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Association between delirium and cognitive change after cardiac surgery

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Abstract

Background. Previous studies provide inconsistent data on whether postoperative delirium (POD) is a risk factor for postoperative cognitive decline (POCD). We thus investigated the relationship between POD and cognitive change after cardiac surgery and assessed the relationship between preoperative cognitive domain scores and POD.

Methods. Postoperative delirium was assessed with the Confusion Assessment Method (CAM) adapted for the intensive care unit and the conventional CAM accompanied by chart review. Cognitive function was assessed with a neuropsychological test battery before elective cardiac surgery and 1 month and 1 yr afterwards. Cognitive change was calculated using the Reliable Change Index (RCI). Multiple linear regression was used to adjust for confounding.

Results. Of the 184 patients who completed baseline assessment, 23 (12.5%) developed POD. At 1 month, the decline in cognitive performance was worse in patients with POD [median composite RCI −1.00, interquartile range (IQR) −1.67 to 0.28] than in patients without POD (RCI −0.04, IQR −0.70 to 0.63, $P=0.02$). At 1 yr, both groups showed cognitive improvement on average compared with baseline (POD patients median composite RCI 0.25, IQR −0.42 to 1.31, *vs* non-POD patients RCI 0.92, IQR 0.18–1.53; $P=0.08$). Correction for differences in age and level of education did not change the results. Patients with POD performed less well than patients without POD on the preoperative Trailmaking test part A ($P=0.03$).

Conclusions. Postoperative delirium is independently associated with cognitive decline 1 month after surgery, but cognitive performance generally recovers in 1 yr. Patients with a predisposition to POD can be identified before surgery by worse performance in an attention task.

Clinical trial registration. NCT00293592.

Key words: cardiac surgical procedures; cognition; delirium; neuropsychological tests

Transient postoperative cognitive decline (POCD) and postoperative delirium (POD) are relatively common complications after surgery. Patients undergoing cardiac surgery are at high risk for both conditions because they are relatively old and often have multiple co-morbidities, including hypertension, diabetes, and previous ischaemic stroke.[1–5] Impaired preoperative overall cognitive function and low level of education[2] increase the risks of both POD and POCD, but the predisposing cognitive profile for both conditions has not yet been fully elucidated. There is limited information on the predictive value of impairment in specific cognitive domains.

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Editor's key points

- Postoperative delirium and postoperative cognitive dysfunction (POCD) are common complications of cardiac surgery.
- It is unknown whether they have a similar aetiology and pathophysiology.
- The authors performed a secondary analysis of the Dexamethasone for Cardiac Surgery (DECS) study database to investigate associations between the two.
- Among patients who developed postoperative delirium, POCD at 3 months was more common.

There is inconsistency in the literature on whether POD increases the risk of POCD.[6] Two recent studies demonstrated an association between POD and subsequent POCD in elderly patients undergoing orthopaedic surgery[7] and cardiac surgery.[8] Both studies used the Mini-Mental State Examination as a global measure of cognitive function.[9] There is, however, longstanding consensus that a battery of neuropsychological tests is required to detect POCD reliably after cardiac surgery.[10] Furthermore, it is currently unclear how postoperative cognitive function evolves over time with respect to the magnitude of the change, changes in overall cognitive function, and changes in different cognitive domains.

The primary aim of this study was to examine the relationship between POD and POCD at 1 month after cardiac surgery, assessed with a battery of neuropsychological tests and based on a comparison with preoperative neuropsychological test performance. Secondarily, we examined whether POD is associated with POCD at 1 yr, whether POD differentially affects specific cognitive domain scores over time, and which preoperative cognitive profile predisposes cardiac surgery patients to develop POD.

Methods

Study design and participants

For this cohort study, we used a subset of the data from the Dexamethasone for Cardiac Surgery (DECS) trial registered in ClinicalTrials.gov (NCT00293592).[11]

This multicentre, double-blind, placebo-controlled trial randomized 4494 patients aged 18 yr or older who were undergoing cardiac surgery with cardiopulmonary bypass to a single high dose of dexamethasone, 1 mg kg^{-1} i.v. injection with a maximum of 100 mg, or placebo at the time of induction of anaesthesia. The use of intraoperative dexamethasone did not reduce the 30 day incidence of major adverse events, a composite of death, myocardial infarction (MI), stroke, renal failure, or respiratory failure, compared with placebo. The study design and the primary results have been described in detail previously.[11]

Data from the present study consist of a subset of the data from two sub-studies of the DECS study. The first was a sub-study of the influence of dexamethasone on the incidence of POD,[12] involving the 768 patients enrolled in the DECS trial at the University Medical Center Utrecht between June 2009 and November 2011, in whom more elaborate delirium data collection was conducted. The second was a pre-planned sub-study within the DECS trial of the effect of dexamethasone on the occurrence of POCD.[13] For this sub-study, 340 patients of the University Medical Center Utrecht, Utrecht, the Erasmus University Medical Center, Rotterdam, and Isala Clinics, Zwolle, provided additional consent (at the time of enrolment in the DECS study) for preoperative and follow-up testing of cognitive function. Between August 2010 and October 2011, 291 patients completed baseline assessment of their cognitive performance (of the 340 who provided informed consent, six were unable to complete the baseline neuropsychological assessments, and 43 could not do so for logistical reasons).[13] Of these 291 patients, 184 were also enrolled in the delirium sub-study. Dexamethasone appeared to have no effect on POD and POCD.[12 13]

All 184 patients who participated in and completed both sub-studies (elaborate delirium screening and cognitive function testing) were included in the present cohort to evaluate the association between postoperative delirium and cognitive change after cardiac surgery. Additional exclusion criteria for this additional sub-study were evident mental illness or significantly impaired vision, hearing, or motor skills (e.g. hemiplegia). Dexamethasone appeared to have no effect on POD and POCD.[12 13] Data on patient, clinical, and surgical characteristics were prospectively collected in the DECS trial database.[11] The Medical Ethics Committee of the University Medical Centre Utrecht approved this study, and written informed consent was obtained from all patients.

To define true cognitive decline beyond natural variation in test performance, from the cardiology outpatient clinic we recruited as control subjects a group of volunteers with documented coronary artery or valve pathology but without elective surgery. In this group, the same neuropsychological test battery and protocol was used by the same investigators as the trial participants, assessing cognition twice with an interval of 1 month.[13]

Delirium assessment

Delirium was assessed by trained research personnel using a previously validated method.[14] This included daily assessment by a research nurse using the Confusion Assessment Method (CAM) adapted for the ICU (CAM-ICU)[15] in the ICU setting, the CAM[16] when the patient was transferred to the ward, a chart review over the previous 24 h to identify key words suggestive of delirium (e.g. confused, agitated, drowsiness, disorientated, delirious),[17] the results of twice daily CAM(-ICU) assessments conducted by the bedside nurse, and the administration of antipsychotic medication. If any of these indicators were present, the patient was scored as delirious. Patients who were deemed to be unarousable as determined by a Richmond Agitation Sedation Scale (RASS)[18] score of −4 or −5 were not evaluated for delirium.[19] Patients were assessed on the first 4 days after surgery at a fixed point during the day whenever possible.

Neuropsychological assessment

Cognitive function was assessed 1 day before surgery (baseline), at 1 month after cardiac surgery, and at 1 yr follow-up. If possible, patients were assessed in the hospital by trained research personnel. In order to maximize the completeness of cognitive follow-up, patients who were unable to come to the hospital for follow-up were offered the option to have the neuropsychological tests administered at their home. Total test time was approximately 30–40 min, depending on the patient's speed of comprehension and execution.

The following tests[20] were administered: Corsi block-tapping task (spatial memory), Rey auditory verbal learning [immediate recall (short-term verbal memory) and delayed recall (intermediate-term verbal memory)], grooved pegboard (motor skills),

Trailmaking test [part A (attention) and part B (executive function)], Digit Span forward and backward (Wechsler Adult Intelligence Scale, Revised; verbal memory; see Supplementary Appendix A).

To obtain an overall score of baseline cognitive performance, we first calculated a z-score for each raw test score of each patient by subtracting the total group mean from the patient's individual score and dividing the residue by the group SD. In timed tasks, scores were inverted so that a higher z-score always indicated better cognitive performance. Then, an overall Z-score was calculated as the mean of the z-scores of the eight test variables and used as a baseline composite cognitive outcome measure. To control for natural variation and practice effects in cognitive test performance during follow-up, we used the Jacobson and Truax' Reliable Change Index (RCI).[21] This approach yields a z-score for every individual test by subtracting from the follow-up score the baseline test score and the mean change on that test in the control group and dividing the result by the SD of the change in the control group. In timed tasks, RCI values were inverted as described above. For the composite RCI, the sum of the z-scores of the different tests was divided by the SD of this sum in the control group.[13] Psychometric test scores from the control group are presented in Supplementary Appendix B.

Study outcomes

The primary study outcome was change in cognitive performance from baseline to 1 month after surgery. Secondly, cognitive performance was assessed at 1 yr. In addition, we assessed the influence of POD on individual cognitive test scores at 1 month and 1 yr after surgery. Finally, the association between preoperative cognitive test performance and the occurrence of POD was investigated.

Statistical analysis

The sample size of this cohort study was determined by the available number of 184 patients within the DECS trial in whom both the presence of POD and cognitive functioning were measured prospectively. Continuous baseline variables were presented as mean or median values, depending on distribution, and compared with Student's unpaired *t*-test or the Mann–Whitney *U*-test, as appropriate. Binary data were presented as percentages and analysed using the Pearson χ^2 test or Fisher's exact test based on minimal cell count. Categorical data were compared using an analysis of variance. For the primary outcome (change in cognitive performance at 1 month as represented by the continuous, composite RCI values), we tested the between-group difference (POD *vs* no POD) using the Mann–Whitney *U*-test. Linear regression analysis was performed to study the association between POD and change in cognitive performance at 1 month and at 1 yr, adjusting for randomization to dexamethasone or placebo, age, and level of education. To study the association between preoperative cognitive tests and POD, we tested the between-group difference (POD *vs* no POD) using logistic regression analysis and adjusted for the same covariables. The analyses were performed using IBM SPSS version 21 (SPSS Inc., Chicago, IL, USA). All reported *P*-values were two sided, and a significance level of $P<0.05$ was used.

Results

Between August 2010 and October 2011, 184 patients involved in the delirium sub-study underwent the neuropsychological preoperative baseline assessment. Of these, 176 (95.7%) completed the 1 month follow-up and 146 (79.3%) the 1 yr neuropsychological follow-up. Of the 184 patients who completed the baseline assessment, 23 (12.5%) patients developed delirium during their postoperative hospital stay. In the POD group, one patient died (5%) between the 1 month and 1 yr follow-up and one refused follow-up (5%), so that the total number lost to follow-up was two (9%). In the group without POD, three patients (2%) died and 25 (17%) refused follow-up; therefore, the total number lost to follow-up was 28 (18%). Figure 1 shows the enrolment flowchart and loss to follow-up.

Baseline patient, clinical, and surgical characteristics of the 176 patients who completed the 1 month follow-up are presented in Table 1. Patients who developed POD were significantly older, more often had peripheral vascular disease, and had a higher EuroScore compared with non-delirious patients. The incidence of delirium and baseline characteristics, except for serum creatinine and left ventricular function, were comparable between the group of patients with complete follow-up and the group without 1 yr follow-up (data not shown).

Change in cognitive performance at 1 month

At 1 month, both patient groups showed a negative change in cognitive performance, based on the composite RCI. The decrease in performance was significantly greater in patients who had been delirious compared with those without delirium [median composite RCI −1.00, interquartile range (IQR) −1.67 to 0.28, *vs* −0.04, IQR −0.70 to 0.63; $P=0.02$]. The unadjusted β was −0.99 [95% confidence interval (CI) −1.59 to −0.39, $P=0.001$]. Adjusting for the possible confounders mentioned above with multiple linear regression resulted in a β of −0.91 (95% CI −1.53 to −0.28, $P=0.005$).

Change in cognitive performance at 1 yr

At 1 yr follow-up, positive median composite RCI scores were found, indicating improved performance compared with the preoperative baseline in both groups. The median composite RCI score was less positive in patients who had POD (median composite RCI 0.25, IQR −0.42 to 1.31) than in patients without POD (0.92, IQR 0.18–1.53; $P=0.08$), suggesting less improved scores in the POD group, but this difference was not statistically significant. Multivariable regression analysis did not change the results (unadjusted $\beta=-0.58$, 95% CI −1.13 to −0.03; adjusted $\beta=-0.40$, 95% CI −0.98 to 0.18; $P=0.17$).

Postoperative delirium and postoperative scores on individual neuropsychological tests

The raw neuropsychological test results at 1 month and 1 yr and the adjusted changes from baseline are presented in Tables 2 and 3. Change from baseline in the grooved pegboard and the Trailmaking test part B significantly differed between delirious and non-delirious patients at both time points. In the POD group, persistent decline was seen on the grooved pegboard, and initially more severe decline recovering to minimal decline was seen at the Trailmaking test part B compared with improved performance on both tests in the non-delirious group.

Preoperative cognitive assessment and POD

As shown in Table 4, consistently lower preoperative scores were recorded in the group who developed POD compared with the group who did not. However, except for the Trailmaking test

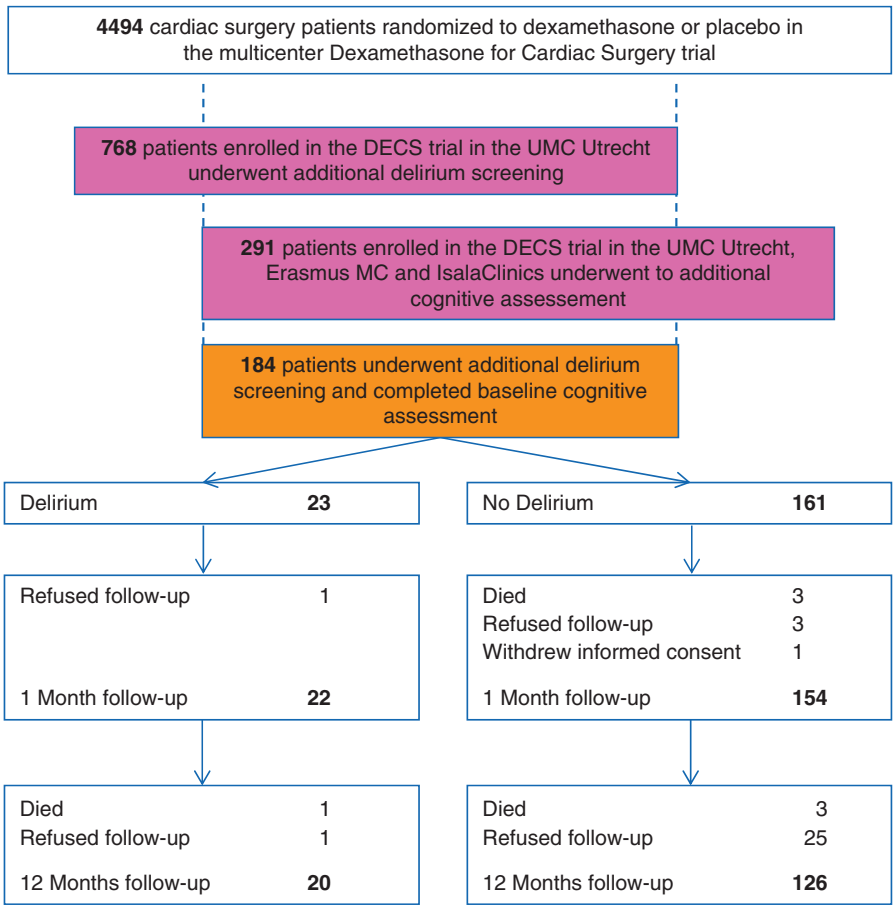

Fig 1 Enrolment flowchart.

part A, these differences did not reach statistical significance after adjusting for potential confounders.

Discussion

We assessed the relationship between POD and cognitive change at 1 month after cardiac surgery and found that patients with POD had a greater decline in cognitive performance than those without POD. However, at 1 yr the patients with and without POD showed an improved cognitive performance compared with preoperative baseline cognitive levels, without a statistically significant difference between the two groups. Adjustment for differences in age and level of education did not change the results.

These findings are concordant with previous research, indicating that POD is an independent risk factor for POCD in the immediate postoperative trajectory.[6–8] Previous studies on cognitive function assessed after a longer duration of follow-up were less consistent.[6–8] In our study, we observed over the course of 1 yr, on average, an improvement in cognitive performance compared with baseline in patients with and without POD.

The relationship between POD and POCD is complex and not yet fully elucidated. Both entities share many risk factors, such as increasing age, low level of education, and underlying comorbidities,[1–5 8] and might be viewed as two expressions of the same underlying process of pre-existing decreased cognitive reserve,[23] as opposed to other evidence supporting a more independent, possibly causal, relationship between delirium and cognitive impairment.[7 8 21] A causal relationship could have important clinical implications, because delirium would then be one of the few modifiable risk factors for POCD, opening up possibilities for prevention. The magnitude of the influence of delirium as an independent risk factor for POCD is difficult to determine. Previous research in the field of POCD has already shown that cognitive function may recover over time.[6 8] Delirium might influence the speed and extent of recovery. In the present study, both groups showed, on average, cognitive improvement compared with baseline scores, but this effect was less pronounced in the delirious group. Furthermore, we did find consistent differences between both groups on the grooved pegboard and Trailmaking test part B, indicating that suffering from a delirium might especially influence fine motor skills and executive functions. In the present study, we found lower baseline scores on all but the WAIS digit span tests for the

Table 1 Patient, clinical, and surgical characteristics. *Data are shown as number of patients (percentages) or †median (interquartile range). ‡The level of education was classified according to Dutch norm data using the system of Verhage, ranging from 1 (no education) to 7 (university). ¶Definition of myocardial infarction: the presence of new Q waves or a new left bundle branch block on the ECG, combined with a biomarker (creatine kinase–MB or troponin) elevation of more than five times the upper reference limit. §Higher EuroScores present increased risk of perioperative mortality.[22] ‖Definition of left ventricular function classes: moderate, ejection fraction of 30–50%; poor, ejection fraction of < 30%. #Statistically significant. **Pearson χ^2. ††Fisher's exact test. ‡‡Analysis of variance. COPD, chronic obstructive pulmonary disease; CABG, coronary artery bypass grafting; ECG, electrocardiogram; MB, myocardial band

Characteristic	Delirious (*n*=22)	Non-delirious (*n*=154)	*P*-value
Male sex*	12 (54.5)	115 (74.7)	0.05**
Age (yr)†	78.1 (74.6–82.7)	65.5 (57.0–72.2)	<0.001#
Weight (kg)†	74.0 (63.0–84.0)	80.0 (71.0–90.0)	0.03#
Education†,‡	5 (3–6)	5 (4–6)	0.81
Hypertension*	14 (63.6)	83 (53.9)	0.39**
Diabetes mellitus*	4 (18.2)	24 (15.6)	0.76††
COPD requiring treatment*	6 (27.3)	19 (12.3)	0.10††
Previous stroke*	3 (13.6)	9 (5.8)	0.18††
Peripheral vascular disease*	7 (31.8)	17 (11.0)	0.02#,††
Recent myocardial infarction*,¶	0 (0.0)	9 (5.8)	0.60††
Serum creatinine (μmol litre^{-1})†	87.5 (78.0–109.3)	91.5 (80.0–105.3)	0.64
EuroScore†,§	8.0 (6.0–9.3)	4.0 (2.0–7.0)	<0.001#
Left ventricular function‖			0.35‡‡
Moderate	2 (9.1)	32 (20.8)	
Poor	1 (4.5)	3 (1.9)	
Dexamethasone treatment*	8 (36.4)	75 (48.7)	0.36**
Type of surgery*			
Isolated CABG	2 (9.1)	41 (26.6)	0.07**
Valve surgery	17 (77.3)	103 (66.9)	0.33**
Time to extubation (h)†	8.0 (6.8–12.3)	7.0 (6.0–10.0)	0.14
Cardiopulmonary bypass time (min)†	121.5 (89.5–154.5)	103 (77.0–152.5)	0.18
Cross-clamp time (min)†	92.0 (71.0–123.3)	78.0 (59.0–120.0)	0.17
Repeat surgery*	3 (13.6)	14 (9.1)	0.45††

Table 2 Raw neuropsychological test results at 1 month and change from baseline (z-score). *Positive values indicate improvement, whereas negative values indicate decline in test performance. In timed tasks, lower scores reflect better performance. The RCI values of these variables were inverted so that positive RCI values always indicate improvement and negative RCI values indicate decline in test performance. †Statistically significant. *P*-values are for the adjusted z-scores and were calculated with multiple linear regression analysis. IQR, interquartile range; RAVL, Rey auditory verbal learning; RAVL IR, Ray auditory verbal learning immediate recall; RAVL DE, Ray auditory verbal learning delayed recall; RCI, Reliable Change Index; WAIS, Wechsler Adult Intelligence Scale

Test	Delirious (*n*=22)				Not delirious (*n*=154)				
	Raw score (IQR)		Z-score (IQR)		Raw score (IQR)		Z-score (IQR)		*P*-value
Corsi blocks (total score)	30	(23–36)	−0.59	(−0.93 to +0.30)	40	(35–54)	−0.04	(−0.57 to +0.36)	0.06
RAVL (IR)	34	(27–43)	+0.09	(−0.63 to +1.23)	43	(34–50)	+0.26	(−0.55 to +0.91)	0.55
RAVL (DR)	5	(4–7)	+0.15	(−0.71 to +0.24)	8	(5–11)	+0.15	(−0.61 to +0.53)	0.93
Grooved pegboard* (s)	105	(92–176	−0.76	(−1.7 to +0.57)	81	(69–96)	+0.08	(−0.41 to +0.71)	<0.001†
Trailmaking test A* (s)	48	(35–66)	−0.03	(−0.95 to +0.89)	34	(26–44)	+0.05	(−0.41 to +0.35)	0.11
Trailmaking test B* (s)	84	(65–168)	−0.67	(−1.96 to +0.26)	58	(40–86)	−0.06	(−0.45 to +0.28)	<0.001†
WAIS digit span (span)	5	(5–6)	−0.12	(−1.08 to −0.12)	5	(5–7)	−0.12	(−1.08 to +0.83)	0.32
WAIS digit span (total)	13	(11–14)	−0.42	(−1.32 to +0.46)	14	(12–16)	−0.43	(−1.32 to +0.46)	0.83

group that later on developed delirium. After adjusting for the difference in age and education between both groups, the Trailmaking test part A remained discriminative between both groups, which might indicate that impaired attention at baseline might predispose to development of delirium. Earlier studies on dysfunction in specific cognitive domains predictive for the development of delirium did show an association with impairment in executive functions tested with the Trailmaking test part B[24] and with more complex executive function tasks,[25] which we were unable to find in the present study.

Our study had several strengths. We used a well-validated, rigorous method of delirium detection, combining the results of standardized observations by research personnel with data available from standard clinical patient care.[14] This allowed us to capture the fluctuating nature of the condition. Staff availability 7 days per week enabled us to minimize missed observations and

Table 3 Raw neuropsychological test results at 1 yr and change from baseline (z-score). *Positive values indicate improvement, whereas negative values indicate decline in test performance. In timed tasks, lower scores reflect better performance. The RCI values of these variables were inverted so that positive RCI values always indicate improvement and negative RCI values indicate decline in test performance. †Statistically significant. *P*-values are for the adjusted z-scores and were calculated with multiple linear regression analysis. IQR, interquartile range; RAVL, Rey auditory verbal learning; RAVL IR, Ray auditory verbal learning immediate recall; RAVL DE, Ray auditory verbal learning delayed recall; RCI, Reliable Change Index; WAIS, Wechsler Adult Intelligence Scale

Test	Delirious (*n*=20)				Not delirious (*n*=126)				
	Raw score (IQR)		Z-score (IQR)		Raw score (IQR)		Z-score (IQR)		*P*-value
Corsi blocks (total score)	40	(35–42)	+0.29	(−0.28 to + 0.87)	54	(40–60)	+0.64	(0.00 to + 1.04)	0.30
RAVL (IR)	38	(29–44)	+0.81	(−0.32 to + 1.13)	46	(35–54)	+0.65	(0.00 t + 1.62)	0.81
RAVL (DR)	7	(5–10)	+0.76	(0.0 to + 1.14)	9	(6–12)	+0.76	(0.00 to + 1.14)	0.44
Grooved pegboard* (s)	99	(88–148)	−0.56	(−1.05 to − 0.21)	77	(65–92)	+0.21	(−0.28 to + 0.63)	0.003†
Trailmaking test A* (s)	46	(34–63)	−0.04	(−0.58 to + 0.83)	35	(28–47)	−0.08	(−0.32 to + 0.38)	0.97
Trailmaking test B* (s)	86	(55–152)	−0.06	(−0.96 to + 0.59)	51	(36–73)	+0.17	(−0.17 to + 0.66)	0.03†
WAIS digit span (span)	5	(5–6)	0.00	(−0.96 to + 0.72)	6	(5–7)	0.00	(−0.96 to + 0.96)	0.95
WAIS digit span (total)	14	(12–15)	0.00	(−0.44 to + 1.33)	15	(13–18)	+0.44	(−0.44 to + 1.33)	0.56

Table 4 Neuropsychological test results at baseline. *In timed tasks, lower scores reflect better performance. †Statistically significant. CI, confidence interval; IQR, interquartile range; OR, odds ratio; RAVL, Rey auditory verbal learning; RAVL IR, Ray auditory verbal learning immediate recall; RAVL DE, Ray auditory verbal learning delayed recall; WAIS, Wechsler Adult Intelligence Scale

Test	Delirious (IQR) (*n*=22)	Not delirious (IQR) (*n*=154)	Unadjusted OR	(95% CI)	*P*-value	Adjusted OR	(95% CI)	*P*-value
Corsi blocks (total score)	33 (24–42)	40 (30–48)	0.97	(0.94–1.01)	0.09	0.99	(0.95–1.03)	0.54
RAVL (IR)	34 (26–37)	39 (32–47)	0.94	(0.89–0.98)†	0.01	0.98	(0.92–1.04)	0.50
RAVL (DR)	5 (3–7)	7 (5–10)	0.76	(0.64–0.90)†	0.002	0.85	(0.70–1.04)	0.11
Grooved pegboard* (s)	102 (86–158)	85 (72–102)	1.02	(1.01–1.03)†	0.001	1.01	(0.99–1.02)	0.31
Trailmaking test A* (s)	52 (39–60)	37 (28–47)	1.06	(1.03–1.09)†	<0.001	1.04	(1.00–1.09)†	0.03
Trailmaking test B* (s)	90 (53–113)	61 (41–90)	1.01	(1.00–1.02)†	0.03	1.00	(0.99–1.02)	0.71
WAIS digit span (span)	6 (5–6)	6 (5–7)	0.85	(0.60–1.22)	0.38	0.76	(0.45–1.15)	0.16
WAIS digit span (total)	13 (11–15)	14 (11–17)	0.93	(0.82–1.05)	0.22	0.90	(0.78–1.04)	0.16

ensure complete follow-up. For logistic reasons, we limited our observation period to the first 4 days after surgery. Being a tertiary centre, a significant part of the patient population with uncomplicated recovery returned to their referring centres within a week after the surgery. This approach might have missed delirium that developed later in the postoperative trajectory. The impact of this limitation is likely to be small, because previous studies showed that the vast majority of delirium in this population is clinically apparent during the first 3 days after surgery.[26 27] Our study population was relatively young compared with other research in the field, which may have resulted in a relatively low incidence of POD. However, our incidence corresponds closely to a similar, large trial by Katznelson and colleagues[28] that reported an incidence of 11.9% in 1528 cardiac patients.

Research on POCD has been hampered by the lack of consensus on strict definitions for POCD based on neuropsychological test methods.[23] We chose a combination of neuropsychological tests, covering a broad range of cognitive domains vulnerable for postoperative change, including the core battery recommended by the 1995 consensus statement.[10] We presented a continuous outcome to avoid arbitrary dichotomization and were able to show improvement in performance. Furthermore, we corrected for learning effects and natural fluctuation in test results by comparing our patients with a non-surgical control group who had similar characteristics.[21] Loss to follow-up was low, especially at 1 month, with a follow-up rate of 95.7%.

Our study has some limitations. The primary study outcome and focus in our analysis was the change in cognitive performance from baseline to 1 month after surgery. Results from the other analyses should be interpreted as hypothesis generating. Overcorrection for learning might have occurred by using a control group with no intervention, who might not have been exposed to the same amount of psychological stress, depression, or both at baseline, which is known to exist in cardiac surgery patients in the period before their intervention. We did not collect data on subjective patient outcomes and the experienced burden of impairment. Therefore, we can make no statements about the clinical impact of the cognitive decline that we measured with our neuropsychological test battery. We believe that in general at 1 month follow-up, patients are still recovering from their cardiac surgery, and the clinical relevance of POCD at this follow-up moment might be limited. Like many other studies, our study suggests that perioperative factors might affect cognitive performance in the first months after surgery, but not in the long term. Including subjective assessments of postoperative cognitive change at different time points in future research might generate valuable information on the clinical impact of the cognitive decline.

In conclusion, this study showed that POD is independently associated with cognitive decline 1 month after surgery. Secondary outcomes indicate that POD is not associated with cognitive decline 1 yr after surgery and that cognitive performance generally recovers in the year after the operation, except for the specific cognitive domains of motor skills and executive function. Patients with a predisposition to POD are characterized by worse performance in attention-requiring tasks.

Authors' contributions

Study design: C.J.K., D.D.
Data collection: A.C.S., T.H.O.
Data analysis: A.C.S., T.H.O.
Writing the paper: A.C.S., D.S.V.
Critical revision of the paper: D.S.V., A.J.C.S., C.J.K., D.D.

Supplementary material

Supplementary material is available at *British Journal of Anaesthesia* online.

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