Thirty-day Outcomes in Indigenous Australians Following Coronary Artery Bypass Grafting

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ABSTRACT

Background

Indigenous Australians have higher rates of cardiovascular disease and co-morbidities compared to their non-Indigenous counterparts.

Aims

We sought to evaluate whether Indigenous status *per se* portends a worse prognosis following isolated coronary artery bypass grafting (CABG).

Methods

The outcomes of 778 Indigenous Australians (55±10 years; 32% female) enrolled in the Australian and New Zealand Society of Cardiac and Thoracic Surgeons registry were compared to 36,124 non-Indigenous Australians (66±10 years; 21% female) following isolated CABG. In a secondary analysis, patients were propensity-matched by age, gender, renal function, diabetes, and ejection fraction (778 individuals in each group).

Results

Indigenous Australians were younger and more likely to be female, current smokers, to have diabetes, hypertension, renal impairment, heart failure, and previous CABG (all $p<0.04$). Indigenous patients had fewer bypasses with arterial conduits (including less internal mammary artery use), and a higher number of distal vein anastomoses ($p<0.001$). Post-operative bleeding rates were higher in indigenous patients ($p=0.001$). However, in-hospital and 30-day all-cause mortality, and rates of 30-day readmission were similar between both groups, though cardiac mortality was higher

in the Indigenous cohort (1.5% vs. 0.8%, $p=0.02$). With propensity-matching, rates of post-operative complications were similar amongst the two groups, with the exception of bleeding, which remained higher in Indigenous Australians ($p=0.03$).

Conclusions

Despite procedural differences and higher rates of baseline co-morbidities, Indigenous Australians do not have worse short-term outcomes following isolated CABG. Given the higher rates of baseline co-morbidities and lower rates of arterial conduit use, it will be essential to determine long-term outcomes.

INTRODUCTION

The disparity between Indigenous and non-Indigenous Australians in terms of health outcomes is well recognized, with cardiovascular disease being the leading contributor to premature death in the Indigenous population [1, 2]. Despite younger age at presentation with acute coronary syndromes, Indigenous patients have higher mortality rates than their non-Indigenous counterparts [3-5] potentially reflecting the increased prevalence of baseline co-morbidities, such as diabetes and obesity [6].

However, several studies suggest that the increased incidence and mortality of coronary artery disease (CAD) in Indigenous populations is not fully explained by the difference in traditional CAD risk factors [7, 8]. Geographical remoteness and reduced rates of coronary revascularization in Indigenous populations [3, 9-12] have been postulated to account for this increased mortality, though conflicting reports demonstrate comparable rate of CAD prevalence among urban Indigenous Australians compared with those in remote areas [13], and rates of revascularization similar to non-Indigenous Australians [14].

Given these disparate data, it is currently unclear whether Indigenous background itself portends a worse prognosis following acute coronary syndrome (ACS) or coronary revascularization.

We aimed to establish whether Indigenous Australians had similar in-hospital and 30-day outcomes to their non-Indigenous counterparts following isolated coronary artery bypass grafting (CABG). Furthermore, we endeavored to determine whether Indigenous status independently predicts outcome or is simply a marker of high-risk patients.

METHODS

Patient population

We analysed the in-hospital and 30-day clinical outcomes in 36,902 consecutive patients undergoing isolated CABG between June 2001 and December 2012 at the 28 Australian hospitals contributing to the Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS) Cardiac Surgery Database. Patients undergoing other cardiac surgery at the time of their CABG, such as valve replacement, were excluded. For the purpose of this study, patients were divided into two groups: those of Indigenous Australian origin and those of non-Indigenous origin. Patients were identified as Indigenous Australians in the ANZSCTS Registry by self-identification or by notation in hospital administrative data (which are collected from each patient at admission). We then performed a secondary analysis where patients were propensity-matched (1:1) by age, gender, renal function, diabetes, and left ventricular ejection fraction (778 patients in each group).

ANZSCTS Registry

The ANZSCTS database contains detailed information pertaining to all cardiac surgery undertaken at participating hospitals. The database has been previously described in detail [15-17]. Briefly, demographic, clinical and procedural characteristics of consecutive patients undergoing cardiac surgery are prospectively recorded on case report forms using standardized definitions for all fields. The database is coordinated by the Centre of Cardiovascular Research and Education in

Therapeutics, a research body within the Department of Epidemiology and Preventative Medicine (Monash University, Melbourne, Australia). The data are subject to an external quality audit program, performed on site to evaluate the completeness and accuracy of the database contents; data accuracy has been 97%, which compares favorably to other large registries [16]. The Ethics Committee of each participating hospital had previously approved the use of de-identified patient data contained within the database for research and waived the need for individual patient consent ('opt-out consent') [15].

Clinical Outcome Definitions

Early post-operative outcomes were analysed. These included: in-hospital mortality; 30-day mortality; peri-operative myocardial infarction, defined as two or more of (1) enzyme level elevation, (2) new wall motion abnormality or (3) new Q waves on serial electrocardiograms; new renal failure, defined as two or more of (1) creatinine increased to >0.2 mmol/L, (2) a doubling or greater increase in creatinine over pre-operative value or (3) a new requirement for dialysis/haemofiltration; prolonged ventilation, defined as ventilation for greater than 24 hours; deep sternal infection, defined as requiring wound debridement with one of positive culture or treatment with antibiotics; cardiac inotrope use for low cardiac output syndrome.

Statistical analysis

Continuous variables are expressed as mean $\pm$ SD, and categorical data are expressed as numbers/percentages. Continuous variables were compared using Student's *t* test.

Categorical variables were compared using Fisher's exact or chi-square tests as appropriate. Independent predictors of 30-day mortality were determined using multiple logistic regression models for variables with a p value <0.10 in simple logistic regression models. All calculated p values were 2 sided, and a p value <0.05 was considered significant. Statistical analysis was performed using Stata 12.0 (StataCorp, Texas, USA) and SPSS for Windows version 17.0 (SPSS, Munich, Germany).

RESULTS

Baseline characteristics

Indigenous Australians were younger and more likely to be female, current smokers, have diabetes mellitus, have higher baseline creatinine, hypertension, previous CABG, recent thrombolysis and a family history of premature CAD ($p<0.03$ for all; Table 1). They were less likely to have a history of peripheral vascular and cerebrovascular disease ($p<0.04$ for both), but there was no significant difference in body mass index (BMI) or history of chronic lung disease.

Clinical presentation and procedural characteristics

Indigenous Australians were less likely to present with an acute coronary syndrome as their indication for CABG, and despite lower left ventricular ejection fraction

(LVEF), were less likely to have New York Heart Association Class III or IV symptoms ($p<0.002$ for all; Table 2). However, there was no difference in rates of pre-operative resuscitation, cardiogenic shock or use of inotropes or intra-aortic balloon pump.

Rates of left main disease were significantly lower in the Indigenous group ($p<0.001$) though there was no difference in number of diseased vessels between the groups (Table 2). The Indigenous cohort had less internal mammary artery use as well as less arterial anastomosis use overall, but higher use of venous conduits (Table 3). They also had lower cross-clamp and cumulative cardiopulmonary bypass times ($p<0.001$).

Outcomes

Indigenous patients experienced more peri-operative MI but less post-operative renal impairment, arrhythmia and need for inotropes ($p<0.04$ for all; Table 4). There was no difference in the incidence of return to theatre, sternal wound infection or prolonged ventilation. At thirty-days, there was no difference in all-cause mortality, though cardiac death was higher in Indigenous Australians (1.5% vs. 0.8%, $p=0.02$; Table 5). Hospital re-admission rates were similar in both groups, though bleeding complications rates were higher in the Indigenous cohort (4.1% versus 2.3%, $p=0.001$).

With propensity matching, all in-hospital and thirty-day outcomes were not significantly different between the groups with the exception of bleeding which remained higher in the Indigenous group (4.1% versus 2.2%, $p=0.03$).

DISCUSSION

In this multi-centre cohort study, Indigenous Australians were younger at presentation for isolated CABG with far higher rates of baseline comorbidities. Despite this, both groups had similar all-cause in-hospital and 30-day mortality, with varied post-operative complication rates, which, with the exception of increased bleeding in the Indigenous group, were comparable with propensity matching.

Our finding of Indigenous patients presenting for coronary bypass operation ten years earlier than their non-Indigenous counterparts is consistent with other reports [18-20]. Furthermore, the Indigenous cohort consisted of a higher percentage of female patients compared with the non-Indigenous group. It is now well documented that the pre-menopausal protection from CAD appears to be absent in Indigenous women [3, 5], though the reasons for this remain unclear. It is possible that the presence of multiple modifiable risk factors such as diabetes mellitus, dyslipidaemia, and smoking outweigh the protective effects of younger age and female gender.

We observed lower rates of arterial conduit use in Indigenous Australians, and in particular, internal mammary artery (IMA) use, which may be driven by lower rates of left main disease. Interestingly, the survival benefit expected from less left main coronary disease was not observed [21]. With propensity matching the difference in left main disease was no longer significantly different, but the lower rate of IMA use in Indigenous patients remained. Operator and institutional preference may account for this difference, with the majority of Indigenous patients receiving their CABG at

the same few centres. Furthermore, Indigenous patients were more likely to have had prior CABG (12.5% versus 6.1%), during which their IMA may have been utilized. The well-described superiority of arterial grafts over venous with regard to long-term patency and mortality [22-25] suggests that over time the IA cohort will have worse outcomes.

Increased rates of post-operative bleeding were observed in the Indigenous cohort. The recognized risk factors for post-CABG bleeding of low BMI, older age and female gender [26, 27] do not appear to account for this difference, as both groups had similar mean BMI and the increased bleeding persisted despite propensity matching for age and gender. Thrombolysis and emergency surgery are also unlikely contributors as initially increased rates of thrombolysis in Indigenous Australians became comparable with propensity matching and time from MI to CABG was longer for Indigenous compared to non-Indigenous Australians in both analyses. Pre-operative hemoglobin, anti-platelet and anti-thrombotic use as well as history of clotting abnormalities are not recorded as part of the ANZSCTS registry but may account for some of the observed difference.

There are several limitations pertaining to our analysis. It is possible that we have underestimated the number of Indigenous Australian patients in our registry for several reasons. One is that some Indigenous Australians may not feel comfortable identifying themselves as Indigenous as they may feel treatment will be impacted. The second reason is there may be reluctance by administrative and medical staff to ask individual patients whether they identify as an Indigenous Australian.

Nevertheless, this study reports a very large cohort of patients with known Indigenous status. Though re-admission and mortality are recorded at 30 days, rates of other complications, such as MI and stroke, are not. In view of the increased prevalence in Indigenous Australians of co-morbidities that may also contribute to these complications [28, 29] as well as concerns regarding medication adherence [30], it is possible that a difference in post-operative morbidity may exist between the groups despite similar mortality. While it is reassuring that outcomes following CABG are similar, we only have short-term results, and long-term outcomes may be worse in Indigenous Australians owing to greater baseline comorbidities and lower use of arterial conduits in their surgery.

CONCLUSIONS

Despite comparable rates of short-term outcomes, the higher prevalence of baseline co-morbidities as well as increased use of venous grafts in Indigenous Australians suggest that the two groups will diverge over time. Close follow-up and aggressive optimization of modifiable cardiovascular risk factors are crucial in ensuring that long-term outcomes are not worse for Indigenous Australians.

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Tables

Table 1: Baseline Characteristics of the Overall Cohort

	Indigenous Australians n=778	Non- Indigenous Australians n=36,124	P value
Age, years $\pm$ SD	54.6 $\pm$ 10.4	66.2 $\pm$ 10.3	<0.0001
Female, n (%)	251/778 (32)	7,426/35,346 (21)	<0.0001
Diabetes mellitus	435/778 (56)	11,879/35,301 (34)	<0.0001
Insulin-requiring DM	134/778 (17)	3,124/35,346 (8.8)	<0.0001
Hypertension	642/778 (83)	27,976/35,299 (79)	0.026
Current smoker	350/645 (54)	5,465/23,743 (23)	<0.0001
Family history of CAD	339/714 (48)	13,679/32,498 (42)	0.004
Pre-op creatinine, μ mol/L $\pm$ SD	136.1 $\pm$ 173	101.3 $\pm$ 81	<0.0001
Dialysis	60/778 (7.7)	494/35,306 (1.4)	<0.0001
Cerebrovascular disease	65/778 (8.4)	3,807/35,297 (11)	0.030
Peripheral arterial disease	54/778 (6.9)	4,255/35,297 (12)	0.000
Respiratory disease	104/778 (13)	4,308/35,299 (12)	0.327
BMI, kg/m ² $\pm$ SD	28.7 $\pm$ 5.9	28.6 $\pm$ 4.9	0.541

Data are number (%), unless otherwise stated. Abbreviations: SD = standard deviation; DM = diabetes mellitus; CAD = coronary artery disease; BMI = body mass index. Respiratory disease is defined as any chronic lung disease; with mild being on any chronic bronchodilator therapy, moderate on chronic oral steroid therapy aimed at lung disease, and severe a room air pO₂ <60 mmHg or CO₂ >50 mmHg or mechanical ventilation for chronic lung disease.

Table 2: Preoperative Cardiac Status

	Indigenous Australians n=778	Non- Indigenous Australians n=36,124	P value
MI [CABG timing since MI event]			<0.0001
≤ 6 hours	10/560 (1.8)	329/18,908 (1.7)	
6-24 hours	8/560 (1.4)	467/18,908 (2.5)	
1-7 days	84/560 (15)	4,615/18,908 (24)	
8-21 days	185/560 (33)	4,791/18,908 (25)	
>21 days	273/560 (49)	8,703/18,908 (46)	
Angina type:			<0.0001
Stable	450/583 (77)	21,697/30,868 (70)	
Unstable	133/583 (23)	9,171/30,868 (30)	
History of heart failure	142/778 (18)	4,963/35,283 (14)	0.001
Heart failure at current admission	61/174 (35)	2,174/6,129 (36)	0.91
NYHA Class:			<0.0001
I or II	666/778 (86)	28,359/35,346 (80)	
III or IV	112/778 (14)	6,987/35,346 (20)	
Cardiogenic shock	6/778 (0.8)	588/35,296 (1.7)	0.052
Resuscitation within 1 hour pre- op	5/778 (0.6)	330/35,297 (0.9)	0.40
Arrhythmia	51/778 (6.6)	3,238/35,286 (9.2)	0.01
Inotropes	12/778 (1.5)	576/35,294 (1.6)	0.85
Previous CABG	21/168 (13)	1,124/18,476 (6.1)	0.001
Previous PCI	113/209 (54)	4,877/8,146 (60)	0.09
Thrombolysis (same admission)	17/152 (11)	394/7,575 (5.2)	0.005
LVEF, %±SD	51.0±15	55.1±13	<0.0001
Left main stenosis >50%	133/777 (17)	9,389/35,272 (27)	<0.0001
No. of diseased vessels			0.68
One	51/777 (6.5)	1,898/35,283 (5.4)	
Two	174/777 (22)	8,159/35,283 (23)	
Three	552/777 (71)	25,221/35,283 (72)	

Data are number (%), unless otherwise stated. Abbreviations: NYHA = New York Heart Association dyspnoea scale.

Table 3: Coronary Bypass Data

	Indigenous Australians n=778	Non- Indigenous Australians n=36,124	P value
Cumulative cross-clamp time, min $\pm$ SD	50.3 $\pm$ 27.6	65.0 $\pm$ 32.1	<0.0001
Cumulative cardiopulmonary bypass time, min $\pm$ SD	78.2 $\pm$ 37.8	90.1 $\pm$ 39.0	0.0001
IABP	44/777 (5.7)	1,969/35,303 (5.6)	0.92
Ventricular assist device	0/775 (0)	51/35,302 (0.1)	0.29
IMA used	684/777 (88)	33,208/35,333 (94)	0.0001
No. of anastomoses with arterial conduits			<0.0001
0	129/777 (16)	1,877/35,327 (5)	
1	501/777 (65)	12,202/35,327 (35)	
2	80/777 (10)	9,685/35,327 (27)	
3	45/777 (6)	7,404/35,327 (21)	
≥ 4	22/777 (3)	4,159/35,327 (12)	
No. of anastomoses with venous conduits			<0.0001
0	122/777 (16)	12,804/35,324 (36)	
1	192/777 (25)	8,908/35,324 (25)	
2	279/777 (36)	8,440/35,324 (24)	
3	143/777 (18)	4,079/35,324 (12)	
≥ 4	41/777 (5)	1,093/35,324 (3)	

Data are number (%), unless otherwise stated. Abbreviations: IABP = Intra-aortic balloon pump.

Table 4: Post-op data

	Indigenous Australians n=778	Non- Indigenous Australians n=36,124	P value
Peri-procedural MI	11/771 (1.4)	243/35,260 (0.7)	<0.0001
Return to theatre	46/774 (5.9)	1,723/35,286 (4.9)	0.18
Inotropes for longer than 4 hours	237/759 (31)	11,508/28,209 (41)	<0.0001
Inotropes for low cardiac output syndrome	126/759 (17)	5,552/28,306 (20)	0.04
New cardiac arrhythmia	141/774 (18)	10,157/35,287 (29)	<0.0001
New renal impairment	16/774 (2.1)	1,223/35,284 (3.5)	0.04
Deep sternal wound infection	9/774 (1.2)	228/35,285 (0.6)	0.08
Ventilation >24 hours	72/774 (9.3)	2,965/35,286 (8.4)	0.37

Data are number (%), unless otherwise stated. Abbreviations: MI = Myocardial infarction.

Table 5: Outcomes

	Indigenous Australians n=778	Non- Indigenous Australians n=36,124	P value
Total mortality	18/778 (2.3)	636/35,346 (1.8)	0.29
Cardiac death	12/778 (1.5)	284/35,346 (0.8)	0.02
30-day mortality	15/717 (2.1)	538/35,059 (1.5)	0.23
Bleeding complication	32/778 (4.1)	800/35,346 (2.3)	0.001
30-day hospital readmission	75/705 (10.6)	3,336/34,690 (9.6)	0.36

Data are number (%), unless otherwise stated. Bleeding complication is defined as bleeding requiring return to theatre.

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