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This is the published version of a paper published in *Critical Care Medicine*.

Citation for the original published paper (version of record):

Claesson Lingehall, H., Smulter, N., Lindahl, E., Lindkvist, M., Engström, K G. et al. (2017)
Preoperative Cognitive Performance and Postoperative Delirium Are independently Associated
With Future Dementia in Older People Who Have Undergone Cardiac Surgery: A Longitudinal
Cohort Study.

Critical Care Medicine, 45(8): 1295-1303

<https://doi.org/10.1097/CCM.0000000000002483>

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Preoperative Cognitive Performance and Postoperative Delirium Are Independently Associated With Future Dementia in Older People Who Have Undergone Cardiac Surgery: A Longitudinal Cohort Study*

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*See also p. 1411.

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All authors have done substantial contributions to conception and design. Dr. Lingehall helped in data collection, data interpretation, selection of statistical methods, data analysis, and preparation of article. Ms. Smulter helped in data collection, data interpretation, and preparation of article. Dr. Lindahl helped in data interpretation and preparation of article. Dr. Lindkvist helped in selection of statistical methods, data interpretation, data analysis, and preparation of article. Dr. Engström helped in study design, data interpretation, and preparation of article. Dr. Gustafson helped in study design, data interpretation, and preparation of article. Dr. Olofsson helped in study design, data interpretation, and preparation of article. All authors have read and approved the final version of the article.

This study was supported by grants from the Heart Foundation of Northern Sweden, the Erik and Anne-Marie Detlof Foundation, the Dementia Foundation, the Borgerskapet in Umeå Research Foundation, Gamla Tjänarinnor, the Medical Faculty at Umeå University, the University of Umeå, the County Council of Västerbotten, and the Strategic Research Program in Care Sciences, Sweden.

Drs. Lindahl and Olofsson disclosed receiving funding from the Heart and Lung Foundation; their institutions received funding from the Dementia Foundation, Strategic Research Program in Care Sciences, Sweden, and Gamla Tjänarinnor; they also received support for article research from the Heart and Lung Foundation of Northern Sweden, the Erik and Anne-Marie Detlof Foundation, the Dementia Foundation, the Borgerskapet in Umeå Research Foundation, Gamla Tjänarinnor, the Medical Faculty at

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DOI: 10.1097/CCM.0000000000002483

Umeå University, the University of Umeå, the County Council of Västerbotten, and the Strategic Research Program in Care Sciences, Sweden. The remaining authors have disclosed that they do not have any potential conflicts of interest.

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Objective: To investigate if postoperative delirium was associated with the development of dementia within 5 years after cardiac surgery.

Design: Longitudinal cohort study.

Setting: Cardiothoracic Division, Umeå University Hospital, Sweden.

Patients: Patients aged 70 years old or older ($n = 114$) scheduled for routine cardiac procedures with cardiopulmonary bypass without documented dementia were enrolled in 2009.

Intervention: Structured assessments were performed preoperatively, 1 and 4 days after extubation, and 1, 3, and 5 years postoperatively.

Measurements and Main Results: Patients were assessed comprehensively, including cognitive and physical function, coexisting medical conditions, demographic characteristics, and medications. Diagnoses of delirium, depression, and dementia were made according to Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision criteria. During the 5-year period, 30 of 114 participants (26.3%) developed dementia. Postoperative delirium had occurred in 87% of those who later developed dementia. A multivariable logistic regression model showed a lower preoperative Mini-Mental State Examination score ($p < 0.001$; odds ratio, 0.68; 95% CI, 0.54–0.84) and the occurrence of postoperative delirium ($p = 0.002$; odds ratio, 7.57; 95% CI, 2.15–26.65) were associated with dementia occurrence.

Conclusions: Our findings suggest that older patients with reduced preoperative cognitive functions or who develop postoperative delirium are at risk of developing dementia within 5 years after cardiac surgery. Cognitive functions should be screened for preoperatively, those who develop postoperative delirium should be followed up to enable early detection of dementia symptoms, and management should be implemented. (*Crit Care Med*; 45:1295–1303)

Key Words: cardiac surgery; cardiovascular disease; delirium; dementia, older people

Delirium after cardiac surgery commonly, occurs in 25–67% of patients (1–4). Delirium is a neuropsychiatric syndrome characterized by a change in cognition fluctuates, develops over a short period of time and has an underlying cause (5). Old age, diabetes, volume load during operation (6), and low preoperative Mini-Mental State Examination (MMSE) score (7) are risk factors for delirium after cardiac surgery. Postoperative delirium (POD) is often characterized by initial decline and a prolonged period of cognitive impairment after cardiac surgery (2).

Dementia is a general term used to describe cognitive impairment that interferes with daily life (5). Associations of cardiovascular disorders (CVD) with mild cognitive impairment (MCI) and dementia have been found (8, 9). Other reported risk factors for dementia are diabetes (10) and depression (11). In a meta-analysis including elderly hospitalized patients, delirium was associated with increased risks of institutionalization for dementia and death (12). In a population-based study of the oldest old (aged ≥ 85 yr), a history of delirium was shown to be associated with accelerated cognitive decline and an eight-fold increased risk of dementia (13).

A Swedish study showed that approximately 17% of individuals aged 75 years old or older had dementia and that the prevalence had decreased from the late 1980s to the early 2000s despite an increase in survival rate (14). However, a population-based cohort (aged ≥ 85 yr) study from northern Sweden showed that the age-specific prevalence of dementia had increased over 5 years, from 26.5% to 37.2%. The proportion of those who had undergone cardiac surgery more than doubled during the same period, from 2.1% to 4.7% (15). The authors discussed that one possible interpretation could be that old people who survived surgery were exposed to a greater risk of dementia development due to their coexisting CVD (15). Furthermore, in a systematic review investigating long-term outcomes in patients undergoing cardiac surgery showed that patients who exhibit POD had a greater likelihood of cognitive and functional decline (16). Few studies have examined the long-term consequences of POD and the development of cognitive decline and dementia in older patients (≥ 70 yr) who have undergone cardiac surgery (2, 17).

Thus, the aim of this study was to investigate whether or not POD is associated with the development of dementia among patients aged 70 years old or older during a 5-year follow-up to cardiac surgery with cardiopulmonary bypass (CPB). We hypothesized that dementia risk would be increased in patients with POD.

METHODS

This study was part of a longitudinal cohort study involving 153 consecutive patients aged 70 years old or older who underwent cardiac surgery with CPB between February and October 2009 at the Cardiothoracic Department of Umeå University Hospital, Sweden.

The inclusion criteria were being scheduled for cardiac surgery including coronary artery bypass grafting, aortic replacement, and/or repair with and without procedures involving the ascending aorta, mitral valve, or combinations thereof. Exclusion criteria were acute procedures (within 24 hr, due to administrative reasons and preoperative testing), documented psychiatric disease or dementia, severe visual/ hearing problems and not fluent in Swedish. All participants received a standardized general anesthesia including propofol, midazolam, fentanyl, pancuronium, and isoflurane in air/oxygen. Propofol infusion was continued until extubation in the ICU. Postoperative pain relief generally encountered oral paracetamol and oxycodone and, if necessary, IV ketobemidone.

Approval was obtained from the regional ethical review board Umeå Sweden (Dnr 08-169M, Dnr 2010-34-32, Dnr 2011-315-32M, and Dnr, 2014-107-32M).

Participants and Procedures

One hundred forty-two patients completed baseline assessment in 2009 (Fig. 1). These patients were invited to three follow-ups at 1, 3, and 5 years after surgery. Follow-ups included home-visits with comprehensive assessments. Inclusion criteria for the present study was that the participants had completed assessments of cognition, depression, delirium, and physical function required for the diagnosis of dementia. Exclusion criterion was death before 5-year follow-up without documented dementia. Nineteen died (malignant disease $n = 8$, cardiovascular diseases $n = 7$, cerebrovascular diseases $n = 1$, and infections $n = 3$), and nine declined participation during these 5 years. Thus, the final study sample consisted of 114 participants (Fig. 1). Those excluded ($n = 28$) were comparable to the study cohort in terms of age, education, preoperative MMSE score, depression, and proportion of patients experiencing POD. The relative proportion of women and those with severe heart failure were somewhat more frequent in the excluded group than

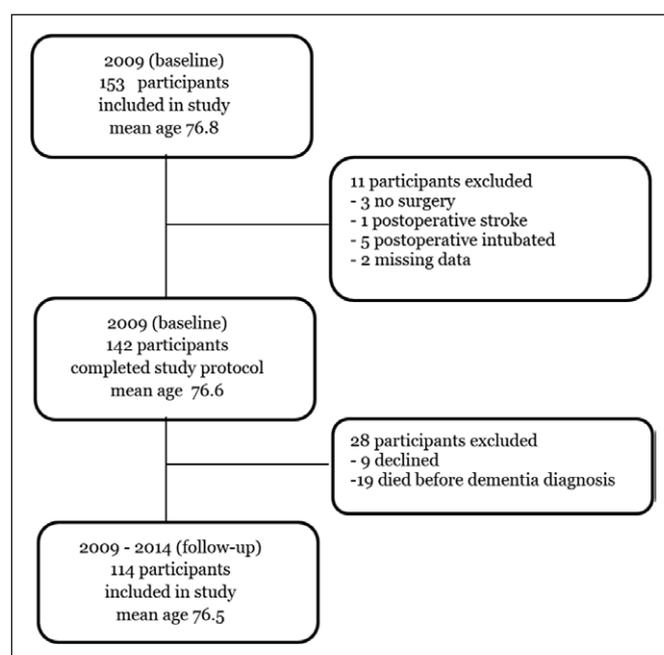


Figure 1. Flow chart of the study protocol.

in the analyzed cohort. Structured assessments were performed preoperatively (T1) and 1 and 4 days after extubation (T2 and T3, respectively) and 1, 3, and 5 years after surgery (T4, T5, and T6, respectively). Six participants declined participation at T4 and/or T5, but overall 88.6% participated in all six interviews at T6.

Assessments

Two specialized registered nurses followed the participants throughout the 5-year study period. Assessments of cognitive and physical function were performed and coexisting medical conditions, demographic characteristics, and drug prescriptions were collected during face-to-face interviews with patients, healthcare professionals, and, when necessary, next of kin. During the 5-year follow-up period, five participants moved and underwent similar assessment by telephone.

The MMSE was used to assess patients' cognitive function, which is scored from 0 to 30 (18). Five participants were interviewed via telephone. It has been shown that using MMSE by telephone versus face-to-face interviews strongly correlates ($r = 0.85$) (19). None of the five participants interviewed by telephone had signs of cognitive impairment indicating dementia. The Organic Brain Syndrome (OBS) scale was developed for the clinical evaluation of various behavioral, psychiatric, and emotional symptoms that appear in cases of organic brain disorders, such as delirium, depression, and dementia in older people (20,

21). The OBS scale data are based on observations and interviews with participants, caregivers, and next of kin. Physical function status was assessed using the Katz Staircase of independence in activities of daily living (ADL), including instrumental ADL (I-ADL) and personal ADL (P-ADL) (22). In this study, I-ADL and P-ADL were assessed and scores were dichotomized (independent/dependent). Depressive symptoms were assessed using the 15-item Geriatric Depression Scale (GDS-15). Scores in GDS-15 range from 0 to 15, higher scores indicating more depressive symptoms (23). The scale has a high sensitivity and specificity for detecting depression (24). Ongoing treatment with antidepressants prescribed for depressive disorders was considered to indicate depression and information from OBS.

The same diagnostic procedures for POD, depression, and dementia were used for all participants. After completing the study, a nurse and a physician specialized in geriatric medicine used MMSE and OBS assessments to diagnose POD according to criteria of the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition, Text Revision (DSM-IV-TR) (5). The same physician performed the final interpretations of all collected data. The diagnosis of dementia and depression was based on the DSM-IV-TR criteria (5) by reviewing and evaluating repeated documentations and assessments (the GDS-15 and OBS for depression and MMSE and OBS for dementia).

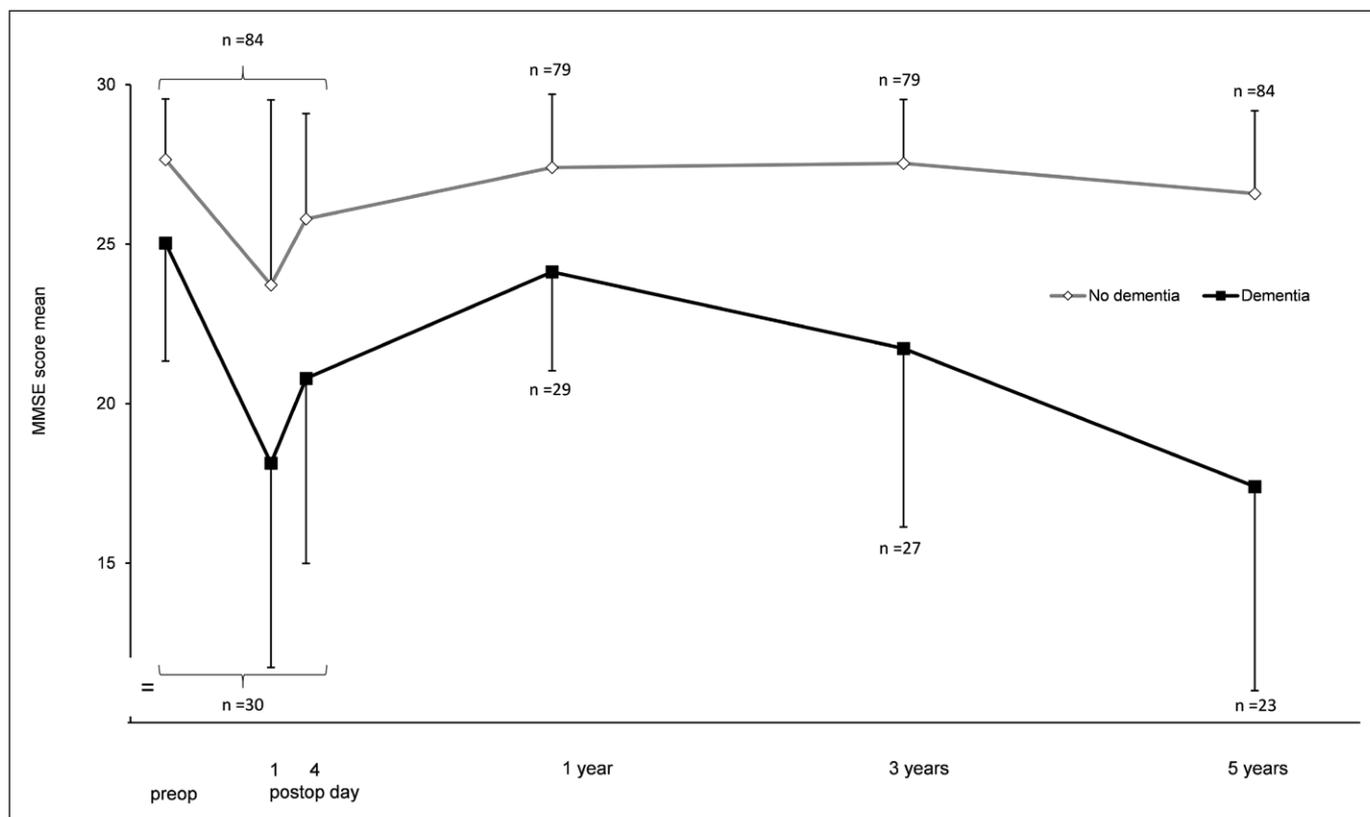


Figure 2. Mini-Mental State Examination (MMSE) scores over time in participants with and without dementia. The time axis is plotted in day and years on a log scale and reflect mean and sd. Inclusion 2009 (T1 = preoperative, T2 = postoperative day 1, T3 = postoperative day 4; mean age, 76.5 yr); 1-year 2010 (T4; mean age, 77.6 yr), 3-year 2012 (T5; mean age, 79.8 yr), and 5 years (T6; mean age, 81.6 yr) after surgery. Differences were significant ($p < 0.05$, t test) at all time points and decline in MMSE score over time was steeper for those with dementia ($p < 0.001$, generalized estimating equation analysis). Mean (sd) MMSE score, without dementia/dementia: T1 = 27.7(1.9)/25.0(3.7), T2 = 23.7(5.8)/18.1(6.4), T3 = 25.8(3.3)/20.8(5.8), T4 = 27.4(2.3)/24.1(3.1), T5 = 27.5(2.0)/21.7(5.6), and T6 = 26.6(2.6)/17.4(6.4).

Statistical Analysis

Baseline characteristics of the participants were separated into preoperative, operative, and postoperative variables. Continuous variables were expressed as means and SDs; categorical data were expressed as numbers and percentages. Changes in MMSE score over time (T1–T6) were investigated in participants with and without development of dementia (Fig. 2) and in participants with and without POD (Fig. 3). For an overview, differences between these groups at each time point were explored using independent-samples *t* tests (complemented with nonparametric tests). To investigate differences between groups in decline in MMSE over time while adjusting for multiple measurement of each participant, generalized estimating equations including a cross-term between group and time was used. Gamma distributed outcome with identity link function was used due to the non-normality of MMSE and a completely general correlation structure was assumed to adjust for multiple measurements.

Univariate logistic regression analyses were used to estimate associations between dementia as dependent against independent variables. Variables at *p* < 0.10 were selected for multivariable analysis. Tests for variable interaction were conducted using cross-terms.

Preoperative and operative/postoperative variables were analyzed separately in two multivariable models, using backward elimination (*p* < 0.05). Finally, a combined multivariable model including all final preoperative, operative, and postoperative variables was constructed. Age and sex were included in all multivariable models, due to their assumed principal importance. Statistical significance was defined as *p* value of less than 0.05. The results of logistic regression models are presented as odds ratios with 95% CI. All analyses were performed using SPSS software (version 21.0 for Windows; IBM, Armonk, NY).

RESULTS

Overall baseline characteristics (*n* = 114) and by dementia group are shown in Table 1. The mean age of the 114 participants was 76.5 years. None had a documented dementia diagnosis prior to surgery, but 7.9% (9/114) had preoperative MCI. Sixty-four of 114 (56.1%) developed POD. In total, 30 participants (26.3%) developed dementia during the 5-year follow-up period. At 1-, 3-, and 5-year follow-ups, 6, 9, and 15 participants were identified with a dementia diagnosis (mean age of participants with dementia, 77.5, 79.8, and 81.6 years, respectively). Of the 30 participants who developed dementia,

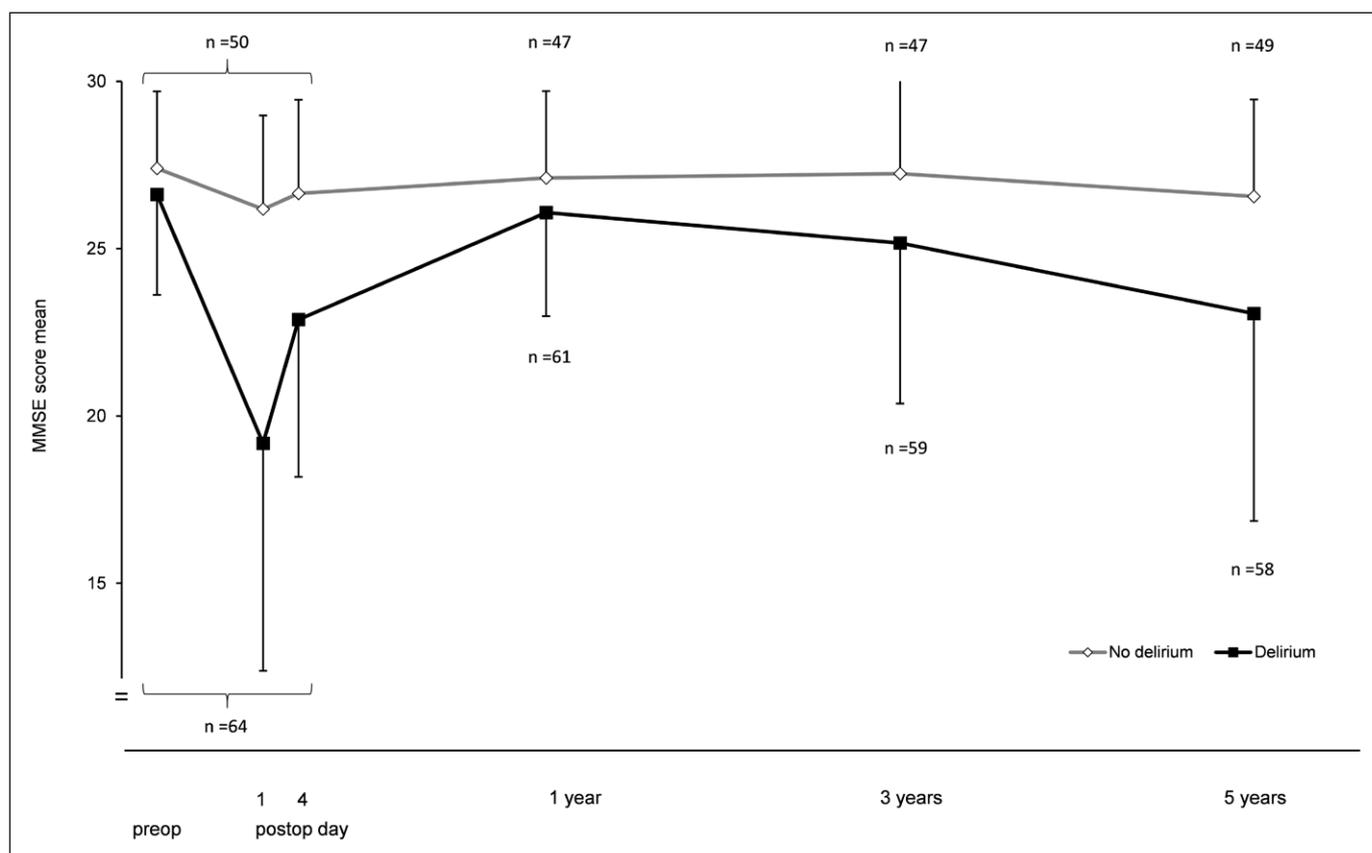


Figure 3. Mini-Mental State Examination (MMSE) scores over time in participants with and without delirium. The time axis is plotted in day and years on a log scale and reflect mean and SD. Inclusion 2009 (T1 = preoperative, T2 = postoperative day 1, T3 = postoperative day 4; mean age, 76.5 yr); 1-year 2010 (T4; mean age, 77.6 yr), 3-year 2012 (T5; mean age, 79.8 yr), and 5 years (T6; mean age, 81.6 yr) after surgery. No significant difference was observed at T1 or T4 (*p* < 0.05, *t* test) and decline in MMSE score over time was steeper for those with dementia (*p* < 0.001, generalized estimating equation analysis). Mean (SD) MMSE score, no delirium/delirium: T1 = 27.4(2.3)/26.6(3.0), T2 = 26.2(2.8)/19.2(6.8), T3 = 26.7(2.8)/22.9(4.7), T4 = 27.1(2.6)/26.1(3.1), T5 = 27.2(2.8)/25.2(4.8), and T6 = 26.6(2.9)/23.1(6.2).

TABLE 1. Participants' Baseline Demographics in Total, and Among Those With and Without Dementia in an Univariate Logistic Regression Analysis

Characteristics	All Patients (n = 114)	Without Dementia (n = 84)	Dementia	Univariate, p
Preoperative variables				
Age (yr)	76.5±4.4	75.9±3.9	78.3±5.1	0.010 ^a
Sex (female)	35 (30.7)	29 (34.5)	6 (20.0)	0.14 ^b
Body mass index	26.6±3.9	26.7±3.9	26.2±3.8	0.56
Impaired vision	104 (91.2)	75 (89.3)	29 (97.7)	0.25
Impaired hearing	27 (23.7)	19 (22.6)	8 (26.7)	0.65
Living with partner	70 (61.4)	56 (66.7)	14 (46.7)	0.06 ^a
Numeric rating scale of pain (0–10, n = 83/30)	1.7±2.0	1.7±2.0	1.9±2.2	0.60
Instrumental-activities of daily living (dependent)	39 (34.2)	26 (31.0)	13 (43.4)	0.22
Personal-activities of daily living (dependent)	4 (3.5)	1 (1.2)	3 (10.0)	0.06 ^a
MMSE score (0–30)	27.0±2.8	27.7±1.9	25.1±3.6	0.0001 ^a
MMSE score (< 24)	9 (7.9)	1 (1.2)	8 (26.7)	0.0017 ^c
Education ≥ 7 yr	54 (47.4)	46 (54.8)	8 (26.7)	0.010 ^a
Geriatric Depression Scale score (0–15)	2.3±2.0	2.3±2.0	2.3±2.1	0.91
Depression	14 (12.3)	7 (8.3)	7 (23.3)	0.04 ^a
Sleeping disorder	35 (30.7)	29 (34.5)	6 (20.0)	0.14
Diabetes	19 (16.7)	11 (13.1)	8 (26.7)	0.09 ^a
Cerebrovascular history	17 (14.9)	12 (14.3)	5 (16.7)	0.75
Malignant disease	9 (7.9)	8 (9.5)	1 (3.3)	0.30
Myocardial infarction (previous)	46 (40.4)	32 (38.1)	14 (46.7)	0.41
New York Heart Association Functional Classification				
I (class)	4 (3.5)	3 (3.6)	1 (3.3)	0.92
II (class)	31 (27.2)	24 (28.6)	7 (23.3)	0.91
III (class)	66 (57.9)	47 (56.0)	19 (63.3)	0.87
IV (class)	13 (11.4)	10 (11.9)	3 (10.0)	0.94
Left ventricular function (reduced)	33 (28.9)	23 (27.4)	10 (33.3)	0.54
Systolic arterial blood pressure mm Hg	139.5±21.2	139.1±20.2	140.6±24.2	0.74
Diastolic arterial blood pressure mmHg	75.2±10.3	75.1±9.9	75.4±11.5	0.87
Previous cardiac surgery	6 (5.3)	5 (6.0)	1 (3.3)	0.32
Previous percutaneous coronary intervention	18 (15.8)	15 (17.9)	3 (10.0)	0.32
No. of drugs prescribed	5.7±2.4	5.7±2.2	5.6±2.7	0.95
Anticoagulants	100 (87.7)	76 (90.5)	24 (80.0)	0.14
β-blockers	82 (71.9)	63 (75.0)	19 (63.3)	0.23
Calcium channel blockers	32 (28.1)	23 (27.4)	9 (30.0)	0.56
Antilipemic agents	79 (69.3)	64 (76.2)	15 (50.0)	0.009 ^a
Antidepressants	6 (5.3)	3 (3.6)	3 (10.0)	0.194
Diuretics	42 (36.8)	26 (31.0)	16 (53.3)	0.032 ^a
Renin–angiotensin–aldosterone system blockers	67 (58.8)	50 (59.5)	17 (56.7)	0.79

(Continued)

TABLE 1. (Continued). Participants' Baseline Demographics in Total, and Among Those With and Without Dementia in an Univariate Logistic Regression Analysis

Characteristics	All Patients (n = 114)	Without Dementia (n = 84)	Dementia	Univariate, <i>p</i>
Operative and postoperative variables				
Coronary artery bypasses grafting isolated	67 (58.8)	52 (61.9)	15 (50.0)	0.26
Valve procedures isolated	23 (20.2)	14 (16.7)	9 (30.0)	0.12
Combined procedures	24 (21.1)	18 (21.4)	6 (20.0)	0.87
Operation time (hr)	2.9±0.9	3.0±0.9	2.7±0.8	0.11
Cardiopulmonary bypass time (hr)	1.4±0.6	1.4±0.6	1.4±0.6	0.97
Ventilator time (hr)	6.9±3.3	6.5±2.8	7.9±4.4	0.06
ICU time (hr)	22.3±19.4	21.5±21.8	24.6±9.7	0.47
Postoperative delirium	64 (56.1)	38 (45.2)	26 (86.7)	0.0004 ^a
Blood loss (L)	0.4±0.4	0.5±0.4	0.4±0.2	0.77
Volume load, blood excluded (L)	3.8±1.1	3.8±1.2	3.7±0.9	0.52
Cerebrovascular injuries	4 (3.5)	1 (1.1)	3 (10)	0.06 ^a

MMSE = Mini-Mental State Examination.

^aVariables tested in the multivariable models, with a $p < 0.10$.

^bVariables added at multivariable testing due to their expected principal importance rather than its statistical influence at univariate testing.

^cVariables ($p < 0.10$) avoided in the multivariable models because of covariability against other used parameter.

p values refer to univariate logistic regression analyses. Data are presented as mean ± sd or *n* (%). Combined procedures are combination of coronary artery bypasses and/or valve surgery and/or intervention of the ascending aorta.

26 (87.7%) had developed POD and 8 (26.7%) of them had preoperative cognitive impairment (MMSE < 24). Among those 30, there was one death at 3 years and five deaths at 5 years.

Participants who developed dementia had significantly lower MMSE scores than those without dementia before and after cardiac surgery, as well as throughout the follow-up period ($p < 0.001$). The decline in MMSE score from baseline (over year 1 and year 3) to year 5 was greater among participants who developed dementia than among those who did not ($p < 0.001$) (Fig. 2).

Preoperative MMSE score did not differ between those who did and did not develop POD. No interaction effect was present between preoperative MMSE score and POD.

However, both groups differed significantly at the 3- and 5-year follow-ups. The mean MMSE scores decline was greater among participants with POD than among those without ($p < 0.001$) (Fig. 3)

Univariate logistic regression analyses showed significant differences between those who did and did not develop dementia. Participants diagnosed with dementia were older, had lower preoperative MMSE scores, were less educated, and were less commonly treated with antilipemic agents. Of those who developed dementia, compared with control participants, the prescription of standard-type diuretic drugs was more frequent, and they more often were diagnosed with depression (Table 1).

No significant interaction between independent variables was detected in relation to dementia. A multivariable logistic regression model identified the following preoperative variables

associated with dementia: male sex, lower preoperative MMSE score, not living with a partner, and not being treated with antilipemic agents. Analyses of operative and postoperative variables showed that age and POD were associated with dementia. In the final combined model, lower preoperative MMSE score and POD remained significantly associated with the development of dementia within 5 years after surgery (Table 2) and there was no significant interaction between MMSE score and POD.

DISCUSSION

We found that 26.3% of participants with no documented preoperative diagnosis of dementia developed this condition within 5 years after cardiac surgery and that 87% of those also had developed POD. All participants' MMSE scores declined over time, but this decline was more prominent among those who developed dementia. Lower preoperative MMSE score and POD was associated with the development of dementia within 5 years after cardiac surgery.

Other studies conducted among older people in different settings have shown that delirium is a strong risk factor for dementia (12, 13, 25, 26). Results of this present study support the study hypothesis that risk of dementia is increased in patients with POD after cardiac surgery.

In the present study, more than one fourth of participants with a mean age of 76.5 years developed dementia within 5 years. Developing dementia increases with age. A review that investigated an European population estimated prevalence of dementia were

TABLE 2. Logistic Regression Analyses Displaying Factors Independently Associated With Dementia, Within 5 Years After Cardiac Surgery

Variable (Unit)	Univariate					Multivariate				
	p	Wald	OR	CI low	CI high	p	Wald	OR	CI low	CI high
Preoperative variables										
Age (yr)	0.01	6.67	1.13	1.03	1.25	0.18	1.77	1.08	0.96	1.22
Sex (female)	0.14	2.13	0.47	0.17	1.29	0.02	5.58	0.19	0.05	0.76
MMSE score (0–30)	<0.0001	15.14	0.70	0.58	0.84	0.0004	12.42	0.70	0.57	0.85
Living with partner	0.06	3.64	0.44	0.19	1.02	0.04	4.32	0.30	0.09	0.93
Education (\geq 7 yr)	0.01	6.62	0.30	0.12	0.75					
Personal activities of daily living (dependent)	0.06	3.57	9.22	0.92	92.39					
Depression	0.04	4.27	3.35	1.06	10.54					
Diabetes	0.09	2.82	2.41	0.86	6.75					
Antilipemic agents	0.01	6.80	0.31	0.13	0.75	0.03	4.60	0.31	0.11	0.90
Diuretics	0.03	4.62	2.55	1.09	5.99					
Operative and postoperative variables										
Age (yr)	0.01	6.67	1.13	1.03	1.25	0.03	4.81	1.13	1.01	1.25
Sex (female)	0.14	2.13	0.47	0.17	1.29	0.23	1.43	0.52	0.17	1.53
POD	0.0004	12.65	7.87	2.52	24.53	0.0039	11.10	5.75	1.75	18.89
Ventilator time ICU (hr)	0.06	3.45	1.12	0.99	1.27					
Cerebrovascular history	0.06	3.57	9.22	0.92	92.39					
Combined preoperative, operative, and postoperative variables										
Age (yr)						0.13	2.26	1.09	0.97	1.23
Sex (female)						0.13	2.29	0.38	0.11	1.33
MMSE score (0–30)						0.0005	12.09	0.68	0.54	0.84
POD						0.0016	9.94	7.57	2.15	26.65

MMSE = Mini-Mental State Examination, OR = odds ratio, POD = postoperative delirium.

Preoperative variables: Nagelkerke $R^2 = 0.39$, overall % = 86. Postoperative variables: Nagelkerke $R^2 = 0.28$, overall % = 73.7. Combined preoperative, operative, and postoperative variables: Nagelkerke $R^2 = 0.42$, overall % = 79.82.

3.2–3.6% (70–74 yr), 5.8–6.0% (75–79 yr), 11.8–12.2% (80–84 yr), and 24.5–24.8% (\geq 85 yr) (27). In a more recent review, the prevalence of dementia among European people with 70–75 years old was 7.6%, 75–80 years 13.4%, and the prevalence in those 80–85 years old was 21.3% (28). There are few studies addressing dementia after cardiac surgery. Studies have shown that patients undergoing cardiac surgery have a greater risk of developing dementia compared with those who had undergone revascularization with percutaneous coronary intervention (8, 29). A review showed no convincing evidence between on- and off-pump procedures and neurological dysfunction after cardiac surgery has a causal role in progression of dementia, independent of pre-existing cognitive impairment or neurocognitive impairment (30). These studies are not comparable to our study due to methodological differences since their mean ages were lower compared to the present study and POD was not investigated. However, the prevalence of dementia seems to be higher in our study than in other studies.

The interface between delirium and dementia in older people remains poorly understood, but delirium seems to be a marker of a vulnerable brain (31). In the present study, 56% of participants developed POD, similar to previously reported findings from patients undergoing cardiac surgery (1, 2). The question of whether POD prevention can reduce the risk of cognitive decline and future dementia after cardiac surgery remains unanswered. However, the risk of POD can be predicted before cardiac surgery (32, 33). Results of the present study suggest that dementia can be predicted using preoperative cognitive screening with MMSE and POD assessment during hospitalization. In the present study, preoperative MMSE scores did not differ between participants who did and did not develop POD. However, the etiology of POD is multifactorial and related to underlying predisposing and precipitating risk factors (34). It might not be surprising that older patients develop POD because many simultaneous noxious stimuli of cardiac surgical

procedures and treatment affect patients during hospitalization (6, 7). Furthermore, we found that participants who developed POD regained preoperative MMSE scores 1 year after surgery, similar to the results reported by Saczynski et al (2). However, the present study indicates that POD might have long-term effects on cognitive function, which may increase the risk of dementia development. The long-term decline in mean MMSE score was significantly greater among participants with POD than among those without, and the risk of developing dementia after POD was increased almost seven-fold. In addition, 26% of those diagnosed with dementia had low MMSE scores before surgery. These observations support results of previous studies, which documented a greater risk of progression to dementia among older people with MCI (35, 36). In the present study, MMSE scores declined by only 0.2 points per year among participants who did not develop dementia or did not develop POD. Our findings support those of a longitudinal study of healthy old people (age > 70 yr), which showed that cognitive decline cannot be attributed to age alone (37).

This study has limitations. As participants were intermittently examined after extubation for POD 1 and 4 days after surgery, POD may have been missed in some participants. Unfortunately, The Society of Critical Care Medicine's guidelines was not used (38). We were unable to record factors related to hospitalization, such as pharmacological interactions (anesthesia, pain relief, and treatment of POD); this may have affected participants' postoperative cognitive performance. Furthermore, five participants were offered a structured interview by telephone but MMSE scores were recalculated. During follow-up, we had no access to medical records at local hospitals. Nevertheless, we received important information from assessments and interviews with healthcare professionals and next of kin. A larger cohort would have been desirable or having a control group without the need for cardiac surgery. Participants who developed dementia after cardiac surgery may also have been exposed to other brain injuries after surgery so this must be taken into account when interpreting our results. Finally, although differences in educational levels were observed among participants with and without dementia, the role of education in MMSE performance was taken into account (39).

CONCLUSIONS

Our findings suggest that older patients with reduced preoperative cognitive functions (low MMSE score) and those who develop POD are at risk of dementia development during 5 years after cardiac surgery. The cognitive functions of older patients undergoing cardiac surgery should be screened preoperatively. Patients who develop POD should be followed up to enable early detection of dementia symptoms, and management should be implemented.

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