Delirium during Hospitalisation

*Incidence, Risk Factors, Early Signs* and
*Patients' Experiences of Being Delirious*

BY

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Abstract

Delirium is common among old patients admitted to hospital, but is often a neglected problem in patient care. The principal aim of this thesis was to evaluate aspects of delirium in relation to incidence, risk factors, behavioural changes, cognitive function and health-related quality of life (HRQOL). A further aim was to describe patients’ experiences of being delirious. The study was prospective, descriptive and comparative, with repeated measures (six-month follow up). The sample consisted of 225 consecutive patients, aged 65 years or older, who were to be operated on due to hip fracture or hip replacement. Exclusion criteria were serious cognitive disorder or delirium on admission. Data were collected via frequent daily observations, cognitive functioning tests (MMSE), HRQOL questionnaires (SF-36) and interviews. Delirium was assessed according to the DSM-IV criteria. A total of 45/225 became delirious, with an incidence of 24.3% among patients undergoing hip fracture surgery and 11.7% among those with hip replacement surgery. A predictive model for delirium included four factors: impaired hearing, passivity, low cognitive functioning, and waiting more than 18h for hip fracture surgery. Disorientation and urgent calls for attention were the most frequent behavioural changes in the prodromal phase prior to delirium. Delirium in connection with hip fracture revealed deteriorated HRQOL and cognitive functioning when measured at a six-month follow-up. The experience of being delirious was described by the patients as a sudden change of reality. Such an experience gave rise to strong emotional feelings, as did recovery from delirium. Nurses’ observations of behavioural changes in old patients with impaired cognitive function may be the first step in managing and reducing delirium. The predictive model of delirium ought to be tested further before use in clinical practice.

Keywords: delirium, Acute confusional state, hip surgery, hip fracture, replacement surgery, cognitive function, MMSE, Follow-up, health-related quality of life, HRQOL, SF-36

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<tr>
<td>ACS</td>
<td>Acute Confusional State, synonymous with delirium</td>
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<td>DSM-IV</td>
<td>Diagnostic and Statistical Manual of Mental Disorders, ed. 4</td>
</tr>
<tr>
<td>D group</td>
<td>Patients who met delirium criteria, in contrast to the NonD group</td>
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<td>HRQOL</td>
<td>Health-related quality of life</td>
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<td>ICU</td>
<td>Intensive Care Unit</td>
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<td>ICU syndrome</td>
<td>Denomination for “Delirium”, often used at ICU</td>
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<td>MMSE</td>
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Introduction

Delirium/Acute Confusional State (ACS) is a disturbance of consciousness with reduced ability to focus, sustain, or shift attention. Further, there is a change in cognition (e.g. memory impairment, disorientation or perceptual disturbance) that develops over a short period of time and tends to fluctuate during the course of the day \(^1\). Delirium is common among old patients in hospitals \(^2\, \text{and} \,3\) and in various settings in old-age care \(^4\).

Delirium / acute confusional state

The word “confusion” is frequently used in common speech, both by professional caring staff and non-professionals. However, it is seldom defined. It is used synonymously with e.g. disoriented, inability to think clearly and coherently, clouding of consciousness or some degree of mental disorder. Moreover, more than 60 synonyms of “delirium” have been found in the literature \(^5\). It has been suggested that “acute confusional state” (ACS) should be the only accepted synonym for delirium \(^2\,\text{and} \,6\).

The criteria for delirium are presented in the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV, see Box 1) \(^1\). In the 1987 edition of the DSM-III-R \(^7\), however, the criteria for delirium were more specific than those in the fourth edition published in 1994. Lipowski \(^6\) stated in 1992 that there was no consensus on how to define or measure delirium. However, in the past decade, instruments have been developed for measuring delirium. In many studies, delirium has been defined in accordance with the DSM criteria \(^5\,\text{and} \,8-13\).

It is not unusual that old patients develop behavioural changes during their hospital stay and display one or more symptoms of delirium. They seldom meet all the criteria for delirium. That condition is known as subsyndromal delirium \(^14\). In the prodromal phase of delirium, however, these symptoms precede an episode of full-blown DSM-defined delirium. This phase involves alterations in behaviour, affect and sleeping pattern, and symptoms and periods of lucid intervals may fluctuate \(^15\).

It has been shown that delirium may have varying symptoms and time course, and it may not be possible to determine any pattern of delirium characteristics or changes over time \(^16\). The prevalence of individual symptoms of delirium varied greatly in 8 studies reviewed by Meagher &
Trzepacz. For example, the reported frequencies of clinical symptoms for disorientation varied between 43% and 100%, of poor attention 17% and 100%, of memory disorder 64% and 90%, and of language disorder between 41% and 93%.

Recent studies investigating psychomotor subtypes of delirium showed that an average of 16% had no psychomotor disturbance, and the hypo- and hyperactive subtypes represented on average 25% and 28%, respectively. The mixed type (both hypo- and hyperactive) was most common and represented on average 47% of the cases.

Box 1: DSM-IV criteria for delirium

(a) Disturbance of consciousness (i.e. reduced clarity of awareness of the environment) with reduced ability to focus, sustain or shift attention

(b) Change in cognition (such as memory deficit, disorientation or 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 the 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

Incidence, prevalence and occurrence of delirium

The reported incidence and prevalence rates of delirium during hospitalisation ranged from 0% to 85% in a review by Forman. In another review of postoperative delirium, incidence was 0-74%. In medical and surgical general hospital inpatients 10-18% became delirious at some point during their hospital stay. At a general surgery department, the incidence rate was 18% and at an ICU, 70%. At general medical departments the reported incidence rates ranged from 5% to 48%. Furthermore, patients undergoing elective cardiac surgery displayed a delirium incidence of 14% and those undergoing major elective surgery of 11%. 
Several studies concerning delirium among patients undergoing hip surgery have shown an incidence/prevalence rate ranging from 9.5% to 60% depending on whether patients with cognitive impairment were included or not. In some studies, the incidence of delirium was reduced as a result of intervention programmes related to hip surgery or in other care settings. The interventions differed between the studies and concerning hip surgery they included e.g. staff education, active nutrition, co-operation between geriatricians and orthopaedic surgeons, geriatrics consultations, cognitive screening, pain control and consultative service by a delirium resource nurse, oxygen therapy, early surgery, preventing and treating perioperative blood pressure drop, orientation regarding time, place and situation, and continuity of care. In one study, the benefit of intervention among delirious hip surgery patients (consultation by a geriatric psychiatrist and follow-up by a liaison nurse) had minor effects when measured eight weeks after discharge. Intervention studies have also been reviewed. Cole and colleagues stated that intervention studies designed to prevent delirium have methodological problems because of the heterogeneity of the patient populations and interventions. They suggest that preventive intervention trials should be conducted with target populations specified by age, level of cognition, severity of illness, and other risk factors for delirium. It is difficult to evaluate the effects of individual elements of an intervention programme as these elements may vary in relation to each other. To develop effective intervention programmes in the long term, studies of interventions should focus on one variable at a time.

Risk factors associated with delirium

In several studies, a variety of factors have been found to be related to delirium. Individual differences may exist in the susceptibility to delirium, and some patients may become delirious even in the course of a mild infection with fever. Inouye presented a model for delirium according to which patients with high vulnerability (e.g. high age, severe dementia, illness or other predisposing factors) may develop delirium despite a relatively benign insult (e.g. one dose of sleeping drug). Patients with high vulnerability and the precipitating factor of psychoactive drugs were found to have a 56-fold increased probability of delirium. Conversely, patients with low vulnerability may be relatively resistant to developing delirium, requiring multiple harmful insults to do so.

Lipowski identified three classes of risk factors for delirium: predisposing, facilitating and precipitating factors. Three general predisposing factors have been established: 60 years of age or older, brain damage (e.g. cognitive impairment) and chronic brain disease. A uniform
finding is that older patients are at higher risk of postoperative delirium, as are patients with pre-existing cognitive impairment and/or dementia, epilepsy, malignancy, and high systolic blood pressure. It has also been reported that patients undergoing surgery for hip fracture are at high risk of delirium. Further, male sex and the existence of several medical diagnoses have also been reported as predisposing factors for delirium.

Several psychosocial and environmental variables may contribute to or facilitate the appearance of delirium. Psychosocial stress, sleep deprivation, sensory underload or overload and immobilisation may facilitate delirium onset, increase its severity and influence its duration and course. One of the most common causes of delirium was reported to be life changes such as transfer to an unfamiliar environment or death of a spouse. Postoperative sleep satisfaction was also shown to be markedly poor among hip surgery subjects who experienced delirium. Also impaired sight and hearing were associated with delirium. A recent study found that the hospital unit as such (i.e. ICU and presumably long-term care unit), number of room changes, absence of a clock/watch or reading glasses, and physical restraints were significantly related to an increase in delirium severity scores, while noise, lighting level, the presence of a calendar or use of hearing aid did not increase the severity scores.

According to the DSM-IV criteria, delirium is caused by the direct physiological consequences of a general medical condition. In a study where independent precipitating factors for delirium were identified, the relative risk of becoming delirious was found to be 4.4 for patients suffering from malnutrition. The use of a catheter carried a relative risk of 2.4, and, using more than three drugs per day gave a relative risk of 2.9. Fever and hypothermia have been associated with delirium as have electrolyte disturbances, anaemia, perioperative blood pressure drop, hypoxia. The use of psychoactive drugs or other drug reactions, especially anticholinergic drugs have been associated with delirium. Several studies have demonstrated that vascular diseases of the brain, e.g. stroke and transient ischemic attacks (TIA), are precipitating organic factors for the development of delirium. However, a given pathogenic factor need not be sufficient to precipitate delirium. Predisposing and facilitating factors also co-determine onset, severity, and duration. Francis and colleagues classified the possible causes of delirium into eight categories (drug-induced, infection, fluid-electrolyte or metabolic disturbance, intracranial process, low perfusion, alcohol and drug withdrawal, and sensory/environmental causes). It has been suggested that psychosocial factors alone may precipitate delirium. However, Lipowski has stated that it is not clear whether predisposing and
facilitating factors can induce delirium in the absence of precipitating organic factors.

Delirium onset, duration, and outcome

In most cases, delirium occurs between the 1st and 6th day of hospitalisation. The most common time of onset appears to be between 24h and 48h after admission to hospital. In a study at a surgery/orthopaedic department, the highest delirium incidence was reported on the 3rd postoperative day.

There are different opinions about the duration of delirium. Lipowski stated that delirium tends to last weeks rather than days in older people. In a study at a geriatric assessment department, the duration of delirium was 8±9 days, whereas in other studies the duration was shorter. In a study at medical departments, 75% of the delirium episodes lasted less than 24h and the great majority of these recovered before discharge.

Several studies have demonstrated that patients with delirium run a higher risk of dying than do non-delirious. In some studies, however, delirium was not found to be associated with increased mortality after adjustment for confounding variables, such as age, gender, cognitive impairment and comorbidity.

Delirium is also associated with poor recovery. In a study of hospitalised old people, 16% of patients with delirium were later institutionalised, compared with 3% of the non-delirious. However, in a group of patients with delirium on admission, institutionalisation after 3 years was delayed in the intervention group compared with controls. The intervention included systematic support provided by a specialist nurse and one rehabilitation period per year in a rehabilitation centre.

Cognitive function after delirium

Cognitive function has been assessed in connection with delirium onset in several studies, mostly by the Mini-Mental State Examination (MMSE). Few studies have focused on delirium and its relation to cognitive function and HRQOL in a longer perspective. Lipowski stated that delirium may increase the risk of dementia, and there is some evidence that patients who develop postoperative delirium represent a subgroup at risk of prolonged and even permanent cognitive disorder or dementia. In a recent follow-up study, the prevalence of dementia was investigated among non-demented patients operated on for hip fracture 5 years earlier. It was found that 69% of those who became delirious postoperatively had developed dementia, compared with 20% of the non-delirious group. In a 2-year follow-up...
study where cognitive function was assessed by use of a telephone version of the MMSE, the decline was 3.2 points in 11 delirium cases. In 81 controls, however, the MMSE sum score was unchanged. In two studies not focusing on delirium as such, the cognitive function decreased between 1.2 and 1.3 points over 2-3 years in non-demented older people (≥75 years). Izaks studied people aged 85 years and above, and found that the median change in MMSE was -4 points after three years.

Health-related quality of life after delirium

The concept of health related quality of life (HRQOL) concerns function and wellbeing in connection with disease and treatment. A common instrument for measuring HRQOL is the SF-36. Studies examining HRQOL following hip fracture have shown that patients often experience a decrease in HRQOL after fracture repair and healing. In a case-control study of 92 community-dwelling patients, it was found that despite age and gender matching, a group of hip fracture patients scored significantly worse 6-12 months after the surgery than did non-fractured patients in all eight domains of the SF-36. In another study enrolling 32 hip surgery patients, HRQOL was significantly reduced after three months in the domains of physical function (-51%), vitality (-24%) and social function (-26%). In contrast, the HRQOL was almost the same after 6 months as it was pre-fracture in all SF-36 domains but physical role.

The HRQOL outcomes are different for hip fractured patients than for patients undergoing hip arthroplasty, and 6-12 months after surgery, most studies found that patients undergoing hip arthroplasty had improved HRQOL in all domains. A 6-year follow-up study found that a decline in cognitive performance was significantly associated with poor HRQOL ratings.

Patients’ experiences of being delirious

Some studies have investigated patients’ experiences and memories after a transient delirium attack, especially at intensive care units (ICU) where delirium also is common. The state has been named “the ICU syndrome”. Granberg et al interviewed ICU patients about their experiences of being delirious. Patients described their experiences as ‘dreams, crazy dreams, nightmares, stupid fantasies, changes of perspective or illusions’, and although the experiences were unreal they appeared real when they occurred. In a Finnish study, the authors found that patients talked about their anxiety when they were on the “threshold between awareness and unawareness”. The way nurses spoke, touched, gestured and were silently
present was important for the patients’ feelings of security during the delirium. Granberg and colleagues 133 presumed that trust and confidence in nurses or significant others and the feelings of trust in self-control seemed to reduce the risk of delirium.

Fagerberg and Jönhagen 136 found that ‘experiencing threat’ was the key component of the patients’ experiences of delirium along with three other components; ‘being suspicious’, ‘wide-open senses’ and ‘need to escape’. The patients’ experiences were focused on feelings of shame and guilt, humiliation, and fear of recurrence. They also sought reasons for the delirium onset. One case study explored the delirious patient’s behaviour and interaction with nurses during the delirium and found that the nurses and the patient were unable to enter each other’s world 137. The patient was found to communicate about events from his/her life and wanted to get out of bed and be together with the family, whereas the nurses communicated from their medical point of view and wanted to keep the patient in bed. Fawdry 138 also reported on case studies concerning two patients who expressed a fear of having lost their mind while confused, and of becoming senile. One of them described the delirium experience as ‘being outside looking in’, and said that it was impossible to understand or respond to questions. The fear seemed to increase when questions were put too rapidly and when nursing personnel talked about the patient but not to her.

Caring for patients with delirium

Patients’ experiences during the delirium episode are often associated with intense fear 133, but may still go undetected by nurses and physicians 66,131,139,149. One explanation may be that nurses fail to recognise delirium in patients with dementia 150. Another explanation may be that patients with delirium who are agitated are easy to detect, but in the hypoactive type of delirium the patient is often somnolent 21, lethargic and displays mood instability 20 and delirium is therefore hard to detect. The hyperactive variant of delirium appears to be documented more often 151, and environmental strategies are significantly more often used in the management of patients with hyperactive delirium 152.

Patients with delirium need the attention of nurses and should be subjected to adequate nursing interventions. In one study, patients with delirium seemed to be lonely because they had fewer interactions with significant others than had lucid patients 29. During the delirium phase, patients are at higher risk of falling out of bed 22, and they have more problems than non-confused patients with mobility, dressing, hygiene,
physical and psychological safety, communication, work, recreation, and learning. Further, patients with delirium recover poorly, and risk prolonged or permanent cognitive disorder.

Early recognition of delirium is essential to be able to give adequate medical treatment and nursing care. Inouye suggests that national strategies should be developed to improve the recognition of delirium and the awareness of its clinical implications. There is no consensus on the appropriate treatment of delirium, although the American Psychiatric Association has drawn up a treatment guideline that merits consideration. Gustafson and colleagues have also presented a guideline for the treatment of delirium.

Despite the vast number of studies on delirium, there are still some knowledge gaps, especially concerning early detection of delirium, and predictive symptoms and signs preceding the delirium onset. The methods for studying these are time-consuming and valid instruments are rare.

Screening study

Before starting the main study, a screening was conducted to find settings with a high incidence of delirium and to test the usability of protocols to be used. The screening study was conducted in April-May 1994 at departments of general and orthopaedic surgery, general medicine and infectious diseases at a county hospital in Sweden. It was a prospective cross-sectional study of a consecutive sample of a total of 448 patients admitted to 15 wards (30 patients per ward). Nurses in charge collected the data on 11 of the wards and the author did so on the remaining 4 wards.

A total of 210 patients from general medicine, 105 from general surgery, 75 from orthopaedic surgery, and 58 from the department of infectious diseases were included in the screening. The mean age was 63±19 years; 48% were women. The patients were monitored until discharge and the nurses contacted the author when a delirious state was suspected. The author confirmed the delirium diagnosis within an hour by use of DSM-III criteria and the Mini-Mental State Examination (MMSE).

The incidence of delirium was 2.2% (10/448) and the duration was 1-4 days. The average age was 85±5 years in patients who met the delirium criteria. Three of the 10 patients were still delirious at discharge and 1 died during hospitalisation. Four of 210 (1.9%) of those who were cared for in general medicine became delirious, and 6 of 75 (8%) at the orthopaedic department. At the orthopaedic department, 5 of the 6 patients with delirium underwent hip-related surgery, and the incidence of delirium was 21% in the oldest patients (≥80 years) who underwent hip surgery.
Since these results indicated that old patients admitted to hospital for hip surgery were at highest risk of delirium, the data collection in the present thesis was conducted in that patient group.
Aims

The aims of the thesis were:

- to investigate the incidence and duration of delirium in connection with hip surgery and to identify possible risk factors for delirium (I)
- to delineate behavioural changes from admission to hospital, during the prodromal phase of delirium, up to delirium onset (II)
- to describe hip surgery patients’ experiences of being delirious (III)
- to compare changes in cognitive function and health-related quality of life (HRQOL) six months after hip surgery in patients who had become delirious in connection with surgery with those who had not (IV)
Patients and methods

Design and setting
The main study (papers I-III) was prospective and included observations and interviews. It was carried out at the department of orthopaedic surgery at a county hospital in Sweden. The data were collected over more than six months in two separate periods (spring 1996 and spring 1997). A follow-up study (paper IV) was performed six months after discharge from hospital. It was conducted mostly in the patients’ homes, but also in community settings where some of the patients lived. The design was descriptive and comparative, with repeated measures.

Patients

Paper I
During six months (18th February to 31st May 1996 and 9th January to 9th April 1997), 341 hip surgery patients aged ≥65 years were admitted to the department of orthopaedic surgery. Of those, 37 patients did not want to take part in the study and 71 were excluded (62 were excluded because they were already delirious on admission according to the DSM-IV criteria or scored less than 11 on the MMSE. Seven patients were unable to communicate because of aphasia or deafness and 2 were too ill to participate). Eight patients were missed. Thus, a total of 225 patients were included (Figure 1). Of those, 85 were operated on because of cervical hip fracture, 64 because of trochanteric hip fracture, and 76 underwent hip replacement surgery. The mean age was 80±8 years; 67% were women.

Paper II
To be able to observe behavioural changes in the prodromal phase of delirium, it was necessary to make as frequent observations as possible among the oldest patients as they were at highest risk of delirium. Of the
225 patients who participated in the main study, 111 were 80 years or older and destined for this part of the study. Eight of the 111 patients had insufficient observation data. The remaining 103 patients were included in this part of the study (Figure 1). The mean age was 87±4 years; 70% were women.

Paper III
Forty-five of the 225 patients participating in the main study became delirious during hospital stay (I). After recovering from delirium (n=37), the patients were asked whether they had any memories from the delirium episode. Most patients (n=19) did not remember anything apart from short fragments, or did not seem to understand what the data collector was talking about. Excluded from the interviews were: 7, who were hastily discharged with no opportunity for interviewing, and 2 who declined the interview. Nine patients, however, said that they remembered and were interviewed about their experiences of being delirious, but only 6 of them were able to contribute remembered experiences. Furthermore, 6 out of 24 patients with attacks of nightly confusion were interviewed to obtain a greater number of interviews (Figure 1). The mean age of the interviewed patients was 80±6 years; 75% were women.

Paper IV
In the main study, 42 of the 45 patients who became delirious during their hospital stay were 75 years or older. Thus, the follow-up described in paper IV was carried out among all 160 patients who belonged to that age group. The inclusion criterion in paper IV was that patients had performed the MMSE twice, on admission and on discharge (to find the “best” cognitive function during hospital stay, as the MMSE performance could be impaired because of medication and pain). Of the 160 patients, 147 were eligible for the follow-up study. At the time of the follow-up, 11 had died, and 21 declined to participate (Figure 1). Thus, paper IV reports findings for the remaining 115 patients. Their mean age was 83±6 years; 70% were women. This paper also reports changes in HRQOL in the 92 patients who were able to complete the SF-36 questionnaire twice during the hospital stay and at follow-up.
Patients aged ≥ 65 years undergoing hip surgery
n=341

71 excluded
37 declined, 8 missed

Paper I
n = 225

Patients aged ≥ 80
n = 111

8 insufficient data

Patients aged 75-79
n = 49

11 died
21 declined
13 insufficient data

Paper II
n = 103

Patients aged ≥ 65-74
n = 65

Paper IV
n = 115

Paper III
Interviews with; 9 pat. after delirium
6 patients after nightly confusion

Figure 1: Patients included in papers I-IV
Measurements

Both qualitative (III) and quantitative (I-II, IV) methods were used in. Table 1 gives an overview of the instruments and protocols used for data collection. Each instrument and protocol is described below.

Table 1: Instruments and protocols used for data collection

<table>
<thead>
<tr>
<th>Instrument /Protocol</th>
<th>Admission</th>
<th>Hospital stay</th>
<th>Discharge</th>
<th>Follow-up</th>
<th>Paper</th>
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<td>Interview guide about delirium experiences</td>
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<td>III</td>
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DM-IV criteria for delirium

Onset of delirium was determined by use of the DSM-IV criteria for delirium related to a general medical condition 1. Patients were considered to have experienced delirium when DSM-IV criteria a-d were fulfilled (see box 1, p. 2). The fulfilment of the criteria was defined as follows:
**Criterion a** was manifested by reduced ability to engage the patient in social conversation, e.g. if the questions had to be repeated because the patient’s attention wandered, or if the patient was easily distracted by irrelevant stimuli.

**Criterion b** was fulfilled if the patient had memory impairment (i.e. could not give an account of when or what the latest meal consisted of, or some other significant occurrences for the patient in recent hours) was disoriented with respect to time, place or person, perceptual disturbances (misinterpretations, illusions or hallucinations) or language disturbances (i.e. impaired ability to name objects, or irrelevant or incoherent speech).

**Criterion c** was fulfilled as the patient was not delirious on admission.

**Criterion d** was considered fulfilled because the hip fracture patients were admitted to hospital and were subjected to surgery and/or had undergone surgery.

**Mini Mental State Examination (MMSE)**
Cognitive function was measured by the Mini-Mental State Examination (MMSE)\(^{117}\). The MMSE includes 11 items that evaluate general domains of cognitive functioning; orientation (in time and space, 10 points), registration (of three words, 3 points), attention and calculation (spelling a word backwards, 5 points), recall (remembering the three words, 3 points) and language (to name a pencil and a watch, to repeat a sentence, to understand and effect an oral 3-step instruction and a written instruction, to write a sentence, and, to draw a geometric figure; in all, 9 points). The maximum score is 30 points, with mild cognitive decline present at scores from 21 to 24, moderate from 11 to 20, and severe cognitive decline from 0 to 10 points\(^ {13}\).

**SF-36**
The Swedish version of the SF-36 questionnaire\(^ {122}\)\(^ {157}\)\(^ {158}\) was used to determine the patients’ health-related quality of life (HRQOL). SF-36 is a standardised health status questionnaire composed of 36 items which measures the following eight domains of HRQOL: physical functioning (PF), limitations in usual role activities due to physical health problems (RP), bodily pain (BP), general health perceptions (GH), vitality (VT), social functioning (SF), limitations in usual role activities because of emotional problems (RE), and mental health (MH). A high score indicates a positive health status. The lowest score is 0 and the highest 100 in each health domain. The SF-36 has been validated for Swedish conditions\(^ {122}\). The data were
analysed according to the SF-36 instruction manual, where age-matched comparative data are available 122.

Structured protocol A
The structured protocol A was based on findings from previous research on factors that predispose to, facilitate and precipitate delirium 2. It included data on patient’s age, sex, cohabitation, sight and hearing, current medication, the presence of chronic diseases, and previous documentation of delirium or dementia. Furthermore, data about X-ray examinations, surgery or other events, such as catheterisation, were included. The type of room (number of beds), the frequency of visitors and length of the hospital stay were also registered. The protocol also included 15 items (yes/no) on the patient’s situation on the ward compared with patients in general. The items covered sleep and rest, loneliness, passivity, restlessness, well-being, aggressiveness, interaction with other patients or visitors, and activities/occupation during hospitalisation.

In a pre-test before the data collection, eight nurses used the structured protocol to evaluate ten patients who had recently been discharged from the ward. There was a high degree of agreement in the assessment of the patients’ situation on the ward. Further, after the data collection in the screening study that preceded the present thesis 156, interrater reliability based on nurses’ assessments was analysed. The agreement between the nurses involved in the assessments varied between 94% and 99.7% (mean value 97.9%).

Delirium protocol B
A special protocol was used to record data at the time of delirium onset, e.g. time for onset, duration, body temperature, pulse, blood pressure, and type of room (number of beds). Also recorded were change of location at the ward, medication changes and alterations of physical health during the 24 hours prior to delirium onset, and notes were made concerning whether the patient remembered the delirium episode after recurrence or not.

Nightly confusion protocol C
Protocol C was designed to provide knowledge about cases of nightly delirium or nightly confusion. If the patients had such symptoms, the nurses in charge were asked to fill in protocol C, which included the same data about the delirium criteria as in the observation protocol D (yes/no). It also included notes about analgesic and sedative medication given during the night.
Observation protocol D

An observation protocol with dichotomous variables (present or absent) was constructed to register the patient’s behaviour, activity, mind and mood at the moment the observation was made. Observation protocol D comprised items on the patient’s state of mind, activity and behaviour, e.g. visits, conversation, call for help, anxiety, irritation, pain, smiling, engagement, passivity and activity. During the whole data collection period, the interrater reliability of the observation protocol was continuously tested (40 times in all) with a variation in percentage agreement from 78% to 100% (mean value agreement = 96%).

Daily field notes

In the daily field notes, the data collectors’ impressions of “the patient’s day” were written down and categorised as behaviour, activity, alertness and, in particular, events that were unusual for the patient group. The notes were written down during the entire hospital stay and these notes were also used when the structured protocol A (on the patient’s situation on the ward) was filled in.

Interview guide

After recovering from delirium, the patients who said they remembered the delirium onset were interviewed to acquire knowledge about their experiences and reflections on being delirious. An interview guide was constructed including questions on what the patients remembered about the delirium episode, their feelings and thoughts during and after delirium, and how they experienced the nurses’ attention and care during that period. The opening question was “Please, tell me what you remember about the delirium episode”.

Procedure

Main study (papers I-III)

In the main study, the author and three specially trained registered nurses collected the data. During daytime, the patients were recruited at the emergency department. Patients who were admitted to the emergency department at night were enrolled the next morning. After informed consent, the MMSE and the DSM-IV criteria for delirium were used to confirm the absence of delirium and severe cognitive decline (MMSE <11 points). The
patients received the SF-36 questionnaire on admission and were instructed to complete it during their hospital stay.

Observations of delirium were made daily, from admission to the ward to discharge every second to fourth hour from 8 a.m. to 9 p.m., 5 days a week and during Saturdays and Sundays from 8 a.m. to 5 p.m. (with some exceptions). However, it was not possible to make these observations during the first postoperative hours at the intensive care unit. At all observations, the DSM-IV criteria for delirium were used and notes were made in the “Daily field notes”. For the oldest patients (80 years or older), the Observation protocol D was also filled in during the observations from admission to hospital and up to two days postoperatively. In those patients who developed delirium, the observations continued through the whole delirium period. At delirium onset, the MMSE was performed, and the Delirium protocol B was completed. If the patients had nightly confusions, the nurses in charge had been asked to fill in protocol C.

When the patients recovered from delirium, they were asked if they remembered the delirium period. The patients who did so were asked to participate in an interview and were requested to choose the place where the interview should take place. Mostly, they preferred to stay in their rooms. Two of the patients were interviewed in their own homes. The author made all interviews, each of which lasted 10-30 minutes. The interview was performed as a conversation with the patient and all interviews started with the same opening question: “Please, tell me what you remember about the delirium episode”. The interviewer listened actively and used probing questions when necessary. The interviews were tape-recorded and transcribed verbatim before analysis.

At discharge, the MMSE was performed again, and the part of the Structured protocol A dealing with the patients’ situation on the ward was filled in. To confirm these assessments, patients were asked for their own opinion about the hospital stay.

Follow-up (paper IV)

Six months after discharge, all patients aged 75 or more were contacted and invited to participate in the follow-up. At follow-up, the MMSE was performed and the SF-36 questionnaire was filled in. A structured interview about current health, social situation and rehabilitation time was also carried out, but that part is not presented in this thesis. The follow-up was carried out in the patients’ homes and the entire visit lasted between 45 and 75 minutes.
Quantitative data analyses

Besides descriptive statistics, the chi square ($\chi^2$) test was used for group comparisons of nominal data, the unpaired t-test was used for comparisons between independent groups (I, II, IV); and the paired t-test for comparisons between dependent groups (IV). Pearson’s correlation coefficient was used in paper IV. In small groups and in variables with skewed distribution, non-parametric statistics were used (Mann Whitney U test and Wilcoxon signed rank test).

Additional analyses of risk factors for delirium were done using multiple logistic regression analysis. These are presented in the summary section of this thesis. Independent variables for these analyses were selected by identifying significant variables (chi-square tests) between the dependent variable and each possible risk factor 159.

StatView 5.0 for Macintosh was used for all statistical calculations. P values ≤ 0.05 were considered significant in all papers.

In order to control for confounding factors, a matched control group was used. The group was selected from the 180 non-delirium patients matched for age, MMSE score, type of hip surgery and gender (I).

In the follow-up (IV), the MMSE score at follow-up was compared with the highest score in hospital. Each individual’s highest MMSE score was chosen because pain and analgesics may have influenced the MMSE scoring during the hospital stay.

The SF-36 norms for the general Swedish population aged ≥ 75 years, elaborated and described by Sullivan and colleagues 122, were used to provide comparative data (IV).

Qualitative data analysis

Experiences of delirium (III) were analysed with qualitative content analysis 160,161. Further, a metaphor based on the categories from the content analysis was used to make the findings easier to understand. Metaphors have been described as being richer than a simple description of the collected interview data and may help the reader to see the pattern of the findings162.

The tape-recorded interviews were transcribed verbatim as carefully as possible, with repetitions, hesitations and pausing. The quotations presented in paper IV were sometimes reworded for readability, but their meaning not altered 163.

The data were analysed in four steps by two researchers. First, the texts were read through several times. During that reading, notes were made in the margin (single words, short phrases). In the second step, the words and phrases were grouped together to form preliminary categories. In the third step, each of these categories was allocated a colour, which was used when
marking up the transcripts. This way the entire transcripts were divided into categories. The same colours were then put together in new documents. During the fourth step, each category was divided into subcategories. Steps 2, 3, and 4 were repeated several times to arrive at a final categorisation that both researchers could agree upon. During these repeated analyses, the categories were sorted into three main categories, the pattern which yielded the metaphor.

Ethical considerations

The Research Ethics Committee at the Faculty of Medicine in Uppsala University approved the study 1995 (Dnr: 313/95).

In the main study, the author and three registered nurses collected the data. The author alone collected the data at follow-up. All patients participated after oral and written informed consent and in consultation with relatives if these were present at the emergency department. Patients with severe cognitive decline (MMSE < 11) were not included. The patients were also informed of the possibility to withdraw at any time.

The author performed the interviews concerning the delirium experiences (III). When the interview was completed and the tape recorder was turned off, the conversation went on until the patients seemed to be satisfied and became composed.

When conducting research in patients with cognitive disorder or dementia it is necessary to be aware of that some of these patients are not able to give informed consent. It can be discussed whether the patients with moderate cognitive decline to the fully understood the effect of participation in the main-study. However, the general impression is that the patients seemed to appreciate the frequent visits and the small talk with the data collectors during the observations.
Results

Incidences and duration of delirium (I, IV)

From now on, patients will be designated as belonging to the “D” group if they met the delirium criteria during the hospital stay and “NonD” if they did not.

The overall incidence of delirium was 20% among the 225 patients undergoing hip-related surgery. The higher the age, the higher the incidence of delirium (Table 2). This was also true of lower cognitive functioning, as the incidence was 8% in hip-fractured patients with normal MMSE scoring and 54% among those with moderate cognitive decline. The incidence of delirium was significantly higher in hip-fractured patients compared with those who underwent hip replacement surgery (24.3% vs. 11.7%; $\chi^2=4.30$; df=1; $p=.04$). In the hip-fractured patients the incidence of delirium was 21.4% among those with cervical hip fracture and 28.1% among those with trochanteric hip fracture (I).

All but eight patients in the D group met the delirium criteria postoperatively (mean 24h± 21h after surgery). During the entire period of hospitalisation, 79% of D patients experienced short nightly confusions.

Table 2: Incidence of delirium in different age groups (n=225)

<table>
<thead>
<tr>
<th>Age group</th>
<th>Total (n)</th>
<th>Delirious (n)</th>
<th>Incidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>65 – 69</td>
<td>30</td>
<td>1</td>
<td>3%</td>
</tr>
<tr>
<td>70 – 74</td>
<td>35</td>
<td>2</td>
<td>6%</td>
</tr>
<tr>
<td>75 – 79</td>
<td>49</td>
<td>6</td>
<td>12%</td>
</tr>
<tr>
<td>80 – 84</td>
<td>48</td>
<td>11</td>
<td>23%</td>
</tr>
<tr>
<td>85 – 89</td>
<td>30</td>
<td>10</td>
<td>33%</td>
</tr>
<tr>
<td>90 – 94</td>
<td>28</td>
<td>12</td>
<td>43%</td>
</tr>
<tr>
<td>≥95</td>
<td>5</td>
<td>3</td>
<td>60%</td>
</tr>
</tbody>
</table>
The duration of delirium was less than 1 day in 18 patients, 1-2 days in 10 and more than 2 days in a further 9 patients. Eight patients (18%) were still delirious at the time of discharge. The length of hospital stay among delirious hip surgery patients did not differ significantly from those in the NonD group (7.6±5.4 days versus 6.7±3.8 days), but they were discharged to rehabilitation units to a greater extent (73.3% versus 51.6%; χ²=6.01; df=1; p=.02) (I).

At the time of the 6-month follow-up among patients aged 75 years or older, 5/39 (12.8%) in the D group and 6/108 (5.6%) in the NonD groups had died. This difference was not significant (IV).

Risk factors for delirium (I)
The 45 patients in the D group were significantly older than the 180 in the NonD group (85±7 years vs. 78±7 years old, respectively; t=5.53; df=223; p=.0001). Sixty-nine percent in the D group were women as were 67% in the NonD group. There were significant differences between the two groups in all variables examined concerning risk factors during the hospital stay (Table 3).

Delirium was more common in patients with hip fracture compared with patients undergoing hip-replacement surgery. Delirium also occurred more often in older patients and patients with lower MMSE scores. To control for these confounding variables, a control group (n=45) was selected from the 180 NonD patients matched for age, MMSE, sex and reason for surgery. The factors significantly related to delirium were associated with poor communication and social isolation, e.g. impaired hearing and passivity. Further, the D group was more often admitted from community elderly care (Table 4).

Patients who subsequently became delirious interacted poorly with others during hospitalisation. During the observations, 15 out of 32 D patients did not speak to anybody but the data collectors before the onset of delirium. All spoken interaction with the caring staff was related to receiving assistance, e.g. with washing, eating or visiting the toilet. The speaking tended to be “necessary talk” about the current action (i.e. “take it easy” and “it hurts”, a short reply “yes/no” to a question or “thanks for the help”).

In order to understand the relative impact of different risk factors for delirium, multiple logistic regression analysis was performed, using the possible risk factors as independent variables (Table 5). The analysis showed that four factors were significantly related to onset of delirium: (1) impaired hearing (OR 4.09), (2) waiting for surgery≥18 hours (OR 3.63), (3) passivity (OR 2.75), and (4) MMSE score (OR 0.82). The MMSE score has a negative coefficient. Therefore the odds ratio here means that for each point dropped
on the MMSE, the risk for delirium increased by 22% (1/0.82=1.22) (Table 5).

### Table 3: Possible risk factors in 45 patients who developed delirium during hospital stay and 180 patients who did not

<table>
<thead>
<tr>
<th></th>
<th>D patients</th>
<th>NonD patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Admitted from home for the aged or nursing homes</td>
<td>18 (40) ****</td>
<td>16 (9)</td>
</tr>
<tr>
<td>MMSE score on admission ± SD</td>
<td>20.7 ±5.2 ****</td>
<td>26.1 ± 3.7</td>
</tr>
<tr>
<td>Age ± SD</td>
<td>85.4 ± 7.2 ****</td>
<td>78.3 ± 7.8</td>
</tr>
<tr>
<td>Cerebrovascular /brain disease</td>
<td>9 (20) ***</td>
<td>6 (3)</td>
</tr>
<tr>
<td>Psychopharmacological drugs on admission</td>
<td>13 (29%) **</td>
<td>22 (12)</td>
</tr>
<tr>
<td>Surgery ≥18 h. after admission to emergency unit</td>
<td>21 (54) ***</td>
<td>26 (24)</td>
</tr>
<tr>
<td>Impaired hearing</td>
<td>32 (71) ****</td>
<td>46 (26)</td>
</tr>
<tr>
<td>Impaired sight</td>
<td>19 (42) ****</td>
<td>26 (14)</td>
</tr>
<tr>
<td>Slept often in daytime</td>
<td>13 (30) **</td>
<td>17 (10)</td>
</tr>
<tr>
<td>More passive</td>
<td>19 (44) ****</td>
<td>18 (10)</td>
</tr>
<tr>
<td>Less talkative</td>
<td>25 (58) ****</td>
<td>34 (20)</td>
</tr>
<tr>
<td>Not interacting with other patients</td>
<td>31 (72) ****</td>
<td>49 (30)</td>
</tr>
<tr>
<td>Reported to disturb other patients</td>
<td>6 (14) ****</td>
<td>1 (0.6)</td>
</tr>
<tr>
<td>Not reading papers /books</td>
<td>35 (81) ****</td>
<td>50 (29)</td>
</tr>
<tr>
<td>Not occupied at the ward</td>
<td>38 (88) ****</td>
<td>77 (45)</td>
</tr>
</tbody>
</table>

n.s.= non significant;  * p<.05;  ** p<.01;  *** p<.001;  **** p<.0001

### Table 4: Risk factors for delirium in 45 patients who developed delirium during hospital stay and 45 matched controls

<table>
<thead>
<tr>
<th></th>
<th>D group</th>
<th>NonD</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td>Impaired hearing</td>
<td>32 (71)</td>
<td>18 (40)</td>
<td>$\chi^2=7.6; \text{df}=1; p&lt;.01$</td>
</tr>
<tr>
<td>Admitted from home for the aged or nursing homes</td>
<td>18 (40)</td>
<td>8 (18)</td>
<td>$\chi^2=4.4; \text{df}=1; p&lt;.05$</td>
</tr>
<tr>
<td>Not interacting with other patients</td>
<td>31 (72)</td>
<td>18 (46)</td>
<td>$\chi^2=4.7; \text{df}=1; p&lt;.05$</td>
</tr>
<tr>
<td>Not reading papers or books</td>
<td>35 (81)</td>
<td>24 (59)</td>
<td>$\chi^2=4.2; \text{df}=1; p&lt;.05$</td>
</tr>
<tr>
<td>Passive behaviour</td>
<td>19 (44)</td>
<td>10 (24)</td>
<td>$\chi^2=3.9; \text{df}=1; p&lt;.05$</td>
</tr>
<tr>
<td>Reported to disturb other patients</td>
<td>6 (14)</td>
<td>0 (0)</td>
<td></td>
</tr>
</tbody>
</table>
Table 5: Logistic regression indicating factors significantly related to onset of delirium

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>P value</th>
<th>Odds ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impaired hearing</td>
<td>1.41</td>
<td>.006</td>
<td>4.09</td>
<td>1.50 to 11.17</td>
</tr>
<tr>
<td>Surgery ≥18h after admission to emergency unit</td>
<td>1.29</td>
<td>.011</td>
<td>3.63</td>
<td>1.35 to 9.73</td>
</tr>
<tr>
<td>Passivity</td>
<td>1.01</td>
<td>.056</td>
<td>2.75</td>
<td>0.97 to 7.75</td>
</tr>
<tr>
<td>MMSE</td>
<td>-0.20</td>
<td>.0004</td>
<td>0.82</td>
<td>0.74 to 0.92</td>
</tr>
</tbody>
</table>

Model $\chi^2 = 54.31; df = 1; p < .0001$

Behavioural changes before delirium onset (II)

One hundred and three patients who were 80 years and older were included in this part of the study; 32 of them became delirious during the hospital stay and 71 did not. A total of 55 patients experienced episodes of behavioural changes during the study period. Of these, 21 subsequently became delirious (D group), and the remaining 34 belonged to the NonD group. In the D group, 66% of the patients had behavioural changes before delirium onset. In the NonD group this figure was 48% (n.s.). The mean age in the D group was 88.6±5 years and in the NonD group 86.8±4 years. Below, the D and NonD groups are compared with regard to behavioural changes.

Anxiety was the most frequent behavioural change in both groups. Almost half of the D group became disoriented, compared with 12% of the NonD group ($\chi^2=7.0; df=1; p=0.008$). Although not frequent and mostly not significant, increased psychomotor activity, urgent calls for attention ($\chi^2=3.9; df=1; p=0.05$), perceptual disturbance, and reduced attention tended to be more frequently represented in the D group. Decreased psychomotor activity, memory impairment, incoherent speech and a lowered level of consciousness were almost as frequent in both groups (Figure 2). In the D group, anxiety, disorientation, decreased and increased psychomotor activity were common during the final six hours before delirium onset (Figure 3).
Figure 2: Behavioural changes during hospital stay in the D group (n=21) before delirium onset and in the NonD group (n=34) up to 48 hours postoperatively.

Figure 3: Number of patients with behavioural changes ≤ 6h before delirium onset (n=21)
Experiences of being delirious (III)

Most patients with transient delirium said that they did not remember anything about the delirium episode or seemed not to understand the questions about it. Fifteen patients reported that they had some memories of the delirium and were interviewed about their experiences. Although they seemed to remember the delirium occasion when they were asked about it, one patient denied having been delirious when she was interviewed, and one did not remember anything about the episode although the interviewer confronted the patient with events that had actually happened during the delirium. A third patient talked about the situation when she had fallen and fractured her hip, but seemed not to remember anything else. Therefore, the findings below were based on interviews with 12 of the 15 patients.

The qualitative analysis yielded three main categories: entry into delirium, experiences during delirium and exit from delirium. These and the subcategories are presented in Table 6.

The entry into delirium was experienced as a sudden change of reality, in which the environment was completely transformed and the nurses became total strangers. In some cases, the entry into delirium could be associated with basic unfulfilled physiological needs, like freezing or thirst.

The experiences during delirium were described as dramatic scenes with terrifying sights that gave rise to strong feelings of fear, panic and anger. One patient saw rats coming out of the ventilator, and in the neckband of the overalls hanging on the wall she saw mummified heads stretching out. There were fire and floods. Further, the experiences were characterised by opposite pairs. They took place in the hospital but at the same time somewhere else; they were both real and unreal; it was like dreaming but still being awake.

The exit from the delirium was associated with disparate feelings. There were feelings of fear, dissociation, and remorse but also of relief. The feeling of ‘dreaming’ could suddenly be broken when someone interrupted it and entered the room. Almost all patients said that they thought about the delirium event after they had recovered. Some patients expressed the fear of becoming senile or mad. The delirium could also be used as a learning occasion that prepared the patients to handle the situation if they became delirious again. The interview was also appreciated because it gave them the opportunity to talk about the delirium.

The main categories of the delirium experience could be illustrated with a metaphor. It was like a journey through day and night, from twilight and midnight til daybreak and daylight, where daylight might symbolise reality. Thus, in the twilight the delirium onset was noticed as a sudden change of
reality. In the midnight phase, the daylight was missing and the delirium patients had lost touch with reality; they were elsewhere, in another place and in another time. But just as the night can be starry and moonlit, fragments of their reality and normality could appear through the delirium experiences. At daybreak, when the daylight returned, the patients noticed that they had recovered from the delirium. The daylight symbolises how the patients reflect on and cope with the delirium episode.

Table 6: Experiences of being delirious in 12 patients – main categories, categories and subcategories

<table>
<thead>
<tr>
<th>Main categories</th>
<th>Categories</th>
<th>Subcategories</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entry into delirium</td>
<td>Sudden change of reality</td>
<td>Preceding unfulfilled need</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sudden change of reality</td>
</tr>
<tr>
<td>Experiences during</td>
<td>Contradictions</td>
<td>Real – unreal</td>
</tr>
<tr>
<td>delirium</td>
<td></td>
<td>Awake – dreaming</td>
</tr>
<tr>
<td></td>
<td></td>
<td>In hospital – elsewhere</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Frightening – pleasurable</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Present – past</td>
</tr>
<tr>
<td>Dramatic scenes</td>
<td>Life-threatening or death</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Fire or flood</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Shut in and impossible to escape</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Flight</td>
</tr>
<tr>
<td>Strong emotional</td>
<td>Anger</td>
<td></td>
</tr>
<tr>
<td>feelings</td>
<td>Fear</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Panic</td>
<td></td>
</tr>
<tr>
<td>Difficulties in</td>
<td>Heard but did not understand</td>
<td></td>
</tr>
<tr>
<td>communicating</td>
<td>Spoke but was not listened</td>
<td></td>
</tr>
<tr>
<td></td>
<td>to</td>
<td></td>
</tr>
<tr>
<td>Exit from delirium</td>
<td>Suddenly back to reality</td>
<td></td>
</tr>
<tr>
<td>Feelings after</td>
<td>Fear</td>
<td></td>
</tr>
<tr>
<td>delirium</td>
<td>Relief</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Discomfort</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Remorse</td>
<td></td>
</tr>
<tr>
<td>Integration of</td>
<td>Meaning and importance</td>
<td></td>
</tr>
<tr>
<td>delirium</td>
<td>Ignorance</td>
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<td>Learning occasion</td>
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<td>Useful experience</td>
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Cognitive function in relation to delirium (IV)

At the follow-up, the mean ages for the D and NonD groups were 85±5 and 83±6 years, respectively; 69% and 70%, respectively, were women. The patients who had been delirious scored significantly lower than did nonD patients on the MMSE both on admission (20.7 points vs. 26.1; p=.0001) and discharge (20.4 vs. 25.8; p=.0001).

The MMSE score at follow-up was compared with the highest individual score in hospital. The total MMSE decline in the D group at follow-up was 2.6 points (Z=2.3, p=.03) and 0.9 in the NonD group (Z=3.2, p=.002). The difference between the groups (1.7 p) was not significant (Z=-0.9, p=.36). The MMSE decline from hospital stay to follow-up tended to be independent of the reason for surgery. For patients who underwent hip replacement surgery (n=26) the MMSE scoring decreased by 1.3 points (Z=1.3, p=.02) and the hip-fractured patients (n=89) by 1.4 points (Z=3.7; p=.001).

From hospital stay to follow-up, two patients lowered their MMSE sum score substantially. Both belonged to the D group and scored 25 and 26, respectively, on the MMSE during the hospital stay, but scored 5 and 3 points, respectively, at follow-up. If these two patients had been excluded from the analysis above, the difference between the two groups would have decreased from 1.7 points (2.6 p minus 0.9 p) to 0.5 points (1.4 p minus 0.9 p).

Health-related quality of life in relation to delirium (IV)

During the hospital stay, the health-related quality of life (HRQOL) profiles in the D and NonD groups were almost equal (±10) to that of the Swedish reference group aged 75 years and older (SRef-75) except for physical functioning and, for the D group, bodily pain. The tendency at follow-up was that the D group HRQOL score was almost equal to or lower (SF -23; p<.05; all other n.s.) than during hospital stay, with one exception (role emotional; +21, n.s.). The NonD group scored almost equal or higher at follow-up (PF +19, p<.05; GH +5, p<.05; RE +25, p<.05; MH +7, p<.05; the remaining were n.s.).

There was a substantial difference in the HRQOL profile depending on the reason for surgery. At follow-up, the hip-replacement patients (n=21) had improved their HRQOL considerably. They scored significantly higher in all domains and even higher than the SRef-75 (figures 4a, b).

During hospital stay, HRQOL did not differ significantly between D and NonD hip-fractured patients, except for bodily pain, which was lower in the
NonD group. At follow-up, however, the D group scored significantly lower than the NonD did in physical functioning (mean value (mv)=21 vs. 34; z=1.92, p=.05) and vitality (mv=39 vs. 54; z=2.12, p=.03). The NonD group almost reached their hospital scores in all domains but role physical. Compared with SRef-75, all domains but bodily pain, general health and role emotional were scored lower at follow-up in both D and NonD hip-fracture patients (Figures 4 c, d).

Cognitive function and HRQOL
During hospital stay, cognitive function correlated negatively with bodily pain (r=-0.23; p=.03) but positively with general health (r=0.24; p=.03). At follow-up, cognitive function correlated with physical function (r=0.25; p=.02).
Figure 4a: HRQOL in patients undergoing hip replacement (n=21)
PF = physical functioning; RP = role physical; BP = bodily pain; GH = general health; VT = vitality; SF = social functioning; RE = role emotional; MH = mental health

Figure 4b: HRQOL in patients with hip-fracture (n=71)
Figure 4c: HRQOL in hip-fractured D patients (n = 15)

Figure 4d: HRQOL in the hip-fractured NonD patients (n = 56)
Discussion

The results depict what happened before delirium onset, during delirium and six months afterwards. Figure 5 gives an overview of the most important results during this time period. The results are discussed below under three main headings; before, during, and after delirium.

Before delirium onset

Risk factors for delirium

Old age, cognitive impairment, pre-existing cerebrovascular or brain diseases, and the use of psychopharmacological drugs were factors predisposing to or precipitating delirium, which is in line with several other studies. Factors that facilitated delirium onset were impaired hearing, passivity, poor communication, and social isolation. Earlier studies have also reported that delirious patients more often have impaired hearing or vision.

Behavioural changes were common among hip surgery patients during the hospital stay, both in those who later became delirious and in those who did not. However, the behavioural changes were different and more numerous in the D group than in the NonD group. These behavioural changes could be identified hours and sometimes days before delirium onset. The most common behavioural change in both D and NonD groups was anxiety. Therefore, anxiety is unlikely to be a dominant marker for the approaching delirium. However, disorientation, decreased psychomotor activity and urgent calls for attention may be markers, as these behavioural changes were the most dominant six hours immediately before delirium onset.

It is necessary to pay attention to each behavioural change as that may precede delirium. Nurses ought to give these patients special attention and interact with them, in order to prevent delirium. Intervention programs have been conducted with the intention of reducing delirium in hip surgery patients, but these interventions have not been directed towards activation of, and communication with the patient.
Figure 5: Model of predisposing and predicting variables before delirium, experiences of being delirious and outcome after 6 months
Is it possible to predict an approaching delirium?

The multiple logistic regression analysis showed that four of the risk factors above were significantly related to the onset of delirium. Patients with impaired hearing had 4 times higher risk of delirium than did those with normal hearing. Patients who waited for surgery for more than 18 hours had a 3.6 times higher risk compared to those who waited less than 18 hours. If the patient was more passive than patients in general, the risk of delirium was almost 3 times higher. The fourth factor, cognitive function assessed by the MMSE, showed that for each one-point drop in the MMSE, the risk of delirium increased by 22%. If these four factors are present in combination with high age, the risk of an approaching delirium is high. This simple predictive model, based on the presence of 4 risk factors can be used to identify old patients at high risk of delirium, but should be tested in further studies before it can be incorporated in a delirium prevention protocol for bedside use.

Some predictive models have been presented in earlier studies. Pompeji \textsuperscript{169} found cognitive impairment, burden of comorbidity, depression, and alcoholism to be predictors, whereas O’Coffey \textsuperscript{170} used logistic regression and found three predictive factors: dementia, severe illness, and elevated serum urea. Inouye \textsuperscript{82} reported vision impairment, severe illness, cognitive impairment, and high blood urea nitrogen/creatinine ratio to be predictive factors. All these studies included patients older than 70 years, but since different variables were used in the regression analysis, the models differ. Cognitive impairment, however, seems to be present in most predictive models.

During delirium

Twenty percent of the 225 patients developed delirium during their hospital stay, which means that the incidence of delirium was lower than in other comparable studies \textsuperscript{9,11,39,40,42,44-48,50}. This may partly be explained by the fact that patients who were delirious on admission or had a severe cognitive decline were not included. It may also be possible that the frequent daily observations and incidental small talk with the patients during the data collection had an intervention effect, and thereby reduced the incidence of delirium.
Patients’ own experiences during delirium

Patients with transient delirium were asked about their memories and experiences of the delirium period. Most patients with impaired cognitive functioning (MMSE < 25) did not remember the delirium episode or could not/did not want to talk about it. The higher the MMSE, the more the patients remembered. This is not surprising because memory disturbances are one of the symptoms of dementia. As in other studies, the delirium experiences were associated with strong fear, insecurity, panic and anger. Changes of the perception of reality were related not only to the entry into delirium, but remained during the entire delirium phase. It is not surprising that delirium patients may scream or fight to escape experiences that they think are real; and it may be hard for the nursing staff to handle the strong emotional feelings related to the delirium. However, it ought to be possible to interact with the delirium patient if the nurses are aware of the patient’s changed conception of reality and the difficulty to communicate during delirium.

Two of the patients said that the entry into delirium was associated with thirst and cold, respectively. The onset of delirium may be associated with basic physiological needs in other patients too, although it was not mentioned in the interviews. Delirium onset is also common in intensive care departments, where sleeplessness, pain and severe illness are common threats to basic needs. If unfulfilled basic needs in addition to the medical condition facilitates the occurrence of delirium, the incidence might be reduced quite simply by adequate nursing. In a recent study, severe pain increased the risk of delirium. Patients receiving low doses of parenteral morphine were more likely to develop delirium than those who received more analgesics. Inouye asserts that delirium incidence can serve as a measure of the quality of hospital care because delirium cases may be reduced by interventions targeting cognitive impairment, immobility, sleep deprivation, vision and hearing impairment, and dehydration.

After delirium

Patients who recovered from delirium had disparate feelings of fear, discomfort, remorse and relief, and they explicitly appreciated the interview and the opportunity to talk about their experiences. The nurses have to be sensitive to the patient’s experience and listen to the explicit and implicit questions posed by the patient. To be able to communicate with patients about their transient delirium after they have recovered, it might be of value to document behavioural changes and other significant behaviour during the delirium.
Cognitive function

Although delirious patients most often recover after one or two days, the delirium experience may be the beginning of a rapid progressive dementia or reduced cognitive ability. In this study the deterioration of the MMSE score was 2.6 points in the D group in the follow-up, compared with other studies, where the cognitive decline in older people was between 1.2 and 4 points when measured after 2-3 years. Thus, the cognitive decline in the follow-up was too great to be a normal 6-month change in cognitive function in older patients. This is in line with Francis and Kapoor’s two-year follow-up study of patients from general medical wards, where 11 delirium patients indicated a significantly greater decline on the MMSE than did 81 controls. The follow-up was performed in the patients’ homes (or nursing homes/ other residence for aged). One study has reported that patients tested at home achieved significantly higher scores than when they were tested at the clinic. Therefore, the true deterioration may be greater than that shown in the present study, given that the MMSE measurements during hospitalisation were performed in an unfamiliar environment, when the patients were presumably more tired and dazed by pain and drugs than during the follow-up.

In order to determine diminished cognitive functioning, it is recommended to use a cognitive test (e.g. MMSE) on admission and at discharge for patients at risk of delirium, and to use an observation protocol to recognise behavioural changes. If patients who have suffered from delirium have lower MMSE scores on discharge than on admission, nurses are recommended to advise the patient’s families to consult a gerontologist about the cognitive decline. The nurses are also recommended to carefully study existing guidelines for the prevention and treatment of delirium. To be noticed, patients with prodromal delirium symptoms or full-bloomed delirium should always be examined by a physician as well, because delirium by definition has a precipitating organic cause, and such medical or pharmacological causes have to be treated.

Health related quality of life

In the long term, delirium affects not only cognitive function but also quality of life. It has been shown that several patients with hip fracture never reach their pre-fracture HRQOL. This tends to be in line with the present findings, showing that physical functioning was still low at follow-up, and role physical, vitality and social functioning were lower than during hospital stay. Patients also experienced more bodily pain. The hip-replacement patients, on the contrary, had considerably lower HRQOL scores during the hospital stay than did hip-fractured patients. But for the former patient group
the surgery was a necessary condition for improving HRQOL, which is also well documented in other studies.\textsuperscript{126-129}

When examining the hip fracture group with regard to the delirium experience, patients in the D group scored lower at follow-up in physical functioning and vitality sub-scales than did those who did not experience delirium. An explanation of why patients with delirium have poorer physical outcomes after fracture repair may be that they were older and had lower cognitive function than NonD patients and therefore a lower capacity for rehabilitation. Carmelli and colleagues\textsuperscript{130} found that a decline of cognitive performance was significantly associated with poor HRQOL ratings. However, Marcantonio and colleagues\textsuperscript{91} found that delirium was associated with poor functional recovery after hip fracture even after adjustment for age and pre-fracture cognitive and functional impairment. However, it is necessary to plan the post-hospitalisation care for hip-surgery patients by informing their families and staff in community elderly care about the likelihood of an ongoing need for support and care.

Several studies have pointed out the greater risk of delirium patients dying\textsuperscript{68,70,72,81,108,111,176}. This was also suggested in the present study, where 11 patients had died at the 6-month follow-up. Of these, 12.8% belonged to the D group and 5.6% to the NonD group (n.s.). However, in the main study as well as in other studies investigating delirium, the study population was old, and the D group was even older than the NonD group. Thus, the greater risk of dying in the D group need not be related to delirium. It may be due to higher age and other confounding variables\textsuperscript{43,71}.

Methodological considerations

Data collection

In the main study, data were collected during 6 months divided in 2 time periods and including 225 patients. The intention was to collect the data during the time of the year when snow and cold weather causes more frequent falls outdoors and thereby more hip fractures. However, most patients fell indoors, why the reason for data collection did not really matter.

The reason for exploring patients aged $\geq$80 years in the study of behavioural changes (II) was because they belonged to the oldest age group, which was at the highest risk of delirium. This has also been found in other studies\textsuperscript{40,48,67,69,71,73-75}. For the same reason, patients aged $\geq$75 were explored at follow-up (IV), as 42/45 in the D group belonged to that age group and it was desirable to include as many D patients as possible.
Some behavioural changes in the D and NonD groups may have been missed, as the very frequent observations were limited to the oldest age group, but also because the observations were intermittent. However, it is not likely that any delirium cases were missed, as the observations were frequent in the oldest group, and those who were younger than 80 years were observed at least every 4th hour or 3 times a day. If patients younger than 80 years demonstrated behavioural changes, they were observed more frequently too.

Measurements

Delirium
The DSM criteria for delirium were used to determine delirium onset 1, and changes in the patients’ mental state and behaviour were observed at frequent daily observations. It was both methodologically and ethically impossible to administer a standard instrument such as the MMSE, as the observations concerning delirium would be performed daily and frequently. When planning the main study in 1994-1995, few instruments were available 177, and they had not been used frequently. As they did not seem to be adapted very well to the DSM criteria, it was decided that the DSM criteria were preferable for assessing delirium. From the middle of the 1990s, the development and testing of delirium instruments have increased 173,178-182. In recent studies, the confusion assessment method (CAM) has often been used to assess delirium 183. It is a validated instrument, which is easy to administer, and can be recommended in all clinical settings as a screening instrument for delirium.

MMSE
The MMSE 117 is well tested and was easy to administer. It has been discussed whether the MMSE is a valid instrument for measuring cognitive functioning in old age, because the scoring is influenced by impaired sight and hearing 184,185. In the present thesis, however, the focus is not on the MMSE scoring per se, but on the individual change in scoring. That some patients scored one or several points lower because of impaired hearing and sight was not significant for the results in paper IV, as they did so during both the hospital stay and the follow-up.

The MMSE scores for hip-fractured patients on admission were probably artificially low in some cases. Pain and analgesics influenced the scoring, and some patients scored two points lower at the casualty department when
performing the written part of MMSE. On the other hand, some patients scored lower at discharge than on admission. These patients had been relocated to the rehabilitation departments only a few days after surgery, and their MMSE scores might be lower because they were still receiving analgesics. In view of this, the individual’s highest MMSE score during the hospital stay was compared with the score at follow-up. Thereby, the effects of any deteriorated MMSE scores during the hospital stay were reduced as far as possible.

**SF-36**

The SF-36 was chosen for measuring HRQOL, as it has been used in old age groups in several studies. Test-retest reliability and convergent validity has been shown to be fairly good among residents in a nursing home, who scored ≥ 17 points on the MMSE. Some of the patients had impaired sight or a deteriorated cognitive function and therefore had difficulties completing the SF-36 form. In these cases, the data collectors read the questions. At follow-up, all patients but one answered the questions orally. Apart from the fact that it would have taken too long for the patients to complete the questionnaires by themselves, and some patients were unable to do so, because they had impaired sight or were cognitively impaired. The cases where the administration of the SF-36 was different may be a threat against its validity. However, the results in paper IV concerning HRQOL were in line with other studies concerning hip surgery outcome.

Validity and reliability of the study-specific protocols and interviews

In the main study, the author and three registered nurses collected the data collection. Prior to data collection the assisting nurses were trained to perform the observations. They were instructed about the criteria for delirium and trained to assess the patients and to fill in the observation protocols. During the first week, the author participated in the data collection together with the three nurses in order to validate the observations.

Protocol A showed a satisfactory agreement between nurses, between nurses and the author (in the screening study that preceded present thesis), but also between the author and patients (I). Prior to discharge, the patients’ psychosocial situation on the ward was to be assessed (I). The whole hospital stay was to be considered, but not the delirium period. However, behaviour during the prodromal delirium may have influenced the assessment as behavioural changes often preceded delirium onset.

The percentage agreement for protocol D is satisfactory, as it varied between 78% and 100%, and the mean value for agreement was 96%.
All interviews but two were performed during the hospital stay, and there was no time to make supplementary interviews. It is debatable whether the six patients with nightly confusion who participated in the interviews experienced delirium or not. However, their reports were included in the analysis as they concurred with the reports of patients with delirium established during daytime.

As the respondents mostly belonged to the oldest old age group (≥80 years), and these interviews were analysed 5-6 years later, it would neither be ethically justifiable nor methodologically possible to trouble these patients to read the analysis and the interpretation of the interviews. Further, it is not possible to remember or confirm the interviews after such a long time. Trustworthiness is satisfactory, as the findings tend to be congruent with other studies examining delirium experiences. During the analysis, the authors discussed themes and sub-themes until agreement was reached. The analysis was also discussed at seminars with other researchers.
Conclusions

- The overall incidence of delirium was 20%. The higher the age and the lower the cognitive functioning, the higher the risk of delirium.
- It is possible to predict an approaching delirium episode. Significant predictors were impaired cognitive function, impaired hearing, passivity, and long wait for surgery.
- It is possible to observe behavioural changes prior to delirium onset. The most important behavioural changes were disorientation, increased psychomotor activity, urgent calls for attention, perceptual disturbance, and reduced attention.
- The experience of delirium is associated with fear, panic and anger that patients have to reflect upon after recovery.
- Delirium related to hip fracture is associated with a reduced cognitive functioning and poorer health-related quality of life six months later.
- Research is needed to further test the predictive model for delirium that was presented in this thesis.

Proposals for clinical practice

There are several risk factors for delirium. Besides old age, the most important risk factors demonstrated in the present thesis are; impaired cognitive function, impaired hearing, passivity, and a long wait for surgery. Important behavioural changes prior to delirium were decreased psychomotor activity, disorientation, and urgent calls for help. When admitting an old person to hospital for orthopaedic surgery, the following should be considered in order to prevent delirium:

- Assess MMSE at admission to confirm whether the patient has impaired cognition.
- Use a short structured observation protocol including items on passivity, disorientation, psychomotor activity and urgent calls. Also, make notes about the patient’s hearing.
- Be aware that the waiting time for surgery should be as short as possible (should not exceed 18 hours).
• Try to activate patients who are passive (at least those with impaired hearing).
• Patients who develop delirium despite such measures should be given an opportunity afterwards to talk about what happened during the delirium attack. Also, assess the MMSE at discharge as well if the patient has been delirious during the hospital stay.
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A doctoral dissertation from the Faculty of Medicine, Uppsala University, is usually a summary of a number of papers. A few copies of the complete dissertation are kept at major Swedish research libraries, while the summary alone is distributed internationally through the series *Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine*. (Prior to October, 1985, the series was published under the title “Abstracts of Uppsala Dissertations from the Faculty of Medicine”.)