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Postoperative delirium in elderly patients is associated with subsequent cognitive impairment

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Abstract

Background. We examined the risk for postoperative delirium (POD) in patients with mild cognitive impairment (MCI) or dementia, and the association between POD and subsequent development of MCI or dementia in cognitively normal elderly patients.

Methods. Patients ≥65 yr of age enrolled in the Mayo Clinic Study of Aging who were exposed to any type of anaesthesia from 2004 to 2014 were included. Cognitive status was evaluated before and after surgery by neuropsychological testing and clinical assessment, and was defined as normal or MCI/dementia. Postoperative delirium was detected with the Confusion Assessment Method for the intensive care unit. Logistic regression analyses were performed.

Results. Among 2014 surgical patients, 74 (3.7%) developed POD. Before surgery, 1667 participants were cognitively normal, and 347 met MCI/dementia criteria. The frequency of POD was higher in patients with pre-existing MCI/dementia compared with no MCI/dementia {8.7 *vs* 2.6%; odds ratio (OR) 2.53, [95% confidence interval (CI) 1.52–4.21]; $P<0.001$}. Postoperative delirium was associated with lower education [OR, 3.40 (95% CI, 1.60–7.40); $P=0.002$ for those with <12 *vs* ≥16 yr of schooling]. Of the 1667 patients cognitively normal at their most recent assessment, 1152 returned for postoperative evaluation, and 109 (9.5%) met MCI/dementia criteria. The frequency of MCI/dementia at the first postoperative evaluation was higher in patients who experienced POD compared with those who did not [33.3 *vs* 9.0%; adjusted OR, 3.00 (95% CI, 1.12–8.05); $P=0.029$].

Conclusions. Mild cognitive impairment or dementia is a risk for POD. Elderly patients who have not been diagnosed with MCI or dementia but experience POD are more likely to be diagnosed subsequently with MCI or dementia.

Key words: aged, humans, male, female; anaesthesia, general; delirium; dementia; mild cognitive impairment; surgery

Delirium is a neurobehavioural syndrome caused by dysregulated neuronal activity attributable to systemic disturbances that presents clinically with acute confusion, inattention, disorganized thinking, and fluctuating mental status. Major predisposing factors in hospitalized patients include older age, alcohol use, and poor functional and cognitive status.[1 2] Although many patients who develop delirium during hospitalization initially appear to recover, evidence suggests that

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Editor's key points

- The relationships between postoperative delirium and preoperative mild cognitive impairment or dementia were analysed in a large cohort of elderly patients.
- Postoperative delirium was more frequent in patients with baseline cognitive impairment.
- Diagnosis of cognitive impairment on follow-up was more frequent in patients who had previously experienced postoperative delirium.

delirious episodes portend long-term cognitive decline.[3] For example, elderly patients who were considered to be cognitively normal before hospital admission and experienced delirium during their hospital stay were more likely to be diagnosed with incident dementia within several years compared with those who did not experience delirium.[4–8] In addition, several studies suggest that non-demented surgical patients who develop postoperative delirium (POD) are also at risk for long-term cognitive impairment.[2,9–12] Although many of these studies excluded patients with frank confusion or dementia before surgery, they all included patients with lesser degrees of cognitive impairment. The association between POD and long-term changes in cognition in patients who are considered cognitively normal before surgery is not clear.

The ability to assess cognition clinically has improved substantially with the introduction of diagnostic criteria for mild cognitive impairment (MCI; i.e. cognitive impairment that has no to minimal impact on daily functioning).[13 14] The Mayo Clinic Study of Aging (MCSA), a population-based longitudinal cohort study, examines the incidence and prevalence of MCI and dementia in Olmsted County, MN, USA, including risk factors for these conditions,[15] using strict MCI diagnostic criteria.[13 14] We have used MCSA in previous work to examine the association between receiving general anaesthesia and developing MCI or dementia.[16]

One of our aims was to validate previous findings that the rate of POD is increased in patients who have a clinical diagnosis of MCI or dementia at the time of surgery. However, our main interest was to conduct the analysis of patients enrolled in the MCSA and test the hypothesis that surgical patients who are cognitively normal as determined by lack of MCI or dementia on a preoperative MCSA assessment and who develop POD are at increased risk for subsequent development of MCI or dementia. A preliminary analysis of these data was published previously.[17]

Methods

In 2004, Mayo Clinic epidemiologists and neurologists assembled a large prospective population-based cohort of Olmsted County, MN, USA, residents to study the decline in cognitive function with ageing.[14 15 18] The primary aim of the MCSA is to examine risk factors for progression from normal cognitive function to MCI and dementia.[15] In the present study, we used MCSA resources to examine the association between cognitive status and POD in elderly patients who underwent surgery.

Study participants

Patient consent for inclusion in retrospective studies (consistent with Mayo Clinic Institutional Review Board policies and Minnesota Statute 144.295) was obtained. For initial recruitment to the MCSA, Olmsted County residents who were 70–89 yr old on October 1, 2004, were identified, randomly selected, and invited to participate in the study.[15] In 2008, ongoing recruitment was initiated using the same protocols as baseline, and in 2012, the lower limit of the age criterion was reduced to 50 yr of age. The present study includes all participants enrolled and examined in person in the MCSA study from November 2004 to February 2014 who underwent surgeries and procedures under anaesthesia at Mayo Clinic in Rochester, MN, USA after enrolment; we included only participants who were ≥65 yr of age at enrolment.

Assessment of cognition

Details regarding diagnostic procedures for assessment of cognition and diagnosis of MCI or dementia in the MCSA cohort have been described.[14 19] Briefly, MCSA participants received detailed assessments of cognitive status at baseline and at follow-up visits every 15 months. Baseline assessments included questionnaires assessing memory and risk factors (based on family and medical history), neurological evaluation, and neuropsychological and laboratory (apolipoprotein E genotyping) evaluation. The neurological evaluation included the Short Test of Mental Status,[20] modified Hachinski Ischemic Scale,[21 22] modified Unified Parkinson's Disease Rating Scale,[23] and a questionnaire developed to elicit neurological conditions that could influence cognition. The neuropsychological evaluation included subtests of the Wechsler Adult Intelligence Scale-Revised and Wechsler Memory Scale-Revised,[24] and assessed performance in four cognitive domains: memory, executive function, language, and visuospatial skills.[25] A study partner (informant) completed the Clinical Dementia Rating Scale[26] to assess functioning of the subject and dementia severity when present. The diagnosis of normal cognition, MCI, dementia, or Alzheimer's dementia was made by consensus, taking into account all data collected. Participants were re-evaluated at 15 month intervals to assess changes in neurocognitive status and to detect incident MCI or dementia using the same protocol used at the baseline evaluation. Given that surgery or acute illness may affect cognition, participants were always evaluated at least 1 month after an acute illness or surgical procedure.

Assessment of delirium

Delirium was detected using the standardized Confusion Assessment Method (CAM-ICU).[27] The CAM-ICU is a standardized approach for assessment of delirium in the intensive care unit (ICU),[2 27] and was validated for use in both intubated and non-intubated ICU patients. A recent study found that the CAM-ICU has high specificity (≥98%) but low sensitivity (18%) when used for detection of delirium in non-ICU patients.[28] Where the specificity and sensitivity fall out in our cohort is not known, as CAM-ICU is not validated as a research tool on this patient population. This instrument closely correlates with the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* criteria for delirium, along with the Mini-Mental Status Examination, Visual Analog Scale for Confusion, and digit span test. After receiving proper training, a healthcare professional can evaluate patients using this tool within 3 min.[29 30]

The CAM-ICU algorithm is based on the following four cardinal features of delirium: (1) acute onset and fluctuating course; (2) inattention; (3) disorganized thinking; and (4) altered level of consciousness. According to CAM-ICU, a diagnosis of delirium requires the presence of features 1, 2, and either 3 or 4 (Supplementary Table S1). In our practice, CAM-ICU has been

applied to all hospitalized surgical patients upon admission and every 12 h thereafter since January 2004. It is also repeated if there are interim changes in mental status. In the immediate postoperative period, before each CAM-ICU assessment, the Richmond Agitation and Sedation Scale (RASS) is also applied.[31] The degree of sedation or agitation is scored on a 10-point RASS scale from −5 (unarousable) to +4 (combative), with a score of 0 equating to an alert and calm patient.[32] Deeply sedated patients (RASS −4 or −5) are not assessed for delirium. The RASS is assessed upon admission and discharge from the postanaesthesia care unit and on wards every 12 h or when deemed clinically necessary. Patients with acceptable RASS scores who are mechanically ventilated are assessed with CAM-ICU using non-verbal communication (by squeezing the hand on command or by holding up fingers).[30] The CAM-ICU instrument has been validated in both intubated and non-intubated patients.[33] For all patients in the MCSA who had surgery requiring anaesthesia after 2004, CAM-ICU reports were reviewed from electronic medical records to identify episodes of postoperative delirium, which we defined as a CAM-ICU positive event that occurred within the first 72 h after surgery. Patients who had at least one CAM-ICU positive score for delirium before surgery were excluded.

Outpatients at our institution are not assessed using CAM-ICU but rather with a set of questions that assesses orientation to time, place, and birthday. If a patient fails to respond appropriately to these questions at the planned time of discharge, the nurse initiates the 'acute confusion nursing order set', which includes administering CAM-ICU and contacting the primary provider for hospital admission if the patient continues to be disoriented. Therefore, we assume that our methods capture instances of POD in patients undergoing surgery regardless of admission status.

Medical and surgical history

The following information was retrieved from the MCSA database: patient characteristics, education level [<12 yr (did not complete high school), 12 yr (high school graduate), 13–15 yr (some college or technical school), and ≥16 yr (4 yr college degree or more)], past medical history, and apolipoprotein E status. Surgeries were classified in the following five major categories: (1) cardiac/vascular/thoracic; (2) general (abdominal, ear, nose and throat, reconstructive, urological, gynecological); (3) neurosurgery; (4) orthopaedic; and (5) miscellaneous (includes minor surgeries such as dermatological, ophthalmological, and other radiological procedures). For all participants, medical records were reviewed for episodes of anaesthesia care (general, regional, and monitored anaesthesia care) from 2004 to the present. Anaesthetic exposures were retrieved from medical records and cross-checked with the electronic anaesthesia database Data Mart (Microsoft), a structured query language relational data warehouse that provides access to all electronic medical records data for patients across Mayo Clinic in Rochester.

Statistical analyses

The sample for the present study was limited to participants enrolled in MCSA from 2004 to 2014 who underwent procedures and surgeries requiring anaesthesia care after enrolment. For those who had multiple procedures, only the first procedure was analysed. As MCI and dementia fall within a common spectrum of cognitive decline,[34] we combined them into a single category for analysis.

To test the hypothesis that individuals with prevalent MCI or dementia are at increased risk for POD, this end point was analysed using logistic regression, with preoperative cognitive status (normal *vs* MCI or dementia) as the explanatory variable of interest. Preoperative cognitive status was defined as normal *vs* MCI or dementia based on the participant's status determined at their most recent MCSA study visit before surgery. In addition to univariate analysis, a multivariable analysis was performed using stratified logistic regression, with type of surgery used as a stratification variable. Covariates included in the multivariable analysis known to be associated with MCI or dementia included age, education, sex, apolipoprotein E status,[35] and time from most recent MCSA study visit to surgery.

To test the hypothesis that cognitively normal individuals who experienced POD are at increased risk for subsequent development of MCI or dementia, we included in analyses participants who were not diagnosed with MCI or dementia at their most recent MCSA visit before undergoing a surgery with anaesthesia and who had at least one MCSA follow-up visit after their surgery. The frequency of MCI or dementia at the first MCSA study visit after the surgical procedure was the primary outcome and was analysed using logistic regression, with POD (yes *vs* no) as the explanatory variable of interest. In addition to univariate analysis, a multivariable analysis was performed, which adjusted for characteristics known to be associated with MCI or dementia including age, education, sex, apolipoprotein E status, midlife dyslipidaemia, hypertension, and diabetes mellitus.[35] In addition, covariates were included for time from most recent MCSA study visit to surgery, co-morbidities present at the time of surgery, and time from surgery to the next MCSA visit. In all instances, findings were summarized using the odds ratio (OR) and corresponding 95% confidence interval (CI). A value of $P<0.05$ was considered statistically significant. Analyses were performed using SAS 9.4 statistical software (SAS Institute Inc., Cary, NC, USA).

Results

Of the participants enrolled in the MCSA from November 29, 2004 to March 26, 2014, 2018 underwent a surgical procedure requiring anaesthesia at Mayo Clinic in Rochester, MN, USA, subsequent to enrolment. Of these, four patients were excluded because they developed delirium while in the hospital before surgery. Thus, 2014 patients are included in the analysis. The mean (SD) age at the time of surgery was 80 (6) yr. General anaesthesia was used in 1075, monitored anaesthesia care in 778, and regional anaesthesia in 161 patients. Of the 2014 patients, 1036 (51%) were discharged on the day of surgery (i.e. were outpatients), 254 (13%) were discharged on the day after surgery, and 724 (36%) remained in the hospital for ≥2 days after surgery.

The median (interquartile range) time from the most recent MCSA study visit to surgery was 8.8 (4.1–14.2) months. Selected patient and surgical characteristics are presented in Table 1. Overall, 74 (3.7%) patients developed POD. The frequency of POD increased significantly with age and fewer years of education. In addition, the rate of POD differed across surgical procedures, being more frequent after orthopaedic, major cardiovascular, and thoracic procedures. Postoperative delirium was more common in men compared with women (Table 1).

At the time of the most recent MCSA study visit before surgery, 1667 (83%) participants were cognitively normal, and 347 (17%) met criteria for MCI or dementia (316 MCI, 31 dementia). The frequency of POD was significantly higher in patients with

Table 1 Frequency of postoperative delirium according to selected patient and procedural characteristics. *Results are from univariate logistic regression analyses. CI, confidence interval; ENT, ear nose and throat; OR, odds ratio

		Postoperative delirium	Logistic regression*		
Characteristic	N	*n* (%)	OR	95% CI	P-value
Age (yr)					<0.001
≤74	414	6 (1.5)	1.0	Reference	
75–79	547	14 (2.6)	1.8	(0.7–4.7)	
80–84	531	21 (4.0)	2.8	(1.1–7.0)	
85–89	392	21 (5.4)	3.8	(1.5–9.6)	
≥90	130	12 (9.2)	6.9	(2.5–18.8)	
Sex					0.010
Female	953	24 (2.5)	1.0	Reference	
Male	1061	50 (4.7)	1.9	(1.2–3.1)	
Education (yr)					0.002
≥16	645	15 (2.3)	1.0	Reference	
13–15	535	28 (5.2)	2.3	(1.2–4.4)	
12	662	18 (2.7)	1.2	(0.6–2.4)	
<12	172	13 (7.6)	3.4	(1.6–7.4)	
Type of surgery					<0.001
General/urology/ENT	539	13 (2.4)	1.0	Reference	
Cardiac/vascular/thoracic	252	17 (6.8)	2.9	(1.4–6.1)	
Miscellaneous/minor procedures	676	11 (1.6)	0.7	(0.3–1.5)	
Neurosurgery	74	3 (4.0)	1.7	(0.5–6.1)	
Orthopaedic	473	30 (6.3)	2.7	(1.4–5.3)	

prevalent MCI or dementia compared with those who were cognitively normal (8.7 *vs* 2.6%; $P<0.001$). After adjustment for other potential confounders, pre-existing MCI or dementia remained significantly associated with an increased risk for delirium [OR, 2.53 (95% CI, 1.52–4.21); $P<0.001$; Table 2 and Supplementary material Table S2].

Of the 1667 participants who were assessed as cognitively normal at the last MCSA visit before surgery, 1152 (69%) returned for a subsequent MCSA visit after surgery. Of these, the median (interquartile range) time from surgery to the first subsequent MCSA study visit was 9.0 (4.6–12.7) months. At the first postsurgery MCSA visit, 109 participants (9.5%) met criteria for MCI or dementia. The frequency of MCI or dementia at the first follow-up MCSA visit was significantly higher in patients who experienced POD *vs* those who did not (33.3 *vs* 9.0%; $P<0.001$). After adjustment for other potential confounders, POD remained significantly associated with an increased risk for subsequent diagnosis of MCI or dementia [OR, 3.00 (95% CI, 1.12–8.05); $P=0.03$; Table 2 and Supplementary material Table S3]. Details of the patients who were assessed at their last MCSA visit before surgery as cognitively normal, developed POD, and had an MCSA follow-up visit after surgery are shown in Supplementary material Table S4.

Discussion

We confirmed previous findings that in a general surgical population elderly patients with MCI at the time of surgery are at higher risk for clinically evident POD compared with patients without MCI. Our main finding is that elderly patients who are cognitively normal at a detailed assessment performed before surgery and who experience clinically evident POD are more likely to develop MCI or dementia subsequently compared with those who do not experience POD.

A considerable search of the literature suggests that delirium in community or hospitalized non-surgical patients is associated with long-term cognitive decline.[4–8 36 37] Evidence suggests a similar relationship for surgical patients who develop POD,[10–12] including two studies performing longitudinal assessments.[2 9] Some studies excluded patients with frank dementia at baseline,[2 4 8 11 36] whereas others included patients with milder forms of cognitive impairment as assessed with the Mini-Mental Status Examination.[9] None of these studies included formal assessment of preoperative MCI, such that all are likely to have included some patients with cognitive impairment. At the same time, other studies show that impaired cognitive function before surgery is a risk factor for developing POD;[1 38 39] of these, two specifically used MCI to define preoperative impaired cognition.[40 41] In the present study, we confirm this finding in a general surgical population. Thus, it is possible that an association between POD and long-term cognitive impairment reflects the fact that POD is a stressor and a marker for pre-existing changes in cognitive function that predicts later long-term functional and cognitive decline.

In two longitudinal studies, repeated postoperative measurements of cognitive function were performed in patients without dementia.[2 9] In both studies, it was found that POD was more common in patients with lower preoperative cognitive scores (assessed with either the Mini-Mental State Examination[2] or the General Cognitive Performance Score[9]), and POD was associated with a transient decline in cognitive function (throughout the first month after surgery). In both studies, it was also found that when these differences in preoperative cognitive function were adjusted for during analysis, POD was not associated with greater changes in cognitive scores compared with those with no delirium from preoperative baseline 1 yr after surgery. However, during 3 yr of repeated follow-up assessments in patients undergoing major

Table 2 Association between preoperative cognitive status and delirium (No. 1), and association between postoperative delirium and subsequent diagnosis of MCI or dementia (No. 2), in those with preoperative normal cognitive status. *Analysis No. 1 includes all patients to assess whether most recent cognitive status before surgery is associated with postoperative delirium. Adjusted analyses were performed using stratified logistic regression, with type of surgery included as a stratification variable. Additional covariates included in the model were age (using a penalized spline), sex, education level, APOE-ϵ4 genotype, and time from most recent MCSA visit to surgery. There were 31 observations excluded from the multivariable analysis because of missing APOE-ϵ4 genotype. †Analysis No. 2 includes 1152 patients who were cognitively normal before surgery and returned for at least one MCSA study visit after surgery. Among these patients, logistic regression was used to assess whether postoperative delirium was associated with diagnosis of MCI or dementia at their next MCSA follow-up visit. In addition to those used in analysis No. 1, patient co-morbidities and the time from surgery to the next MCSA visit were included as covariates in the adjusted analysis. Five observations were deleted from adjusted analysis because of missing APOE-ϵ4 genotype. Of 515 participants who were cognitively normal before surgery but did not return for a subsequent MCSA visit, 196 died (53 died ≤6 months after surgery; 30, 18, and 95 died 6.1–12.0, 12.1–18.0, and >18 months after surgery, respectively) and 319 were still alive at the time of analysis (36 with time from surgery of ≤6 months; 37, 28, and 218 with time from surgery of 6.1–12.0, 12.1–18.0, and >18 months, respectively). APOE-ϵ4, apolipoprotein ϵ4; CI, confidence interval; MCI, mild cognitive impairment; MCSA, Mayo Clinic Study of Aging; OR, odds ratio

			Unadjusted			Adjusted		
Analyses	***N***	**Outcome [*n* (%)]**	**OR**	**(95% CI)**	***P*-value**	**OR**	**(95% CI)**	***P*-value**
No. 1*		Postoperative delirium						
Preoperative cognitive status								
Normal cognition	1667	44 (2.6)	1.00	Reference		1.00	Reference	
MCI/dementia	347	30 (8.7)	3.49	(2.16–5.64)	<0.001	2.53	(1.52–4.21)	<0.001
No. 2† (cognitively normal patients)		Subsequent MCI/dementia						
Postoperative delirium								
No	1131	102 (9.0)	1.00	Reference		1.00	Reference	
Yes	21	7 (33.3)	5.05	(1.99–12.79)	<0.001	3.00	(1.12–8.05)	0.029

non-cardiac surgery,[2] those who experienced POD had significantly greater relative long-term cognitive decline. Neither of these studies specifically examined the association between POD and later cognition among those with normal preoperative cognition.

Our results suggest that even in patients who are cognitively normal after surgery, POD is still associated with later cognitive decline, as measured by the development of MCI or dementia. The association between POD and subsequent MCI or dementia can be interpreted within the conceptual framework of cognitive trajectories proposed to explain perioperative changes in cognition.[42] Within this framework, cognitive function declines at varying rates with ageing, and clinical diagnoses such as MCI and dementia are made when the trajectory crosses a detectable threshold. Patients with cognitive function that is approaching the threshold are deemed to have low cognitive reserve. Surgery represents an event that could both cause transient changes in cognition and alter the trajectory of decline. The relationship between POD and later cognitive decline has at least two potential interpretations within this framework. First, POD could be a marker for patients with accelerated preoperative cognitive decline that is more likely to be associated with diminished cognitive reserve. Although patients can recover from acute POD caused by the insult of surgery, they then return to their accelerated trajectory and are more likely to manifest later clinical diagnoses once their cognition declines below the threshold detectable with current diagnostic tools. Second, POD itself could produce injury, thus accelerating the trajectory of decline.[43–46] However, studies showing that immediate postoperative decreases in cognition associated with POD appear to be transient make this latter interpretation less likely.[2 9] The distinction between these interpretations is clinically relevant, because interventions exist that focus on modifiable risk factors for prevention of delirium,[47–49] with especially compelling evidence from the ICU settings with introduction of 'pain, agitation, and delirium guidelines'.[50] Specifically, evidence is accumulating that certain measures (e.g. reduction of benzodiazepine use, shorter intubation time) can reduce the incidence and severity of delirium.[33 50 51] In that context, if delirium, *per se*, accelerates the trajectory of cognitive decline,[45 46] prevention of POD may improve the long-term cognitive outcome. Alternatively, if POD is merely a marker for the risk rather than a cause, prevention of delirium may not affect long-term cognitive outcome, and these specific aspects of perioperative delirium must be the focus of future studies.

Limitations

This study had several limitations in addition to those already discussed. First, although the study benefited from rigorous preoperative cognitive assessments, a median of 8.8 months elapsed from the time of the last cognitive assessment until surgery. This is a relatively brief time when assessing typical changes in cognitive function, but some patients might have developed MCI within this interval. However, the fact that the incidence of POD was much lower in these cognitively normal individuals than in those with MCI or dementia argues that we were indeed able to distinguish between patients who were not cognitively normal. Second, almost one-third of patients were not available for postoperative MCSA follow-up, which could bias our estimates on the frequency of MCI after surgery. It is also important to note that the proportion of patients with POD was lower in those who returned for a follow-up MCSA visit compared with those who did not. Third, the time from surgery to the next follow-up visit varied, such that all patients were not sampled at the same point of their postoperative cognitive trajectory. Fourth, the routine

clinical use of CAM-ICU as a means to ascertain POD, although common in the literature, has not been specifically validated in our surgical practice. Finally, the overall incidence of POD obtained by reviewing medical records appears to be low compared with other studies,[1 52] which suggests incomplete ascertainment using routine clinical *vs* prospective research assessments. However, several other factors might contribute to our lower delirium rates, as follows: (1) more than one-half of the procedures were performed on an outpatient basis, including many using monitored anaesthesia care, and these patients might be less likely to develop POD; (2) only 36% of patients were hospitalized for >2 days, and longer hospitalizations are associated with delirium; (3) our window used to define POD (72 h) was shorter than some other studies;[11 12] (4) we excluded high-risk patients with any preoperative CAM-ICU positive assessments for delirium; and (5) it is possible that the low sensitivity of CAM-ICU when used for non-critically ill hospitalized patients (18%)[28] results in missing detection of 'mild' instances of delirium.

In conclusion, elderly patients without a preoperative diagnosis of MCI or dementia who experienced POD detected by routine clinical surveillance were more likely to be diagnosed subsequently with MCI or dementia. Postoperative delirium may be related to underlying cognitive deficits and may be a consequence or marker of emerging cognitive impairment. These findings suggest that elderly surgical patients who experience POD should receive extended neurocognitive follow-up, as they might be at increased risk for cognitive dysfunction. More research is needed to determine whether the measures designed for prevention of POD may affect subsequent cognitive trajectories.

Authors' contributions

Study conception and design: J.S., R.O.R., T.N.W., D.S.K., R.C.P., D.O.W.
Acquisition of data: J.S., R.O.R., T.N.W., A.N.C., A.C.H., D.R.S., D.O.W.
Data analysis: J.S., R.O.R., T.N.W., A.N.C., A.C.H., D.R.S., D.O.W.
Interpretation of data: J.S., R.O.R., T.N.W., D.S.K., R.C.P., A.N.C., A.C.H., D.R.S., D.O.W.
Final approval of the version to be published: J.S., R.O.R., D.S.K., R.C.P., A.N.C., A.C.H., D.R.S., D.O.W.
Full access to all of the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis: J.S., D.R.S., R.O.R.
Final responsibility for the decision to submit for publication: J.S., D.R.S., R.O.R.

Supplementary material

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

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Declaration of interest

D.S.K. served as past deputy editor for the journal *Neurology*; he currently serves on a Data Safety Monitoring Board for Lundbeck Pharmaceuticals and for the Dominantly Inherited Alzheimer's Disease Treatment Unit. He is an investigator in clinical trials sponsored by Biogen, Lilly, and TauRX and receives research support from the US National Institutes of Health.
R.C.P. is chair of Data Monitoring Committees for Pfizer and Janssen Alzheimer Immunotherapy and has served as a consultant for Roche, Merck, and Genentech. He receives royalties from the publication of *Mild Cognitive Impairment*, published by Oxford University Press.
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