

From DEPARTMENT OF CLINICAL SCIENCES,
DANDERYD HOSPITAL
DIVISION OF ORTHOPAEDICS
Karolinska Institutet

and

Sophiahemmet University College
Stockholm, Sweden

**GENDER DIFFERENCES IN
PATIENTS WITH HIP FRACTURE
ASPECTS ON CARE AND RECOVERY**

Bodil Samuelsson



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To Manda and Hampus

ABSTRACT

Hip fractures in the elderly are common and impose a substantial burden on the healthcare system. This fracture population consists of many subgroups that often require differentiated and extensive acute and postfracture care. The aim of this thesis was to basically characterise a hip fracture population at time of admission, present postoperative results and discuss aspects that may influence recovery. Gender differences are specifically addressed.

Study I, II and IV derive from a consecutive series of 2213 patients with hip fracture admitted to four major hospitals in Stockholm, while Study III was a small pilot study.

In *Study I* we investigated the effect of time-to-surgery on: ability to return to own home, incidence of pressure ulcers, length of stay (LOS), and mortality. Patients who had surgery within 24, 36 or 48 hours were compared with those who had surgery later. The ability to return to own home was affected in patients who had to wait longer than 36 and 48 hours. The incidence of pressure ulcers and LOS increased at all time limits.

In *Study II* we investigated gender differences in two subgroups, characterized by normal cognitive function versus cognitive dysfunction, and whether such differences influenced patient ability to: return to own home, regain walking ability and perform activities of daily living (ADL). Cognitive function was assessed by the Short Portable Mental Status Questionnaire (SPMSQ). Dysfunction was equally common by gender. Patients with normal function (SPMSQ 8-10) were younger and healthier, resided more often in their own homes and were able to manage ADL independently, with no gender differences. In patients with dysfunction (SPMSQ 0-7), men had more comorbidity on admission, greater loss of walking ability and higher mortality after the fracture episode. We found that cognitive status was the overarching most important factor for predicting outcome.

In *Study III* we examined gastric emptying time of 400 ml carbohydrate rich drink in ten elderly women with acute hip fracture, and compared results with two reference groups of healthy women. The mean half gastric emptying time in the study group was 57 ± 5 (39-82) minutes, to be compared with 58 ± 4 (41-106) and 58 ± 5 (33-72) in the two reference groups. No adverse event was observed during anesthesia. Consequently, it should be possible to give patients a carbohydrate-rich drink before surgery instead of ordering strict fasting (NPO), which in turn could improve the patients' chances to recover and regain prefracture status.

In *Study IV* we focused on gender differences in complications; specifically on factors associated with common general complications. Complications were common with an incidence of 59% in men and 56% in women (ns). Most common were urinary tract infection, pressure ulcer, cardiac complications and pneumonia. Male gender emerged as an independent risk factor for suffering from pneumonia, and female gender for urinary tract infection. Besides gender, time-to-surgery, cognitive function, cardiovascular and pulmonary disease on admission were independent risk factors for suffering complication.

In conclusion, there are gender differences among patients admitted to a hospital for acute hip fracture, both with regard to status on admission and outcome. Cognitive dysfunction, equally common among women and men, has a major impact on incidence of complication and functional recovery. Men with cognitive dysfunction are at greater risk. With increased awareness of risk factors and gender bias, along with reduced waiting time for surgery, it should be possible to decrease complication incidence and improve outcome. We found no evidence for prolonged gastric emptying time of a carbohydrate-rich beverage, which implies it may be possible to provide patients with a carbohydrate-rich drink before surgery instead of adhering to strict fasting.

LIST OF PUBLICATIONS

- I. Al-Ani AN, **Samuelsson B**, Tidermark J, Norling Å, Ekström W, Cederholm T, Hedström M. Early operation of patients improved ability to return to independent living – a prospective study of 853 patients. *J Bone Joint Surg Am.* 2008 Jul;90(7):1436-42.
- II. **Samuelsson B**, Hedström M, Ponzer S, Samnegård E, Söderqvist A, Cederholm T, Säaf M, Thorngren KG, Dalen N. Gender differences and cognitive aspects on functional outcome after hip fracture - a 2 years' follow up of 2,134 patients. *Age Ageing.* 2009 Nov;38(6):686-92.
- III. **Samuelsson B**, Hellström PM, Al-Ani AN, Hedström M. Gastric emptying in nine elderly patients with hip fracture: normal emptying time of 400 ml Carbohydrate-rich drink. Submitted.
- IV. **Samuelsson B**, Hedström M, Ponzer S, Söderqvist A, Al-Ani A, Ekström W, Mattiasson A-C, Thorngren K-G, Cederholm T, Dalén N. Gender differences in comorbidity and complications after hip fracture - a prospective cohort study of 1,955 Swedish patients. Manuscript.

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LIST OF ABBREVIATIONS - DEFINITIONS

ADL	Activity of Daily Living
ASA	American Society of Anesthesiologists Scale
CI	Confidence Interval
EPUAP	European Pressure Ulcer Advisory Panel
HF	Hip Fracture
ICD-10	International Classification of Disease
ICN	International Council of Nurses
MCI	Mild Cognitive Impairment
MMSE	Mini Mental State Examination
NOS	Not Other Specified
PU	Pressure Ulcer
SAHFE	Standardised Audit of Hip Fractures in Europe
SPMSQ	Short Portable Mental Status Questionnaire
SPSS	Statistical Package for the Social Sciences
UTI	Urinary Tract Infection
WHO	World Health Organization

Sex, gender

Gender is used to describe those characteristics of women and men which are socially constructed, while sex refers to those which are biologically determined (WHO 2002). In this thesis, the term gender was used in the meaning of both sex and gender; the two concepts were not diversified.

Cognitive dysfunction, cognitive impairment

Any cognitive disorders; delirium, dementia, amnesic disorders or NOS (not other specified, a syndrome of cognitive impairment that does not meet the criteria for delirium, dementia or amnesic disorders)

Independent living, own home

Community dwelling, living in their own homes or in a communal setting without health care facilities

Institutional living

Residential care setting, an institutional dwelling where older people have specialist health care professionals available at all times

INTRODUCTION

Hip fractures are the most devastating of the osteoporotic fractures. Apart from an increased mortality rate, hip fractures are associated with morbidity and a high risk of postoperative complications and will affect patients' future mobility, social functioning, quality of life and autonomy. The prevalence of hip fractures increases exponentially with age and constitutes a major public health problem since these patients often require extensive acute and post-fracture care, including rehabilitation and social services.

The hip fracture population is heterogenic, consisting of many subgroups of patients, and outcomes therefore vary for a variety of reasons. Our knowledge concerning epidemiology, etiology, surgery and care has increased over the past decades. Generally speaking, women are more prone to suffer from hip fractures, while affected men are at increased risk for mortality.

Sex (referring to the biological dimension) and gender (referring to the sociocultural dimension) are major determinants of health and disease in many conditions, but little attention has been paid to the influence of sex and gender on care and outcome after hip fracture.

The aim of this thesis was to basically characterise hip fracture patients, and to illuminate factors that may influence recovery. Special focus is paid to sex and gender differences (referring to both sex and gender).

BACKGROUND

HIP FRACTURES

Incidence and definition

The risk of sustaining a hip fracture increases with advancing age, and constitutes a major public health problem worldwide. About half of the total number of hip fractures in Sweden occur between the ages of 80 and 89 years¹, and about two thirds of the patients are women, although sex distribution seem to be changing toward a larger proportion of men²⁻³. This trend break has also been reported from other western countries⁴⁻⁶. However, for demographic reasons due to an increasing number of old people, the absolute number of fractures will remain high.

Hip fractures, including the proximal femur, may be defined as femoral neck fractures (cervical or intracapsular) or inter/subtrochanteric fractures (extracapsular). The incidence of the two types is almost equal, with a slight predominance for the former. Sex distribution differs somewhat, with extracapsular fractures being more common in women^{1,7}. In intracapsular fractures, surgical treatments include primary osteosynthesis (with screws or pins) or artificial hip joint replacement. Inter/subtrochanteric fractures are usually treated with dynamic hip screws or medullary nailing^{1,8}.

Etiology: osteoporosis and falls

Hip fractures comprise almost 20% of all osteoporotic fractures⁹ and are commonly associated with a minor fall which, because of osteoporosis and therefore fragile bone, produces sufficient force to break the bone¹⁰⁻¹¹.

Osteoporosis is a systematic skeletal disease characterized by decreased bone mass. It mainly affects the elderly and leads to increased risk of sustaining a fracture. One in three women and one in eight men above the age 50 have been reported to suffer from osteoporosis¹². Considered together with the higher life expectancy of women, this may explain most of the increased risk in women for sustaining fragility fractures.

The reason that women are at higher risk of developing osteoporosis is multifactorial. Briefly, women having mainly primary causes, reflecting hormonal balance, while the condition in men more often is a consequence of secondary causes, such as other diseases¹³⁻¹⁴. The World Health Organization (WHO) has established criteria for the diagnosis of osteoporosis and have determined bone density levels that predict higher risks of sustaining fractures¹⁵.

The incidence of osteoporosis and hip fracture also varies among different populations worldwide, with Scandinavia having the highest known incidence in the world. In Sweden, with 9.4 million inhabitants, 70 000 fractures due to osteoporosis

occur annually, including 18 000 hip fractures¹⁶. Recently, a trend toward osteoporosis fractures occurring later in life has been reported among women^{2-3, 17}.

Almost all hip fractures occur as a result of a fall, most commonly indoors during daily activities, such as walking or rising from sitting to standing or vice versa¹⁸⁻¹⁹. The etiology of falls in older people is complex and multifactorial; falls are usually caused by combinations of predisposing factors and trigger events. Predisposing factors include morbidity, functional disability, previous falls, intake of medication²⁰ and aging, with deterioration of postural control²¹⁻²². Emotional stress has also been identified as a trigger of falls leading to hip or pelvic fracture²³.

In elderly people, the numbers of falls has been reported to be greater among men, but the proportion of fractures following falls is greater among women¹⁸.

Young and middle-aged patients

In younger people (<50), hip fractures are rare, as reflected by the literature. Moreover, patients < 50 years are not reported to all national quality registers, which makes it more difficult to survey larger cohorts in this age group. Many studies dealing with hip fractures in young patients are case reports, or deal with highly specific issues, such as stress fractures among military personnel²⁴, or hip fractures due to sports injuries or high-energy trauma²⁵. Generally speaking, there is a larger proportion of male patients who fracture their hip in these younger age groups, and fracture is more often due to high-energy trauma²⁶⁻²⁹. However, in these relatively young patients with hip fractures due to high-energy trauma, bone density has been reported to be lower compared with controls or the general population^{26, 30-31}.

Middle-aged patients (age 50-65) also differ from the older population by virtue of a higher proportion of men^{30, 32-33}. Patients with a hip fracture due to low-energy trauma in this group usually have manifest osteoporosis, and several studies have also shown that they are predisposed to suffer from new fractures³⁴⁻³⁶. However, many of these fracture patients are otherwise quite healthy and highly functional prior to the fracture incident, and a majority will regain their prefracture mobility after surgery^{1, 33}.

Aging

Internationally, old people are defined as age 60 years or older, and the very old as aged 80 or older³⁷. In Sweden, the corresponding figures are 65 and 85, respectively. The discrepancy in definitions of old people is explained by cultural and socioeconomic reasons and by expected survival among people in relatively good health. Chronological and biological ages certainly do not always harmonize, as the former is determined by years and the latter by frailty.

Among the very old, irrespective of what definition is used, an increased prevalence of different diseases and decline in general function are common, and falls and therefore fractures are frequent. Patients sustaining hip fractures are at increased risk for death compared with the non hip fracture control population, who otherwise share the same

status³⁸⁻⁴²; this may be interpreted as an indication that elderly patients with hip fracture have a higher biological age.

Generally speaking, gender differences in aging are complex. Women have a longer life expectancy; in fact, women in all age groups have a higher survival rate than men⁴³. As a result, elderly men more frequently have a wife to care for them, while women tend to be more dependent on their children or the healthcare system⁴³.

Cognitive disorders

Cognitive disorders increase with increasing age⁴⁴⁻⁴⁵, and are therefore common in hip fracture populations. Cognitive disorders, including dementia and delirium, play a major role in poor outcomes after surgery⁴⁶.

Dementia includes several subtypes, is described as a syndrome caused by disease of the brain and is usually of progressive nature. Symptoms of dementia include deterioration of memory, thinking, orientation, comprehension, calculation, learning capacity, language and judgment skills⁴⁷.

Delirium, or acute confusional state, is often associated with cerebrovascular insufficiency and characterized by a disturbance of consciousness and changes in mentation. Delirium is a temporary state that fluctuates, which may last from a couple of hours to several days of patients with hip fracture⁴⁸. Patients with dementia diseases are at higher risk for delirium, and delirium has been reported to occur in between 4-53% in hip fracture populations⁴⁸.

Mild cognitive impairment (MCI) refers to the transitional state between the cognitive changes of normal aging and very early dementia⁴⁹. It has been found to be frequent among patients at high risk of developing dementia, such as patients with Parkinson's disease⁵⁰ or patients with vascular disease⁵¹. The incidence of MCI in a general elderly population has been reported to be approximately 16% in persons not suffering from dementia, with even higher numbers among men⁵².

Several mental tests are available for to assess a patient's cognitive function. The Short Portable Mental Status Questionnaire (SPMSQ) has been reported to be easy to administer and has been validated with rates of sensitivity and specificity similar to the often used Mini Mental State Examination (MMSE)⁵³. The SPMSQ has also been shown to be a valuable tool to predict outcome after hip fractures^{48,54}. It is usually administered verbally, but could also be administered in writing when needed (hearing problems, language problems, etc.). It should be kept in mind that although the SPMSQ is a valuable screening tool developed to detect cognitive disorders, it does not differentiate between dementia and delirium or other mental disorders⁵⁵.

AWAITING SURGERY

Time to surgery for a patient with hip fracture is commonly unpredictable and often more than 24 hours⁵⁶⁻⁵⁷, which is a time limit that has been reported to have a negative effect on outcome⁵⁸. This may be due to several reasons, including the patient's stress level related to the fracture, pain and immobilization. These factors, in conjunction with

lengthy fasting, may cause an array of more or less serious consequences that will affect individuals differently depending on their general health status on admission.

Fasting guidelines

The guidelines for fasting in preparation for elective surgery allow clear fluids until 2-4 hours before induction of anesthesia in patients without reported risks of pulmonary aspiration. However, the guidelines for patients considered to be at increased risk of delayed gastric emptying, including emergency patients with acute fractures requiring surgery, are usually advised to rigidly follow preoperative fasting standards. This often means the “nil per os” order for clear fluids/liquids and solids overnight, or a minimum of six hours fasting preceding induction of anesthesia ⁵⁹.

Gastric emptying

Gastric emptying is the process by which food is delivered to the small intestine at a rate and in a form that optimizes intestinal absorption of nutrients. The rate of gastric emptying is subject to alteration by physiological, pharmacological and pathological conditions ⁶⁰.

In healthy individuals, a meal normally empties from the stomach within six hours, a light meal within four hours and clear fluids within two hours ⁶⁰. However, apart from considerable individual variation ⁶¹, several known factors may affect gastric emptying. For example, premenopausal women have a slower emptying rate than men of all ages, while old men have a slower rate than young men ⁶²⁻⁶³. Injury and stress are factors that can theoretically have a negative influence on gastric emptying; the use of parenteral opioid analgesics may also have a negative impact ⁶⁴. A number of comorbid states, including diabetes mellitus ⁶⁵, renal insufficiency ⁶⁶ and gastroesophageal reflux ⁶⁰ are also considered to be risk factors for delayed gastric emptying.

Insulin resistance

Patients with acute hip fractures commonly have a different metabolic situation compared with patients undergoing elective surgery, where normal metabolism before surgery is to be expected. The trauma induced by the fracture itself results in a cascade release of stress hormones that cause major metabolic alterations by mobilizing substrates from all energy stores: glucose from glycogen, fat from adipose tissue and protein mainly from skeletal muscles. All stress hormones also counteract the actions of insulin and together with the fasting condition itself induce a state of insulin resistance, which will further aggravate catabolism ⁶⁷. The combination of these two catabolic factors renders the patient vulnerable to additional metabolic stressors in preparation for surgery. Preoperative insulin resistance will also influence postoperative recovery, since insulin is a major anabolic hormone ⁶⁸⁻⁶⁹. Once established, insulin resistance is likely to persist for at least a couple of weeks, even with relatively limited surgery.

Carbohydrate-rich beverage

The alternative to strict fasting, i.e. clear liquids 2-3 hours before induction of anesthesia, has been shown to be safe in preparing for elective surgery, which has

created opportunities for development of other beverages that can be administered close to surgery. A carbohydrate-rich beverage given shortly before surgery has been shown to reduce discomfort⁷⁰⁻⁷⁵ and to have a beneficial effect on postoperative nutritional parameters, muscle strength and mobilization⁶⁸.

Previous studies in gastric emptying of 400 ml of a carbohydrate-rich drink*

First author	Year	Method	Study population	n	F/M	Ages
Gustafsson	2008	Paracetamol	Diabetes (+controls)	25 (10)	12/23	45-73
Hausel	2001	Aspiration	Elective surgery	252	168/84	34-69
Henriksen	2003	Aspiration	Elective surgery	48	28/21	44-82
Lobo	2009	MR**	Healthy volunteers	20	10/6	39-55
Nygren	1995	Isotopic marker	Elective (+controls)	6 (7)	9/4	46 (42)
Protic***	2010	Paracetamol	Hip fracture	110	84/26	66-91

*50 kcal, 12.6% carbohydrates/100ml ** Magnetic resonance imaging *** 200 ml

COMPLICATIONS

Hip fracture causes not only suffering, but potentially a wide spectrum of directly or indirectly related complications.

There are numerous classifications of complications in the literature, making comparisons among studies difficult. One definition used by Fritzell et al defines complications as general or specific, early or late, and major or minor with regard to possible consequences⁷⁶. The most commonly occurring complications in a hip fracture population are associated with the patient's general health status and comorbidity, and can be classified as minor or major. Common general complications include pressure ulcer, cardiac disorders, urinary tract infection, acute confusional state (delirium) and pneumonia.

Patients with more comorbidity on admission are at higher risk for incident-related (fracture episode) complications than those who are healthier⁷⁷. One indicator of the patient's initial medical condition, including comorbidity, is the anesthesiologist's ASA assessment of physical status prior to surgery⁷⁸. Patients who score high on the ASA classification are at high risk for suffering major complications, and consequently have a higher mortality risk related to the fracture⁷⁷.

However, the ASA classification gives no detailed information about individual patient requirements, which is essential for care planning. To identify patients at risk for malnutrition, delirium, pressure ulcer or repeated falls, other specific assessment instruments are available, as for example the Modified Norton scale⁷⁹. The use of such established risk assessment procedures on admission reportedly decreases the incidence of complications⁸⁰.

Pressure ulcer

Pressure ulcer is one of the most common general complications in hip fracture patients, with a reported incidence ranging from 4% to 55%⁸¹⁻⁸⁶. The consequences

may be extensive, including pain, restricted living situation for the patient⁸⁷⁻⁸⁸, prolonged hospital stay and sometimes additional months of intense nursing care after discharge from the hospital following acute fracture care⁸⁹. The cost of pressure ulcers is therefore high, both for the patient and for the healthcare system⁹⁰⁻⁹¹.

Definition

The European Pressure Ulcer Advisory Panel (EUPAP) has defined pressure ulcer as localized damage to the skin and underlying tissues, caused by disruption of the blood supply to the area, as the result of pressure, shear or friction or a combination of any of these⁹²: EUPAP has agreed on the following classification system for pressure ulcers:

Stage 1	Non-blanchable erythema of intact skin. Discoloration of the skin, warmth, edema, induration, or hardness may also be used as indicators, particularly in individuals with darker skin.
Stage 2	Partial thickness skin loss involving epidermis, dermis, or both. The ulcer is superficial and presents clinically as an abrasion or blister.
Stage 3	Full thickness skin loss involving damage to or necrosis of subcutaneous tissue that may extend down to, but not through, underlying fascia.
Stage 4	Extensive destruction, tissue necrosis, or damage to muscle, bone, or supporting structures with or without full thickness skin loss.

Risk factors

Historically, pressure ulcers have been considered to result from poor nursing practices, stated as such by Florence Nightingale in the nineteenth century “If he (a patient) has a bedsore, it is generally the fault not of the disease, but of the nursing”⁹³. In recent years, perhaps due to large studies specifically focusing on risk factors, the attitude has changed toward considering pressure ulcer to be an indicator of quality of care, involving all healthcare professionals⁹⁴.

Today a variety of intrinsic (patient-related) and extrinsic (environment-related) pre-existing risk factors for sustaining pressure ulcers are defined^{81-82, 84-85, 95-98}, such as poor nutritional status, poor physical function, cognitive impairments, high ASA score and advanced age. Care-related factors that may contribute include inadequate pain relief and nutritional support, long waiting time before surgery and duration of the surgical procedure itself. Thus, to avoid pressure ulcers it is important for all healthcare professionals to be aware of the risk factors, both intrinsic and extrinsic, and be involved in providing care.

Pneumonia

In addition to the suffering that pneumonia causes patients after hip fracture, it increases the risk of developing other major complications and for mortality⁹⁹⁻¹⁰⁰. Pneumonia demands intense medical care and ultimately a prolonged hospital stay. The literature, with some inconsistency, has reported that time to surgery increases risk of developing pneumonia^{97, 101-102}. Incidence of pneumonia is consistently reported to be higher in men^{99, 103}.

Cardiac complications

Cardiac complications, including cardiac insufficiency, arrhythmia and myocardial infarction, have been reported to be a frequent cause of death in the wake of fracture¹⁰⁴⁻¹⁰⁶; higher incidence of cardiac complications has been reported in men¹⁰⁶. Most patients with hip fracture who suffer from cardiac complications have a prior history of cardiovascular disease¹⁰⁶. Heart failure has even been reported to be a risk factor for sustaining orthopedic fractures¹⁰⁷.

Urinary tract infection

Women are especially prone to urinary tract infections for reasons that are not yet well understood, but one woman in five develops these infections during her lifetime. Risk factors, in addition to female gender, include advanced age, diabetes or other diseases that affect the immune system. Only about 20% of urinary tract infections occur in men. Among men, prostate problems are a risk factor. Urinary catheters comprise a common care-related risk factor¹⁰⁸.

Among hip fracture patients, the incidence of urinary tract infections has been reported to be between 4% and 23%^{102, 105-106, 109-111}, and has also been reported as a cause for prolonging hospital stay^{109, 112}.

RECOVERY

A significant number of patients do not recover from hip fracture. In Sweden, the four-month mortality-rate has been reported to be 13% in women, and 24% in men¹¹³. This may be due to several reasons, some of which we cannot influence, and others that we can. Many of the patients belong to the very old (>85), and are in poor general health at time of admission, indicating frailty, in reality a high biological age. However, the fracture itself exerts an independent effect, which we may conclude from the increased mortality rate compared with the general population^{38-42, 114}.

All studies on hip fracture patients in the Western world report an increased risk of mortality in men compared with women, but the reasons are still poorly understood. Possibly, a higher risk of sustaining major complications could be one explanation^{99, 103}. Others suggest factors such as high ASA score, more severe comorbidity or poor nutritional status on admission, indicating frailty^{78, 103, 115-117}.

One independent risk component for poor outcome in both men and women is cognitive dysfunction, including both dementia and delirium^{48, 54, 98, 118-123}.

The influence of gender

Several studies have been published dealing with different aspects of this subject, but gender (sociocultural context) has been most thoroughly explored in the social sciences, where the concept of gender struggles to distinguish itself from sex (biological context)¹²⁴. In contrast, in the healthcare setting, both sociocultural and biological factors should be analyzed simultaneously; what is biological is also socially determined, and vice versa¹²⁵⁻¹²⁶. Gender bias is a complex issue, but in the context of health care it means that female/male personnel treat female/male patients differently, which is also supported in the literature^{125, 127-128}.

To detect gender difference in health care, statistics need to be presented by gender. Since 2006, the National Board of Health and Welfare in Sweden requires gender-sensitive analyses from the national quality registers; consequently, most of these registers now report results by gender and some also include detailed analyses of findings¹²⁹⁻¹³⁰.

The national register RIKSHÖFT, has reported that women have a poorer walking ability¹³¹; prior history of fracture and fear of falling are more common among women, factors shown to have a negative impact on walking ability¹³²⁻¹³³. Gender differences in functional recovery after geriatric rehabilitation following hip fractures is reported with inconsistent results: showing either no difference¹³⁴⁻¹³⁸, a disadvantage for women¹³⁹⁻¹⁴⁰, or a disadvantage for men¹¹⁶.

It should be kept in mind that the majority of patients admitted with hip fracture will survive and recover to live for many more years³⁵. Although many will function at a lower level, a significant number will still retain independence⁵⁷. This fact highlights the importance of defining all risk factors for poor outcome that we can influence and taking appropriate action to do so. It has been shown that multidisciplinary strategies designed to promote a consistent approach to outcome-focused care, such as “clinical pathways” and “care pathways,” have positive effects on outcome¹⁴¹. Such pathways may include fast track to surgery¹⁴², early mobilization¹⁴³⁻¹⁴⁴, individual care planning¹⁴⁵, and geriatric or community-based rehabilitation^{46, 141}. In other words, recovery depends on multiple factors and it is crucial to identify all those factors that we can influence in order to do the most good for all patients.

AIMS

GENERAL AIM

The general aim was to investigate and describe gender differences in patients with hip fractures and to illuminate factors that may influence care and recovery.

SPECIFIC AIMS

Study I

To investigate whether timing of surgery in hip fracture patients influenced ability to return to independent living, risk for development of pressure ulcers, length of hospital stay, or mortality during the first four months.

Study II

To describe the total population of patients sustaining hip fracture within a geographically defined urban area of Sweden in 2003 and to investigate the potential importance of gender and cognitive function for returning to own home, regaining walking ability and restoring ADL function in this population

Study III

To investigate whether 400 ml of a carbohydrate-rich beverage could be administered to patients with hip fracture awaiting surgery without incurring a risk of pulmonary aspiration – a pilot study

Study IV

To describe gender differences in hip fracture patients > 64 years regarding comorbidity and general complications, and to find factors associated with general complications.

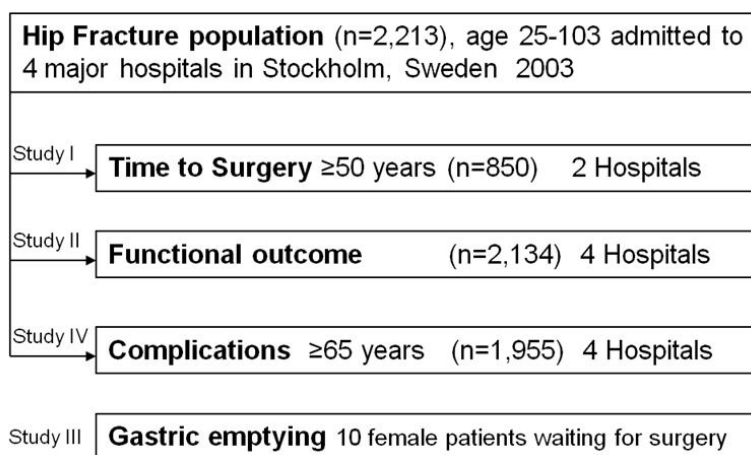
METHODS

DESIGN AND GEOGRAPHICAL CONTEXT

Studies I, II and IV were derived from a prospective cohort study (n=2,213). The study was conducted in four major hospitals in Stockholm County, with a catchment serving about 1.4 million of the 1.9 million inhabitants of Stockholm.

Paper III was a pilot study with quasi-experimental design, conducted at Danderyd Hospital, Stockholm and included ten patients. Results were compared with two reference groups of healthy individuals.

Flow chart study I-IV



PATIENTS AND PROCEDURE

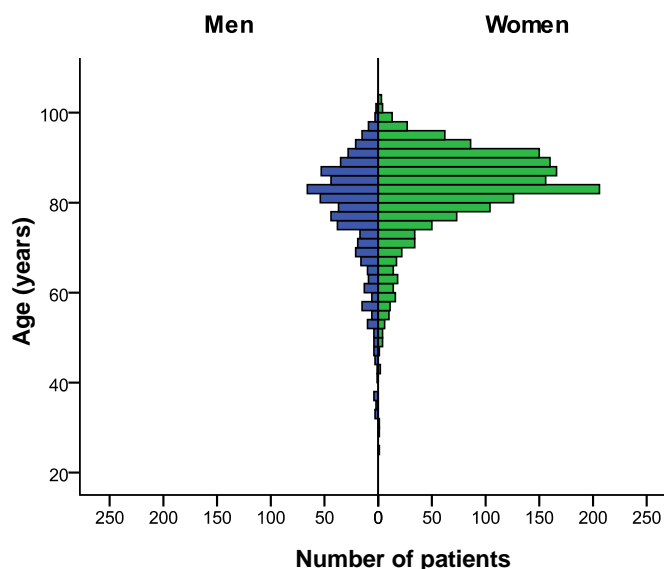
Study I, II and IV

Virtually all patients with hip fracture consecutively admitted to any of the four hospitals between January 1 and December 31, 2003 were included. Trained independent study nurses assessed the patients on admission and conducted structured interviews according to protocol. In cases where patients were unable to provide answers, a proxy was asked. In cases where the patient/proxy did not wish to participate in interviews, only data from medical records were used. If the study nurses did not have an opportunity to meet with the patient during the hospital stay, questionnaires were completed at a later date using medical records and telephone interviews with patients/proxies.

On admission, fractures were classified by experienced orthopaedic surgeons, while ASA classification⁷⁸ was carried out by the attending anaesthesiologist. ASA 1 indicates a complete healthy person; ASA 2, a person with a mild systematic disease; ASA 3 a person with severe systematic disease that is incapacitating, ASA 4, a person with an incapacitating disease that is a constant threat to life; ASA 5, a moribund patient

who is not expecting to live 24 hours with or without surgery. Only one patient in the study was classified as ASA 5. Complications were recorded as such if medical treatment had been initiated by a physician, with the exception of pressure ulcers, which were commonly recorded by the responsible nurse who initiated treatment. Patients were followed up after four, 12 and 24 months, mostly by telephone interviews, but also face-to-face or using mailed questionnaires. Patients who did not want to participate in interviews were followed up using the hospital discharge register and, in cases of readmission, by reviewing medical records. Mortality data were obtained from the hospital discharge register. For study I, we retrospectively reviewed medical records in two of the four hospitals to add information on the exact time (by hour) for admission and for surgery start, reasons for delay before surgery (patient-related or system-related), when the fracture occurred, and diagnosis (if any) or known history of dementia (in those cases SPMSQ was not assessed).

The figure below illustrates the age and sex distribution of the whole study population (2213 patients).



Study III (pilot study)

Ten patients admitted for acute hip fracture to Danderyd Hospital, Stockholm, Sweden, were recruited to the study. Inclusion criteria, apart from fracture, were female gender and age ≥ 75 years. Excluded were patients with severe cognitive impairments, patients with known gastro-oesophageal reflux or other gastrointestinal motility disorders. The study was conducted in the morning, which allowed at least four hours of fasting before surgery, since only patients who were scheduled for surgery in the afternoon were asked to participate. Due to fracture-related pain, a half-supine position was allowed during intake of the beverage, and additional intravenous morphine was permitted during the study as needed according to standard procedure for hip fracture patients.

Two hundred ml of the carbohydrate-rich drink was given before, and another 200 ml after intake of 1.5g of paracetamol dissolved in 100 ml of water, for a total volume of 500 ml. A time limit for intake was set to 30 minutes. The carbohydrate drink consisted of an iso-osmolar carbohydrate-rich solution (50 kcal, 12.6% carbohydrates/100ml).

Plasma samples were obtained for measurement of plasma paracetamol concentration at 0, 15, 30, 60, 120 and 180 minutes after the patient had completed intake of the beverage and the paracetamol solution. After immediate centrifugation, plasma samples were kept frozen at -20° C until analysis. Half-emptying time (T_{50}) was defined as the period from the end of beverage intake with paracetamol until 50% of gastric emptying was achieved. The gastric emptying profile was estimated after conversion of plasma paracetamol concentration to cumulative concentrations, i.e. total absorption of the drug. In this way we obtained a gastric emptying curve from 0% to 100%, adapted to a third-degree polynomial.

The results were compared with two reference groups of 20 gender-matched patients who participated in earlier studies of gastric emptying with similar experimental design. One group consisted of 10 women, age 45-71 years, with osteoarthritis who were planned for hip replacement surgery. The other 10 were healthy female volunteers, age 28-55.

INSTRUMENTS

The National Quality Register - RIKSHÖFT (SAHFE)

The main study protocol was based on The Standardized Audit of Hip Fracture in Europe (SAHFE)¹⁴⁶, which includes a primary form, a four-month assessment and an optional form (“Q-reg”)¹⁴⁷.

Baseline data included age, sex, comorbidities, residential status, walking ability, ASA grade, type of fracture, surgery technique, location of pressure ulcer, if any (on admission, during hospital stay and at discharge), use of established risk assessment, length of hospital stay (by date), place of discharge and in-hospital mortality. Comorbidities were recorded as follows: cardiovascular disease, stroke, respiratory disease, renal disease, diabetes, rheumatoid disease, Parkinson’s disease and malignant disorders. Complications after surgery were recorded as follows: pressure ulcer, cardiac complication, pneumonia, urinary tract infection, wound infection (deep and superficial), myocardial infarction, renal failure, gastrointestinal bleeding, stroke, deep venous thrombosis and pulmonary embolism.

The four-month follow-up questionnaire included data on current residence, walking ability, ADL status, complications and mortality. The same form was completed again at 12 and 24 months.

The Short Portable Mental Status Questionnaire

Cognitive status was assessed at time of inclusion using the Short Portable Mental Status Questionnaire (SPMSQ)⁵⁵, which is a 10-item questionnaire.

- 1 What are the date, month, and year?
- 2 What is the day of the week?
- 3 What is the name of this place?
- 4 What is your telephone number or alt. street address?
- 5 How old are you?
- 6 When were you born?
- 7 Who is the current prime minister?
- 8 Who was prime minister before him?
- 9 What was your mother's maiden name?
- 10 Can you count backward from 20 by 3's?

Scoring:

- 0-2 errors:** normal mental functioning
- 3-4 errors:** mild cognitive impairment
- 5-7 errors:** moderate cognitive impairment
- 8-10 errors:** severe cognitive impairment

Walking ability

Walking ability was measured: (Study I)

- Alone outdoors
- Outdoors, only if accompanied
- Alone indoors, but not outdoors
- Indoors, only if accompanied
- Unable to walk

And by use of walking aids: (Study II and IV)

- Able to walk without aids
- One aid (stick, crutch, tripod or hemi-walker)
- Two aids (stick, crutch, tripod or hemi-walker)
- Frame (walking frame or rollator)
- Wheelchair/bedbound

Katz index of Activities of Daily Living

Katz Index of Activities of Daily Living encompasses six basic functions: bathing, dressing, toileting, transfer, continence and feeding¹⁴⁸.

- Index A: Independence in all six functions
- Index B: Independence in all but one.
- Index C-G: Dependence in bathing and at least one other function

Bathing	(sponge bath, tub bath or shower) - Receives either no assistance or assistance in bathing only one part of body
Dressing	Gets clothes and gets dressed without any assistance except for tying shoes
Toileting	Goes to toilet room, uses toilet, arranges clothes and returns without any assistance (may use cane or walker for support and may use bedpan/urinal at night)
Transferring	Moves in and out of bed and chair without assistance (may use cane or walker)
Continence	Controls bowel and bladder completely by self (without occasional “accidents”)
Feeding	Feeds self without assistance (except for help with cutting meat or buttering bread)

STATISTICAL METHODS

Statistical methods - overview				
	Study I	Study II	Study III	Study IV
Chi square	x	x		x
T-test	x	x		x
Kruskal Wallis	x		x	
Logistic regression	x	x		x
Linear regression	x			

The statistical analyses were conducted using SPSS for Windows (Chicago, Illinois).

Mean, standard deviations and percentages were used for descriptive purposes. Non-parametric data were tested using Pearson’s chi square test. Normally distributed independent variables were tested for differences using the Student t test. The Kruskal-Wallis test was used to compare variables measured on an ordinal scale or continuous data not normally distributed. In study III, statistical evaluation of differences between groups was assessed using the Kruskal-Wallis test with Dunn’s post hoc test.

Regression analyses

Regression analyses were performed to find predictors for specific outcomes (Study I, II and IV). The selected factors used for study I and II were factors that previously had been reported to be predictors of the particular outcome in question. In study IV, all baseline variables that correlated with each outcome were selected for analyses.

To find independent predictors, the selected factors were univariately tested and entered into the models. Independent variables were either dichotomized or dummy coded with the best item used as reference. Stepwise procedures were used in all models. *P*-values of <0.05 were considered significant.

In study I, three separate regression analyses using the different cut-off limits for delay before surgery were performed for each outcome. Cut-off limits were set at 24, 36 and 48 hours. The following variables were considered: (1) return to own home: age, gender, prefracture walking ability, prefracture ADL, whether patient was living with someone, ASA score, treatment modality, reoperation, reason for delay before

surgery (2) pressure ulcer: age, gender, prefracture walking ability, prefracture ADL, dementia, ASA score, duration of surgery (3) length of hospital stay: age, gender, prefracture living conditions, prefracture walking ability, prefracture ADL, dementia, ASA score, fracture type, reoperation, reason for delay before surgery

In study II, the following variables were considered to be possible predictors: age, gender, living alone, ASA grade (1-2 vs 3-4), fracture type (intra capsular vs. extra capsular), comorbidity (0-1 vs. 2-6), SPMSQ (8-10 vs. 0-7+dementia), ADL (Katz index) and walking ability (using walking aids).

In study IV, age and class variables were dichotomized for the final models (after first undergoing univariate testing): age (<85 vs. ≥85), ADL (Katz A-B vs. C-G), and walking ability (no/one aid vs. two/frame).

METHODOLOGICAL CONSIDERATIONS

Generally

In the main cohort study, our intention was to include all patients admitted for hip fracture. However, in spite of thorough reviews of patients scheduled for surgery in the four participating hospitals, the possibility that we missed some patients cannot be excluded. If so, that number should be small, and consequently we do not consider this to be a relevant problem regarding our results and conclusions. Due to the difference in etiology (not osteoporosis), patients with pathological fractures (n=79) were excluded from analyses.

Certain methodological issues were not considered in the analyses: patients who did not speak Swedish (or have assistance with translation) were included using only information from medical records and therefore some data are systematically missing in this specific subgroup of patients.

The four hospitals had similar logistic processes and care procedures, with the exception of one, where patients >65 years were cared for in the geriatric wards instead of an orthopaedic ward. In that hospital, geriatric rehabilitation was included in the acute care process, but whether this practice had an independent effect on outcomes was not evaluated.

Study I and IV

Pressure ulcers were commonly recorded according to nursing notes, which some publications consider to be an unreliable source¹⁴⁹. Something else to consider may be the lack of certain presumed risk factors that were not included in the analyses; e.g. nutritional parameters as serum albumin and body mass index (BMI). The reason was a large amount of missing data; in the case of BMI, a lack of scales to weigh immobilized patients on the wards at the time of the study, and in the case of serum albumin this analysis was not included in routine screening. Another consideration might be lack of information about what happened between the time of fracture and admission, and the duration or reason for wounds reported on admission.

Study I

The reason for not including all patients in Study I was because of the extensive extra work with additional reviews of medical records that would have been required (as described in Patients and procedure); however, according to our calculations, we considered the number of patients in two hospitals (850) to be sufficient for power.

Study II and IV

The choice of logistic regression analyses to determine predictors may be challenged by alternative methods. However, most studies in this field use regression analyses, which facilitate comparisons with previous studies.

In study IV, all baseline variables were tested for correlation with each outcome measurement. When correlations are tested in a large data set, the risk of mass significance needs to be considered. Performing regression analyses diminishes this risk. There are however other possible uncertainties with this method; unknown confounders and interactions. In study IV, all variables in the regression models were tested for interactions, but not in Study II, which would have been optimal.

Study III

Assessing pain and nausea preoperatively, and evaluation of the postoperative period would have been appropriate.

ETHICAL CONSIDERATIONS

Ethical considerations arise when conducting interviews with patients/proxies in vulnerable situations. Many elderly patients with hip fracture have dementia or other cognitive disorders and therefore cannot personally take part in a study.

But, it is also important to include frail patients in studies, since they belong to a group that should be especially interesting for evidence-based care improvements. Any inconvenience incurred through assessment of cognitive status or the interview process must be weighed against such benefits. The ethics committee therefore agreed that even patients/proxies who did not provide “informed consent” could be monitored with regard to information not deemed to be potentially harmful for the patient in any way.

Hence, all patients admitted for hip fracture were monitored in the main cohort study (Study I, II and IV), including patients who were unable to provide informed consent or participate in the interviews. In cases where patients were unable to provide relevant answers, a proxy respondent, i.e. relative or caregiver, was consulted instead. In cases where the patient/proxy declined participation in interviews, only data from medical records were used.

In all cases where a study nurse received information suggesting technical or other complications during the follow-up period, a visit to an orthopaedist was arranged.

The studies were approved by the local ethics committee (Dnr. 2002/206, 2002/123), and conducted in accordance with the ethical principles of the Declaration of Helsinki (Helsinki Declaration 1989). This thesis also complied with the ICN Code of Ethics for Nurses (ICN 2006).

SUMMARY OF RESULTS

PAPER (I)

Research questions: Does timing of surgery influence (1) ability to return to independent living, (2) development of pressure ulcers, (3) length of hospital stay, (4) mortality at four months?

Results: Patients who had to wait more than thirty-six and forty-eight hours between admission and surgery were less likely to return to independent living within four months, whereas no significant difference was observed with adherence to the twenty-four-hour cut-off limit. Incidence of pressure ulcers and length of hospital stay including rehabilitation increased with duration at all the three cut-off limits. Delay before surgery did not affect the four-month mortality rate.

Additional observation: No gender differences concerning delay before surgery were observed.

PAPER (II)

Research question: What characterises a hip fracture population in Stockholm 2003? What impact do gender and cognitive function have on (1) return to own home, (2) retained walking ability, (3) retained physical function (ADL)?

Results: More than half of the patients had cognitive dysfunction (SPMSQ 0-7, or diagnosed or documented dementia), with equal gender distribution (not shown).

SPMSQ	n	%
8-10	910	41
3-7	563	25
0-2	401	18
Missing	194	9
Dementia*	145	7

* Included in missing

Women were more apt to live alone and had poorer walking ability than men. They were also more frequently treated with prosthesis and more likely to be discharged to rehabilitation units.

Walking aids at baseline – total study population

	Women		Men	
	n	%	n	%
No aid	602	38	242	40
One aid	170	11	95	16
Two aids	29	2	21	4
Walking frame	728	46	208	34
Wheel chair/bedridden	47	3	38	6
Total number*	1576		604	

*Missing: n=33 (1.5%)

The subgroup of patients with *normal cognitive function* (SPMSQ 8-10) were younger compared with the total population. These men had less comorbidity compared with the men in the total population; however, there was no statistically significant difference in comorbidity between the two genders. Almost all patients resided in their own homes and were independent in ADL, with no gender difference. Patients in the *dysfunction group* were older compared with the total population. They also had more comorbidity, poorer physical function and fewer resided in their own homes (60% women, 68% men). Comorbidity was higher in men than in women, but men lived in their own homes more often, with a spouse.

Logistic regression analyses showed that cognitive function had the most powerful effect on retaining physical function and return to own home. Prefracture walking ability had more influence than cognitive function on retained walking ability.

Return to own home* after four months

Baseline variable	Score Chi-Square	<i>p</i>
Cognitive function (SPMSQ 0-7 vs. 8-10)	153.7897	<0.001
Activities in daily living (Katz)	58.9355	<0.001
Age	28.6639	<0.001
Living alone (yes vs. no)	13.6632	0.011
ASA (1-2 vs. 3-4)	5.4719	0.019

* Own home or in a communal setting without healthcare facilities

Regain good walking ability* after four months

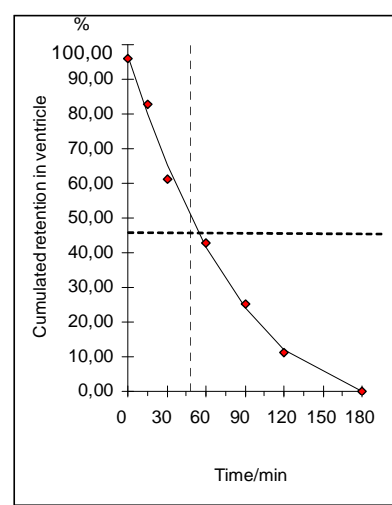
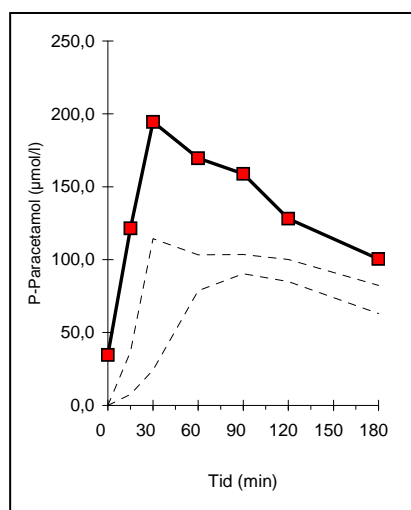
Baseline variable	Score Chi-Square	<i>p</i>
Walking ability	434.6048	<0.001
Cognitive function (SPMSQ 0-7 vs. 8-10)	42.1377	<0.001
Age	10.9011	0.001
Living alone	7.6534	0.022
ASA (1-2 vs. 3-4)	5.1269	0.024

*Without use of walking aids, or with one or two canes

PAPER (III)

Research question: Do elderly patients with acute hip fracture have prolonged gastric emptying time (with accompanying risk of pulmonary aspiration) compared with non-fracture reference groups?

Results: The gastric emptying profile was normal for each of the nine patients in the hip fracture group, including the two patients who required pain relief with morphine. One patient was excluded due to nausea and vomiting. The mean gastric half-emptying time was 57 ± 5 (39-82) minutes in the hip fracture group, to be compared with 58 ± 4 (41-106) and 58 ± 5 (33-72) minutes in the two reference groups.



The figures to the left shows the plasma paracetamol concentrations obtained from one patient. The figure to the right shows the gastric emptying profile, estimated after conversion of plasma paracetamol concentration to cumulative concentrations, i.e. total absorption of the drug. In this way we obtained a gastric emptying curve from 0% to 100%, adapted to a third-degree polynomial.

Additional observation: No adverse event during anesthesia was observed in any the ten patients.

PAPER (IV)

Research question: What are the gender differences in patients with hip fracture regarding (1) comorbidity, (2) complications? Which factors are associated with the most common general complications?

Results: Comorbidity: gender differences were found in specific comorbid conditions; e.g. men had a history of more strokes, Parkinson's disease and malignancy. History of cardiovascular disease was equally common in women and men. Complications: Fifty-nine percent of men and 56% of women (ns) suffered from one or more complications. Most common were urinary tract infection (30% women, 23% men, $p=0.001$), pressure

ulcer (20% men, 18% women ns), cardiac complications (18% men, 13% women, $p=0.018$) and pneumonia (14% men, 6% women, $p<0.001$).

After logistic regression analyses, male gender emerged as a risk factor for pneumonia and female gender as a risk factor for urinary tract infection. Gender, age, ASA, time-to-surgery, cardiovascular or pulmonary disease and cognitive function emerged as the most frequently occurring significant variables.

Additional observations:

Eighty-two percent of all patients with cardiac complications had a history of cardiovascular disease, and more than 70% suffered from additional complications. Within four months, 25% of the women and 41% of the men with this complication had died.

The table below provides detailed information about grade and location at three different times during hospitalization. There were no gender differences in pressure ulcer in terms of incidence, grade or location (not shown).

Location and grade of pressure ulcers					
	I	II	III	IV	Total
At admission					
Sacrum	43	16	11	4	
Heels	10	7	9	1	
Other part of the body	23	29	7	1	
<i>Total</i>	<i>76</i>	<i>52</i>	<i>27</i>	<i>6</i>	<i>161</i>
During primary care					
Sacrum	185	75	30	8	
Heels	73	30	12	1	
Other part of the body	48	46	9	2	
<i>Total</i>	<i>306</i>	<i>151</i>	<i>51</i>	<i>11</i>	<i>519</i>
On discharge					
Sacrum	161	94	32	7	
Heels	64	36	15	1	
Other part of the body	46	43	9	2	
<i>Total</i>	<i>271</i>	<i>173</i>	<i>56</i>	<i>10</i>	<i>510</i>

Figures given in numbers

DISCUSSION

The overarching aim of this thesis was to investigate and describe gender differences in patients with hip fractures, and to illuminate aspects that may have influence on care and recovery. Two studies were carried out to investigate gender differences with respect to background factors and outcome, one study investigates the influence on outcome of prolonged waiting time for surgery, and in a pilot study we investigated whether a carbohydrate drink may be given to elderly patients instead of having them observe strict fasting. The most important findings are discussed below.

Gender differences

Study II and IV showed that women had higher chronological age, lived alone more often and had poorer walking ability. Men seemed to have a higher biological age based on greater comorbidity, but no difference was found as measured by ASA score. The men suffered more major complications, and had a higher mortality rate. Apart from the ASA score, our findings are in line with previous studies^{40, 150-153}.

However, when dividing the population into subgroups by cognitive function (Study II), not only were age, comorbidity and outcome dissimilar between the two groups, but gender differences as well. Among patients with normal cognitive function, no gender differences were found in comorbidity, or in recovery in terms of regaining previous walking ability, physical function or returning to own home. In fact, not even mortality differed in this group, which is an interesting finding as mortality is consistently reported to be higher in male populations¹⁵⁴.

Still, some gender differences in the two subgroups (normal cognitive function vs. cognitive dysfunction) were similar: women had higher age, lived alone more often, and had poorer walking ability. Gender differences in choice of surgical method among patients with intracapsular fractures were also similar in the two subgroups. Interestingly, in cases of the same kind of fracture and equivalent comorbidity (not shown), women were more likely to receive a prosthesis in both groups, an issue that deserves consideration in future studies.

Walking ability

Study II addressed poorer walking ability among women, possibly due to increased fear of falling, and partly as a result of the living situation, since women live alone more often, frequently in a block of flats, which creates issues making it more difficult for them to walk outdoors. Because we have more complete information about use of walking aids, we based our measurement of walking ability on this question, rather than on reported ability to walk with or without assistance. We found that men did not use walking frames as often as women did, which is consistent with previous reports on Swedish hip fracture populations¹⁵⁵, and even among the general population in Sweden¹⁵⁶. Alternatively, gender differences in use of walking aids could conceivably be attributable to sociocultural factors: “doing gender” - men

might not like the idea of showing physical weakness¹⁵⁷, a concept possibly confirmed by the discrepancy between reported disability in the general population and use of walking aids by men¹⁵⁶. Another contributing factor could be living situation, since most elderly men have a wife to help with support, while women living alone are more dependent on their children or the healthcare system¹⁵⁸. The distribution of use of walking aids prior to the fracture incident in our patient population, is consistent with figures reported from RIKSHÖFT^{131, 155}.

Important to note: despite previous reports of poor prognostic outcome in patients with cognitive dysfunction¹³⁴, our study showed that pre-fracture walking ability rather than cognitive function had the greatest impact on regaining walking ability. This could be interpreted to mean that patients with cognitive dysfunction who have good walking ability should be able to regain their prefracture walking skills.

However, many patients in the cognitive dysfunction group lived in institutional care settings, and accordingly did not receive as much rehabilitation as patients who live in their own homes, which might have contributed to their overall poor recovery¹⁴³. This hypothesis was also later tested in a substudy of patients with severe cognitive dysfunction (SPMSQ 0-2) derived from the same population, where rehabilitation in patients with severe cognitive dysfunction was evaluated¹⁵⁹. The results indicated better outcome for patients discharged to geriatric rehabilitation compared with those discharged to institutional care settings, despite equivalent prefracture walking ability.

Case control studies indicate that hip fracture may activate a person's "functional decline", and consequently the biological aging process^{38, 40}. However, more aggressive care, including clinical procedures that optimise care programmes and rehabilitation tailored to patient requirements, may have a positive effect on such decline⁴⁶.

Complications

The incidence of complications in the study population was high, with 59% of men and 56% of women suffering one, or more than one, complication, indicating that treatment and care of hip fracture may have been suboptimal. One way to avoid complications could be to reduce waiting time before surgery, as shown in study I and IV.

Pressure ulcer

In study I, where we analysed waiting time at two hospitals, we found that about half of the patients were operated within 24 hours, two thirds within 36 hours and 87% within 48 hours. The results showed that longer waiting time was associated with increased occurrence of pressure ulcer, consistent with previous studies^{58, 160}. We found no gender differences either in waiting time or pressure ulcers, which came as a relief. But subsequently we asked ourselves why men, who had higher comorbidity, did not have a higher incidence of pressure ulcers, leading us to consider the

possibility of gender bias (female/male staff treating female/male patients differently). In addition to a long waiting period before surgery, we found that pulmonary disease, high age and poor physical function were predictors. Exploring the question of gender bias requires a different study design.

The incidence of pressure ulcers in hip fracture populations varies widely in the literature, from 4% to 55%^{81-86, 98}. This variation is partly due to different definitions. For example, according to the European Pressure Ulcer Advisory Panel (EPUAP), grade I, included in Study IV, should be recorded as a 'warning signal', and be omitted from calculation of either prevalence or incidence rates¹⁶¹. Moreover, difficulties in differentiating grade I pressure ulcers from moisture lesions have been described¹⁶¹⁻¹⁶². For both these reasons, we decided to omit grade I when calculating the effect of waiting time before surgery on pressure ulcer (Study I). However, to us it seems more likely that pressure ulcers are underreported by nurses¹⁴⁹, and given the fact that most studies include grade I in their reports^{82, 84, 86, 98}, we decided to reconsider grade I as a complication in study IV. When doing so, the incidence of pressure ulcers in the total study population was 18% in women and 20% in men. This gender difference was not significant; in addition, no other differences were found, in either grade or location (data not shown). This finding is consistent with most previous studies^{81-83, 163}, but is contradicted by a few that report a disadvantage to the favour of either women^{162, 164} or men¹⁶⁵.

A decrease in grade I and simultaneous increase in grade II-III can be tracked in the table providing detailed information about grade and location at three different times during hospitalization; this may be interpreted to mean that a significant number of grade I ulcers worsened during hospital stay. However, interventions may have been carried out in the ward to prevent further progress of observed grade I, and the increase in number of grade II may have resulted from new observations. One study reported that 22.1% of grade I ulcers in an acute care setting deteriorated to a higher stage¹⁶², which theoretically supports this assumption. However, we performed no further analyses to explore this matter.

In study IV, logistic regression analyses confirmed previously reported predisposing factors such as high age, reduced physical function and pulmonary disease^{82, 166}. However, one previously reported risk factor, diabetes⁸², did not correlate with pressure ulcer in our study, which could indicate that this risk factor is known, and consequently more interventions are carried out to prevent complications in these patients.

The negative effect of long waiting time before surgery, as previously reported^{58, 85}, was confirmed in Study I and IV. However, possible care-related confounders that were not evaluated included poor nutritional parameters (due to prolonged fasting), analgesics, sedatives (due to increased anxiety in patients with cognitive dysfunction), unsuitable patient positioning or clothing. In a study of pressure ulcer prevalence in Europe⁸², no association was found between long waiting time before surgery and pressure ulcer, possibly explained by awareness of risks and knowledge of preventive measures in departments where long waiting times were common. Most pressure ulcers can be prevented by appropriate interventions. One improvement may be a carbohydrate drink rather than strict fasting⁶⁸, which is why Study III was focused on whether elderly patients could be given a carbohydrate drink. However, in this pilot study, we did not evaluate any effects.

Despite diverse patient characteristics and various definitions of pressure ulcer, most pressure ulcers can be avoided through adequate care; reported incidence can probably be used as a quality of care indicator. Another reported quality of care indicator is use of risk assessments for developing pressure ulcer⁸⁰, which was not a significant part of the present study, since only about 7% of patients in our study were assessed to be at risk of pressure ulcer according to nursing notes.

Cardiac complications

We defined cardiac complication as the need for new medications other than the patient's regular medication regimen, which also usually involving medical consultation. By this definition, the incidence of cardiac complications was 13% in women and 18% in men, myocardial infarction not included. These figures may seem high, and they are possibly influenced by two factors: criteria that included both arrhythmia and heart failure, and the longer follow-up period (four months), rather than just the initial hospital stay. By comparison, reported incidence of inpatient postoperative heart failure among hip fracture patients ranges from 5% to 11%^{106, 167}.

About 67% of the total study population had a history of cardiovascular disease at time of admission, and among patients who suffered a cardiac complication, this figure was 80%. Although not further investigated, it seems likely that chronic heart failure is a common diagnosis among patients with a history of cardiovascular disease. Chronic heart failure is a syndrome that may lead to cardiac decompensation (worsening) in response to other concurrent illness such as pneumonia, arrhythmias, failure to maintain fluid restriction, medication, anaemia, excessive fluid, or medications that cause fluid retention¹⁶⁸⁻¹⁶⁹, and probably also by the stress related to the fracture. To prevent cardiac complications, awareness should be increased about patients who have

cardiac disease at time of admission and all care providers should remain alert for such complications in these patients. In study IV, we showed that delay in time-to-surgery was associated with more cardiac complications. Although no adjustment was made for reason for delay, this association suggests negative consequences of long waiting times before surgery, which includes fasting, and we believe the latter finding is pertinent to the discussion on creating rational fast-track pathways for these patients¹⁷⁰⁻¹⁷¹.

Urinary tract infections

By defining urinary tract infection as one requiring treatment, irrespective of origin or symptoms, incidence in our study was 30% in women and 23% in men. These figures are about the same as those previously reported in Sweden^{109, 167}, but more than twice as high compared with other studies^{106, 110}. Although the data included four months of follow-up, only a few more cases were observed after primary care visits (not shown), indicating that most infections occurred while the patient was hospitalised for the fracture.

We found only two factors that correlate with urinary tract infection: age and female gender, which is in line with previous knowledge of bacteruria among elderly women in general, and specific in hip fracture populations with reported incidence of 38% on admission^{108-109, 112}. According to standard procedure at that time in the four hospitals, almost all patients in the study had an indwelling urinary catheter, probably > 2 days, which has been reported to increase the risk for infection^{112, 172}. However, since we did not record the number of days, we could not evaluate the effect of time. In other words, there may be an additional confounder in women, since they may have had more difficulty urinating in the preoperative situation, and possibly had their indwelling catheter in place for a longer time.

It seems plausible that urinary catheters could be used less often, or for a shorter period of time. However, the risk of urinary tract infection must be weighed against the risks of overfilled bladder and urinary retention, as well as with the discomfort and pain related to the alternative, intermittent catheterisation, when patients repeatedly fail to empty the bladder by normal urination. All these issues are under study, and new guidelines are expected.

One interesting additional finding was that mortality rate was lower among patients with urinary tract infection, compared with the total study population, and no gender difference was shown. One interesting thought is that this observation may be due to the use of antibiotics in this group, which may have prevented other infections. However, this may simply be a coincidental finding, so no conclusion can be drawn, but we do consider this matter worthy of additional study in another setting, perhaps using national quality registers.

Cognitive function

According to SPMSQ, about half of the total study population suffered from cognitive dysfunction. The table below shows the distribution of SPMSQ scores. No gender differences were found in incidence, severity or missing data (not shown). Due to a relatively large amount of missing data (16%), we reviewed medical records

at two hospitals for history of dementia. In this way, we found an additional 145 patients who were merged into the subgroup of patients identified by SPMSQ as having cognitive dysfunction: in study I, patients were considered as having dementia with an SPMSQ score of 0-2 or diagnosis of dementia, whereas in Studies II and IV we assigned patients without dysfunction to a normal cognitive function group.

In study II, where patients with normal cognitive function (SPMSQ 8-10) were compared with patients having any degree of cognitive dysfunction (SPMSQ 0-7 + dementia), almost all patients in the normal cognitive function group returned to their own home after four months, whereas a large number of patients in the dysfunction group did not. Although we did not separate patients with severe dysfunction from those with mild to moderate (SPMSQ 3-7), we could still conclude that cognitive function *per se* matters: 68% of the men and 60% of the women were admitted from their own home, but only 42% and 36% respectively still lived there four months after the fracture episode. This finding was confirmed by regression analysis in Study II, and also by additional observations in Study I, where only a few patients with diagnosed dementia or SPMSQ 0-2 had returned to their own home after four months.

CONCLUSIONS AND CLINICAL IMPLICATIONS

There are gender differences among patients admitted to a hospital for acute hip fracture, both with regard to status on admission and outcome. Cognitive dysfunction, equally common among women and men, has a major impact on incidence of complication and functional recovery. Men with cognitive dysfunction are at greater risk.

- Early surgery for patients with hip fracture improved ability to return to independent living, reduced risk of developing pressure ulcers and shortened hospital stay compared with outcome after late surgery.
- Women were older, lived alone more often and had poorer walking ability compared with men. They were more often treated with prosthesis and sent to rehabilitation units.
- Male gender was associated with a higher risk for loss of walking ability and death, but only in patients with cognitive dysfunction.
- Cognitive dysfunction was equally common in women and men and cognitive function *per se* was the single most important factor for returning to own home and regaining physical function.
- Among patients with normal cognitive function, no gender differences were found in comorbidity, recovery to prefracture skills or mortality.
- We found no evidence for prolonged gastric emptying time of a carbohydrate-rich beverage in nine elderly women with acute hip fracture.
- More than half of patients with hip fracture had a complication; patients with cognitive dysfunction, cardiovascular or pulmonary disease were particularly prone to suffer a complication.
- Men had more comorbidity on admission, were at greater risk of developing pneumonia and had a higher mortality rate.

Clinical implications

With increased awareness of risk factors and gender bias, along with reduced waiting time for surgery, it should be possible to decrease complication incidence and improve outcome. We found no evidence for prolonged gastric emptying time of a carbohydrate-rich beverage, which implies it may be possible to provide patients with a carbohydrate-rich drink before surgery instead of adhering to strict fasting.

POPULÄRVETENSKAPLIG SAMMANFATTNING

Höftfrakturer är vanligt förekommande, i synnerhet bland äldre, och innebär utöver ett lidande för patienten också en stor belastning på hälso- och sjukvården.

Patienterna har olika behov avseende det akuta omhändertagande, rehabilitering och andra hjälpinsatser. Avhandlingens övergripande syfte var att beskriva en höftfrakturpopulation avseende skillnader mellan kvinnor och män, bakgrundsfaktorer samt faktorer som kan påverka återhämtningen efter operation. Olika aspekter som kan påverka återhämtningen diskuterades. Delstudier I, II och IV härrör från en population på 2 213 patienter med höftfraktur som behandlades vid fyra sjukhus i Stockholm. Delstudie III är en pilotstudie. Patienternas kognitiva funktion mättes med ett validerat instrument, the Short Portable Mental Status Questionnaire (SPMSQ).

I *delarbete I* undersökte vi om väntetiden från ankomsten till sjukhus till operation påverkade möjligheten att återvända till eget boende, förekomst av trycksår, vårdtid och dödlighet. Patienter som opererades inom 24, 36 respektive 48 timmar jämfördes med de som opererades senare. Möjligheten att återvända till eget boende minskade bland dem som fick vänta mer än 36 och 48 timmar. Förekomsten av trycksår ökade efter varje angiven tidsgräns, liksom vårdtiden. Vi fann inga könsskillnader vare sig med avseende på väntetid, eller uppkomst av trycksår.

I *delarbete II* undersökte vi skillnader mellan kvinnor och män bland patienter med normal respektive nedsatt kognitiv funktion, och möjligheten att återvända till eget boende, återfå gångförmågan, samt förmågan att klara dagliga aktiviteter (ADL). Över hälften av både kvinnorna och männen hade nedsatt kognitiv funktion. I gruppen med normal funktion (SPMSQ 8-10) var könsskillnaderna få; generellt sett var patienterna yngre och friskare, bodde oftare i eget hem och kunde sköta sina dagliga aktiviteter utan hjälp. I gruppen med nedsatt kognitiv förmåga (SPMSQ 0-7), hade männen fler andra sjukdomar än kvinnorna och sämre förmåga till återhämtning. Kognitiv funktion hade sammantaget stor betydelse för återhämtningen.

I *delarbete III* undersökte vi om det är möjligt att ge patienter en kolhydratdryck nära inpå (2-3 timmar) operation istället för strikt fasta, vilket idag är den vanliga rutinen. Vi mätte magtömningshastigheten av 400 ml kolhydratdryck hos tio äldre kvinnor med höftfraktur, och jämförde resultaten med två grupper friska kvinnor. Medeltömningsstiden skiljde sig inte mellan grupperna.

I *delarbete IV* fokuserade vi på könsskillnader och riskfaktorer avseende vanliga komplikationer upp till fyra månader efter frakturen. Fler än hälften av både kvinnorna och männen drabbades av en eller flera komplikationer. Vanligast var urinvägsinfektion, trycksår, hjärtsvikt och lunginflammation. Risken att drabbas ökade: vid lång väntetid till operation, om patienten hade kognitivt nedsatt funktion samt vid hjärt- eller lungsjukdom. Männen hade större risk att drabbas av

lunginflammation, och kvinnorna av urinvägsinfektion.

Sammanfattningsvis fanns skillnader mellan kvinnor och män, både avseende riskfaktorer och komplikationer. Nedsatt kognitiv förmåga innebar sämre återhämtning, i synnerhet för männen. Fler än hälften av både kvinnorna och männen drabbades av en eller flera komplikationer i samband med frakturen. Risken för vanliga komplikationer, som trycksår och hjärtsvikt, minskade med kortare väntetid till operation.

Magtömningstiden hos de nio äldre patienter som undersöktes i pilotstudien var normal, vilket kan innebära en möjlighet att ge patienter med akut höftfraktur en dryck istället för strikt fasta före operation.

Några tankar om framtida förbättringsarbeten

En stor förändring har skett på senare tid avseende väntetid till operation, och de flesta patienter opereras nu inom 24 timmar. Det finns dock alltså behov av förbättringar, i det akuta omhändertagandet såväl som eftervården.

- Kognitiv funktion visade sig ha stor betydelse för återhämtningen. Att identifiera dessa patienter, som kan behöva särskilda åtgärder, är en förutsättning för att kunna planera för vården på bästa sätt för den enskilda patienten. Här finns ett behov av interventionsstudier för att hitta vägar att förbättra prognosen för patienter med nedsatt kognitiv funktion.
- En kolhydratdryck i väntan på operation är en möjlig väg för att minimera den katabola fasen postoperativt och därmed påskynda återhämtningen. Större studier behövs för att selektera patienter som utan ökad risk för aspiration i samband med operationen kan ges en kolhydratdryck, och för att utvärdera effekter.
- Med ökad medvetenhet hos vårdpersonal om risken för hjärtkomplikationer hos patienter med hjärtsjukdom kanske dessa komplikationer kan minskas; här finns behov av en kunskapsinventering och vidare studier.
- Resultaten tyder på att det finns ett behov av att undersöka om män och kvinnor behandlas olika av vårdpersonal, och om det påverkar kvaliteten på vården.

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