DELIRIUM IN OLD PATIENTS WITH FEMORAL NECK FRACTURE

Risk Factors, Outcome, Prevention and Treatment

by

Maria Lundström
When I am an old woman, I shall wear purple
With a red hat which doesn't go, and doesn't suit me.
And I shall spend my pension on brandy and summer gloves
And satin sandals, and say we've no money for butter.
I shall sit down on the pavement when I'm tired
And gobble up samples in shops and press alarm bells
And run my stick along the public railings
And make up for the sobriety of my youth.
I shall go out in my slippers in the rain
And pick the flowers in other peoples' gardens
And learn to spit...........
But maybe I ought to practice a little now?
So people who know me are not too shocked and surprised
When suddenly I am old, and start to wear purple.

(Warning by Jenny Joseph)
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PAPERS I-IV

Dissertations from the Department of Community Medicine and Rehabilitation,
Geriatric Medicine, Umeå University, 1983-2004
ABSTRACT

Delirium is probably the most common presenting symptom of disease in old age. Delirium, as defined in DSM-IV, is a neuropsychiatric syndrome characterized by disturbance in attention and consciousness, which develops over a short period of time and where the symptoms tend to fluctuate during the course of the day. The overall aim was to increase knowledge about the risk factors and outcome of delirium in old patients with femoral neck fracture and to develop and evaluate a multi-factorial intervention program for prevention and treatment of delirium in these patients.

In a prospective study of 101 consecutive patients with a femoral neck fracture, 29.7% were delirious before surgery and another 18.8% developed delirium postoperatively. Of those who were delirious preoperatively all but one remained delirious postoperatively. The majority of those delirious before surgery were demented, treated with drugs with anticholinergic properties (mainly neuroleptics), had had previous episodes of delirium and had fallen indoors. Patients who developed postoperative delirium had perioperative falls in blood pressure and seemed to have more postoperative complications, such as infections. Patients with preoperative delirium had a poorer walking ability on discharge compared to patients with postoperative delirium only.

In a five-year prospective follow up study 30 out of 78 (38.5%) non-demented patients with a femoral neck fracture developed dementia. Twenty out of 29 (69%) who were delirious postoperatively developed dementia compared to 10 out of 49 (20%) who were not delirious during hospitalization (p<0.001). Twenty-one (72.4%) of those with postoperative delirium died within 5 years compared to 17/49 (34.7%) of those who remained lucid postoperatively (p=0.001).

A non-randomized multi-factorial intervention study with the aim of preventing and treating delirium among patients with femoral neck fracture (n=49) showed that the incidence of delirium was significantly lower than reported in previously published studies. The incidence of other postoperative complications was also lower and a larger proportion of the patients regained independent walking ability and could return to their previous living conditions on discharge.

A similar multi-factorial intervention program evaluated as a randomized controlled trial including 199 femoral neck fracture patients showed that fewer intervention patients than controls suffered postoperative delirium (56/102, 55% vs. 73/97, 75%, p=0.003). For
intervention patients the postoperative delirium was also of shorter duration (5.0±7.1 days vs. 10.2±13.3 days, p=0.009). Eighteen percent in the intervention ward and 52% of controls were delirious after the seventh postoperative day (p<0.001). Intervention patients suffered from significantly fewer in-hospital complications, such as decubital ulcers, urinary tract infections, nutritional complications, sleeping problems and falls, than controls. Total postoperative hospitalization was shorter in the intervention ward (28.0±17.9 days vs. 38.0±40.6 days, p=0.028).

In conclusion, pre- and postoperative delirium is common and seems to be associated with various risk factors, which require different strategies for prevention and treatment. Delirium is also associated with the development of dementia and a higher mortality rate. Multi-factorial intervention programs can successfully be implemented and result in the reduction of delirium, fewer complications and shorter hospitalization.

Keywords: delirium, femoral neck fractures, dementia, risk factors, RCT, intervention, multi-factorial, outcome, mortality

I en prospektiv studie, av 101 konsekutiva patienter med cervikal höftfraktur, var 29.7% deliriösa före operationen och ytterligare 18.8 % utvecklade delirium efter operationen. Av dem som var deliriösa före operationen förblev alla utom en deliriös efter operationen. Majoriteten som var deliriösa före operationen var dementa, behandlades med läkemedel med antikolinerg effekt (övervägande neuroleptika), hade haft tidigare episoder med delirium och hade ramlat inomhus. Patienter som utvecklade delirium efter operationen hade blodtryckssfall under operationen och drabbades av fler komplikationer efter operationen som t.ex. infektioner. De patienter som var deliriösa före operationen hade sämre gångförmåga vid utskrivningen jämfört med dem som bara var deliriösa efter operationen.

En uppföljningsstudie av 78 konsekutiva icke demente patienter, 65 år och äldre, som drabbats av fraktur på lårbenshalsen visade att trettio (38.5%) av de 78 patienterna utvecklade demens inom en femårs period. Tjugo utav 29 (69%) som hade ett delirium efter operationen utvecklade demens jämfört med 10 av 49 (20%) som ej blev deliriösa efter operationen (p<0.001). Tjugoen (72.4%) av dem som hade ett postoperativt delirium dog inom fem år jämfört med 17/49 (34.7%) av dem som ej blev deliriösa efter operationen (p=0.001).

En icke- randomiserad multifaktoriell interventionsstudie som inkluderade 49 patienter med cervikal höftfraktur, 65 år och äldre, som vårdades på en akutgeriatrisk rehabiliteringsavdelning visade att förekomsten av delirium var signifikant lägre jämfört med tidigare publicerade studier. Förekomsten av andra postoperativa komplikationer var också
lägre och en större andel av patienterna återfick sin tidigare självständiga gångförmåga och en större andel kunde återvända till sitt tidigare boende vid utskrivningen.

En annan interventionsstudie av 199 patienter, 70 år eller äldre, som randomiserades postoperativt till ortopedisk kontrollavdelning eller till en geriatrisk interventionsavdelning resulterade i att färre patienter var deliriösa efter operationen i interventionsgruppen jämfört med kontrollgruppen (56/102, 55% mot 73/97, 75%, p=0.003). Delirium efter operationen i interventionsgruppen varade kortare tid (5.0±7.1 dagar mot 10.2±13.3 dagar, p=0.009) trots att 27% av patienterna med delirium efter operationen skrevs ut med ett pågående delirium från kontrollgruppen jämfört med ingen från interventionsgruppen (p=0.001). Arton procent av patienterna i interventionsgruppen hade fortfarande delirium efter sjunde dagen efter operationen jämfört med 52% i kontrollgruppen (p=0.001). Patienter i interventionsgruppen hade signifikant färre komplikationer som t.ex. trycksår, urinvägsinfektioner, nutritions- eller sömnproblem och fall. Den totala vårdtiden efter operationen för interventionsgruppen var i genomsnitt tio dagar kortare (28.0±17.9 dagar mot 38.0±40.6 dagar, p=0.028).

ABBREVIATIONS

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>A.D.</td>
<td>Anno Domini</td>
</tr>
<tr>
<td>B.C.</td>
<td>Before Christ</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence Interval</td>
</tr>
<tr>
<td>DSM-III</td>
<td>Diagnostic and Statistical Manual of Mental Disorders, Third edition</td>
</tr>
<tr>
<td>DSM-III-R</td>
<td>Diagnostic and Statistical Manual of Mental Disorders, Third edition-revised</td>
</tr>
<tr>
<td>DSM-IV</td>
<td>Diagnostic and Statistical Manual of Mental Disorders, Fourth edition</td>
</tr>
<tr>
<td>GDS-15</td>
<td>The Geriatric Depression Scale (15 item version)</td>
</tr>
<tr>
<td>ICD-10</td>
<td>The International Classification of Diseases and Related Health Problems, Tenth revision</td>
</tr>
<tr>
<td>LPN</td>
<td>License Practical Nurse</td>
</tr>
<tr>
<td>MMSE</td>
<td>Mini Mental State Examination</td>
</tr>
<tr>
<td>NS</td>
<td>Not Significant</td>
</tr>
<tr>
<td>OBS Scale</td>
<td>Organic Brain Syndrome Scale</td>
</tr>
<tr>
<td>OR</td>
<td>Odds Ratio</td>
</tr>
<tr>
<td>Reg. OT</td>
<td>Registered Occupational Therapist</td>
</tr>
<tr>
<td>RN</td>
<td>Registered Nurse</td>
</tr>
<tr>
<td>RPT</td>
<td>Registered Physiotherapist</td>
</tr>
<tr>
<td>SD</td>
<td>Standard Deviation</td>
</tr>
</tbody>
</table>
ORIGINAL PAPERS

The thesis is based on the following Papers, which will be referred to in the text by their Roman numerals:


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INTRODUCTION

In Sweden the number of old people especially the oldest old, is increasing, leading in turn to an increasing age-related diseases such as stroke, dementia, arthrosis, heart failure and injuries such as hip fractures. In the Swedish population of approximately 9 million, 19 000 people every year sustain a hip fracture.\(^1\) It is unusual to sustain a hip fracture before 50 years of age but after that age the risk increases, especially for woman. The lifetime risk of sustaining a hip fracture for a woman is 20% in Sweden and the mean age of patients with a hip fracture is 81 years.\(^1\) Other known risk factors for hip fracture, apart from being over 50 years of age and of female sex are e.g. low bone mass, low body weight, estrogen deficiency, earlier fracture, tendency to fall, immobilization, low level of physical activity, reduced vision, stroke, dementia, diabetes mellitus, previous hip fracture and cigarette smoking.\(^2\)-\(^5\) In Sweden the total annual cost for hip fracture during the first 4 months after incidence is estimated at approximately 1.3 billion Swedish crowns and during the first year the calculated costs are 3 billion Swedish crowns annually.\(^1\)

Many in-hospital complications after hip fracture surgery have been reported including delirium, urinary retention, incontinence, urinary tract infections, deep vein thrombosis and falls.\(^6\) The old hip fracture patients have complex needs since they are frail and many have dementia, stroke or depression, which leads to a reduction in brain capacity and a lower threshold for delirium.\(^4\),\(^7\)-\(^9\)

Delirium

Delirium is probably the most common presenting symptom of disease in old age (≥65 years). Delirium is poorly recognized and is frequently mistaken for dementia or depression and is therefore often underdiagnosed.\(^10\)-\(^12\) Delirium in general is reversible but patients with delirium have a poor prognosis.\(^12\) The delirium syndrome was mentioned and observed as early as 2,500 years ago by the Greek physician Hippocrates. Hippocrates said, according to a translation of Sprengell C, “When a delirium or raving is appeased by sleep, it is a good sign”. Another aphorism from Hippocrates is “Difficulty of breathing and delirium in continual fevers are mortal”. Hippocrates did not use the original Greek or Latin word for “delirium”, he used several Greek words to refer to it but when Sprengell translated Hippocrates work in the early eighteenth century he used the word “delirium”.\(^13\) The first time the word “delirium”
was mentioned in medical literature was by Celsus (25 B.C.-A.D. 50). Who, although he was not a physician, compiled the first great medical work since Hippocrates

**Definition, terminology and subtypes of delirium**

Definition and terminology

Diagnostic criteria and the terminology of delirium have changed over the years. The DSM-III-R criteria (Table 1) from 1987 were replaced by DSM-IV in 1994 which has been in use since then. Delirium as defined in DSM-IV is a neuropsychiatric syndrome characterized by reduced ability to focus, sustain or shift attention, the occurrence of cognitive changes such as memory loss, disorientation, language disturbance, or the development of a perceptual disturbance. A delirium develops over a short period of time (usually hours to days) and tends to fluctuate over the course of the day. There also has to be evidence from the history, physical examination, or laboratory findings that delirium is caused by the direct physiological consequences of a general medical condition (Table 2).

As mentioned, the terminology for “delirium” has changed over the years and in the literature there are many words, over 65 in all, that are used as synonyms for “delirium” including “acute confusional state” (ACS), “confusion”, “acute brain failure” and “acute brain syndrome”. The term “Delirium” has been the consensus term since the late 1980s and it has been suggested that “acute confusional state” should be the only acceptable synonym for delirium.

Subtypes

Delirium can be classified into three subtypes, the hyperactive-hyperalert, the hypoactive-hypoalert and the mixed type. Hyperactive delirium (i.e. restlessness/agitation, irritability and aggression) is more easily detected compared to hypoactive delirium (i.e. latency in reaction and in response to verbal stimuli and psychomotor slowing). Patients with a mixed type fluctuate between the hyperactive and the hypoactive type. Patients with hypoactive delirium seem to have a poorer prognosis than patients with hyperactive delirium. Delirium can also be categorized into psychotic, emotional or in a mixed type with both an emotional and a psychotic profile.
Table 1. Diagnostic criteria for delirium according to DSM-III-R: 

| A. | Reduced ability to maintain attention to external stimuli (e.g., questions must be repeated because attention wanders) and to appropriately shift attention to new external stimuli (e.g., perseverates answer to a previous question). |
| B. | Disorganized thinking, as indicated by rambling, irrelevant, or incoherent speech. |
| C. | At least two of the following: |
|     | (1) reduced level of consciousness, e.g., difficulty keeping awake during examination |
|     | (2) perceptual disturbance: misinterpretations, illusions, or hallucinations |
|     | (3) disturbance of sleep-wake cycle with insomnia or daytime sleepiness |
|     | (4) increased or decreased psychomotor activity |
|     | (5) disorientation to time, place, or person |
|     | (6) memory impairment, e.g., inability to learn new material, such as the names of several unrelated objects, after five minutes, or to remember past events, such as history of current episode of illness |
| D. | Clinical features develop over a short period of time (usually hours to days) and tend to fluctuate over the course of the day. |
| E. | Either (1) or (2): |
|     | (1) evidence from the history, physical examination, or laboratory tests of a specific organic factor (or factors) judged to be etiologically related to the disturbance |
|     | (2) in the absence of such evidence, an etiologic organic factor can be presumed if the disturbance cannot be accounted for by any non-organic mental disorder, e.g., Manic Episode accounting for agitation and sleep disturbance |

Table 2. Diagnostic criteria for delirium according to DSM-IV: 

| A. | Disturbance of consciousness (i.e. reduced clarity of awareness of the environment) with reduced ability to focus, sustain, or shift attention. |
| B. | A change in cognition (such as memory deficit, disorientation, language disturbance) or the development of a perceptual disturbance that is not better accounted for by a pre-existing, established, or evolving dementia. |
| C. | The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during course of the day. |
| D. | There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition. |
Epidemiology of delirium

Delirium is a common disorder among hospitalized old patients with a reported prevalence among medical in-patients of between 10 and 30% and a incidence during hospitalization of between 4 and 30%. The prevalence and incidence of delirium in surgical patients is also high, for example: in old patients undergoing cardiac surgery delirium occurs in 23 to 32% and in patients operated on for elective hip surgery delirium occur in 4 to 27%.

As can be seen in Table 3 delirium among patients undergoing an acute operation due to hip fracture is reported to be higher and to occur in 5-61%. Four to 33% develop delirium before the hip fracture surgery or before admission and an additional 5 to 41% develop delirium postoperatively (Table 3). Delirium is a common cause of falls thus some old people are already delirious before the fracture occurs. As delirium, by definition, has a specific etiologic organic factor this indicates that these patients have some often undetected acute disorder that has caused the prefracture delirium. Falls, like delirium, are also often caused by acute diseases and should be regarded as a symptom of acute disease or drug side effect until proven otherwise. The great majority of hip fractures are caused by a fall.

The prevalence and incidence of delirium varies among studies and is not only a result of differing prevention and treatment strategies. Several studies with a lower prevalence and incidence of delirium have often excluded patients with dementia or aphasia or excluded patients with signs of cognitive impairment or delirium on admission but there are studies which have excluded patients with dementia or aphasia and yet still have a high occurrence of delirium. The varying prevalence can also be explained by the different use of diagnostic criteria, which have changed over the years. Laurila et al. compared the DSM-IV classification with DSM-III, DSM-III-R, and ICD10 and found that DSM-IV identifies more subjects as delirious, particularly among those with previous dementia.
<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Age</th>
<th>Delirium preoperatively</th>
<th>Developed delirium postoperatively</th>
<th>Occurrence of delirium during hospitalization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Williams et al. 1985</td>
<td>170</td>
<td>≥60</td>
<td>-</td>
<td>-</td>
<td>52</td>
</tr>
<tr>
<td>Williams et al. 1985 (intervention sample)</td>
<td>57</td>
<td>≥60</td>
<td>-</td>
<td>-</td>
<td>44</td>
</tr>
<tr>
<td>Berggren et al. 1987</td>
<td>57</td>
<td>&gt;64</td>
<td>9</td>
<td>35</td>
<td>44</td>
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<tr>
<td>Gustafson et al. 1988</td>
<td>111</td>
<td>≥65</td>
<td>33</td>
<td>28</td>
<td>61</td>
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<td>Brännström et al. 1989 &amp; 1991</td>
<td>35</td>
<td>≥61</td>
<td>-</td>
<td>-</td>
<td>43</td>
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<td>Mullen and Mullen 1985</td>
<td>400</td>
<td>≥60</td>
<td>-</td>
<td>-</td>
<td>26</td>
</tr>
<tr>
<td>Bowman 1997</td>
<td>17</td>
<td>Mean age 80 years</td>
<td>-</td>
<td>-</td>
<td>47</td>
</tr>
<tr>
<td>Edlund et al. 1999</td>
<td>54</td>
<td>≥40</td>
<td>19</td>
<td>9</td>
<td>28</td>
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<tr>
<td>Gustafson et al. 1991 (intervention sample)</td>
<td>103</td>
<td>≥65</td>
<td>29</td>
<td>19</td>
<td>48</td>
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<tr>
<td>Brauer et al. 2000</td>
<td>571</td>
<td>≥50</td>
<td>4</td>
<td>5</td>
<td>9</td>
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<tr>
<td>Dolan et al. 2000</td>
<td>682</td>
<td>≥65</td>
<td>14</td>
<td>-</td>
<td>14</td>
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<tr>
<td>Sörensen Duppils et al. 2000</td>
<td>149S</td>
<td>≥65</td>
<td>-</td>
<td>-</td>
<td>24</td>
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<tr>
<td>Marcantonio et al. 2000</td>
<td>126</td>
<td>≥65</td>
<td>-</td>
<td>-</td>
<td>41</td>
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<tr>
<td>Andersson 2001</td>
<td>208¶</td>
<td>≥65</td>
<td>-</td>
<td>-</td>
<td>20</td>
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<tr>
<td>Galanski et al. 2001</td>
<td>37#</td>
<td>≥60</td>
<td>Non delirious on admission</td>
<td>41</td>
<td>41</td>
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<tr>
<td>Millisen et al. 2001 (intervention vs. control)</td>
<td>60 vs. 60</td>
<td>Median age 82 vs. 80</td>
<td>-</td>
<td>-</td>
<td>20 vs. 23</td>
</tr>
<tr>
<td>Millisen et al. 2002</td>
<td>55</td>
<td>≥65</td>
<td>-</td>
<td>-</td>
<td>20</td>
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<tr>
<td>Zakriya et al. 2002</td>
<td>168**</td>
<td>≥50</td>
<td>-</td>
<td>-</td>
<td>28</td>
</tr>
<tr>
<td>Adunsky et al. 2003</td>
<td>281</td>
<td>≥60</td>
<td>16</td>
<td>15</td>
<td>31</td>
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<tr>
<td>Gruber-Baldini et al. 2003</td>
<td>674‡</td>
<td>≥65</td>
<td>29</td>
<td>-</td>
<td>37</td>
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<tr>
<td>Morrison et al. 2003</td>
<td>541§§</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>16</td>
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<tr>
<td>Schuurmans et al. 2003</td>
<td>92††</td>
<td>≥70</td>
<td>-</td>
<td>-</td>
<td>20</td>
</tr>
<tr>
<td>Edelstein et al. 2004</td>
<td>921‡‡</td>
<td>≥65</td>
<td>-</td>
<td>-</td>
<td>5</td>
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<tr>
<td>Kagansky et al. 2004</td>
<td>102†††</td>
<td>≥75</td>
<td>6</td>
<td>6</td>
<td>12</td>
</tr>
</tbody>
</table>

- The studies have not assessed, mentioned and/or calculated these figures.
* Patients with a medically validated history of chronic mental impairment were excluded.
† Only fully lucid patients were included.
‡ Only patients living in community dwellings were included.
§ Patients delirious on admission or patients with aphasia were excluded.
¶ Patients with mental disease, already confused or difficult to communicate with were excluded.
# Patients with severe dementia or aphasia were excluded.
** Patients with a dementia diagnosis or delirious on admission were excluded.
§§ Patients delirious at the first interview (within 48 hours of admission) were excluded.
†† Patients suspected of being delirious on admission were excluded.
††† Those patients with dementia who not could answer a simple questionnaire were excluded.
††† Patents with severe dementia, severe hearing loss, or visual impairment that could interfere with reliable cognitive tests were excluded.
Aetiology and risk factors for delirium

Cerebral hypoxemia is known to be associated with development of delirium. Hypoxemia is often caused by e.g. sleep-apnea syndrome, anaemia, severe hypotension, pulmonary diseases, and heart failure; all conditions which are probably common among old people undergoing hip surgery. Postoperative delirium has been reported to be precipitated by perioperative hypotension, hypoxemia and anaemia and can be prevented and treated by avoiding or treating such complications.

Hypercortisolism due to different kinds of stress is probably an important precipitating mechanism for delirium that can be prevented both by preventing and treating medical complications as well as by providing optimal care from the patient’s perspective. Stress caused by the injury, admission to hospital and the operation itself seem to contribute to delirium, probably mediated by hypercortisolism. Hypercortisolism seems to be common in hip fracture patients. The combination of hypercortisolism and factors endangering the cerebral oxygen metabolism seems to be an especially dangerous combination for the brain. The combination of hypercortisolism and hypoxemia seem to be common in hip fracture patients which might contribute to the particularly high prevalence of delirium in patients undergoing acute hip fracture surgery.

Many predisposing and even more precipitating causes of delirium have been reported in reviews. In Table 4 risk factors or causes of delirium in hip fracture patients are listed and old age, dementia, cognitive impairment, previous stroke, depression, impaired hearing, impaired vision and treatment with drugs with anticholinergic properties seem to be the most important risk factors for delirium. Dementia or cognitive impairment seem to be an especially important risk factor for the development of delirium e.g. in one study performed on a delirium ward showed that among the 169 delirious patients 40% had a dementia diagnosis and another 30% had mild cognitive impairment, which is in many cases an early sign of dementia.

Among patients with a hip fracture delirium is associated with more postoperative complications compared to those who do not develop delirium. In-hospital complications that have been reported as being associated with delirium in patients with hip fracture are hypoxemia, decubital ulcers, feeding problems, pain, urinary incontinence, temperature >38°C, self-destructive behaviour and infections such as urinary tract infections.
<table>
<thead>
<tr>
<th>Risk factors for or causes of delirium</th>
<th>Studies that have found such an association</th>
<th>Studies that have not found such an association</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>Berggren 1987, Gustafson 1988, Edlund 1999, Galanski 2001</td>
<td>None</td>
</tr>
<tr>
<td>Cardiovascular diseases</td>
<td>Gustafson 1988</td>
<td>None</td>
</tr>
<tr>
<td>Heart failure</td>
<td>Dolan 2000, Zakriya 2002</td>
<td>None</td>
</tr>
<tr>
<td>Hypoxemia</td>
<td>Berggren 1987, Gustafson 1991</td>
<td>None</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>Gustafson 1988, Berggren 1987</td>
<td>Schuurmans 2003</td>
</tr>
<tr>
<td>Pain</td>
<td>Bowman 1997</td>
<td>None</td>
</tr>
<tr>
<td>Polypharmacy</td>
<td>Kagansky 2004</td>
<td>Schuurmans 2003</td>
</tr>
</tbody>
</table>
Drugs with anticholinergic properties

<table>
<thead>
<tr>
<th>Use of antidepressants</th>
<th>Berggren 1987\textsuperscript{37}, Gustafson 1988\textsuperscript{42}</th>
<th>None</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of benzodiazepines</td>
<td>Gustafson 1988\textsuperscript{42}, Brännström 1989\textsuperscript{38}</td>
<td>None</td>
</tr>
<tr>
<td>Use of neuroleptics</td>
<td>Berggren 1987\textsuperscript{37}, Gustafson 1988\textsuperscript{42}, Brännström 1989\textsuperscript{38}</td>
<td>None</td>
</tr>
</tbody>
</table>

*On the border of significance
† Including both patients with hip fracture and patients undergoing elective hip surgery.
‡ Also including previous transient ischemic attacks (TIA) or epilepsy

Patients’ experience of delirium

Studies have shown that patients who have been delirious remember what they experienced during the delirium episode and that they often experience things as terrifying and threatening.\textsuperscript{71-74} The patients describe situations during the delirium episode as being very real; they felt as if they are dreaming but at same time they knew they were awake.\textsuperscript{74} The patients reported that they saw and heard frightening things that did not exist and they misinterpreted what they saw or heard.\textsuperscript{73, 74} The patients also felt that, during the delirium episode, they were neither provided with any help in removing these threats nor received any explanations for their experience and retrospectively they were afraid of a recurrence if they should become ill in the future.\textsuperscript{72, 73} Moreover the patients had feelings of remorse, shame and embarrassment about things they had said or done towards the staff, spouses and friends during the delirium episode.\textsuperscript{72-74}

Outcome of delirium

Patients with delirium have a poor prognosis. For example among patients in general internal medicine or acute geriatric units delirium has been reported to be associated with prolonged hospitalization\textsuperscript{75, 76} and increased mortality.\textsuperscript{77-79} The outcome and prognosis for patients with delirium after hip fracture is also poor, they are hospitalized for longer periods,\textsuperscript{9, 37, 42, 57} and fewer of them can return to their previous independent living arrangements.\textsuperscript{9, 38, 45} Delirious patients operated on for a hip fracture also have poorer functional recovery,\textsuperscript{36, 42, 45, 48, 57} poorer recovery of basic activities in daily living,\textsuperscript{43, 57} and a increased mortality\textsuperscript{9, 44, 57} compared to those who do not develop delirium.
Delirium and development of dementia

Another reported consequence of delirium in old people is that delirium is associated with the development of dementia. Delirium is, to date, an incurable progressive brain disease and is defined, according to DSM-IV criteria, as a development of multiple cognitive deficits manifested by both memory impairment (impaired ability to learn new information or to recall previously learned information) and one (or more) of the following cognitive disturbances: (a) aphasia, (b) apraxia, (c) agnosia, (d) disturbance in executive functioning (i.e., planning, organizing, sequencing, abstracting). The cognitive deficits also cause significant impairment regarding social or occupational functioning and represent a significant decline from a previous level of functioning. Each subtype of dementia e.g. Alzheimer’s disease and vascular dementia are specifically defined.

In a three-year follow up study of patients aged 65 years and older admitted to general medicine service who at baseline had the diagnosis ‘delirium-no dementia’, nine out of fifteen were found to have developed dementia. In a study of non-demented older patients (aged 65 years and above) living in community dwellings (n=37) and admitted to hospital for acute delirium the incidence of dementia during a two-year follow up was found to be 38%. Furthermore, among 20 non-demented people (aged 85 years or above) who had been diagnosed as having had an episode of delirium during a three-year observational period, 13 were found to have developed dementia. None of these studies included patients with postoperative delirium. In a study, among non-demented patients with a hip fracture, it was shown that patients with delirium on admission to hospital were almost twice as likely to be cognitively impaired at a two-year follow up.

Delirium and intervention studies

Several studies have been performed to evaluate intervention programs aimed at preventing and treating delirium and its underlying causes but only a few of these studies have been evaluated as randomized trials with positive results. Among patients in general internal medicine a few intervention studies have been performed and only two have produced any positive results regarding the reduction in the occurrence of delirium. The first of these successful intervention studies was a multi-component risk-factor, non-randomized, intervention study aimed at preventing the development of delirium in older patients admitted to general internal medicine. This intervention resulted in a reduction in the number and duration of episodes of delirium. The second successful
intervention study was a randomized intervention study aimed at investigating whether a program of education and a reorganization of the nursing and medical care improved the outcome for older delirious patients. This study resulted in a reduction in the duration of delirium, length of hospital stay and a lower in-hospital mortality in delirious patients.

Among studies on patients operated on for hip fracture several intervention studies have shown that postoperative delirium can be prevented and treated (Table 5). However only one of these studies was a randomized controlled trial and the effect of the intervention bordered on significance and focused mainly on prevention and treatment of medical complications.

To date, it seems that multi-factorial, multi-professional interventions are the most effective, according to the studies performed on patients in general internal medicine.
<table>
<thead>
<tr>
<th>Trial</th>
<th>Design</th>
<th>Intervention</th>
<th>Results</th>
</tr>
</thead>
</table>
| Williams M, et al. 1985<sup>39</sup> | Intervention study compared to historical control n=57/170 ≥ age 60 mean age 81/79 | Interpersonal and environmental nursing intervention related to the following problems:  
  • Strange environment  
  • Altered sensory input  
  • Loss of control  
  • Disruption of life pattern  
  • Immobility  
  • Pain  
  • Disruption of elimination patterns | Incidence of delirium (43.9% vs. 51.5%, NS); but the difference was significant (P<0.02) when controlled for baseline differences. |
| Gustafson Y, et al. 1991<sup>46</sup> | Intervention study compared with historical control from the same orthopaedic department n=103/111 ≥ age 65 mean age 80/79 | Pre- and post-operative geriatric assessments and intervention  
  • Oxygen therapy  
  • Early surgery  
  • Prevention and treatment of falls in perioperative blood pressure  
  • Treatment of postoperative complications | Lower incidence, (47.6% vs. 61.3%,p< 0.05), severity, (6.8% vs. 29.7% with severe delirium, p<0.001) and shorter duration of delirium. Fewer postoperative complication such as decubital ulcers and injurious falls  
Mean length of stay on orthopaedic ward was shorter (11.6 days vs. 17.4 days, p<0.001) |
| Marcantonio E, et al. 2001<sup>61</sup> | Randomized intervention study n=62/64 ≥ age 65 mean age 78/80 | Daily proactive geriatric consultation that made targeted recommendations based on a structured protocol, which included 10 modules. | Lower incidence (32% vs. 50%, p=0.04) and severity (12% vs. 29%, p=0.02) of delirium. The difference did not remain significant after adjustment for baseline differences. |
| Milisen K, et al. 2001<sup>50</sup> | Longitudinal prospective before/after design n=60/60 mean age 82/80 |  
  • Education of nursing staff  
  • Systematic cognitive screening  
  • Consultative service from a delirium resource nurse, a geriatric nurse specialist, or a psychogeriatrician  
  • Use of a scheduled pain protocol | Less severe delirium (p<0.005) and shorter duration (median 1 day vs. 4 days, p=0.03) of delirium. |
**Rationale for this thesis**

Delirium is a far too common disorder among old patients; it has many predisposing and precipitating factors, and is associated with poor prognosis. For patients who have experienced episodes of delirium the experience is often frightening and they are afraid that there will be a recurrence if they should become ill in the future. Few studies have been successful in reducing delirium and, to my knowledge, no study preformed as a randomized controlled trial in patients with hip fracture has resulted in a reduction in the duration of delirium and thus the length of hospitalization. However, a combination of good nursing and medical care, reducing stress by creating a safe and secure caring situation and by preventing complications such as hypotension, hypoxemia, anaemia, urinary retention, infections, pain, malnutrition, thrombosis and constipation, seems to be a prerequisite for the prevention and treatment of delirium. Therefore, it is important to increase our knowledge about delirium and to develop and implement intervention programs able to reduce the suffering of older patients and the care and treatment costs.
AIMS OF THIS THESIS

The overall aim was: to increase knowledge about the risk factors and outcome of delirium in old patients with femoral neck fracture and to develop and evaluate a multi-factorial intervention program for prevention and treatment of delirium in these patients.

The specific aims were:

- To investigate the differences between preoperative and postoperative delirium regarding predisposing, precipitating factors and outcome, in older patients admitted to hospital with femoral neck fractures (Paper I).

- To investigate whether delirium in older patients with femoral neck fractures is associated with an increased risk of developing dementia and a higher mortality rate (Paper II).

- To investigate whether a reorganization of nursing and medical care, could reduce the incidence of postoperative delirium and improve functional outcome in patients treated for femoral neck fractures (Paper III).

- To investigate, in a randomized study, whether a postoperative multi-factorial intervention program, including comprehensive geriatric assessment, management and rehabilitation, reduces delirium and improves outcome in patients with femoral neck fractures (Paper IV).
METHODS

This thesis involves three samples of patients from two different hospitals. Papers I, II and IV concern two samples of patients from Norrland’s University Hospital in Umeå, Sweden and Paper III one sample of patients from Piteå River Valley Hospital in Piteå, Sweden. A schematic overview of the studies and the characteristics of the samples is presented in Tables 6 and 7.

Subjects and settings

Papers I and II

The populations in Papers I and II are based on 103 consecutive patients, 65 years and above, operated on for fractured neck of the femur at the Department of Orthopaedic Surgery at Norrland’s University Hospital in Umeå. This sample was a part of a intervention program for prevention and treatment of delirium consisting of geriatric consultation, oxygen therapy, early surgery, prevention and treatment of perioperative blood pressure falls and treatment of postoperative complications. The inclusion dates ran from December 1986 to January 1988. The only exclusion criteria were age under 65 and the patient’s refusal to participate. All other patients were included regardless of diagnosis. Among these 103 patients there were three participants who entered the study twice since they sustained a second femoral neck fracture during the inclusion period. Paper I included 101 patients/cases since it was impossible to verify whether two of the 103 patients/cases did or did not have preoperative delirium. The population in Paper II is based on 100 consecutive patients (for those three patients with a second hip fracture, only the first fracture was included). Pre-fracture dementia was diagnosed in 22 of these 100 patients according to the DSM-IV criteria for organic brain disorders. These patients were then excluded, thus 78 non-demented patients remained for inclusion in Paper II. These 78 non-demented patients were followed for five years and all survivors received a home visit five years after the hip fracture. The five-year follow up visits were performed between 1991-1993.

The operation performed on all patients was internal fixation with hook-pins, according to Hansson under spinal anesthesia.
Paper III
In Paper III the population were based on 49 consecutive patients aged 65 years and above. All patients were operated on for fractured neck of the femur at the ward for Acute Rehabilitation, which was a part of the Department of Geriatric Medicine at the Piteå River Valley Hospital in Piteå, Sweden. The study ran from January to December 1993 and the only exclusion criteria were age under 65 and the patient’s refusal to participate. All other patients were included regardless of diagnosis. Nine patients who met the inclusion criteria were not included due to failure in inclusion routine, these patients tended to be older than the study sample (mean age 83.8 years vs. 79.7 years). Internal fixation was used for all patients, and performed using von Bahr screws.\textsuperscript{90} One patient was operated on under ketamin anaesthesia and all the others under spinal anaesthesia.\textsuperscript{37}

Paper IV
Paper IV included 199 patients, aged 70 years or above, consecutively admitted to the Orthopaedic Department at the Norrland’s University Hospital in Umeå, Sweden, between May 2000 and December 2002 with femoral neck fractures. The patients were randomized to postoperative care at a geriatric ward with a special intervention program, based on the program developed in Paper III, or to conventional care at the orthopaedic department. Exclusion criteria were: age under 70, severe rheumatoid arthritis, severe hip osteoarthritis, severe renal failure, pathological fracture and patients who were bedridden before the injury. Two hundred and fifty-eight patients fulfilled the inclusion criteria but 59 patients declined or did not participate in the study for other reasons (Figure 1). These 59 patients tended to be more often admitted from their own apartment/house (p=0.009) and were more likely to be males (p=0.033) but there was no difference in age (p=0.354) compared to the 199 patients included.

Depending of the degree of dislocation (Garden I-IV)\textsuperscript{91} various operation methods were used. Fractures with minor dislocation (Garden I-II) (n=69) were treated with two hook-pins (Swemac Orthopedica\textsuperscript{®}) and dislocated fractures (Garden III-IV) (n=111) with bipolar hemiarthroplasty (Link\textsuperscript{®}). Basocervical fractures (n=17) were operated on using a dynamic hip screw (DHS, Stratec Medical\textsuperscript{®}). Two patients should have had arthroplasty but one had a resection of the femoral head due to a deterioration in medical status and one died before
Most (174/199, 87%) of the operations were performed under spinal anesthesia, the remaining operations (24/199, 12%) where performed under general anesthesia.

<table>
<thead>
<tr>
<th>Context of the study</th>
<th>Paper I</th>
<th>Paper II</th>
<th>Paper III</th>
<th>Paper IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Orthopaedic unit</td>
<td>Orthopaedic unit</td>
<td>Geriatric/Rehabilitation unit</td>
<td>Orthopaedic units vs. Geriatric unit</td>
<td></td>
</tr>
<tr>
<td>Type of study</td>
<td>Prospective clinical assessment</td>
<td>5-year prospective follow up study</td>
<td>Prospective intervention study compared to historical controls in the same and other hospitals</td>
<td>Randomized controlled trial</td>
</tr>
<tr>
<td>Number of subjects</td>
<td>101 patients ≥ age 65 years</td>
<td>78 non-demented patients ≥ age 65 years</td>
<td>49 patients ≥ age 65 years</td>
<td>199 patients ≥ age 70 years</td>
</tr>
<tr>
<td>Method of data collection</td>
<td>Observations Assessments Interviews Medical charts</td>
<td>Observations Assessments Interviews Medical charts</td>
<td>Observations Assessments Interviews Medical charts</td>
<td>Observations Assessments Interviews Medical charts</td>
</tr>
<tr>
<td>Assessment scales</td>
<td>OBS Scale MMSE</td>
<td>OBS Scale MMSE</td>
<td>OBS Scale</td>
<td>OBS Scale MMSE GDS-15</td>
</tr>
<tr>
<td>Diagnostic criteria</td>
<td>Re-evaluated by DSM-IV</td>
<td>Re-evaluated by DSM-IV</td>
<td>DSM-III-R</td>
<td>DSM-IV</td>
</tr>
<tr>
<td>Statistical analysis</td>
<td>Pearson chi-square test Fisher’s exact test Student’s t-test Multivariate logistic regression analyses</td>
<td>Pearson chi-square test Fisher’s exact test Student’s t-test Multivariate logistic regression analyses</td>
<td>Pearson chi-square test Fisher’s exact test Student’s t-test Yates’ corrected chi-square test Bonferroni adjustment</td>
<td>Pearson chi-square test Fisher’s exact test Student’s t-test Multivariate logistic regression analyses</td>
</tr>
</tbody>
</table>
Table 7. Baseline characteristics of the patients in the four Papers

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Paper I (n=101)</th>
<th>Paper II (n=78)</th>
<th>Paper III (n=49)</th>
<th>Paper IV (Intervention n=102, Control n=97)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean±SD (Range)</td>
<td>79.5±7.7 (65-102)</td>
<td>79.1±8.1 (65-102)</td>
<td>79.7±7.5 (65-98)</td>
<td>82.3±6.6 (70-100) / 82.0±5.6 (70-96)</td>
</tr>
<tr>
<td>Sex, men/woman (%)</td>
<td>27.7/72.3</td>
<td>23.1/76.9</td>
<td>34.7/65.3</td>
<td>27.5/72.5 / 23.7/76.3</td>
</tr>
<tr>
<td>Impaired hearing (%)</td>
<td>29.7</td>
<td>30.8</td>
<td>22.4</td>
<td>44.6* / 41.5*</td>
</tr>
<tr>
<td>Impaired vision (%)</td>
<td>22.8</td>
<td>23.1</td>
<td>51.0</td>
<td>40.7† / 36.5†</td>
</tr>
<tr>
<td>Dementia (%)</td>
<td>20.8</td>
<td>0</td>
<td>22.4</td>
<td>27.5 / 37.1</td>
</tr>
<tr>
<td>Previous stroke (%)</td>
<td>29.7</td>
<td>30.8</td>
<td>26.5</td>
<td>28.4 / 21.5§</td>
</tr>
<tr>
<td>Depression (%)</td>
<td>10.9</td>
<td>10.3</td>
<td>12.2</td>
<td>32.4 / 47.4¶</td>
</tr>
</tbody>
</table>

* 8 missing value in intervention group and 15 missing value in the control group
† 11 missing value in intervention group and 23 missing value in the control group
§ 4 missing value in the control group
¶ 2 missing value in the control group
Figure 1. Flow chart for the randomized trial (Paper IV).
Data collection

Scales

The Organic Brain Syndrome Scale (OBS Scale)\textsuperscript{92} consists of two main parts: the disorientation subscale, a questionnaire of 15 items, and the confusion subscale, an observation schedule containing 39 clinical features. The disorientation subscale measures the patient’s orientation to time, place and own identity with a maximum score of 45 (higher score indicates increased disorientation). The confusion subscale describes different cognitive, perceptual, emotional and personality changes and fluctuations in the clinical states and is based on observations and interviews with the patients and interviews with the caregivers.

A modified version of the Organic Brain Syndrome Scale was used in all Papers in this thesis. The modified version of the OBS Scale is adjusted for hip fracture patients which means that variables affected by the hip fracture per se are excluded.\textsuperscript{37} In the modified OBS Scale, which also includes two main parts, the disorientation subscale consists of 12 items and the confusion subscale, an observation schedule of 21 clinical features. The disorientation subscale, a questionnaire, measures the patient’s orientation to time, place and own identity with a maximum score of 36 (higher score indicates increased disorientation). The confusion subscale describes different cognitive, perceptual, emotional, and personality changes and fluctuations in the clinical states and is based on observations and interviews with the patients and interviews with the caregivers.

The original OBS Scale has been compared with other assessment scales and has been shown to have good concurrent validity.\textsuperscript{92} The modified version of the OBS Scale has been compared to the Confusion Assessment Method (CAM) and showed 100\% agreement in a study regarding the diagnosis of postoperative delirium in patients undergoing Coronary Artery Bypass Surgery (CABG).\textsuperscript{24} In two previous studies the inter-rater reliability between the assessors using the modified version of the OBS Scale was tested and found to be over 90\% for all variables in both studies.\textsuperscript{37, 42} In another study the inter-rater reliability between the assessors was found to be above 95\%.\textsuperscript{38, 43} The OBS Scale offers a broad description of reported and observed signs of organic brain syndromes as well as fluctuations in the patients’ clinical state. The OBS Scale thus offers the opportunity to register more signs and symptoms than a pure interview or observation instrument.\textsuperscript{92}
The Mini Mental State Examination (MMSE)\textsuperscript{93} was used to assess cognition. The MMSE is scored from 0 to 30 points and a score below 24 indicates cognitive impairment.\textsuperscript{94} The MMSE has shown good reliability and validity\textsuperscript{93-95} (Papers I, II and IV).

The Geriatric Depression Scale (GDS-15, shorter version)\textsuperscript{96, 97} was used to assess depression in Paper IV. This scale has 15 items and scores of between five and nine indicates mild depression while ten or more indicates moderate to severe depression. GDS-15 has been shown to have a high sensitivity and high specificity in a community sample of the oldest old.\textsuperscript{98}

Study procedures

Diagnosis

Delirium

In Papers I and II the patients were tested on admission, and on days 1, 3 and 7 after surgery using the modified OBS Scale and observed every day regarding both fluctuations in mental state and the detection of medical complications. Patients with cognitive impairment detected by the OBS Scale testing were also tested with the MMSE. The survivors were visited and assessed using the OBS Scale and the MMSE in their homes five years after the fracture.

In Papers I and II the results of the assessments and the OBS Scale testing were analyzed and the patients were diagnosed regarding delirium during hospitalization according to DSM-III criteria\textsuperscript{99} independently by three of the Paper’s authors (BB, GB, and YG). In the few cases where there was disagreement regarding diagnosis, each case was discussed until a consensus was reached. In Papers I and II one of the author (YG) reanalyzed all assessments and documentation to decide whether the patients met the DSM-IV criteria for delirium during hospitalization and at the 5-year follow up.

In Paper III all patients were observed almost every day pre- and postoperatively and assessed on days 1 and 7 postoperatively using the modified OBS Scale. A specialist in geriatric medicine analyzed all assessments and documentation to decide whether the patients met the DSM-III-R criteria for delirium.\textsuperscript{15} All four co-workers who assessed the patients were employed on the ward, the patients were thus observed almost everyday of the week and in addition other members of the staff were interviewed regarding e.g. diurnal variation.
In Paper IV all patients were observed almost every day pre- and postoperatively and tested once between days 3-5 using the modified OBS Scale and any changes in the patients mental state were also documented in the nurses’ and medical records. Delirium on discharge was registered if the patient was delirious during the last 24 hours of hospitalization according to the nurses’ records. One nurse from the orthopaedic department was employed half-time on the study and was trained to carry out assessments using the Mini Mental State Examination (MMSE), the Organic Brain Syndrome Scale (OBS Scale) and the Geriatric Depression Scale (GDS-15) on the geriatric intervention ward. Similarly a nurse in the intervention ward was also employed half-time on the study carrying out the same assessments but in the control wards. The same two nurses also worked half-time each as regular nurses in the opposite ward than in which they performed the assessments. An occupational therapist and a physiotherapist were also employed to assess the patients in the project. Finally, a specialist in geriatric medicine, who was not working in either of the two wards and did not know which group the patients were randomized to, analyzed all assessments and documentation including all patients’ medical and nurses’ records to decide whether the patients met the DSM-IV criteria for delirium.

Symptoms of cognitive disturbance during the first eight postoperative hours were not registered as delirium but were ascribed to the immediate effects of drugs from the pre-medication and/or anaesthetic (Papers I-IV).

**Dementia**

In Papers I and II all patients were assessed pre- and postoperatively to verify any preoperative dementia diagnosis. Their pre-fracture mental state was assessed by means of interviews with relatives or caregivers. They were e.g. asked about pre-fracture memory problems, orientation and about previous episodes of delirium. Dementia was diagnosed according to DSM-IV criteria using to the same procedure as for delirium (see above).

In Paper II pre-fracture dementia was diagnosed in 22 of the 100 patients according to the DSM-IV criteria for organic brain disorders. These patients were excluded, thus 78 non-demented patients remained for inclusion in Paper II. Patients and/or their caregivers were interviewed six months and five years after surgery regarding living conditions and health. All medical records from all hospital admissions and outpatients reception were reviewed and all diagnoses were registered. For the patients who died during the 5 years the dementia diagnosis was based on documentation from outpatient visits, from hospital records and/or
death certificates. Cognitive decline during the last month of life was not diagnosed as dementia. The majority of these patients were assessed at the Department of Geriatric Medicine, Norrland’s University Hospital, which is the only hospital in the catchment area. The department of Geriatric Medicine is responsible for all dementia assessment in the primary catchment area of the hospital and specialists in geriatric medicine from this department are the responsible physicians for everyone living in residential care in Umeå. All patients who are offered apartments in residential care facilities, such as group livings for the demented, first undergo a full dementia assessment. Patients with dementia living in their own homes are also in most cases assessed and supported by the outpatient dementia clinic at department of Geriatric Medicine. This means that for almost all the patients in this study there was extensive documentation in their records regarding cognitive and functional level as well as diagnoses of dementia and delirium. Finally 44 of those 47 who were still alive after 5 years were tested in their homes using both the OBS Scale and the MMSE. The disorientation subscale scores in the modified OBS Scale strongly correlate with the MMSE scores (Pearson r=-0.899, p=<0.001) at the time of the follow up (Paper II).

In Paper III the patients’ pre-fracture mental state was assessed by means of interviews with relatives or caregivers and a review of their nursing and medical records. Dementia was diagnosed according to DSM-III-R criteria. The majority of the patients were assessed at the Department of Geriatric Rehabilitation, Piteå River Valley Hospital, which is the only hospital in the catchment area. This department is also responsible for all dementia assessment in the primary catchment area of the hospital. A unique epidemiological study of dementia was performed in the catchment area of this hospital which means that all persons with a cognitive impairment severe enough to require medical attention was assessed in the Piteå River Valley Hospital.100

In Paper IV a specialist in geriatric medicine blindly analyzed all assessments and documentation including all patients’ medical and nursing records to decide whether the patients met the DSM-IV criteria for dementia. Assessments with the OBS Scale and the MMSE at four and twelve month were also used to validate any dementia diagnoses.
Depression

In Papers I, II and III the diagnosis of depression was mainly based on documentation in the medical records, often in combination with ongoing treatment with antidepressants and with depressive symptoms observed and registered by the OBS Scale. The rating of depression according to the OBS Scale has been compared to the Montgomery-Åsberg Depression Rating Scale (MADRS) and found to have a high correlation.\(^{101}\)

In Paper IV a specialist in geriatric medicine analyzed all assessments and documentation including all patients’ medical and nursing records to decide whether the patients met the DSM-IV criteria for depression.\(^{16}\) Depression before hospitalization was diagnosed after an evaluation of earlier diagnoses documented in the records, and current treatment with antidepressants. Depression during hospitalization was diagnosed if the patients were currently being treated with antidepressants and if the screening with the GDS-15 indicates depression in combination with depressive symptoms observed and registered by the OBS Scale.

Hearing and vision

Patients’ hearing and vision were tested on the first occasion when assessment with the OBS Scale was performed. The patients were assessed as having impaired hearing if they could not hear a normal speaking voice from a distance of one meter with or without a hearing aid and impaired vision if they not could read a newspaper with or without glasses (Papers I-IV).

Blood pressure

Blood pressure was measured every 5 minutes during the operation and blood pressure falls in relation to blood pressure before the spinal anesthesia were registered in percentages (Papers I and II).

Further relevant information about the patients’ living conditions, on-going treatments and diagnoses etc. were obtained from the patients themselves, their spouses, nursing and medical staff and medical records (Papers I-IV).
Follow up (Papers I-IV)
In Papers I and II the patients and/or their caregivers, were interviewed six months after surgery regarding living conditions and health. In Papers I and II the patients were followed regarding mortality for 3 and 5 years respectively. All survivors were visited and assessed 5 years after the fracture. In Paper III the patients or their caregivers were interviewed 6 months after surgery, when their living conditions and walking ability were recorded. Mortality during the six months after the hip fracture was also registered. In Paper IV the patients were visited and assessed at 4 and 12 months by the study group. Mortality during the first year after the hip fracture was also registered.

Study design
Paper I was performed as a prospective study with a six-month follow up and Paper II was performed as a 5-year prospective follow up study.

Paper III was performed as a non-randomized intervention study where all the data concerning patient characteristics were compared with historical cohorts of corresponding patients in the same and other hospitals. The inclusion criteria and assessment methods were identical in control studies I and II and in the current intervention study. Because of different inclusion criteria in control study III, the intervention sample was matched as closely as possible to the inclusion criteria in the earlier study. The same inclusion criteria as in that study (control III) were adopted for the current sample resulting in 45 patients remaining for comparison. Only patients able to communicate on admission to hospital are included in the comparisons.

In Paper IV all patients had the same preoperative treatment in the orthopaedic ward. The patients were randomized to postoperative care in a geriatric ward with a special intervention program or to conventional care in the orthopaedic department. This was done using sealed, opaque envelopes stratified according to operation method. All participants received an envelope while in the emergency room but the envelope was not opened until immediately before surgery to ensure similar preoperative treatment. The staffing at the orthopaedic ward was 1.01 nurses/aids per bed and 1.07 nurses/aids per bed on the intervention ward. A similar proportion of other professionals worked in both wards but in the intervention ward they had developed a plan which included more teamwork. The staff on the intervention ward were
fully aware of the nature of the study and the staff on the control ward were informed that a new care program was being evaluated on the geriatric ward.

**Intervention programs (Paper III and IV)**

The intervention program in Paper III was based on previous research in Umeå and Piteå and on a literature review.\(^{37-39, 41-43, 46}\) The intervention program in Paper IV was based on the same program as reported in Paper III.

In Paper III there was a total reorganisation of the nursing and medical care of patients with femoral neck fractures and the intervention program consisted of ten items:

1. All members of staff received 2 weeks training in caring, rehabilitation, teamwork and medical knowledge including sessions about delirium, risk factors, prevention and treatment. The education preceded the reorganisation of the care.

2. All femoral neck-fracture patients were admitted to the geriatric rehabilitation unit from the emergency ward. Orthopaedic surgeons and geriatricians co-operated in the treatment of the patient. The motto in the ward was, ‘We don’t move disabled patients if the doctor is healthy and can walk independently’.

3. Medical prevention and treatment of delirium patients: all patients were operated on as quickly as possible, as a more favourable outcome has been reported for hip fracture patients operated on immediately after admission.\(^{102}\)

   Hypoxemia has been reported to be common among hip fracture patients and also to be associated with postoperative delirium.\(^{37, 46, 103}\) It was, therefore, considered important to prevent hypoxemia. Oxygen-enriched air was administered throughout the operation and the immediate postoperative period. All patients were treated with a Positive Expiratory Pressure bottle (PEP-bottle) several times a day to prevent atelectasis and pneumonia.\(^{104}\)

   Patients who develop postoperative delirium were assessed and treated for complications that could be associated with delirium, e.g. anaemia, heart failure, urinary tract infections, urinary retention, pneumonia, deep vein thrombosis and pulmonary embolism.\(^{26, 42, 46, 47, 105}\) The aim of this intervention was mainly to reduce the duration and severity of the delirium, as it has been found that prolonged delirium is associated with several postoperative complications.
Treatment of postoperative complications in delirious patients probably reduces the stress and thereby the duration and severity of delirium. Pain-reducing pills were distributed as soon as the patient woke up in the morning, in order to facilitate the ensuing training. All patients received low-molecular heparine as a thrombosis prophylactic.

4. The team carried out the planning of individual care on the day of admission and rehabilitation was started as soon as possible. The members of the team met the patient, his/her family and each other both formally and informally during the hospital stay or during home visits. On the basis of the data collected by its members, the team collectively formulated the main and secondary goals, in co-operation with the patient. Each member of the team was responsible for fitting his/her data collection into the whole, for defining his/her own tasks and ensuring that these tasks were carried out with regard to the whole. The teamwork was thus performed according to an interdisciplinary rehabilitation team process.

All patients were assigned two contact people, one of whom was a registered nurse and the other a licensed practical nurse both with primary care responsibility for the patient.

5. Small teams of staff worked closely with the patient, watching the patient’s state of well-being and adjusting the training to that particular level of well-being, which may vary from day to day, even from hour to hour.

6. Physiotherapists and occupational therapists participated in the team and were on the ward all day and co-operated effectively and closely with all the staff. Much of the training took place in the patient’s room, but there were special rooms and equipment for training on the ward.

Patients were encouraged all hours of the day and all days of the week to perform all the activities or parts of activities in all situations that they could manage. All staff members were involved in the training.

7. A new building specifically designed for rehabilitation was erected in 1992. All the patients’ rooms are single or double, spacious and fitted with a shower room and toilet. Every patient has his/her own bedside phone to facilitate close contact with friends and relatives. There are four dining rooms on the ward designed for eight patients each. The eating, living
and training environment on the ward is excellent. There are no set visiting hours and relatives are encouraged to stay with the patients and even to stay the night, especially if the patient was uneasy or delirious.

8. The staff adjusted to the individual needs of the patient instead of the patient having to adjust to the group. The patients were allowed to wake up at a time that suited them, to drink morning tea/coffee in peace and quiet before getting washed, dressed and going to the breakfast room. In short, the patients were allowed to wake up and prepare themselves for the training at their own pace.

9. The good eating environment includes nicely laid tables and food taken from a serving dish by the patients themselves as far as possible. Nutritional and protein drinks were served every day in attractive glasses. The drinks were prepared on the ward by the staff and made to look good and appetising.

10. The patient did not change ward during the course of care (including the need of in-hospital rehabilitation) from admission to discharge. They did not even change rooms during their entire stay on the ward, which also meant that they always met members of the same team.

Difference in intervention program in Paper IV compared to that in Paper III
Before the intervention started the staff in Paper III received a 2 weeks course in e.g. caring and rehabilitation of patients with hip fractures and stroke. The education also focused on prevention, detection and treatment of complications such as delirium. In Paper IV the staff received a similar course but the duration was only four days.

The intervention ward in Paper IV was situated in a 24-bed geriatric unit specializing in geriatric orthopaedic patients in the Geriatric Department at Norrland’s University Hospital in Umeå. This Department of Geriatrics was moved in 1996 in to a new building specifically designed for geriatric care and rehabilitation with the same exclusive environment as in Piteå (Paper III) except that there was only one dining room per 24 patients.

Further differences: the intervention program in Paper III also included preoperative care since all patients were admitted to the intervention ward preoperatively. In Paper IV the intervention patients received their preoperative care at the Orthopaedic Department since the
intervention program concerned postoperative care at the geriatric unit specializing in geriatric orthopaedic patients. In both intervention studies the patients received oxygen-enriched air during and after the operation. In Paper IV the patients also received oxygen-enriched air preoperatively (in the ambulance, at the emergency ward and on the orthopaedic ward before surgery). The patients in Paper III did not receive oxygen-enriched air preoperatively on regular basis. In Paper IV the patients received blood transfusion if B-haemoglobin, g/l, was <100; for those at risk of delirium or those already delirious the limit was <110 g/l. In Paper III the patients received blood transfusion on an individual basis not according to any specific protocol.

In Paper III the orthopaedic surgeons and geriatricians co-operated in the treatment of the patients but in Paper IV the geriatricians had the responsibility for the patients and the orthopaedic surgeons came to the ward once a week for consultation.

Control groups (Papers III and IV)

In Paper III the control group comprised historical cohorts of corresponding patients in the same (control III) and other hospitals (control I and II). Controls I and II consisted of two studies on delirium, one control and one medical intervention, including all patients 65 years of age and above consecutively admitted to the Orthopaedic Department of Norrland’s University Hospital in Umeå. Control study I consisted of 111 consecutive patients (28 men and 83 women, mean age 79.3 years, range 65-95 years) operated on for femoral neck fracture from March 1983 to June 1984 (control I), and the second control study (II) included 103 consecutive patients (28 men and 75 women, mean age 79.5 years, range 65-102) operated on for femoral neck fracture from December 1986 to January 1988.

Control study III comprised an earlier study from the same hospital as the intervention study was performed in and included all patients 60 years of age and above admitted for treatment of femoral neck fractures. Patients with severe communication problems were excluded. Thirty-five patients (7 men and 28 women, mean age was 78.2, range 61-88 years) were included from April 1983 to May 1984.

In Paper IV the control group consisted of those patients who were randomly assigned to receive their postoperative care in the Orthopaedic Department according to the usual postoperative care routines, which included checks for e.g. oxygen saturation, haemoglobin,
nutrition, decubital ulcers, bladder and bowl function, home situation etc. The checks were not carried out according to any specific program, as in the intervention ward, and were thus not performed systematically. The physiotherapist on the ward worked to mobilize the patients together with the ordinary staff (licensed practical nurses and registered nurses). The occupational therapist on the ward met only those patients who were going to return home, for consultation about assistive devices and adjustments to the patient’s home. The patients who needed further in-hospital rehabilitation were admitted to a geriatric ward, but not the intervention ward.

**Data analyses**

Univariate analyses using the Pearson chi-square test, Student’s t-test and the Fisher’s exact test were performed to analyze group differences in Papers I-IV. In Paper III the Yates’ corrected chi-square was also used. A p value of <0.05 was regarded as statistically significant in all Papers. In Paper I variables which showed statistically significant differences were included in multivariate logistic regression analyses to find the factors that were independently associated with the development of preoperative and postoperative delirium. In Paper II variables showing statistically significant differences between groups were included in multivariate logistic regression analyses to find the factors associated with the development of delirium and of dementia. In Paper III a Bonferroni adjustment for multiple comparisons was performed. In Paper IV multivariate logistic regression analyses were used to control for case-mix between the control and the intervention sample.

**Ethical approval**

On admission all patients (Papers I-IV) were asked verbally (also in writing in Paper IV) if they were willing to participate in the study after being informed about the study and that their participation or refusal would not affect their medical or nursing care in any way. In those patients with cognitive impairment/dementia or delirium the next of kin was also asked.

The Ethical Committee of the Faculty of Medicine at Umeå University approved the studies (Papers I, II and IV). Paper III was performed and evaluated as a Clinical Research and Development project at Piteå River Valley Hospital and was approved by the hospital authorities there.
RESULTS

Delirium before and after Operation for Femoral Neck Fracture (Paper I)

Forty-nine of the 101 patients (48.5%) were delirious on admission or developed delirium during their stay on the ward. Thirty of those 101 patients (29.7%) were delirious on admission or developed delirium before surgery, and another nineteen (18.8%) developed delirium postoperatively. All but one of the patients who were delirious preoperatively remained delirious postoperatively. Twenty-nine of the 99 patients (29.3%) whom it was possible to assess for more than one week had delirium or episodes of delirium during a period of at least one week. Twenty-three out of 28 (82.1%) who were already delirious before the operation were delirious for more than one week compared to only 6 out of 18 (33.3%) who developed delirium postoperatively (p<0.001). It was not possible to assess one patient who was delirious preoperatively and one patient who had delirium only postoperatively after one week.

A larger proportion of patients who were delirious before surgery (n=30) were demented (60.0% vs. 4.2%, p<0.001) and treated with drugs with anticholinergic effects (46.6% vs. 19.7%, p=0.006) or neuroleptics (43.3% vs. 11.3%, p<0.001) compared to those who were not delirious preoperatively (n=71). Patients who were delirious before surgery had also had previous episodes of delirium (67.0% vs. 8.4%, p<0.001), had fallen indoors (90.0% vs. 67.6%, p=0.004), seemed to fall more often during the night (35.7% vs. 18.8%, P=0.077) and more of them suffered from constipation (28.0% vs. 4.3%, p<0.001). Some of the patients were reported to have been delirious when they fell. A multivariate logistic regression analysis showed that dementia was the factor to be independently associated with preoperative delirium (odds ratio (OR)= 34.00; 95% confidence interval (CI)= 8.66-133.49, Model Chi-square 38.0, p<0.001, concordant 85%).

Patients who developed delirium postoperatively (n=19) were more often male (47.4% vs. 11.5%, p=0.001), had more perioperative blood pressure falls measured as a percentage (31.4±16.5 vs. 22.9±13.2, p=0.029) and seemed to have more postoperative complications such as infections like pneumonia (10.5% vs. 0%, p=0.069) and urinary tract infection (47.4% vs. 25.0%, 0.071) and depressed mood (52.1% vs. 19.2%, p=0.056) compared to those who
remained lucid (n=52) during their stay on the ward. Multivariate logistic regression modelling revealed that perioperative blood pressure falls (%) and male sex was the factors to be independent associated with postoperative delirium (OR=1.06; 95% CI=1.02-1.10 and OR=4.13; 95% CI=1.32-12.98, respectively, Model Chi-square 12.3, p=0.002, concordant 82%).

The predisposing and precipitating factors differed between those who developed delirium preoperatively and those who developed delirium postoperatively (Table 8). Those who were delirious before surgery were more often demented, being treated with drugs with anticholinergic effects (mainly neuroleptics), had had previous episodes of delirium and had more often fallen indoors than those who developed delirium after surgery. Eighteen out of 21 patients with dementia were delirious during their stay on the ward and all 18 were delirious before surgery.

Patients who developed delirium after surgery more often had pronounced perioperative blood pressure falls than those who were already delirious before surgery (Table 8). The two multivariate logistic regression models described above confirmed that there were different predisposing and precipitating factors for delirium in patients who were delirious before surgery and those who developed delirium postoperatively.

The outcomes also differed between those patients who were delirious before surgery and those who developed delirium postoperatively. Delirium that developed postoperatively seemed to have a shorter duration (Table 8). A larger proportion of those who developed delirium postoperatively could walk independently on discharge compared to those who were delirious before surgery. Patients who developed delirium postoperatively also had a lower long-term mortality than those who were delirious preoperatively (Table 8).

Delirium was more common in men (22/28, 78.6% compared to 26/73, 35.6% in women, p<0.001). This was true both for those with preoperative delirium and those who developed postoperative delirium. As shown in Table 9 the men with femoral neck fractures were in poorer health than the women, except that more female patients had hypertension and were treated with diuretics. Men also suffer more postoperative complications and had a higher long-term mortality.
Table 8. Comparison between patients who developed postoperative delirium and those who were already delirious on admission (all of whom remained delirious postoperatively)

<table>
<thead>
<tr>
<th></th>
<th>Delirious preoperatively (n=29)</th>
<th>Delirious postoperatively only (n=19)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean,SD)</td>
<td>81.4±5.6</td>
<td>80.0±8.1</td>
<td>0.490</td>
</tr>
<tr>
<td>Men</td>
<td>13 (44.8)</td>
<td>9 (47.4)</td>
<td>0.862</td>
</tr>
<tr>
<td>Admitted from independent living (n=24 vs. 19)</td>
<td>3 (12.5)</td>
<td>12 (63.2)</td>
<td>0.001</td>
</tr>
<tr>
<td>Walked independently before the fracture (n=26 vs. 18)</td>
<td>24 (92.3)</td>
<td>17 (94.4)</td>
<td>1.000</td>
</tr>
<tr>
<td>Previous delirium</td>
<td>20 (69.0)</td>
<td>2 (10.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Urinary incontinence</td>
<td>16 (55.2)</td>
<td>3 (15.8)</td>
<td>0.013</td>
</tr>
<tr>
<td>Dementia</td>
<td>18 (62.1)</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Drugs with anticholinergic effect</td>
<td>14 (48.3)</td>
<td>3 (15.8)</td>
<td>0.021</td>
</tr>
<tr>
<td>Neuroleptics</td>
<td>13 (44.8)</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fracture indoors, (n=27 vs. 19)</td>
<td>27 (100)</td>
<td>15 (78.9)</td>
<td>0.024</td>
</tr>
<tr>
<td>Fracture at night</td>
<td>10 (34.5)</td>
<td>2 (10.5)</td>
<td>0.086</td>
</tr>
<tr>
<td>Cognitive testing on admission (mean,SD)* (n=27 vs. 19)</td>
<td>25.1±9.7</td>
<td>3.6±3.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Blood pressure during operation ≤80 mmHg</td>
<td>3 (10.3)</td>
<td>6 (31.6)</td>
<td>0.065</td>
</tr>
<tr>
<td>Blood pressure fall as percentage (mean,SD)</td>
<td>21.7±12.9</td>
<td>31.4±16.5</td>
<td>0.028</td>
</tr>
<tr>
<td>Days of delirium (mean,SD)</td>
<td>3.9±1.2</td>
<td>2.8±1.8</td>
<td>0.036</td>
</tr>
<tr>
<td>Delirium for more than one week (n=46)</td>
<td>23/28 (82.1)</td>
<td>6/18 (33.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pneumonia postoperatively</td>
<td>6 (20.7)</td>
<td>2 (10.5)</td>
<td>0.305</td>
</tr>
<tr>
<td>Urinary tract infection</td>
<td>10 (34.5)</td>
<td>9 (47.4)</td>
<td>0.372</td>
</tr>
<tr>
<td>Length of stay in the orthopaedic department (mean,SD)</td>
<td>11±10.8</td>
<td>15±9.6</td>
<td>0.489</td>
</tr>
<tr>
<td>Return to independent living at discharge (n=3 vs. 12)</td>
<td>1 (33.3)</td>
<td>6 (50.0)</td>
<td>1.000</td>
</tr>
<tr>
<td>Regained independent walking ability on discharge (n=23 vs. 16)</td>
<td>5 (21.7)</td>
<td>13 (81.2)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Regained independent walking ability at 6 months (n=24 vs.17)</td>
<td>12 (50.0)</td>
<td>14 (76.5)</td>
<td>0.028</td>
</tr>
<tr>
<td>Dead at 3 years</td>
<td>21 (72.4)</td>
<td>6 (31.6)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

*Higher score = worse test result (range 0-36 points)
Table 9. Differences between males and females with femoral neck fracture

<table>
<thead>
<tr>
<th></th>
<th>Men (n=28)</th>
<th>Women (n=73)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (mean,SD)</strong></td>
<td>80.8±6.1</td>
<td>79.1±8.2</td>
<td>0.258</td>
</tr>
<tr>
<td>Impaired vision</td>
<td>10 (35.7)</td>
<td>13 (17.8)</td>
<td>0.055</td>
</tr>
<tr>
<td>Impaired hearing</td>
<td>12 (42.9)</td>
<td>18 (24.7)</td>
<td>0.073</td>
</tr>
<tr>
<td>Dementia</td>
<td>9 (32.1)</td>
<td>12 (16.4)</td>
<td>0.082</td>
</tr>
<tr>
<td>Parkinson’s disease</td>
<td>4 (14.3)</td>
<td>0 (0)</td>
<td>0.005</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1 (3.6)</td>
<td>25 (34.2)</td>
<td>0.002</td>
</tr>
<tr>
<td>Benzodiazepines</td>
<td>3 (10.7)</td>
<td>19 (26.0)</td>
<td>0.095</td>
</tr>
<tr>
<td>Diuretics</td>
<td>5 (17.9)</td>
<td>29 (39.7)</td>
<td>0.038</td>
</tr>
<tr>
<td>Postoperative pneumonia</td>
<td>6 (21.4)</td>
<td>2 (2.7)</td>
<td>0.005</td>
</tr>
<tr>
<td>Preoperative and postoperative delirium</td>
<td>22 (78.6)</td>
<td>26 (35.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dead after 1 year</td>
<td>6 (21.4)</td>
<td>10 (13.7)</td>
<td>0.341</td>
</tr>
<tr>
<td>Dead after 2 year</td>
<td>13 (46.4)</td>
<td>11 (15.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Dead after 3 year</td>
<td>18 (64.3)</td>
<td>23 (31.5)</td>
<td>0.003</td>
</tr>
</tbody>
</table>
Dementia after delirium in patients with femoral neck fractures (Paper II)

Thirty (38.5%) of the 78 non-demented patients were already delirious on admission or developed delirium during their hospital stay. Eleven of them were delirious preoperatively and all but one remained delirious postoperatively.

Patients who were delirious postoperatively (n=29) were more often men, had worse results on cognitive testing on admission, had previously had delirium, were diagnosed as diabetic and had a higher level of S-creatinine. Furthermore, a higher proportion had systolic blood pressure falls during the operation and postoperative complications such as pneumonia, urinary tract infections, depressed mood and a longer stay in hospital (15.5 days vs. 10.6 days; p=0.014). Multivariate logistic regression modelling revealed that systolic blood pressure falls to ≤ 80 mmHg during the operation, diagnosis of diabetes, worse results on cognitive testing on admission and male sex were the factor independently associated with postoperative delirium (OR=31.80; 95% CI=2.63-383.98, OR=8.08; 95% CI=1.22-53.57, OR=1.19; 95% CI=1.06-1.34, OR=13.35; 95% CI=2.94-60.63, respectively, Model Chi-square 40.9, p<0.001, concordant 84%).

All eleven who were already delirious preoperatively developed dementia within a five-year period (Figure 2). Twenty out of the 29 patients (69%) who were delirious postoperatively developed dementia compared to 10 out of 49 patients (20%) who remained lucid after the operation (p<0.001). A significantly higher proportion of patients who developed dementia had been diagnosed as diabetics, had had previous episodes of delirium, was delirious postoperatively, had a longer stay in hospital and worse results on cognitive testing on admission compared to those who did not develop dementia. A multivariate logistic regression analysis resulted in three factors being identified as independently associated with the development of dementia. These three factors were: diabetes, postoperative delirium and worse results on cognitive testing on admission (OR=13.82; 95% CI= 1.35-141.12, OR=5.66; 95% CI= 1.31-23.56, OR=1.18; 95% CI= 1.02-1.37, respectively, Model Chi-square 31.9, p<0.001, concordant 79%).

Twenty-one out of 29 (72.4%) patients with postoperative delirium died within 5 years compared to 17/49 (34.7%) of those who remained lucid postoperatively (p=0.001).
Figure 2. Development of dementia and mortality in five-year follow up.
Reorganization of nursing and medical care to reduce the incidence of postoperative delirium and improve rehabilitation outcome in elderly patients treated for femoral neck fractures (Paper III)

One fifth (n=10) of the 49 patients were already delirious preoperatively, 30.6% (n=15) were delirious or developed delirium postoperatively but only 16.3% (n=8) remained delirious after one week. The absolute majority (89.3%) of those who came from independent living could return home and 84% could walk independently with or without walking-aids on discharge. The length of stay was 12.5±8.4 days (range 2-54) including the total in-hospital rehabilitation time.

Comparisons with control I and II.

There were only minor base-line differences in the three groups (the intervention ward from Piteå River Valley Hospital and the two controls from the Orthopaedic Department at Norrland’s University Hospital in Umeå) of patients treated for femoral neck fractures in the two hospitals. For example there were more patients with impaired vision, constipation and receiving treatment with analgesics in the intervention sample than in the two control studies. When the Bonferroni correction for probabilities was made, only impaired vision remained as a significant difference between the samples.

The intervention resulted in a much lower incidence and a shorter duration of delirium in the intervention group than in either of the two control studies (Table 10). The rehabilitation outcome regarding walking ability and the possibility of returning home on discharge were much better for the intervention group despite a short total length of hospital stay (Table 10).

It should be noted that the hospitalisation time in the two studies from Umeå includes only the stay on the orthopaedic ward. More than one third of the patients in both the Umeå studies were discharged to the geriatric rehabilitation unit. In the current intervention study the ward stay also included the time needed for rehabilitation.

There were fewer complications in the intervention study than in the control studies, for example fewer patients suffered from urinary retention (2.0% vs. 18.9%, p=0.004) and decubital ulcers (0% vs. 12.6%, p=0.009) compared to control I.
Table 10. Incidence of postoperative delirium, ward stay, walking ability, living condition and mortality in the intervention and the two control studies from the Orthopaedic Department at Norrland’s University Hospital in Umeå

<table>
<thead>
<tr>
<th></th>
<th>Intervention (n=49)</th>
<th>Control I (n=111)</th>
<th>Control II (n=103)</th>
<th>p-value*</th>
<th>p-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative delirium</td>
<td>20.4</td>
<td>33.3</td>
<td>29.1</td>
<td>0.098</td>
<td>0.253</td>
</tr>
<tr>
<td>Postoperative delirium</td>
<td>30.6</td>
<td>61.3</td>
<td>47.6</td>
<td>&lt;0.001</td>
<td>0.047</td>
</tr>
<tr>
<td>Delirium ≥7 days</td>
<td>16.3</td>
<td>39.6</td>
<td>29.1</td>
<td>0.004</td>
<td>0.088</td>
</tr>
<tr>
<td>Length of hospital stay (mean)</td>
<td>12.5§</td>
<td>17.4‡</td>
<td>11.6‡</td>
<td>&lt;0.001</td>
<td>0.003</td>
</tr>
<tr>
<td>No walking aids before fracture</td>
<td>38.8</td>
<td>77.5</td>
<td>64.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Walking independently with or without walking aids on discharge</td>
<td>83.8</td>
<td>58.3</td>
<td>60.2</td>
<td>0.002</td>
<td>0.005</td>
</tr>
<tr>
<td>Walking independently with or without walking aids at six months</td>
<td>80.5</td>
<td>75.3</td>
<td>77.8</td>
<td>0.509</td>
<td>0.726</td>
</tr>
<tr>
<td>Independent living before fracture</td>
<td>57.1</td>
<td>47.7</td>
<td>56.3</td>
<td>0.273</td>
<td>0.923</td>
</tr>
<tr>
<td>Proportion returning to independent living on discharge</td>
<td>89.3</td>
<td>62.3</td>
<td>53.4</td>
<td>0.010</td>
<td>0.001</td>
</tr>
<tr>
<td>Proportion still living independently at six months</td>
<td>80.0</td>
<td>71.7</td>
<td>75.9</td>
<td>0.979</td>
<td>0.659</td>
</tr>
<tr>
<td>In-hospital mortality</td>
<td>2.0</td>
<td>2.7</td>
<td>5.8</td>
<td>0.805</td>
<td>0.298</td>
</tr>
<tr>
<td>Six-month mortality</td>
<td>16.3</td>
<td>16.2</td>
<td>12.6</td>
<td>0.986</td>
<td>0.536</td>
</tr>
</tbody>
</table>

* The difference between Control I and the intervention.
† The difference between Control II and the intervention.
§ Also includes the rehabilitation time
‡ Only the orthopaedic ward stay

Comparison with control III

There were no significant differences between the intervention sample (cared for in the ward of acute rehabilitation) and the control sample (cared for in a ward of general surgery) from the same hospital regarding the clinical characteristics of the patients (e.g. previous concurrent diagnoses such as dementia or stroke and regular use of drugs such as neuroleptics and benzodiazepines).

The difference in postoperative delirium (42.9% vs 26.7%) does not reach statistical significance (Table 11). However, the difference in rehabilitation outcome was significantly better for the patients in the intervention study. A larger proportion could return home directly and a larger proportion could walk independently on discharge despite a short total length of hospital stay (Table 11). It should also be noted that in this control study almost half the patients were discharged to the geriatric clinic for rehabilitation. During the intervention study
all patients received all their rehabilitation in the same ward and no patient was discharged for rehabilitation elsewhere.

Table 11. Incidence of postoperative delirium, ward stay, walking ability and living condition in the intervention and the Piteå control study

<table>
<thead>
<tr>
<th></th>
<th>Intervention (n=45)</th>
<th>Control III (n=35)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperative delirium</td>
<td>26.7</td>
<td>42.9</td>
<td>0.129</td>
</tr>
<tr>
<td>Length of hospital stay (mean)</td>
<td>12.9*</td>
<td>12.8†</td>
<td></td>
</tr>
<tr>
<td>No walking aids before fracture</td>
<td>40.0</td>
<td>45.7</td>
<td>0.608</td>
</tr>
<tr>
<td>Walking independently with or without walking aids on discharge</td>
<td>88.6</td>
<td>60.0</td>
<td>0.003</td>
</tr>
<tr>
<td>Walking independently with or without walking aids at six months</td>
<td>84.6</td>
<td>78.2</td>
<td>0.482</td>
</tr>
<tr>
<td>Living independently before fracture</td>
<td>60.0</td>
<td>77.1</td>
<td>0.104</td>
</tr>
<tr>
<td>Proportion returning to independent living on discharge</td>
<td>92.6</td>
<td>33.3</td>
<td>0.018</td>
</tr>
<tr>
<td>Proportion still living independently at six months</td>
<td>84.6</td>
<td>78.2</td>
<td>0.482</td>
</tr>
</tbody>
</table>

* Also includes the rehabilitation time
† Only the orthopaedic ward stay
Prevention and treatment of postoperative delirium in old people with femoral neck fracture – a randomized controlled trial (Paper IV)

Fewer intervention patients than controls were delirious postoperatively (56/102, 55% vs. 73/97, 75%, p=0.003) and the duration of postoperative delirium was also shorter (5.0±7.1 days vs. 10.2±13.3 days, p=0.009) (Table 12). None of the intervention patients was delirious at discharge (p<0.001). Eighteen percent of intervention patients were delirious after the seventh postoperative day compared with 52% of the controls (p<0.001).

Intervention patients suffered fewer complications during hospitalization and complications were more common among patients with postoperative delirium (Table 13).

More assessments of underlying causes of delirium were documented in the nurses’ records in the intervention ward compared to in the control ward (2.28±1.25 vs. 0.90±0.90, p<0.001). Similarly more treatments (1.69±1.56 vs. 0.56±0.98, p<0.001) for underlying causes of delirium were also documented. Delirious control patients on the other hand were more often given sedatives (20/48, 41.7% vs. 6/39, 15.4%, p=0.008) and opioid drugs (29/47, 61.7% vs. 12/39, 30.8%, p=0.004) on demand than those in the intervention ward.

Intervention patients had a shorter total postoperative hospitalization (28.0±17.9 days vs. 38.0±40.6 days, p=0.028) than controls, which was also true for intervention patients with postoperative delirium (31.4±19.3 days vs. 43.6±42.7 days, p=0.032). Delirium per se was associated with prolonged hospitalization. Similar proportions of patients could return to their previous places of residence on discharge despite the shorter ward stay (Table 13). Mortality during hospitalization and at the 4- and 12-month follow up did not differ significantly between the intervention and control samples (data not shown).

All differences between the intervention and control wards remained unchanged even when adjustment was made for a different case-mix in the two wards (Table 14).
The duration of postoperative delirium in patients with dementia in the intervention ward was 3.2±4.1 days compared to 12.8±17.6 days in the control ward (p=0.003). In addition, 15 patients with dementia in the control ward were still delirious on discharge in contrast to none from the intervention ward (p<0.001).

Table 12. Delirium in patients on the intervention ward vs. the control ward.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All patients</th>
<th>Patients delirious postoperatively</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention ward (n=102)</td>
<td>Control ward (n=97)</td>
</tr>
<tr>
<td>Delirium during hospitalization</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Delirium preoperatively n=101, 97 vs. 55, 73</td>
<td>59 (58)</td>
<td>74 (76)</td>
</tr>
<tr>
<td>Delirium only preoperatively n=101 vs. 97</td>
<td>3 (3)</td>
<td>1 (1)</td>
</tr>
<tr>
<td>Delirium only postoperatively n=101 vs. 97</td>
<td>37 (36)</td>
<td>44 (45)</td>
</tr>
<tr>
<td>Delirium on day 1 n=101, 96 vs. 56, 73</td>
<td>39 (39)</td>
<td>70 (73)</td>
</tr>
<tr>
<td>Delirium on day 2 n=100, 94 vs. 56, 72</td>
<td>32 (32)</td>
<td>69 (73)</td>
</tr>
<tr>
<td>Delirium on day 3 n=100, 93 vs. 56, 71</td>
<td>30 (30)</td>
<td>64 (69)</td>
</tr>
<tr>
<td>Delirium on day 4 n=100, 92 vs. 56, 70</td>
<td>24 (24)</td>
<td>51 (55)</td>
</tr>
<tr>
<td>Delirium on day 5 n=100, 90 vs. 56, 68</td>
<td>24 (24)</td>
<td>46 (51)</td>
</tr>
<tr>
<td>Delirium on day 6 n=100, 88 vs. 56, 66</td>
<td>14 (14)</td>
<td>32 (36)</td>
</tr>
<tr>
<td>Delirium on day 7 n=98, 87 vs. 55, 66</td>
<td>12 (12)</td>
<td>32 (37)</td>
</tr>
<tr>
<td>Delirium after day 7 n=100, 87 vs. 56, 66</td>
<td>18 (18)</td>
<td>45 (52)</td>
</tr>
<tr>
<td>Delirium on discharge</td>
<td>0</td>
<td>20 (21)</td>
</tr>
<tr>
<td>Duration of delirium in days, mean±SD</td>
<td>2.7±5.6</td>
<td>7.7±12.3</td>
</tr>
</tbody>
</table>
Table 13. Diagnoses and presenting symptoms for study patients during hospitalization.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>All patients</th>
<th>Patients delirious postoperatively</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Intervention ward (n=102)</td>
<td>Control ward (n=97)</td>
</tr>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Anemia</td>
<td>n=102, 96 vs. 56, 73</td>
<td>88 (86)</td>
</tr>
<tr>
<td>Constipation</td>
<td>n=102, 95 vs. 56, 72</td>
<td>38 (37)</td>
</tr>
<tr>
<td>Decubital ulcers</td>
<td>n=101, 97 vs. 56, 73</td>
<td>9 (9)</td>
</tr>
<tr>
<td>Depression</td>
<td>n= 101, 97 vs. 56, 73</td>
<td>50 (50)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>n=102, 96 vs. 56, 73</td>
<td>22 (22)</td>
</tr>
<tr>
<td>Heart failure</td>
<td>n= 101, 95 vs. 55, 72</td>
<td>6 (6)</td>
</tr>
<tr>
<td>Infections:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>n=102, 96 vs. 56, 73</td>
<td>5 (5)</td>
</tr>
<tr>
<td>Urinary infection</td>
<td>n=102, 96 vs. 56, 73</td>
<td>32 (31)</td>
</tr>
<tr>
<td>Other infections</td>
<td>n=101, 96 vs. 55, 73</td>
<td>18 (18)</td>
</tr>
<tr>
<td>Sleeping problems</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td></td>
<td>2 (2)</td>
</tr>
<tr>
<td>Nutritional complications</td>
<td></td>
<td>25 (25)</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td></td>
<td>2 (2)</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Stomach ulcers</td>
<td>n=101, 97 vs. 55, 73</td>
<td>3 (3)</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>n=93, 90 vs. 56, 69</td>
<td>16 (16)</td>
</tr>
<tr>
<td>Falls</td>
<td></td>
<td>12 (12)</td>
</tr>
<tr>
<td>MMSE*, mean±SD</td>
<td>n=93, 90 vs. 56, 69</td>
<td>17.4±8.2</td>
</tr>
<tr>
<td>OBS Scale*: **; mean±SD, n=94, 90 vs. 55,69</td>
<td>10.1±10.8</td>
<td>12.5±11.4</td>
</tr>
<tr>
<td>GDS-15*, mean±SD</td>
<td>n=81, 68 vs. 46, 48</td>
<td>5.2±3.6</td>
</tr>
<tr>
<td>Length of hospital stay, mean±SD</td>
<td></td>
<td>28.0±17.9</td>
</tr>
<tr>
<td>Return to own house/apartment on discharge</td>
<td>n=64, 55 vs. 31, 35</td>
<td>48 (75)</td>
</tr>
</tbody>
</table>

* Assessed at day 3-5 postoperatively
** Disorientation subscale (higher score indicates increased disorientation)
Table 14. Multivariate logistic regression analysis to control for baseline differences between the postoperative delirious patients in the intervention and control wards. Included variables: dementia, ward, age, sex and the variable (depression) that differed between the intervention and control sample.

<table>
<thead>
<tr>
<th>Independent variable</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dementia</td>
<td>3.51</td>
<td>1.53-8.00</td>
</tr>
<tr>
<td>Ward</td>
<td>2.81</td>
<td>1.43-5.52</td>
</tr>
<tr>
<td>Depression</td>
<td>1.20</td>
<td>0.92-3.98</td>
</tr>
<tr>
<td>Age</td>
<td>1.07</td>
<td>1.01-1.13</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.87</td>
<td>0.86-4.08</td>
</tr>
</tbody>
</table>

Model Chi-square 37.43; p<0.001, concordant 68.5%.
DISCUSSION

This thesis shows that pre- and postoperative delirium in old patients suffering femoral neck fracture is common and appears to be associated with a variety of risk factors. A large proportion of those delirious before surgery were demented, being treated with drugs with anticholinergic properties (mainly neuroleptics), had had previous episodes of delirium and had fallen indoors. Patients who developed postoperative delirium had perioperative falls in blood pressure and seemed to have more postoperative complications, such as infections (Paper I). This thesis also shows that a large proportion of patients who are delirious during treatment for femoral neck fracture, develop dementia and have a higher mortality rate than those who are not delirious (Paper II). Furthermore, this thesis shows that postoperative delirium can be successfully prevented and treated which also results in fewer in-hospital complications, a shorter period of hospitalization and an improved rehabilitation outcome (Papers III and IV).

Predisposing and precipitating factors for delirium

Preoperative delirium in Paper I was associated with pre-existing dementia, treatment with drugs with anticholinergic effects (mainly neuroleptics) and previous episodes of delirium. This indicates that the majority of those patients had a prefracture organic brain disorder or were being treated with drugs that interfere with higher cortical functions. Due to multicollinearity it is not possible to decide which of neuroleptics or drugs with anticholinergic properties that was the most important risk factors, after dementia, for preoperative delirium. Neuroleptics might have been prescribed for treatment of delirium prefracture and can thus be a confounder rather than a risk factor for delirium. Constipation was also associated with preoperative delirium. Taking drugs with anticholinergic effects is a well-known risk factor for both delirium and for constipation. This result supports the opinion that prescribing drugs with anticholinergic properties should be avoided in old people and especially in patients with dementia. Patients with preoperative delirium had more often fallen indoors and seemed to fall more often during the night. Some of the patients were also reported to have been delirious when they fell. In a previous paper describing an intervention to combat delirium it was found that injurious falls were reduced when the incidence of delirium was reduced, indicating that delirium is an important risk factor for falls. Another recently published study found that delirium were the most common precipitating symptom
among those who fell in residential care facilities.\textsuperscript{30} In Paper IV it was found that reduced duration of delirium was also associated with fewer falls during hospitalization.

Severe perioperative falls in blood pressure, which could be partly prevented by properly performed anesthesia, seemed to contribute to postoperative delirium. This has also been shown in previous papers.\textsuperscript{37, 46}

Few studies have focused on preoperative delirium and its predisposing factors. One study which excluded those with dementia found that preoperative delirium was associated with age, heart failure and previous stroke.\textsuperscript{36} Another study found that those with preoperative delirium were older, had lower prefracture mobility and were more cognitively impaired than those who developed delirium postoperatively.\textsuperscript{53} This study also showed that predisposing factors for developing preoperative delirium were dementia, prefracture mobility and low MMSE score. Studies on postoperative delirium have either excluded patients with preoperative cognitive impairment or analyzed risk factors for postoperative delirium regardless of whether the patients were delirious preoperatively.\textsuperscript{27, 34, 36, 37, 39, 57} The precipitating factor for postoperative delirium found in Paper I was perioperative hypotension and male sex. Previous studies in hip fracture patients\textsuperscript{37, 42} have shown that postoperative delirium was associated with other perioperative complications such as infections and hypoxemia. One probably explanation that those precipitators for delirium were not found in Paper I was that the patients were included in an intervention program. That intervention aimed at prevention and treatment of delirium by means of oxygen therapy, early surgery, prevention and treatment of perioperative falls in blood pressure and treatment of postoperative complications such as infections.\textsuperscript{46} This earlier paper\textsuperscript{46} and other studies have shown that perioperative hypotension, anaemia and hypoxemia, all factors endangering the oxygenation of the brain, seem to be both important and preventable precipitating factors for postoperative delirium after various types of hip surgery.\textsuperscript{37, 46, 61} Postoperative complications, such as infections, are also important and treatable precipitating factors for postoperative delirium.\textsuperscript{46, 61} A large proportion of hip fracture patients seem to have fallen due for example to urinary tract infections\textsuperscript{30, 31} but many of these infections are neither detected nor treated preoperatively.

Men, in comparison to women, seem to be at a higher risk of developing delirium both preoperatively and postoperatively in this study, which can only be partially explained by the fact that the males seem to be more frail, as is also demonstrated by the higher long-term mortality among the men. The poorer outcome for men might at least partly be caused by the higher incidence of delirium.
There is to date only one other study that has found that male patients have a higher risk of developing delirium among studies on patients with hip fracture.57

Outcome of delirium
A larger proportion of those who only developed delirium postoperatively, reported in Paper I, regain independent walking ability compared to those who were delirious before surgery. The poorer rehabilitation prognosis, for those with preoperative delirium, is probably due to their pre-fracture clinical characteristics, such as a pre-existing dementia. This is in accordance with two previously published studies which showed that delirium preoperatively was associated with dementia and with adverse functional recovery.36, 53 One of the studies36 excluded patients with a preoperative dementia diagnosis but both studies showed that preoperative delirium was associated with poor functional recovery. Since in many cases, according to Paper II, delirium might be an early sign of an undetected dementia it is not surprising that delirious patients have a poorer long-term prognosis.

Dementia and mortality
The main finding in Paper II is that a large proportion of patients who were delirious when treated for femoral neck fracture, have developed dementia after five years and had a higher mortality rate than those who were not delirious. Furthermore, patients with diabetes, the majority with vascular co-morbidity, were also found to have an increased risk of developing dementia. This association has recently been confirmed by the findings of the Kungsholmen project.112

The finding, that a large proportion of patients with delirium developed dementia, is similar to the results from other recently published studies.78, 81, 82 None of these studies included patients with preoperative and/or postoperative delirium. However in a study, among non-demented patients with a hip fracture, it was shown that patients with delirium on admission to hospital were nearly twice as likely to be cognitively impaired at a two-year follow up.36

The finding, in Paper II, that those who were already delirious on admission or developed postoperative delirium have significantly worse test results concerning recognition and orientation on admission might indicate that preoperative and/or postoperative delirium can sometimes be a marker of undetected or undiagnosed organic brain disorder.
The finding that patients with femoral neck fractures who were delirious postoperatively had an increased risk of developing dementia and a higher mortality rate raises the question of whether postoperative delirium is a marker of undetected dementia and/or whether prevention of postoperative delirium can reduce the risk of developing dementia. The possibility cannot be excluded that postoperative delirium, which seems to be precipitated by potentially brain damaging mechanisms, may contribute to the development of dementia. It has been shown for example that prevention of falls in systolic blood pressure and cerebral hypoxia can prevent patients from becoming delirious postoperatively. It is not known, however, whether these interventions have any impact on the development of dementia. It is important to observe that half the patients with postoperative delirium in Paper II did not develop dementia during the 5-year follow-up period, which confirms that delirium is a reversible condition at least if it is reversed quite quickly.

**Prevention and treatment of delirium**

The aim of Paper III was to investigate the effects of an intervention program on delirium and its associated complications in patients treated for femoral neck fractures. The most important results were the lower incidence and the shorter duration of delirium compared to other previous studies. There were also fewer postoperative complications of other kinds and a larger proportion of patients could return to their previous dwellings and walk independently with or without walking-aids on discharge, after a short total hospitalization time.

Unfortunately it was not possible to perform this intervention study (Paper III) as a randomized controlled trial for organisational reasons in the hospital. The second intervention study (Paper IV), based on the same program, was therefore performed and evaluated as a randomized controlled trial.

A multi-factorial program with systematic assessment, prevention and treatment of complications causing or prolonging delirium such as urinary tract infections, hypoxemia, anaemia, constipation and nutritional complications might have contributed to the shorter duration of delirium in the intervention studies. This in turn probably contributed to the reduced incidence of postoperative complications such as falls and decubital ulcers, which in fact mainly occurred in delirious patients. The lower incidence of such complications might also have contributed to the shorter period of hospitalization. The patients in the intervention groups were cared for by a geriatric team working according to a protocol designed to
prevent, detect and treat postoperative delirium. As seen in Paper IV, it seems that patients with dementia have benefited the most from the intervention program. They probably have the lowest threshold for delirium, but delirium is probably in general often regarded as an unavoidable part of the dementia syndrome. This view, alas, does not encourage any assessment being made of underlying preventable and treatable causes of the delirium or the necessary actions being taken. This neglect gives rise to unnecessary morbidity and incurs costs. In the intervention ward in Paper IV delirium was also regarded as a complication with an underlying cause also in patients with dementia. A more widespread application of basic geriatric principles in surgical wards would no doubt have a great impact from both a humanitarian and an economic point of view.

All femoral neck fracture patients in Paper III were admitted to the geriatric rehabilitation unit from the emergency ward and after the operation the patients returned to the same ward and even to the same room and remained there until discharged from the hospital. All patients in Paper IV were admitted to the orthopaedic ward from the emergency room and were randomized immediately before surgery to ensure the same preoperative treatment. The preoperative care in Paper IV unfortunately was not always carried out according to the protocol, resulting for example in a mean waiting time for operation of more than one day (mean) (24.7±16.6 hours), which might have contributed to the high incidence of preoperative delirium. Some patients were also admitted to other hospital wards preoperatively, due to lack of beds in the orthopaedic department, which might also have prolonged the waiting time for the operation and resulted in treatment not being performed according to the preoperative treatment protocol. The oldest and frailest patients should have surgical priority and this is perhaps easier to implement in a small hospital with a smaller catchment area, as there are, for example, fewer different kinds of operations to compete with, compared to the situation in a university hospital. The hip fracture surgery in a university hospital, as in Paper IV, has to compete with more kinds of surgery than in a smaller hospital, as in Paper III. If the patients with a high risk of delirium are not given priority care the increased risk of complications will increase hospitalization and costs. If the humanitarian and medical arguments do not convince hospital managers, the obvious economical incentives should do so.

When analyzing the nurses’ records in Paper IV it was found that in the control ward, nurses administered more sedative drugs and analgesics when the patients were delirious. Patients inevitably have some degree of pain after an operation, but if the patients were worried,
restless, in excessive pain or delirious the reason for them being in this state was not investigated. Instead delirious patients in the control ward were frequently treated with analgesics and sedative drugs. One side effect of analgesics can be delirium but on the other hand severe pain can also contribute to the development of delirium.\textsuperscript{55} From this perspective nurses and physicians have a responsibility to investigate why the patients are delirious, worried or in pain and assess them for underlying causes, and the physician has the responsibility to prescribe adequate treatment for any underlying causes before relieving the symptoms. Pain after fracture surgery cannot be entirely avoided but since the demented or delirious patient has difficulties communicating, it is important that this problem is properly addressed in acute surgical/orthopaedic wards.

In contrast to the nurses in the control ward the nurses in the intervention ward documented a more systematic assessment and treatment of the underlying causes of delirium. There were only a few patients who received symptomatic treatment with e.g. sedative drugs or analgesics in the intervention ward. Symptomatic treatment may have disguised acute symptoms of disease especially in the control ward and thus led to a delay in the adequate diagnosis and treatment of complications.

It seems that the different assessment and treatment strategies in the two wards probably have contributed to the shorter duration of delirium, fewer complications and shorter hospitalization experienced in the intervention ward.

**Methodological considerations and limitations**

It is difficult to differentiate between dementia and delirium and it is especially difficult in a given situation to decide whether or not a delirious patient has an underlying dementia disorder.\textsuperscript{13, 113} However, the patients in Papers I and II were observed over a period that was long enough to allow for the detection of changes in their mental state and they were tested with the OBS Scale several times. Their prefracture mental state was also assessed by means of interviews with relatives or caregivers and their medical records were studied. Simultaneously with this study, the authors YG, GB and BB were collaborating in another study, using the same OBS Scale. In that study their agreement was above 95\% on all occasions regarding the diagnoses of dementia and delirium.\textsuperscript{20, 101} The three authors had also cooperated in two previous studies were the interrater reliability of each sub-scale of the modified OBS Scale was tested and the agreement then between the assessors (YG, GB and BB) was higher than 90\% in both studies.\textsuperscript{37, 42} In a third study where two of the authors (BB
and YG) cooperated the interrater reliability was above 95% between the assessors.\textsuperscript{38, 43} The diagnoses of delirium and dementia fulfilled the DSM-IV criteria. In Papers I and II, one of the authors (YG) performed the great majority of the ratings with the OBS Scale, and the remainder of the ratings were made by the co-authors GB and BB. The patients were also followed for five years and all survivors were tested using the OBS Scale and MMSE. Some of the delirious patients might have had a “preclinical” Alzheimer disease since they later developed cognitive impairment with social consequences and fulfilled the DSM-IV criteria for dementia. These procedures support the reliability of the delirium and dementia diagnoses, and may also support the high percentage of delirium found in Papers I and II.

The method used in Paper II to detect the development of dementia after surgery for hip fracture might lead to an underestimation of the incidence of dementia, since not all patients were cognitively tested before they died. This is probably especially true of patients with delirium since this group had a higher mortality rate meaning that fewer were assessed before they died and that they also had a shorter observation period in which to develop dementia. However, comprehensive information was found in the medical records and in the nurses’ documentation about the patients’ cognition and behaviour during their hospital or nursing-home care before they died. A large proportion of patients who died showed terminal cognitive decline but cognitive decline during the last month before death was not diagnosed as dementia. Dementia diagnoses in the death certificates in some cases were also verified by post-mortem histopathology of the brain.

In Paper III the patients were systematically assessed using the OBS Scale and observed during a period of time long enough to allow detection of changes in their mental state. Their pre-fracture mental state was also assessed by means of interviews with relatives or caregivers and from their medical records. As the four co-workers who assessed all the patients were employed on the ward, the patients were observed almost every day of the week and in addition other members of the staff were interviewed regarding e.g. diurnal variation.

In Paper III, from a methodological point of view, a randomised experimental study would have been preferable to the use of historical controls. However, the total reorganisation of the hospital made this impossible. Thus, because of the method used, the results should be interpreted with some caution. However, during the intervention study and the three Swedish control studies,\textsuperscript{38, 42, 46} the routines from admission to discharge were carefully observed and no differences between the study periods have been found, other than those described in the
intervention program. It should also be observed that the patients in the various studies are comparable regarding most of the relevant background variables. During all four Swedish studies (present intervention and the three Swedish control studies\textsuperscript{38, 42, 46}) the patients were observed and tested using the same methods and at similar intervals and the diagnosis of delirium was made by the same physician. The caregivers were also interviewed about the patients at similar intervals and to the same extent in all these studies.

Fortunately, the opportunity to evaluate the program in a randomized controlled trial came some years later, which resulted in Paper IV.

In Paper IV the patients were only tested once between days 3-5 postoperatively using the modified OBS Scale but changes in the patient’s mental state were also documented in the nurses’ and medical records. The two nurses employed by the study worked in the intervention and control ward respectively. One registered physiotherapist was employed half-time in the study and half-time on the intervention ward and one occupational therapist was employed full time in the project, for assessing the patients. The patients were thus observed almost every day of the week and other members of the staff were also interviewed regarding e.g. diurnal variation. The terminology used for documenting symptoms of delirium in the records was not always consistent. This varying terminology might have led to both an overdiagnosis and an underdiagnosis of delirium. Previous studies have reported poor documentation and an underdiagnosis of delirium, based on documentation in the records.\textsuperscript{10, 51}

Therefore, if anything, the interpretation of the results is that there is probably some underestimation of the incidence and prevalence of delirium in Paper IV.

To achieve a correct diagnosis of delirium in the two groups a geriatrician, who did not work on any of the wards, and who did not know to which group the patients were randomized, decided whether the patients were delirious or not according to the documented assessments performed by the two study nurses. The two nurses carried out the assessments in patients on the ward where they did not work. Our interpretation therefore is that we have reduced the risk that the effect of the intervention could be due to different assessment routines in the two groups or that the nurses assessed patients in their own department.

Since the staff in the control ward in Paper IV knew about the evaluation of the intervention but did not know the content of this intervention, the effect could not be explained by the common study effect alone. Nor could the effect be explained by increased staffing in the geriatric ward since there was almost no difference in this respect between the wards.
The study in Paper IV showed a higher frequency of delirium in both the intervention (58%) and the control group (76%) compared to the non-randomized intervention study (31%) performed at the Piteä River Valley Hospital. The higher frequency of delirium was perhaps partly due to that the sample in the second intervention study (Paper IV) had a higher mean age (82.2±6.2 vs. 79.7±7.5) and that a larger proportion of the patients had dementia (32% vs. 22%). Another probable explanation for the difference in the occurrence of delirium between the two intervention studies could be that the patients in Paper IV a had longer waiting time for operation than the patients in Paper III (24.7±16.6 hours vs. 17.8±19.7 hours, p=0.014) which together might have contributed to the high proportion of preoperative delirium in Paper IV. A further explanation could be that in Paper IV 56% of the patients had arthroplasty and in Paper III all patients had internal fixation with von Bahr screws which means that a larger proportion of the patients in Paper IV had more extensive operations. Furthermore, we cannot exclude the possibility that the change of ward immediately after the operation for patients in the intervention group may have contributed to the continuing high prevalence of delirium in the intervention ward in Paper IV.

Several studies with a lower incidence of delirium have often excluded patients with dementia or aphasia or patients with signs of cognitive impairment or delirium on admission, which will inevitably result in a lower incidence of delirium.27, 33, 34, 39, 48 The study in Paper IV had several patients who were not included which is a disadvantage. Twenty-one of those suffered their fracture in other hospital wards and was not detected by the study staff until it was too late for randomization. Another 27 non-randomized patients occurred because inclusion routine failed. This could partly be explained by the large number of people working at the Emergency Department and the Orthopaedic Department. It is difficult to organize the whole staff to work for the best interests of the study, since new members of staff are constantly being employed. As mentioned earlier, missing cases seem to have been more often admitted from their own apartment/house and were more likely to be males. They seemed to be healthier and they could have reduced the proportion of delirious patients if they had been included in the study.

When comparing the two interventions (Papers III and IV) it seems that the effects of the intervention program in Paper III were better than those of the intervention program in Paper IV e.g. lower prevalence of delirium (31% vs. 58%), fewer complications (e.g. decubital ulcers 0% vs. 9% and urinary retention 2% vs. 16%) and more patients could return to their
previous independent living on discharge from hospital (89% vs. 75%). This could partly be explained by the fact that the intervention program in Paper III included both postoperative and preoperative care. The intervention program in Paper IV included only postoperative care. Thus the patients in Paper III received all their pre- and postoperative care on the same ward and even in the same room. The intervention patients in Paper IV received their preoperative care at the orthopaedic department and the postoperative care in a geriatric unit specializing in geriatric orthopaedic patients.

**Multi-factorial and multi-professional interventions**

The two intervention studies (Papers III and IV) in this thesis show that postoperative delirium can be successfully prevented and treated resulting in a shorter total period of hospitalization and an improved rehabilitation outcome. Several other intervention studies have also shown that postoperative delirium after hip fracture surgery can be prevented and treated.\(^39, 46, 50, 61\) However, only one of the previous studies has been evaluated as a randomized study and it seems that the present multi-factorial and interdisciplinary intervention programs have better effects than the intervention in that study.\(^61\)

The content of the intervention studies in Papers III and IV was based on a modified theoretical model of possible pathophysiological mechanisms of delirium in patients with hip fracture. The original model was presented in a thesis by Gustafson\(^114\) and has been slightly modified in the present thesis (Figure 3).

The intervention programs have focused as far as possible on all steps in the model:

2. Prevention of hypercortisolism by avoiding stressful situations for the patients and by preventing complications. Creating opportunities for the patients to be orientated as to day, time and person by ensuring the presence of e.g. clocks, calendars, mirrors and good lighting.
3. Breaking the vicious circle of delirium by creating a safe and secure environment and ensuring that the delirious patients can rest e.g. by prescribing sedatives preferable clomethiazol.
4. Prevention, detection and treatment of complications such as hypotension, pain, urinary retention, decubital ulcers, falls, and infections such as urinary tract infection and pneumonia.
5. Avoiding to prescribe drugs with anticholinergic effects.
6. All meals supplied to contain proper nutritional value, individually adjusted for each patient. Nutritional and protein drinks, as a nutritional supplement, supplied to all patients every day.

7. Early mobilization and rehabilitation, which is an important part of preventing complications thus probably leads to a reduction of stress.

This intervention complies with various professions aspects of good care. To comply with all steps in the model the patients needs to be cared for by a multi-professional team.

To be successful, intervention programs seem to have to be multi-factorial and interdisciplinary and include the assessment and treatment of underlying causes as well as the prevention and treatment of factors endangering cerebral metabolism. Excellent nursing care also seems to be a prerequisite for a successful intervention. The present interventions were multi-factorial and also involved the entire staff (RN, LPN, RPT, Reg. OT, Dietician, Social Worker, Geriatrician and Orthopaedic Surgeon), which may explain the positive results.

Successful intervention programs among patients in general internal medicine have also been multi-factorial and interdisciplinary. One such successful intervention study which included patients admitted to general internal medicine was a multi-factorial intervention. It resulted in a reduction of the duration of delirium, length of hospital stay and in-hospital mortality in delirious patients. Another of these successful intervention studies on medical in-patients was a multi-component risk-factor intervention study aimed at preventing the development of delirium in older patients and resulted in a reduction in the number and duration of episodes of delirium.

Interventions including only single measures, such as staff education have not proven effective. Nor have interventions based only on consultations or guidelines had any major impact if they did not involve all the staff and several aspects of caring for the patients. It seems that the most effective interventions have been performed in wards that included staff with geriatric competence which is also supported by the results from Papers III and IV. The most successful intervention programs have included several aspects of good medical and nursing care and the total effect of the multi-factorial intervention program seems to be greater than the sum of the separate parts.
Figure 3. A simplified model for the possible pathophysiology of delirium in old patients. Modified with permission of Gustafson (1991). 114
GENERAL CONCLUSIONS

- Pre- and postoperative delirium is common and seems to be associated with different risk factors. The results from this study stress the importance of identifying the risk factors for delirium and the mechanisms involved in the development of delirium. The variety of factors associated with preoperative and postoperative delirium imply the need for a variety of strategies for prevention and treatment.

- Delirium is associated with the development of dementia and a higher mortality rate. Patients who develop delirium should therefore be assessed for any underlying organic brain disease since new prevention and treatment opportunities for dementia, both vascular and degenerative, are available which might postpone the progression of the disease.

- Postoperative delirium can be successfully prevented and treated by a team applying comprehensive geriatric assessment, management and rehabilitation. A reduced incidence of delirium results in fewer complications and a shorter hospitalization period.

- Successful intervention programs seem to have to be multi-factorial and interdisciplinary and include geriatric competence, assessment and treatment of underlying causes as well as the prevention and treatment of factors endangering the cerebral metabolism. Implementing this inexpensive intervention program will probably have a great humanitarian and economic impact and is probably applicable to surgery on old people in general.

- The high prevalence of delirium in Paper IV (both control and intervention) might indicate that the intervention program in Paper III, which also included preoperative care, might have been even more effective than the postoperative intervention in Paper IV.
Clinical implications and implications for future research

Delirium seems to be one of the most important predictors of outcome for the old patient with a fractured hip. The results from Paper I stress the importance of identifying the risk factors for delirium and the mechanisms involved in the development of delirium. The various factors associated with preoperative and postoperative delirium imply the need to use a variety of strategies for prevention and treatment. As delirium, by definition, has identifiable causes and is reversible, greater efforts should be made in the care, assessment and treatment of these patients.

Postoperative delirium may be an early sign of dementia and/or it may contribute to the development of dementia. Several studies have shown that postoperative delirium can be prevented and treated but whether or not it has any impact on the development of dementia remains unknown. More research in the field is needed. Nevertheless, patients who develop delirium should be assessed for any undetected, underlying organic brain disease since new prevention and treatment opportunities for dementia, both vascular and degenerative, are available which might postpone the progression of the disease.

Today, in industrialized countries most surgical hospital beds are occupied by old people—an increasing trend worldwide. The intervention studies in this thesis show that postoperative delirium can be successfully prevented and treated by a team applying comprehensive geriatric assessment, management and rehabilitation. A reduced incidence of delirium results in fewer complications and shorter hospitalization. Implementing this inexpensive intervention program will probably have a great humanitarian and economic impact and would probably be applicable to surgery on old people in general. Therefore, the organization of surgical wards should be reconsidered and adapted to the needs of the oldest and most frail patients.

However, even if the intervention studies in this thesis show that delirium can be successfully prevented and treated, the prevalence of delirium remains too high. Further research into the evaluation of intervention programs for the prevention and treatment of delirium is necessary e.g. a more efficient prevention of hypoxemia and of hypercortisolism. Perhaps drugs to reduce the oxygen metabolism of the brain and drugs for the treatment of hypercortisolism
may be an option in the future. Research into how to improve prevention of other complication is also needed. More research is also needed concerning the pathophysiology of delirium which in turn is a prerequisite for a more effective pharmacological treatment of delirium.
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