Development of dementia in patients with femoral neck fracture who experience postoperative delirium—A three-year follow-up study

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Objectives: It remains unclear to what extent postoperative delirium (POD) affects the incidence of dementia in hip fracture patients, and the methods used to detect delirium and dementia require validation. The aim of this study was to investigate the development of dementia within 3 years of femoral neck fracture repair surgery, with a focus on POD as a potential predictive factor.

Methods: Patients were assessed for cognition, delirium, depression, psychological wellbeing, and nutritional status during their hospitalization as well as 4, 12, and 36 months after the operation. Logistic regression models were used to analyse factors associated with POD and factors associated with the development of dementia.

Results: The study sample consisted of 135 patients without a history of dementia, of whom 20 (14.8%) were delirious preoperatively and 75 (55.5%) postoperatively. Three years after their operations, 43/135 patients (31.8%) were diagnosed with dementia. A greater portion of patients diagnosed with dementia (39/43, 90.6%) than patients with no dementia (36/92, 39.1%) were included among the 75 patients who had experienced POD ($P < 0.001$). In a logistic regression model, after adjustment for covariates (age, sex, diabetes, delirium pre- and postoperatively, hyperactive delirium, days with delirium, urinary tract infection, and Mini Nutritional Assessment score), POD emerged an independent predictor for the development of new dementia (odds ratio, 15.6; 95% confidence interval, 2.6–91.6) within 3 years after the operation.

Conclusion: Geriatric hip fracture patients who exhibit POD should be monitored closely for the development of dementia.

KEYWORDS
cognitive impairment, femoral neck fracture, geriatrics, logistic regression, mortality

INTRODUCTION

Delirium is a disturbance of awareness accompanied by cognitive impairment that develops over a short period of time, fluctuates, and has, by definition, an underlying cause.$^{1,2}$ A number of studies have provided evidence of an association between postoperative delirium (POD) and subsequent cognitive decline.$^{3-6}$ This association has been observed in hip surgery patients,$^{7-10}$ patients undergoing noncardiac surgery,$^{6}$ and patients with pre-existing cognitive impairment.$^{11}$

Elderly patients may experience POD during their hospitalization following hip fracture repair.$^{12,13}$ In addition to being very disconcerting to patients,$^{14,15}$ POD can impede recovery from hip fracture.$^{16,17}$ It has been associated with longer hospitalization, reduced ability to regain prefracture functional status, risk of altering patients’ living situations, and increased mortality.$^{18,20}$ Moreover, longer duration of POD in hip-fracture patients has been reported to be associated with greater mortality risk within 6 months.$^{21}$ These associations are also seen in patients who develop delirium superimposed on dementia.$^{22}$

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Several research groups have investigated the association between delirium and dementia in patients who have suffered a hip fracture.\(^23\)\(^-\)\(^26\) However, the studies have had a variety of methodological limitations, such as a small sample size (eg, \(N = 78\)),\(^24\) a short follow-up period (eg, 6 months),\(^25\) retroactive delirium diagnosis,\(^23\) heterogenous clinical samples (eg, inclusion of both emergency and elective hip surgery)\(^23\)\(^,\)\(^26\) and no prefracture assessment of dementia.\(^26\) Thus, questions remain regarding the putative association between POD and subsequent dementia. The aim of the present study was to investigate whether POD is a predictor of dementia incidence in patients with a femoral neck fracture within 3 years after hip repair surgery.

2 | METHODS

2.1 | Procedures

The present study is part of a larger randomized intervention study conducted between May 2000 and December 2002 and had a 3-year follow up that was ended in 2005. The whole study design is presented in detail elsewhere.\(^12\)\(^,\)\(^27\) The present study cohort is a subsample of 135 of the 199 participants enrolled in the aforementioned intervention study who did not fulfil the DSM-IV\(^1\) criteria for dementia upon their admission. All included patients were at least 70 years old and were admitted to a university hospital in northern Sweden with a femoral neck fracture. Informed consent was obtained from the patient or the patient’s next of kin if the patient was cognitively impaired. The Ethics Committee of the Faculty of Medicine at Umeå University approved the study (\(\# 00-137\)).

The participants received the same treatment preoperatively but were randomized into either standard or intervention postoperative care. If participants in the control group needed further rehabilitation, they were transferred to a general geriatric ward. The intervention program was conducted by staff who were educated about individual care, rehabilitation, an active approach to the prevention, detection, and treatment of postoperative complications, including POD, and an active nutrition program. The staff worked as a team in applying a meticulous investigation, treatment, and rehabilitation program, as described in detail elsewhere.\(^12\)\(^,\)\(^27\) The number of staff providing care was the same for both the intervention and control groups.

2.2 | Data collection

The participants were observed daily preoperatively and postoperatively by ward nurses. At least 3 times a day and after each shift documentations were performed in nursing records according to routine procedure, including any symptoms or signs of delirium and changes in the patient’s mental state. The patients were also assessed explicitly for cognitive status, depressive symptoms, delirium, morale, hearing and vision, and nutritional status once between 3 and 5 days postoperatively by 2 study nurses (research assistants) who were contracted half-time in the study and trained to carry out the assessments in the 2 wards. Medical and social data were also collected from the participants, relatives, staff, and medical records. The same 2 research assistants re-assessed the participants 4, 12, and 36 months postoperatively in their homes with similar assessments as in hospitalization.

Information regarding prescribed drugs at admission and any complications arising during hospitalization (eg, constipation, sleeping disturbances, and nutritional problems) were obtained from the patients’ medical records. Length of stay in the hospital as well as in-hospital, 1-year, and 3-year mortality data were recorded.

2.3 | Assessment of delirium

The modified Organic Brain Syndrome Scale (OBS scale; 28) was used to screen for delirium. It consists of a 12-item disorientation subscale and a 21-feature observation confusion subscale. The disorientation subscale is a questionnaire that assesses participants’ orientation to time, place, and their own identity (maximum score, 36; higher score indicates worse disorientation). The confusion subscale is designed to reflect various cognitive, psychotic, emotional, and personality changes and fluctuations in the clinical state including, depressed mood, emotional lability, anxiety, restlessness, agitation, aggressive behavior, delusions/hallucinations, and language/speech disturbances. The confusion subscale is applied through direct observation and interviewing of participants and caregivers. Here, the OBS scale was applied to capture symptoms and clinical changes within the prior couple of days. The scale has been shown to have good concurrent validity relative to other delirium assessment instruments\(^28\)\(^,\)\(^29\) and has been used in a variety of settings to diagnose POD.\(^12\)\(^,\)\(^15\)\(^,\)\(^30\)\(^,\)\(^31\) Any delirium-like symptoms and signs within the first 8 postoperative hours were attributed to the immediate effects of peri-operative drugs and not registered as delirium.

2.4 | Additional assessments

The Mini Mental State Examination (MMSE)\(^32\) was used to assess participants’ cognition. MMSE scores range from 0 to 30 points, with lower scores indicating a worse cognitive state. The MMSE has been shown to have good reliability and construct validity and may be used to assess cognitive changes over time.\(^33\)

The presence of depression before hospitalization was determined based on an evaluation of earlier diagnoses in the patients’ medical

Key points

- Of 135 patients with a femoral neck fracture and no history of dementia, more than half experienced delirium postoperatively.
- Nearly one third of participants had developed dementia 3 years after the operation, and more than 90% of those who developed dementia had postoperative delirium during hospitalization.
- Postoperative delirium was independently associated with subsequent development of dementia within 3 years, while diabetes seemed to exert a protective effect.
- Patients who develop postoperative delirium after femoral neck fracture should be afforded special attention because this syndrome may be a harbinger of cognitive decline and dementia.
records and current antidepressant prescriptions. Patients were considered to be having depressive symptoms during hospitalization if they were currently being treated with antidepressants and shown to have depressive symptoms on the Geriatric Depression Scale-15 (score > 5 indicative of depressive symptoms)\textsuperscript{34,35} in combination with depressive symptoms being observed and registered with the OBS scale.

The Mini Nutritional Assessment (MNA)\textsuperscript{36} was used to assess participants’ nutritional status. The MNA has a total score of 30: a score > 24 indicates a well-nourished subject, a score of 17–23 indicates risk of malnutrition, and a score < 17 is considered indicative of malnourishment or insufficient protein calorie intake.\textsuperscript{37} The participants’ quality of life, morale, and subjective well-being were assessed with the Philadelphia Geriatric Centre Morale Scale (maximum score, 17; higher score indicates higher morale or better quality of life).\textsuperscript{38}

Participants who were unable to read 4-mm block letters at a reading distance, with or without glasses, were considered vision impaired. Hearing was considered impaired if the participant could not hear a normal speaking voice at a 1-m distance, with or without a hearing aid.

2.5 \textbf{Diagnosis of delirium, dementia, and depression}

After the study was finished (after 2005), all assessments (including those done during hospitalization 3–5 days, at 4–12–and 36-months follow-ups) and documentations (including participants’ medical and nursing records during hospitalization and death certificates) were analysed by a specialist in geriatric medicine who was not involved in the patient’s care nor in their follow-ups to ascertain whether each participant met the DSM-IV-TR criteria for delirium, dementia, or depression; the geriatrician also classified the type of delirium evidenced (hypo, hyper, or mixed) based on DSM-IV-TR criteria. The geriatrician first evaluated all assessments performed by the research assistants, and this was performed totally blinded. In the next step, he read and analysed all documentation in the records with regard to any signs or symptoms indicating delirium for each day. This step was not possible to perform totally blind. The records we used included documentation from about 6,500 days, and therefore it was difficult for the geriatrician to know the patients’ group allocation.

2.6 \textbf{Statistical analyses}

To describe group differences (with vs without POD; with vs without dementia), univariate analyses were performed; Student t test for continuous variables and chi-square tests for categorical data, or Fisher exact tests when the expected count was less than 5. Logistic regression models were used to analyse factors associated with POD and factors associated with development of dementia. For each model, variables with a $P$-value \textless{} 0.10 were included in regression modelling. MMSE results ($>$0.4 Spearman rank correlation coefficient) and neuroleptic agent use (too few events) were not included as factors. The analyses were conducted in SPSS version 23. A $P$-value < .05 was regarded as significant.

3 \textbf{RESULTS}

Of the 135 participants in the study, 20 (14.8%) had experienced delirium preoperatively and 75 (55.5%) experienced POD (Figure 1). The demographic, preoperative clinical, and immediate postoperative clinical characteristics of the participants who later developed POD (POD group) and those who did not (non-POD group) are compared...
in Table 1. Preoperatively, participants who had POD tended to be older (83.1 ± 6.1 vs 81.0 ± 6.2, \( p < 0.001 \)), were more likely to be diagnosed with depression upon admission (41% vs 15%, \( p < 0.001 \)), and were less likely to have been living independently before sustaining the fracture compared with those who did not have POD (75% vs 90%, \( P = 0.023 \), Table 1). During the postoperative hospitalization period, relative to participants who did not experience POD, participants who experienced POD had a higher incidence of postoperative complications, ie, constipation (51% vs 32%, \( P = 0.026 \)), sleeping problems (43% vs 25%, \( P = 0.032 \)), urinary tract infection (24% vs 10%, \( P = 0.035 \)), and hip luxation (8% vs 0, \( P = 0.033 \)), as well as longer average hospital stays (45.2 ± 37.0 vs 23.9 ± 21.0, \(<0.001\), Table 1). Logistic regression modelling indicated that depression at the time of admission and postoperative urinary tract infection were independently associated with POD (data not shown).

Follow-up data for these 2 groups collected at 3 time points (4, 12, and 36 months) are compared in Table 2. At each follow-up time point, surviving patients in the POD group had greater incidences of dementia (13% vs 0%, \( P = 0.004 \)) and depression (63% vs 25%, \( P < 0.001 \)), lower MMSE scores (20.4 ± 5.2 vs 26.2 ± 3.5, \( P < 0.001 \)), and lower MNA scores (22.5 ± 3.9 vs 24.9 ± 3.2, \( P < 0.001 \)) than surviving patients in the non-POD group. Geriatric Depression Scale scores were similar between the 2 groups at the last follow-up time point, but significantly higher in the POD group than in the non-POD group at the former follow-up time points. Mortality between 12 months and 36 months was greater for the POD group than the non-POD group (28% vs 13%, \( P = 0.036 \), but too few deaths in other time periods to analyse).

### Table 1: Comparison of characteristics at baseline and during hospitalization between patients who experienced POD (N = 75) and those who did not (N = 60) within a total cohort of 135 patients with no diagnosis of dementia before undergoing hip surgery

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>POD</th>
<th>No POD</th>
<th>( P^d )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age ± SD, years</td>
<td>83.1 ± 6.1</td>
<td>81.0 ± 6.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No. men/no. women</td>
<td>19/56</td>
<td>15/45</td>
<td>0.965</td>
</tr>
<tr>
<td>Living independently, N (%)</td>
<td>56 (75)</td>
<td>54 (90)</td>
<td>0.023</td>
</tr>
<tr>
<td>Impaired vision 69/56, N (%)</td>
<td>27 (39)</td>
<td>18 (32)</td>
<td>0.418</td>
</tr>
<tr>
<td>Impaired hearing 72/52, N (%)</td>
<td>29 (40)</td>
<td>26 (50)</td>
<td>0.431</td>
</tr>
<tr>
<td>Heart diseaseb 74/59, N (%)</td>
<td>41 (56)</td>
<td>32 (54)</td>
<td>0.893</td>
</tr>
<tr>
<td>Previous stroke 73/60, N (%)</td>
<td>19 (26)</td>
<td>11 (18)</td>
<td>0.291</td>
</tr>
<tr>
<td>Diabetes mellitus, N (%)</td>
<td>17 (23)</td>
<td>10 (17)</td>
<td>0.386</td>
</tr>
<tr>
<td>Hypertension 74/57, N (%)</td>
<td>32 (43)</td>
<td>28 (49)</td>
<td>0.503</td>
</tr>
<tr>
<td>Previous hip fracture 75/59, N (%)</td>
<td>12 (16)</td>
<td>7 (12)</td>
<td>0.496</td>
</tr>
<tr>
<td>Depression on admission 75/59, N (%)</td>
<td>31 (41)</td>
<td>9 (15)</td>
<td>0.001</td>
</tr>
<tr>
<td>Neurolepticsc, N (%)</td>
<td>3 (4)</td>
<td>4 (7)</td>
<td>0.700e</td>
</tr>
<tr>
<td>Antidepressantsc, N (%)</td>
<td>25 (33)</td>
<td>8 (13)</td>
<td>0.007</td>
</tr>
<tr>
<td>During hospitalization</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urinary tract infection postop 75/59, N (%)</td>
<td>39 (52)</td>
<td>13 (22)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Constipation postop, N (%)</td>
<td>38 (51)</td>
<td>19 (32)</td>
<td>0.026</td>
</tr>
<tr>
<td>Urinary retention postop, N (%)</td>
<td>18 (24)</td>
<td>6 (10)</td>
<td>0.035</td>
</tr>
<tr>
<td>Sleeping disturbances postop, N (%)</td>
<td>32 (43)</td>
<td>15 (25)</td>
<td>0.032</td>
</tr>
<tr>
<td>Nutritional problems postop, N (%)</td>
<td>32 (43)</td>
<td>9 (15)</td>
<td>0.001</td>
</tr>
<tr>
<td>Hip luxation, N (%)</td>
<td>6 (8)</td>
<td>0</td>
<td>0.033e</td>
</tr>
<tr>
<td>Depression postop 75/60, N (%)</td>
<td>44 (59)</td>
<td>17 (28)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Intervention/control group N</td>
<td>37/38</td>
<td>37/23</td>
<td>0.152</td>
</tr>
<tr>
<td>Mean MMSE score ± SD postop day 3–5</td>
<td>17.7 ± 6.0</td>
<td>25.0 ± 3.3</td>
<td>&lt;0.001f</td>
</tr>
<tr>
<td>Mean MNA score ± SD postop day 3–5</td>
<td>21.8 ± 3.8</td>
<td>24.9 ± 2.6</td>
<td>&lt;0.001f</td>
</tr>
<tr>
<td>Mean GDS score ± SD postop day 3–5</td>
<td>5.5 ± 3.9</td>
<td>3.6 ± 2.8</td>
<td>0.004f</td>
</tr>
<tr>
<td>Mean length of stay ± SD, days</td>
<td>45.2 ± 37.0</td>
<td>23.9 ± 21.0</td>
<td>&lt;0.001f</td>
</tr>
<tr>
<td>In-hospital death, N (%)</td>
<td>4 (5)</td>
<td>3 (5)</td>
<td></td>
</tr>
</tbody>
</table>

\( ^a \)For characteristics for which information was not available for all 135 patients, adjusted Ns for percentages are indicated in the form of POD N/No POD N.

\( ^b \)Including heart failure.

\( ^c \)Prescriptions made upon admission; antidepressants refer to selective serotonin reuptake inhibitors.

\( ^d \)Chi-square tests.

\( ^e \)Fisher exact tests.

\( ^f \)Student t test.

Abbreviations: GDS, 15-item Geriatric Depression Scale; MMSE, Mini Mental State Examination; MNA, Mini Nutritional Assessment; POD, postoperative delirium; Postop, postoperatively; SD, standard deviation.

Significant \( P \) values are in bold typeface.
For parameters for which information was not available for all 135 patients, adjusted Ns for percentages are indicated in the form of POD N/No POD N.

have experienced hyperactive (5.9 ± 6.2 vs 2.4 ± 6.1, P = 0.002). Of those who died, 15 were diagnosed with diabetes (35.7%). The most common cause of death was cardiovascular disease (N = 13), followed by trauma/accident (N = 9), and cancer (N = 8). The mortality rate for patients that had developed dementia was similar to that for those who had not (data not shown).

A logistic regression analysis showed that POD was significantly associated with development of dementia within 3 years (odds ratio 15.582, confidence interval 2.649–91.640, P = 0.002), while...
participants with diabetes seemed to have a reduced risk (odds ratio 0.244, confidence interval 0.065–0.919, \( P = 0.037 \), Table 5). None of the other analysed factors were found to be significantly related to dementia diagnosis.

### 4 DISCUSSION

In this study, nearly a third of 135 patients who suffered a hip fracture with no prior history of dementia developed dementia within 3 years of hip repair surgery, among whom 91% had experienced POD during hospitalization. A logistic regression model showed that POD was independently associated with the development of dementia within 3 years, whereas diabetes emerged as a negative predictor of dementia. Notably, POD was associated with an increased 3-year mortality rate.

The present results are consistent with prior reports suggesting that POD is a strong predictor of later dementia in hip fracture patients.\(^{23,24,26}\) However, there are some methodological differences between these studies. Lundström et al\(^{24}\) employed similar assessments for both delirium and dementia as the present study, but had a smaller cohort and a longer follow-up period (5 years). Five years after the operation, they found that 30/78 patients (38%) were diagnosed with dementia, including 20/29 (69%) who had POD and only 10/49 (20%) who did not. In the present study, 43/135 participants (32%) were diagnosed with dementia by 3 years after the operation; 91% of the patients in the dementia group had experienced POD whereas only 39% of the patients in the no dementia group had experienced POD. In a prospective study of 106 elderly hip fracture patients without prefracture dementia, Krogseth et al\(^{25}\) found that of 29 patients who experienced delirium, 11 (37%) fulfilled the criteria of dementia after 6 months, compared with 5/77 (7%)

### TABLE 3

| Characteristic                  | Dementia 3 Years Postop | No Dementia 3 Years Postop | \( P \)  \\
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age ± SD</td>
<td>84.4 ± 6.2</td>
<td>81.1 ± 6.0</td>
<td>0.004(^{d})</td>
</tr>
<tr>
<td>No. men/no. women</td>
<td>7/36</td>
<td>27/65</td>
<td>0.103</td>
</tr>
<tr>
<td>Living independently, N (%)</td>
<td>33 (77)</td>
<td>77 (84)</td>
<td>0.333</td>
</tr>
<tr>
<td>Impaired vision, N (%)</td>
<td>17/40 (42)</td>
<td>28/85 (33)</td>
<td>0.299</td>
</tr>
<tr>
<td>Impaired hearing, N (%)</td>
<td>19/41 (46)</td>
<td>36/86 (42)</td>
<td>0.634</td>
</tr>
<tr>
<td>Heart disease, N (%)</td>
<td>20/42 (48)</td>
<td>53/91 (58)</td>
<td>0.252</td>
</tr>
<tr>
<td>Previous stroke, N (%)</td>
<td>12/42 (28)</td>
<td>18/91 (20)</td>
<td>0.260</td>
</tr>
<tr>
<td>Diabetes mellitus, N (%)(^{a})</td>
<td>5 (12)</td>
<td>22 (24)</td>
<td>0.096</td>
</tr>
<tr>
<td>Hypertension, N (%)</td>
<td>18 (42)</td>
<td>42/88 (48)</td>
<td>0.527</td>
</tr>
<tr>
<td>Previous hip fracture, N (%)</td>
<td>6 (14)</td>
<td>13/91 (14)</td>
<td>0.959</td>
</tr>
<tr>
<td>Depression on admission, N (%)</td>
<td>15 (35)</td>
<td>25/91 (27)</td>
<td>0.381</td>
</tr>
<tr>
<td>Neuroleptics, N (%)</td>
<td>0</td>
<td>7 (7)</td>
<td>0.096(^{e})</td>
</tr>
<tr>
<td>Antidepressants(^{b}), N (%)</td>
<td>13 (30)</td>
<td>20 (22)</td>
<td>0.285</td>
</tr>
</tbody>
</table>

\(^{a}\) Of 27 participants with diabetes, 15 had died by the 3-year follow-up time point.

\(^{b}\) Selective serotonin reuptake inhibitors.

\(^{c}\) Chi square test.

\(^{d}\) Student t test.

\(^{e}\) Fisher exact test.

Abbreviations: Hyper, hyperactive; hypo, hypoactive; POD, postoperative delirium; postop, postoperatively; preop, preoperatively; SD, standard deviation. Significant \( P \) values are in bold typeface.
without delirium ($P < 0.001$), and further found that delirium was a strong predictor of dementia after 6 months. Their study had a far shorter follow-up period than the present study, and they assessed preoperative cognitive status with the short-form Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE). Neither the present study nor the 2003 study by Lundstrom and colleagues

### TABLE 4  Comparison of clinical scale scores during hospitalization and at follow-up assessments between patients with ($N = 43$) and without ($N = 92$) dementia diagnosis during the study period

<table>
<thead>
<tr>
<th>Assessmenta</th>
<th>Mean Score ± SD</th>
<th>Dementia 3 Years Postop</th>
<th>No Dementia 3 Years Postop</th>
<th>$P^b$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Postop days 3-5 during hospitalization</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMSE, 40/84</td>
<td>17.0 ± 6.4</td>
<td>22.6 ± 5.2</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>OBS, 41/84</td>
<td>10.1 ± 7.9</td>
<td>3.8 ± 6.2</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GDS-15, 36/81</td>
<td>4.1 ± 3.2</td>
<td>4.9 ± 3.8</td>
<td></td>
<td>0.277</td>
</tr>
<tr>
<td>PGCMS, 36/81</td>
<td>10.6 ± 3.2</td>
<td>10.2 ± 3.8</td>
<td></td>
<td>0.563</td>
</tr>
<tr>
<td>MNA, 40/80</td>
<td>22.2 ± 3.5</td>
<td>23.6 ± 3.7</td>
<td></td>
<td>0.034</td>
</tr>
<tr>
<td><strong>4-month follow-up</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMSE 42/77</td>
<td>19.0 ± 5.4</td>
<td>25.3 ± 3.7</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>OBS 42/77</td>
<td>7.0 ± 5.9</td>
<td>1.5 ± 2.4</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GDS-15 41/76</td>
<td>4.2 ± 2.8</td>
<td>4.1 ± 3.2</td>
<td></td>
<td>0.829</td>
</tr>
<tr>
<td>PGCMS 40/76</td>
<td>11.0 ± 3.0</td>
<td>11.4 ± 3.5</td>
<td></td>
<td>0.559</td>
</tr>
<tr>
<td>MNA 42/76</td>
<td>22.4 ± 3.9</td>
<td>24.3 ± 3.6</td>
<td></td>
<td>0.012</td>
</tr>
<tr>
<td><strong>12-month follow-up</strong></td>
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<td></td>
</tr>
<tr>
<td>MMSE 43/70</td>
<td>17.7 ± 6.4</td>
<td>25.6 ± 4.3</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>OBS 42/70</td>
<td>8.4 ± 6.3</td>
<td>1.4 ± 4.2</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GDS-15 40/68</td>
<td>4.8 ± 3.2</td>
<td>4.5 ± 3.4</td>
<td></td>
<td>0.611</td>
</tr>
<tr>
<td>PGCMS 40/68</td>
<td>11.0 ± 3.7</td>
<td>11.6 ± 3.2</td>
<td></td>
<td>0.328</td>
</tr>
<tr>
<td>MNA 42/67</td>
<td>21.5 ± 3.8</td>
<td>24.7 ± 3.1</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>36-month follow-up</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MMSE 31/44</td>
<td>15.6 ± 5.6</td>
<td>26.9 ± 2.4</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>OBS 32/44</td>
<td>12.3 ± 8.4</td>
<td>0.4 ± 0.6</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GDS-15 28/44</td>
<td>4.0 ± 2.6</td>
<td>3.3 ± 2.6</td>
<td></td>
<td>0.250</td>
</tr>
<tr>
<td>PGCMS 30/43</td>
<td>11.2 ± 4.5</td>
<td>12.0 ± 3.0</td>
<td></td>
<td>0.327</td>
</tr>
<tr>
<td>MNA 33/43</td>
<td>21.7 ± 3.7</td>
<td>25.7 ± 2.2</td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

$^a$For parameters for which information was not available for all 135 patients, adjusted Ns for reported means are indicated in the form of Dementia group N/No dementia group N.

$^b$Student t test.

Abbreviations: GDS-15, 15-item Geriatric Depression Scale; MMSE, Mini Mental State Examination; MNA, Mini Nutritional Assessment; OBS, Organic Brain Syndrome Scale; PGCMS, Philadelphia Geriatric Centre Morale Scale; postop, postoperatively; SD, standard deviation.

Significant $P$ values are in bold typeface.

### TABLE 5  Logistic regression modelling of factors associated with the development of dementia within 3 years after hip repair surgery

<table>
<thead>
<tr>
<th>Independent Variable</th>
<th>B</th>
<th>Wald Statistic</th>
<th>$P$</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.060</td>
<td>1.952</td>
<td>0.162</td>
<td>1.062</td>
<td>0.976–1.156</td>
</tr>
<tr>
<td>Sex</td>
<td>0.508</td>
<td>0.619</td>
<td>0.432</td>
<td>1.662</td>
<td>0.469–5.891</td>
</tr>
<tr>
<td>Diabetes</td>
<td>-1.411</td>
<td>4.347</td>
<td>0.037</td>
<td>0.244</td>
<td>0.065–0.919</td>
</tr>
<tr>
<td>Delirium preop</td>
<td>0.624</td>
<td>0.709</td>
<td>0.400</td>
<td>1.867</td>
<td>0.437–7.982</td>
</tr>
<tr>
<td>Delirium postop</td>
<td>2.746</td>
<td>9.228</td>
<td>0.002</td>
<td>15.582</td>
<td>2.649–91.640</td>
</tr>
<tr>
<td>Hyperactive delirium</td>
<td>0.338</td>
<td>0.305</td>
<td>0.581</td>
<td>1.402</td>
<td>0.423–4.645</td>
</tr>
<tr>
<td>Days with delirium</td>
<td>-0.056</td>
<td>1.822</td>
<td>0.177</td>
<td>0.946</td>
<td>0.872–1.025</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>0.314</td>
<td>0.337</td>
<td>0.562</td>
<td>1.369</td>
<td>0.474–3.949</td>
</tr>
<tr>
<td>MNA score</td>
<td>-0.010</td>
<td>0.021</td>
<td>0.885</td>
<td>0.990</td>
<td>0.861–1.138</td>
</tr>
</tbody>
</table>

Nagelkerke $R^2 = 0.380$.

Abbreviations: CI, confidence interval; MNA, Mini Nutritional Assessment; OR, odds ratio; postop, postoperatively; preop, preoperatively.

Significant Wald significance $P$ values are in bold typeface.
included such a formal assessment, but rather relied upon medical records. In a study of patients in Brazil, Wacker et al. observed a 10-fold increased risk of subsequent dementia in patients who experienced POD; they used the IQCODE, but delirium was diagnosed by retrospective chart review. Analogous results have been obtained in different medical populations. In a study of 51 community-dwelling patients admitted in an acute delirious state but without dementia, Rahkonen et al. found that half of such patients were diagnosed with dementia within 2 years of being admitted. Furthermore, in a population-based study of 199 non-demented very old subjects (≥85 years old), 13/20 subjects (65%) with delirium at baseline were found to have dementia 3 years later. In yet another population-based study of an elderly cohort, delirium emerged as a strongly significant risk factor (8-fold increased risk) for dementia. Here, we observed an association between POD duration and subsequent development of dementia in our univariate analysis, but this association was not significant in the regression model. A similar association has been reported for non-hip-fracture patient populations. Altogether, these studies identify delirium as an important risk factor for dementia, although a causal mechanism underlying this association has yet to be established.

A number of research groups have examined a potential association between POD and subsequent cognitive impairment, rather than a diagnosis of dementia per se. These studies reported that POD following hip surgery was associated with subsequent cognitive impairment. These studies had a variety of methodological limitations, such as using telephone interviews for follow-up assessments, a small study sample, short (4–6 months) follow-up period, and inconsistent age criteria precluding direct inter-study comparisons. Hence, more research with standardized methods, large samples, and similar long follow-up periods is needed.

Our finding that diabetes was associated with a reduced risk of dementia was surprising given that previous studies have shown diabetes to be a positive risk factor for dementia, although this association has been suggested to be less evident among people over 85 years old. Notwithstanding, one prior prospective community-based cohort study showed that diabetes was not an independent risk factor for dementia. Conversely, another study showed that patients with both diabetes and dementia had slower cognitive decline than patients with dementia only and that non-demented patients with diabetes did not exhibit cognitive impairment relative to non-diabetic non-demented controls. Because the present study sample included few participants with diabetes, and some of those in our cohort died during the follow-up period, it was not possible to conduct a meaningful statistical evaluation of the relative incidence of dementia in diabetics as a subgroup. Hence, the emergence of this association in our results should be interpreted with caution.

The present finding that more participants with POD, relative to those without POD, had died by the 3-year follow-up time point is consistent with prior findings. However, one recent study found no association between POD following hip fracture surgery and mortality after adjusting for cognitive impairment severity as determined by the IQCODE. It should be noted that very old patients with multiple comorbidities may be particularly vulnerable to any postoperative complication, including delirium. These patients should be afforded special attention when hospitalized to prevent complications.

4.1 Strengths and limitations

A noteworthy strength of this study is that cognitive assessments were conducted on several occasions (baseline as well as 4, 12, and 36-month follow-ups). Additionally, delirium and dementia diagnoses were made with standardized criteria by one physician who was a specialist in geriatric medicine.

This study has the limitation of not having included preoperative cognitive testing. Cognitive testing was conducted only one time during hospitalization. Secondly, the presence of preoperative delirium was based solely on nurse documentation.

5 Conclusion

Postoperative delirium is a strong predictor of subsequent development of dementia in elderly patients recovering from hip fracture repair surgery. Patients who develop POD after femoral neck fracture should be monitored closely for potential cognitive decline and dementia.

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Conflict of Interest

None declared.

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