# Outcomes of cardiac surgery in Indigenous Australians

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ardiovascular disease is more prevalent among Indigenous Australians than non-Indigenous Australians, and Indigenous Australians present for cardiac surgery about 20 years earlier, on average. This is likely to be due both to higher rates of traditional cardiovascular risk factors and to persistence of rheumatic heart disease.1-4 In addition to differences between Indigenous and non-Indigenous Australians in disease prevalence, there is evidence of disparity in outcomes after acute cardiovascular events such as myocardial infarction.<sup>5,6</sup> While cardiac surgery is highly effective, outcomes for Indigenous patients may be less favourable, owing to more extensive disease at the time of presentation, a higher prevalence of cardiovascular risk factors, difficulty accessing ongoing medical care, and higher mortality from non-cardiovascular causes.

The aim of our study was to explore whether the increased mortality associated with coronary heart disease in Indigenous Australians is normalised after cardiac surgery.

## **METHODS**

#### **Patients**

Data were prospectively collected for 2635 consecutive patients who underwent cardiac surgery at Flinders Medical Centre between January 2000 and December 2005. Flinders Medical Centre is a tertiary referral centre serving the southern region of Adelaide and also providing a cardiac surgical consultation service to the Royal Darwin Hospital. The Flinders cardiac surgical database consists of over 2000 prospectively collected data elements per patient, including baseline patient characteristics, operation details, postoperative complications, and late mortality. Informed consent was obtained for all patients before inclusion in the database.

#### Baseline data and definitions

A structured form was completed for each patient on hospital admission to record age, sex, self-reported Indigenous status (including Torres Strait Islander), cardiovascular risk factors and medical history.

Hypertension was defined by either a documented history of hypertension diagnosed and treated with medication, diet and/or exercise; or a measured systolic

#### **ABSTRACT**

**Objective:** To describe baseline characteristics, operative events and late mortality among Indigenous Australians undergoing cardiac surgery.

**Design, setting and participants:** Prospective study of consecutive patients undergoing cardiac surgery at Flinders Medical Centre in Adelaide between January 2000 and December 2005.

**Main outcome measures:** Operative (30-day) mortality and late mortality after cardiac surgery.

**Results:** Of 2635 patients undergoing cardiac surgery, 283 (10.7%) were Indigenous. Indigenous patients were substantially younger than non-Indigenous patients (mean, 47 [SD, 14] years v 65 [SD, 12] years; P = 0.001) and were more likely to have diabetes (39.6% v 27.3%; P = 0.001), renal dysfunction (3.2% v 1.2%; P = 0.009), and valvular surgery (53.0% v 23.1%; P < 0.001). There was a non-significant trend toward excess operative mortality in Indigenous patients (Indigenous 2.5% v non-Indigenous 1.3%; hazard ratio [HR], 1.67 [95% CI, 0.74–3.75]). But in the under-55-years age cohort, the difference between the two groups was highly significant (Indigenous 3.3% v non-Indigenous 0.4%; HR, 7.99 [95% CI, 1.66–38.50]), even after adjustment for euroSCORE (the European System for Cardiac Operative Risk Evaluation). Survival at 1 and 5 years was 94.0% and 80.6%, respectively, for Indigenous patients compared with 96.7% and 87.7%, respectively, for non-Indigenous patients. There was an excess in euroSCORE-adjusted mortality in the Indigenous cohort overall (HR, 1.46 [95% CI, 1.03–2.07]) that strengthened when restricted to the under-55-years cohort (HR, 6.9 [95% CI, 1.42–33.5]).

**Conclusion:** Indigenous Australians present for cardiac surgery nearly 20 years earlier than non-Indigenous Australians and experience excess age-stratified operative and late mortality.

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blood pressure of >140 mmHg or diastolic pressure of >90 mmHg on at least two occasions

Hyperlipidaemia was defined by a history of hypercholesterolaemia diagnosed by a physician and/or a serum cholesterol level > 5.0 mmol/L.

Diabetes was defined by a previous physician diagnosis or treatment with hypoglycaemic medication.

The European System for Cardiac Operative Risk Evaluation (euroSCORE) is a widely used model for predicting 30-day mortality in patients undergoing cardiac surgery<sup>7</sup> (the higher the euroSCORE, the higher the predicted operative mortality). It was developed from outcomes in 128 European centres and has been validated in European, Japanese, and North American populations. <sup>8-12</sup> Although the euroSCORE model has previously been shown to overestimate operative mortality in an Australian population, it does provide sufficient discrimination between strata of risk. <sup>13,14</sup> Using standard component definitions, we calcu-

lated the logistic euroSCORE for all patients preoperatively (Box 1).<sup>7</sup>

Preoperative renal dysfunction was defined by a serum creatinine level > 200 µmol/L.

Preoperative neurological impairment was defined by a condition affecting ambulation or daily functioning.

Critical preoperative state was defined by preoperative ventricular arrhythmia, acute renal failure, or the need for resuscitation or haemodynamic support.

An assessment of left ventricular systolic function was obtained either by echocardiography or left ventriculography and classified, on the basis of ejection fraction (EF), as moderate systolic impairment (EF, 30%–50%) or severe systolic impairment (EF < 30%).

# Operative characteristics and complications

The type of procedure performed was recorded as the presence of coronary artery bypass grafting, with or without valve replacement or repair. In patients undergo-



Variable

ing left anterior descending artery grafting, use of the left internal mammary conduit was recorded.

Operative mortality was defined as mortality that occurred at any time in hospital during the same admission or within 30 days of surgery. Other complications recorded included permanent stroke (defined by a new persistent neurological deficit); postoperative renal failure (defined by acute or worsening renal failure resulting in either an increase in serum creatinine to  $> 200 \,\mu$ mol/L or twice the baseline creatinine level, or a new requirement for dialysis); and prolonged ventilation ( $> 24 \,\mu$ ) hours).

# Late mortality

Late mortality was defined as all mortality occurring during the period of follow-up, including events within 30 days of surgery. Death after hospital discharge was detected by a search of the National Death Index in December 2006. This national database, maintained by the Australian Institute of Health and Welfare, records data from death certificates. Data linkage was performed between patient records in the Flinders cardiac surgical database and recorded deaths in Australia on the basis of first name, family name, sex, date of birth, postcode of residence and date of most recent contact.

### Statistical analysis

Baseline clinical and procedural variables were stratified by Indigenous status. To control for confounding by preoperative clinical parameters, we used the euroSCORE to model preoperative risk. Calibration and discrimination of the euroSCORE in our population were first examined using the *c* statistic (a measure of concordance) and the Hosmer–Lemeshow goodness-of-fit test. Operative mortality was stratified by Indigenous status in quintiles of the euroSCORE.

Given the marked difference between Indigenous and non-Indigenous people in age of onset of cardiac disease, operative mortality for the entire cohort was first calculated unadjusted, then stratified by age group (<55 years or ≥55 years) and adjusted for euroSCORE as a continuous variable through Cox proportional hazards modelling, after confirming preservation of the proportional hazards assumption. We also tested for interaction between age group, Indigenous status and mortality (operative and late).

For analysis of late mortality, unadjusted Kaplan–Meier survival curves were stratified by age group (< 55 years or ≥ 55 years) and

# 1 Components of the logistic euroSCORE (European System for Cardiac Operative Risk Evaluation)<sup>7</sup>

Definition

variable	Definition			
Patient-related factors				
Age	Continuous			
Sex	Female			
Chronic pulmonary disease	Long-term use of bronchodilators or steroids for lung disease			
Extracardiac arteriopathy	Any one of the following: claudication; carotid occlusion (> 50% stenosis); previous or planned intervention on the abdominal aorta, limb arteries or carotid arteries			
Neurological dysfunction disease	Condition severely affecting ambulation or day-to-day functioning			
Previous cardiac surgery	Requiring opening of the pericardium			
Serum creatinine level	> 200 µmol/L preoperatively			
Active endocarditis	Patient still under antibiotic treatment for endocarditis at the time of surgery			
Critical preoperative state	Any one or more of the following: ventricular tachycardia or fibrillation or aborted sudden death, preoperative cardiac massage, preoperative ventilation before arrival in the anaesthetic room, preoperative inotropic support, intra-aortic balloon counterpulsation or preoperative acute renal failure (anuria or oliguria [< 10mL/hour])			
Cardiac-related factors				
Unstable angina	Rest angina requiring administration of intravenous nitrates until arrival in the anaesthetic room			
Moderate LV dysfunction	LV ejection fraction 30%–50%			
Severe LV dysfunction	LV ejection fraction < 30%			
Recent myocardial infarct	Within the previous 90 days			
Pulmonary hypertension	Systolic pulmonary artery pressure > 60 mmHg			
Operation-related factors				
Emergency	Carried out on referral before the beginning of the next working day			
Procedure other than isolated CABG	Major cardiac procedure other than or in addition to CABG			
Surgery on the thoracic aorta	For disorder of ascending, arch or descending aorta			
Post-infarct septal rupture				
LV = left ventricular. CABG = coronary artery bypass grafting.				

compared by the log-rank test. Adjusted late outcomes in the two groups were compared in patients aged < 55 years using the euro-SCORE as a continuous variable as an overall measure of risk in Cox proportional hazard models.

Other in-hospital events were assumed to occur at the time of surgery. These binary events are reported as counts and proportions of the total, and adjusted for euro-SCORE and age in logistic regression models. Normally distributed variables are expressed as mean (SD), and non-Gaussian variables as median (interquartile range [IQR]).  $\chi^2$  tests were used for comparisons of binary outcomes between groups, and t tests for continuous variables. All analyses were

performed using Stata software, version 10 (StataCorp, College Station, Tex, USA).

# Ethics approval

The study was approved by Flinders Clinical Research Ethics Committee and the Aboriginal Health Research and Ethics Committee of the Aboriginal Health Council of South Australia.

# **RESULTS**

### Baseline patient characteristics

Of the 2635 patients who underwent cardiac surgery, 283 (10.7%) were Indigenous. The mean age of the cohort was 63 years (SD, 13



### 2 Baseline patient data and operative characteristics\*

Characteristic	Indigenous patients $(n = 283)$	Non-Indigenous patients ( $n = 2352$ )	Р
Mean age in years (SD)	47 (14)	65 (12)	0.001
Female sex	114 (40.3%)	658 (28.0%)	< 0.001
Hypertension	143 (50.5%)	1381 (58.7%)	0.007
Hypercholesterolaemia	125 (44.2%)	1545 (65.7%)	< 0.001
Diabetes	112 (39.6%)	643 (27.3%)	0.001
Current smoker	102 (36.0%)	299 (12.7%)	< 0.001
Chronic pulmonary disease	15 (5.3%)	160 (6.8%)	0.3
Previous cardiac surgery	5 (1.8%)	5 (0.2%)	< 0.001
Serum creatinine level > 200 μmol/L	9 (3.2%)	29 (1.2%)	0.009
Unstable angina	19 (6.7%)	281 (11.9%)	0.01
Active endocarditis	6 (2.1%)	23 (1.0%)	0.04
Pulmonary hypertension	24 (8.5%)	26 (1.1%)	< 0.001
Moderate or severe LV dysfunction	53 (18.7%)	268 (11.4%)	< 0.001
Recent myocardial infarct	50 (17.7%)	447 (19.0%)	0.6
Emergency surgery	11 (3.9%)	123 (5.2%)	0.3
Median euroSCORE (IQR)	2.08 (1.49–3.92)	2.59 (1.51–5.13)	< 0.001
CABG	142 (50.2%)	1790 (76.1%)	< 0.001
Single valve surgery ±CABG	98 (34.6%)	492 (20.9%)	< 0.001
Double valve surgery ± CABG	19 (6.7%)	11 (0.5%)	< 0.001
Other procedures	24 (8.5%)	59 (2.5%)	0.2
Mitral valve replacement ±CABG	69 (24.4%)	138 (5.9%)	< 0.001
Implantation of mechanical prosthesis	38 (55.1%)	91 (65.9%)	< 0.001
Mitral valve repair ±CABG	16 (5.7%)	58 (2.5%)	< 0.001
Aortic valve replacement ±CABG	65 (23.0%)	358 (15.2%)	0.001

CABG = coronary artery bypass grafting. euroSCORE = European System for Cardiac Operative Risk Evaluation. IQR = interquartile range. LV = left ventricular.

years), with Indigenous patients being younger than non-Indigenous patients (mean, 47 [SD, 14] years v 65 [SD, 12] years; P=0.001) and more likely to be women (40.3% v 28.0%; P<0.001). The difference between mean ages at operation remained significant for patients undergoing coronary artery bypass grafting alone (Indigenous patients, 52 [SD, 9] years v non-Indigenous patients, 65 [SD, 10] years; P<0.001).

The age difference in the operative cohort was clearly demonstrated by an analysis of the proportion of patients in each age group: 202/283 Indigenous patients (71.4%) and 458/2352 non-Indigenous patients (19.5%) were aged < 55 years.

Non-Indigenous patients were more likely to have the cardiovascular risk factors of hypertension and hypercholesterolaemia, whereas Indigenous patients were more likely to have diabetes and renal dysfunction and to be current smokers (Box 2). Indigenous patients were also more likely to present with moderate or severe left ventricular dysfunction, active endocarditis and pulmonary hypertension. The median euro-SCORE was lower for Indigenous patients than non-Indigenous patients (2.08 [IQR, 1.49-3.92] v 2.49 [IQR, 1.51-5.13]; P < 0.001), owing to the inclusion of age in this score.

## Operative characteristics

Indigenous patients were more likely to undergo either single or double valve surgery. In patients undergoing mitral valve replacement, Indigenous patients were less likely to undergo implantation of a mechanical prosthesis (Box 2).

# Mortality and in-hospital adverse events in entire cohort

Forty-two patients (1.6%) died either within 30 days of cardiac surgery or during the same admission (Box 3). In the overall cohort, euroSCORE was able to discriminate risk of operative mortality (c statistic, 0.75), but overestimated events in all strata (Hosmer–Lemeshow goodness-of-fit, P<0.001). The increasing frequency of operative mortality associated with increasing euroSCORE is evident from the graph in Box 4. There was a non-significant trend towards higher operative mortality in Indigenous patients than non-Indigenous patients (2.5% v 1.5%), whether unadjusted or adjusted for euroSCORE (Box 3).

There was no significant excess in new postoperative renal failure (hazard ratio [HR], 1.3 [95% CI, 0.8–2.0]); ventilation time >24 hours (HR, 1.2 [95% CI, 0.9–1.7]), or postoperative stroke (HR, 0.3 [95% CI, 0.0–2.1]) in the Indigenous group.

At a median follow-up of 45 months (IQR, 25–60 months), there were 293 deaths (11.1%) (Box 3). Indigenous status

#### 3 Operative mortality and late mortality,\* by Indigenous status

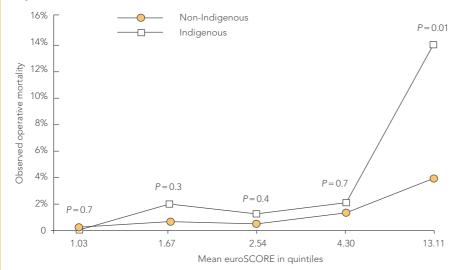
			Unadjusted HR (95% CI)	Α	Adjusted HR <sup>†</sup> (95% CI)		
Outcome	Indigenous patients (n = 283)	Non-Indigenous patients (n = 2352)	Whole cohort	Whole cohort	Age < 55 years	Age ≥ 55 years	P (interaction <sup>‡</sup> )
Operative mortality	7 (2.5%)	35 (1.5%)	1.67 (0.74–3.75)	1.67 (0.74–3.75)	6.90 (1.42–33.50)	na	0.92
Late mortality	36 (12.7%)	257 (10.9%)	1.41 (0.99–1.99)	1.46 (1.03–2.07)	2.70 (1.55–4.67)	0.92 (0.47–1.81)	0.005

HR = hazard ratio. na = not applicable. \* Operative mortality: mortality occurring in hospital during the same admission or within 30 days of surgery; late mortality: all mortality occurring during the period of follow-up, including events within 30 days of surgery. † Adjusted for euroSCORE (European System for Cardiac Operative Risk Evaluation). ‡ Interaction between age group, Indigenous status and mortality.



<sup>\*</sup>Values are number (%) of patients, except where otherwise specified.

# 4 Operative mortality of Indigenous and non-Indigenous patients, divided into quintiles of baseline euroSCORE\*



euroSCORE = European System for Cardiac Operative Risk Evaluation. \* Differences in mortality between Indigenous and non-Indigenous patients were compared using the  $\chi^2$  test, with P values < 0.05 considered statistically significant.

was associated with a borderline-significant excess in late mortality (Indigenous patients, 12.7% v non-Indigenous patients, 10.9%; HR, 1.4 [95% CI, 0.99–2.0]) that became significant when adjusted for euroSCORE (HR, 1.5 [95% CI, 1.03–2.1]).

Survival at 1 and 5 years was 94.0% and 80.6%, respectively, for Indigenous patients compared with 96.7% and 87.7%, respectively, for non-Indigenous patients (Box 5).

# Mortality and in-hospital adverse events in patients under 55 years of age

The mean age of Indigenous patients was substantially lower than the mean age of

non-Indigenous patients. When the analysis was restricted to patients aged <55 years, there was a significant excess in operative mortality among Indigenous patients (Box 6). The difference persisted when adjusted for euroSCORE (Box 3). The operative mortality of Indigenous patients aged <55 years (3.5%) was in fact higher than that for non-Indigenous patients aged  $\geq 55$  years (1.7%).

In patients aged < 55 years, at a median follow-up of 45 months, death occurred in 27/202 Indigenous patients (13.4%) and 26/458 non-Indigenous patients (5.7%) (Box 6). Unadjusted survival curves of patients in the

# alive at 1- to 5-year follow-up after surgery), by Indigenous status and type of surgery Indigenous Non-Indigenous

5 Survival (proportion of patients

	Indigenous patients	Non-Indigenous patients
All surgery*	(n = 283)	(n = 2352)
1-year	94.0%	96.7%
2-year	92.4%	95.6%
3-year	89.6%	92.1%
4-year	87.1%	89.3%
5-year	80.6%	87.7%
CABG <sup>†</sup>	(n = 142)	(n = 1790)
1-year	97.2%	97.5%
2-year	95.6%	95.3%
3-year	93.5%	93.6%
4-year	93.5%	90.6%
5-year	82.2%	89.4%
Valve surgery <sup>‡</sup>	(n = 117)	(n = 503)
1-year	90.6%	95.2%
2-year	89.6%	91.1%
3-year	86.7%	87.0%
4-year	79.6%	83.8%
5-year	79.6%	81.0%

CABG = coronary artery bypass grafting.
\*Whole cohort. † Patients undergoing CABG only.
‡ Patients undergoing valvular surgery with or
without CABG.

two age groups (<55 years and  $\ge 55$  years) (Box 7) showed excess late mortality among Indigenous patients compared with non-Indigenous patients in the younger cohort (HR, 3.0 [95% CI, 1.8-5.3]), which persisted despite adjustment for euroSCORE (HR, 6.9 [95% CI, 1.4-33.5]). By contrast, differences in survival between Indigenous and non-Indigenous patients were not significant in the older cohort, whether unadjusted (HR, 1.2 [95% CI, 0.6-2.3]) or adjusted (HR, 0.9 [95% CI, 0.5-1.8) for euroSCORE. This was primarily due to a low number of Indigenous patients (and hence events) in the older age group (interaction P value for age < 55 years, Indigenous status and mortality, 0.005).

# **DISCUSSION**

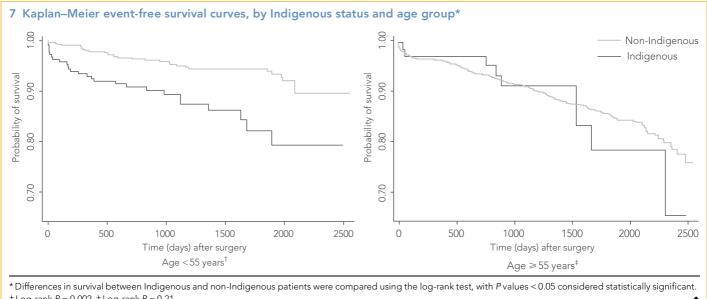
Although not statistically significant overall, the difference in operative mortality between Indigenous and non-Indigenous patients was statistically significant in the younger age group (<55 years). At a median of 45 months' follow-up, there was an

# 6 Operative mortality, in-hospital complications and late mortality, by age group and Indigenous status\*

Age group and Indigenous status	Operative mortality	Postoperative renal failure	Stroke	Late mortality
All patients ( $n = 2635$ )	42 (1.6%)	202 (7.7%)	30 (1.1%)	293 (11.1%)
Non-Indigenous patients aged $\geq 55$ years ( $n = 1894$ )	33 (1.7%)	157 (7.3%)	27 (1.4%)	231 (12.2%)
Non-Indigenous patients aged < 55 years (n = 458)	2 (0.4%)	21 (4.6%)	2 (0.4%)	26 (5.7%)
Indigenous patients aged $\geq 55$ years (n = 81)	0	11 (13.8%)	0	9 (11.1%)
Indigenous patients aged $< 55$ years ( $n = 202$ )	7 (3.5%)	13 (6.5%)	1 (0.5%)	27 (13.4%)

<sup>\*</sup> Operative mortality: mortality occurring in hospital during the same admission or within 30 days of surgery; late mortality: all mortality occurring during the period of follow-up, including events within 30 days of surgery. Figures represent number (%) of patients.





† Log-rank P = 0.002. ‡ Log-rank P = 0.21.

excess in euroSCORE-adjusted mortality in the Indigenous cohort, which again strengthened when restricted to patients under 55 years of age. Adjusting for known predictors of operative and late mortality, Indigenous patients in the younger age group had about seven times greater risk of operative mortality and nearly three times greater risk of late mortality compared with non-Indigenous patients.

The influence of ethnic status on outcomes of cardiac surgery has been described in international settings. In North America, both African-American and South-East Asian populations have been shown to have increased operative mortality after risk adjustment. 15-17

Previous studies of Indigenous Australians have focused on the management of valvular disease rather than cardiac surgery overall. They have revealed high rates of morbidity and mortality following valve surgery, particularly after the implantation of mechanical prostheses. 18-20 In addition, an excess in ageadjusted mortality after percutaneous mitral commissurotomy has been found in an Indigenous cohort compared with a non-Indigenous control group.<sup>20</sup> But, to our knowledge, ours is the first analysis of cardiac surgical outcomes in Indigenous people compared with non-Indigenous people.

Consistent with previous analyses are the differences in baseline characteristics of Indigenous patients presenting with symptomatic cardiovascular disease. 18-20 Not only are there significant age differences, but the severity of heart disease appears different. Rheumatic valvular disease and premature coronary atherosclerosis are both major health problems in Indigenous populations and are responsible for the marked age discrepancy in our cohort presenting for cardiac surgery. However, the younger age of onset and severity of heart disease do not completely explain the adverse outcomes, as disparity in outcomes persisted after risk adjustment. Differences in late mortality must also take into account the known higher rate of non-cardiovascular mortality in Indigenous populations.<sup>1</sup>

Although Indigenous and non-Indigenous patients may not have equal access to sophisticated cardiovascular therapies, our data suggest that cardiovascular mortality in Indigenous patients does not return to that of the overall Australian population even when the most appropriate and effective therapy has been accessed.

A strength of our study was the standardised collection of data and analysis of inhospital outcomes from a large single-centre registry. A limitation was that, after discharge, the assessment of late outcome was based on total mortality rather than repeated cardiovascular events or need for re-operation. There is some evidence to suggest that differences in the timing of mortality reporting in Indigenous populations have the potential to cause underestimation of mortality at the time of follow-up. In addition, we recorded all-cause late mortality rather than death from cardiovascular causes. A larger sample size would allow a more detailed analysis of the mechanisms of adverse outcomes and, potentially, the development of a more accurate operative

risk prediction model for Indigenous patients. Future studies should aim at increasing the sample size of Indigenous patients through national collaboration, while maintaining standardised definitions and data collection methods. Although we used the euroSCORE to adjust for surgical risk, the score has not been validated in the Indigenous population. We acknowledge the limitations of using this measure for risk stratification in the Indigenous population. but it is widely used throughout Australia and we believe it to be the best currently available tool for such a purpose.

While improving access of Indigenous Australians to advanced cardiovascular therapies is a major public health priority, improvements in outcomes will require comprehensive strategies that include attention to the primary and secondary prevention of both coronary artery and rheumatic heart disease.

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### **COMPETING INTERESTS**

None identified.

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