9 cm	
	LVS		2.7 cm	
	EF		60%	
	LV wall (hypokinetic, akinetic, paradoxical motion)		No hypokinesia / akinesia	
	LV wall		IVS upper wall paradoxical motion	
Coronary artery angiogram	Coronary artery	Lesion	Percentage lumen stenosis	Stricture site
	LMS	No		
	LAD	Yes	90	Middle
	Intermediate	No		
	Lcx	No		
	DIAG	No		
	OM1	Yes	60	Proximally
	OM2			
	RCA	Yes	100	Proximally
	PDA			
	MIBI	Not done		
		Number of vessels	3VD	
Operation	Graft			
Details	Pedicled in situ LIMA		LAD	No
	LIMA free			No
	Pedicled in situ RIMA		OM1	No
	RIMA free			No
	Radial		PDA	No
	Venous1		No	
	Venous2		No	
	Venous3		No	
	Native vessels			Yes
	Postoperative angina			No
	Symptom onset years		3 years	
	Coronary artery angiogram repetition			Yes
	Previous cardiac operation		No	
	Kind of previous cardiac operation		None	
	Additional cardiac operation simultaneously with CABG		No	
	Additional comments		None	
	EUROSCORE II: 0.62%			

Preoperative investigations

i) Exercise tolerance test (ETT). The protocol included Bruce protocol max exercise tolerance test. A necessary precondition for this test to be performed was prior discontinuation of any medication that could affect the findings such as b-blockers (BB), calcium antagonists with a negative inotropic effect (verapamil, diltiazem) and ivabradine that should have been discontinued 48 h before the ETT. In addition to the above calcium antagonists belonging to dihydropyridines (nifedipine, amlodipine, *etc.*) as well as nitrates were discontinued 24 h before the ETT.
ii) Echocardiogram.
iii) Coronary artery angiogram – with quantification of lesions. Coronary angiography was performed in all patients with puncture of the right femoral artery. After placing a 5F sheath, the catheter was advanced along the normal arterial course and selective imaging of the left coronary artery in 6 projections and of the right coronary artery in two projections was performed. LV angiogram was performed with a pig tail catheter in a right anterior oblique projection of 30°. Coronary angiogram views were recorded on CD.

All coronary artery findings (abnormal and normal) and the conclusion as to whether it was one (1VD), two (2VD) or three (3VD) vessel disease were recorded in detail.

Operation data

The grafts, which have been placed as well as the coronary vessels on which the anastomoses have been performed respectively, were studied. Any combined cardiac surgery was also recorded.

Arterial graft preparation technique

Preparation of LIMA

The preparation of the LIMA was performed immediately after opening the sternum and before opening the pericardium. The flap of the LIMA was prepared with the accompanying fat and lymph vessels. The preparation was carried out using electric diathermy. The width of the flap was about 1 centimetre. Its preparation started from its emergence at the level of the left subclavian artery until its bifurcation. Surgical clips were placed in the branches of the LIMA. The anastomosis with the coronary vessel was performed with continuous suturing with 8-0 end-to-side or side-to-side prolene suture (Figure 3). It is noted that in patients with chronic obstructive pulmonary disease (COPD), extra-pleural preparation of the LIMA duct was performed avoiding opening of the pleural cavity. In all patients, a technique with reverse octoid closure of the sternal lips with a wire was used.

Preparation of RIMA

The preparation of the RIMA was carried out with the same technique as the LIMA from the level of its emergence from the right subclavian artery and usually to below its bifurcation, so that it has a sufficient length to approach the obtuse marginal (OM) branches of the left circumflex (LCx) or the posterior descending (PDA) branch of the right coronary artery (RCA). The anastomosis of the RIMA to the LCx was done through the transverse sinus of the pericardium (Figure 4).
It should be emphasized, that the in situ pedicled grafts of the LIMA and RIMA that were prepared, were used without the extension distally with a segment of another graft.

Radial artery preparation

In the patients of the study in which a free radial artery graft was used, the left radial artery was prepared, after performing Allen's test in order to check the patency of the collateral circulation. The preparation of the radial artery was performed using the established technique (Figure 5).[1]

Postoperative follow-up

During the postoperative period and after surgical reperfusion, patients are consistently receiving appropriate medication (antiplatelet agents, β-blockers, angiotensin-converting enzyme inhibitors, and statin).
During the postoperative follow-up period, major cardiovascular events were recorded, which included: i) death attributed to cardiac aetiology; ii) myocardial infarction (MI); iii) need for revascularization with percutaneous angioplasty (PCI) or Redo CABG; and iv) stroke.
In the patients who experienced a recurrence of angina pectoris, its duration, the ECG findings as well as the findings from the diagnostic and imaging tests performed (myocardial scintigraphy, coronary angiography) were recorded.
To investigate the patency of grafts, the study protocol included coronary angiography screening of all patients 5 years after CABG surgery.
All study patients underwent a detailed postoperative screening of predisposing cardiovascular risk factors. More specifically, the following factors were recorded:
i) Smoking
ii) Dyslipidaemia
iii) Diabetes mellitus
iv) Arterial hypertension

Statistical analysis

EuroSCORE II was used to calculate predicted perioperative mortality risk. Descriptive statistics were performed. For the quantitative variables, the mean value and standard deviation were calculated, while for the qualitative variables, the frequency and the percentage ratio. The χ^2 test was used to compare between qualitative variables. Differences with a calculated significance coefficient of $p<0.05$ were considered statistically significant. To study the long-term survival of the patients, a Kaplan-Meier curve was created.
A total of 40 protocols were drawn up for an equal number of

patients with all data detailed for each one. Indicatively, Table 1 shows the protocol with the data of the patient of the study with study number (ID).

Results

Preoperative-interoperative characteristics

The demographic data of the patients are presented in detail in Table 2. In Table 3, an analysis of predisposing risk factors is made, and the clinical manifestation of coronary artery disease is presented.

The mean EuroSCORE II value was 1.42±1.1% (range: 0.5-6.9%). The patients underwent diagnostic tests that included, in addition to the clinical examination, ECG, echocardiographic study, ETT, myocardial scintigraphy (MPS) and coronary angiography. Some did not need to undergo an ETT or scintigraphy, but directly had a coronary angiography. Regarding the preoperative angiographic characteristics, 5 patients had a single-vessel disease (1VD), percentage (12.5%), 10 patients had 2-vessel disease (2VD), percentage (25%) and 25 patients had three-vessel disease (3VD), percentage (62.5%). Regarding the ejection fraction: 8 patients (20%), had EF below 50% and 32 patients (80%) had EF above 50%. The mean lipid values were as follows: total cholesterol (mg/dl): 238.95±76.5, HDL cholesterol (mg/dl): 40.15±12.2, LDL cholesterol (mg/dl): 161.23±64.2, serum triglycerides (mg/dl): 154.28±103.4, serum glucose (mg/dl): 144.29±62.6.

Table 4 shows in detail the arterial grafts that were used as well as the target vessels to which they were implanted.

Postoperative follow-up

Overall survival

The average duration of follow-up of the patients was 9.3±4.8 years and ranged from one month to 15.6 years. The Kaplan-Meier survival curve of the study patients is presented in Figure 1. From the Kaplan Meier curve survival analysis, the 30-day mortality, which was attributed to surgery, was 1/40 (2.5%). The 12 month mortality was 3/40 patients (7.5%) and

Table 2. Patient demographics.

Demographics data	Number of patients (n=40)	%
Men	35	87.5
Women	5	12.5
Married	40	100
Men average age (years)	63.5±13.1	
Women average age (year)	70±12	

Table 3. Coronary artery disease risk factors analysis.

	Number of patients (n=40)	Percentage
Risk factor		
Arterial hypertension	31	77.5
Diabetes mellitus		
Diabetes mellitus - diet	5	12.5
Diabetes mellitus - tablets	3	7.5
Diabetes mellitus - insulin	5	12.5
Hyperlipidaemia	36	90
Hypertriglyceridaemia	13	32.5
Smoking	13	32.5
Positive family history	13	32.5
Risk factors combination		
No risk factor	1	2.5
1 risk factor	4	10
2 risk factors	14	35
3 risk factors	12	30
4 risk factors	8	20
5 risk factors	1	2.5
CAD clinical manifestation		
LV anterior wall MI	3	7.5
LV anterior and inferior wall MI	2	5
LV lateral wall MI	0	0
LV inferior wall MI	4	10
NSTEMI ACS	2	5
Stable angina	4	10
Unstable angina	32	82.5
Silent myocardial ischaemia	3	7.5

CAD, coronary artery disease; LV, left ventricular; MI, myocardial infarction; NSTEMI, non ST-elevation acute coronary syndrome; ACS, acute coronary syndrome.

the corresponding actual survival was 92.5%. The 5- and 10-year mortalities were 6/38 patients (15.8%) and 10/30 patients (33.3%), respectively, while the actual survivals were 84.2% and 66.7% at 5 and 10 years respectively. Overall, during the study follow-up time 10/40 patients (25%) died. The average duration from surgery to death was 3.5±2.7 years, with range from 1 month to 7.1 years. 4/10 deaths (40%) occurred during the time period of the first 2 years after the CABG operation, while the same percentage (40%) was found during the time period from 4.5 to 6.5 years after the operation. The 10 patients who died (7 men and 3 women) had a mean age of 66.1±13.5 years. The causes of death of the study patients are presented in detail in Table 5. The majority of deaths 3/10 (30%) were from stroke, while 2/10 (20%) were due to malignancy (prostate and lung). Of the 4/10 deaths (40%) attributable to cardiac causes, there was no death due to recurrence or progression of coronary disease. Two patients suffered acute pulmonary oedema after persistent hypertensive crisis, one patient suffered a ruptured aneurysm of the descending thoracic aorta, and in one patient death was attributed to acute pulmonary embolism. Three of the above patients (2 who died of pulmonary oedema due to hypertensive crisis and one who died of descending aorta rupture) suffered from severe hypertension, their blood pressure being well controlled on medication, but they had discontinued their anti-hypertensive medication. A comparative study of the mortality of two subgroups of patients followed (Figure 2). the first group included 16 patients who underwent CABG using only the two internal mammary arteries (LIMA and RIMA), while the second group included 24 patients in whom in addition to the two internal mammary arteries (LIMA and RIMA) the radial artery (RAD) was also used as a free graft. It was found that mortality was similar in the two subgroups [4/16 (25%) patients of the first group and 6/24 (25%) patients of the second group], as confirmed by the comparative study of the survival curves (Log rank= 0.018, p=0.8).

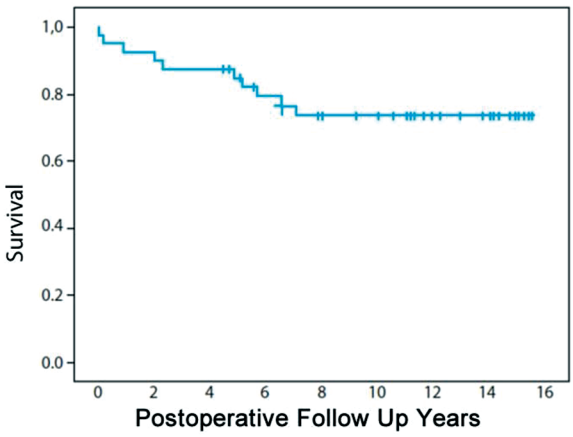

Figure 1. Survival of the patients post-operatively over a follow-up period of 16 years.

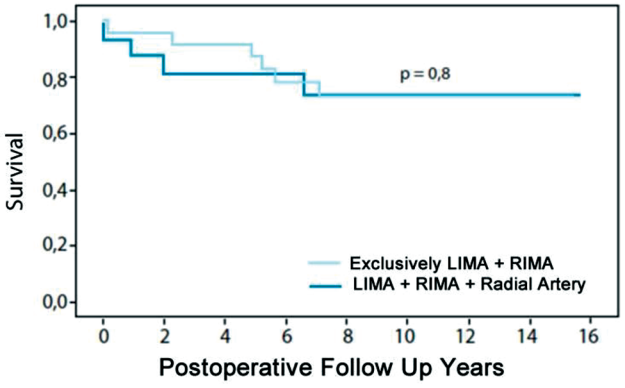

Figure 2. Patient survival in group receiving LIMA + RIMA grafts vs those with LIMA + RIMA + radial grafts.

Table 4. Arterial grafts used and vessel-targets they were implanted.

	LIMA	RIMA	Radial artery
LAD branch / system			
LAD	26		
1st diagonal		2	
Sequential LAD-1st diagonal branch	7		
Sequential LAD-2nd diagonal branch		3	
Sequential LAD-LAD	3		
Intermediate branch		2	
LCx system			
OM1		16	4
OM2		1	
PDA		1	
Sequential OM1-OM2		1	
Sequential OM2-OM3		1	
RCA system			
RCA		5	1
PDA		6	18
Total number of grafts	39	34	24

Major cardiovascular events – morbidity

Table 6 shows the frequency of major cardiovascular events during the total duration of the postoperative follow-up time. In addition to major cardiovascular events, overall morbidity included a 75-year-old patient who presented 7 years postoperatively with unifocal ventricular ectopics (VEs), frequent multifocal ventricular ectopics (multifocal VEs) and couplets. Myocardial scintigraphy (MPS) ruled out myocardial ischemia. The patient was treated with medication (amiodarone 200 mg daily after amiodarone loading dose and a b-blocker). Three patients developed atypical anginal complaints, which were checked by performing coronary angiography. It was found excellent patency of the grafts in all three cases. A 75-year-old patient developed clinical signs of acute congestive heart failure eight years after surgery. He had an angiogram, which showed excellent patency in all grafts (LIMA to LAD, RIMA to OM1 and radial artery to PDA). Further testing showed that the patient had viral myocarditis following a respiratory infection, which caused acute heart failure. The patient received the appropriate medication resulting in the improvement of the symptoms and the remission of the disease. The patient was in NYHA clinical stage II. None of the operated patients of the study showed infection of the middle sternotomy wound, which is a serious complication in patients who undergo an CABG operation, while it occurs more often in patients who use both internal mammary arteries.

Table 5. Causes of death of the study patients

Cause of death (n=10)	Number of patients
Acute pulmonary oedema – heart failure	2
Thoracic descending aorta aneurysm rupture	1
Cerebrovascular accident	3
Malignancy	2
Haematological disease	1
Acute pulmonary embolism	1

Graft patency check

It should be noted that during the post-operative follow-up period, the patients, in addition to performing coronary angiography (Table 7), underwent the following tests to diagnose possible recurrence of coronary artery disease:

i) ETT: 9 patients.
ii) MPS with Thallium (Tl201) or Technitium (Tc99m): 14 patients.
iii) CT coronary angiogram: 1 patient.

Table 6. Major cardiovascular events.

	Number patients (n=40)	Percentage
Cardiac cause - non ischaemic	4	10%
Myocardial infarction	0	0%
Revascularization necessity	0	0%
Cerebrovascular accident	3	7.5%
Total	7	17.5%

Table 7. Graft patency check with a repeat coronary artery angiogram.

	LIMA	RIMA	Radial	Patency
LAD system				
LAD	20	0	0	100%
Diagonal	0	1	0	100%
Sequential LAD-1st diagonal branch	6	0	0	100%
Sequential LAD-2nd diagonal branch	3	0	0	100%
Sequential LAD-LAD	2	0	0	100%
Intermediate branch	0	2	0	100%
Left Cx system				
OM1	0	13	3	100%
OM2	0	1	0	100%
PDA	0	1	0	100%
Sequential O1M-OM2	0	0	0	
Sequential OM2-OM3	0	0	0	
RCA system				
RCA	0	4	1	100%
PDA	0	5	15	100%
Total number of grafts	31	27	19	100%

Of the nine patients who underwent a maximal ETT in Bruce protocol, none had positive or suspicious findings, suggesting residual myocardial ischemia. At the same time, myocardial scintigraphy performed postoperatively in 14 patients did not demonstrate reversible myocardial ischemia, expansion of the pre-existing scar, or new scar formation.

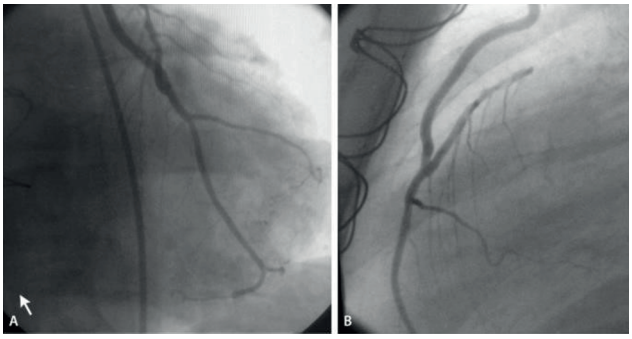

Figure 3. Pedicled in situ LIMA to LAD.

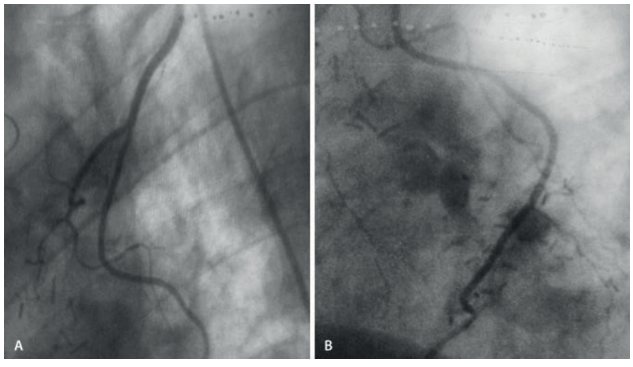

Figure 4. Pedicled in situ RIMA obtuse marginal artery.

CAD risk factors modification

During the postoperative follow-up period of the patients, the guidelines referring to the secondary prevention of cardiovascular disease of the European Society of Cardiology[2] were applied. A statistically significant reduction in the smoking habit was found from 32.5% of patients to only 5% postoperatively ($p<0.01$). Only 40% of the patients in the study achieve the postoperative limits, which are set regarding the control of total cholesterol values, LDL and HDL fractions, as well as triglyceride levels, while in 52.5% of patients some of these limits were not reached. The control of serum glucose levels in the diabetic patients of the study was satisfactory in 2/3 of the patients. The goal of treating arterial hypertension (blood pressure <130/80 mmHg) was achieved in 65% of patients postoperatively compared with 22.5% preoperatively, and this difference proved to be statistically significant ($p=0.01$). From the comparative analysis of CAD risk factors in the patients who survived during the postoperative follow-up period in relation to the patients who died, no statistically significant differences were found (Table 8).

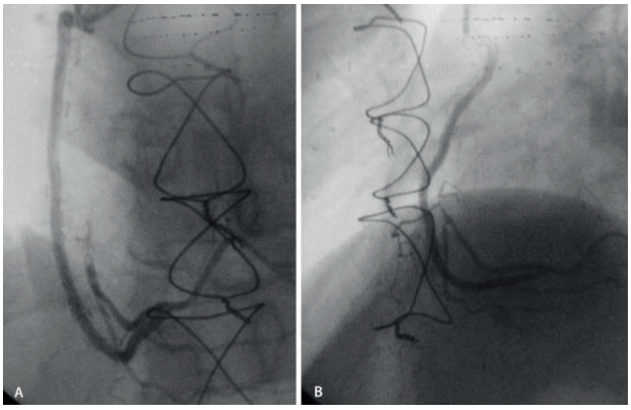

Figure 5. Free radial artery graft to right coronary artery posterior descending branch.

Table 8. Risk factors for coronary artery disease: postoperative comparison between survivors and non survivors during follow up.

Risk factors	Survived (%) (n=30)	Died (%) (n=10)	p
Smoking	1 (3.3%)	1 (10%)	0.8
Hyperlipidaemia	30 (100%)	7 (70%)	0.7
Optimal control	13 (43.3%)	3 (30%)	0.5
Insufficient control	17 (56.7%)	4 (40%)	0.5
Diabetes mellitus	12 (40%)	6 (60%)	0.6
Optimal control Serum glucose ≤130 mg/dl and HbA1c <6	2 (6.7%)	1 (10%)	0.8
Moderate control Serum glucose 131-199 mg/dl and HbA1c 6-7	7 (23.3%)	2 (20%)	0.8
Insufficient control Serum glucose ≥200 mg/dl and HbA1c >7	3 (10%)	3 (30%)	0.5
Arterial hypertension**	10 (33.3%)	10 (33.3%)	

**Optimal blood pressure control is defined the blood pressure target ≤130/80 mm Hg.

Discussion

The present study is the only study in Greece to record the long-term (> 5 years) survival of patients who undergo CABG surgery using only TAMR. A strong element of the study is the average duration of postoperative follow-up of the patients, which exceeded 9 years (9.3±4.8 years) and reached up to 15.6 years. During this period the overall mortality was 25% (none due to myocardial ischaemia), while the actual 10 year survival (i.e. patients who completed 10 years of postoperative follow-up) was 66.7%. There was no difference in the survival of the patients who received only two internal mammary artery grafts (LIMA and RIMA), compared to patients who underwent reperfusion surgery using the two internal mammary arteries (LIMA and RIMA) and a free radial artery graft.

This study also documents the long-term (5 years) patency of arterial grafts and in a total of 32 patients the arterial grafts were 100% patent. This finding may explain the low rates of major cardiovascular events (17.5%) that observed during the postoperative follow-up period – these were all non-coronary artery disease events. The choice of grafts in the surgical treatment of coronary artery disease constitutes, even nowadays, a great challenge. Arterial grafts had already been used since the late 1960s, since the pioneering operations of Kollesov and Green. From the mid-1980s, after the results of the Cleveland Clinic studies, the use of the LIMA to bypass the anterior descending branch of the left coronary artery (LAD) has been established. This increases survival and time free of myocardial infarction, while reducing symptoms and the need for repeated myocardial reperfusion operations.[3,4] The benefit of using the LIMA in terms of improving survival is a consistent finding regardless of age, sex, degree of luminal stenosis, or preoperative left ventricular function.

Well-designed studies in large series of patients since the last decade have demonstrated the superiority of the LIMA over vein grafts in terms of short-term and long-term patency. A key advantage of LIMA is its extremely low sensitivity to atheromatous degeneration, that has been documented with a LIMA as a native vessel and as a bypass graft.[5-9] Given the favourable histological characteristics of the LIMA and the long-term results regarding graft patency and patient survival, the following reasonable question was raised already at the beginning of the last decade: «If one internal mammary artery (1 IMA) is better than none, two internal mammary arteries (2 IMAs) could not they be better than one IMA?»[10] It was therefore proposed to use both IMAs in order to further improve patient survival. At the same time, the expansion of the use of the radial artery as a free graft made the technique of «total arterial myocardial revascularization» possible. This implies the complete avoidance of venous grafts and the use, more commonly, of the two IMAs as well as the radial artery free graft.

To increase the number of possible arterial bypasses and to achieve complete reperfusion, the techniques of sequential anastomoses as well as bifurcating grafts were developed.[8,9] Therefore, based on the above clinical data, the use of not only the left, but also both IMAs, as pedicled in situ and free grafts, with one or more consecutive anastomoses, depending on the desired cardiac surgical technique, began to be applied. Large series of patients and meta-analyses have shown that the use of two IMAs improves not only the quality of life, but also the survival expectancy.[11,12]

According to the study by Popovic *et al*.,[13] the eight-year survival of patients who underwent CABG using the two IMAs was 88% and 66% for ages younger than and older than 65 years, respectively. These data agree with the results of our own study (66.7% actual survival at decade). The researchers concluded that the long-term prognosis is excellent in appropriately selected patients. Age, poor renal function, peripheral arterial disease and left heart failure were adverse prognostic factors.[13] At the same time, clinical studies which have evaluated the progress of atherosclerosis with stenotic lesions in native coronary vessels, which have patent grafts after repeated coronary angiography, are of particular interest. Progression of coronary artery disease over the decade averaged 8% in areas revascularized with a patent IMA graft, while the corresponding rate was 11% in areas revascularized with a patent radial artery and 43% in areas revascularized with a patent vein graft.[8] In 2010, Borges *et al*.[14] demonstrated that CABG using IMA showed a lower progression of coronary disease lesions (17%) compared to vein grafts or percutaneous angioplasty (44%), including restenosis, p<0.001). The higher flow seen in the vein graft is thought to significantly reduce flow through native stenotic coronary lesions and thus further damage deterioration. In addition to rheological factors, IMA endothelium protects against coronary disease progression, possibly through nitric oxide (NO) production, in contrast to vein grafts, thereby preventing platelet aggregation, thrombosis, hyperplasia of the intima and the migration of inflammatory cells, which are blamed for causing coronary artery disease.[7] The IMA has multiple elastic petals, while the muscle element is significantly absent. These particular histological features may explain the reduced propensity for spasm and the development of atherosclerosis.

Regarding the use of the two IMAs, Tatoulis *et al*.[15] published the angiographic results of a large series of 5766 patients who received 991 RIMA grafts. Similar patency was found between the LIMA and RIMA when used in the LAD branch (96.5% *vs* 94.5%), as well as in branches of the LCx artery (90.5% *vs* 88.5%, respectively). In the right coronary artery, patency of the RIMA was significantly reduced, but superior to venous grafts. As found from the above study, the RIMA has similar long-term patency to the LIMA. This observation is confirmed by the results of the present study, which demonstrated a similar patency of both IMAs at five years. Considering the continuous increase in the population's survival expectancy, these results may significantly influence the strategy followed by cardiac surgeons regarding the selection of the most appropriate grafts for performing CABG.

Multiple randomized studies have investigated the patency of the radial artery, mainly as a graft choice in the best target after the LAD branch compared to vein grafts as well as to the RIMA.[16,17]

According to the results of the RAPS[18] and RSVP[19] study, the patency of the radial artery at five years was superior to vein grafts. It should be noted, however, that in the RAPCO study,[20] there was no significant difference in survival between patients in whom the Radial artery was used compared to patients who received a free RIMA graft or vein graft. This finding was also highlighted in the present study, as no difference in overall survival was found between the patients who received only two IMAs compared to those who also received a Radial artery graft in addition to the two IMAs.

It has been found that subgroups of patients, such as patients with preoperative renal dysfunction, may benefit from total arterial reperfusion as it is associated with perioperative morbidity and mortality comparable to the use of an IMA and venous grafts. Elderly patients (age >70 years) are also a special group of patients as they show significant comorbidities. It should be emphasized that TAMR is technically applicable to elderly patients but while it is clear that the use of at least one IMA graft improves survival even in 80-year old patients, the advantages of TAMR diminish with age. Researchers argue that there is no benefit from this strategy in patients over 70 years of age. The series of patients in our study included a significant number of elderly patients (mean age 63.5±13.1 years for men and 70±12 for women). The results of the study demonstrate that TAMR is safe and effective in the group of patients over 70 years of age. However, increasing surgical experience as well as long-term follow-up of large series of patients are necessary to draw safer conclusions.[21,22]

The present study concerned patients with a relatively low surgical risk (mean EuroSCORE II value: 1.42%). At the same time, comorbidity was limited, with the main disease being diabetes mellitus, which required insulin treatment and concerned 12.5% of the patients in this series. It has been shown that patients with diabetes mellitus show an increased risk of complications from the median sternotomy wound due to the use of the two IMAs. Literature data report an increase in the incidence of complications from mid-sternotomy trauma from less than 1% to approximately 3%. In the series of 40 patients of the study, no infections of the middle sternotomy wound were found, a finding that reinforces the safety of the method. It has been found that the skeletonized preparation of IMAs can contribute to the reduction of complications from the chest wall, as the blood supply to the sternum through the intercostal branches is maintained.[23] Nevertheless, in the series of patients under study, the technique followed was the preparation of the grafts of the IMA with a flap, without complications arising from the surgical wound.

Despite scientific evidence from large patient series and meta-analyses that the use of two IMAs is superior to one IMA, data from the large, worldwide database of the Society of Thoracic Surgeons National Adult Cardiac Surgery Database demonstrate that in 2011 only 4.4% of patients used both IMAs. The main reason is the technical difficulty of preparing and performing anastomoses of the two IMAs, as well as the risk of contamination of the median sternotomy wound. It is indisputable that more time is required for the preparation of the two IMAs. At the same time, the need to perform successive anastomoses increases the complexity of the operation. The results of the Arterial Revascularization Trial (ART study), which is the only randomized study with a sufficient statistical sample (3102 patients were randomized), showed that "when compared with single arterial graft (SAG), both mammary arterial grafts (MAG) and total arterial graft (TAG) represent valuable strategies to improve clinical outcomes following coronary artery bypass grafting but TAG can potentially provide further benefit".[24] Also the PREVENT IV study which investigated the venous graft failure showed that 42.8% of the venous graft had a failure at a 12-18 moths' time.[25]

Conclusions

There is no consensus among members of the cardiac surgical community regarding the identity of the graft that is most appropriate after the LIMA in the anterior descending branch (LAD). According to the results of this study, TAMR is considered safe and effective and is associated with satisfactory long-term survival. In concordance with the results from large series of patients and multicentre studies there was no difference in survival between those patients who had only IMA grafts placed and those who had grafts from the IMA and the Radial artery, in this study. The present study suggests that even in elderly patients the results can be excellent.[20,21] The limitations of the study should be emphasized, that the patients come from a single reference centre, while there was no control group. However, these the first long-term survival results of patients, who underwent TAMR in Greece, and the basis for conducting multicentre studies, which will compare the various surgical methods in larger groups of patients.

In conclusion, the present study results suggest that TAMR should be used as the preferential revascularisation strategy in ischaemic heart disease patients undergoing coronary artery bypass grafting (CABG).

References

1. Collins P, Webb CM, Chong CF, et al. Radial artery versus saphenous vein patency (RSVP) trial investigators. Radial artery versus saphenous vein patency randomized trial: five-year angiographic follow-up. Circulation 2008;117:2859-64.
2. Perk J, De Backer G, Gohlke H, et al. European Guidelines on cardiovascular disease prevention in clinical practice (version 2012). The Fifth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of nine societies and by invited experts). Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Eur Heart J 2012;33:1635-701.
3. Weiss AJ, Zhao S, Tian DH, et al. A meta-analysis comparing bilateral internal mammary artery with left internal mammary artery for coronary artery bypass grafting. Ann Cardiothorac Surg 2013;2:390-400.

4. Kollosof VI. Mammary artery – coronary artery anastomosis as method of treatment of angina pectoris. J Thorac Cardiovascu Surg 1970;60:469-82.
5. Lytle BW, Blackstone EH, Sabik JF, et al. The effect of bilateral internal thoracic artery grafting on survival during 20 postoperative years. Ann Thorac Surg 2004;78:2005-12.
6. Damgaard S, Steinbróchel DA, Kjaergard HK. An update on internal mammary artery grafting for coronary artery disease. Curr Opin Cardiol 2005;20:521-4.
7. Taggart DP, Altman DG, Gray AM, et al. Randomized trial to compare bilateral vs. single internal mammary coronary artery bypass grafting: 1 year results of the Arterial Revascularization Trial (ART). Eur Heart J 2010; 31:2470-81.
8. Dimitrova KR, Hoffman DM, Geller CM, et al. Arterial grafts protect the native coronary vessels from atherosclerotic disease progression. Ann Thorac Surg 2012;94:475-81.
9. Cameron A, Davis KB, Green G, Schaff HV. Coronary bypass surgery with internal-thoracic-artery grafts - effects on survival over a 15-year period. N Engl J Med 1996;334:216-9.
10. Puskas JD, Kilgo PD, Kutner M, et al. Off-pump techniques disproportionately benefit women and narrow the gender disparity in outcomes after coronary artery bypass surgery. Circulation 2007;116:I192-9.
11. Lytle BW. Bilateral internal thoracic artery grafting. Ann Cardiothorac Surg 2013;2:485-92.
12. Galbut DL, Kurlansky PA, Traad EA, et al. Bilateral internal thoracic artery grafting improves longterm survival in patients with reduced ejection fraction: a propensity- matched study with 30-year follow-up. J Thorac Cardiovasc Surg 2012;143:844-53.
13. Popovic B, Voillot D, Maureira P, et al. Bilateral internal mammary artery bypass grafting: long-term clinical benefits in a series of 1000 patients. Heart 2013;99:854-9.
14. Borges J, Lopes N, Soares P, et al. Five-year follow-up of angiographic disease progression after medicine, angioplasty, or surgery. J Cardiothorac Surg 2010;5:91.
15. Tatoulis J, Buxton BF, Fuller JA. The right internal thoracic artery: the forgotten conduit - 5,766 patients and 991 angiograms. Ann Thorac Surg 2011; 92:9-15.
16. Tsuneyoshi H, Komiya T, Shimamoto T, et al. The second best arterial graft to the left coronary system in off-pump bypass surgery: a propensity analysis of the radial artery with a proximal anastomosis to the ascending aorta versus the right internal thoracic artery. Gen Thorac Cardiovasc Surg 2015;63:335-42.
17. Schwann TA, Hashim SW, Badour S, et al. Equipoise between radial artery and right internal thoracic artery as the second arterial conduit in left internal thoracic artery-based coronary artery bypass graft surgery: a multi-institutional study. Eur J Cardiothorac Surg 2016;49:188-95.
18. Deb S, Cohen EA, Singh SK, Une D, Laupacis A, Fremes SE; RAPS Investigators. Radial artery and saphenous vein patency more than 5 years after coronary artery bypass surgery: results from RAPS (Radial Artery Patency Study). J Am Coll Cardiol 2012;60:28-35.
19. Collins P, Webb CM, Chong CF, Moat NE; Radial Artery Versus Saphenous Vein Patency (RSVP) Trial Investigators. Radial artery versus saphenous vein patency randomized trial: five-year angiographic follow-up. Circulation 2008;117:2859-64.
20. Buxton BF, Raman JS, Ruengsakulrach P, et al. Radial artery patency and clinical outcomes: five-year interim results of a randomized trial. J Thorac Cardiovasc Surg 2003;125:1363-70.
21. Kinoshita T, Asai T, Murakami Y, et al. Efficacy of bilateral internal thoracic artery grafting in patients with chronic kidney disease. Ann Thorac Surg 2010;89:1106-11.
22. Medalion B, Mohr R, Frid O, et al. Should bilateral internal thoracic artery grafting be used in elderly patients undergoing coronary artery bypass grafting? Circulation 2013;127:2186-93.
23. Toumpoulis IK, Theakos N, Dunning J. Does bilateral internal thoracic artery harvest increase the risk of mediastinitis? Interact Cardiovasc Thorac Surg 2007;6:787-91.
24. Taggart DP, Gaudino MF, Gerry S, et al. Effect of total arterial grafting in the Arterial Revascularization Trial. J Thorac Cardiovasc Surg 2022;163:1002-1009.e6
25. Hess CN, Lopes RD, Gibson CM, et al. Saphenous vein graft failure after coronary artery bypass surgery: Insights from PREVENT IV. Circulation 2014;130:1445-51.