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Mortality and recurrent cardiac events after coronary artery bypass graft: long term outcomes in a population study

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Objective: To determine 30 day mortality, long term survival, and recurrent cardiac events after coronary artery bypass graft (CABG) in a population.
Design: Follow up study of patients prospectively entered on to a cardiothoracic surgical database. Record linkages were used to obtain data on readmissions and deaths.
Patients: 8910 patients undergoing isolated first CABG between 1980 and 1993 in Western Australia.
Main outcome measures: 30 day and long term survival, readmission for cardiac event (acute myocardial infarction, unstable angina, percutaneous transluminal coronary angioplasty or reoperative CABG).
Results: There were 3072 deaths to mid 1999. 30 day and long term survival were significantly better in patients treated in the first five years than during the following decade. The age of the patients, proportion of female patients, and number of grafts increased over time. An urgent procedure (odds ratio 3.3), older age (9% per year) and female sex (odds ratio 1.5) were associated with increased risk for 30 day mortality, while age (7% per year) and a recent myocardial infarction (odds ratio 1.16) influenced long term survival. Internal mammary artery grafts were followed by better short and long term survival, though there was an obvious selection bias in favour of younger male patients.
Conclusions: This study shows worsening crude mortality at 30 days after CABG from the mid 1980s, associated with the inclusion of higher risk patients. Older age, an acute myocardial infarction in the year before surgery, and the use of sephenous vein grafts only were associated with poorer long term survival and greater risk of a recurrent cardiac event. Female sex predicted recurrent events but not long term survival.

Western Australia is a large, geographically isolated state with a population approaching two million and low emigration rates. Until 1993 Western Australia had a single cardiothoracic surgical unit, which allows us to report population based figures for operative (30 day) mortality, long term survival, and recurrent major cardiac events after isolated coronary artery bypass graft (CABG) surgery among 8910 patients.

Operative mortality has been reported from single sites around the world for over 30 years. Recently, national bodies such as the Society of Thoracic Surgeons (STS) in the USA[1] and the Society of Cardiothoracic Surgeons in the UK[2] have amassed very large databases; other bodies operating at state and regional levels, such as those from New York,[3] Ontario,[4] and northern New England,[5] have provided risk adjusted operative mortality for very large populations.

Long term outcomes of CABG have been reported from North American[6–8] and European[9] databases, clinical trials[10] and the CASS (coronary artery surgery study) registry.[11] An important finding from long term follow up of patients from databases is the survival benefit conferred by arterial revascularisation.[12 13]

Within Australia, operative mortality among 12 000 subjects (1978–90) from one site has been reported,[14] as has the recurrence of symptoms within 10 years in the 4001 patients undergoing surgery between 1970–82[15] in the state of South Australia. Other reports are of small numbers, with even the most recent based on fewer than 2000 patients. The present population based study provides contemporary long term outcomes among patients who underwent isolated first CABG surgery from 1980 to March 1993.

METHODS

The data for the study were obtained by record linkage of three information systems: the cardiothoracic surgery clinical database, hospital morbidity data (HMD), and the Australian national death index.

The databases

The Department of Cardiothoracic Surgery at Royal Perth Hospital maintained a record of all cardiac and thoracic surgery undertaken, collecting information on public and private cases from 1978 to 1993. Records of isolated first CABG surgery were extracted to form the base set of data for this report. The Royal Perth Hospital ethics committee gave permission for access to the database and to hospital records.

The confidentiality of health information committee at the Health Department of Western Australia approved access to the information held in the state's HMD system. This system has recorded each public and private admission to an acute care hospital throughout Western Australia since 1971 and includes identifying information by which multiple records for a patient are collated under a unique root number. This enables a patient's contacts with the hospital system to be tracked. The Centre for Health Services Research at the

Abbreviations: AMI, acute myocardial infarction; CABG, coronary artery bypass graft; CI, confidence interval; HMD, hospital morbidity data; IMA, internal mammary artery; PCI, percutaneous catheter intervention; STS, Society of Thoracic Surgeons; CASS, coronary artery surgery study

Table 1 Characteristics of subjects by period of surgery

	1980–4	1985–9	1990–3	p Value
Number (total n=8910)	2640	3225	3045	
Male sex (%)	82	78	75.6	
Mean (SD) age (years)	57.6 (9.1)	61.3 (9.2)	63 (9.7)	<0.001
Median age men (years)	57	61	63	
Median age women (years)	62	65	67	
AMI previous year (%)	23.1*	23.2	19.3	
Mean (SD) number grafts	3.30 (1.3)	3.38 (1.3)	3.5 (1.3)	<0.001
⩾3 grafts (%)	72.7	75.8	77.6	<0.001
PCI in same admission (%)	0.9	1.8	1.3	
Age ⩾70 years (%)	8.5	20	27.7	<0.001

*1981–4. AMI, acute myocardial infarction; PCI, percutaneous catheter intervention.

University of Western Australia has linked the HMD with the state birth, death, cancer, and mental health registers to create the Western Australian Health Services linked database.[16] We merged the CABG surgery data with the 1980–96 subset of the Western Australia linked database to provide an extended collection of over 1.5 million records from which to derive morbidity and mortality outcomes.

To identify deaths of members of our cohort occurring outside Western Australia we obtained permission to search the national death index.

The committee for human rights at the University of Western Australia approved the study protocol.

Record linkage
The primary linkage used a public health system unique identifier for the majority of cases, plus date of birth and phonetic algorithm software to match names for admissions to private hospitals. Coding anomalies and spurious and missing data in key variables were corrected with information from original hospital records. Linkage to the national death index used date of birth and phonetic algorithm software to match by name, a process reported to have a sensitivity and a specificity of 88.8% and 98.2%, respectively.[17] In addition, we verified all matches with moderate or low probability against the state death and electoral rolls to ensure complete ascertainment of mortality. The linkage resulted in the identification of an additional 53 deaths. Overall, < 2% of deaths occurred outside Western Australia.[18]

Outcomes
Record linkage allowed us to determine operative mortality (defined as death within 30 days after the day of surgery), long term survival, and survival to a recurrent major cardiac event (first readmission for acute myocardial infarction (AMI), unstable angina, or repeat revascularisation procedure or a cardiac death).

Variables
The candidate independent variables available from the data were age, sex, period of surgery, recent AMI, number of grafts, use of an internal mammary artery (IMA) graft, and a percutaneous catheter intervention (PCI) in the same admission as the CABG. Recent AMI referred to infarction at any time in the year before the index CABG. Persons undergoing CABG in 1980 were excluded from these analyses, as data from the preceding year were not available. A PCI performed during the same admission as a CABG was used as an indicator of urgent surgery. In this context the CABG operations mostly would have been emergency surgery following failed angioplasty, although the date and time of the PCI were not recorded. The period 1990–3 was analysed separately to determine more accurately the association between the use of IMA grafts and outcomes. This variable had not been reliably documented earlier, as the surgical database, since its inception in the late 1970s, was not designed to capture changes in surgical technique. A field for IMA grafts was not added until after their use had become commonplace following the publication of the seminal paper by Loop and colleagues in 1986.[12] Nor could the use of IMA grafts be confirmed from the HMD, as a clinical code to distinguish them from saphenous vein grafts was not available before the *International classification of diseases*, ninth revision, clinical modification, in 1988, was adopted in Western Australia in 1989.

Statistical methods
To study trends over time we divided cases by year of the first CABG into three periods: 1980–4 (n = 2640), 1985–9 (n = 3225), and 1990 to March 1993 (n = 3045). We compared the characteristics of patients in each period using one way analysis of variance for means and the χ^2 test for categorical variables. The crude mortality at 30 days for each period was age standardised using the age structure of the cohort as the standard. Bivariate logistic regression was used to determine the factors predictive of mortality at 30 days. All candidate variables were entered into the models. There were significant univariate associations between the period of surgery and all other candidate variables and a significant interaction between period and age in the multivariate analysis for 30 day mortality. In models that included "period" the relation between period and 30 day mortality was regularly significant but with extreme confidence intervals. The confounding made interpretation of period as an independent variable difficult. These results are therefore not presented.

Non-parametric estimates of survival and survival free of a major recurrent cardiac event at 5, 10, 15, and 18 years were determined by the Kaplan-Meier method. We used the log rank test to compare the survival of the groups and the Cox proportional hazards model to determine the correlates of survival and event-free survival, with assumptions of proportionality being checked using log-minus-log plots. As there was a significant interaction between sex and the use of an IMA graft, data for male and female patients were modelled separately for the period 1990–3.

All tests were two tailed with a probability value of $p \leq 0.05$ considered significant. The 95% confidence intervals (95% CI) are reported. The data were analysed using SPSS for Windows version 9.0 (SPSS Inc, Chicago, Illinois, USA) statistical software.

RESULTS
Between January 1980 and March 1993, 8910 patients underwent isolated first CABG, with 3072 deaths to July 1999. The median follow up for survival was 9.4 years (maximum 19.5 years).

The median age at surgery rose throughout the study period (table 1). The proportion of those 70 years or older at operation increased from 5% in 1980 to 32% in 1993 and the proportion of women coming to surgery grew from under 16% to 27%.

The mean number of grafts placed increased over time; the proportion of single artery grafts fell from 9% in 1980–4 to

Table 2 Thirty day mortality (crude and age standardised) and cumulative incidence of repeat CABG to three years by period

	Total (%)	1980–4 (%)	1985–9 (%)	1990–3 (%)	2p
30 day mortality					
Total (crude)	1.9	0.5	2.8	2.3	<0.001
Men (crude)	1.6	0.4	2.7	1.6	<0.001
Men (age adjusted)	1.5	0.5	2.6	1.3	
95% CI		0.46 to 0.54	2.54 to 2.66	1.31 to 1.55	
Women (crude)	3.0	1.1	3.0	4.3	0.005
Women (age adjusted)	2.4	1.2	3.0	3.7	
95% CI		1.1 to 1.34	2.89 to 3.15	3.59 to 3.86	
Cumulative incidence of repeat CABG to three years					
Total		1.4	1.1	0.6	
Men		1.5	1.1	0.7	
Women		1.1	1.4	0.7	

CABG, coronary artery bypass graft; CI, confidence interval.

5.5% in 1990–3. Among those having an IMA graft in the period 1990–3, the mean (SD) age was 61 (9.5) years, significantly younger than those having only saphenous vein grafts (64 (9.6) years, $p < 0.001$). In the last full year of the study, 1992, 87% of those 50 years or younger had an IMA graft and the proportion fell to 50% for those over 70 years of age.

The lower proportion in 1990–3 of patients who had had an AMI in the year before surgery (table 1) may reflect the increasing time on the waiting list for non-urgent surgery, which was more than a year towards the latter part of the study period, or a falling clinical threshold for coronary revascularisation.

Operative (30 day) mortality

The operative (30 day) mortality was lowest in the earlier period, 1980–4 (table 2). Overall, 30 day mortality was significantly associated with age, rising from 0.7% in those under 60 years to 2.5% in 60–69 year olds and 6.4% in those over 80 years ($p < 0.001$). A PCI in the same admission and female sex increased risk while the use of an IMA graft significantly reduced risk. Table 3 shows the odds ratios and CIs for the covariates of early mortality. In 1990–3, increasing age was significantly associated with poorer outcome for both male and female patients, while the use of an IMA was associated with significant reduction in risk at 30 days for women only.

Among the subjects who had a repeat operation (n = 765) the operative mortality at 30 days was 8.6%. All of those requiring a second repeat operation (n = 26) survived the perioperative period.

Long term survival

The median survival for patients undergoing CABG was 16.5 years (95% CI 16.0 to 18.0 years). Survival estimated by the Kaplan-Meier method was 89% at 5 years, 73% at 10 years, 56% at 15 years, and 45% at 18 years for men, with corresponding figures for women of 87%, 70%, 51%, and 39% (fig 1A). The overall poorer survival for women was influenced by the greater difference in 1985–9, the only period in which survival for the sexes was significantly different. Survival was better for subjects in the 1980–4 group than for those who had surgery in the following decade (fig 2). Survival worsened with increasing age (fig 3A). IMA grafts in the period 1990–3 appeared to have a considerable effect on survival (fig 4A). Table 4 shows the results of the multivariate analysis of long term survival.

Heart disease and stroke were recorded as the cause of late death in nearly 60% of cases, with cancer accounting for a further 13%.

Recurrent cardiac events

The median time to the first major cardiac event was 10.0 years (95% CI 9.8 to 10.2 years), with event free survival, as for mortality, being significantly better for the 1980–4 group. Estimates of survival free of a new event were 93% at 1 year, 78% at 5 years, 50% at 10 years, and 25% at 15 years. Female sex was associated with an increased likelihood of a recurrent event (fig 1B), as was increasing age (fig 3B). In patients from 1990–3 an arterial graft appeared to reduce the risk for a recurrent event (fig 4B). The maximum follow up for this

Table 3 Factors associated with 30 day survival

	Odds ratio	95% CI	2p
30 day survival (overall)			
Age (per year)	1.08	1.06 to 1.10	<0.0001
PCI in same admission	3.26	1.48 to 7.18	0.004
IMA used	0.50	0.28 to 0.89	0.019
Female sex	1.39	1.003 to 1.94	0.047
Recent AMI	1.21	0.88 to 1.66	0.25
>3 grafts	0.92	0.64 to 1.32	0.65
Period 1990–3			
Age (per year)	1.09	1.05 to 1.12	<0.0001
Female sex	2.53	1.47 to 4.37	0.0009
PCI at same admission	3.38	0.94 to 12.09	0.06
>3 grafts	0.77	0.43 to 1.37	0.38
IMA used*	0.77	0.38 to 1.6	0.49
Recent AMI	0.97	0.58 to 1.6	0.91
Men			
Age (per year)	1.09	1.05 to 1.14	<0.0001
Women			
Age (per year)	1.08	1.02 to 1.13	<0.0001
IMA used	0.14	0.03 to 0.6	0.008

*Internal mammary artery (IMA) graft–sex interaction p = 0.039.

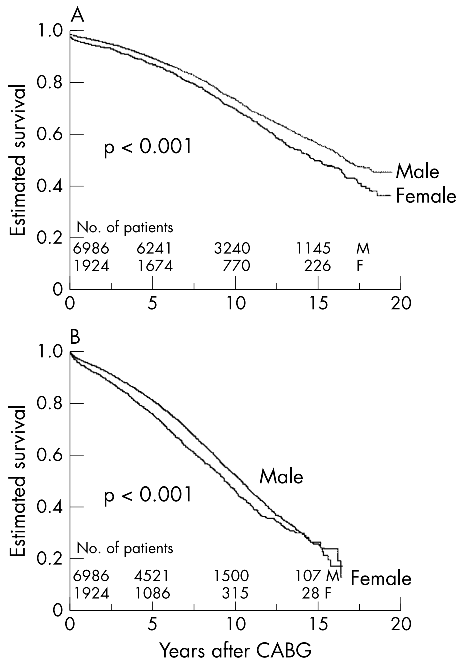

Figure 1 (A) Long term survival by sex. (B) Survival to recurrent event by sex.

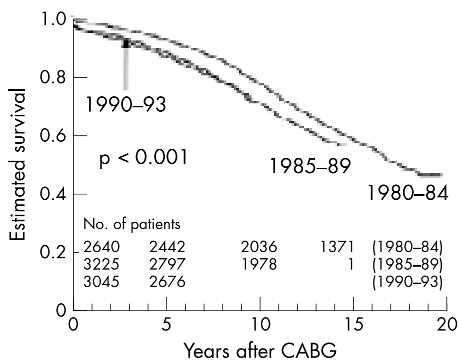

Figure 2 Long term survival by period of surgery.

period was 6.5 years, with a mean event-free survival of 5.3 (95% CI 5.2 to 5.4) years for those with saphenous vein grafts alone compared with 5.7 (95% CI 5.6 to 5.8) years for patients with an IMA graft.

Table 4 shows the covariates for survival to a first recurrent cardiac event.

The likelihood of a cardiac death as the first recurrent cardiac event increased with age (2.5% under 40 years, 20% for the oldest).

The median time to repeat operation (n = 735) was 8.4 (mean 8.1, maximum 16.4) years. The incidence of repeat CABG within three years was greatest among those who had surgery in the 1980–4 period (table 2). There was no apparent association between use of an IMA and the need for a reoperation within three years, though the numbers are small—10 end points among 1217 subjects with IMA (0.8%) versus 10 in 1828 subjects (0.5%) with only saphenous vein grafts.

Length of stay postoperatively varied little throughout the 1980s (median nine days) and fell to eight days in the early 1990s. Stay increased with age, with a median of 12 days for those over 80 years. Only older age and female sex were significantly associated with length of stay (data not shown).

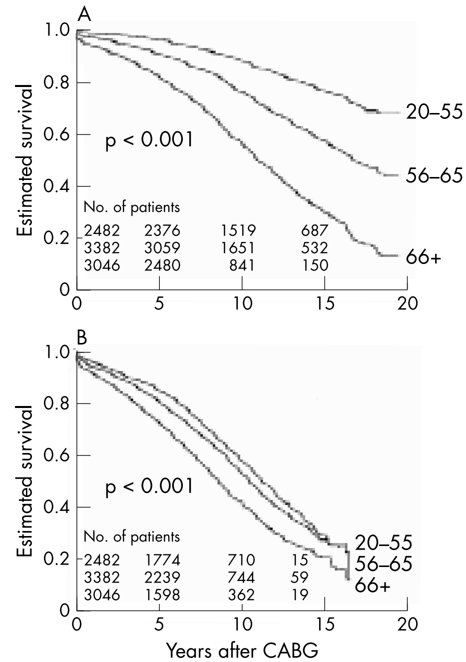

Figure 3 (A) Long term survival by age group. (B) Survival to recurrent event by age group.

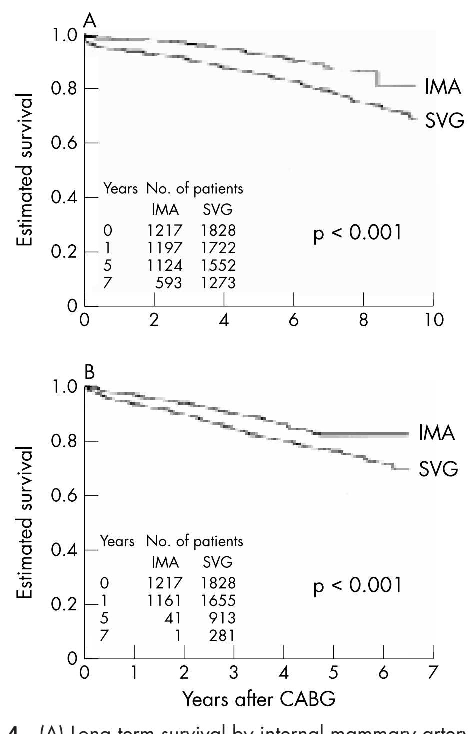

Figure 4 (A) Long term survival by internal mammary artery (IMA) versus saphenous vein graft (SVG) alone. (B) Survival to recurrent event by IMA versus SVG alone.

DISCUSSION

Thirty day operative mortality in this study was < 2% overall and remained under 3% despite the increased age of the patients and more complex coronary disease in the latest period. These crude figures are consistent with those from other centres. One Australian site recently reported a risk adjusted comparison of operative mortality with the STS database for 1867 patients from 1996 to 1998. The observed (crude) mortality was 2.25% and the expected, using the STS

Table 4 Factors associated with long term survival and survival to cardiac event

	Hazard ratio	95% CI	2p
Survival			
Age (per year)	1.07	1.06 to 1.08	<0.0001
AMI previous year	1.17	1.09 to 1.27	<0.0001
IMA used	0.66	0.55 to 0.77	<0.0001
⩾3 grafts	1.1	1.01 to 1.19	0.026
Female sex	0.91	0.84 to 0.99	0.04
PCI in same admission	1.04	0.76 to 1.41	0.81
Survival (1990–3)			
Age (per year)	1.07	1.05 to 1.07	<0.0001
IMA used	0.63	0.52 to 0.76	<0.0001
PCI in same admission	1.78	1.003 to 3.18	0.048
AMI previous year	1.15	0.98 to 1.3	0.08
Female sex	0.88	0.74 to 1.06	0.175
⩾3 grafts	1.12	0.92 to 1.37	0.26
Survival to cardiac event			
Age	1.02	1.019 to 1.26	<0.0001
AMI previous year	1.23	1.15 to 1.31	<0.0001
Female sex	1.13	1.04 to 1.22	0.002
IMA used	0.83	0.72 to 0.97	0.018
⩾3 grafts	0.95	0.88 to 1.02	0.18
PCI in same admission	1.09	0.84 to 1.43	0.50
Survival to cardiac event (1990–3)			
Age	1.027	1.02 to 1.03	<0.0001
AMI previous year	1.32	1.13 to 1.54	0.0003
IMA used	0.69	0.59 to 0.83	<0.0001
⩾3 grafts	0.79	0.66 to 0.94	0.008
Female sex	1.16	0.98 to 1.38	0.07
PCI in same admission	1.33	0.75 to 2.4	0.32

model, was 2.41%.[19] We do not have sufficient data contemporaneous with that of the STS to make a similar comparison.

Operative mortality in Western Australia has risen over time as surgery has been extended to an older and sicker population. This change probably also reflects the widespread use of angioplasty in lower risk patients. A large series from the Cleveland Clinic covering a similar period to our study found that, while crude operative mortality had risen in 1993–4 (3.44%) compared with 1986–8 (2.47%, p=0.013), when adjusted for increased preoperative risk, hospital mortality was not significantly worse (2.79% during 1986–8 versus 2.94% during 1993–4).[20]

No risk adjusted data for long term outcomes are available. Unadjusted survival to five years among patients in Western Australia (89%) is comparable to that reported from other cohorts in Australia of 88%[20] and 91%,[15] though these are not contemporaneous, being a decade earlier.

The most obvious trend over time is the increasing age at which people came to surgery, with the greatest proportional increase seen in those over 70 years. This was accompanied by increased perioperative risk, as well as reduced long term survival. The crude operative mortality at 30 days in our patients (> 70 years 3.5%, > 80 years 6.4%) compares favourably with that from other large, contemporaneous cohorts.[22–24]

When age was taken into account, women were at no disadvantage compared with men for long term survival, although they were at increased risk during the perioperative period. This finding of equivalent long term outcome but short term disadvantage has been reported among the patients in the CASS registry[11] and from several other cohorts.[25–27] Suggested explanations for the increased risk among women include physiological factors, comorbidities associated with older age, and underuse of proven treatments.[28–30]

The reduction in risk for those receiving an IMA graft in our cohort increased progressively with time since surgery. The very early and pronounced divergence in our cohort (4% at 12 months and 6% at three years) contrasts with that reported from the 9600 strong cohort from Belgium, where there was no difference in survival at one year and the use of an arterial graft was associated with improved survival of just 1% at three years for a "median" patient.[31] The greater benefit found among our patients is almost certainly associated with their selection on the basis of clinical and demographic factors that, in addition to the IMA graft, favour survival. Like others, we found that older patients, those requiring surgery urgently, and women were less likely to receive an arterial graft.[32]

Recurrent events are so idiosyncratically defined and reported in the wider literature that no comparisons can be drawn. In our study age, a recent AMI and female sex were associated with increased risk of the composite end point of admission for AMI, angina, or a revascularisation procedure or a cardiac death, while the use of an IMA graft appeared to be beneficial. While there are no large randomised controlled trials of arterial versus vein grafts alone, improved survival free from myocardial infarction, hospitalisation for cardiac causes, cardiac reoperation or any cardiac event is reported from clinical databases for patients with IMA grafts.[12 13] The observational studies are, however, at risk from the selection biases apparent in our cohort—patients receiving arterial grafts are more likely to be male, younger, and undergoing elective surgery.

Our finding of significantly reduced risk of a cardiac event associated with a greater number of grafts in 1990–3 may be related to the greater proportion of those having an IMA graft when the number of grafts was three or more, or it may indicate more complete revascularisation.

While randomised controlled trials set the standards for both unbiased determination of the efficacy and safety of treatments and the collection of uniform, complete, and validated data, clinical trials of CABG surgery represent a tiny proportion of the procedures performed and involve a select population. Contemporary information about the outcomes of changing surgical revascularisation techniques in changing populations is gleaned from databases, which, if of sufficient size and well managed, can generate knowledge about the large scale use of procedures in non-select populations and can lead to improved health care.[5 8 9 33] Although both clinical and administrative databases fall short of the standard set by clinical trials for the collection of data[34] and are open to confounding, prognostic models for five year survival derived from a large observational database and the three major randomised trials produced comparable results.[35]

Though national and regional databases are established in several countries and provide risk adjusted comparative and prognostic information based on very large series, there is no agreed national or international definition of the variables for a minimum dataset. Nor are the resources available to provide complete, validated data from each potential participating site, certainly within Australia. Though mortality follow up was complete, the clinical information available from our database was limited. The resources needed to maintain a growing database over years were insufficient to ensure high quality and complete data on patient related and operative variables for examination as possible covariates of survival. We had available age, sex and previous CABG but neither left ventricular function nor urgency of surgery, using instead an angioplasty in the same admission as an indicator of urgent surgery.

HMD need to be used cautiously in clinical research because of changes to the coding of disease over the decades.[36–38] This is especially so for longitudinal studies, as changing requirements for clinical detail to meet the needs of health policy and changes to funding arrangements have influenced the information recorded. We chose not to use HMD to study risk factors such as impaired renal function, hypertension, or diabetes, as these have been more thoroughly coded in recent years than previously. Despite these limitations the electronic linkage of three databases allowed us to retrieve information about the long term outcomes of CABG in a whole population that would not otherwise have been obtainable.

Conclusion

In a large Australian population we found low 30 day operative mortality and good long term survival to almost 20 years in patients undergoing CABG surgery. The prime importance of age as a determinant of both early and late outcomes is clear but we were unable to establish whether the influence was age per se or comorbidities. Operative mortality increased fivefold (0.5% to 2.7%) over the decade of the 1980s, steadying to 2.4% in 1990–3, and was associated with the increasing age of the patients, a greater proportion of women, and less single vessel coronary artery disease treated with surgery. The importance of collecting uniform, good quality data to enable risk adjusted comparisons at regional and national levels has been recognised and will improve the future reporting of outcomes.

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IMAGES IN CARDIOLOGY

Torsades de pointes in Prinzmetal's variant angina

A 49 year old woman with history of angina at rest and syncope was admitted for evaluation. During hospitalisation the patient was resuscitated following a cardiac arrest. Left cardiac catheterisation revealed coronary arteries without significant stenoses. Upright tilt testing and electrophysiological study were negative. Two weeks after discharge a symptomatic out-of-hospital ventricular tachycardia was recorded. The patient repeatedly experienced paroxysmal episodes of typical angina lasting up to 15 minutes. At rehospitalisation continuous telemetric electrocardiographic monitoring documented ST segment elevations (panel A) with premature ventricular contractions and short runs of torsades de pointes ventricular tachycardia (panel B). A spontaneous normalisation of ST segments with transient ST segment depression was observed 12 minutes after the symptoms and ECG changes had begun (panel B). Repeat coronary angiography on the following day showed spontaneous coronary artery spasms in multiple arteries (solid arrows in panels C and E) with transient occlusion of the first obtuse marginal branch of the left circumflex artery (open arrows in panel F). After intracoronary administration of glyceryl trinitrate there was normalisation of the coronary artery diameters (panels D and F) and ECG abnormalities.

The findings confirm that life threatening ventricular arrhythmia may occur in Prinzmetal's variant angina. Subsequently, the patient was treated with slow release molsidomine 16 mg, slow release isosorbide dinitrate 120 mg, and nifidipine 60 mg daily. During a follow up period of nine months, the patient was free of symptoms.

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