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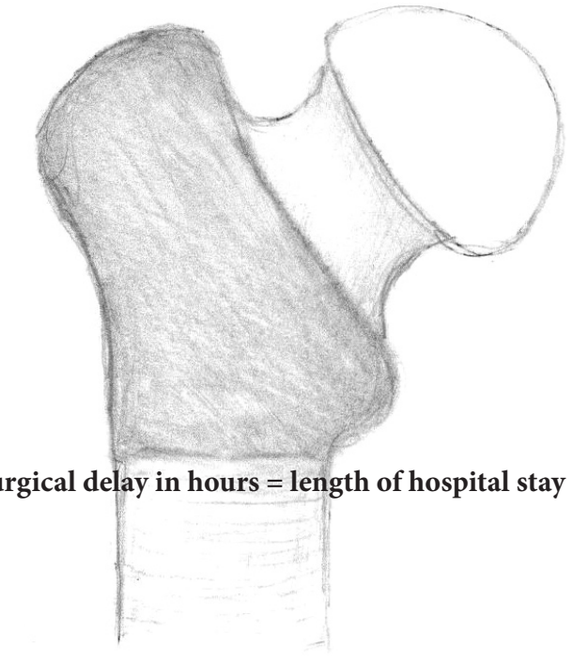

0.148 X surgical delay in hours = length of hospital stay in days

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

اقْرَأْ بِاسْمِ رَبِّكَ الَّذِي خَلَقَ * خَلَقَ الْإِنْسَانَ مِنْ عَلَقٍ * اقْرَأْ وَرَبُّكَ الْأَكْرَمُ * الَّذِي عَلَّمَ بِالْقَلَمِ * عَلَّمَ الْإِنْسَانَ مَا لَمْ يَعْلَمْ *

I GUDS. DEN NÅDERIKES. DEN BARMHÄRTIGES NAMN!

LÄS! I din Herres namn, Han som har skapat-. * Skapat människan av en grodd som sätter sig fast! * Läs! Din Herre är den Främste Givaren, * som har lärt [människan] pennans bruk. * Lärt människan vad hon inte visste!

Quran. Surah Al-'ALAQ (GRODDEN) - 96

Dedicated to everyone who will benefit from this work
I hope the God Allah will accept this work from me

Tuva Larsson, 14 years old, International English School Bromma (IESB), is gratefully acknowledged for providing cover illustration representing the hip

ABSTRACT

Hip fractures, the most serious osteoporosis-related fractures, mainly affect older people. The functional outcome for many hip fracture patients remains to be improved. Hip fractures in young patients are uncommon, but lifelong disability may prevail. The aim of this thesis was to examine possibly modifiable factors correlated with functional outcome in older subjects with hip fracture. Furthermore, to study background data and trauma mechanism in young and middle-aged patients with femoral neck fracture. Finally, the frequency of osteoporosis and sarcopenia in younger patients with a hip fracture was examined.

Study I A total of 850 patients with hip fractures were included. Outcomes including return to independent living, pressure ulcer (PU), length of hospital stay (LOS), and mortality were considered in relation to time between admission and surgery. Patients operated upon later than 36 and 48 hours after admission were less likely to return to independent living while there was no significant difference when using the 24-hour cut-off limit. The incidence of PU and LOS in the groups operated on later was increased at all 3 cut-off limits. The mortality rate did not differ.

Study II A total of 246 patients with femoral neck fracture and cognitive impairment were included. All were able to walk before the fracture. Significant predictors of preserved walking ability and ADL function at 4- and 12-month follow-up were: discharge to rehabilitation unit, walking ability, and ADL function prior to fracture, whereas surgical method was not. Patients discharged to rehabilitation unit were less likely to be wheelchair bound at any follow-up occasion.

S*tudy III* Included were 27 young (20-49 years of age) and 158 middle-aged (50-69 years of age) patients with a femoral neck fracture. They were studied regarding trauma mechanisms and risk factors for osteoporosis and hip fracture. A minority of both the young and middle age group had a high-energy trauma as a cause for the hip fracture. Life style factors and other non-trauma related risk factors appeared to be main contributors to the occurrence of the hip fracture in both age groups

Study IV The study population was the same as in *Study III*. Bone mineral density (BMD) and fat-free mass (FFM) were determined by Dual X-ray Absorptiometry (DXA). FFM index (FFMI) was calculated as the ratio of FFM (kg) and height squared. One third of the study population had FFMI below the 10^{th} percentile of a of an age- and gender-matched reference population, i.e. indicating sarcopenia. All young patients had a femoral neck BMD below the mean for age and 90% of the middle-aged patients had osteopenia (56%) or osteoporosis (34%).

In conclusion, the result of this thesis indicates that early operation of patients with hip fracture improves the ability to return to independent living, reduces the incidence of pressure ulcers and reduces the length of hospital stay. Discharge to rehabilitation unit, a factor we can influence, and previous function were both associated with preserved walking ability and ADL function in cognitively impaired patients with hip fracture. A minority, both in the young and middle-aged patients had a high-energy trauma as a cause for the hip fracture. And most of these patients have one or more risk factors for hip fracture and low BMD regardless of the trauma mechanism. One third has signs of sarcopenia i.e. low muscle mass.

LIST OF PAPERS

I. Early operation on patients with a hip fracture improved the ability to return to independent living. A prospective study of 850 patients.
Al-Ani AN, Samuelsson B, Tidermark J, Norling A, Ekström W, Cederholm T, Hedström M. J Bone
Joint Surg Am. 2008 Jul; 90(7):1436-42.

II. Does rehabilitation matter in patients with femoral neck fracture and cognitive impairment? A prospective study of 246 patients.
Al-Ani AN, Flodin L, Söderqvist A, Ackermann P, Samnegård E, Dalén N, Sääf M, Cederholm T, Hedström M.
Arch Phys Med Rehabil. 2010 Jan; 91(1):51-7.

III. One or More Risk Factors for Osteoporosis in the Majority of Young and Middle-Aged Patients with a Femoral Neck Fracture Regardless of Trauma Mechanism.
Al-Ani AN, Neander G, Samuelsson B, Blomfeldt R, Ekström W, Hedström M.
In manuscript.

IV. Low Bone Mineral Density and Fat Free mass in Young and Middle-Aged Patients with a Femoral Neck Fracture.
Al-Ani AN, Cederholm T, Neander G, Blomfeldt R, Ekström W, Hedström M.
Submitted.

LIST OF ABBREVIATIONS

ADL	Activities of Daily Living
ASA	America Society of Anesthesiologists
AUDIT	Alcohol Use Disorder Identification Test
BC	Body composition
BMD	Bone mineral density
BMI	Body mass index
CI	Confidence interval
DXA	Dual X-ray absorptiometry
EQ-5D	The 5-Dimentional Scale of the EuroQol
FFM	Fat-free mass
FFMI	Fat-free mass index
FM	Fat mass
FMI	Fat mass index
FRAX	Fracture assessment tool
HA	Hemiarthroplasty
HRQoL	Health related quality of life
LOS	Length of hospital stay
MCI	Mild cognitive impairment
MMSE	Mini-Mental State Examination
NHANES III	The Third National Health and Nutrition Examination survey
OR	Odds Ratio
PU	Pressure Ulcer
QCT	Quantitative Computed Tomography
sBMD	Standardized bone mineral density
SD	Standard deviation
SHFG	Stockholm Hip Fracture Group
SPA	Single photon absorptiometry
SPMSQ	Short Portable Mental Status Questionnaire
WHO	World health organization

CONTENTS

1 BACKGROUND

1.1 HIP FRACTURE

1.1.1 Definition

Hip fractures are defined as fracture of the proximal part of the femur. The majority of hip fracture are intracapsular (cervical) or extracapsular (trochanteric) while basocervical and subtrochanteric fractures are less frequent [1].

1.1.2 Classification

There are different classification systems for hip fractures. The cervical fractures are classified according to Garden[2] dividing cervical fractures according to degree of dislocation in the anterior-posterior view into 4 types (Garden 1 to 4). However due to the difficulty to differentiate between Garden 3 and 4, a more practical classification, i.e. undisplaced (Garden 1 and 2) and displaced (Garden 3 and 4) are more commonly used[3]. Jensen-Michaelsen (J-M) classification is frequently used for classification of trochanteric fractures into stable (undisplaced and displaced two-part fractures) and unstable (three-and four parts fractures)[4]. The less common subtrochanteric fractures are classified according to Seinsheimer classification[5]

1.1.3 Surgical treatment

Femoral neck fractures are generally treated by internal fixation or hip arthroplasty depending on degree of displacement, patient's age and functional demand. Trochanteric and subtrochanteric fractures are treated by internal fixation by means of Sliding Hip Screw or intramedullary nails.

1.2 WAITING TIME FOR OPERATION

Waiting time for operation has long been discussed with main emphasis on mortality and post-operative complications with contradicting results[6-12]. Some studies have shown that prolonged waiting time for operation was associated with increased incidence of pressure ulcer and increased length of hospital stay[9,10,13]. A limited number of prospective trials have analyzed the influence of waiting time for surgery on the patient's ability to return to independent living[13-15] with some controversies. There is a need to study the effect of prolonged waiting time for operation on functional outcome especially the patient's ability to return to independent living which is of crucial importance.

The term early operation does not represent a standard parameter in the published literature. While most studies used 24 hours to define early operation carried out within 24 hours of admission or injury[16-20]. Others used 48 hour as a cut-off limit for early operation[10,21] or 72 hours[12,22].

Limitations of previous studies investigating waiting time for operation are the retrospective design in some, different cut-off limits for definition of early and late

operation in others and different follow up times. However, one common major limitation is that the time interval for the waiting period is calculated from the date of admission to the date of operation (i.e. calendar days), instead of the more precise calculation of number of hours from the exact time of admission to the operation.

Furthermore, many studies report patients operated within the same day of admission as < 24 hours while those operated day one after admission as > 24 hours. This misunderstanding is widespread in the literature. It is obvious that patients operated within the same day of admission without knowing the exact time for admission and operation could have waited anything between 0-24 hours. However, it is less obvious that even patients operated the day after admission could have been waited < 24 hours (it could be from few hours and upward). This imply that many patients will be misclassified when the exact times of admission and operations are not registered and may explain some of the diverging reports in the literature. Currently it is advised to use the exact time of admission and operation when calculating the waiting time for surgery.

Another potential flaw is to determine the interval between the injury and admission, since the time of the injury is often difficult to decide and in most situations is less exact. This is especially true for many of the hip fracture patients with cognitive impairment. One way to overcome this difficulty is to exclude all patients not admitted to the hospital on the same day of the injury.

1.3 CATABOLISM IN HIP FRACTURE PATIENTS

Hip fracture patients are mainly older adults with high prevalence of malnutrition[23-26]. As the patients with a hip fracture are already in a catabolic state initiated by their injury, these patients have a different metabolic situation from that in elective surgical patients with a basically normal metabolism before the operation.

A long waiting time for surgery means a long fasting time and several days of low caloric intake[27] which aggravate the catabolism. Studies have shown that fasting itself will induce a state of insulin resistance and catabolism[28].

Catabolism (Greek kata = downward + ballein = to throw) is the set of metabolic pathways that break down molecules into smaller units and release energy[29]. Catabolism therefore provides the chemical energy necessary for the maintenance and growth of cells during stress periods by breakdown of carbohydrates, fat and proteins.

The stress response to injury or trauma involves hormonal and metabolic changes which follow injury or trauma and are part of the systemic reaction to injury. The so-called classic catabolic hormones known since the early 20th century are cortisol, glucagon, and adrenaline (and other catecholamines).

In recent decades, many more substances with catabolic effects have been discovered, including pro-inflammatory cytokines[30]. Moreover, recent studies shown that the stress response in elderly hip fracture patients may differ than in young patients with exaggerated cortisol response[31].

The longer this stress period prevails the more of the body tissues will be broken down. Especially protein degradation is stimulated by the increased cortisol and cytokine concentrations. Predominantly skeletal muscle is broken down and there may be marked

weight loss and muscle wasting in patients after major surgical or traumatic injury[32]. Muscle break down will ultimately result in loss of muscle function. The elderly patients with hip fracture have little muscle reserve[24,33] and the pre-operative stress period needs to be minimized. And factors that might aggravate the stress response in these vulnerable patients should be avoided. Such factors are long fasting time, long periods of severe pain and prolonged immobilization in bed.

1.4 COGNITIVE IMPAIRMENT

Cognitive impairment is a descriptive term of all types of decline in cognitive function like memory, learning ability, orientation, intelligence, problem solving, reaction time, abstractions etc. Cognitive impairment is a continuum of different conditions from Mild Cognitive Impairment (MCI) to dementia. MCI is recently recognized as a clinical entity which is thought to be a transient state between normal aging and dementia[34]. MCI may be associated with functional impairment[35].

The most common causes of cognitive impairment in elderly are dementia and delirium[36]. Studies have shown that between 10%-56% of all hospitalized elderly patients have cognitive impairment and the rates are 3-6 times higher in hip fracture patients than other hospitalized patients[37,38]. The reason for this is that dementia is a risk factor for fall and fracture[39-45]. Moreover the trauma and the following stress, hospitalization and pain might affect the central nervous system resulting in delirium after a hip fracture.

It is important that all hip fracture patients are screened at admission for cognitive impairment. Besides measures to prevent and treat the delirium, a thorough understanding of the ability of a patient with a hip fracture to cooperate and follow postoperative regimens is crucial in the planning of the surgical treatment and the postoperative rehabilitation[46].

As the number of older people increases worldwide the number of patients with cognitive impairment will also rise[47]. Previous studies have shown that cognitive impairment is an important predictor of poor prognosis after hip fracture regarding walking ability, ADL, and return to independent living[48-51]. However, a few recent studies have reported that cognitive impairment per se does not significantly affect the functional gain in elderly patients with hip fracture if they were referred to rehabilitation[38,52,53]. Limitations of these studies include the small number of patients and the short follow-up periods.

Some studies indicate that hip fracture patients with cognitive impairment receive suboptimal care compared to cognitively intact patients[54,55]. Others have studied whether the type of surgical procedure affects functional outcome in patients with hip fractures and cognitive impairment[56,57]. Nonetheless, prospective studies investigating other potential predictors of long-term functional outcome in patients with hip fracture and cognitive impairment are lacking.

1.5 HIP FRACTURE IN YOUNG AND MIDDLE-AGED SUBJECTS

Femoral neck fracture in young adults (< 50 years old) are rare and account for only about 3% of the total hip fracture population[58-61]. The existing knowledge regarding demographics, risk factors as well as the mechanism of trauma in these patients are limited. The majority of the studies are retrospective including small numbers of patients[58,59,61,62]. Traditionally, energy traumas are often considered the leading cause of hip fracture at this age[58,59,63-65].

Hip fracture in the middle-aged subjects is seldom studied as an entity on its own. Instead, it is more commonly considered combined with hip fractures in the more frail elderly patients[66-68]. Besides, hip fracture quality registers like Swedish National Hip Fracture Registry (RIKSHÖFT)[1] includes only patients with hip fracture 50 years of age or older. The rationale behind this is the exponential increase in the incidence of hip fracture after this age. However, the background data, risk factors and the mechanism of trauma the middle-aged subjects might differ from those of elderly patients. Moreover, the majority of the middle-aged patients are still within the working age group. Early identification of patients at higher risk may facilitate timely started treatment of specific conditions that might be the cause of early osteoporosis and fracture.

Risk factors for osteoporosis and hip fracture are well described in the literature which includes life style related factors like smoking, high alcohol consumption, physical inactivity and other clinical risk factors like hypogonadism, early menopause, antiepileptic use, corticosteroid use or use of psychopharmaca, previous fracture in adult life for the patients or their parents, chronic disabling liver, lung or neuromuscular disease, diabetes mellitus, rheumatoid arthritis, underweight etc.[69-74]. However, the rate of these risk factors in the young and middle-age subjects with hip fracture is less well known.

1.6 BMD AND DXA

Bone mineral density (BMD) is a major determinant of bone strength. Densitometry by itself is first described for more than 100 years ago as dentist attempted to quantify the bone density in the mandible[75,76].

When an X-ray beam passes through a tissue some the energy will be attenuated by the tissue and the other part will be transmitted through the tissue. The ability of the tissue to attenuate X-rays is largely determined by tissue density. Different tissues will therefore attenuate/transmit X-ray photon energy differently. If it is possible to quantify the degree of attenuation, than it is possible to quantify tissue density as well. This is the basic principle behind absorptiometric techniques.

The absorption of X-rays is very sensitive to the calcium content of the tissue. This ability is utilized to calculate bone mineral content in the scanned bone. By dividing this amount by the measured area, an aerial bone mineral density (g/cm^2) can be calculated since the scan is two dimensional. The first densitometers were developed 1960s using single source of radiation and the technique is called single photon absorptiometry (SPA)[77]. SPA were only able to measure peripheral sites like forearm and heel because the measured site needed to be immersed in water to eliminate the effect of overlying soft tissue.

With development of densitometers with dual energy radiation source, central sites like the hip and the spine were readily examined without the need for water bath. The recently developed fan beam techniques shorten the scan time to 10-30 seconds for the hip and less than five minutes for the whole body.
The Dual X-ray Absorptiometry (DXA) is nowadays the most accurate and most commonly used non-invasive technique for measuring of bone mineral density (BMD) which is measured in g/cm^2. An absolute value is than related to either mean BMD in young healthy reference population or to mean BMD in a reference population of the same age and gender, where the number of standard deviations from the reference mean value denotes the T-score or the Z-score, respectively.

There are other non-invasive techniques used for measurement of BMD, e.g. Quantitative Computed Tomography (QCT) which gives volumetric bone density (g/cm^3); however QCT is more expensive and provides a higher radiation dose.

1.7 BODY COMPOSITION AND DXA

Determination of body composition (BC) is an important method for assessment of nutritional status of the patients. Anthropometric methods like body mass index (BMI), skinfold thickness and upper arm muscle circumference measurements are simple and widely used but less accurate methods for these purposes. A more accurate and valid method for measurement of BC is DXA. The photon attenuation principle mentioned above is used. The three components of body namely bone mineral, fat and lean (muscle) mass have different attenuation properties. The amounts of photon attenuation are measured at two different energies and numerous algorithms and software are used by various manufacturers for calculation of the three components[78].

The whole body DXA examination usually takes less than five minutes with patients lying in supine position. The radiation effective dose is small (5-7 μSV). Fat-free mass (FFM) is the sum of lean body mass and bone mineral. To eliminate the differences in FFM and body fat mass associated with differences in height, fat-free mass index (FFMI) and fat mass index (FMI) could be calculated by dividing the absolute values in kg by the square height in meter (kg/m^2)[79].

1.8 SARCOPENIA

Sarcopenia, which is defined as reduced muscle mass and muscle function[80] is mainly observed in the older population, but might also affect younger subjects due to illness or inactivity. Previous research have shown that low muscle mass is associated with increased risk for fall and fracture and could partly explain the increasing risk for hip fracture with increasing age[81-83]. However, knowledge about muscle mass in the young and middle-aged patients with femoral neck fracture is poor. Examination of body composition and their relations to trauma mechanism is interesting as such knowledge may indicate the need for specific preventive interventions in these particular age groups

1.9 RISK FACTORS FOR HIP FRACTURE

1.9.1 Osteoporosis

The reasons for hip fracture are multifactorial. Osteoporosis is a major contributing factor. Osteoporosis is a systemic skeletal disease that is relatively new in the medical field. The World Health Organization (WHO) defines osteoporosis 1993 as "A systemic skeletal disease characterised by low bone mass and microarchitectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture risk". The impact of osteoporosis as major risk for fragility fractures is widely recognized as a major health problem and the age-adjusted incidence of fragility fractures are increased in the Western countries[84].

In 1994, WHO published diagnostic criteria for definition of osteoporosis based on BMD at the hip, lumbar spine or forearm in postmenopausal women. These criteria were originally developed for epidemiological purposes, but it has become used even for clinical purposes. Recent advances in DXA measurement indicated that the same *T*-score derived from different sites and different techniques yields different information on the prevalence of osteoporosis and fracture risk. For these reasons a new reference standard for description of osteoporosis has been developed. The rationale behind these criteria are described by Kanis et al[85] and the following four categories are given for adult men and women using DXA measurement at the femoral neck. The recommended reference range is the Third National Health and Nutrition Examination Survey (NHANNES III) as reference data base for femoral neck measurements in women aged 20-29 years old.

1-Normal. A BMD value higher than 1 SD below the young adult female reference means (*T*-score $\geq$ -1 SD).
2-Osteopenia. A BMD value more than one 1 SD below the young female adult mean, but less than 2.5 SD below this value (*T*-score < -1 and > -2.5 SD).
3-Osteoprosis. A BMD value 2.5 SD or more below the young female adult mean (T-score $\leq$ -2.5 SD).
4- Sever osteoporosis (established osteoporosis). A T-score score $\leq$ -2.5 SD and one or more osteoporotic fracture.

In the young age patients (20-49 years), Z-score below -2 SD are considered as low bone mineral density (osteoporosis) according to recommendation by the International Society of Clinical Densitometry[86]

A number of risk factors for low BMD, i.e osteoporosis are identified like female gender, increasing age, genetic risk factors, physical inactivity, smoking, nutritional factors and low body weight[69,87,88]. Moreover, several factors for secondary causes for osteoporosis are identified. These includes type I (insulin dependent) diabetes, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hypogonadism or premature menopause (< 45 years), chronic malnutrition, or malabsorption and chronic liver disease[89].

It is estimated that hip fracture risk is increased by 2.6 fold with each standard deviation (SD) decrease in the femoral neck BMD[90]. Thus an individual with *Z*-score of -2 at the hip would have 2.6^2 or 7-fold higher risk than an individual with average BMD (Z-score = 0). Studies indicate that BMD has low sensitivity but high specificity for fracture prediction[91]. This means that the majority of patients with fracture would have a normal BMD but the fracture risk is high in patients with osteoporosis[92].

For these reasons a fracture assessment tool (FRAX®), has been developed by WHO to evaluate the fracture risk of patients[70]. It is based on individual patient models that integrate the risks associated with clinical risk factors as well BMD at the femoral neck. The FRAX® output is a 10-year probability of hip fracture and the 10-year probability of a major osteoporotic fracture (clinical spine, forearm, hip or shoulder fracture). However, it can only be used in patients 40 years and older[93]. The FRAX® models have been developed from studying population-based cohorts from Europe, North America, Asia and Australia.

1.9.2 Other risk factors

Although low BMD is a major risk for fracture there are several other clinical risk factors that contribute to fracture risk. Some of these factors are BMD dependent and others are independent of BMD. The predictive value of BMD can be enhanced by use of other factors, such as biochemical indices of bone resorption and clinical risk factors[94]. These clinical risk factors include age, a parental history of hip fracture, smoking, use of systemic corticosteroids, previous fracture in adult life, excess alcohol intake and rheumatoid arthritis. Furthermore, other risk factors like cognitive impairments and factors that increases fall risk are important contributing factors in the older populations[39,40,95]

2 AIMS OF THE STUDIES

STUDY I

The primary aim was to investigate whether the timing of surgery in hip fracture patients was associated with the patient's ability to return to independent living. The secondary aims was to study whether the timing of surgery had any influence on the Patient's risk of developing pressure ulcers, the length of the hospital stay, and mortality at 4 months follow up.

STUDY II

The aim was to find factors associated with preserved walking ability and ADL at 4- and 12-month follow-up in patients with femoral neck fracture and cognitive impairment.

STUDY III

The aim was to study the young and middle-aged patients with femoral neck fracture with main emphasis on background data and risk factors for osteoporosis and hip fracture.

STUDY IV

The aim was to examine BMD and body composition in the young and middle-aged patients with femoral neck fracture and their relation to the trauma mechanisms.

3 PATIENTS

3.1 ETHICS

The studies were conducted according to the Helsinki Declaration[96], and the protocols were approved by the local ethics committee. Written consent was obtained from all patients who participated in the studies. In patients with severe cognitive impairment, the informed consent was given by a close relative or caregiver whenever possible. The ethics committee agreed that even patients/proxies who did not provide "informed consent" could be included with regard to information not deemed to be potentially harmful for the patients.

3.2 INCLUDED PATIENTS

Patients included in Study I and II were derived from a large cohort study, the Stockholm Hip Fracture Group study. In this study all patients admitted for hip fracture to the four university hospitals in Stockholm (Danderyd Hospital, Stockholm Söder Hospital, Karolinska University Hospital, at Huddinge, and at Solna) during one year (2003) were consecutively included (n = 2213).
A flow chart presentation of the included patients in each study is shown in figure 1.
Age and gender distribution for all included patients (n = 2113) are presented in figure 2.

Figure 1. Flow chart showing included patients in each study.

Included in
- *study I* were 850 patients with hip fracture (≥ 50 years old) admitted to Danderyd Hospital and Karolinska University Hospital, at Huddinge.
- *study II* were 246 patients (≥ 66 years old) with femoral neck fracture and cognitive impairment.
- *study III and IV* were 185 young and middle age patients (20-69 years old) with femoral neck fractures admitted to four university hospitals in Stockholm between September 2002 and May 2006.

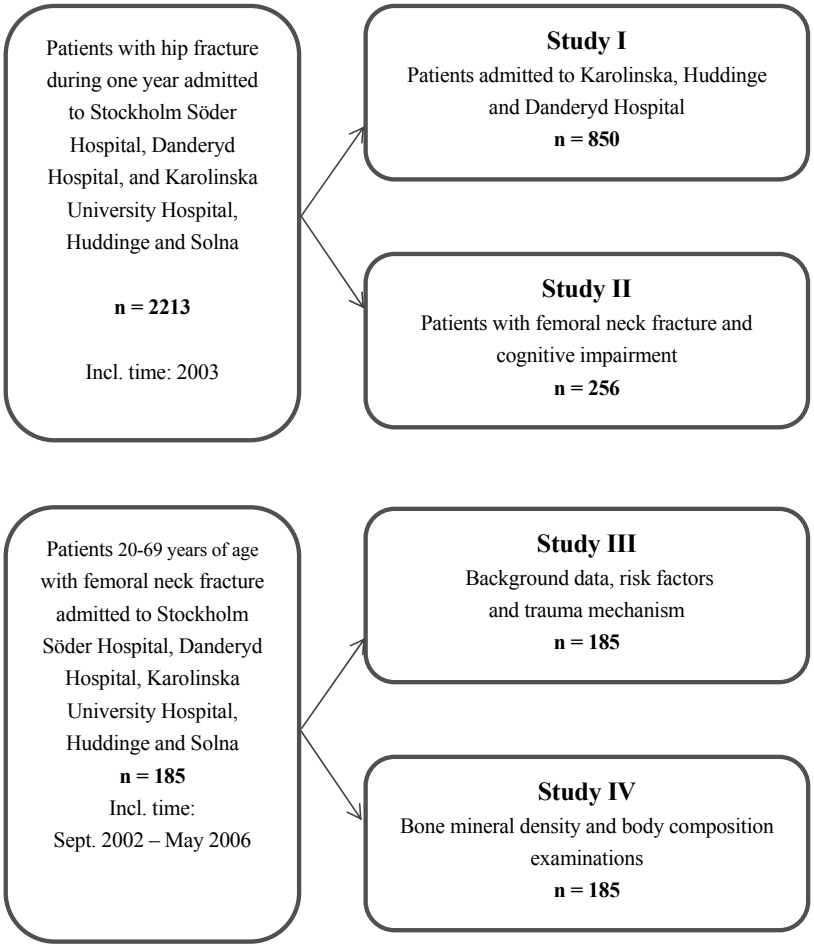
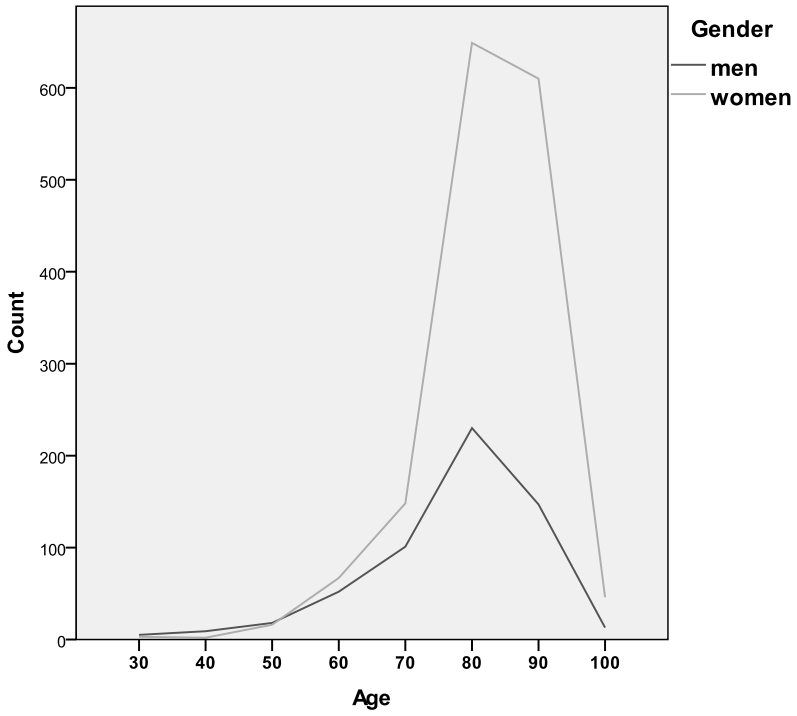


Figure 2. Age and gender distribution for all hip fracture patients admitted during one year (2003) to four hospitals in Stockholm.



3.2.1 Study I

3.2.1.1 Inclusion

The study group in this prospective study consisted of 850 consecutive patients with an acute hip fracture who were (≥ 50 years of age) admitted to two major hospitals (Danderyd and Karolinska University Hospital, at Huddinge) in Stockholm, Sweden, during one year (2003). Thirty-one patients with a pathological fracture and seventy-five patients who arrived at the hospital later than one calendar day after the time of injury were excluded. Thus, the remaining 744 patients were included in the analyses. Mean age 81 years (SD 9).

3.2.1.2 Follow up

Five hundred and two patients who had been admitted from an independent living situation were still alive at four months and were therefore available for the analysis of the ability to return to independent living within four months. Among the forty-two patients with dementia only thirteen patients (31%) were able to return to independent living. No additional analysis was performed in this group because of the limited number of patients. Of the 456 patients (91%) without dementia, 80% of them were able to return to independent living within four months.

3.2.2 Study II

3.2.2.1 Inclusion

Included were 246 patients (≥ 66 years) with femoral neck fractures and cognitive impairment defined as previously diagnosed dementia or SPMSQ (0-2 points) and able to walk with or without walking aids admitted to four university hospitals in Stockholm during one year (2003). Mean age was 84 years (SD 6). A total of nineteen patients (8%) died before hospital discharge. Of the remaining 227 patients, 81 (36%) were discharged to rehabilitation units, and 146 (64%) were discharged directly to their previous place of residence.

3.2.2.2 Follow up

The numbers of patients who died prior to 4-month and 12-months follow-ups were 58 (24%) and 99 (40%), respectively. Of the survivors at the 4 and 12 moths follow-up, information on walking ability and use of walking aids was available for 162 (86%) and 130 (86%) respectively. Among survivors at the 4-month and 12-month follow-ups, information on ADL was available for 162 patients (86%) and 122 (83%) patients, respectively.

3.2.3 Study III and IV

Included were 185 young and middle-aged patients (20-69 years) with femoral neck fracture admitted to the four university hospitals in Stockholm between September 2002 and May 2006.
Inclusion criteria:

- Absence of sever cognitive impairment (SPMSQ ≥ 3).
- Absence of psychotic disease.
- Independent living.
- Able to walk with or without walking aids.

Exclusion criteria:

- Displaced fracture > 48 hours.
- Pathological fracture.
- RA or other previous pathology involving the fractured hip.
- Chronic renal failure.
- Hyperparathyroidism.

To examine how representative our study patients were, registrations of all hip fracture patients were done during one year (2003). The analysis showed that 80% of the young patients and 50% of the middle-aged patients were included in the present study (Figure 3). The study population had better ASA-score, EuroQol, ADL Katz index and less use of walking aids. This discrepancy probably due to the fact that patients from institutions, those with severe cognitive impairment or unable to walk not were included in the study. Otherwise there were no differences in gender distribution, rate of smoking or fracture type (Table 1).

Figure 3. Flow chart of all patients with femoral neck fracture (1121/2213) during one year (2003).

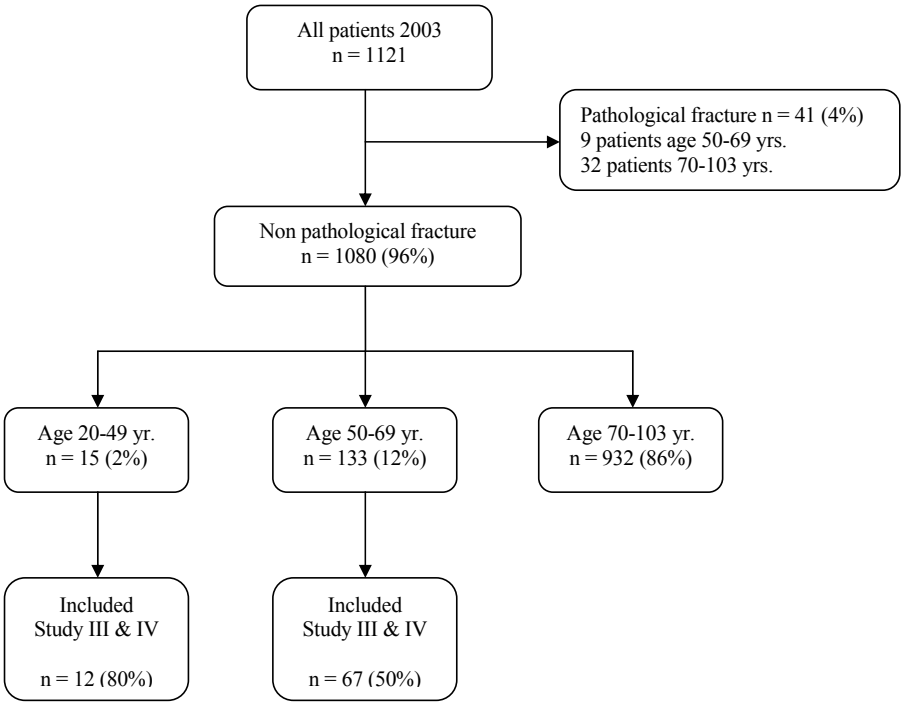


Table 1. Characteristics of the included (young and middle aged) patients compared with none included during one year (2003).

	All patients	**Included**	**Non-Included**	***p*-value**
Number (%)	148 (100)	79 (53)	69 (47)	
Age mean (SD)	60 (8)	57 (9)	62 (6)	< 0.001
Age distribution n (%)				
15-49 yr	15 (10)	12 (15)	3 (4)	0.029
50-69 yr	133 (90)	67 (85)	66 (96)	
Gender n (%)				
Men	63 (43)	36 (46)	27 (39)	0.429
Women	85 (57)	43 (54)	42 (61)	
ASA score[a] n (%)				
1	35 (24)	31 (41)	4 (6)	< 0.001
2	62 (43)	32 (42)	30 (44)	
3	43 (30)	12 (16)	31 (46)	
4	4 (3)	1 (1)	3 (4)	
Comorbidities[b] n (%)				
0	71 (49)	50 (63)	21 (32)	0.002
1	31(21)	12 (15)	19 (29)	
2	30 (20)	12 (15)	18 (27)	
≥ 3	13 (10)	5 (7)	8 (12)	
EuroQol mean[c] (SD)	0.74 (0.28)	0.85 (0.22)	0.63 (0.35)	< 0.001
Living alone[d] n (%)				
Yes	57 (42)	30 (38)	27 (47)	0.314
No	80 (58)	49 (62)	31(53)	
ADL Katze n (%)				
A	119 (84)	73 (92)	46 (74)	0.009
B	9 (6)	3 (4)	6 (10)	
C-G	13 (10)	3 /4)	10 (16)	
Smoking[f]	51 (36)	26 (51)	25 (49)	0.377
Walking aids[g] n (%)				
None	104 (71)	71 (90)	33 (49)	< 0.001
one stick	14 (10)	4 (5)	10 (15)	
Two sticks or frame	28 (29)	4 (5)	24 (36)	
Fracture type n (%)				
Displaced	98 (66)	49 (62)	49 (71)	0.249
Un-displaced	50 (34)	30 (38)	20 (29)	

[a] missing n = 4, [b] missing n = 3, c missing n = 20, [d] 11 patients from Institution , [e] missing n = 7
f missing n = 8, g missing n = 2

4 METHODS

4.1 INCLUSION DATA

4.1.1 Study I and II

At the time of inclusion the following variables were recorded: age, sex, pre-fracture living condition, walking ability, walking aids, ADL Katz index, previous diagnosis of dementia, SPMSQ, number of comorbidities, ASA score, discharge to rehabilitation, post-operative complications, fracture type and treatment modality. In patients with severe cognitive impairment, the living condition, walking ability, use of walking aids and ADL were assessed by means of a report by a proxy (a close relative or caregiver). Proxy-patient agreement is in general good for concrete observable variables and moderately reliable for subjective variables[97,98]. In addition in *Study I* waiting time for operation and reason for delay for surgery were recorded.

4.1.2 Study III and IV

At admission, patients basics characteristics were registered; age, gender, the prefracture living conditions, walking ability, ADL Katz index, ASA score, number of co-morbidities, walking ability, use of walking aids, quality of life before the fracture, alcohol consumption AUDIT, smoking, previous history of falling during the last year, previous fractures for patients and their parents as well as the mechanism of injury. The following variables were registered as risk factors for osteoporosis and fracture[69-71] which includes life style factors like smoking, high alcohol AUDIT score, and other risk factors like hypogonadism, early menopause, antiepileptic use, corticosteroid use or use of psychopharmaca, previous fracture in adult life for the patients or their parents, chronic disabling liver, lung or neuromuscular disease, diabetes mellitus, rheumatoid arthritis and underweight.

4.2 FOLLOW UP

4.2.1 Study I

The four-month follow-up was carried out by telephone interviews, regular out patient's visits or using mailed questionnaires. In case of re-admissions patients medical records were reviewed. The total length of hospitalization, including rehabilitation during the first four months, was calculated from the date of admission.
Living conditions at 4 months and before fracture were compared. Mortality data were obtained from the hospital discharge register.

4.2.2 Study II

The follow-ups at 4 and 12 months were carried out via telephone interviews with the proxy. All patients reporting problems were scheduled for a re-check, including x-ray examinations. Date of death was registered when appropriate. Walking ability, ADL index, healing complications, reoperation, general major complications (e.g. pneumonia, heart failure, myocardial infarction, pulmonary embolism, renal failure, cerebrovascular accident, gastrointestinal bleeding), and place of residence were recorded.
Walking ability (outdoors, indoors, or unable to walk) at 4-month and 12-month follow-ups was compared with walking ability at admission and categorized as "preserved walking ability" if no change had occurred. ADL Katz index at follow-up was compared with corresponding ADL index at admission and similarly categorized. Length of hospital stay (LOS), including stay at the rehabilitation unit was calculated from the date of admission.
Mortality data were obtained from the hospital discharge register.

4.3 WAITING TIME FOR OPERATION

In *Study I* the exact time of admission to the emergency ward and start of surgery was registered. Waiting time for operation (h) is defined as the time between hospital admission and start of operation. We compared patients who had surgery within any of the three cut-off limits (24, 36, and 48 hours) with those who had the operation later, i.e., patients who had the operation before 24 hours were compared with those who had the operation after 24 hours and so on. The reason for a delay of surgery was defined as patient-related, i.e. medical reasons, or as system-related, i.e. unavailability of operating theatre for different reasons.

4.4 LIVING CONDITION

The living conditions of the patients in all 4 studies were recorded as independent (own home or block of service flats) or institutionalized (living in nursing home or residential care home for demented patients). Patients from independent living conditions were also recorded whether they were living alone or together with someone.

4.5 WALKING ABILITY

Walking ability in all 4 studies was categorized as walking outdoors (alone or accompanied), indoors (alone or accompanied) or unable to walk.

4.6 WALKING AIDS

The uses of walking aids in all 4 studies were recorded as follows:
none, one aid (cane or crutch), two aids (two canes or two crutches), walking frame or wheel-chair.

4.7 ADL

The Katz index of activities of daily living (ADL) indicates independence or dependence in bathing, dressing, going to the toilet, transferring, continence, and feeding[99]. ADL index A indicates independence in all six functions, and index B indicates independence in all but one of the six functions. Indexes C through G indicate dependence in bathing and at least one other function.

4.8 ASA

The ASA physical status classification system was adopted by the American Society of Anesthesiologists (ASA) in 1963. The ASA score asses the fitness of the patient before surgery according to five categories[100]:

- ASA 1: A normal healthy patient.
- ASA 2: Patient with mild systemic disease.
- ASA 3: Patient with severe systemic disease.
- ASA 4: Patient with severe systemic disease that is a constant threat to life.
- ASA 5: Moribund patient who is not expected to survive with or without surgery.

ASA classifications were carried out by the attending anaesthesiologists.
In *Study I and II* ASA classes were categorized as ASA 1-2, ASA 3 and ASA 4-5.
In *Study III* the original classification were used.

4.9 PRESSURE ULCER

A PU is defined as damage to skin and underlying tissues caused by pressure, shear or friction, or a combination of these factors[101]. Pressure ulcers were classified according to the Treatment Guidelines of the European Pressure Ulcer Advisory Panel (EPUAP)[101,102].

Grade I:	indicates non-blanchable erythema of intact skin.
Grade II:	partial-thickness skin loss involving epidermis, dermis, or both; the ulcer is superficial and presents clinically as an abrasion or blister.
Grade III:	full thickness skin loss involving damage to or necrosis of subcutaneous tissue that may extend down to, but not through, the underlying fascia.
Grade IV:	extensive destruction, tissue necrosis, or damage to muscle, bone, or supporting structures with or without full-thickness skin loss.

Non-blanchable erythema is frequently assessed incorrectly as blanchable erythema [103]. Therefore, patients with a grade-II, III, or IV ulcer were classified as having a pressure ulcer (Study I). Pressure ulcers were recorded by the responsible nurse.

4.10 SPMSQ

There are several instruments that can be used for screening of cognitive function including Short Portable Mental Status Questionnaire (SPMSQ) and Mini-Mental State Examination (MMSE). The most widely used screening test for cognitive function is the MMSE test, which consists of 13 items. It involves manual handling and drawing, which preferably is conducted when the patient is sitting. Therefore, the MMSE is not perfect for assessing cognition in bed-bound patients, such as subjects with a recent acute hip fracture.

SPMSQ is a validated instrument for assessment of cognitive function. The SPMSQ has been validated as having a similar sensitivity and specificity to that of the MMSE[104,105]. Smith et al[106] in a review article concluded that the SPMSQ test is as good screening test for cognitive impairment as the MMSE. The SPMSQ is simple to administer, the interrater reliability was not considered to be a problem and the test-retest reliability has been shown to be good ($r = 0.80$)[104].

The Short Portable Mental Status Questionnaire (SPMSQ) is a ten item questionnaire that assesses the patient's cognitive function and classifies it into four levels of cognitive function. The questionnaire and the classification of cognitive function are shown in Table 2.

Table 2. The Short Portable Mental Status Questionnaire.

	Questionnaire	Correct answer	Incorrect answer
1.	What is the date today?	1 points	0 points
2.	What day of the week is it?	1 points	0 points
3.	What is the name of this place?	1 points	0 points
4.	What is your telephone number or, alternatively, street address?	1 points	0 points
5.	How old are you?	1 points	0 points
6.	When were you born?	1 points	0 points
7.	Who is the prime minister now?	1 points	0 points
8.	Who was prime minister before him or her?	1 points	0 points
9.	What was your mother's maiden name?	1 points	0 points
10.	Subtract 3 from 20 and keep subtracting 3 from each new.	1 points	0 points

8-10	correct answers: *Intact cognitive function*
6-7	correct answers: *Mild cognitive impairment*
3-5	correct answers: *Moderate cognitive impairment*
0-2	correct answers: *Severe cognitive impairment*

4.11 QUALITY OF LIFE

The health related quality of life (HRQoL) was rated by using the EQ-5D[107] and patients were asked to rate their HRQoL the week before the fracture. We used the preference scores (EQ-5D index scores) generated from a large UK population (UK EQ-5D index Tariff)[108] when calculating the scores of our study population. An EQ-5D index score of 0 indicated the worst possible health status and a score of 1 indicated full health. The EQ-5D is validated for use in elderly patients with hip fracture[109].

4.12 ALCOHOL AUDIT

Alcohol consumption was evaluated with Alcohol Use Disorder Identification Test (AUDIT) which is a validated instrument that identifies hazardous and harmful alcohol use, as well as possible dependence[110]. It consists of ten items supposed to measure three different aspects of drinking, i.e. alcohol use (the first 3 items), dependence (the following 4 items) and problems resulting from drinking (the last 3 items). Studies indicate that the AUDIT has good sensitivity (an average of 0.86) and specificity (average of 0.89) at a threshold requirement of 8 points[111,112]. For women, a lower limit of 5 is advised. The test-retest reliability for AUDIT is good (0.97)[113].

4.13 BONE MINERAL DENSITY MEASUREMENT WITH DXA

Bone mineral density (BMD) was examined by Dual Energy X-ray Absorptiometry (DXA) using Hologic QDR-4500A densitometer (Hologic, Inc., Waltham, MA. USA) in one center (Karolinska Hospital, Solna), GE Lunar DPX-L in another center (Danderyd Hospital) and GE Lunar Prodigy (Madison, WI, USA) in the other two centers (Karolinska Hospital, Huddinge and Stockholm Söder Hospital). Both the un-fractured hip (femoral neck, total hip, trochanter region and Ward´s triangle) and the whole body BMD were determined.

The leg rotating fixators provided by the manufacturer were used to standardize the position of the patients during DXA-examination of the hip. Results were obtained both as absolute areal density values in grams per square centimeter and as standard deviation units related either to the mean value for young healthy adults (T-score) or to the age- and sex-matched mean value (Z-score). The T- and Z-scores were calculated using the manufacturer's standard normal reference database.

To decrease the variation in bone mineral density between different centers, equations for a standardized bone mineral density (sBMD) for sub-regions of the femur [114] were used to create sBMD for the total hip and femoral neck. The DXA examinations of the hip were performed in 160 patients (87%). In 151 (94%) of them the DXA examination was made within two weeks after admission and in 9 patients (6%) within 3-24 weeks after the fracture.

The WHO criteria for diagnosis of osteoporosis were used in the middle aged patients (50-69 years). T-score values greater than or equal to -1 SD were considered to be normal. T-score values < -1 and > -2.5 SD were considered as osteopenia, whereas a T-score value less than or equal to -2.5 SD were considered as osteoporosis[71]. In the young patients (20-49 years), Z-score below -2 SD was considered as a low bone mineral density i.e.

osteoporosis, according to recommendations by the International Society of Clinical Densitometry[86].

4.1 MECHANISM OF TRAUMA

In S*tudy III and IV* the mechanism of trauma was classified as low-energy trauma (simple fall), sport injury (mainly bicycling, ice skating) and high-energy trauma (traffic accident, riding accident and fall from height).

4.2 BODY COMPOSITION MEASUREMENT WITH DXA

Body composition (BC) was examined with whole-body DXA in 171 patients (92%). In 161 patients (94%) DXA were performed within two weeks after admission and in 10 patients (6%) within 3-24 weeks after the fracture. Lean body mass, fat mass and bone mineral content were obtained as absolute values in kg. Fat-free mass (FFM) is the sum of lean body mass and bone mineral. To eliminate the differences in FFM and body fat mass associated with differences in height, fat-free mass index (FFMI) and fat mass index (FMI) was calculated by dividing the absolute values in kg by the square height in meter (kg/m2)[79].

For definition of sarcopenia, cut-off values for FFMI below the 10th percentile for age and sex matched European reference population[79] was used as described by Kyle et al[115]. No standardization was performed for body composition as several studies have shown good correlation between different DXA systems (R2 = 0.85 to 0.99)[116,117].

4.3 STATISTICAL METHODS

The statistical software used was SPSS 19.0 for Windows (IBM, SPSS Statistics). Normally distributed independent variables were tested for differences with the Student t test. The Kruskal-Wallis test was used to compare variables measured on an ordinal scale or continuous data not normally distributed. Contingency tables were tested for differences with the chi-square test. Logistic regression analyses were performed to adjust dichotomous variables, and linear regression analyses were used to adjust continuous variables. Covariables used in the regression analyses as possible confounders were specified for each analysis. Factors that had previously been reported to be good predictors of the particular outcome were used for adjustments and were first tested in a univariate analysis. Possible confounders were entered into a stepwise regression model to identify independent predictors of outcome. A p value of < 0.05 was considered significant.

5 SUMMARY OF THE STUDIES

5.1 STUDY I

Early operation on patients with a hip fracture improved the ability to return to independent living. A prospective study of 850 patients.

Objective: The impact of waiting time for surgery on patients with hip fracture was studied with a main focus on mortality and post-operative complications. Since hip fracture is a leading cause of institutionalization of older people, there is a pressing need to find modifiable factors that may impact the patient's ability to return to independent living.

Methods: Included were 850 patients ≥ 50 years, living independently who were admitted to two hospitals in Stockholm (Danderyd and Karolinska, Huddinge) over a twelve-month period 2003. Patients with pathological fracture (n = 31) and patients who presented to the hospital more than 24 hours post-fracture (n = 75) were excluded. The exact time of hospital admission and surgery were recorded. Three cut-off limits (24, 36, and 48 hours) were defined for comparison of early and late surgery.

Results: Only 48% of patients had surgery within 24 hours of admission. About 69% of delayed operations, i.e. > 24 hours of admission were due to system reasons, i.e. lack of resources, while 31% were related to patient factors i.e. medical reasons.

- Return to independent living: The analysis included only patients without dementia (n = 456). Among patients operated within 24 hours, 85% were able to return to independent living, compared to 82% in those who were operated > 24 hours after admission; OR 0.86 (95% CI; 0.45 to 1.65), (p value NS). The corresponding figures using the 36-hour cut-off were 86% and 77%, OR 0.44 (95% CI; 0.21 to 0.90), ($P < 0.05$) and for the 48-hour cut-off 85% and 73%, OR 0.33 (95% CI; 0.14 to 0.78), ($p < 0.01$), respectively. The differences were adjusted for age, gender, pre-fracture walking ability, whether patient lived with someone, ASA score, treatment modality, re-operation and reason for delay of surgery.

- Pressure ulcers: Six percent of patients operated within twenty-four hours developed pressure ulcers, compared with 10% of patients who had surgery later, OR 2.19 (95% CI; 1.21 to 3.96), ($P < 0.01$). The corresponding figures for the thirty-six-hour cut-off limit were 6% and 15%, OR 3.42 (95% CI; 1.94 to 6.04), ($p < 0.001$), and for the forty-eight hour cut-off limit 6% and 20%, OR 4.34 (95% CI; 2.34 to 8.04), ($p < 0.001$), respectively. The analyses were adjusted for age, pre-fracture walking ability, dementia, ASA score, and duration of surgery.

- Length of hospital stay: Median length of hospital stay including rehabilitation was 14 days for patients operated within 24 hours compared with 18 days for those operated later ($p < 0.001$). The corresponding figures for the 36-hour cut-off limit were 15 and 19 days ($p < 0.001$) and for the 48-hour cut-off limit 15 and 21 days ($p < 0.001$), respectively. A linear regression analysis showed a significant relationship between waiting time for surgery (hours) and length of hospital stay (days) after adjustment for age, pre-fracture living conditions, pre-fracture walking ability, dementia, ASA score, re-operation, and reason for surgical delay ($p < 0.01$). The following formula was calculated: hospital stay in

days = (0.148 x delay in hours). Accordingly, total length of hospital stay was increased by one day for every 6.75 hours of surgical delay.
- Mortality: Four-month mortality was 14.5% with no significant difference between early and late surgery at all three cut-off limits.
Conclusions: Early surgery on patients with hip fractures is associated with improved ability to return to independent living, reduced incidence of pressure ulcers, and shortened hospital stay. High priority should be given to reduce the system-related delays, i.e. those caused by lack of resources.

5.2 STUDY II

Does rehabilitation matter in patients with femoral neck fracture and cognitive impairment? A prospective study of 246 patients

Objective: Patients with cognitive impairment have a higher rate of falls and fractures. As the number of older people increases worldwide, the number of hip fracture patients with impaired cognitive function will also rise. Previous studies have shown that hip fracture patients with cognitive impairment have poor prognosis with reduced walking ability and increased need for ADL support, as well as an increased burden on patients, relatives, and society. Factors associated with preservation of walking ability and ADL functions after hip fracture need to be identified in this group of patients.
Methods: Included were 246 patients with femoral neck fracture, ≥ 66 years of age, with cognitive impairment, i.e. a diagnosis of dementia and/or SPMSQ score 0-2 points, but capable of walking. Walking ability (outdoors, indoors, or unable to walk) and ADL Katz index (A to G) at 4- and 12-month follow-ups were compared with admission scores, and categorized as "preserved walking ability" and "preserved ADL index" if no change had occurred. Length of hospital stay, including rehabilitation, was recorded. Patients who became wheelchair-bound at 4 and 12 months were also recorded. The following factors were used in the stepwise multiple logistic regression analyses to identify factors associated with specific outcomes: age, gender, ASA score, walking ability, ADL Katz index, fracture type, surgical method, discharge to rehabilitation, re-operations, and major complications.
Results: Sixty-three patients (25%) had undisplaced fractures and were operated with internal fixation. One hundred eighty-three patients (75%) had a displaced fracture. Of these, 70 (38%) were operated with internal fixation, 70 (38%) underwent uncemented hemiarthroplasy (HA) using Austin Moore implants, and 43 (24%) underwent cemented HA using the Exeter™ stem with a large head.

One hundred patients were admitted from their own homes and 70% of them were discharged to rehabilitation units after surgery, while 125 patients were admitted from institutions, of which 8% (n = 10**)** were discharged to rehabilitation.
- Preserved walking ability: At 4-month follow-up 62% of patients had preserved walking ability. The corresponding figure at 12 months was 57%. Discharge to rehabilitation units was a factor associated with preserved walking ability at both time points, with OR 2.84 (95% CI; 1.16 – 6.90), (p = 0.022) at 4-month follow-up and OR 2.83 (95% CI; 1.10 – 7.26), (p = 0.03) at 12-month follow-up. For both follow-up time points, walking ability prior to fracture was also significantly related to post-operative walking capacity, whereas surgical method was not. The logistic regression analyses were

adjusted for age, gender, ASA score, fracture type, and surgical method. The model correctly predicted preserved walking ability in 76% of patients at both time points.
- Preserved ADL Katz index: At 4- and 12-month follow-up respectively, 57% and 48% of patients had preserved ADL index. Again discharge to rehabilitation unit were significantly associated with preserved ADL index at both time points: OR 4.24 (95% CI; 1.61 – 11.17), (p = 0.003) at 4-month and OR 5.33 (95% CI; 1.44 – 19.65), (p = 0.012) at 12-month follow-up, respectively. Pre-fracture ADL status was also significantly associated with preserved ADL index, while surgical method was not. The model correctly predicted preserved ADL index in 70% of patients at 4 months and 80% at 12 months.
- Wheelchair dependence: At 4-month follow-up, 22% of patients were wheelchair-bound. The corresponding figure for 12-month follow-up was 28%. Patients discharged to a rehabilitation unit were less likely to become wheelchair-bound, OR 0.26 (95% CI; 0.08–0.83), (p = 0.024) at 4-month and OR 0.36 (95% CI; 0.13–0.99), (p = 0 .049) at 12-month follow-up. At 4-month follow-up, major reoperations, major complications, and age were also significant related to post-operative wheelchair dependence. The model correctly predicted wheelchair dependence in 78% of patients. At 12-month follow-up, only major complications and discharge to rehabilitation unit were significant. The model correctly predicted wheelchair dependence in 72% of patients. Surgical method was not significant at either time point. The logistic regression analyses were adjusted for age, gender, ASA score, fracture type, walking aids prior to fracture, and surgical method.
Conclusions: Discharge to rehabilitation, a factor over which we have control, rather than surgical method was the strongest factor associated with preserved walking ability and ADL index in patients with femoral neck fracture and cognitive impairment. The patient's degree of function prior to fracture (a factor over which we have no control) displayed corresponding relationships. It is likely that patients with impaired cognitive function have difficulties coping with their new situation after hip fracture and may need more support from a rehabilitation team. Availability of rehabilitation should be improved.

5.3 STUDY III

One or More Risk Factors for Osteoporosis in the Majority of Young and Middle-Aged Patients with Femoral Neck Fracture, Regardless of Mechanism of Trauma

Objective: In the older population, 98% of hip fractures result from simple falls. However, the majority of studies in young patients with hip fractures have reported an increased incidence of high-energy trauma. Studies on middle-aged patients are sparse. The aims of this study were to investigate background data, explore risk factors for osteoporosis and fractures, and record mechanism of trauma among young and middle-aged patients with femoral neck fracture.
Methods: Included were 185 consecutive young and middle-aged patients (20-69 years) with femoral neck fracture who were capable of walking. At inclusion several variables were registered including age, gender, ASA score, and medications. Alcohol consumption was evaluated using the Alcohol Use Disorder Identification Test (AUDIT). The following variables were considered to be risk factors for osteoporosis and fracture and included lifestyle factors such as smoking and high alcohol AUDIT score, as well as other risk factors such as hypogonadism, early menopause, use of antiepileptics, corticosteroids, or psychopharmaca, previous fracture in adult life for patients or their parents, chronic

disabling hepatic, pulmonary, or neuromuscular disease, diabetes mellitus, rheumatoid arthritis, and underweight. The mechanism of injury was classified as low-energy trauma (simple falls), sport injury (mainly bicycling, ice skating), and high-energy trauma (traffic accident, riding accident, and falls from height).

Results: There were 27 patients (15%) in the young age group (20-49 years) and 158 patients (85%) in the middle age group (50-69 years).

- Background data: In the young age group 70% were men, compared with 44% in the middle age group, ($p = 0.001$). The majority of young patients, 67%, had an ASA score of 1, compared with 32% of middle-aged patients ($p = 0.004$). Thirty per cent used medications, compared with 61% of the middle-aged patients ($p = 0.01$). Frequency of smoking was 22% among young patients, compared with 43% among middle-aged patients ($p = 0.04$). A total of 47 patients (26%) reported high alcohol consumption according to AUDIT in both age groups. Of the patients with high alcohol consumption the fracture was due to low-energy trauma in 92%, sport injury in 4%, and high-energy trauma in 4%. The corresponding figures for patients with low alcohol consumption were 70%, 21%, and 9%, respectively ($p = 0.011$).

- **Risk factors**: One or more risk factors for osteoporosis and fractures were present in 81% of the young age group and 82% of middle-aged patients ($p=0.92$). Among patients with low-energy trauma, 86% had one or more risk factors for osteoporosis and fractures. Corresponding figures for sport injury were 66% and 79% for young and middle-aged patients with high-energy trauma ($p = 0.019$).

- Mechanism of trauma: In the young age group, fractures occurred as a result of low-energy trauma in 44%, sport injury in 41%, and high-energy trauma in only 15%. The corresponding figures for middle-aged patients were 80%, 13%, and 7% respectively ($p < 0.001$).

Conclusions: High-energy trauma was the cause of hip fracture in a minority of both young and middle-aged patients, in contrast to what has been reported earlier in the young age patients. It would seem that lifestyle factors and other non-trauma related risk factors appear to be the main contributors to the occurrence of hip fracture in both age groups. Further studies are needed to investigate the importance of individual risk factors in young and middle-aged patients with hip fracture. Middle-aged patients have higher morbidity and higher medication use compared with the young group of patients, which might have an effect on hip fracture outcome

5.4 STUDY IV

Low Bone Mineral Density and Fat-free mass in Young and Middle-Aged Patients with Femoral Neck Fracture

Objective: Low bone mass and reduced muscle mass are predisposing factors for fracture and are seen mainly in the older population. Knowledge regarding bone mass and muscle mass in younger age groups with femoral neck fracture is limited. The aim of this study was to examine bone mineral density (BMD) and body composition in young and middle-aged patients with hip fracture. We also wanted to study whether there was a relationship between BMD, body composition, and mechanism of trauma.

Methods: Included were 185 young and middle-aged patients (20-69 years) with femoral neck fractures. Bone mineral density (BMD) and lean body mass and fat mass (FM) were

determined by DXA. Fat-free mass (FFM) is the sum of BMD and lean body mass. FFM index (FFMI) and FM index (FMI) were calculated as the ratio of FFM (kg), FM (kg), and height squared (m^2). Body mass index (BMI) was calculated in a similar way, using ratio of body weight and height squared. Mechanisms of trauma were classified as low-energy trauma, sport injury, or high-energy trauma.

Results:

-Bone mineral density (BMD): In the young patient group, BMD at the femoral neck was below mean for age in all patients, and 26% had osteoporosis (i.e. Z-score ≤ -2 SD). Among middle-aged patients, 90% had osteopenia (56%), (i.e. T-score value < -1 and >-2.5 SD) or osteoporosis (34%), (i.e. T-score ≤ -2.5 SD) at the femoral neck. Median sBMD for the femoral neck was 702, 740, and 803 mg/cm^2 ($p = 0.018$) in patients with low-energy trauma, sport injury, and high-energy trauma, respectively. These variations remained significant after adjustments for gender ($p = 0.015$) and age group ($p = 0.036$).

- Body composition: In all, 59% of patients had normal weight (i.e. BMI 18.5-24.99) and 38% were overweight or obese (i.e. BMI > 25). Only five patients (3%) were underweight by the WHO cut-off of BMI < 18.5, whereas 11 patients (9%) had BMI < 20, which is usually used as a cut-off for underweight in Western societies. However, DXA scans revealed that 36% of the whole study population had a FFMI below the 10^{th} percentile of an age- and gender-matched reference population (i.e. sarcopenic). Median FFMI was 15.9, 17.7 and 17.5 kg/m^2 ($p = 0.001$) in patients with low-energy trauma, sport injury, and high-energy trauma, respectively. Median FMI was 7.7, 6.1 and 7.0 kg/m^2 ($p = 0.044$) in patients with low-energy trauma, sport injury, and high-energy trauma, respectively. Differences in FFMI due to mechanism of trauma remained significant after adjustments for gender ($p = 0.001$) and age group ($p = 0.001$). Variations in FMI were lost after adjustments for gender ($p = 0.117$) and age group ($p = 0.06$).

Conclusions: The vast majority of young and middle-aged patients with femoral neck fracture had a BMD below mean for age, regardless of mechanism of trauma, while about one quarter to one third had osteoporosis. Our findings suggest that BMD should be measured in all young and middle-aged patients (20-69 years) with hip fracture, regardless of mechanism of trauma. Furthermore, the high incidence of low muscle mass despite apparently normal or high BMI suggests that sarcopenia may be a predisposing factor for hip fracture. Future intervention studies should consider measures to counteract both osteoporosis and sarcopenia in these age groups.

6 DISCUSSION

The overall aim of this thesis was to assess the effect of some less considered risk factors for the outcome after hip fracture surgery, as well as to focus on groups of hip fracture patients that are somewhat outside the main stream of hip fracture research, i.e. patients with cognitive impairments and younger patients.

First, the effect of waiting time for operation on outcome was evaluated (*study I*). Next, hip fracture patients with cognitive impairment were focused in order to find factors associated with preserved walking ability and ADL (*Study II*). The third objective was to describe background data and risk factors in young and middle-aged patients with femoral neck fracture (*Study III*), and finally to investigate body composition together with BMD in young patients with hip fracture (< 70 years old) and their relation to trauma mechanisms in this particular age groups (*Study IV*)

6.1 WAITING TIME FOR OPERATION

One of the major goals of hip fracture managements is to enable patients to regain prefracture level of function and living conditions, not just to achieve a successful surgical management[118,119]. Our results indicate that prolonged waiting time for hip fracture surgery is associated with deteriorated ability to return to independent living, higher incidence for pressure ulcers and longer hospital stay. The negative influence of prolonged waiting time for operation was still significant after adjustment for several confounding factors including the reason for late operation indicating that the delay per se is an important factor. For this reason, the indication of time-consuming preoperative investigations of the hip fracture patients should be balanced against the expected negative influence of prolonged waiting time. However, in study I the major reason for delays were not due to prolonged medical examinations, but rather system related, e.g. unavailability of operating theatre for a variety of reasons. More efforts are needed to analyze and in the future avoid system-related causes of delay of surgery.

Our results from study I are consistent with a study by Siegmeth et al (2005) reporting that early operation was related to improved ability to return to the original residence[13]. Furthermore, Fox et al (1994) showed that system-related delays for surgery could predict the need for discharge to nursing home care.

Several other studies have investigated the influence of patient related factors on the ability to return to previous independent living e. g. age, cognitive function, living with someone, comorbidity and mobility.[15,48,119-126]. However, the majority of these factors cannot be influenced by the health care providers, whereas waiting time for surgery is indeed a factor that can be.

The hip fracture patients are in general elderly with low BMI and low muscle mass[23-25,127]. The normal stress reaction to a trauma usually starts within minutes after the injury with an increased secretion of catabolic hormones[128,129]. The inducing factor for this hormonal reaction is partly the afferent neuronal impulses from the site of injury. Long waiting for surgery imply longer time of severe pain and prolongs the period of metabolic stress with increased catabolism and breakdown of skeletal muscle. It has been shown that treatment with analgesics has little inhibitory effect on the stress response[130].

Hip fracture patients usually receive suboptimal amounts of calories and fluids[27] peri-operatively, which further aggravates the catabolic reaction and insulin resistance[131]. Ironically, Symeonidis et al showed that malnourished patients had longer waiting time for operation compared to patients without malnutrition[132]. Both the stress reaction and the following insulin resistance will accelerate the process of muscle loss and weakness that normally develops after a hip fracture[24,33].

Hip fracture patients are at increased risk for pressure ulcer, and a PU incidence of between 9% and 66% has been reported[133-135]. The majority of these PU appeared during the first 48 hours after admission[135]. Several studies have shown that long waiting time for surgery increased the incidence of pressure ulcer in these patients[9,133,136,137]. Patients are usually lying immobilized in bed until surgery and it is known that prolonged immobilization is the main cause of pressure ulcer development[138]. PU develops after prolonged mechanical pressure that cause ischemia of the underlying tissue. Microscopic changes have been observed with pressure of 70 mm already after two hours[139]. Supine patients get sores on the sacrum and the heels and these are the most common sites for pressure ulcer in hip fracture patients[136,140].

A long immobilization, usually a result of a long waiting time for surgery, is known to affect several organs including the respiratory system with atelectasis and increased risk for pneumonia. The latter being one of the most common complications after a hip fracture[139,141].

Our finding that a delay of the operation was associated with an increase in LOS has also been reported by several others[13,14,142-144]. Siegmeth et al (2005) reported that the increase of LOS can be calculated from the delay of surgery in hours, after adjustment for the ASA score, mental score, and prefracture walking ability. They reported that a delay of 7.85 hours until surgery increased the hospital stay by one day. This finding was similar to our observation in study I, i.e. LOS was increased by one day with every 6.75-hour delay of surgery[13].

In conclusion, prolonged waiting times for surgery should be avoided in hip fracture patients.

6.2 COGNITIVE IMPAIRMENT AND HIP FRACTURE OUTCOME

The result of *study II* demonstrated that discharge to rehabilitation, rather than type of surgical procedure, predicted preserved walking ability, ADL and less wheelchair reliance in patients with femoral neck fracture and cognitive impairment. As expected, the likelihood of preserving the walking ability was also dependent on prefracture function similar to what others have found[145,146].

Postsurgical rehabilitation of older patients with hip fracture is essential for regaining prefracture level of function[147]. In spite of this patients with cognitive impairment are not considered to be good candidates for rehabilitation after hip fracture[148,149]. More recent studies have shown that patients with cognitive impairment can regain pre-fracture mobility after hip fracture if they are discharged to rehabilitation units. Huusko et al (2000) showed in a randomized controlled trial that hip fracture patients with mild to

moderate cognitive impairment often can return to independent living if they were discharged for geriatric rehabilitation[150]. Moreover, Beloosesky et al (2002) in a prospective longitudinal study found that pre-fracture motor function rather than cognitive level was the important predictive factor for motor gain after hip fracture[145].

Lenze et al (2004) verified that the association between cognitive impairment and poor functional outcome in patients with hip fracture was actually mediated via rehabilitation participation[151] Others have reported that a high-intensity functional weight-bearing exercise program for older people living in institutions is useful regardless of cognitive function[152].

Since publication of the *study II*, new studies have come to similar results as ours. Morghen et al (2011) showed in a prospective cohort study that walking independence is achievable after hip fracture surgery and rehabilitation, and can be maintained at one year even in those with moderately severe or severe cognitive impairment[153]. Dubljanin-Racpopoć et al (2010) pointed that in spite of cognitive impairment, elderly patients with hip fracture can benefit from participation in rehabilitation programmes[154].

The common procedure, at least in Sweden and other western countries[155] is that subjects already residing in an institution seldom are considered for discharge to a rehabilitation unit after a hip fracture. Beaupre et al (2007) reported that only 10% of patients admitted from long-term care were discharged to inpatient rehabilitation, compared with 79% of community-dwelling patients[155], which is similar to our findings.

It is likely that patients admitted from residential care facilities are frailer than those living independently, this could also affect long-term outcome. However, the current study also supports previous findings by Munin et al, in a prospective cohort study[156], [157] who demonstrated that patients with hip fracture discharged to inpatient rehabilitation units had superior functional outcome at 12 and 24 weeks compared with patients treated in skilled nursing homes, even after controlling for important covariates Our finding that the previous living situation was the strongest factor related to discharge to rehabilitation units, even after adjusting for relevant confounding factors, are in line with above mentioned studies.

The previous living situation accounted for 81% of variations in the discharge to rehabilitation (*Sudy II*). Patients admitted from institutions have shorter hospital stay in general and are discharged from the acute hospital as soon as they are medically stable[158]. This could be explained by a widespread notion that patients admitted from institutions do not need to be considered for rehabilitation programs outside their usual living setting. Logically, the assumption would be that it is easier for patients with cognitive impairment to get rehabilitation in a familiar environment. However, the findings of this study show that these patients were less likely to preserve walking ability, ADLs index and more prone to be wheelchair bounded than patients discharged to geriatric rehabilitation units. It is reasonable to believe that there is a general lack of rehabilitation capacity, physiotherapists, and knowledge in residential care institutions.

Our results showed that about one third of all patients with cognitive impairment were wheelchair users at the 12-month follow-ups. Similar findings were reported by Blomfeldt et al (2005)[56]. We found that discharge to rehabilitation units was related to reliance on a wheelchair in patients with cognitive impairment and a hip fracture, after 4 months and 12 months follow up. Major re-operations were only significantly related to reliance on

wheel-chair at 4-months. An early healing complication with a following major reoperation means two major traumas to these already fragile patients. On the other hand, patients might have a chance to recover if re-operation were delayed after 4 months.

In conclusion, current results indicate that discharge to a rehabilitation unit, a factor that we can influence, was a significant predictor for preserved walking ability and ADL Katz index, irrespective of the surgical method. Patients admitted from institutions like nursing homes and residential care homes were less likely to be discharged to rehabilitation units. This could be explained by a different patient selection but it could also be a result of a systematic organizational misconception. Further studies are needed to investigate the extent and the quality of rehabilitation provided after hip fracture in nursing- and residential care homes.

6.3 YOUNG AND MIDDLE AGED PATIENTS WITH HIP FRACTURE

A minority of the young hip fracture patients had a high-energy energy trauma as the cause for the hip fracture, in contrast to what has been reported earlier in the young patients[58,59,63-65]. Still some report findings in line with ours[61,62,159,160]. This controversy could have several reasons. For example, the frequency of traffic accidents - a major cause of energy trauma in several studies may vary between countries. Another explanation may be that the prevalence of osteoporosis differs over the world. Sweden together with Norway has the highest prevalence of osteoporosis. A third reason cold be that in some studies sport injuries are considered as a high-energy trauma [61].

We chose to consider sport injury as a separate group. Hip fracture due to fall during sport activity has not been addressed before as an important cause of hip fracture. Such fall related hip fractures were more frequent in the young age group compared to the middle-aged patients in whom the fracture occurred most commonly after low-energy trauma. Similar results are reported by others[161,162]. It is possible that the differences regarding trauma mechanisms are caused by increased osteoporosis with increasing age and/or by decreased lean body mass that might increase fall tendency in the middle age patients. Interestingly, we found that middle-aged patients had not only significantly lower BMD, but also lower FFMI compared to the younger age group.

The great majority of the young patients had a good physical health according to ASA score, in contrast to the middle-aged patients. Furthermore, the middle-aged patients had many co-morbidities and several medications, e.g. antiepileptic, cardiovascular and anti-diabetics drugs, factors that have all been related with an increased risk for hip fracture[62,161].

Besides, the results from *study III* show a high rate of smoking in the middle-aged patients compared to the average for Swedish middle-aged population (20%)[163]. This is consistent with the results by Holmberg et al (2005) which showed smoking to be a risk factor for hip fracture in the middle-aged population[161]. A recent meta-analysis by Kanis et al (2005) reported that smokers have increased risk for any fracture and the highest risk was observed for hip fracture[164].

A higher alcohol consumption was found in both the young and middle-aged patients with femoral neck fracture compared to the general Swedish population (13%)[163]. Several

authors have reported similar results[59,61,62,162]. Excessive consumption of alcohol is a well-recognized cause of secondary osteoporosis, particularly in men[165].

The results of *Study III* indicate that greater part of the young and middle-aged subjects with hip fracture have one or more risk factors for osteoporosis and fracture regardless of the trauma mechanism. Similar results had been reported by several authors[62,159]. These results might indicate that hip fractures in young subjects might be a sign of early osteoporosis leading to fractures already after moderate traumas. The result of *Study IV* confirm that the major part of these young patients had a femoral neck BMD below the mean for age irrespective of the trauma mechanism and one third to one fourth of them had osteoporosis.

Patients with low-energy trauma had significantly lower BMD and FFMI compared to patients with other trauma mechanisms (*study IV*). Boden et al (1990) and Lofthus et al (2006) similarly revealed that there were inverse correlation between the degree of BMD loss and the energy level of injury, i.e. the greater loss of BMD the less energy is needed for causing a fracture[62,159].

Our results (*Study IV*) revealed that about one third of the *middle-aged* patients had osteoporosis which is high compared to previous reports on the prevalence of osteoporosis; i.e. 13% and 5% in 50-69 years old Swedish women and men, respectively[166]. Furthermore, 49% of the women and 64% of the men in this age group was found to have osteopenia. This is more than expected due to previous reports, i.e. 47% and 28% in 50-69 years old Swedish women and men, respectively[166]. Most likely the majority of individuals with osteopenia will develop osteoporosis within the coming 10 years[167].

Body composition in young and middle-aged patients with hip fracture is not well studied previously. Anthropometric measures, e.g. BMI, are feasible practical methods that crudely describe a patient's nutritional status. FFMI is recently suggested as a method of describing fat-free mass that is adjusted for height[79]. Moreover, FFMI and FMI of an European reference population from Switzerland published by Shutz et al[79] permits comparison of our patients with hip fracture with those of similar age, gender and ethnicity.

Using BMI in our group of young and middle-aged patients only 3% were classified as being underweight; i.e. BMI < 18.5, whereas 9% had BMI below 20 kg/m^2. On the other hand one third were found to have FFMI below the 10th percentile of a European reference population. The latter is a cut-off that has been suggested to delineate malnutrition or sarcopenia[168]. Kyle et al found that 25% of the acutely ill and 37% of chronically ill patients displayed FFMI below this level at hospital admission[169]. Broadwin et al (2001) reported that subjects in the lowest quintile of FFM percentage were more likely to have functional disability than those in the highest quintile[170]. And Baumgartner et al showed that low skeletal muscle mass increase the risk for physical disability and falls[171].

Our results highlight that the young and middle-aged patients with hip fracture especially after low-energy trauma not only display an increased prevalence of osteoporosis, but also have low height adjusted fat-free mass, i.e. sarcopenia. Sarcopenia is related to an increased risk for fall in spite of an apparently normal BMI. Future intervention studies should take into consideration measurements to counteract both osteoporosis and low

muscle mass. A low FFM mass may be masked by high FM which might reflect a more sedentary lifestyle in our society. Thus, BMI is not enough to describe body constitution of hip fracture patients, and it may be suggested that the use of body composition measurements may add valuable information, beyond BMD, for treatment decisions for the hip fracture patients.

6.1 STRENGTHS AND LIMITATIONS

Certain strengths and limitations of the studies need to be further discussed.

Study I An alternative design could have been a randomized controlled trial where patients would be randomized to various waiting times. However, this approach could be inappropriate from an ethical point of view. Consequently, the best approach is a prospective cohort study including a large number of consecutive patients. The crucial part of our study was the logistic regression analyses, especially the selection of the factors used for adjustments. To the best of our knowledge, we selected factors that had previously been reported to be good predictors of the particular outcome studied. The major strength of the study was that we were able to include prospectively a large number of consecutive patients with high-quality data. A prerequisite for this was that the data were collected by specially trained research nurses who were designated for this task and worked in close cooperation with researchers in the Stockholm Hip Fracture Group. An important part of the data collection was the recording of the exact times of admission and operation.

Study II Data were collected only from proxies as the patients were selected because of their severe cognitive impairment. No reliability testing of the proxy-given information was performed. Proxy-patient agreement is in general good for concrete observable variables and moderately reliable for subjective variables[97,98]. Like other studies in this field, group selection was based on clinical decision rather than randomization. However, the patients were similar in cognitive function, age, sex, ASA score, fracture type, surgical method, and walking ability before the fracture. Yet, it could be that data relevant for the decision of discharge to rehabilitation units were not collected. The patient's nutritional status is also an important factor for functional re-gain independently of cognitive impairment. An alternative design for a study aimed to evaluate the effect of rehabilitation would be a randomized controlled trial. However, this approach might as well be questionable from an ethical point of view. Consequently, the second best approach is a prospective cohort study including consecutively admitted patients. One strength of this study was the choice of easily recognizable outcome variables: walking outside, inside, or unable to walk, and Katz ADLs index. Moreover, the dropout rate was fairly low

Study III Not all the young and middle-aged patients with femoral neck were included during the study period. To examine how representative our study patients were, registrations of all hip fracture patients were done during one year (2003). The analysis showed that 80% of the young patients and 50% of the middle-aged patients were included in the present study. The study population had better ASA-score, EuroQol, ADL Katz index and less use of walking aids. This discrepancy was probably due to the fact that patients from institutions, those with severe cognitive impairment or unable to walk were not included in the study. Otherwise, there were no differences in gender distribution, rate of smoking or fracture type.

Another limitation of this study was that not all risk factors for osteoporosis were registered such as low calcium intake and physical inactivity. However, the aim of this study was report the occurrence of the most established risk factors in the young and middle-aged hip fracture population. And as we aimed to treat all the patients with internal fixation for follow up design, patients with hyperparathyroidism, RA or other pathology involving the hip were not included.

Study IV A strength of this study is that most DXA examinations were performed in close proximity to the injury. Still, ten patients were examined by DXA more than two

weeks after the fracture which might affect the result. However, the analysis was repeated excluding those patients, a procedure that provided only minor differences on the results. Another limitation is that due to the multicenter nature of the study, patients were not examined by the same type of DXA equipment. To compensate for this a standardized bone mineral density (sBMD) for sub-regions of the femur[114] were used to create sBMD for the total hip and femoral neck. No such standardization for body composition was used as several studies have shown good correlation between different DXA systems[116,117].

7 CONCLUSIONS

7.1 STUDY I

Early operation on patients with a hip fracture improves their ability to return to independent living, reduces the risk of pressure ulcers, and shortens the hospital stay compared with the outcome after a late operation. The first priority should be to reduce the large number of system-related delays, i.e. those caused by a lack of resources.

7.2 STUDY II

Discharge to rehabilitation rather than surgical method was the strongest factor associated with preserved walking ability and ADL in eldely hip fracture patients with cognitive impairments. It is likely that patients with impaired cognitive function have difficulty coping with their new situation after hip fracture and need more support from a rehabilitation team. Availability of rehabilitation should be improved.

7.3 STUDY III

A minority of both the young and middle-aged patients had a high-energy trauma as the cause for the hip fracture. Life-style factors and other non-trauma related risk factors appeared to be main contributors to the occurrence of the hip fracture in both the young and middle-aged patient groups. Further studies are needed to investigate the importance of individual risk factors.

7.4 STUDY IV

A large majority of young and middle-aged patients with femoral neck fracture had osteopenia or osteoporosis at the femoral neck. One third of patients were sarcopenic. Patients with a low-energy trauma had the lowest femoral neck BMD and the lowest FFMI. Future intervention studies should take in consideration measures to counteract both osteoporosis and sarcopenia.

8 SAMMANFATTNING PÅ SVENSKA

Höftfraktur är den mest allvarliga osteoporosrelaterad frakturen och drabbar främst äldre personer. Efter en höftfraktur förlorar många sin tidigare gångförmåga och 20-50% kan heller aldrig återvända till eget boende. Det funktionella utfallet för många patienter med höftfraktur kan förbättras. Höftfrakturer hos unga patienter är ovanliga men följden kan bli ett livslångt funktionshinder.

Syftet med avhandlingen var att undersöka påverkbara faktorer som var associerade med funktion hos äldre patienter med höftfraktur. Vidare att studera bakgrundsdata, riskfaktorer samt traumamekanismer hos unga och medelålders patienter med höftfraktur. Vi avsåg också att undersöka förekomsten av benskörhet och sarkopeni (dvs. låg muskelmassa) hos unga patienter.

Studie I 850 patienter med höftfraktur studerades med avseende på möjlighet att återvända till eget boende, förekomsten av trycksår och vårdtidens längd i relation till väntetid inför operation. Patienter som fick vänta mer än 36 timmar innan de blev opererade återvände i lägre utsträckning till eget boende. Förekomsten av trycksår liksom vårdtiden ökade i grupperna som opererades senare än 24 timmar efter ankomst till sjukhus.

Studie II 246 patienter med höftfraktur och nedsatt kognitiv funktion (inkl. demenssjukdom) studerades med avseende på orsaker relaterade till post-operativt funktionsutfall. För att kunna bevara gångförmågan och den dagliga ADL funktionen var vistelse på rehabiliteringsklinik efter operationen av betydelse, men även gångförmåga och ADL-funktion före skadan var av betydelse. Patienter som skrivits ut till rehabiliteringsenhet var också i mindre grad rullstolsbundna vid båda uppföljningarna efter 4 och 12 månader.

Studie III 27 unga (20-49 år) och 158 medelålders (50-69 år) patienter med höftfraktur studerades med avseende på det våld som åstadkommit frakturen, bakgrundsdata samt riskfaktorer för benskörhet och höftfraktur. En minoritet av både åldersgrupperna hade varit med om ett kraftigt våld. Vi fann en eller fler riskfaktorer för osteoporos och fraktur hos majoriteten av patienterna.

Studie IV 185 patienter som deltog i studie III undersöktes med Dual X-ray absorptiometry (DXA) för bestämning av bentäthet och kroppssammansättning. Fett-fri massa (FFM) index (FFMI) beräknades som förhållandet mellan FFM (kg) och längd (m) i kvadrat, med syfte att korrigera det absoluta talet för muskelmassa för längden.

En tredjedel av studiepopulationen hade FFMI under den 10:e percentilen för en ålders- och gender matchad referenspopulation, vilket indikerar förekomst av sarkopeni. Alla unga patienter hade en bentäthet i lårbenshalsen som var under medelvärdet för ålder, och 90% av de medelålders patienterna hade låg bentäthet (56%) eller osteoporos (34%).

Sammanfattningsvis noterades att tidig operation av patienter med höftfraktur förbättrar möjligheten att återvända till ett eget boende, reducerar incidensen av trycksår och minskar vårdtidens längd. Utskrivning till rehabiliteringsenhet, en faktor som vi kan påverka, och tidigare funktion var faktorer som var förknippade med bevarad gångförmåga och ADL funktion hos äldre patienter med höftfraktur och nedsatt kognitiv funktion. En minoritet av både yngre och medelålders patienter hade hög energi trauma som orsak till höftfraktur. Majoriteten av patienterna hade en eller flera riskfaktorer för

höftfraktur och låg bentäthet som var oberoende av traumamekanismen. En tredjedel hade tecken på sarkopeni.

9 ملخص ABSTRACT IN ARABIC

إن كسور الورك هي الكسور الأكثر خطورة من بين الكسور المتعلقة بهشاشة العظام، وهي تصيب المسنين بالدرجة الأولى. ويبقى من اللازم تحسين النتائج الوظيفية لدى الكثير من المرضى المصابين بكسر الورك. وعلى الرغم من أن كسور الورك لدى الشباب غير شائعة، إلا أنها قد تؤدي إلى عجز دائم.

تهدف هذه الأطروحة إلى دراسة العوامل القابلة للتعديل والمرتبطة بتحقيق نتائج وظيفية أفضل لدى المرضى المسنين المصابين بكسر الورك. كما تهدف إلى دراسة بيانات الخلفية وآلية الحادث لدى المرضى الشباب ومتوسطي الأعمار المصابين بكسر في عنق الفخذ. كما نريد أيضاً أن نفحص مدى شيوع هشاشة العظام وانخفاض كتلة العضلات (sarcopenia) لدى المرضى الشباب المصابين بكسر الورك.

الدراسة I اشتملت على 850 مريضاً مصاباً بكسر الورك. وقد تمت دراسة النتائج؛ العودة إلى الحياة المستقلة، وقرحة الضغط (PU)، وطول فترة الإقامة في المستشفى (LOS)، والوفيات. المرضى الذين أجريت لهم عملية جراحية بعد أكثر من 36 و48 ساعة بعد دخولهم إلى المستشفى كانوا أقل احتمالاً للعودة إلى الحياة المستقلة، في حين أنه لم يكن هناك اختلاف هام عند تطبيق حدّ الـ 24 ساعة. وقد ازداد حدوث قرحة الضغط وطول فترة الإقامة في المستشفى لدى المجموعات التي خضعت للعملية الجراحية لاحقاً في كل الحدود الثلاثة، أما معدّل الوفيات فلم يتغيّر.

الدراسة II اشتملت على 246 مريضاً مصاباً بكسر في عنق الفخذ وبضعف الإدراك. وكانوا جميعاً قادرين على المشي قبل إصابتهم بالكسر.

العوامل الهامة في الحفاظ على القدرة على المشي والفعاليات اليومية عند متابعة الـ 4 أشهر و12 شهراً كانت الإحالة إلى قسم إعادة التأهيل ومدى القدرة على المشي والقيام بالفعاليات اليومية قبل الإصابة بالكسر، في حين أنه لم تكن هناك أهمية لنوعية الجراحة المتبعة. وكان المرضى الذين تمت إحالتهم إلى قسم إعادة التأهيل أقل عرضة للاعتماد على الكرسي المتحرك في كلتا المتابعتين.

الدراسة III اشتملت على 27 مريضاً شاباً (20-49 عاماً) و158 مريضاً في متوسط العمر (50-69 عاماً) مصابين بكسر في عنق الفخذ، وقد جرت دراستهم من منظور آلية الحادث وعوامل احتمالات الإصابة بهشاشة العظام وكسر الورك.

كانت النسبة الأقل بين مجموعتي الشباب ومتوسطي الأعمار قد تعرضوا لحادث خطير كان هو السبب وراء إصابتهم بكسر الورك. ويبدو أن عوامل نمط الحياة وعوامل احتمالات الإصابة بهشاشة العظام تساهم إلى حدّ كبير في حدوث كسر الورك في كلتا المجموعتين.

الدراسة IV اشتملت على نفس الأشخاص الذين اشتملت عليهم *الدراسة III*. تم تحديد كثافة العظام (BMD) والكتلة الخالية من الدهون (FFM) بواسطة قياس الامتصاص بالأشعة السينية المزدوجة (DXA). تم حساب مؤشر الكتلة الخالية من الدهون (FFMI) كمعدل الكتلة الخالية من الدهون ومربع الطول، وهي قيمة تصف كتلة العضلات المعدلة حسب الطول. وكان مؤشر الكتلة الخالية من الدهون لدى ثلث الأشخاص الذين اشتملت عليهم الدراسة أقل من 10 بالمائة من الفئة المرجعية، وهذه علامة انخفاض كتلة العضلات. كل المرضى الشباب كانت لديهم كثافة العظام في عنق الفخذ أقل من المتوسط بالنسبة لعمرهم، و90% من فئة المرضى المتوسطي الأعمار كانوا مصابين بنقص كثافة العظم (osteopenia), (56%) أو هشاشة العظام (osteoporosis), (34%).

وفي النتيجة، فإن إجراء العمل الجراحي المبكر للمصابين بكسر الورك يحسّن من إمكانية القدرة على العودة إلى الحياة المستقلة، ويقلل من حدوث قرحة الضغط، كما يقلل من طول فترة الإقامة في المستشفى. الإحالة إلى قسم إعادة التأهيل، وهو عامل يمكننا التأثير فيه، وكذلك الأداء الوظيفي قبل الإصابة هي عوامل مرتبطة بالحفاظ على القدرة على المشي والقيام بالفعاليات اليومية لدى المرضى المصابين بضعف الإدراك وبكسر الورك. النسبة الأقل من المرضى الشباب ومتوسطي الأعمار المصابين بكسر عنق الفخذ كانوا قد تعرضوا لحادث خطير أدّى إلى الإصابة بالكسر. أما الأغلبية فكان لديهم عامل واحد أو أكثر من عوامل احتمالات الإصابة بهشاشة العظام وبانخفاض كثافة العظام، بغض النظر عن آلية الحادث. ثلث هؤلاء المرضى كانت لديهم علامات انخفاض كتلة العضلات.

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