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Clinical Investigation

CLINICAL INVESTIGATION

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