

# Comorbidities and Ventricular Dysfunction Drive Excess Mid-Term Morbidity in an Indigenous Australian Coronary Revascularisation Cohort



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## Background

There is a paucity of data in regards to longer term morbidity outcomes in Indigenous Australian patients undergoing coronary artery bypass grafting (CABG). No comparative data on re-infarction, stroke or reintervention rates exist. Outcome data following percutaneous coronary intervention (PCI) is also extremely limited. Addressing this gap in knowledge forms the major aim of our study.

## Methods

This was a single centre cohort study conducted at the Townsville Hospital, Australia which provides tertiary adult cardiac surgical services to the northern parts of the state of Queensland. It incorporated consecutive patients (n = 350) undergoing isolated CABG procedures, 2008–2010, 20.9% (73/350) of whom were Indigenous Australians. The main outcome measures were major adverse cardiac or cerebrovascular events (MACCE) at mid-term follow-up (mean 38.9 months).

## Results

The incidence of MACCE among Indigenous Australian patients was approximately twice that of non-Indigenous patients at mid-term follow-up (36.7% vs. 18.6%; p = 0.005; OR 2.525 (1.291–4.880)). Following adjustment for preoperative and operative variables, Indigenous Australian status itself was not significantly associated with MACCE (AOR 1.578 (0.637–3.910)). Significant associations with MACCE included renal impairment (AOR 2.198 (1.010–4.783)) and moderate-severe left ventricular impairment (AOR 3.697 (1.820–7.508)). An association between diabetes and MACCE failed to reach statistical significance (AOR 1.812 (0.941–3.490)).

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<b>Conclusions</b>	Indigenous Australians undergoing CABG suffer an excess of MACCE when followed-up in the longer term. High rates of comorbidities in the Indigenous Australian population likely play an aetiological role.
<b>Keywords</b>	Indigenous Australians • Coronary artery disease • Coronary artery bypass grafting • Coronary artery disease risk factors

## Introduction

For the purpose of this study the term Indigenous Australians is used to encompass both Aboriginal Australians and/or Torres Strait Islander peoples.

Indigenous Australians experience poorer health outcomes than non-Indigenous Australians. Estimates of a life expectancy gap of 10.6 and 9.4 years exist for Indigenous Australian males and females respectively born 2010–2012 when compared to non-Indigenous Australians [1]. Ischaemic heart disease (IHD) represents the leading specific cause of death in both Indigenous Australian males and females. Recent estimates show IHD representing the greatest contributor to the disparity in life expectancy between Indigenous and non-Indigenous Australian males accounting for 18.8% of the mortality gap [2]. IHD also accounts for 9.5% of the mortality gap between Indigenous and non-Indigenous Australian females with diabetes accounting for 21.4% [2].

Cardiac surgery, in the form of coronary artery bypass grafting (CABG), may represent an integral part of the treatment regimen of a patient with more advanced coronary artery disease. Relatively limited research exists in regards to CABG in the Australian Indigenous population. Available evidence indicates, that in comparison to non-Indigenous Australians, Indigenous patients:

- Present for CABG at a much younger age [3–6].
- Experience higher rates of preventable risk factors including renal impairment [5–7].
- Present with higher rates of left ventricular dysfunction and heart failure preoperatively [5,6].
- Experience excess perioperative morbidity [6,7].
- Have reduced long-term survival [6].

There is a paucity of data in regards to longer term morbidity outcomes in Indigenous Australian patients undergoing CABG. No comparative data on re-infarction, stroke or reintervention rates exist. This is not isolated to the cardiac surgical population. Very limited follow-up data exists in regards to Indigenous Australian patients undergoing percutaneous coronary interventions (PCI) [8]. Addressing this significant gap in knowledge of clinical outcomes in Indigenous Australian patients undergoing coronary revascularisation forms the major aim of our study.

## Methods

### Setting

A retrospective cohort study was conducted out of The Townsville Hospital which provides tertiary adult cardiac surgical

services to the northern parts of the state of Queensland. The catchment area includes the vast majority of the Cairns–Atherton, Cape York, Mount Isa, Torres Strait and Townsville–Mackay Indigenous regions as defined in the 2011 Census of Population and Housing [9]. The Indigenous Australian population of these regions combined is estimated, from the most recent census data available, to be 67,926 forming 10.4% of the total population in these regions [10].

### Study Period and Indigenous Identification

Consecutive patients who underwent isolated CABG at Townsville Hospital between August 2008 and March 2010 formed the study cohort. A pragmatic balance was struck between the ability to thoroughly follow-up the cohort and statistical power. The patients identified as being of Aboriginal and/or Torres Strait Islander descent at hospital admission.

### Perioperative Data

Patient demographics, cardiovascular risk factors, preoperative cardiovascular status, operative interventions and perioperative outcome measures were entered prospectively into a systemised database and retrospectively assessed. Definitions were as defined within the Australian & New Zealand Society of Cardiac & Thoracic Surgeons (ANZSCTS) National Cardiac Surgery Database Program Data Definitions Manual Version 3.0 [11]. Perioperative mortality was defined as death within the initial hospital admission or occurring within 30 days postoperatively.

Predicted perioperative mortality was calculated retrospectively from database variables. The model used was a 12-variable multiple logistic regression model for predicting risk of 30-day mortality for patients undergoing cardiac surgery. This risk prediction model was developed from, and validated in, the Australian cardiac surgical population [12].

Remoteness was defined using the Australian Standard Geographical Classification (ASGC) method and was based upon a patient's residential address at the time of surgery [13]. Given relatively small numbers, patients were defined as remote (if they resided in remote or very remote areas) or non-remote (from major cities, inner regional or outer regional areas) [13].

### Mid-Term Outcomes

Patient follow-up was conducted initially in the form of a telephone interview and subsequently a questionnaire to the last known residential address if the patient had no recorded telephone number or was unable to be contacted via the telephone. If these methods were unsuccessful, telephone contact was made with the patient's listed next of kin, listed

general practitioner or local health care service. These sources were used only to enable patient contact and not for exchange of study information. Major adverse cardiac or cerebrovascular events (MACCE), or the lack of these, were confirmed by hospital patient record search and the search of a statewide public hospital database. Current self-reported postoperative smoking status was also recorded at follow-up. Patients unable to be contacted directly were excluded from mid-term outcome analysis (apart from survival analysis) unless a clearly defined MACCE event was noted in the process of statewide public hospital database search and subsequent record review—this event only was then included in the mid-term outcome analysis. A National Death Index (NDI) Linkage was performed by the Australian Institute of Health and Welfare (AIHW) to capture deaths not recorded on the statewide public hospital database or occurring interstate. Probabilistic matching of records provided by the NDI was based upon patient name, date of birth, sex, date of last contact and state of residence. Survival data was considered complete. The composite outcome MACCE included all-cause mortality, stroke, repeat revascularisation and myocardial infarction (MI). Stroke was defined as a focal, central neurological deficit lasting >72 hours or which resulted in irreversible brain damage or body impairment not caused by trauma. Repeat revascularisation was defined as any repeat percutaneous coronary intervention (PCI) or CABG. Myocardial infarction was defined differently depending if diagnosed perioperatively or following discharge from hospital. Perioperative MI was defined as within the ANZSCTS National Cardiac Surgery Database Program Data Definitions Manual Version 3.0 by the presence of at least two of the three criteria of a troponin rise >20 µg/L, new regional wall motion abnormalities and serial electrocardiograms (ECGs) demonstrating new Q waves ≥0.03 ms in two contiguous leads [11]. Following hospital discharge the diagnosis of MI included non-ST segment elevation myocardial infarction (NSTEMI) and ST segment elevation myocardial infarction (STEMI). Clinical diagnosis required the presence of at least two of a typical chest pain syndrome, TnI >0.04 µg/L or diagnostic ECG changes.

Cardiovascular death was as per the definition proposed by the Standardized Data Collection for Cardiovascular Trials Initiative [14]. This definition included deaths resulting from “acute MI, sudden cardiac death, death due to heart failure (HF), death due to stroke, death due to cardiovascular (CV) procedures, death due to CV haemorrhage, and death due to other CV causes” [14]. For the purposes of the study undetermined causes of death were presumed cardiovascular deaths.

## Statistical Analysis

All univariate analyses were conducted using Fisher’s exact test for categorical variables and one of the Wilcoxon rank sum or two-sample unpaired t-tests for each continuous variable. Unadjusted odd ratios (OR) and 95% confidence intervals (CI) were calculated for each mid-term outcome categorical variable, where an OR greater than one denoted higher odds in the Indigenous Australian cohort.

Survival curves were constructed for the analysis of postoperative survival (in months), using the Kaplan-Meier estimator. For analyses estimated survival functions for each group were compared using the log-rank test under the null hypothesis that the two survival functions were equal.

Adjustment for the influence of preoperative and operative variables on the composite outcome MACCE was performed using multiple logistic regression. Variables previously demonstrated to influence long-term outcomes post CABG were selected for the model [15,16]. Geographical remoteness was also included in the model due to the previously demonstrated association between increasing levels of remoteness and deaths from ischaemic heart disease in Australia [17]. Statistical significance of each explanatory variable was assessed using the Likelihood Ratio test, under the null hypothesis that the select variable was not predictive of the odds of MACCE, whilst controlling for other variables. The area under the curve (AUC) was computed to assess the model with a value in excess of 0.7 considered representative of good model fit.

All results were based on the 5% level of statistical significance.

Analyses for perioperative variables were conducted using PASW Vers. 18 (SPSS Hong Kong). Adjustment for predicted perioperative mortality and all mid-term outcomes analysis was conducted in R, Version 2.13.0. Survival analyses for postoperative survival were conducted in MATLAB.

## Ethical Review

Ethics approval was obtained from the Townsville Health Service District Human Research Ethics Committee and the University of Queensland School of Medicine. Support for the research was gained from the local Indigenous Australian community via the Townsville District Executive Director for Indigenous Health. Ethical approval for conduct of the NDI linkage was provided by The Australian Institute of Health and Welfare Ethics Committee.

## Results

### Demographics and Risk Factors (Table 1)

Isolated CABG procedures were performed on 350 patients during the study period with 20.9% (73/350) being Indigenous Australian. Indigenous Australian patients undergoing isolated CABG were on average 7.6 years younger than non-Indigenous patients and a higher proportion were female (35.6% vs 20.2%;  $p = 0.008$ ).

Significantly higher rates of current smoking, diabetes, dyslipidaemia and renal impairment were observed within the Indigenous Australian cohort. Although the predicted rate of perioperative mortality was lower in the Indigenous Australian CABG cohort due to the younger age structure of the cohort, this difference was not statistically significant (1.07 vs. 1.34%;  $p = 0.394$ ). A significantly higher proportion of Indigenous Australian patients resided in remote areas.

**Table 1** Preoperative Risk Factors.

	Isolated CABG Patients		P-value
	Non-Indigenous n = 277	Indigenous Australians n = 73	
Age-years (Mean ± SD)	63.2 ± 10.6	55.6 ± 10.3	p < 0.001
Gender (Female)	20.2% (56/277)	35.6% (26/73)	p = 0.008
Smoker ever	73.9% (204/276)	76.7% (56/73)	p = 0.763
Smoker current	18.5% (51/276)	31.5% (23/73)	p = 0.023
Family history	36.7% (101/275)	44.9% (31/69)	p = 0.216
Diabetes	28.2% (78/277)	58.3% (42/72)	p < 0.001
Dyslipidaemia	72.2% (200/277)	84.9% (62/73)	p = 0.033
Obesity (BMI > 30)	35.1% (97/276)	33.3% (24/72)	p = 0.890
Renal Impairment (GFR < 60)	16.7% (46/276)	27.8% (20/72)	p = 0.042
Dialysis	0.4% (1/277)	6.8% (5/73)	p = 0.002
Hypertension	78.0% (216/277)	82.2% (60/73)	p = 0.520
Cerebrovascular disease	8.3% (23/277)	5.6% (4/72)	p = 0.621
Peripheral vascular disease	7.6% (21/277)	4.2% (3/72)	p = 0.435
Respiratory disease	10.1% (28/276)	4.2% (3/72)	p = 0.161
ASGC remoteness status — Remote	9.8% (27/276)	45.2% (33/73)	p < 0.001
Predicted perioperative mortality (Mean ± SD)	1.34 ± 2.58%	1.07 ± 1.93%	p = 0.394

Abbreviations: ASGC, Australian Standard Geographical Classification; GRF, glomerular filtration rate; SD, standard deviation; BMI, body mass index.

## Cardiac Status (Table 2)

Rates of MI, documented heart failure and New York Heart Association (NYHA) classification did not differ significantly between the cohorts. Despite this, significantly higher rates of moderate or severe left ventricular impairment were present among Indigenous Australians (31.9 vs. 17.8%; p = 0.014).

The pattern of coronary artery disease differed between Indigenous Australian and non-Indigenous patients. Higher rates of significant left main disease were evident in the non-Indigenous group (39.4% vs. 23.3%; p = 0.013). A non-significant excess in rates of triple vessel disease was observed in the Indigenous Australian cohort (78.1% vs. 68.6%; p = 0.148).

**Table 2** Preoperative Cardiac Status.

Variable	Isolated CABG Patients		P-value
	Non-Indigenous n = 277	Indigenous Australians n = 73	
Prior myocardial infarction	66.8% (185/277)	72.6% (53/73)	p = 0.398
Myocardial infarction <7 days	14.8% (41/277)	8.2% (6/73)	p = 0.178
Angina	70.8% (196/277)	60.6% (43/71)	p = 0.115
Unstable angina	15.9% (44/276)	5.6% (4/71)	p = 0.032
CCF	6.5% (18/277)	4.2% (3/72)	p = 0.586
NYHA III-IV	11.9% (33/277)	11.1% (8/72)	p = 1.000
Preoperative inotrope support	2.2% (6/277)	2.8% (2/72)	p = 0.671
Previous CABG	2.9% (8/276)	1.4% (1/73)	p = 0.691
Previous valve procedure	0% (0/276)	0% (0/73)	p = 1.000
Previous PTCA	10.1% (28/276)	5.5% (4/73)	p = 0.262
Moderate or severe LV impairment (LVEF < 45%)	17.8% (49/275)	31.9% (23/72)	p = 0.014
Left main stenosis >50%	39.4% (109/277)	23.3% (17/73)	p = 0.013
3-vessel disease	68.6% (190/277)	78.1% (57/73)	p = 0.148

Abbreviations: CABG, coronary artery bypass grafting; CAD, coronary artery disease; CCS, Canadian Cardiovascular Society; CCF, Congestive Cardiac Failure; LV, left ventricular; NYHA, New York Heart Association; PTCA, percutaneous transluminal coronary angioplasty.

**Table 3** Surgical Intervention.

CABG Patients	Isolated CABG Patients		
	Non-Indigenous n = 277	Indigenous Australians n = 73	P-value
Non-elective procedure	29.6% (82/277)	19.2% (14/73)	0.079
No. of grafts (mean ± SD)	2.97 ± 1.00	2.93 ± 0.75	p = 0.731
IMA	86.6% (240/277)	78.1% (57/73)	p = 0.097
X-Clamp time (minutes) (Mean ± SD)	51.8 ± 18.6 (n = 252)	50.3 ± 17.5 (n = 69)	p = 0.562
CPB time (minutes) (Mean ± SD)	74.7 ± 24.7 (n = 256)	76.0 ± 27.8 (n = 71)	p = 0.700

Abbreviations: CABG, coronary artery bypass grafting; SD, standard deviation; IMA, internal mammary artery.

### Surgical Intervention (Tables 3 and 4)

There were no statistically significant differences observed with regards to the urgency of procedures conducted, cross clamp and cardiopulmonary bypass times, or the mean number of grafts performed. Reduced internal mammary artery utilisation was noted in the Indigenous Australian isolated CABG group although this was not statistically significant (78.1% vs. 86.6%;  $p = 0.097$ ). Reasons for the internal mammary artery not being utilised in the Indigenous Australian isolated CABG cohort are shown in Table 4.

### Perioperative Outcomes (Table 5)

No significant difference in perioperative mortality was observed between Indigenous Australian and non-Indigenous CABG cohorts (4.1% vs. 2.5%;  $p = 0.441$ ).

**Table 4** Reasons for IMA Graft Not Utilised in Indigenous Australian Isolated CABG Cohort.

Reason	Total (n = 16)
No LAD disease	2
<b>LIMA Issue</b>	
Atherosclerotic disease	1
Dissection/Trauma	2
<b>LAD Issue</b>	
Endarterectomy with long arteriotomy requiring reconstruction	2
Distal disease (LIMA short)	1
Small target with diffuse disease	1
Infarcted LAD territory with severe ischaemic cardiomyopathy	1
<b>Patient Factors</b>	
Unstable Patient	2
AV fistula left arm	1
<b>No reason stated</b>	3

Abbreviations: LAD, left anterior descending coronary artery; LIMA, left internal mammary artery; AV, arteriovenous.

Significantly lower rates of atrial fibrillation were observed in the Indigenous Australian cohort (13.7% vs. 25.3%;  $p = 0.041$ ). No other significant differences in regards to postoperative morbidity were evident between the cohorts.

Rates of readmission within 30 days of discharge did not differ between Indigenous Australian and non-Indigenous patients.

### Mid-Term Outcomes (Tables 6 and 7)

Patients were followed for a mean of  $38.9 \pm 5.9$  months. Follow-up was complete in 82.6% (74.0% Indigenous Australian patients, 84.8% non-Indigenous patients). Thirty-two (32) deaths occurred during the follow-up period, 9.1% of the cohort. No significant difference in survival was noted between Indigenous Australian and non-Indigenous patients (Figure 1). However, the mean age of death of Indigenous Australian CABG patients was substantially younger than non-Indigenous patients (56.8 vs. 69.7;  $p = 0.005$ ).

Cause of death was able to be determined in 75.6% of deaths (34/45) (81.8% (9/11) Indigenous Australian patients, 73.5% (25/34) non-Indigenous patients). No significant differences in rates of cardiovascular death were evident between Indigenous Australian and non-Indigenous CABG groups.

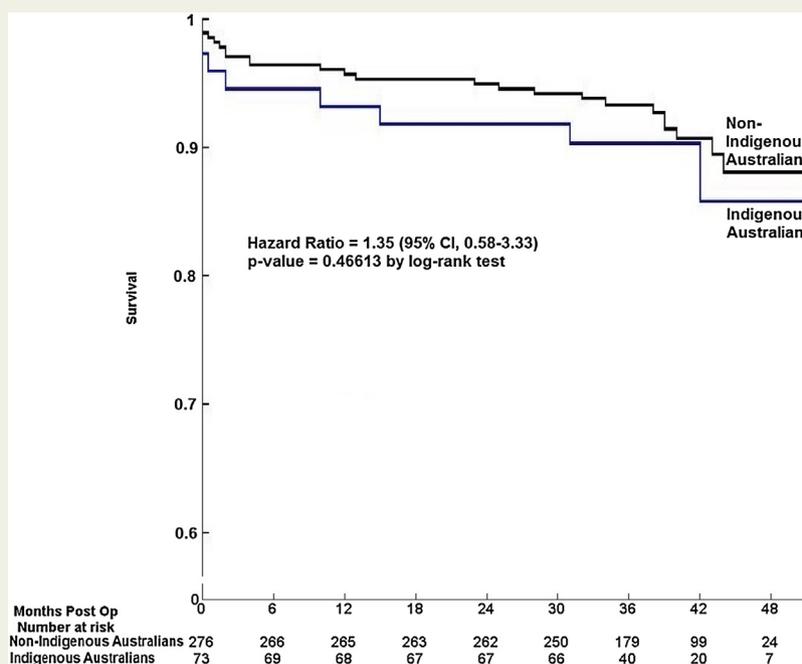
Despite survival being similar between both groups, Indigenous Australian patients who underwent CABG experienced MACCE at almost twice the rate of their non-Indigenous counterparts (36.7% vs. 18.6%;  $p = 0.005$ ; OR 2.525 (1.291–4.880)). Rates of stroke (7.1% vs. 2.1%;  $p = 0.073$ ; OR 3.518 (0.674–16.966)) and MI (17.5% vs. 8.0%;  $p = 0.045$ ; OR 2.432 (0.946–5.929)) were more than double that of the non-Indigenous cohort and appeared to be the main contributing factors to the excess of MACCE observed in the Indigenous Australian CABG group. Rates of repeat revascularisation did not vary significantly between Indigenous Australian and non-Indigenous CABG groups.

Following adjustment for preoperative and operative variables, Indigenous Australian status itself was not significantly associated with MACCE (AOR 1.578 (0.637–3.910)  $p = 0.324$ ) (Table 7). Independent associations with MACCE from the adjusted model were renal impairment ( $p = 0.047$ ) and moderate-severe left ventricular impairment ( $p = < 0.001$ ). There also appeared to be association between

**Table 5** Perioperative Outcomes — CABG patients.

Postoperative Outcomes	Isolated CABG Patients		P-value
	Non-Indigenous n = 277	Indigenous Australians n = 73	
Intubation >24 hrs	5.4% (15/277)	1.4% (1/72)	p = 0.210
ICU length of stay >1 night	17.4% (48/276)	27.8% (20/72)	p = 0.065
Atrial fibrillation	25.3% (70/277)	13.7% (10/73)	p = 0.041
Pneumonia	0.4% (1/277)	2.7% (2/73)	p = 0.112
Renal failure	1.8% (5/277)	1.4% (1/73)	p = 1.000
AMI	0.4% (1/277)	0% (0/73)	p = 1.000
CVA	0.4% (1/277)	0% (0/73)	p = 1.000
Deep sternal infection	2.9% (8/277)	2.7% (2/73)	p = 1.000
Readmission <30 days	11.1% (30/271)	11.4% (8/70)	p = 1.000
Perioperative mortality	2.5% (7/277)	4.1% (3/73)	p = 0.441

Abbreviations: AMI, acute myocardial infarction; CVA, cerebrovascular accident; ICU, intensive care unit.



**Figure 1** Kaplan Meier survival estimator isolated coronary artery bypass graft (CABG) cohort.

diabetes and MACCE although this failed to reach statistical significance (AOR 1.812 (0.941–3.490); p = 0.075).

### Postoperative Smoking Status (Table 6)

A significantly higher proportion of Indigenous Australian CABG patients continued to smoke at follow-up in comparison to the non-Indigenous cohort (27.7% vs. 14.2%; p = 0.031). However, in relative terms, large proportions of both Indigenous Australian and non-Indigenous preoperative current smokers continued to smoke.

### Discussion

This study of consecutive patients undergoing isolated CABG surgery at Townsville Hospital included 73 Indigenous Australian patients. At 20.9% of the cohort this makes this the largest reported proportion of Indigenous Australians undergoing CABG in an Australian centre to date. It demonstrates a significant over-representation of Indigenous Australians in a CABG cohort at a hospital where Indigenous Australians form 10.4% of the population of the catchment

**Table 6** Mid-term Outcomes.

MACCE	Isolated CABG Patients		P-value	Odds Ratio (95% CI)
	Non-Indigenous n = 276	Indigenous Australians n = 73		
MACCE	18.6% (45/242)	36.7% (22/60)	0.005	2.525 (1.291–4.880)
Death Any Cause	8.7% (24/276)	11.0% (8/73)	0.503	1.291 (0.479–3.145)
Stroke	2.1% (5/235)	7.1% (4/56)	0.073	3.518 (0.674–16.966)
MI	8.0% (19/237)	17.5% (10/57)	0.045	2.432 (0.946–5.929)
Repeat revascularisation	3.0% (7/236)	3.7% (2/54)	0.676	1.257 (0.124–6.863)
Age of death (Years) (Mean ± SD)	69.7 ± 10.2	56.8 ± 11.3	0.005	N/A
Cardiovascular death	4.7% (13/276)	6.8% (5/73)	0.550	1.486 (0.401–4.636)
Post operative — Smoking at follow-up	14.2% (30/212)	27.7% (13/47)	0.031	2.311 (1.001–5.138)

Abbreviations: MACCE, major cardiac or cerebrovascular event; CABG, coronary artery bypass grafting; CI, confidence interval; MI, myocardial infarction.

**Table 7** Adjusted Odds Ratios MACCE.

	Isolated CABG Patients	
	AOR (95% CI)	P-value
Age	1.001 (0.969–1.034)	0.967
Female sex	1.443 (0.683–3.050)	0.336
Indigenous Australian status	1.578 (0.637–3.910)	0.324
Smoker	1.203 (0.585–2.472)	0.616
Diabetes	1.812 (0.941–3.490)	0.075
Renal impairment (GFR <60)	2.198 (1.010–4.783)	0.047
Cerebrovascular disease	2.225 (0.756–6.549)	0.147
Peripheral vascular disease	1.864 (0.615–5.654)	0.271
Prior MI	0.901 (0.446–1.819)	0.771
NYHA III-IV	1.061 (0.365–3.083)	0.914
Obesity (BMI > 30)	0.882 (0.439–1.770)	0.723
Moderate or severe LV impairment (LVEF < 45%)	3.697 (1.820–7.508)	<0.001
3-vessel disease	1.937 (0.874–4.296)	0.104
Non-elective procedure	1.267 (0.629–2.554)	0.507
ASGC remote or very remote	0.717 (0.265–1.938)	0.512
IMA	0.551 (0.251–1.206)	0.136

Area under the curve (AUC) 0.765.

Abbreviations: CABG, coronary artery bypass grafting; AOR, adjusted odds ratio; GFR, glomerular filtration rate; NYHA, New York Heart Association; BMI, body mass index; LV, left ventricular; LVEF, left ventricular ejection fraction; MI, myocardial infarction; IMA, internal mammary artery; ASGC, Australian Standard Geographical Classification.

area [10]. This highlights the significant disadvantage of the Indigenous Australian population in regards to ischaemic heart disease.

This is the first study comparing the longer term morbidity outcomes of Indigenous Australians undergoing CABG to those of non-Indigenous Australians. A significant excess of morbidity in the Indigenous Australian cohort is demonstrated at mid-term follow-up. It is likely that it is excessive levels of comorbidities including renal dysfunction and diabetes and higher rates of left ventricular dysfunction in the

Indigenous Australian CABG cohort which is largely responsible for the surplus of MACCE observed in the group. Excess rates of renal impairment and diabetes have almost been universally reported in a range of clinical settings in the Indigenous Australian population to date while excess rates of left ventricular dysfunction and heart failure have commonly been reported in the CABG literature [5,6,18–21]. These findings highlight the importance of programs targeting both the prevention and management of diabetes, renal disease and heart failure in the Australian Indigenous

population. The development of models to better manage heart failure in Indigenous Australian patients and the continued implementation of recommendations from peak bodies addressing the epidemic of both diabetes and renal disease in the Indigenous Australian population will conceivably result in a reduction of the disparity in IHD outcomes between Indigenous and non-Indigenous Australians [22–24].

No significant differences were observed in regards to all cause and cardiovascular mortality between Indigenous Australian and non-Indigenous CABG cohorts during the follow-up period. When mean age of death however is considered, it is clear that Indigenous Australian patients undergoing CABG suffer an excess of premature mortality with deaths occurring, on average, 13 years younger than non-Indigenous patients (56.8 years vs. 69.7 years;  $p = 0.005$ ). Prabhu et al., in a series from Adelaide, demonstrated excess longer term mortality in Indigenous Australians undergoing isolated CABG (HR 1.30 (95% CI: 1.03–1.64;  $p = 0.03$ ) [6]. Survival analysis for Prabhu's study was conducted at a later stage of follow-up (median 7.5 years) than our study. Given the excess of MACCE observed at mid-term follow-up in our Indigenous Australian CABG cohort it is likely that we may see a significant divergence in our Indigenous and non-Indigenous survival curves, consistent with that demonstrated by Prabhu et al., in the longer term. It is also interesting in Prabhu's study that, following correction for variables including sex, recent MI, smoking, a history of stroke as well as left ventricular ejection fraction, diabetes and renal disease (but excluding age) Indigenous Australian patients did not appear to be at increased risk of mortality in the longer term (AHR 0.89 (95% CI: 0.70–1.14;  $p = 0.37$ ). Again, this appears to suggest that it is the excess of comorbidities and other factors in the Indigenous Australian population, rather than Indigenous status per se, which is responsible for the reduced long-term survival in the Indigenous Australian population following CABG.

A concerning feature identified in the Indigenous Australian isolated CABG cohort, particularly given the younger age structure of the group, was a non-statistically significant reduction in the utilisation of the internal mammary artery (IMA) as a bypass conduit (78.1% vs. 86.6%;  $p = 0.097$ ). The use of an IMA as a bypass conduit has proven benefits in regards to reduction of long-term morbidity and mortality over the use of saphenous vein alone [15]. Reduced IMA utilisation in Indigenous Australian patients has also been noted in a series from Melbourne and in recently published data from the ANZSCTS database [5,7]. Racial disparities in the utilisation of the IMA are not isolated to the Australian population with patients from non-Caucasian races in the United States less likely to receive an IMA graft [25]. A potential explanation for not using an IMA as a bypass conduit may be patient instability and the need to hasten conduit availability. This does not appear the case from our data with no statistically significant difference detected in regards to the urgency of procedures conducted between the Indigenous Australian and non-indigenous CABG cohorts. In fact, the rates of non-elective procedures were lower, although

not significantly so, in the Indigenous Australian isolated CABG cohort (19.2% vs. 29.6%;  $p = 0.079$ ). Reasons behind this reduced utilisation of the IMA in our Indigenous Australian cohort are shown in Table 4. Given the younger age structure of the Indigenous Australian CABG cohort and the benefit gained in regards to long-term morbidity and mortality with the use of IMA grafts, utilisation of the IMA in Indigenous Australian patients needs to be maximised. Similarly, a trend towards higher rates of triple vessel disease without an observed increase in the mean number of bypass grafts performed per patient in the Indigenous Australian cohort may suggest an element of under grafting. Again, particularly given the young age structure of the Indigenous Australian cohort, grafting strategies need to be optimised.

Consistent with previously published series in regards to CABG in the Indigenous Australian population, we observed younger patients with high levels of comorbidity and left ventricular impairment in our Indigenous Australian cohort [3–7]. Despite this, no significant difference was evident in regards to perioperative mortality, again a finding consistent with other series reporting on the subject [5–7]. A trend towards more prolonged intensive care unit (ICU) admissions was observed in the Indigenous Australian cohort despite lower rates of postoperative atrial fibrillation and a trend towards shorter duration of intubation. This prolonged ICU requirement is likely reflective of the significant preoperative comorbidity burden observed in the Indigenous Australian cohort.

Follow-up proved more difficult in the Indigenous Australian CABG cohort. Follow-up rates were significantly lower for Indigenous Australian patients when compared with the non-Indigenous group (74.0% vs. 84.8%;  $p = 0.037$ ). Follow-up rates were particularly low in Indigenous Australian patients from remote regions (66.7% vs. 80.0% non-remote; data not shown). These levels of loss to follow-up may impact results. Follow-up difficulties have previously been encountered in research on Indigenous Australian patients undergoing cardiac surgical procedures [3]. Indigenous Australians living in remote communities have been shown to have reduced access to telecommunications services when compared to the broader Australian population [26]. Strategies we used to negate this included utilising the assistance of local health services to put researchers in contact with patients in remote communities as well as the use of posted questionnaires when telephone contact was not possible. Despite this, follow-up rates remained lower for remote Indigenous Australian patients which is likely at least partially attributable to the reduced access to telecommunication services in these regions.

A weakness of this study is that details of secondary preventative strategies, apart from postoperative smoking, which may impact upon medium and longer term outcomes, have not been detailed. A significantly higher proportion of Indigenous Australian patients continued to smoke following CABG when compared to the non-Indigenous cohort. Persistent smoking in itself has been shown to adversely affect mortality post CABG although one study suggests

these effects may only begin to be seen 4 years postoperatively [27]. When compared to rates of current smoking preoperatively, significant proportions of both Indigenous and non-Indigenous patients continued to smoke following their surgery reflecting poor rates of cessation in both cohorts rather than a failure of secondary prophylactic strategies in the Indigenous Australian cohort alone.

This study also represents a single centre study. Despite the proportion of Indigenous Australians undergoing isolated CABG at our centre being the highest reported in the literature to date (20.9%), the applicability of the findings to the Australian Indigenous population as a whole is debatable. However, there is no nationally representative data reporting on longer term outcomes of Indigenous Australian patients undergoing coronary revascularisation. Demonstrated associations between renal dysfunction and diabetes and the occurrence of MACCE in the study cohort are relevant to the Indigenous Australian population as a whole given the significant excesses of these conditions affecting this population group [5,6,18–21].

Given the higher rates of adverse outcomes experienced in the longer term by the Indigenous Australian CABG cohort the question must be raised as to how to improve this [6]. As outlined above, continued focus on strategies to reduce the impact of diabetes, renal impairment and heart failure in the Indigenous Australian population is required as a preventative strategy. From a cardiac surgical perspective, given comparable perioperative outcomes, the focus of cardiac surgical research on Indigenous Australian patients undergoing CABG should potentially be directed toward the post-operative period and whether a form of enhanced clinical follow-up may produce benefits in regards to reducing the excess of longer term MACCE and mortality in the Indigenous Australian CABG population. Clinical follow-up of CABG patients in this study following discharge generally consisted of a GP visit usually within 1 week and surgical review at approximately 6 weeks. Patients were then typically discharged to the care of their local general practitioner or health service. Whether enhanced multidisciplinary follow-up after discharge involving regular input from relevant specialities including cardiology, endocrinology and nephrology would have benefits on reducing adverse outcomes following CABG in Indigenous Australian patients would be a particular area of interest. Research into this could be potentially conducted through expansion of already successfully implemented programs [28–30].

## Conclusion

Ischaemic heart disease is a leading contributor to the both morbidity and mortality in the Indigenous Australian population. Indigenous Australians undergoing surgical coronary revascularisation suffer an excess of MACCE when followed-up in the mid- to longer term. High rates of comorbidities evident in the Indigenous Australian population likely play an aetiological role. Continued focus on strategies to reduce

the impact of diabetes, renal impairment and heart failure in the Indigenous Australian population is essential to reduce the mortality gap experienced by Indigenous Australians secondary to IHD. Whether enhanced follow-up strategies in Indigenous Australian patients after CABG may reduce the excess of MACCE in this population is a question which remains to be answered.

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## Competing Interests

None declared.

## References

- [1] AIHW. Australia's Health 2014. Australia's Health Series no. 14. Cat. no. 178. Series No. 14. ed. Canberra: Australian Institute of Health and Welfare, 2014.
- [2] Australian Institute of Health and Welfare 2014. *Mortality and life expectancy of Indigenous Australians: 2008 to 2012. Cat. no. IHW 140*. Canberra: AIHW.
- [3] Kejriwal NK, Tan JT, Vasudevan A, Ong M, Newman MA, Alvarez JM. Follow-up of Australian Aboriginal patients following open-heart surgery in Western Australia. *Heart Lung Circ* 2004;13(1):70–3.
- [4] Lehman SJ, Baker RA, Aylward PE, Knight JL, Chew DP. Outcomes of cardiac surgery in Indigenous Australians. *Med J Aust* 2009;190(10):588–93.
- [5] O'Brien J, Reid C, Tran L, Baker R, Newcomb A, Smith J, et al. Thirty-day outcomes in Indigenous Australians following coronary revascularisation. *Global Heart* 2014;9 Supplement(1 supplement):e157.
- [6] Prabhu A, Tully PJ, Bennetts JS, Tuble SC, Baker RA. The morbidity and mortality outcomes of indigenous Australian peoples after isolated coronary artery bypass graft surgery: the influence of geographic remoteness. *Heart Lung Circ* 2013;22(8):599–605.
- [7] Elahi M, Matata B, Yui M. Ethnicity and adverse operative outcomes among Australian patients undergoing first-time isolated coronary artery bypass graft surgery. *Int Surg* 2008;93(6):358–65.
- [8] Tiong K. Clinical Outcomes of Percutaneous Coronary Interventions for Indigenous and Torres Straits Australians (ATSI) in Far North Queensland. *Heart Lung Circ* 2008;17S:S158.
- [9] ABS 2012. *Census of Population and Housing – Counts of Aboriginal and Torres Strait Islander Australians, 2011*. ABS Catalogue no. 2075.0. Canberra: ABS.
- [10] Australian Bureau of Statistics 2011. 2011 Census of Population & Housing 'Cairns – Atherton, Cape York, Mount Isa, Torres Strait and Townsville-Mackay (Indigenous Regions), Remoteness Areas, Indigenous status. <http://www.abs.gov.au/websitedbs/censushome.nsf/home/tablebuilder>.
- [11] ASCTS 2008. *ASCTS National Cardiac Surgery Database Program. Data Definitions Manual. Version 3.0 2008*.
- [12] Billah B, Reid CM, Shardey GC, Smith JA. A preoperative risk prediction model for 30-day mortality following cardiac surgery in an Australian cohort. *Eur J Cardiothorac Surg* 2010;37(5):1086–92.
- [13] Australian Institute of Health and Welfare 2004. *Rural, regional and remote health: a guide to remoteness classifications*. AIHW cat. no. PHE 53. Canberra: AIHW.
- [14] Hicks K, Hung HMJ, Mahaffey KW, Mehran R, Nissen SE, Stockbridge NL, et al. Standardized Definitions for Cardiovascular and Stroke End Point Events in Clinical Trials – Draft Definitions for Testing November 9, 2012. <https://www.cardiac-safety.org/think-tanks/ecrf-forms-for-posting/Draft%20Definitions%20for%20Testing%20November%209-%202012%20with%20MI%20Preamble%20CLEAN.pdf>.

- [15] Loop FD, Lytle BW, Cosgrove DM, Stewart RW, Goormastic M, Williams GW, et al. Influence of the internal-mammary-artery graft on 10-year survival and other cardiac events. *N Engl J Med* 1986;314(1):1–6.
- [16] Shahian DM, O'Brien SM, Sheng S, Grover FL, Mayer JE, Jacobs JP, et al. Predictors of long-term survival after coronary artery bypass grafting surgery: results from the Society of Thoracic Surgeons Adult Cardiac Surgery Database (the ASCERT study). *Circulation* 2012;125(12):1491–500.
- [17] Australian Institute of Health and Welfare 2011. *Cardiovascular disease: Australian facts 2011. Cardiovascular disease series*. Cat. no. CVD 53. Canberra: AIHW.
- [18] Katzenellenbogen JM, Sanfilippo FM, Hobbs MS, Briffa TG, Ridout SC, Knuiman MW. Aboriginal to non-Aboriginal differentials in 2-year outcomes following non-fatal first-ever acute MI persist after adjustment for comorbidity. *Eur J Prev Cardiol* 2012;19(5):983–90.
- [19] McGrady M, Krum H, Carrington MJ, Stewart S, Zeitz C, Lee GA, et al. Heart failure, ventricular dysfunction and risk factor prevalence in Australian Aboriginal peoples: the Heart of the Heart Study. *Heart* 2012;98(21):1562–7.
- [20] Randall DA, Jorm LR, Lujic S, O'Loughlin AJ, Eades SJ, Leyland AH. Disparities in revascularization rates after acute myocardial infarction between aboriginal and non-Aboriginal people in Australia. *Circulation* 2013;127(7):811–9.
- [21] Teng TH, Katzenellenbogen JM, Thompson SC, Sanfilippo FM, Knuiman M, Geelhoed E, et al. Incidence of first heart failure hospitalisation and mortality in Aboriginal and non-Aboriginal patients in Western Australia, 2000–2009. *Int J Cardiol* 2014;173(1):110–7.
- [22] Diabetes Australia. Aboriginal and Torres Strait Islanders and Diabetes Action Plan. 2013. <http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.636.7708&rep=rep1&type=pdf>.
- [23] Kidney Health Australia. National Chronic Kidney Disease Strategy – Executive Summary 2006. [http://kidney.org.au/cms\\_uploads/docs/national-ckd-strategy-ex-summary-2006.pdf](http://kidney.org.au/cms_uploads/docs/national-ckd-strategy-ex-summary-2006.pdf).
- [24] Iyngkaran P, Majoni V, Nadarajan K, Haste M, Battersby M, Ilton M, et al. AUSTRALIAN Indigenous Chronic Disease Optimisation Study (AUSI-CDS) prospective observational cohort study to determine if an established chronic disease health care model can be used to deliver better heart failure care among remote Indigenous Australians: Proof of concept-study rationale and protocol. *Heart Lung Circ* 2013;22(11):930–9.
- [25] Tabata M, Grab JD, Khalpey Z, Edwards FH, O'Brien SM, Cohn LH, et al. Prevalence and variability of internal mammary artery graft use in contemporary multivessel coronary artery bypass graft surgery: analysis of the Society of Thoracic Surgeons National Cardiac Database. *Circulation* 2009;120(11):935–40.
- [26] Australian Communications and Media Authority *Telecommunications in Remote Indigenous Communities*: Commonwealth of Australia, 2008.
- [27] van Domburg RT, Meeter K, van Berkel DF, Veldkamp RF, van Herwerden LA, Bogers AJ. Smoking cessation reduces mortality after coronary artery bypass surgery: a 20-year follow-up study. *J Am Coll Cardiol* 2000;36(3):878–83.
- [28] Corpus R. The Indigenous Cardiac Outreach Program. *Heart Lung Circ* 2014;23(1):e35.
- [29] McKenzie S, Goodman A, Mahoney R, Corpus R, Brown M. The Economic Savings of Queensland's Indigenous Cardiac Outreach Program. *Heart Lung Circ* 2013;22(S1):S254.
- [30] Tibby D, Corpus R, Walters DL. Establishment of an innovative specialist cardiac indigenous outreach service in rural and remote Queensland. *Heart Lung Circ* 2010;19(5–6):361–6.