Prevalence of Dementia 7.5 Years after Coronary Artery Bypass Graft Surgery

Lisbeth A. Evered, B.Sc., M.Biostat., Ph.D., Brendan S. Silbert, M.B., B.S., F.A.N.Z.C.A., David A. Scott, M.B., B.S., Ph.D., F.A.N.Z.C.A., Paul Maruff, Ph.D., David Ames, B.A., M.D., F.R.C.Psych., F.R.A.N.Z.C.P.

ABSTRACT

Background: Although postoperative cognitive dysfunction (POCD) is well described after coronary artery bypass graft (CABG) surgery, a major concern has been that a progressive decline in cognition will ultimately lead to dementia. Since dementia interferes with the ability to carry out daily functions, the impact has far greater ramifications than cognitive decline defined purely by a decreased ability to perform on a battery of neurocognitive tests. The authors hypothesized that early cognitive impairment measured as baseline cognitive impairment is associated with an increased risk of long-term dementia.

Methods: The authors conducted a prospective longitudinal study on 326 patients aged 55 yr and older at the time of undergoing CABG surgery. Dementia was classified by expert opinion on review of performance on the Clinical Dementia Rating Scale and several other assessment tasks. Patients were also assessed for POCD at 3 and 12 months and at 7.5 yr using a battery of neuropsychologic tests and classified using the reliable change index. Associations were assessed using univariable analysis.

Results: At 7.5 yr after CABG surgery, the prevalence of dementia was 36 of 117 patients (30.8%; 95% CI, 23 to 40). POCD was detected in 62 of 189 patients (32.8%; 95% CI, 26 to 40). Due to incomplete assessments, the majority (113 patients), but not all, were assessed for both dementia and POCD. Fourteen of 32 (44%) patients with dementia were also classified as having POCD. Preexisting cognitive impairment and peripheral vascular disease were both associated with dementia 7.5 yr after CABG surgery. POCD at both 3 (odds ratio, 3.06; 95% CI, 1.39 to 9.30) and 12 months (odds ratio, 4.74; 95% CI, 1.63 to 13.77) was associated with an increased risk of mortality by 7.5 yr.

Conclusions: The prevalence of dementia at 7.5 yr after CABG surgery is greatly increased compared to population prevalence. Impaired cognition before surgery or the presence of cardiovascular disease may contribute to the high prevalence.
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OF adults older than 65 yr who undergo coronary artery bypass graft (CABG) surgery, a significant proportion suffer postoperative cognitive dysfunction (POCD) in the months after surgery.[1–3] POCD refers to an objectively measured decline in cognition after anesthesia and surgery. It is based solely on a decrease in cognitive performance detected by a change in performance on a battery of neuropsychologic tests administered by a trained examiner. Many studies have documented the incidence of POCD in the months and years after cardiac anesthesia and surgery. When these tests are administered before hospital discharge, POCD is detected in 14 to 48% of patients.[2,4–8] Cognitive impairment persists in approximately 30% of cardiac surgery patients for 6 weeks and in approximately 25% for 3 months.[2,4–6]

Despite the difficulties inherent in long-term follow-up, several investigators have attempted to determine the incidence of POCD over periods greater than a year to determine the extent to which POCD after cardiac

What We Already Know about This Topic

- Although postoperative cognitive dysfunction (POCD) is well described after coronary artery bypass graft (CABG) surgery, it is unclear if a progressive decline in cognition will ultimately lead to dementia.
- The authors investigated whether baseline POCD is associated with an increased risk of long-term dementia in a prospective longitudinal study on 326 patients aged 55 yr and older at the time of undergoing CABG surgery.

What This Article Tells Us That Is New

- The prevalence of dementia at 7.5 yr after coronary artery bypass graft surgery is greatly increased compared to population prevalence. Impaired cognition before surgery or the presence of cardiovascular disease may contribute to the high prevalence.

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surgery is long lasting. Newman *et al.*[2] identified an incidence of POCD of 42% 5 yr after cardiac surgery. An increased incidence at 5 yr was also found by Stygall *et al.*[9] although other investigators have identified either no decline[10] or minimal changes after 5 yr.[11]

The primary objective of cardiac surgery is to improve clinical and functional outcome. Therefore, it is important to identify not only whether POCD is present as a long-term adverse event but also whether its presence impacts negatively on the functional activities of daily life. Newman *et al.*[12] used a number of tests to assess quality of life after cardiac surgery and showed that decreased quality of life correlated with poor cognitive function at 5 yr after cardiac surgery.

A major concern after cardiac surgery has been that progressive decline in cognitive function will ultimately lead to dementia. This is important because dementia has profound consequences for patients, families, society, and ultimately the economy. The prevalence of dementia has been steadily increasing as the population ages, and any exacerbation after cardiac surgery would have profound implications on healthcare management of the elderly and the economy. To date, there has been no prospective evaluation of dementia after cardiac surgery. Several retrospective studies, such as case-controlled database analyses or retrospective meta-analyses on the incidence of dementia after noncardiac surgery, have provided conflicting results.[13–18]

There has, thus, been a call for a prospective study of the incidence of dementia after anesthesia and surgery to provide high-level evidence to resolve this issue.[19] This has become increasingly important because not only is the incidence of dementia increasing as the population ages, but also anesthesia and surgery is an increasingly common procedure in the elderly.[20] Moreover, if baseline cognitive function or POCD is indeed an antecedent of dementia, the identification and management of these may offer an avenue for averting the descent into dementia.

The aims of this study were to prospectively identify the prevalence of dementia at 7.5 yr after CABG surgery and relate this to baseline cognition and POCD at 7.5 yr.

Materials and Methods

Subjects and Study Design

We conducted a prospective longitudinal study on patients who had undergone first-time elective CABG surgery and were enrolled in a study comparing cognitive outcomes after being randomized to receive either high- or low-dose fentanyl anesthesia.[21] The outcome for POCD up to 12 months has been previously published and showed no significant difference in cognitive outcomes between the high- and low-dose fentanyl groups.[21] After the 12-month assessment, patients were invited to participate in this follow-up study. The long-term follow-up was scheduled at 7.5 yr. The trial was registered in the Australian New Zealand Clinical Trials Registry (ACTRN12605000285651). The St. Vincent's Hospital Human Research Ethics Committee (Melbourne, Victoria, Australia) approved the study at each of three participating sites, and written informed consent was obtained from all participants.

Eligible patients were aged ≥55 yr at entry, were fluent in English, had no previous neurologic deficit, and were amenable to undergo neuropsychological testing. Exclusion criteria included history of stroke or transient ischemic attack, treatment with sedatives, and a clinical history of dementia.

Neuropsychologic Testing

The test battery consisted of the Consortium to Establish a Registry for Alzheimer's Disease-Auditory Verbal Learning Test (CERAD-AVLT), Digit–Symbol Substitution Test, Trail Making Test Parts A and B, Controlled Oral Word Association Test, Semantic Fluency Test, and the Grooved Pegboard Test (dominant and nondominant hands). The National Adult Reading Test was used to estimate intelligence quotient. All of these tests have been described elsewhere.[21] The results are given as the number of correct responses or the time taken to complete the test. All patients underwent baseline testing within 1 week before their procedure.

A control group was used for the purpose of calculating POCD using the reliable change index (RCI).[22] This group constituted 51 subjects recruited from the community as part of a parallel investigation, the Australian Cognition Evaluation study (ACTRN12607000049471).[23] These subjects were aged 60 yr and older, had large joint osteoarthritis, and had no surgery planned for the next 12 months. Otherwise, they met the inclusion and exclusion criteria for the CABG surgery patients. These participants underwent neuropsychologic testing with the same battery of tests, and at the same time intervals, as the study patients to 12 months.

RCIs were determined by subtracting the preoperative score (X_1) from the postoperative score (X_2), giving Δ_X for each individual participant for a given task. The mean expected change for the controls Δ_Xc, calculated in the same way, was then subtracted from this, removing any practice effect. This score was then divided by the SD for the change in test results of the control group SD(Δ_{Xc}), controlling for the expected variability. These scores were then used to create a combined test score ($Z_{combined}$) using the sum of Z scores for each test ($\sum Z_{a,b,c,d,etc.}$) divided by the SD of this summation in the control group [SD($\sum Z_{control}$)]. POCD was defined in an individual when their RCI score was less than −1.96 on more than or equal to 2 tests, and/or their combined z-score was less than −1.96.

We used preexisting cognitive impairment (PreCI) as a measure of baseline cognitive function because it has been used widely before anesthesia and surgery.[24–26] Preexisting cognitive deficit was classified where patients demonstrated a deficit of more than or equal to 2 SD below published norms in more than or equal to 2 tests.[26]

Postoperative testing was completed at 7 days, 3 months, 12 months, and 7.5 yr. Testing was done at the patient's home to provide a more relaxed and stress-free environment.[27]

Test scores were analyzed to identify POCD using the RCI.[22,28] As 7.5 yr had not elapsed since the control group were first tested, we employed the RCI method of Van Dijk *et al*.[29] using control data to 12 months.

Dementia

Dementia was classified by an experienced academic old-age psychiatrist (D.A.) with over two decades' experience in the regular use of the clinical dementia rating (CDR) and assessment of dementia using clinical review. He is chair of the Australian Biomarker Imaging and Lifestyle Diagnostic Group, which uses clinical review for the classification of mild cognitive impairment and dementia.[30] The global CDR represents a five-point ordinal scale, where CDR value of 0 indicates no dementia, and CDR value of 0.5, 1, 2, and 3 indicate questionable, mild, moderate, and severe dementia, respectively. This scale can also be classified as the CDR sum of boxes, an 18-point ordinal scale (0 to 18) providing a more sensitive measure of impairment, which has been advocated as the best tool for clinical trial outcomes.[31] Patients who were unable to provide an informant were not included in the classification of dementia. Tasks completed in addition to the CDR that informed the classification of dementia included the following:

1. The Informant Questionnaire for Cognitive Decline in the Elderly[32]
2. The recall component of the CERAD-AVLT (part of the POCD neuropsychologic battery but not used for classification of POCD)
3. The mini-mental state examination[33]
4. Instrumental Activities of Daily Living Questionnaire[34]
5. The Geriatric Depression Score[35]

The psychiatrist made diagnoses based on all cognitive and functional data collected from subject and informant at the home visit, but blind to previous and algorithm-derived diagnoses. He also rerated every CDR based on data obtained at the visit in order to ensure consistency of rating on this instrument. As has been the case with research conducted by the developers of the CDR, some subjects who met criteria for dementia still had an overall CDR rating of 0.5.

Statistical Analysis

As this was a follow-up study, no *a priori* power calculations were undertaken. Since there was no difference in the incidence of POCD between those receiving high-dose fentanyl and those receiving low-dose fentanyl when assessed to 12 months in the original study,[21] these groups (fentanyl dose) were combined for the purpose of the current study. Group comparisons were made using unpaired *t* tests or ANOVA for continuous variables, the Spearman ranked correlation coefficient or Kruskal-Wallis test for ranked data, and chi-square or Fisher exact test for dichotomous variables. One-way ANOVA was used to assess any differences between participants, those lost to follow-up, and controls. Associations were determined using univariable analysis (appendix 1). Cox proportional hazard regression was used for investigation of associations between POCD and mortality. Tests were performed using STATA (version 12.0; Stata Corp., USA). A probability value of <0.05 was taken to indicate statistical significance.

Results

There were 326 patients in the original study who were eligible to enroll in this follow-up study.[21] We were unable to locate 50 patients at 7.5 yr afterward, but we have included their results to 12 months. The remaining 276 patients were considered for inclusion in this long-term follow-up. The patient flow profile is shown in figure 1. For assessment of dementia, 72 patients were unable to provide an informant and were therefore unable to be classified for dementia. Of the analyzed cohort, 117 of 193 (60.6%) completed dementia classification and 189 of 193 (97.9%) patients completed long-term POCD follow-up assessment, with 113 completing both assessments; four patients were assessed for dementia without being assessed for POCD (fig. 1).

The demographic and outcome data for both groups analyzed and those lost to follow-up are shown in table 1. Differences between groups were observed only for diabetes and the rate of POCD at 12 months, which were both higher in the group lost to follow-up.

Patient and control group characteristics are shown in table 2. Patients were younger, had a higher proportion of males, and had a higher incidence of cardiovascular risk factors than controls. The long-term follow-up assessment was completed at a median of 7.4 (interquartile range, 6.1 to 9.0) yr when the patients' mean age was 75.2 ± 7.3 yr.

Dementia was classified in 36 of 117 (30.8%) patients (95% CI, 23 to 40) at the 7.5-yr assessment. Four of these patients undertook the dementia assessment but did not complete the battery for POCD classification. Table 3 demonstrates the outcome scores for cognitive tests and Instrumental Activities of Daily Living (IADL) for dementia patients *versus* nondementia patients. All test scores except CERAD-AVLT immediate were significantly lower

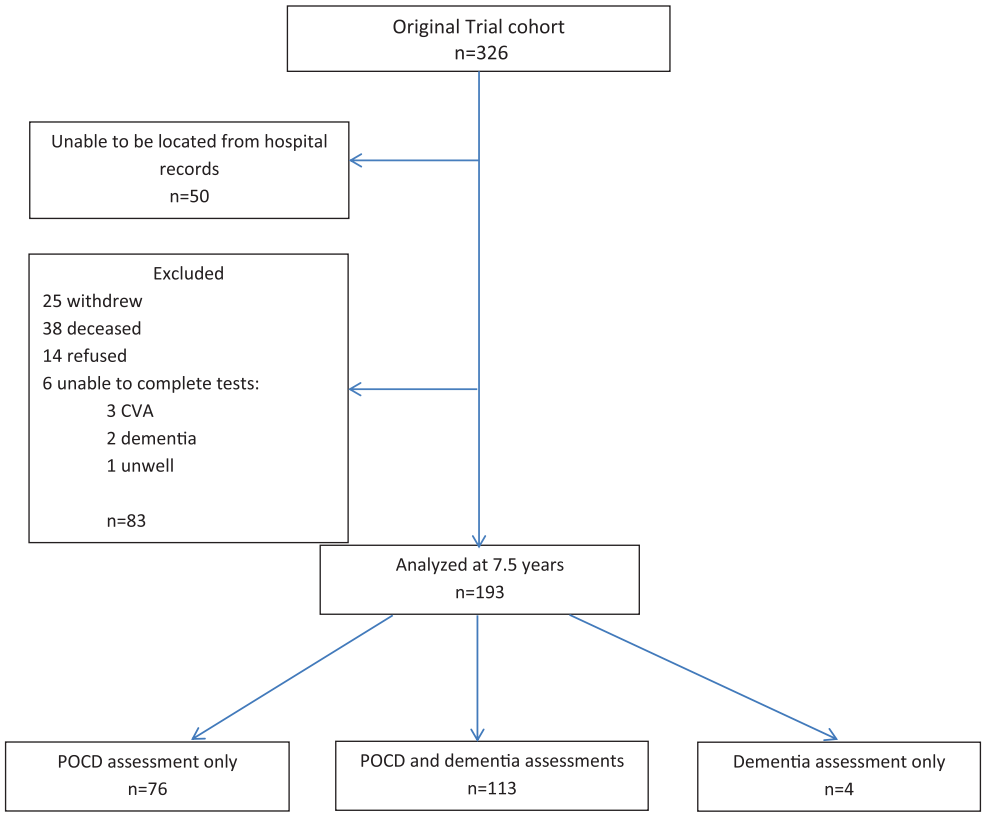

Fig. 1. Trial profile for assessment at 7.5 yr after coronary surgery. CVA = cerebrovascular accident; POCD = postoperative cognitive dysfunction.

Table 1. Data for Patients Completing 7.5-yr Assessment *versus* Loss to Follow-up

	POCD or Dementia (n = 80)	POCD and Dementia (n = 113)	Loss to Follow-up (n = 133)	*P* Value
Age (yr)	67.6 (8.2)	67.7 (7.0)	68.4 (7.8)	0.65
Gender (M/F)	59/21	89/24	104/29	0.68
Height (cm)	168.7 (10.3)	171.1 (8.4)	170.5 (9.0)	0.19
Weight (kg)	81.2 (15.7)	82.0 (11.8)	83.0 (15.8)	0.67
Body mass index (kg/m^2)	28.5 (5.4)	28.0 (4.0)	28.5 (4.7)	0.70
Diabetes	21 (26%)	21 (19%)	45 (34%)	0.03
Hypertension	53 (66%)	85 (75%)	94 (71%)	0.40
Peripheral vascular disease	12 (15%)	18 (16%)	18 (14%)	0.16
History of myocardial infarct	32 (40%)	59 (52%)	61 (46%)	0.24
History of smoking	48 (60%)	84 (74%)	99 (74%)	0.05
Hypercholesterolemia	58 (72%)	90 (80%)	98 (74%)	0.44
Estimated intelligence quotient	107.4 (10.4)	109.4 (9.2)	109.0 (9.8)	0.34
Apolipoprotein E4 positive	22 (34%)	28 (31%)	29 (27%)	0.63
Preoperative medications				
Statins	41 (51%)	81 (72%)	83 (63%)	0.01
β-Blockers	49 (61%)	65 (58%)	70 (53%)	0.49
ACE inhibitors	28 (35%)	36 (32%)	52 (39%)	0.47
Cognitive impairment				
PreCI	26 (32%)	31 (27%)	48 (36%)	0.35
POCD 3 mo	8 (10%)	13 (12%)	15 (13%)	0.83
POCD 12 mo	8 (10%)	2 (2%)	13(12%)	0.01

Data are presented as mean (SD) or n (%); three groups compared using one-way ANOVA.
ACE = angiotensin-converting enzyme; F = female; M = male; POCD = postoperative cognitive dysfunction; PreCI = preexisting cognitive impairment.

Table 2. Patient and Control Demographics and Medical History

	POCD or Dementia (n = 80)	POCD and Dementia (n = 113)	Controls (n = 51)	*P* Value
Age (yr)	67.5 (8.2)	67.7 (7.0)	72.0 (7.2)	< 0.01
Gender (M/F)	59/21	89/24	13/38	< 0.01
Height (cm)	168.7 (10.3)	171.1 (8.4)	166.0 (8.6)	< 0.01
Weight (kg)	81.2 (15.7)	82.0 (11.8)	75.3 (17.3)	0.02
Body mass index (kg/m^2)	28.5 (5.4)	28.0 (4.0)	27.2 (5.0)	0.28
Diabetes	21 (26%)	21 (19%)	6 (12%)	0.13
Hypertension	53 (66%)	85 (75%)	34 (67%)	0.32
Peripheral vascular disease	12 (15%)	8 (7%)	3 (6%)	0.11
History of myocardial infarct	32 (40%)	59 (52%)	7 (14%)	< 0.01
History of smoking	48 (60%)	84 (74%)	20 (39%)	< 0.01
Hypercholesterolemia	58 (73%)	90 (80%)	26 (51%)	< 0.01
Estimated intelligence quotient	107.4 (10.4)	109.4 (9.2)	115.4 (9.0)	< 0.01
Apolipoprotein E4 positive	22 (34%)	28 (31%)		
Preoperative medications				
Statins	41 (51%)	81 (72%)	21 (45%)	< 0.01
β-Blockers	49 (62%)	65 (58%)	6 (13%)	< 0.01
ACE inhibitors	28 (35%)	36 (32%)	11 (23%)	0.39

Data are presented as mean (SD) or n (%); three groups compared using one-way ANOVA.

ACE = angiotensin-converting enzyme; F = female; M = male; POCD = postoperative cognitive dysfunction.

Table 3. Assessment Scores at 7.5 Yr for Dementia *versus* No Dementia

Assessment	Dementia (n = 36)	No Dementia (n = 81)	*P* Value
CDR-SB	2.2 (2.9)	0.0 (0.1)	< 0.001
IQCODE	3.30 (0.57)	2.89 (0.46)	< 0.001
CERAD-AVLT	15.5 (3.2)	16.5 (3.3)	0.15
CERAD-AVLT (delayed recall)	2.4 (1.9)	3.5 (1.8)	0.006
MMSE	24.8 (4.6)	26.9 (2.5)	0.003
IADL	33.8 (11.8)	41.4 (4.0)	< 0.001

Data are presented as mean (SD).

CDR-SB = clinical dementia rating sum of boxes: 0 (no dementia) to 18 (severe dementia); CERAD-AVLT = Consortium to Establish a Registry for Alzheimer's Disease Auditory-Verbal Learning Test (number of words); IADL = instrumental activities of daily living: 0 (worst) to 45 (no decline); IQCODE = Informant Questionnaire for Cognitive Decline in the Elderly (>3 reflects decline); MMSE = mini-mental state examination: 0 (worst) to 30 (best).

for those patients who met criteria for dementia. The test scores for the cognitive battery used to test for POCD for those with and without dementia at 7.5 yr are shown in appendix 2.

POCD was classified in 62 of 189 (32.8%; 95% CI, 26 to 40%) patients at 7.5 yr. Of those assessed for both dementia and POCD (n = 113), 14 of 32 (44%) with dementia also met criteria for POCD. Eight of 36 (22.2%; 95% CI, 10 to 39%) patients with POCD at 3 months had died by 7.5-yr follow-up, compared to 20 of 267 (7.5%; 95% CI, 5 to 11%) without POCD (P < 0.01). Similarly for those with POCD at 12 months, 6 of 23 (26.1%) patients (95% CI, 10 to 48%) had died by 7.5 yr, while only 20 of 276 (7.2%; 95% CI, 4 to 11%) without POCD at 12 months died (P < 0.01). A classification of POCD at 3 months or at 12 months was associated with an increased risk of mortality at 7.5 yr postoperatively, adjusted odds ratio (OR) of 3.06 (95% CI, 1.39 to 9.30) at 3 months and adjusted OR of 4.74 (95% CI, 1.63 to 13.77) at 12 months. Figure 2 shows the Cox proportional hazard survival curve for POCD at 12 months and mortality risk, adjusted for age and intelligence quotient.

Preexisting cognitive impairment was identified in 105 of 326 (32.2%; 95% CI, 27 to 38) patients at baseline. There was no difference in the incidence of PreCI between the original study sample (105/326 [32.2%]) and either the subgroup completing 7.5 yr dementia assessment (33/117 [32.7%]) or the subgroup completing 7.5 yr POCD assessment (55/189 [29.1%]). Patients with PreCI were significantly more likely to be classified with dementia at 7.5-yr follow-up (15/33; 45.5%) compared with those without PreCI (21/84; 25.0%; P = 0.03). POCD at 3 (36/303, 11.8%) or 12 months (23/300, 7.7%) was associated with POCD at 7.5 yr (62/189, 32.8%; P < 0.01, P = 0.03, respectively) but was not associated with dementia at 7.5 yr (36/117, 30.8%; P = 0.60, P = 0.16, respectively).

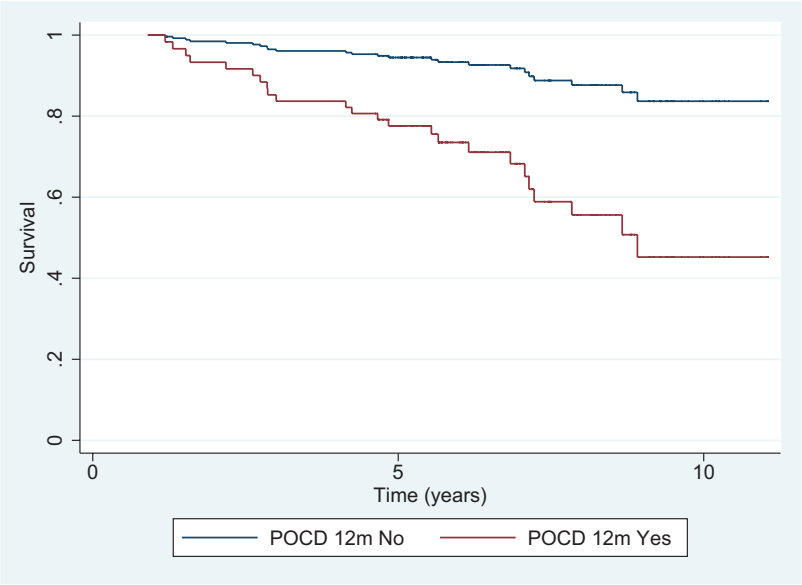

Fig. 2. Adjusted Cox proportional hazard ratio curve for postoperative cognitive dysfunction (POCD) at 12 months and mortality risk.

Table 4. Univariable Odds Ratios for Predictors of 7.5-yr Dementia

	Univariable Regression	
Predictor	Odds Ratio (95% CI)	*P* Value
Dementia 7.5 yr		
Age at enrolment	1.02 (0.97–1.08)	0.48
Estimated IQ	0.96 (0.92–1.00)	0.07
PreCI	2.50 (1.07–5.82)	0.03
Peripheral vascular disease	7.43 (1.84–29.99)	0.01

IQ = Intelligence quotient; PreCI = preexisting cognitive impairment.

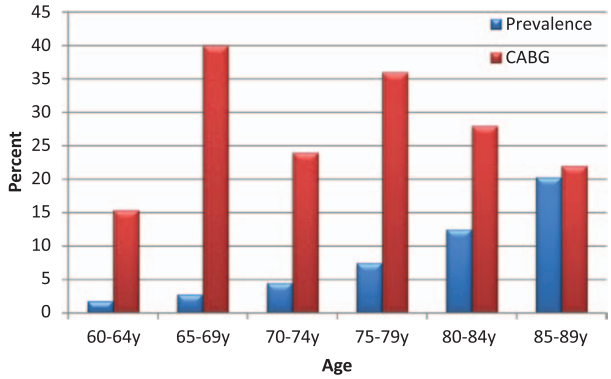

Fig. 3. Prevalence of dementia 7.5 yr after coronary artery bypass graft (CABG) surgery by age group *versus* corresponding population data.

Univariable analysis of all demographic and comorbid variables (appendix 1) demonstrated that dementia at 7.5 yr was associated with PreCI (OR, 2.50 [95% CI, 1.07 to 5.82]) and with peripheral vascular disease (OR, 7.43 [95% CI, 1.84 to 29.99]; table 4).

Discussion

This prospective study shows that at 7.5 yr after CABG surgery, the prevalence of dementia is 30.8% in patients aged 55 yr and older at the time of surgery and whose mean age at the time of assessment was 75.2 yr. The population prevalence of dementia in Australia is 9% for individuals aged 65 yr and older,[36] and this is consistent with other world regions (fig. 3).[37] The high prevalence of dementia 7.5 yr after CABG surgery greatly exceeds that found in general population studies. A diagnosis of dementia using expert assessment is likely to give a greater prevalence than reliance on clinical reporting of dementia, which is used in population studies (especially when done retrospectively). Although there are reports of the prevalence of dementia in retrospective studies after CABG surgery,[13,38] we were unable to find any reports comparing prevalence using retrospective outcomes with the prevalence when dementia is assessed by expert opinion.

A prevalence of 30.8% of dementia after CABG surgery is in direct contrast to the few retrospective studies, which have sought an association between CABG surgery and dementia. Knopman *et al.*[38] retrospectively identified 24 CABG surgery patients from the medical records of 557 cases of dementia in a population case-controlled study of dementia and were unable to find an association. Seitz *et al.*[13] examined 15 case-controlled studies (both cardiac and noncardiac surgery) and found no association between surgery and dementia. Recognizing the limitations of case-controlled studies, the authors called for prospective studies to provide high-level evidence, echoing the same call from a consensus statement at the First International Workshop on Anesthetics and Alzheimer's disease.[19]

The increased prevalence of dementia in the long term after CABG surgery may be the consequence of the

anesthesia and surgery, or alternatively it may be due to the natural decline in cognition in elderly patients who have cardiovascular disease severe enough to warrant cardiac surgery. We did not follow a nonsurgical control group with concomitant cardiovascular disease, so are unable to distinguish these two issues. Selnes *et al.*[39] and Selnes and Gottesman[40] have shown that patients with cardiac disease exhibit the same cognitive decline whether they were treated surgically or medically, which suggested that anesthesia and surgery with cardiopulmonary bypass were not implicated in the genesis of cognitive decline. This view is supported by Newman *et al.*,[41] who showed dementia incidence to be increased by 30% after 5 yr in patients with a history of cardiovascular disease, further supporting that cardiovascular disease increases the prevalence of dementia.

In contrast, a retrospective study by Lee *et al.*[42] found that the adjusted risk of dementia up to 6 yr after CABG surgery *versus* percutaneous transluminal coronary angioplasty was 1.71 (95% CI, 1.02 to 2.87; $P = 0.04$), suggesting that patients undergoing CABG surgery were at an increased risk for dementia compared to patients with cardiovascular disease who did not undergo CABG surgery.

In addition to the prevalence of dementia, we also found that 32.8% of patients met criteria for POCD at 7.5 yr after CABG surgery. This was preceded by a high rate of early decline at 3 months, followed by apparent recovery[21] before further decline at 7.5 yr, reflecting a similar postoperative cognitive trajectory to that described by Newman *et al.*[2] However, not all investigators have found such a rate of POCD 5 yr after CABG surgery,[9,11,39] and one investigation was unable to find persistent long-term POCD.[10]

The choice of control group has a direct effect on the rate of POCD. We used 12-month control data to calculate 7.5-yr incidence of POCD, following the work of Van Dijk *et al.*,[29] who used 3-month data to calculate the long-term incidence of POCD. If further cognitive deterioration occurred during subsequent years in the control group, this would tend to overestimate the incidence of POCD in the study group at 7.5 yr. In addition, the use of a control group with little cardiovascular disease may have inflated the true incidence of POCD in patients who have undergone CABG surgery.

Loss to follow-up in studies tracking long-term POCD ranges from 34 to 42%. The loss to follow-up in the current study is 41%, which is in keeping with other long-term follow-up studies. This is explicable when one takes into account the long time period until the final testing and the many reasons for loss to follow-up that are unavoidable over this time period (fig. 1). The onset of dementia is a slow process, and protracted studies on dementia are all prone to patient attrition. In this study, diabetes and the rate of POCD at 12 months were both higher in the group lost to follow-up, which would suggest that if these variables are associated with long-term outcome, this group would likely perform worse than the groups who completed 7.5-yr assessments.

Previous studies of cognitive decline after CABG surgery have employed measurements of cognitive function (*e.g.*, POCD) rather than the direct assessment of dementia. Not surprisingly, in this prospective study, we observed an overlap between these two classifications. Forty-four percent of patients with dementia were also classified with POCD at 7.5 yr, indicating incomplete overlap between dementia and POCD. POCD has been the construct most often used after cardiac surgery to attribute cognitive decline, but relies solely on the results of objective cognitive testing and does not take into account other limitations required for a diagnosis of dementia. Over half the patients with POCD did not classify with dementia, indicating that daily function may be maintained, even though cognitive decline is demonstrable on neuropsychologic testing. This is supported by the scores observed in the tools used to assess dementia (table 3), where significant differences were observed between those with dementia and those without dementia, except for the CERAD-AVLT (which is a component of the neuropsychologic battery used to assess POCD).

Baseline cognitive impairment defined by PreCI was present in 32.2% of patients, consistent with previous studies before cardiac surgery.[24] PreCI was predictive of dementia at 7.5 yr. Selnes *et al.*[43] observed that cognitive decline was related to preoperative cognitive status and occurred to a greater extent in patients with cardiovascular disease (regardless of surgical or medical treatment) than healthy controls. This agrees with population studies that show that subtle cognitive impairment precedes dementia,[44] and suggests cognitive decline after CABG surgery may share characteristics with the nonsurgical population. Peripheral vascular disease was also a predictor of dementia, which reinforces the association of cardiovascular disease with dementia. Newman *et al.*[41] similarly demonstrated that individuals with peripheral vascular disease were 2.5 times more likely to develop dementia, suggesting peripheral vascular disease may reflect part of a disease process that contributes to dementia. In summary, the risk factors for long-term dementia after CABG surgery share risk factors found in population studies, which have not specifically focused on CABG surgery.

Early postoperative cognitive impairment assessed as POCD was predictive of long-term POCD, but not long-term dementia. This may be due to PreCI representing a static measure of preoperative cognition, while POCD is a measurement of change that is subject to baseline performance.

Death up to 7.5 yr was associated with POCD at 3 (OR, 3.06; 95% CI, 1.39 to 9.30) and at 12 months (OR, 4.74; 95% CI, 1.63 to 13.77). POCD has previously been shown to be associated with increased mortality at 1 yr postoperatively after noncardiac surgery.[45]

Limitations of this study include the lack of a formal assessment of dementia at baseline, such that we are only able to identify a prevalence (not incidence) of dementia at 7.5 yr. However, it is unlikely any patients with dementia were enrolled at baseline because all patients underwent a full battery of neuropsychologic testing at baseline, being required to complete all tests at this time point, and no patient was enrolled who had a known diagnosis of mild cognitive impairment, dementia, or any identified cognitive complaint. Another limitation, common to all long-term follow-up studies, is the reduced number of participants completing 7.5-yr dementia and POCD assessments. There was no difference in the incidence of PreCI in the whole cohort (32.2%) or either of the subgroups completing dementia assessment at 7.5 yr (32.7%) or POCD assessment at 7.5 yr (29.1%), indicating baseline cognition was consistent across these groups. Thus, these findings are likely generalizable to the rest of the original sample. A further limitation as a result of the small available sample size is our inability to identify any impact of other demographic or comorbid factors utilizing multivariable analysis techniques. Finally, for dementia, we did not follow a nonsurgical group with concomitant cardiovascular disease, and therefore we have used population data for comparison. Taken together, these limitations may have led to either an increased or a decreased estimate of the dementia prevalence.

In conclusion, we have demonstrated that older individuals undergoing CABG surgery are at an increased risk of dementia in the ensuing 7.5 yr compared to population data. We also identified an association between POCD at 3 and 12 months and mortality to 7.5 yr. Since baseline cognitive function is an important predictor of long-term dementia, this suggests that appropriate preoperative cognitive assessment may allow identification of vulnerable individuals.

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Competing Interests

The authors declare no competing interests.

Correspondence

Address correspondence to Dr. Silbert: Department of Anaesthesia and Acute Pain Medicine, St. Vincent's Hospital, PO Box 2900, Fitzroy, Victoria 3065, Australia. brendan.silbert@svha.org.au. Information on purchasing reprints may be found at www.anesthesiology.org or on the masthead page at the beginning of this issue. ANESTHESIOLOGY's articles are made freely accessible to all readers, for personal use only, 6 months from the cover date of the issue.

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Appendix 1. Demographic and Comorbid Variables at Baseline

Age	Gender
Height	Weight
Body mass index	Obesity*
Estimated IQ	History of or current smoking*
Hypertension*	Diabetes*
Hypercholesterolemia*	Peripheral vascular disease*
History AMI*	History of TIA
ApoE positive	CVRF
β-Blockers	Preexisting cognitive impairment
ACE inhibitors	Anesthetic group
Statins	Left ventricular function
Aspirin	Instrumental activities of daily living
Geriatric Depression Scale	Family history of Alzheimer disease
CCF	Time to assessment
Death up to 7.5 yr	

*CVRF (cardiovascular risk factors) are composed of the composite of seven variables and ranked 0 to 7.

ACE = angiotensin-converting enzyme; AMI = acute myocardial infarction; ApoE = apolipoprotein E; CCF = congestive cardiac failure; IQ = intelligence quotient; TIA = transient ischemic attack.

Appendix 2. Test Scores at 7.5 Yr in Individuals with Dementia and without Dementia

Assessment	Dementia (n = 30)	No Dementia (n = 80)	*P* Value
CERAD-AVLT	15.5 (3.2)	16.5 (3.3)	0.15
DSST	29.5 (10.7)	34.0 (10.0)	0.04
TMT A	64.3 (28.2)	54.3 (32.9)	0.14
TMT B	166.9 (87.8)	126.8 (65.8)	0.01
COWAT	32.0 (10.7)	33.8 (11.3)	0.46
CERAD semantic fluency	15.0 (4.3)	16.5 (4.7)	0.14
GPBD	109.7 (33.8)	104.2 (24.6)	0.35
GPBND	131.8 (54.8)	122.4 (40.8)	0.33

All data are presented as mean (SD).

CERAD = Consortium to Establish a Registry for Alzheimer's Disease-semantic fluency (animals); CERAD-AVLT = Consortium to Establish a Registry for Alzheimer's Disease-Auditory Verbal Learning Test; COWAT = Controlled Oral Word Association Test; DSST = Digit Symbol Substitution Test; GPBD = Grooved Peg Board Test, Dominant; GPBND = Grooved Peg Board Test, Nondominant; TMT A = Trail Making Test Part A; TMT B = Trail Making Test Part B.