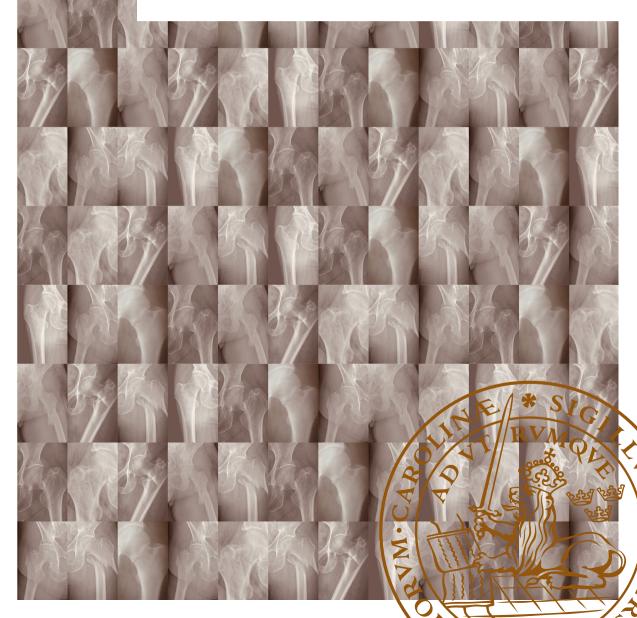


On hip fractures in adults under the age of 60

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On hip fractures in adults under the age of 60

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Sebastian Strøm Rönnquist



DOCTORAL DISSERTATION

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Abstract

The understanding of patients under the age of 60 with hip fractures have been influenced by preconceptions that fractures are due to high-energy trauma and the risk of osteoporosis is low. The patients' perspectives have seldomly been presented and the surgical results were insufficiently described. This thesis project was developed in response to the relative lack of research on this patient group.

In a prospective, multicenter, mixed general population-based cohort study, Paper I collected detailed information on the injury, demographics, epidemiology, lifestyle factors, comorbidity and general health, and DXA was performed at the time of the fracture. Paper II described the fracture classification, and analyzed whether trauma mechanism and osteoporosis determined the fracture pattern. In a qualitative interview study, Paper III illuminated the lived experience of recovery after a hip fracture. Paper IV analyzed national register data to describe the rate of conversion to secondary arthroplasty after internal fixation of displaced and undisplaced femoral neck fractures.

Adults under the age of 60 constituted approximately 5% of the total hip fracture population. More than half of the fractures occurred in men and most were aged 50-59. Two thirds of the fractures were displaced or unstable and intracapsular fractures were most common. Two thirds suffered their fractures after low-energy trauma, two thirds had previous disease(s), and half had a previous fracture. On DXA, we found a high prevalence of osteopenia (57%) and osteoporosis (31%). Trauma mechanism and bone mineral density did not explain different hip fracture patterns. The recovery after a hip fracture was a protracted process with lingering pain, functional, and psychosocial challenges and support of rehabilitation was inadequate. After initial internal fixation, a secondary arthroplasty was performed in 25% of displaced and 8% of undisplaced femoral neck fractures at five years.

Existing preconceptions should be traded for a nuanced understanding of patients under the age of 60 with hip fractures. A thorough health investigation and DXA assessment is warranted in all patients, regardless of age and trauma mechanism. A long term follow up is justified considering lingering challenges in recovery and the risk of a need for conversion to secondary arthroplasty after internal fixation of femoral neck fractures. Rehabilitation should be diversified and meet the demands of younger patients suffering hip fractures.

Svensk sammanfattning

Höftfraktur är välstuderat bland äldre, medan litteraturen om de yngre patienterna har varit sparsam. Den generella uppfattningen av yngre patienter med höftfraktur har influerats av förutfattade meningar; att yngre bryter höften på grund av högenergetiskt trauma, missbruk, eller för att de är multisjuka – inte på grund av osteoporos (benskörhet). Det råder också en uppfattning om att vilken typ av höftfraktur en patient får styrs av traumamekanismen, ju högre energi i skademomentet desto värre – mer felställd eller instabil – fraktur. Ännu mindre har skrivits om de yngre patienternas egna upplever att drabbas av en höftfraktur och även resultaten efter operation för collumfrakturer (lårbenshalsbrott) var bristfälligt beskrivna. För att komplettera kunskapen om yngre individer som drabbas av höftfrakturer utvecklades doktorandprojektet, med målet att svara på de övergripande frågorna:

- Vem är det som bryter höften i yngre ålder?
- Vad avgör frakturmönstret?
- Hur påverkas livet och hur upplever patienterna återhämtningen efter en höftfraktur?
- Hur är det kirurgiska resultatet hos yngre patienter?

Delarbete I och II utgår från forskningsprojektet HöftFraktur hos vuxna Under 60 år (HFU-60). HFU-60 är en kohortstudie baserad på den allmänna befolkningen från fyra ortopediska kliniker i Sverige och Danmark, där patienter under 60 år med höftfraktur har bjudits in att delta i studien. Avsikten med HFU-60 studien var att analysera demografi, epidemiologi, förekomst av osteoporos, frakturbehandling och resultaten efter höftfraktur för unga patienter.

Delarbete I undersökte vilka patienterna är som drabbas av höftfraktur i yngre ålder; vi analyserade detaljerad information om skademekanismen bakom höftfrakturen, demografi, epidemiologi, livsstilsfaktorer, samsjuklighet och generell hälsa. Dessutom mättes bentätheten med DXA kort tid efter frakturen. Delarbete II beskrev frakturtyperna stringent enligt AO/OTAs frakturklassifikation och undersökte om det fanns ett samband mellan typ av höftfraktur, traumamekanism och osteoporos. Delarbete III var en kvalitativ intervjustudie, som baserades på en subgrupp av HFU-60 patienterna, där patienternas egna upplevelser av att bryta höften belystes.

Delarbete IV analyserade nationella registerdata från Svenska Frakturregistret och Svenska Ledprotesregistret för att beskriva frekvensen av omoperation med höftprotes i de fall när osteosyntes (spikning/skruvning) av collumfrakturer misslyckades.

Vi fann att vuxna under 60 år utgjorde cirka 5% av den totala höftfrakturpopulationen. Mer än hälften av frakturerna skedde hos män och de flesta patienter var i åldern 50–59 år. Två tredjedelar av frakturerna var felställda eller instabila och höftfrakturer innanför ledkapseln var vanligare än dem utanför ledkapseln. Två tredjedelar ådrog sig frakturen vid lågenergitrauma, två tredjedelar hade tidigare sjukdom(ar), och hälften hade haft en tidigare fraktur. Vid bentäthetsmätning fann vi en hög förekomst av osteopeni (delvis sänkt benmassa) (57%) och osteoporos (31%), men osteoporos och traumamekanism avgjorde inte frakturmönstret. Att återhämta sig efter en höftfraktur var en långsam process som innehöll kvardröjande smärta, funktionella och psykosociala svårigheter och stödet i rehabiliteringen var bristfälligt. Efter osteosyntes av collumfrakturer utfördes omoperation med höftprotes hos 25% av dem med felställda frakturer och 8% av dem med icke felställda frakturer.

Förutfattade meningar bör ersättas av en nyanserad förståelse av vilka de yngre med höftfraktur grundlig hälsoundersökning patienterna är. En samt bentäthetsmätning är befogat för alla patienter, oavsett ålder och traumamekanism. Långtidsuppföljning är motiverad; särskilt med tanke på långvariga svårigheter i återhämtningen efter en höftfraktur i kombination med risken för både tidiga och sena komplikationer efter osteosyntes av collumfrakturer, vilket kan kräva Rehabiliteringen omoperation med höftprotes. efter höftfrakturer bör individualiseras och möta kraven även från yngre patienter.

List of papers

- I. Frailty and osteoporosis in patients with hip fractures under the age of 60 – a prospective cohort of 218 individuals. Sebastian Strøm Rönnquist, Bjarke Viberg, Morten Tange Kristensen, Henrik Palm, Jens-Erik Bech Jensen, Carsten Fladmose Madsen, Kristina E Åkesson, Søren Overgaard, Cecilia Rogmark. Osteoporosis International. 2022 May 1;33(5):1037–55.
- II. Trauma mechanism and bone mineral density did not impact hip fracture type – a multicenter cohort of patients under 60 years of age. Sebastian Strøm Rönnquist, Bjarke Viberg, Morten Tange Kristensen, Henrik Palm, Jens-Erik Bech Jensen, Carsten Fladmose Madsen, Kristina E Åkesson, Søren Overgaard, Cecilia Rogmark. Manuscript 2022.
- III. Lingering challenges in everyday life for younger patients with hip fractures – a qualitative study of the lived experience during the first three years. Sebastian Strøm Rönnquist, Hilda K Svensson, Charlotte Myhre Jensen, Søren Overgaard, Cecilia Rogmark.

Manuscript 2022.

IV. Rate of conversion to secondary arthroplasty after femoral neck fractures in 796 younger patients treated with internal fixation: a Swedish national register-based study. Sebastian Strøm Rönnquist, Johan Lagergren, Bjarke Viberg, Michael Möller, Cecilia Rogmark.

Acta Orthopaedica. 2022 Jun 14;93:547-53.

Abbreviations

AO	Arbeitgemeinschaft für Osteosynthesefragen / AO Foundation
AP	Antero-posterior
ASA	American Society of Anesthesiologists
BHW-PA	Board of Health and Welfare physical activity questions
BMD	Bone mineral density
CI	Confidence interval
DXA	Dual energy x-ray absorptiometry
FNF	Femoral neck fracture
FRAX®	Fracture Risk Assessment Tool
HFU-60	Hip Fractures in adults Under 60 years of age
ICD-10	International Classification of Diseases, tenth revision
IF	Internal fixation
NHANES III	Third National Health and Nutrition Examination Survey
SAR	Swedish Arthroplasty Register
SFR	Swedish Fracture Register
WHO	World Health Organization
UN	United Nations

Thesis at a glance

Paper	Questions and study design	Main results	Conclusion	Perspective
I	Who fractures their hip in younger age? Prospective, multicenter, cohort study, n=218.	Most of the fractures occurred in men (58%), in patients aged 50-59 years (68%), and after low-energy trauma (68%). 1/3 of the patients had no disease, 1/3 had 1 disease, and 1/3 had multiple comorbidities. Half of the patients had a previous fracture. Smoking (42%), alcohol (29%), and drug use (8%) were more common than in the general population. Vitamin D was low in half of the patients. On DXA investigation, the prevalence of osteopenia (57%) and osteoporosis (31%) were high compared to reference population data.	This was a heterogeneous group with a high degree of frailty and numerous risk factors for fractures. The prevalence of osteopenia and osteoporosis was high.	Younger patients with hip fractures should be thoroughly investigated, including DXA investigation.
11	What causes the fracture pattern? Prospective, multicenter, cohort study, n=218.	Femoral neck fractures constituted 58% (2/3 were displaced), pertrochanteric fractures 34% (2/3 were unstable), basicervical (5%), and subtrochanteric (4%), i.e., intracapsular fractures (63%) were more common than extracapsular. Another concurrent fracture was seen in 7 patients. Analyses on the associations between fracture type, trauma mechanism, and DXA result did not reach statistical significance, though clinically important findings were seen.	Most fractures were unstable/ displaced and the anatomical location was mainly intracapsular. Most fractures resulted from low- energy trauma. Trauma mechanism and BMD did not impact hip fracture type.	The high prevalence of low BMD calls for awareness of the risk of osteoporosis associated with hip fractures regardless of age and trauma type.

Paper	Questions and Study design	Main results	Conclusion	Perspective
111	How is life affected after a hip fracture? Qualitative interview study, n=19.	Lingering pain and feelings of weakness, disability and physical inability were expressed by participants. The provided care and rehabilitation were perceived as adapted to elderly patients, not to the needs of younger individuals.	The lived experience of sustaining a hip fracture in patients under 60 years includes challenges in everyday life, even years after the injury.	Other pathways of care and rehabilitation, and improved information, are suggested to meet diverse demands of all patients with hip fractures.
IV	What is the surgical outcome in younger patients? National register study, n=796.	Most fractures occurred in men (59%), in patients aged 50-59 years (63%), and after low-energy trauma (77%). Secondary arthroplasty was performed in 108 patients. Coversion rates for dFNF at 1, 2, and 5 years were: 1y: 9% (95% CI 6–12), 2y: 17% (CI 13–21), 5y: 25% (CI 20–30). For uFNF, conversion rates were: 1y: 3% (CI 1–5), 2y: 5% (CI 3–8), 5y: 8% (CI 5–11). Age 50-59 had an increased risk of conversion for uFNF compared to patients aged <50. Mortality rate for patients 50-59 years were 4% (CI 2-6) at 1 year, and 16% (CI 11-20) at 5 years.	Higher rate of conversion for dFNF compared to uFNF during follow-up, at 5 years 25% vs. 8%. Mortality rates were markedly higher for patients aged 50-59, but did not differ between sex or fracture types.	Surgeons and patients should be aware of the risk of conversion to arthroplasty at the time of initial fracture treatment.
DXA: Dual energy x-ray absorptiometry BMD: Bone mineral density dFNF: displaced femoral neck fracture uFNF: undisplaced femoral neck fracture				

Preface

This thesis project was developed in 2014, in response to the scarcity of literature regarding younger patients with hip fractures, especially in comparison to the elderly population, which has been well studied in this regard.

To understand multiple aspects of the phenomenon of hip fractures in adults under the age of 60, a prospective, multicenter, mixed general population-based cohort study called the Hip Fractures in adults under 60 years of age (HFU-60) was designed and initiated. The intention was to provide information on the demography, epidemiology, prevalence of osteoporosis, treatment, and outcomes after hip fracture. In this thesis, Paper I and Paper II come from the HFU-60 study and aim to answer these questions: who fractures their hip at younger ages, and what determines the fracture pattern?

As a sub-study of the HFU-60, the qualitative interview study InterHFU was undertaken using a subset of individuals from the cohort. The rationale behind this qualitative study was to illuminate the patients' experiences of suffering a hip fracture, with a focus on these questions: how is life affected after a hip fracture, and how do patients experience the recovery? The outcomes of this study were explicitly patient-centered, thanks to the study design of Paper III.

To expand the generalizability of the results, in Paper IV, data was retrieved from two national registers, the Swedish Fracture Register and the Swedish Arthroplasty Register. This provided a large cohort that enabled analysis of reoperation with arthroplasty after initial treatment with internal fixation of femoral neck fractures. This provided new and pertinent information on the surgical outcomes in this age group.

This has been an evolving journey, looking forward during the years of working on this project, but also looking back at the works of prior orthopedic surgeons such as Speed, Leadbetter, Garden, and Johansson in Sweden, who all provided essential knowledge on hip fractures beginning almost a century ago (1–4). Alas, you gentlemen of previous generations, even though our understanding of hip fractures has deepened, the femoral neck fracture is still unsolved.

Copenhagen, August 2022

Introduction

A life-breaking event

A hip fracture has been described as a life-breaking event, one that not only breaks a bone but also leaves existential and social cracks (5). Research on older patients with hip fractures makes clear the risks of subsequent functional deficit, persistent pain, fear of falling, and decreased health-related quality of life (6–8). Regarding younger patients, there has been a lack of knowledge about their perspectives (9). Furthermore, orthopedic surgeons tend to have preconceived notions about the characteristics of young and middle-aged patients with hip fractures.

Common preconceptions are that younger patients suffer hip fractures due to highenergy trauma or alcohol/substance use disorder, but not due to osteoporosis (10,11). This perception is underpinned by surgically-oriented studies from trauma centers and low-income countries. The few existing studies suggesting that young and middle-aged patients with hip fractures may have osteopenia and osteoporosis regardless of trauma mechanism were directed to readers interested in bone health (12–15). In addition, these studies were based only on risk factors for osteoporosis or dual-energy x-ray absorptiometry (DXA) years after the fracture – not at the time of the fracture. These shortcomings indicate a need for studies on a population-based cohort with evaluation for osteoporosis by DXA investigation at the time of the fracture.

Another common notion is that hip fracture type and degree of displacement is associated with trauma mechanism, i.e., that a higher trauma energy would lead to a displaced or more unstable fracture type. However, this has not been shown in previous reports. Poorer bone quality has previously been proposed as a reason for a shift toward more unstable fractures in older patients, as the distribution of fracture type differs compared to younger patients (16). Clearly, a better understanding of hip fractures and the possible etiology behind different fracture patterns is needed.

To illuminate younger patients' perspectives, how could their lived experience and path of recovery after sustaining a hip fracture be studied?

Who is younger?

Age and the understanding of who is younger or older is relative. There is no consensus in the literature on the dividing line distinguishing younger from older patients with hip fractures; ages between 40 and 70 years have been used in studies (17,18). Multiple studies have, however, used age 60 as a cut-off between younger and older patients (19–27).

The World Health Organization (WHO) and the United Nations (UN) collaborated in developing the United Nations Decade of Healthy Ageing (2021–2030), focusing on healthy ageing and improving the lives of older people, defined as an age above 60 (28,29).

In the HFU-60 study, 60 years of age was defined as the upper age limit, which coincides with treatment guidelines at the department of origin of the study, where age 60 has been used as a divide in deciding between arthroplasty or internal fixation for displaced FNFs.

Individuals aged under 60 are hence regarded as younger in this thesis and referred to as young, younger, young and middle-aged, or non-elderly.

Epidemiology

Hip fractures are most often suffered by an elderly individual, but 2–11% of hip fractures affect young and middle-aged patients (30,31). From the Swedish Fracture Register (SFR), the total number of adult hip fractures in 2021 was 13,936, and fractures in individuals aged 18–59 years accounted for 616 (4%) (32). In a study on hip fractures in women under age 65, age 45 was found to be the first significant increase in age-related incidence, and most fractures are found in the eldest group of younger patients (12).

Hip fractures in the elderly population are often explained as an expression of comorbidities or frailty in combination with reduced bone quality. However, although fracture risk was higher with a lower bone mineral density (BMD), in a large analysis of self-reported fractures, only one-fourth of hip fractures occurred in individuals with osteoporosis; most fractures occurred in the osteopenic range with T-scores of -1 to -2.5 (33).

From the SFR year report 2020 (16), the fracture type distribution by age visualizes a change in fracture type with higher age, where displaced femoral neck fractures and multifragmentary pertrochanteric fractures are more common at higher ages (Figure 1).

Figure 1 Hip fracture type distribution according to age group

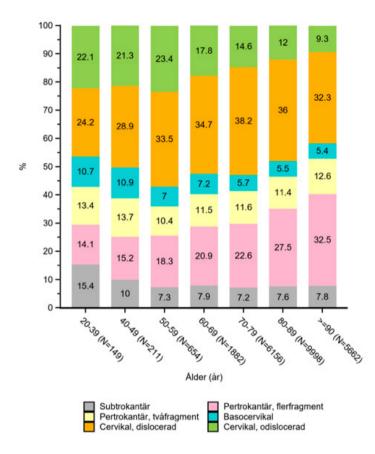


Figure 1 The distribution of hip fracture types changes with higher age. Displaced femoral neck fractures and multifragmentary pertrochanteric fractures are more common in higher ages. Figure from the SFR annual report 2020 (16). Fracture types in English – subtrokantär: subtrochanteric – pertrokantär, flerfragment: pertrochanteric, multifragment – pertrokantär, tvåfragment: pertrochanteric, two fragments – basocervikal: basicervical – cervikal, dislocerad: femoral neck fracture, undisplaced.

The injury

Some hip fractures occur spontaneously, but most fractures occur because of trauma. In the reporting of orthopedic fracture research, a distinction between lowenergy and high-energy trauma is often made, and one would expect there to be universal definitions of these terms. However, there is only consensus regarding low-energy trauma, which is defined as a same-level fall from standing height or less (34). High-energy trauma can refer to traumatic events, like high-speed traffic accidents or falls from a considerable height, e.g. >3m or more (13,30,35,36), but definitions vary. In younger patients, high-energy trauma has previously been proposed as the main reason for hip fractures (24,35,36).

In the HFU-60 study, low-energy trauma was defined as a same-level fall from a standing or sitting position, and all other trauma was defined as "not low-energy trauma", thereby avoiding the need to enumerate specific higher-energy trauma mechanisms.

Hip fracture classification

A hip fracture is a fracture of the proximal part of the femur, but typically excluding fractures of the femoral head itself. Hip fractures can be categorized according to their anatomical location on the femur, but other systems of classification based on fracture morphology, degree of displacement, and sometimes etiology are often used.

Anatomical description

Anatomically, hip fractures can be divided into intracapsular and extracapsular fractures depending on the fracture's location in relation to the hip joint capsule, which extends to the intertrochanteric line, as seen on plain antero-posterior (AP) radiographs. Fractures lateral to the intertrochanteric line are considered extracapsular, and consist of the sub-types pertrochanteric and subtrochanteric hip fractures. Intracapsular fractures are found medial to the intertrochanteric line and consist of femoral neck fractures (FNFs). One classification system based on the anatomical location of the fracture is the WHO International Classification of Diseases, tenth revision (ICD-10). According to ICD-10, hip fractures are classified as S72.0x (where x is 0 or 1 for closed or open fractures, respectively) for femoral neck fractures (37).

AO/OTA classification

Arbeitgemeinschaft für Osteosynthesefragen (AO), currently the AO Foundation, was begun by a group of Swiss surgeons in 1958 to improve treatment of fractures (38). The work included classifying fractures, which in 1996 led to the publication of a Fracture and Dislocation Classification Compendium, a collaboration between AO and the Orthopaedic Trauma Association (OTA), most recently revised in 2018 (39). In the Swedish Fracture Register (SFR), from which data was collected for Paper IV, fractures are classified according to the 2007 revision (40). Hip fractures are classified according to their anatomical location as well as fracture morphology.



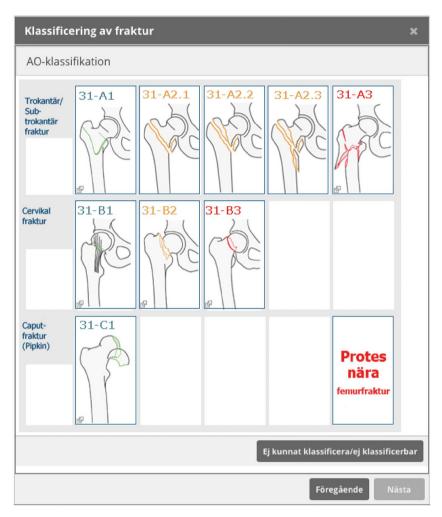


Figure 2 AO/OTA classification of hip fractures in the Swedish Fracture Register. Figure from Sundkvist et al. (41).

Garden's classification

R.S. Garden presented a classification of FNFs, based on the displacement seen on AP radiographs (3). In Garden's classification, FNFs are classified into four types – stage I–IV – but due to high inter-observer variation, it has been reduced to two categories: undisplaced (Garden 1–2) and displaced (Garden 3–4), which is commonly used clinically (42).

Description based on etiology

Hip fractures have also been described according to one of the main etiologies, i.e., osteoporosis. The Fracture Risk Assessment Tool (FRAX®), used to calculate the 10-year probability of fractures based on risk factors, defines hip fractures as a major osteoporotic fracture (together with fractures of the spine, forearm, and shoulder) (43). The FRAX® is intended for use in patients above 40 years of age, and fracture risk cannot be accurately calculated for younger patients.

Treatment

The prognosis in terms of pain, functional outcome, and mortality for a patient with a hip fracture left untreated is poor. In the days when hip fractures in adults were treated with plaster casts, the importance of reduction and firm fixation was emphasized by Leadbetter (2), but he considered aftercare to be most important in hip fracture treatment to preserve life. Today, treatment is generally surgical, with the goal to allow early mobilization, and aftercare remains important.

Regarding the choice of the specific operative treatment, decisions are based on fracture type, degree of displacement, and the patient's age, ideally biological rather than chronological. Principally, the choice of surgical treatment of hip fractures is binary, internal fixation (IF), or joint replacement by arthroplasty.

The surgical outcome after IF of displaced FNFs in older patients is well described. That understanding has led to a change in primary treatment to arthroplasty, due to unacceptably high rates of reoperations (44,45). In younger patients, IF is recommended for these fractures, thereby sparing the native joint (25). However, the rate of conversion to secondary arthroplasty has been insufficiently described. One population-based cohort study reported a conversion rate of 14% but did not distinguish fracture displacement (46), and a smaller case series presented a conversion rate of 22% for displaced fractures (22). More comprehensive results of surgical treatment, based on a large cohort with precise fracture classification, are needed.

In Scandinavia, the treatment for undisplaced FNFs in all ages is currently internal fixation, but in other countries the use of arthroplasty is increasing. Therefore, randomized trials are underway in Scandinavia and the UK to investigate if arthroplasty is a better treatment option for elderly patients (47–49).

Extracapsular fractures are mainly treated by IF, using either sliding hip screw devices or intramedullary nails; nails are usually preferred for unstable pertrochanteric and subtrochanteric fractures (25).

The Swedish Fracture Register

The SFR was begun in 2011 as a national quality register; it prospectively collects data on injury and fracture type according to AO/OTA classification, operative and non-operative fracture treatments, and reoperations – all recorded to the register by the treating physician. Patients answer questionnaires regarding functional performance pre-fracture and one year after the fracture. The coverage for hip fractures in the SFR increased from 18% to 86% during the study period for Paper IV (2012–2018), due to an increased number of hospitals participating in the register (50,51). By 2021, coverage was 100%; all orthopedic departments in Sweden report to the register, which recorded 645,000 fractures at the end of 2021. The completeness was validated and found to be 55% for femoral fractures in 2018, rising to 84% in 2020 (52,53). A validation study found the accuracy of classification by orthopedic surgeons of femoral fractures in SFR to be substantial for AO/OTA group and almost perfect for AO/OTA type (54).

The Swedish Arthroplasty Register

Begun in 1975, the Swedish Knee Arthroplasty Register was the first national quality register in Sweden; it was followed by the Swedish Hip Arthroplasty Register in 1979. The two registers are now united into one national quality register for hip and knee replacement surgery, the Swedish Arthroplasty Register (SAR). The SAR prospectively registers patient data, procedure-related information, and patient-reported outcome measures. Knee replacements are beyond the scope of this thesis and will not be covered further. References to arthroplasty in the thesis indicate arthroplasty of the hip. Regarding hip arthroplasty, all departments performing hip replacements in Sweden report to the SAR, i.e., a coverage of 100%. The completeness for the years of Paper IV (2012–2019) was approximately 98% for total hip arthroplasty (THA), 96% for hemiarthroplasty (HA), and 92% for revisions of THA and HA (55).

Using unique individual personal identification numbers, patients can be followed accurately in and across the registers. Both registers are notified from the population register (the Swedish Tax Agency) in the case of any deaths, and date of death is registered.

Aims

Overall aim

The thesis project aimed to deepen the understanding of hip fractures in younger patients. Research questions were as follows:

- Who fractures their hip at younger ages?
- What determines the fracture pattern?
- How is life affected after a hip fracture, and how do patients experience their recovery?
- What is the surgical outcome in younger patients?

Specific aims

Paper I: To describe the characteristics of a cohort of patients under age 60 with hip fractures, focusing on risk factors for fractures and osteoporosis and analyze BMD at the time of the hip fracture in relation to the general population.

Paper II: To describe the fracture classification in a cohort of patients under age 60 with hip fractures and analyze associations between trauma mechanism, BMD, and fracture type.

Paper III: To illuminate the lived experiences of and the path of recovery for adults sustaining a hip fracture before age 60.

Paper IV: To determine the rate of conversion to arthroplasty from IF due to undisplaced and displaced FNFs in patients under age 60 and to descriptively analyze mortality and the relationship between conversion rate and sex, age, trauma mechanism, and surgeon's experience.

Methods

HFU-60: Paper I and II

Study design

The HFU-60 study is a prospective, multicenter, mixed general population-based cohort study of adult patients under age 60 with hip fractures. The overarching aim of the study is to describe the epidemiology, fracture treatment, and clinical and functional results as well as patient-reported outcomes.

Paper I presents the primary baseline report from the HFU-60 study, providing detailed information on patient and injury characteristics; it describes the demography and epidemiology of hip fractures in young and middle-aged patients, lifestyle factors, comorbidity and general health, and results of DXA investigation at the time of the fracture. The latter feature was analyzed in relation to previous population-based samples. Paper II describes the fracture classifications in the cohort and analyzes associations between trauma mechanism, BMD, and fracture type. Further studies based on the HFU-60 project have been undertaken, and results will be published separately.

Setting

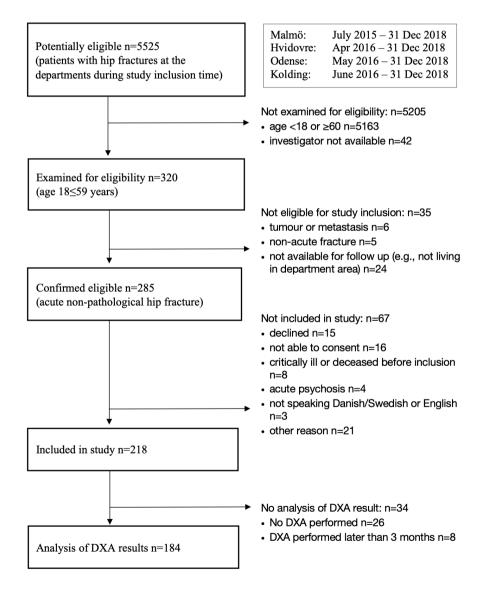
Patients were included at four departments of orthopedics and traumatology in Southern Scandinavia: Skåne University Hospital Malmö in Sweden and, in Denmark, Hvidovre University Hospital, Odense University Hospital, and Lillebaelt University Hospital Kolding. The participating departments belong to public hospitals serving both urban and rural areas; they are responsible for all fracture treatment in their catchment areas, thus the cohort represents all types of trauma and patient profiles. Public healthcare is provided in both Denmark and Sweden; it is free in Denmark and available at low cost in Sweden.

Participants

Patients aged 18 to 59 years presenting with a hip fracture to any of the participating departments were examined for eligibility, regardless of medical, functional, and

cognitive status prior to the fracture. Patients with pathological fractures (i.e., tumor or metastasis), non-acute fractures (i.e., older than four weeks), or not residing in the catchment area were excluded from study participation. Existence of other concurrent injuries was not a reason for exclusion. Of the confirmed eligible patients, 67 were excluded from the HFU-60 cohort; these patients did not consent to participate or were unable to consent due to their medical condition (i.e., they were critically ill, transferred to other departments, or in an acute psychosis) or because they did not speak Swedish, Danish, or English.

Figure 3 Flow chart of inclusion and DXA analysis in HFU-60



Data collection

In HFU-60, multiple variables were collected; recorded variables used in Paper I and II are specified and defined in Appendix Table 5 in the appended Paper I. Data were retrieved via review of medical records and patient interviews, physical activity assessments and functional tests, patient questionnaires on alcohol and drug use, laboratory assessment, and BMD investigation.

The injury was classified according to trauma mechanism, in HFU-60 as either lowor not low-energy trauma and in Paper IV following the registrations in the SFR as low- or high-energy trauma. Low-energy trauma was defined as same-level falls in both HFU-60 and the SFR. Significantly high levels of energy, e.g., falls from heights or traffic accidents, were considered high-energy trauma in the SFR. In HFU-60, the term "not low-energy trauma" was used for trauma other than samelevel falls.

In Paper I, the fracture classification was simplified to either intra- or extracapsular, whereas in Paper II, the full fracture classification recorded in the HFU-60 study was used. This meant that the fractures were classified by orthopedic surgeons according to a predefined protocol fitted to the 2007 revision of the AO/OTA Fracture and Dislocation Classification Compendium (40). Fractures were classified as follows (3,40):

- undisplaced femoral neck (Garden 1-2, AO 31-B1)
- displaced femoral neck (Garden 3-4, AO 31-B3)
- basicervical (AO 31-B2)
- stable pertrochanteric (AO 31-A1 + A2.1)
- unstable pertrochanteric (AO 31-A2.2-3 + A3)
- subtrochanteric (AO 32 until 3cm below lower border of lesser trochanter)

Statistics

Data collected at the local departments was stored securely online using Research Electronic Data Capture (projectredcap.org). Data curation and analysis was performed using IBM SPSS version 26. Continuous variables were assessed for normality and presented as either mean (SD) or median (IQR) depending on normal distribution. Associations between categorical variables were analyzed by chi-square tests, and T-test was used to compare means; a p-value of <0.05 was considered statistically significant.

InterHFU: Paper III

Study design

InterHFU was a qualitative study on a subset of the HFU-60 cohort from Skåne University Hospital Malmö and Odense University Hospital, using a phenomenological hermeneutic method following Lindseth and Norberg (56): a method of text analysis or text interpretation consisting of naïve reading and understanding, structural analysis, and comprehensive understanding.

Participants

Individuals included in the HFU-60 cohort from Malmö or Odense were also eligible for participation in InterHFU, provided they fulfilled the inclusion criteria: speaking Swedish or Danish, ability to individually partake in the interview, minimum six months' time since the hip fracture, and New Mobility Score \geq 3 pre-fracture (57). Of these, 30 participants were purposively sampled and invited, and 19 agreed to participate.

Data collection

Participants were interviewed by two experienced qualitative researchers; data collection continued until no new aspects of experiences were presented. Interviews were initiated with an open-ended question: "Could you tell me about when you sustained your hip fracture and how you have experienced the time after as well as your recovery?" An interview guide with follow-up questions was used if needed, with the intention to keep the interviewee within the focus of the study.

Recorded data was transcribed, and triangulation was performed through comparisons by a bilingual author, evaluating whether the collection of the two national datasets were similarly conducted.

Analysis

Naïve reading involved multiple readings of the text as openly as possible, to grasp the meaning behind the words rather than what was literally stated. The findings from both datasets echoed each other, enabling a joint analysis. In the structural analysis, the text was further studied; units of meaning and units of significance were identified, and themes emerged. Comprehensive understanding involved critical reflection in relation to relevant literature, where the apparent themes were discussed to gain an understanding of the participants' experiences.

National register study: Paper IV

Study design

Paper IV was a longitudinal cohort study based on two Swedish national registers, with analyses of prospectively collected data from the SFR and the SAR. For information on the register setting, please refer to the introduction.

Participants

From the SFR, patients with undisplaced and displaced FNFs treated with parallel pins/screws or sliding hip screw devices during 2012–2018 were included. Other fracture types and spontaneous, pathological, and stress fractures were excluded, as were fractures treated with arthroplasty, intramedullary nail, other types of plate fixation, or non-surgically. In the SAR, secondary arthroplasties were identified by cross-referencing the registers. The unique individual personal identification number carried by all Swedish inhabitants enabled a reliable match between registers, regarding both secondary surgeries and death.

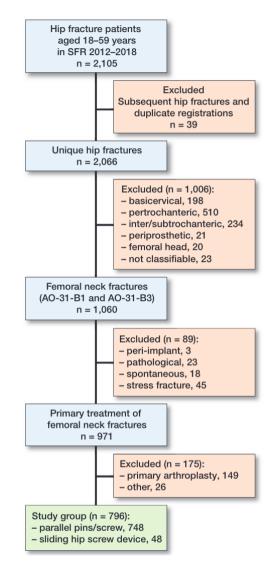
Data collection

Basic epidemiological variables (i.e., sex, age, and trauma mechanism categorized as either low- or high-energy trauma) were collected from the SFR, together with data on the primary fracture treatment (i.e., type of IF and surgeon's experience defined as performed by either a resident or a specialist). From the SAR, data on conversions to arthroplasty were collected and analyzed together with mortality data.

Statistics

Observations were grouped by fracture type (undisplaced or displaced FNF), sex, and age <50 or 50–59. Continuous variables were presented as mean or median, depending on normality, and associations between categorical variables were analyzed using the chi-square test. The rate of conversion was determined as cumulative reoperation rate with 95% confidence interval (CI) at one, two, and five years after the fracture by Kaplan-Meier analysis, which was also used to determine mortality rate. Previously described risk factors for secondary arthroplasty (female sex, higher age, high-energy trauma mechanism, and resident surgeon) (58–61) were analyzed using a Cox proportional hazard regression model. Analysis was performed in IBM SPSS version 26 and R version 4.0.2; a p-value of <0.05 was considered statistically significant.

Figure 4 Flow chart of inclusion in Paper IV



Ethical considerations

The studies included in the thesis (Paper I–IV) were conducted in accordance with the Helsinki Declaration. The HFU-60 study was registered at ClinicalTrials.gov (NCT03848195). Papers I, II, and III were approved by the ethical review boards in Sweden (Regionala etikprövningsnämnden Lund [dnr: 2015/28]) and Denmark (the Regional Health Service and University Research Ethics Committee and the Danish Data Agency [S-20150137]). Participants provided informed consent prior to study enrollment.

Paper IV was approved by the Swedish national ethical review board (Etikprövningsnämnden: Dnr 2019-05024), and data were pseudonymized before extraction from the registers and subsequent analysis.

Data supporting the findings of the studies may be made available upon reasonable request to the corresponding author. The authors have no conflicts of interest with relevance to any of the studies to declare. Funding for the studies was provided by grants from the Greta and Johan Kock Foundation, A. Påhlsson Foundation, H Järnhardt Foundation, Skåne University Hospital Research Fund, the Research and Development Council of Region Skåne, the Swedish Research Council funding for clinical research in medicine, and *Region Syddanmarks forskningsfond* from the Region of Southern Denmark. None of the funders had influence on the scientific work.

Main results

Characteristics of younger patients with hip fractures

Demographics and anthropometrics

From both the HFU-60 (Papers I–II) and the national register study (Paper IV), it was found that the proportion of men incurring hip fractures (58% and 59%, respectively) was larger than women. Approximately two-thirds of the fractures occurred in patients aged 50–59 years, and 83% of the patients in the HFU-60 study were aged 45–59 years. Figure 5 shows a larger proportion of the fractures in higher ages.

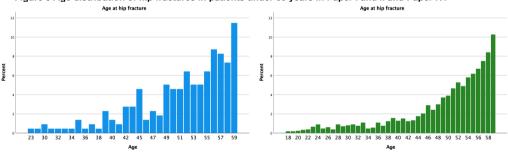


Figure 5 Age distribution of hip fractures in patients under 60 years in Paper I and II and Paper IV.

Figure 5 Age distribution of hip fractures in patients under age 60 in the HFU-60 cohort (Paper I and II, left in blue) and in the SFR cohort 2012-2018 (Paper IV, right in green).

In HFU-60, women had a higher median age than men, and women were significantly overrepresented in the oldest age group; 52% of the women were aged 50-59 versus 35% of the men (p=0.009). A little more than half of the patients lived with another adult, 37% lived alone, and 5% (8% of the men) inhabited an institution (Table 1 in Paper I). Body Mass Index (BMI) was normal in half of the patients, but

women were overrepresented in the underweight as well in the obese categories (p=0.023).

Lifestyle factors

Almost all patients (92%) in the HFU-60 study reported no specific dietary preferences; vegetarians and vegans constituted 3%, as did those on a diabetes diet (Table 2 in Paper I). Less than half of the patients (41%) achieved a score of \geq 11 on the Board of Health and Welfare physical activity questions (BHW-PA) (that is, were physically active corresponding to the WHO-recommended minimum activity level of 150 minutes per week). Smoking was reported by 42% of the cohort, and 16% reported previous smoking (i.e., quit more than two years ago). Validated questionnaires on alcohol (AUDIT) and drug use (DUDIT) were answered by 89% and 87% of the patients, respectively. Hazardous or harmful alcohol use was found in 25% of the women and 31% of the men. On DUDIT, 5% of the women and 10% of the men reported signs of drug-related problems.

Medical history

We found that a third of the patients were healthy, a third had one previous disease, and a third had multiple comorbidities (Table 3 in Paper I). In 144 patients (66%), 313 diseases were found. A larger proportion of women than men were found with any previous disease(s), 71% and 62%, respectively (p=0.025). Diseases that were considered associated with increased risk of hip fracture after literature review and expert discussion (Appendix Table 6 in Paper I) were found in 105 patients (48%); neurological disease, diabetes, psychiatric disease and disability, osteoporosis, and chronic obstructive pulmonary disease were the five most common, accounting for 59% of the diseases potentially associated with hip fracture.

Patients were classified according to the American Society of Anesthesiologists (ASA), and two-thirds were categorized as ASA I-II, i.e., with no or mild systemic disease. The remaining third of the patients were ASA III-IV, with six patients considered ASA IV.

Almost half of the cohort (47%) had incurred a previous fracture in adult life, and 5% had a previous hip fracture. A family history of fragility fractures was reported by almost a fifth of the patients, but an equal fraction could not say whether fragility fractures were present in or absent from the family history.

Previous medication

Medical charts were reviewed, and patients were asked about use of medication during the five years leading up to the hip fracture; 135 patients (62%) had used any

medication regularly. Of these, 70 patients presented 130 pharmacological treatments potentially associated with increased fracture risk (Appendix Table 7 in Paper I). The three most common treatments used (accounting for 40%) were as follows: proton pump inhibitors, selective serotonin reuptake inhibitors, and opioids.

Blood sample results

Pre- and post-operative blood samples were analyzed (Appendix Table 8 in Paper I) adjunctive to the operation, on mean 1.4 (SD 1.1) days before and two (2.4) days after surgery. In the pre-operative samples, CRP and leucocytes were above reference in 30% and 75% of the cases, respectively; hemoglobin was below reference in 37% of the samples. Post-operatively, results below reference in more than a quarter of the samples were seen for sex hormones (85% low estradiol in women, 60% low testosterone in men), vitamin D (52%), albumin (45%), and calcium (29%).

The injury

Most fractures were due to low-energy trauma, accounting for 68% of all fracture types in the HFU-60 and 77% of the FNFs in Paper IV. In Paper I, we found that low-energy traumas were more common in women (78%) than in men (61%) (p=0.007).

Fracture types were classified according to AO/OTA in Paper II and Paper IV. All hip fracture types were included in Paper II, while only FNFs were included in paper IV (Table 1).

Fracture types	n (%)
Undisplaced femoral neck, AO 31-B1	46 (21)
Displaced femoral neck, AO 31-B3	80 (37)
Basicervical, AO 31-B2	11 (5)
Stable pertrochanteric, AO 31-A1 + A2.1	28 (13)
Unstable pertrochanteric, AO 31-A2.2-3 + A3	45 (21)
Subtrochanteric, AO 32	8 (4)

Table 1 Fracture classification in HFU-60 according to AO/OTA. Fractures were classified by orthopedic surgeons according to the 2007 revision of the AO/OTA classification, where basicervical fractures are considered intracapslar and unstable (40). In the HFU-60 cohort, intracapsular fractures (63%) were more common than extracapsular, and two-thirds of the fractures were displaced or unstable. Other concurrent fractures were seen in seven patients (five low-energy trauma, two not low-energy trauma), involving the spine, ribs, the contralateral lower extremity, or the upper extremities.

DXA results

DXA investigation was performed within three months of the hip fracture in 184 patients; 85% were performed within the first post-operative month. The median time to DXA investigation was five days (IQR 3-24). T-score at the lumbar spine, femoral neck, or total hip were osteoporotic (< -2.5) in 31% of the patients, osteopenic (-1 to -2.5) in 57%, and normal T-scores (> -1) were found in 12% (Table 4 in Paper I). Results were similar for women and men, with insignificant differences between low-energy and not low-energy trauma, although a tendency of marginally better results on DXA investigation was seen after not low-energy trauma.

Figure 6 Comparison of mean T-scores, HFU-60 vs. NHANES III

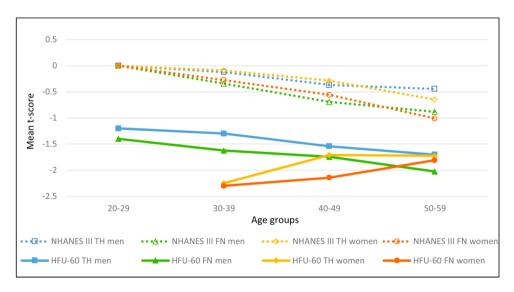


Figure 6 Comparison of mean T-score by age group, HFU-60 vs. NHANES III. Multiple line chart of HFU-60 mean T-scores for women and men compared to NHANES III mean T-scores calculated from BMD data (62). TH total hip, FN femoral neck. NHANES III mean BMD data for age groups were converted to T-scores using the formula: T-score = (measured BMD – young adult mean BMD) / young adult population SD (63). Mean T-scores for HFU-60 were significantly lower than for NHANES III regarding both TH and FN for men (p = <.001), TH for women (p = 0.02), and FN for women (p = 0.03). Figure 2 in Paper I.

Findings were compared with data from the Third National Health and Nutrition Examination Survey (NHANES III), an American general population-based sample,

and mean T-scores were significantly lower for HFU-60 women and men of all age groups (Figure 6). HFU-60 patients' mean T-scores were all osteopenic (-1 to -2.5), whereas NHANES III mean T-scores were normal (>-1) for all age groups.

Fracture classification and association with trauma mechanism and BMD

Most hip fractures in the HFU-60 cohort were of the femoral neck (58%), and twothirds were displaced FNFs. Pertrochanteric fractures were seen in one-third, and two-thirds of these were unstable. A small proportion of the fractures was basicervical (5%) and subtrochanteric (4%).

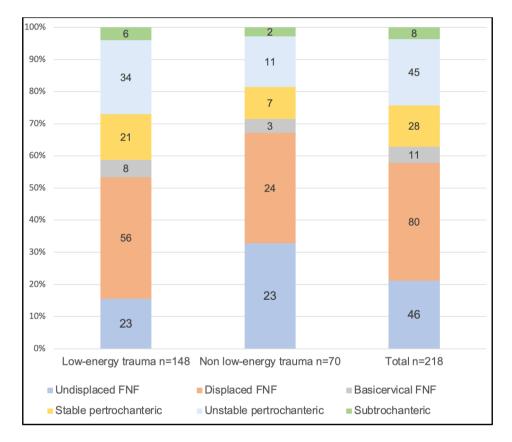


Figure 7 Hip fracture classification divided by trauma mechanism

Figure 7 Hip fracture classification distribution fractioned by percentage, and divided by trauma mechanism. Numbers in fractions are frequencies. FNF: femoral neck fracture. Hip fractures classified according to AO/OTA classifications (40): undisplaced FNF 31-B1; displaced FNF 31-B3; basicervical FNF 31-B2; stable pertrochanteric 31-A1 & 31-A2.1; unstable pertrochanteric 31-A2.2-3 & 31-A3; subtrochanteric AO 32. Figure 2 in Paper II.

Analysis from Paper II on the associations between fracture classification, trauma mechanism, BMD, and a combination of trauma mechanism and BMD did not differ significantly statistically, but clinically important results were found.

A not low-energy trauma fracture was more often intracapsular (71%) than extracapsular (29%) compared to fractures after low-energy trauma, in which a more even distribution was seen -59% and 41% respectively (p=0.07, Table 2 in Paper II). An unstable or displaced fracture was most common in the cohort (66%) and seen more often following low-energy trauma (70%) than after not low-energy trauma (57%), (p=0.06, Table 3 in Paper II).

A normal T-score on DXA was associated with an insignificant tendency towards a lower rate of unstable or displaced fractures, compared to osteoporotic and osteopenic T-scores (Table 3 in Paper II).

Analyses of the combination of trauma mechanism and osteoporotic DXA results showed that osteoporosis was common in both trauma mechanisms, with a higher rate of osteoporosis in low-energy trauma (36%) than not low-energy trauma (22%) (p=0.05). Similar results were found regarding fracture stability and anatomic location (i.e., intra- or extracapsular) in relation to trauma mechanism in combination with osteoporosis.

The lived experience of recovery after hip fracture

In Paper III, interviews were undertaken with 13 women and six men at 0.7 to 3.5 years after sustaining a hip fracture. Patients were aged 32 to 59 years at the time of the hip fracture and presented a variety of characteristics (Table 2 in Paper III). From interviews with participants and through further analysis, the themes presented in Table 2 emerged.

Interviews with young and middle-aged individuals who had suffered hip fractures revealed lingering challenges in everyday life, present years after the fracture. Challenges existed in several dimensions, both corporeal hip-specific and globally psychosocial, affecting the humor and spirit as well as behavior in social settings.

Themes	Examples of quotes
Growing old overnight	"We are all different, you cannot give me the same instructions as an eighty-year-old."
A person lacking capability	"Feeling tired all the time because I do not get the sleep I need because of the pain"
Inconsistent emotions and subsequent consequences	"A low energy trauma hip fracture is an old peoples' disease – so why me?"
Total standstill in midlife	"My neighbor could walk nicely one month after the operation. I am now one YEAR after the operation and I still have problems even though I am younger. This is embarrassing!"
Defy despair	"I want to be exactly the same as before the operation but then I understand, I do not have that strength in the leg because it has taken quite a lot of damage. But I want to return to who I was before. I have so many beautiful shoes to use, ones with really high heels. They have been my motivation to get better (laughs), because I decided I will use them again (laughs)."
Returning to normal	"I think it has taken a long time to get back to normal. And, well, I am not quite sure that I actually am fully back to normal… But now is maybe the new normal."

Table 2 Emerged themes, including exemplar quotes from participant interviews

Pain

Most participants explicitly described experiencing pain from the fractured hip at the time of the interview, with varying intensity and incidence – for some daily, and for others more seldom. Hip pain or a combination of pain from the hip and groin, the back, and radiating pain in the leg was reported by participants. The pain was described as a constant reminder of the fracture, affecting the present but also the future by anticipation of further pain.

Functional impact

Physical limitations following the hip fracture were omnipresent, rendering ordinary activities difficult through pain, limping, stiffness, and loss of physical strength and leg function. Doubt regarding the body's capability and fear of falling led participants to live more cautiously, in anticipation of falls or fear of aggravating symptoms of the hip fracture. Participants living alone were forced to ask for help with ordinary chores, which for some created an unpleasant duality where they felt incapable and diminished, yet thankful for the help. Furthermore, the limitations led to reduced work capacity for some, with prolonged sick-leave or reassignment to other tasks, which also could mean a reduced income.

Psychological impact

Strong emotions were experienced by the participants; a sense of growing old overnight arose when suffering the fracture, and most struggled to believe in a future with full recovery. Having different personae were reported: an overly positive façade expressing confidence in front of others, and another feeling depressed and hopeless when alone. Feelings of sadness and entrapment, self-imposed isolation in combination with external exclusion, and fear of falling preoccupied the latter persona. In an escalation of negative feelings, frustration and anger grew towards those feelings of weakness, helplessness, and dependence. Furthermore, many struggled with an unanswerable question of why they broke their hip – "why did this happen to me?"

Social impact

Negative impacts of the fracture were also present in social contexts, for example, through fear of falling. Participants not only hesitated in familiar situations, in which expectations of others might involve risks of falling or worsening of hip symptoms, but also avoided unfamiliar situations, leading to a more limited life compared to that before the fracture. The social impact included managing the reactions and expectations of others; participants reported that people around them often failed to appreciate the severity of their symptoms and limitations, which in turn generated feelings of shame from the perception that they were overreacting. On the other hand, support from family and maintaining social networks were described as important parts of the path to recovery.

Recovery

Information on the injury, treatment, and prognosis, as well as physical rehabilitation, was provided at the hospital ward after the hip fracture surgery, often while participants were under the influence of analgesics, making it difficult for some to remember information and instructions later during the recovery process. Many described the initiation of the recovery process following the hip fracture as following a standard protocol adapted to elderly patients and as mechanical and oblivious to specific rehabilitation needs. Participants described feeling abandoned after discharge, left alone to seek further support through municipal care or private caregivers. Individually targeted rehabilitation and continuous support of needs were identified as important factors in the recovery process, but most participants described a lack of it.

Conversion to secondary arthroplasty after IF in FNFs

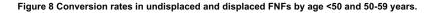
In Paper IV, the rate of conversion to secondary arthroplasty was analyzed in 796 patients under age 60 with undisplaced and displaced FNFs that were initially treated with IF. The cohort with FNFs was defined, and patients were identified from the SFR. Patients were aged 20 to 59 years, 59% were men, and 77% of the fractures were due to low-energy trauma.

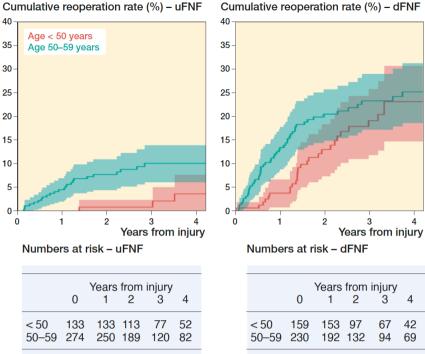
Included fractures were undisplaced (n=407) or displaced (n=389); most were treated with parallel pins/screws (n=748), and only a small part of the cohort (6%) was treated with sliding hip screw devices (n=48). From the SAR, 108 secondary arthroplasties (106 THA, 2 HA) were identified, 28 after undisplaced and 80 after displaced fractures.

In a Kaplan-Meier implant survival analysis, the conversion rates for undisplaced and displaced fractures were identified up to five years after the fracture (Figure 8). The conversion rates were significantly higher at all time points for displaced fractures, both for patients aged <50 years and those aged 50-59 (Table 2b in Paper IV).

The rate of conversion for undisplaced FNFs was 3% (95%CI 1-5) at one year, 5% (CI 3-8) at two years, and 8% (CI 5-11) at five years. For displaced FNFs, the 1, 2, and 5-years conversion rates were 9% (CI 6-12), 17% (CI 13-21), and 25% (CI 20-30), respectively.

In a Cox proportional hazards regression model of risk factors for conversion, age 50-59 had a hazard ratio of 5.2 (95%CI 1.4-20), compared with age <50 in the group with undisplaced FNFs. At five years, a conversion rate of 10% (CI 6-14) was seen in patients with undisplaced fractures aged 50–59 years, compared to 4% (CI 0-8) in patients <50 years. Neither female sex, high-energy trauma, nor resident surgeon could be identified as risk factors (Table 3 in Paper IV).





Cumulative reoperation rate (%) - dFNF

Figure 8 Conversion rates showed as cumulative reoperation rate with 95% confidence intervals presented by fracture type and age classification. uFNF: undisplaced femoral neck fracture, dFNF: displaced femoral neck fracture. Figure 2 from Paper IV.

Mortality in younger patients after hip fracture

In Paper IV, mortality rates were analyzed through Kaplan-Meier analysis. At one year and five years post-fracture, mortality rates were similar between undisplaced and displaced fractures as well as between women and men (Figure 9).

Patients aged 50-59 years had a significantly higher mortality rate compared to patients aged <50. The 1- and 5-year cumulative mortality rates for patients aged <50 years were 0% and 5% (CI 2-7); for patients aged 50–59, it was 4% (CI 2-6) at one year and 16% (CI 11-20) at five years.

Figure 9 Mortality rates by fracture type and sex

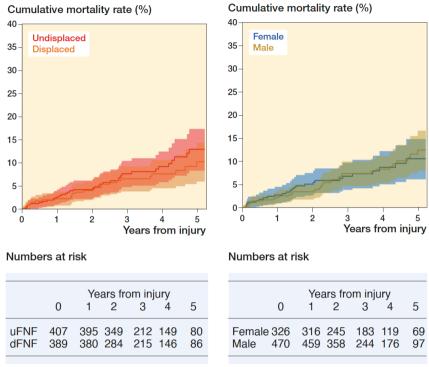


Figure 9 The cumulative mortality rates by fracture type and sex showed similar mortality rates between undisplaced and displaced fractures, as well as between women and men. Figure 3 and 4 in Paper IV.

Discussion

Demographic and physical characteristics of subjects

Young and middle-aged patients with hip fractures formed a heterogenous group, where multiple risk factors for fractures and low bone mass were common. Previous assumptions and preconceptions regarding younger patients do not seem to be valid; most patients are not "addicts", multimorbid, or incurring their fracture through high-energy trauma mechanisms. Indeed, the opposite was true for most patients. We also found a high prevalence of osteopenia and osteoporosis on DXA investigation at the time of the fracture.

Patients aged under 60 constituted circa 5% of the total hip fracture population. Since every twentieth patient presenting with a hip fracture can be expected to be young, all orthopedic surgeons will probably meet and treat these patients. In both the HFU-60 and the SFR cohorts, hip fractures became more common with increasing age (Figure 5). This is also consistent with a large Danish register report where 90% of hip fractures in patients under 65 were found in the ages 40–65 (64). Hence, a hip fracture in the third or fourth decade of life is quite uncommon, approximately accounting for fewer than one in a hundred of all patients with hip fractures.

In younger individuals, hip fractures were more common in men, in contrast to hip fractures among the elderly, an observation that has been previously reported (13,15,35,36). In the HFU-60 cohort, two-thirds of the men were aged below 50, compared to half of the women. The explanation for the difference in age distribution between women and men is probably multifactorial, resulting in young men being at higher risk of hip fractures than young women. Men reported heavier smoking, more alcohol and drug use, and more fractures were seen in men after not low-energy traumas, suggesting a more risk-exposed behavior in men. Nevertheless, proportionally more women than men had a history of previous fractures and comorbidities.

Regarding lifestyle factors, the HFU-60 cohort presented worse characteristics compared to the general population in Sweden and Denmark. Physical activity level was found to be lower than the WHO-recommended 150 min/week in more than half of the cohort; in Sweden and Denmark, around 70% of the general population are physically active \geq 150 min/week (65–67). Smoking was two-and-a-half to four

times as common, harmful alcohol use was almost twice as common in men and more than twice as common in women, and signs of drug-related problems were three times higher than in the general population (68–72). Previous studies of younger patients with hip fractures show varying degrees of smoking and alcohol use but support our findings of higher prevalence than in the general population (12–14,18,23,30,73).

The medical history of the cohort indicates a high degree of frailty in younger patients with hip fractures, and their biological age can be considered more advanced than their chronological age. Two-thirds of the patients in the HFU-60 cohort had no previous disease or only mild systemic disease, i.e., ASA I-II. One-third was classified ASA III-IV with multiple comorbidities, carrying 78% of the disease burden, yet only 3% of the cohort were ASA IV. In previous studies on younger patients with hip fractures, comorbidity has been reported in 9 to 55%, suggesting a variance in the composition of the study populations (14,17,35,74–77). Diseases associated with increased risk of hip fractures were seen in almost half of the cohort, and one-half had also incurred a previous fracture in adult life, suggesting increased risk of hip fractures.

The blood sample results may also reflect frailty and a predisposal for poor bone health and fractures in the cohort. Pathologically low values for vitamin D, albumin, and calcium were common, and most had low sex hormones. However, testosterone and estradiol were analyzed post-operatively after opioids were administered, which may have negatively affected the results (78).

DXA investigation at the time of the hip fracture revealed a high prevalence of osteopenia and osteoporosis in the HFU-60 cohort; only 12% had a normal T-score. Somewhat surprisingly, no normal DXA results were found in patients younger than age 40. Compared to the American population-based NHANES III cohort used as a reference database, the mean T-scores were lower for all age groups in both women and men from the HFU-60 cohort. Our found rates of osteopenia (57%) and osteoporosis (31%) were also much higher than in local population-based samples from Scandinavia – Malmö in Sweden and Tromsø in Norway – which presented rates of osteopenia of 5–9% and of osteoporosis of 0–5% (79,80). Rates of osteopenia and osteoporosis similar to ours were also presented by Al-Ani et al. (18) in their smaller cohort of somewhat older patients with hip fractures from Stockholm, Sweden.

From our findings and the comparisons, it seems reasonable to expect an inferior bone quality in almost all patients under the age of 60 with hip fractures. Furthermore, since we could not identify any particular subgroup with no or only low risk of low BMD, all young and middle-aged patients with hip fractures should be considered at risk and should be investigated accordingly and treated when indicated (81). One could argue that the diagnosis of osteoporosis is a categorical variable, whereas a diminished bone quality is reflected perhaps more correctly by a continuous decrease in T-score. Hence, the group without osteoporosis also contains individuals with lower-than-normal bone quality, but not low enough to be categorized as osteoporotic. As previously mentioned, it has been reported that most fractures, including hip fractures, occur in individuals with osteopenia, not osteoporosis (33). The treatment of osteopenia and osteoporosis is beyond the aim of this thesis; but only briefly mentioned, the cut-off T-score value for treatment and fracture prophylaxis of low bone quality has been discussed, and former guidelines from the National Osteoporosis Foundation also recommended treatment in the osteopenic range for T-scores < -2 (33).

Impact of trauma mechanism and BMD on hip fracture type

Fracture classification in the HFU-60 cohort found intracapsular fractures to be most common (63%), a finding comparable to previous studies, which reported a distribution of approximately three to two between intra- and extracapsular fractures (17,26,36,82). The distribution of the specific fracture types among the intracapsular fractures was comparable to previous reports (36,41). Regarding extracapsular fractures, the proportions of subtrochanteric fractures were higher than ours in previous studies (26,36,82). These studies did not, however, report fractures using AO/OTA classification, making strict comparisons difficult, and thus our findings can be considered sufficiently representative.

The injury leading to the hip fracture was typically a low-energy trauma, i.e., a same-level fall. In the HFU-60 cohort (Paper I & II), two-thirds of the trauma mechanisms were classified as low-energy trauma, as were almost four-fifths in the SFR cohort (Paper IV). A possible explanation for the larger proportion of low-energy trauma in Paper IV might lie in the alternative definition of trauma mechanism in the SFR, whereas in HFU-60, trauma mechanisms other than same-level falls were categorized as not low-energy. This might have led to a classification of intermediate trauma mechanisms as low-energy if they fitted that definition better than the definition of high-energy trauma. Hence, the proportion of low-energy fractures is plausibly more correct based on the HFU-60 cohort. On the other hand, high-energy trauma cannot be distinguished in the HFU-60 cohort but is available from Paper IV.

The inconsequence in the classification of trauma mechanism may be explained by the lack of a uniform definition of what high-energy trauma actually is; although the term often include high-speed traffic accidents and falls from a height (13,30,35,36). Similar criteria can also be used to triage patients to care at designated trauma centers; for example, the Swedish National Trauma Alert criteria specifies car accident >50km/h without seatbelts and falls >5m (83). The fracturing of a bone in

these instances might not be unexpected, as the trauma energy probably exceeds the force required to break even a healthy bone. A definition of an intermediate trauma mechanism, which might be energetic enough to break a healthy bone but not necessarily accompanied by multiple injuries in other organ systems, might be appropriate in future fracture reporting to differentiate trauma mechanisms. However well-defined the criteria, it may still be challenging to correctly grade the energy of the trauma mechanism retrospectively and define when the fracture actually occurred, which has been stated before (81).

In Paper II, no significant associations between trauma mechanism and fracture types could be seen. There was a trend of not low-energy trauma leading to intracapsular fractures more often. Also, low-energy traumas tended to produce unstable or displaced fractures more often than not low-energy trauma. In Paper IV however, the opposite was seen, and high-energy trauma led to displaced FNFs significantly more often. That a trauma mechanism with lower energy would more often produce unstable or displaced fractures may seem counterintuitive and challenges common preconceptions, but this observation suggests that factors beyond the trauma mechanism are implicated in the creation of different fracture patterns.

Experimental biomechanical studies simulating a sideways fall onto the greater trochanter of a cadaver human femur have suggested that fractures of the proximal femur begin with compression of the superolateral cortex of the femoral neck, leading to both intra- and extracapsular fractures (84,85). Similar findings were presented in a clinical study on actual femoral neck fractures in patients treated with arthroplasty, analyzing the fracture site in the resected proximal part of the femur (86). In experimental simulation of fractures, the load was continuously increased until a fracture occurred. The load required to create a fracture varied more than three-fold between the femora used in the biomechanical analyses (84,85). The superolateral femoral neck was found to be the origin of the fractures both in osteoporotic bone as well as in bone with higher T-scores (85).

This suggests that varying properties between the bones require different levels of trauma to fracture them, but the origin of the fractures seems to be the same regardless of degree of trauma and BMD. However, this does not fully explain the reason for different fracture types, especially not where the cranial cortex of the femoral neck is not engaged, e.g., transverse pertrochanteric or subtrochanteric fractures. Another experimental study found that intracapsular fractures were more common at lower failure loads, whereas pertrochanteric and subtrochanteric fractures were more common in femora that required higher loads to break (87). This indicates that intracapsular fractures should be more common after higher energy trauma mechanisms, since a low-energy trauma might be enough to break the hip of a weaker bone – as most of our cohort presented with – resulting in

an intracapsular fracture after a not low-energy trauma mechanism, which was also often seen in our cohort.

Inferior bone quality may partly explain a more severe fracture pattern, and in Paper II we found a somewhat lower rate of unstable or displaced fractures in those with normal bone quality compared to osteopenic and osteoporotic bone. Still, BMD was not significantly associated with fracture type, and inferior bone quality did not by itself explain an unstable or displaced fracture pattern. Neither were different fracture patterns explained by a combination of osteoporosis and trauma mechanism alone. It is probable that other factors of biomechanics and bone properties are also involved in producing different fracture patterns: for instance, the proportion of cancellous to cortical bone, the microarchitecture of the bone, or the skeleton's elasticity.

Lingering challenges and a call for diversified support of recovery

The patient's perspective – challenges after surgery

A hip fracture in young individuals is a sudden, traumatic event that profoundly impacts the individual through many aspects of life. Participants in our qualitative study (Paper III) provided a variety of examples of a hip fracture's negative effects and protracted challenges to everyday life. Through this explicitly patient-centered report, a nuanced picture of the patients' experiences was presented.

The younger patients reported a feeling of growing old overnight, partly due to the type of fracture they suffered but mainly because of the way they were treated by healthcare staff. Care and rehabilitation were described as mechanical and standardized according to the needs of elderly patients, without involving the individual patient in the planning and execution.

Participants reported pain, fear of falling, and negative psychological effects from the hip fracture which damaged integrity, self-worth, and pride. Negative social implications and stories of life being brought to a standstill were common. Economic implications from decreased work ability were also present. The previous description of a hip fracture in the elderly as a life-breaking event seems valid also for younger patients, with negative impact in multiple dimensions of life, which is supported by previous reports (35,9,88–91).

Support from family and social networks, understanding employers, and hope and belief in improvement promoted recovery according to the participants. The need for social support seems as important to our younger participants as it is to elderly individuals, as demonstrated in previous reports (92). However, younger patients described the outside world as struggling to understand the magnitude of limitations and lingering symptoms after a hip fracture, which supports previous findings (88).

According to our participants, there is a lack of individually targeted rehabilitation directed at specific needs relevant for younger individuals. Some patients received individualized rehabilitation, and they described it as greatly contributing towards recovery. Correspondingly, a previous report on hip fractures in patients of all ages stated that only a third found their rehabilitation adequate (93). These results suggest that there is room for improvement in the rehabilitation after hip fractures for all ages.

In the reporting of outcomes after hip fractures, a shift from surgeon-based evaluation to patient-centered assessment has been proposed (11,94). In Paper III, explicitly patient-centered outcomes were reported through the participants' lived experiences. In future evaluations of hip fracture outcomes, it may be of value to add an assessment of psychosocial consequences, as this was accentuated by our participants, and implications were present years after the hip fracture.

In supporting patients when they recover after hip fractures, one should bear in mind that not all individuals reach a full return to the pre-injury state of function and mobility, and that psychosocial consequences affect patients years after the injury (6,11,88,93,95). It is important for future studies to identify those who do and do not recover fully, to better understand what can be expected after a hip fracture.

As surgeons, our job is often considered complete when the patient leaves the operating room and we are satisfied with our work. For the patient who receives surgery for a hip fracture, however, the work has only just begun, and they are often left alone with this burden. It is important for surgeons to inform patients of the lengthy rehabilitation process and the risk of long-term implications after suffering a hip fracture. This information might help to adjust expectations, thus making the patients' burden easier to carry or at least to accept. The addition of diversified rehabilitation tailored to the individual could lessen the burden and result in an improved recovery process. Healthcare services should be able to provide suitable support in recovery for all patients, not merely offer standard geriatric hip fracture rehabilitation.

Could primary treatment of FNFs be better?

The surgeon's perspective – challenges prior to surgery

Fracture of the neck of the femur continues to be regarded as "the unsolved fracture", but its claim to this distinction becomes increasingly insecure. Since the introduction of the Smith-Petersen nail in 1931, unrelenting endeavours have been made to solve this problem [...] The overall picture is one of some confusion but two elementary points of universal agreement are seen to emerge: reduction must be perfect; and fixation must be secure. – *R. S. Garden, 1961* (3).

Since Garden's publication, most elderly patients with displaced FNFs are now treated with primary arthroplasty because the complication rate and the rate of conversion to secondary arthroplasty after IF was deemed to be unacceptably high (44,45,96). Current studies are focusing on whether primary arthroplasty might be a better solution even for undisplaced FNF in the elderly (e.g., the ongoing HipSTHeR study in Sweden, SENSE in Denmark, and FRUITI in the UK), as failures of IF and subsequent conversion to arthroplasty also occur after undisplaced fractures (47–49,97).

In younger patients, arthroplasty has not been considered a universally attractive alternative. Concerns are expressed that the limited longevity of the implant compared to the patient's expected remaining survival would require revision of the arthroplasty (98). Sparing the native femoral head has also been considered beneficial; thus, IF has been the recommended treatment of FNFs in younger patients (25). Different methods to achieve secure fixation are used internationally. In Sweden, two parallel pins or screws are almost uniformly used. The use of three or even four parallel implants is seen in other countries, but there is little evidence that adding extra screws will reduce the risk of complications (59).

Although research on femoral neck fractures has continued to increase since Garden's publication in 1961, it seems that these endeavors have not been sufficient; this fracture is still unsolved (1). Displaced FNFs in younger patients continue to pose a problem, as not all patients heal their fracture uneventfully after IF. As stated by Speed (1) on the treatment of femoral neck fractures, "although the results obtained today show improvement ... there is no guarantee of 100% cure.". That is why this fracture remains unsolved and also where the surgeon's problem presents itself.

The challenge for the treating surgeon lies in pre-operative decision-making, specifically in the selection of the proper treatment for the individual patient; unlike comorbidities and fracture displacement, the surgeon can control this challenge. In Paper IV, we found that most patients heal their fractures after IF of both

undisplaced and displaced FNFs and do not require conversion to arthroplasty. For undisplaced FNFs, our findings confirmed IF as the gold-standard treatment: one in 12 patients underwent conversion to arthroplasty within five years. However, results for displaced FNFs were markedly poorer, where one in four patients treated initially with IF were converted to arthroplasty. Our results are comparable to the few earlier studies on younger patients (22,46).

For some patients, a primary arthroplasty has been proposed as advantageous; previous reports have suggested that alcohol abuse, renal or respiratory disease, osteoarthritis, inflammatory arthritis, and symptomatic hip dysplasia are reasons to choose arthroplasty as a primary treatment of an FNF (11,22). The criteria for patient-selection for either IF or arthroplasty for younger patients without these specified traits are unclear, why the choice of treatment could be arduous. Factors predicting failure of IF have previously been reported in elderly patients; posterior tilt of the femoral neck >20 degrees and anterior tilt >10 degrees in Garden I-II FNFs (99,100), as well as the degree of displacement and fracture comminution (101). In Paper IV, we were not able to perform all the same analyses, since the SFR does not include data on these factors apart from displacement in the form of fracture classification. We found that displaced FNFs had a higher rate of conversion to secondary arthroplasty, suggesting that factors predicting failure of IF in the elderly also might be valid in younger patients. It has previously been shown that time to surgery exceeding 24 hours was associated with a higher failure rate in displaced FNFs treated with IF (22).

Another factor to consider is the longevity of the respective implants. The risk of conversion from IF to arthroplasty should be weighed against the risk of subsequent revisions when choosing arthroplasty as the primary treatment. In a recent register report on survival of THA for all indications, Nugent et al. (98) found a 10-year rate of revision of less than 10% in patients aged 45–60 – much lower than our 25% conversion rate at five years. The lifetime rate of revision was found to be as high as 28% – similar to our conversion rate. However, conversion rates can be expected to increase after even five years post-fracture; a rise in conversion rate from 10% to 14% between five and 10 years in both undisplaced and displaced FNFs was reported by Stockton et al. (46). If a similar increase were true for the displaced FNFs in our register cohort, the 10-year conversion rate would be 35%, somewhat higher than the lifetime revision rate presented by Nugent et al. (98).

The comparison is not fully appropriate, since the results presented by Nugent et al. (98) were for THA performed for all indications. From previous research, it is known that the results regarding implant survival after an arthroplasty due to a hip fracture are somewhat worse than for arthroplasties performed for other reasons (102). Therefore, we could expect the lifetime rate of revision of arthroplasties performed due to FNFs to be higher than 28% presented by Nugent et al. (98). An interesting question would be how the lifetime revision rate of a primary fracture arthroplasty compares to the lifetime conversion rate after initial IF of FNFs, i.e.,

the lifetime risk of major secondary surgery after either primary treatment of a displaced FNF.

From studies on older patients, we know that secondary arthroplasties after initial IF are associated with inferior results regarding revision rate, hip function, and health-related quality-of-life compared to primary fracture arthroplasty (103,104). It has also been shown that patients treated with initial IF of their FNF, in which the native femoral head was spared, did not reach better functional results than those treated with a primary arthroplasty (44,45,105). Consequently, the results speak in favor of arthroplasty as primary treatment of displaced FNFs in the older population, but this has not yet been proven in young and middle-aged patients.

In contrast to the elderly who suffer hip fractures, more younger patients can expect a long survival after their hip fracture. Therefore, long-term results are of interest, which may potentially impact the choice of implant at the initial fracture surgery. An interesting analysis would be a long-term comparison between the first revision of a primary fracture arthroplasty and the secondary arthroplasty after initial failed IF, i.e., a comparison of the results of the secondary surgeries after either primary treatment of displaced FNFs. One could assume – at least in a Swedish setting – that a cohort of patients under 60 years treated primarily with arthroplasty were selected to such treatment for specific reasons, and not representative for most younger patients with FNFs. This may call for a randomized trial with long-term follow-up comparing IF and arthroplasty, similar to the Norwegian trial on patients aged 55-70 years, which recommended THA as primary treatment (106).

Although initial arthroplasty may be the best solution for some patients with an inherently higher risk of fixation failure, most younger patients actually do heal their displaced FNFs; in Paper IV, three in four were not converted to arthroplasty within five years. This speaks in favor of IF as the primary treatment for most young and middle-aged patients, although both surgeons and patients should have realistic expectations and be aware of the risk of complications requiring a secondary arthroplasty during the years following a fracture of the femoral neck.

Higher mortality after hip fracture

The mortality found in Paper IV for young and middle-aged patients with FNFs was similar between undisplaced and displaced fractures, suggesting that the fracture type itself does not pose an increased threat to life. Although one might have expected some characteristics or properties to predispose for a certain fracture type and that this would have had an impact on mortality, no such differences could be identified. Mortality rates were – somewhat surprisingly –similar between women and men. In the elderly, men have a higher risk of dying after suffering a hip fracture (107). In Paper I, younger women were found to have more comorbidities, which may partly explain why the difference in mortality vanished in our young cohort.

As expected, older patients in the cohort (aged 50–59 years) had an increased mortality rate both at one and five years compared to patients under 50. When comparing the mortality for patients aged 50–59 to mortality rates for the general Swedish population of the same ages for the years of the study, the one-year mortality rate of 4% is 10-fold higher, and the five-year mortality rate of 16% is noticeable (108,109). This suggests that although mortality rates are not as high as among the elderly patients, suffering a hip fracture poses an increased threat to life even in younger patients. They may also resemble older patients biologically, although their chronological age is lower.

Limitations and strengths

Considering the evidence pyramid, one could always aspire for higher evidence levels of the studies one conduct. But, both with our research questions and practical issues in mind, we chose the current designs. In particular regarding the outcome after different surgical methods or rehabilitation strategies, randomized trials are preferrable. Such comparative studies will be a natural second step to improve the care chain for young individuals with hip fractures, but initially we need more information about who these patients are and how they fracture and recover. Thus, descriptive cohort studies and a qualitative study became our choice of study designs.

From an international point-of-view, our results may not be generalizable to more than high-income countries with a publicly financed healthcare. Still, we think our underlying message is important, that a patient group should not be looked upon and treated based on preconceived notions. Clinically useful facts must be investigated, and the patients' experience should be sought. A corresponding cohort of young patients in low- and middle-income countries or in a commercialized healthcare setting would most certainly stand forward with other characteristics.

The typical features of Scandinavian healthcare have on the other hand generated some of the strengths of the project. Individuals are admitted to acute orthopaedic care, rehabilitation and follow-up regardless of their socioeconomic status. The participating departments care for all fracture cases in their catchment areas, serving both urban and rural areas. Patients are easily traced via their unique personal identification number, meaning fewer cases with missing data and solid information about mortality. Also, the national quality registers on which Paper IV is based on rely on a long history of register development with the use of personal identity numbers, enabling dependable longitudinal data within and across registers.

The privacy legislation forbids a drop-out analysis of eligible individuals not included in the HFU-60 study; thus, we cannot estimate any possible selection bias. However, three-quarters of the eligible patients were included in this mixed general population-based cohort and we consider the study population to be representative of the heterogeneous group of younger individuals incurring hip fractures. Although our study is one of the largest compared to other clinical studies on corresponding ages, the sample size may limit the statistical power of some of our findings.

The exclusion of some late DXA investigations from the analyses might introduce a selection bias, but DXA performed at the time of the fracture was considered more accurate in the description of the pre-fracture condition. The characteristics of the excluded patients were associated with low BMD as well, with higher median age and ASA-class, a lower proportion of normal BMI, and a higher rate of low-energy trauma compared to patients included in the analyses of DXA results. Hence, the prevalence of osteopenia and osteoporosis in the cohort was probably not overestimated through the exclusion, but might be underestimated.

The participants in Paper III were purposively sampled from the larger HFU-60 cohort; hence, the results cannot be extrapolated to all individuals. Nevertheless, the participants represent a wide variety of characteristics, and our findings are valid as a testimony of experiences of recovery after hip fractures that are important to patients.

In Paper IV, the rate of conversion may have been affected by the treatment with primary arthroplasty of some patients in the age group 50–59, which theoretically reduced the number of FNFs at risk of conversion to arthroplasty. Furthermore, it possibly led to an underestimation of the conversion rate, assuming that these patients were identified as having a higher risk of fixation failure. From an international perspective, the lack of data on whether open reductions were performed and the almost exclusive use of two parallel implants may limit the study. However, there is little evidence that adding extra implants reduces the risk of failure, and open reduction has not been proved to have any clear benefits (11,59,110). Indeed, other outcomes than reoperation are valuable, and patient-reported outcomes are preferable. Nevertheless, conversion to arthroplasty was considered a marker of major hip complications and this outcome was chosen due to the national coverage of the SAR and its high completeness, leading to dependable findings. Our result reflects the everyday practice in non-selected patients and surgeons, rendering generalizability.

Conclusions

Patients under the age of 60 form a heterogenous group. A wide range of different characteristics were seen in demographics, lifestyle factors, previous fractures, and medical history and medications. Some patients showed signs of vitality and health, yet primarily we found a high degree of frailty. Furthermore, risk factors for fractures and osteoporosis were ubiquitous.

On DXA investigation at the time of the fracture, only one in eight had a normal T-score. The prevalence of osteopenia and osteoporosis was high compared to general population-based reference samples, regardless of age and trauma mechanism.

Low-energy trauma was the main trauma mechanism in patients under the age of 60. Most hip fractures were unstable or displaced, and the anatomical location was mainly intracapsular.

Trauma mechanism and BMD did not alone nor in combination sufficiently explain the reasons for different hip fracture patterns.

The lived experience of sustaining a hip fracture includes challenges in everyday life for patients under the age of 60, even years after the fracture. According to the patients, the care and rehabilitation were not adapted to their needs.

Although most patients heal their femoral neck fracture after internal fixation, one in twelve with undisplaced fractures and one in four with displaced fractures needed conversion to a secondary arthroplasty within five years.

Mortality after a hip fracture was higher than in the general population, suggesting that the underlying frailty associated with hip fractures pose a threat to life even in patients under the age of 60.

Clinical perspectives

Regarding patients under the age of 60 with hip fractures, existing preconceptions do not seem valid and should be traded for a nuanced understanding of who these patients are.

A thorough health investigation is warranted given the high degree of frailty and comorbidity in combination with a high prevalence of risk factors for fractures and low bone quality.

Bone quality should be assessed by DXA investigation of all patients with hip fractures, including the youngest patients and regardless of trauma mechanism.

A need for improved information and diversified support in recovery was requested by patients. Healthcare services should be equipped to provide this support.

Both surgeons and patients need to be aware of the risk of complications leading to secondary arthroplasty after internal fixation of femoral neck fractures. This is important in order to inform patients and to plan the follow-up scheme in younger individuals with hip fractures.

Long-term follow-up is justified after hip fractures in patients under the age of 60, primarily concerning a protracted recovery process. In addition, internal fixation of femoral neck fractures carries a risk of early and late developing complications that may require secondary surgery.

Future research in the HFU-60 study

Ongoing, in manuscript:

- Physical activity in young hip fracture patients is associated with healthrelated quality of life and strength; results from the HFU-60 multicenter study.

Anna Gaki Lindestrand, Sebastian Strøm Rönnquist, Bjarke Viberg, Søren Overgaard, Henrik Palm, Cecilia Rogmark, Morten Tange Kristensen.

- How to spot osteonecrosis of the femoral head after internal fixation of femoral neck fractures in younger patients, with implants in situ. The value of MARS MRI versus conventional x-ray.
 Mikael Kindt, Maria L Jönsson, Trine Torfing, Sebastian Strøm Rönnquist, Bjarke Viberg, Søren Overgaard, Cecilia Rogmark.
- Alcohol and drug use in patients younger than 60 years with hip fracture, measured by validated instruments and the clinical eye.
 Sara Svanholm, Sebastian Strøm Rönnquist, Åsa Magnusson, Bjarke Viberg, Carsten Fladmose Madsen, Morten Tange Kristensen, Henrik Palm, Søren Overgaard, Cecilia Rogmark.

Planned papers:

- Outcome after hip fracture in adults under the age of 60 clinical, functional and patient reported results.
- Risk factors for failure after hip fracture treatment in adults under age 60.
- Long term outcome after hip fracture in adults under the age of 60.

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Appendix

Paper I: Frailty and osteoporosis in patients with hip fractures under the age of 60 - a prospective cohort of 218 individuals

Paper II: Trauma mechanism and bone mineral density did not impact hip fracture type – a multicenter cohort of patients under 60 years of age

Paper III: Lingering challenges in everyday life for younger patients with hip fractures – a qualitative study of the lived experience during the first three years

Paper IV: Rate of conversion to secondary arthroplasty after femoral neck fractures in 796 younger patients treated with internal fixation: a Swedish national register-based study

Paper I

ORIGINAL ARTICLE



Frailty and osteoporosis in patients with hip fractures under the age of 60—a prospective cohort of 218 individuals

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Abstract

Summary Research on younger patients with hip fractures is limited. This study adds knowledge on patient and injury characteristics, and DXA was investigated at the time of the fracture. Risk factors for osteoporosis and fractures were numerous among young patients, and osteoporosis was markedly more prevalent than in the general population.

Introduction Knowledge on younger patients with hip fractures is limited. Common preconceptions are that they suffer fractures due to high-energy trauma, alcohol or substance use disorder but not associated to osteoporosis. We aimed to descriptively analyze the characteristics of young and middle-aged patients with hip fractures and examine bone mineral density (BMD) by dual-energy x-ray absorptiometry (DXA) at the time of the fracture.

Methods A prospective multicenter cohort study on adult patients with hip fractures below age 60 collected detailed information on patient characteristics regarding demographics, trauma mechanism, previous fractures, comorbidity and medication, and lifestyle factors. DXA results were compared to population-based reference data.

Results The cohort contains 91 women and 127 men, median age 53 (IQR 47–57). Most fractures, 83%, occurred in patients aged 45–59. Two-thirds of all fractures resulted from low-energy trauma. Half of the patients had prior fractures after age 20. Thirty-four percent were healthy, 31% had one previous disease, and 35% had multiple comorbidities. Use of medication associated with increased fracture risk was 32%. Smoking was prevalent in 42%, harmful alcohol use reported by 29%, and signs of drug-related problems by 8%. Osteoporosis according to WHO criteria was found in 31%, osteopenia in 57%, and normal BMD in 12%.

Conclusion In patients with hip fractures below age 60, risk factors for osteoporosis and fractures were numerous. Moreover, the prevalence of osteoporosis was markedly higher than in the general population. We suggest that young and middle-aged patients with hip fractures undergo a thorough health investigation including DXA, regardless of trauma mechanism.

Keywords DXA · Epidemiology · Hip fracture · Osteoporosis · Young and middle-aged adults

Introduction

Young and middle-aged patients constitute one-tenth of the total hip fracture population [1–4], but the literature is scarce concerning this patient group in comparison to the elderly. Nevertheless, many orthopaedic surgeons have preconceptions regarding who these patients are. Common perceptions are that younger patients suffer hip fractures due to

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high-energy trauma, alcohol or substance use disorder but not due to osteoporosis [5, 6].

These preconceptions could emanate from older studies or studies from low- and middle-income countries, depicting high-energy trauma to be the main cause of hip fractures in younger patients, thereby dismissing any risk of osteopenia and osteoporosis [3, 7, 8]. Studies on samples representing the general Western world population of today suggest that young and middle-aged patients may have both osteopenia and osteoporosis regardless of trauma mechanism [1, 2, 9–12]. However, there are considerable limitations to these studies; conclusions on bone health were not based on dualenergy x-ray absorptiometry (DXA) investigation at the time

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of the fracture but solely on risk factors for osteoporosis, or on DXA measurement years after the hip fracture [1, 2, 9–11]. Only one smaller previous study performed DXA at the time of the hip fracture and found a high rate of low bone mineral density (BMD) in patients aged under 70 years [12].

We designed a prospective multicenter cohort study that assessed BMD by DXA at the time of the hip fracture in adults under 60 years of age and performed comparisons to other DXA reference materials. In addition, detailed information on patient and injury characteristics was obtained as this is not previously well investigated. This is the primary report on baseline results from the "Hip Fracture in adults Under 60 years of age" project (HFU-60), describing the demography and epidemiology of hip fractures in young and middle-aged patients, as well as lifestyle factors, comorbidity, and general health in the cohort together with analysis of DXA results.

Aims

In patients with hip fractures under the age of 60 years, we aimed to descriptively analyze their characteristics, with a focus on risk factors for fractures and osteoporosis, and describe BMD at the time of the hip fracture related to known normal values in the population.

Material and methods

Settings

Patients were included at any of the participating 4 departments of orthopaedics and traumatology in Southern Scandinavia – Lillebaelt Hospital, Odense University Hospital, and Copenhagen University Hospital Hvidovre (Denmark) and Skåne University Hospital Malmö (Sweden). Public health care is provided in both Denmark and Sweden. There is no cost for the patients in Denmark and a small patients' fee in Sweden. The departments participating in the study provide basic and advanced orthopaedic care within their local hospitals and also function as trauma centers for patients in their catchment areas. All hip fracture treatment within the catchment areas is performed at the participating orthopaedic departments. As the aim of the study was to describe the cohort, we did not perform comparisons between the departments or the countries; all included patients were regarded as one common cohort.

Participants

Patients aged 18 to 59 years, who sustained an acute hip fracture (defined by ICD codes S72.00, S72.10, and S72.20) and treated within 4 weeks at any of the participating departments, were eligible for inclusion in the study regardless of medical, cognitive, and functional pre-fracture status. Pathological fractures, i.e. due to tumour or metastases, were excluded. Other concomitant injuries were not a reason for exclusion from the study. The patients' informed consent was obtained before inclusion in the study. Malmö started the inclusion in HFU-60 in July 2015, followed by the other centers in the first half of 2016. Inclusion was closed at all departments 31 Dec 2018.

Data collection

As we have collected multiple variables, all collected data is specified and defined in Appendix Table 5. Data on study participants was retrieved by the following means:

- Review of medical records and patient interviews

Medical charts were reviewed in each hospital. Patients were structurally interviewed post-operatively according to a questionnaire regarding lifestyle and health-related topics in addition to medical history.

From medical charts and patient interview, previous diseases and pharmacological treatment during 5 years prior to the hip fracture as well as information on the present injury were recorded. Review of the literature and expert discussions in the research group led to a selection of specific diseases and pharmacological treatments that may affect the risk of hip fracture (Appendix Tables 6 and 7), the conditions and drugs were chosen due to their known or presumed effects on bone mass, risk of falling, or the ability to hinder or modulate a fall [1, 5, 6, 13]. The specific diseases and medical treatments were recorded, as well all other diagnoses and treatments present in the records. American Society of Anesthesiologists' (ASA) classification for the patients was assessed by the attending anesthesiologist pre-operatively and collected from medical charts [14]. The trauma mechanism was assessed and classified as either low-energy trauma, i.e. a fall from standing or a seated position, or not low-energy trauma if a higher degree of trauma energy led to the hip fracture. Physical activity assessment and functional test

The patients' pre-fracture physical activity level was measured by a validated questionnaire, the Swedish Board of Health and Welfare physical activity questions (BHW-PA), which is a categorical outcome instrument for assessment of physical activity [15]. The total physical activity score is a compound score of the time spent at physical exercise multiplied by two added to everyday physical activity time and is rated from minimal activity (3 points) to maximal activity (19 points) and a score of ≥ 11 indicates fulfilment of recommended WHO activity of ≥ 150 min/week, previously confirmed by accelerometery [16, 17]. In addition, the patients' hand grip strength was measured by a physiotherapist using a Jamar dynamometer; the best of three measurements with the dominant hand was used for analysis [18].

Alcohol and drug use-patient-reported data

Alcohol and drug use were evaluated by the national versions of Alcohol Use Disorders Identification Test (AUDIT) and the Drug Use Disorders Identification Test (DUDIT) in Swedish and Danish. The written validated questionnaires on alcohol and drug use were filled out by the patients during admission regarding their situation preceding the hip fracture. AUDIT was developed by the WHO to identify hazardous or harmful alcohol use. DUDIT is originally a Swedish instrument to identify individuals with drug-related problems. Both have later been translated to multiple languages and are used internationally. AUDIT contains 10 items with a maximum score of 40, and a score > 6 for women and > 8 for men indicates hazardous alcohol use. DUDIT holds 11 items on drug use, maximum score 44, drug-related problems are indicated by ≥ 2 for women and ≥ 6 for men. [19–21]

Laboratory assessment

Blood samples were part of the clinical work-up, taken both pre-operatively and post-operatively (Appendix Table 8). The local hospitals' accredited laboratory reference values were used as cut-off values for normal or pathological test results.

Fracture classification

The hip fracture was classified as either intra- or extracapsular when a local researcher (orthopaedic surgeon) reviewed the pre-operative radiographs (AP and lateral view hip, AP pelvis).

Bone mineral density investigation

DXA scans were performed at each hospital. Measurements were made at the lumbar spine and unfractured hip by local clinical standard regimes within 3 months postfracture. The DXA scanners used within the study came from two different manufacturers, General Electric and Hologic, and showed variability regarding the results on DXA phantom and human control scans. Therefore, we decided to use the DXA results without calibration, as this also represents the clinical setting at the local departments where patients were investigated and eventually diagnosed and treated according to DXA result. We defined osteopenia and osteoporosis by the WHO definitions according to T-score (normal ≥ -1 , osteopenia -2.5 to -1, osteoporosis ≤ -2.5), as proposed by the International Osteoporosis Foundation when investigating younger individuals [22]. The diagnosis was based on the lowest result on lumbar spine, femoral neck, or total hip T-scores, as these sites have been shown to decrease similarly with age [23]. Patients recently investigated by DXA prior to the hip fracture were not re-scanned; the pre-operative results were included in the analysis. Results for patients where DXA was performed later than 3 months post-fracture were excluded from analysis, as BMD has been shown to decrease with time after hip fracture [24]. Mean T-scores for the HFU-60 cohort were compared to the Third National Health and Nutrition Examination Survey (NHANES III) data for hip DXA scans, a sample of the general American population which serves as reference database for hip DXA scans performed on both General Electric and Hologic DXA scanners [25, 26].

Bias

The legislation on personal privacy prohibits us to perform a drop-out analysis of patients confirmed eligible but not included in the study; we cannot estimate the influence of selection bias.

Study size

The current study consists of all 218 eligible patients accepting participation during the inclusion period. The study is mainly descriptive; wherefore, power calculations were not considered necessary.

Ethical considerations

HFU-60 was approved by ethical review boards in Sweden (Regionala etikprövningsnämnden Lund (Diarienummer: 2015/28)) and Denmark (Videnskabsetisk Komité for Region Syddanmark (Projekt ID: s-20150137)), registered at ClinicalTrials.gov (NCT03848195), and conducted in accordance with the Helsinki declaration. All participants gave written informed consent.

Statistics

Data was collected locally and then stored online, available to the participating researchers via password log-in, using Research Electronic Data Capture (REDCap) (projectredcap.org). Analysis of data was performed centrally for all patients, using IBM SPSS version 26. Data was assessed for normality and continuous variables are presented as mean (SD) and median (IQR), depending on normal distribution or not. Analysis of associations in categorical variables was calculated using chi² test and *T*-test was used to compare means. Results are presented separately for women and men in order to describe the cohort most accurately. Patients were also grouped according to DXA result in order to describe risk factors for low BMD.

Results

Of all patients with hip fractures treated at the departments during the study inclusion period, 6% were adults under the age of 60 years. A total of 91 women and 127 men were included in the study, 15 patients declined study participation and 52 eligible patients were not included (Fig. 1).

Demographics

Most hip fractures, 83%, occurred in patients aged 45 to 59 years (Table 1). Women were overrepresented in the oldest age group, with 52% of the women versus 35% of the men

being 55–59 years of age (p=0.009). Fifty-six percent of the patients were actively engaged on the labour market, 26% on early retirement due to poor health, and 11% were unemployed. Just over half of the patients lived together with another adult and 5% (8% of the men) resided in an institution. Half of the patients had a normal body mass index (BMI), and women were overrepresented in the underweight category (p=0.023).

The injury

Two-thirds of the patients suffered their fracture due to low-energy trauma, i.e. a fall from standing or seated position, and more often women (78%) than men (61%) (p=0.007). Intracapsular fractures

Malmö:

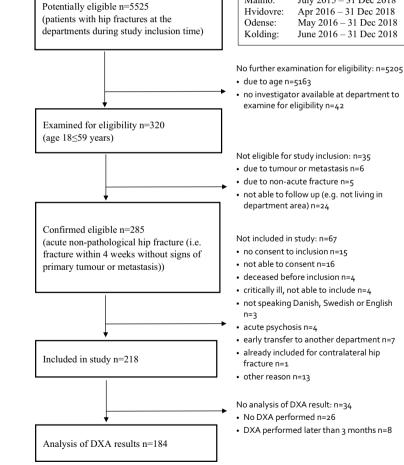


Fig. 1 Flowchart of inclusion and analysis of DXA results



July 2015 - 31 Dec 2018

Table 1 Patients' characteristics

Age	Women $n = 91$	Men $n = 127$	Total $n = 218$
Min-max	23-59 years	28-59 years	23-59 years
Median (IQR)	55 (51–57)	51 (45–56)	53 (47–57)
Age groups: 18–24	1 (1%)	0	1 (.5%)
25–29	0	1 (1%)	1 (.5%)
30-34	3 (3%)	3 (2%)	6 (3%)
35–39	1 (1%)	11 (9%)	12 (6%)
40-44	2 (2%)	15 (11%)	17 (8%)
45-49	11 (12%)	22 (17%)	33 (15%)
50–54	26 (29%)	30 (24%)	56 (26%)
55–59	47 (52%)	45 (35%)	92 (42%)
Occupation	Women $n = 88$	Men $n = 124$	Total $n = 212$
Employed (full/part-time, self-employed)	47 (53%)	72 (58%)	119 (56%)
On sick leave	9 (10%)	3 (2%)	12 (6%)
Early retirement/disability pension	22 (25%)	34 (27%)	56 (26%)
Unemployed (less than 3 years)	3 (3%)	5 (4%)	8 (4%)
Unemployed (more than 3 years)	7 (8%)	7 (6%)	14 (7%)
Does not work (other reason)	0	3 (2%)	3 (1%)
Household circumstances	Women $n = 90$	Men $n = 125$	Total $n = 215$
Living alone	34 (38%)	45 (36%)	79 (37%)
Living with someone else	54 (60%)	70 (56%)	124 (58%)
Lives at institution	2 (2%)	10 (8%)	12 (5%)
Body mass index (kg/m ²)	Women $n = 91$	Men $n = 121$	Total $n = 212$
Mean (SD)	22.96 (±4.62)	24.08 (±3.85)	23.6 (±4.2)
Min-max	13.6-36.1	13.9-35.8	13.6-36.1
BMI distribution:			
Underweight (<18.5)	15 (17%)	6 (5%)	21 (10%)
Normal (18.5-24.99)	42 (46%)	73 (60%)	115 (54%)
Overweight (25.0-29.99)	28 (31%)	37 (31%)	65 (31%)
Obese (> 30.00)	6 (7%)	5 (4%)	11 (5%)
Trauma mechanism	Women $n = 91$	Men $n = 127$	Total $n = 218$
Low-energy trauma	71 (78%)	77 (61%)	148 (68%)
Not low-energy trauma	20 (22%)	50 (39%)	70 (32%)
Fracture type	Women $n = 91$	Men $n = 127$	Total $n = 218$
Intracapsular fracture	55 (60%)	71 (56%)	126 (58%)
Extracapsular fracture	36 (40%)	56 (44%)	92 (42%)

were slightly more common than extracapsular ones (Table 1). No patients were diagnosed with an atypical femur fracture.

Lifestyle factors

Ninety-two percent of the patients reported no specific dietary preferences (Table 2). Regarding physical activity, less than half of the patients reached a BHW-PA score of 11, i.e. a recommended physical activity level of 150 min/week, and hand grip strength showed a wide range, 4.5–80.0 kg. Smokers accounted for 42% of the patients and 16% were previous smokers. AUDIT results ranged from minimum to maximum score and 19 women (25%) and 37 men (31%) reported a hazardous or harmful alcohol use. DUDIT results ranged from 0 to 36 points and 4 women (5%) and 11 men (10%) report signs of drug-related problems.

Medical history

A history of previous disease was common; in all, 313 diseases, both potentially hip fracture associated and other diseases, were found in 144 patients (66%) (Table 3). A total of 105 patients (48%) presented 188 diseases potentially associated with hip fracture and any other disease(s) were present in 98 patients (45%). Women presented a larger proportion than men of both potentially hip fracture associated Table 2 Lifestyle factors

Diet	Women $n = 82$	Men n = 121	Total $n = 203$
Regular diet	78 (95%)	108 (89%)	186 (92%)
Vegetarian/vegan	3 (4%)	3 (2%)	6 (3%)
Diabetes diet	0	7 (6%)	7 (3%)
Other ^a	1 (1%)	3 (3%)	4 (2%)
Physical activity level ^b	Women $n = 85$	Men $n = 122$	Total $n = 207$
Median score (IQR)	9 (6–13)	9 (5-17)	9 (6–15)
Physical activity level score ≥ 11	30 (35%)	54 (44%)	84 (41%)
Hand grip strength (kg)	Women $n = 76$	Men $n = 116$	Total $n = 192$
Min–max	7.1-42.0	4.5-80.0	4.5-80.0
Mean (SD)	28.1 (7.2)	46.1 (13.8)	39.0 (14.6)
Smoking	Women $n = 88$	Men $n = 125$	Total $n = 213$
Never regular smoking	33 (38%)	57 (46%)	90 (42%)
Previous smoker (quit > 2 years ago)	16 (18%)	18 (14%)	34 (16%)
Current smoker (or quit < 2 years ago)	39 (44%)	50 (40%)	89 (42%)
Pack years:	Women $n = 52$	Men $n = 58$	Total $n = 110$
Pack years min-max	0.3-70	0.9-107.5	0.3-107.5
Pack years median (IQR)	25.4 (14.3-38.8)	30 (15-42.4)	29.3 (15-40)
AUDIT ^c	Women $n = 76$	Men <i>n</i> = 118	Total $n = 194$
Hazardous or harmful alcohol use:	19 (25%)	37 (31%)	56 (29%)
AUDIT min-max	0-40	0-36	0-40
AUDIT median (IQR)	4 (1-5.75)	5 (3–9)	4 (2-8)
DUDIT ^d	Women $n = 79$	Men $n = 111$	Total $n = 190$
Signs of drug-related problems:	4 (5%)	11 (10%)	15 (8%)
DUDIT min-max	0–8	0-36	0-36
DUDIT median (IQR)	0 (0-0)	0 (0–0)	0 (0-0)

^aMuslim, milk and cheese free, gluten free, phosphate reduced kidney diet

^bThe Swedish Board of Health and Welfare physical activity questions (BHW-PA), a score of 11 and above fulfils WHO recommendations

^cAUDIT Alcohol Use Disorders Identification Test

^d*DUDIT* Drug Use Disorders Identification Test

and other diseases (p = 0.025). The number of patients with multiple comorbidities is presented in Table 3. Specific diseases potentially associated with increased risk of hip fracture are presented in Appendix Table 6; neurological disease, diabetes, psychiatric disease and disability, osteoporosis, and chronic obstructive pulmonary disease were the most ubiquitous, accounting for 59% of the diseases.

Two-thirds of the patients were classified as ASA I or II, i.e. none or mild systemic disease, and the remaining patients were classified as ASA III–IV (Table 3). Half of the patients had a history of any previous fracture and 5% reported a previous hip fracture. In total, 17% of the cohort reported a family history of fragility fractures.

Previous medication

During the 5 years preceding the hip fracture, 135 patients (62%) had used any regular medication and 70 patients

(32%) had a total of 130 pharmacological treatments from medication groups potentially associated with increased fracture risk (Appendix Table 7). The most common treatments were proton pump inhibitors, selective serotonin reuptake inhibitors and opioids, together they accounted for 40% of the potentially hip fracture associated treatments.

Blood sample results

Blood samples were drawn on mean 1.4 (SD 1.1) days preoperative and mean 2.04 (2.4) days post-operative. Results below reference in more than a quarter of the post-operative samples were found for calcium (29%), albumin (45%), vitamin D (52%), testosterone (60%) in men, and estradiol (85%) in women (Appendix Table 8). Of the pre-operative blood samples, leucocytes and CRP were above reference in 75% and 30%, and hemoglobin was below reference in 37% of the samples. Table 3 Medical history

	Women $n = 91$	Men $n = 127$	Total $n = 218$
Any previous disease	65 (71%)	79 (62%)	144 (66%)
Patients with specific disease(s) potentially associated with hip fracture ^a	52 (57%)	53 (42%)	105 (48%)
Patients with any other disease(s)	49 (54%)	49 (39%)	98 (45%)
Comorbidity (potentially hip fracture asso- ciated and other diseases)	Women $n = 91$	Men $n = 127$	Total $n = 218$
No previous disease	26 (29%)	48 (38%)	74 (34%)
1 comorbidity	25 (28%)	43 (34%)	68 (31%)
2 comorbidities	12 (13%)	20 (16%)	32 (15%)
3 comorbidities	10 (11%)	10 (8%)	20 (9%)
4 comorbidities	8 (9%)	3 (2%)	11 (5%)
5 comorbidities	6 (7%)	1 (1%)	7 (3%)
6 comorbidities	1 (1%)	1 (1%)	2 (1%)
7 comorbidities	1 (1%)	1 (1%)	2 (1%)
8 comorbidities	2 (2%)	0	2 (1%)
ASA classification	Women $n = 91$	Men $n = 127$	Total $n = 218$
ASA I	16 (18%)	44 (35%)	60 (28%)
ASA II	42 (46%)	44 (35%)	86 (39%)
ASA III	31 (34%)	35 (28%)	66 (30%)
ASA IV	2 (2%)	4 (3%)	6 (3%)
Hospital admission	Women $n = 90$	Men $n = 124$	Total $n = 214$
Hospital admission within last year	24 (27%)	27 (22%)	51 (24%)
Previous hip fracture	Women $n = 90$	Men $n = 124$	Total $n = 214$
Yes, contralateral	3 (3%)	6 (5%)	9 (4%)
Yes, ipsilateral	0	1 (1%)	1 (.5%)
Previous fracture (after 20 years of age)	Women $n = 87$	Men $n = 121$	Total $n = 208$
Previous other fracture	44 (51%)	53 (44%)	97 (47%)
Fragility fracture in the family	Women $n = 86$	Men $n = 123$	Total $n = 209$
Yes	21 (24%)	14 (11%)	35 (17%)
No	49 (57%)	82 (67%)	131 (63%)
Do not know	16 (19%)	27 (22%)	43 (21%)

^aSpecific diseases potentially associated with hip fracture are specified in Appendix Table 5

DXA results

A total of 184 patients' DXA scan results were included in the analysis. They were aged 28–59 years, the median was 53 (IQR 47–57) years, compared to a median age of 55 (48–57) for the 26 patients not attending DXA and the 8 patients examined by DXA > 3 months post-fracture who were excluded from the analysis. Median time to DXA investigation from hip fracture surgery was 5 (–324) days, 85% of the analyzed patients had DXA scans within 1 month. T-scores at the lumbar spine, total hip, and femoral neck were normal in 12%, osteopenic in 57%, and osteoporotic in 31% of the patients. The distribution was similar, with no statistically significant differences between women and men or between low-energy and not low-energy trauma mechanisms, but with a tendency of marginally better DXA results among patients with higher than low-energy trauma mechanism (Table 4). In the youngest age groups, none of the patients had normal DXA results. Normal DXA was firstly seen in age group 40–44 and the highest proportion of normal results was found in age group 45–49 (27% normal).

Mean T-scores at the femoral neck and total hip in our cohort were lower in all age groups for both women and men compared to NHANES III data (Fig. 2). NHANES III mean T-scores were all normal (\geq -1), but our cohort's mean T-scores were categorized as osteopenia (<-1 to> -2.5) in all age groups. Mean T-scores for men from our cohort were lower with increasing age, as NHANES III mean T-scores for both men and women were. In contrast, mean T-scores in women from our cohort were higher with increasing age, both at the femoral neck and total hip.

Patient characteristics according to DXA result for 184 patients assessed by DXA are presented by sex in Appendix Table 9. Smoking, lower BMI, a family history of a fragility fracture, and low vitamin D were more frequent Table 4DXA diagnosis bysex, age group, and traumamechanism

	Normal T-score≥ − 1	Osteopenia T-score – 2.5 to – 1	Osteoporosis T-score≤−2.5	
	1-score ≥ - 1	1-score = 2.5 to = 1	$1-score \leq -2.5$	
Sex				
Women $n = 76$	9 (12%)	41 (54%)	26 (34%)	
Men $n = 108$	13 (12%)	64 (60%)	31 (29%)	
Age groups				
25-29 n=1	0	1 (100%)	0	
30 - 34 n = 6	0	4 (67%)	2 (33%)	
35-39 n = 11	0	10 (91%)	1 (9%)	
40–44 <i>n</i> =15	2 (13%)	8 (53%)	5 (33%)	
45–49 <i>n</i> =26	7 (27%)	13 (50%)	6 (23%)	
50-54 n = 51	3 (6%)	31 (61%)	17 (33%)	
55-59 n = 74	10 (14%)	38 (51%)	26 (35%)	
Trauma mechanism				
Low-energy trauma $n = 120$	12 (10%)	65 (54%)	43 (36%)	
Not low-energy trauma $n = 64$	10 (16%)	40 (63%)	14 (22%)	
Total				
n = 184	22 (12%)	105 (57%)	57 (31%)	

Diagnosis based on the lowest T-score on the lumbar spine, femoral neck, or total hip DXA investigation performed at the time of the fracture. Low-energy trauma was defined as a fall from standing or seated position, and any higher degree of trauma energy was classified as not low-energy trauma

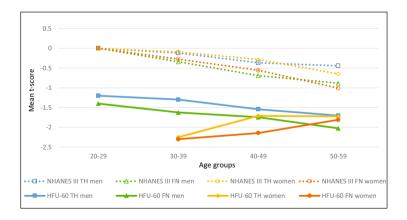


Fig.2 Comparison of mean T-score by age group, HFU-60 vs. NHANES III. Multiple line chart of HFU-60 mean T-scores for women and men compared to NHANES III mean T-scores calculated from BMD data [25]. TH total hip, FN femoral neck. NHANES III mean BMD data for age groups were converted to T-scores using the formula: T-score = (measured BMD – young adult mean BMD) / young adult population SD [23]. Mean T-scores for HFU-60 were significantly lower than NHANES III regarding both TH and FN for men (p = .001), TH for women (p = .020), and FN for women (p = .027)

in both women and men with low DXA results. Previous disease, previous fracture, and a higher number of comorbidities were more common in women with low DXA. For men with low DXA, a higher AUDIT score and hip fracture due to low-energy trauma were more frequent.

Discussion

In the present study on patients with hip fractures under 60 years of age, we found several risk factors for osteoporosis and fractures in our study cohort, and also a high prevalence of osteopenia and osteoporosis upon DXA investigation at the time of the hip fracture.

Demographics

In contrast to hip fractures in the elderly, it has been shown before that the younger the patients, the larger the proportion of men is [3, 7, 9, 11]. Accordingly, 58% of our cohort were men. The explanation is probably a combination of multiple reasons resulting in young men being at higher risk of fractures than young women; in our cohort, the men presented heavier smoking, more alcohol and drug use, and more fractures due to a higher than low-energy trauma mechanism suggesting a more risk-taking behaviour in men.

The fact that only half of the participants were working, compared to four-fifths among the general population 20 to 64 years of age in Denmark and Sweden[27], reflects a socioeconomic distress known to be associated with an increased fracture risk [28].

The injury

Two-thirds of the hip fractures in our cohort were related to low-energy trauma, i.e. a fall from standing or a seated position, in contrast to the preconception that hip fractures in younger patients are caused mainly by high-energy trauma. Previous studies present large variations in trauma mechanisms, depending on inclusion criteria and settings. Studies on general hip fracture populations like ours support our finding that low-energy trauma was the cause for a majority of the fractures [1, 9, 10].

No patients were diagnosed with an atypical femur fracture; considering the previously reported low incidence of 1.74 fractures per 10 000 patient-years [29] and that only 7 patients used bisphosphonates, no atypical femur fractures were expected in the cohort.

Lifestyle factors

The physical activity level in our cohort was lower than a Swedish random population sample measured by the same questionnaire [15]. More than half of our study participants had a lower physical activity level than the recommended minimum according to the WHO of 150 min per week [17]. In contrast, 72% of the general population in Denmark and 66% in Sweden reach the recommended minimum physical activity level [30, 31].

On hand grip strength measurement, 57% of the women and 58% of the men had results lower than the mean from a random population sample of Danish women and men aged 19 to 72 years [18]. Considering that the hand grip strength was lower with increasing age in the general population, our younger cohort performed markedly lower results than the general population of comparable ages.

Smoking was 2.5 to 3.8 times as common in the study cohort than in the general population, where 17% smoke in Denmark and 11% in Sweden [32, 33]. The rate of smokers was also higher than in most other young hip fracture cohorts [1, 2, 34] but on par with Al-Ani et al. [12].

Among our study participants, harmful use of alcohol and drug-related problems were much more common than what is reported from the general population in the countries. One quarter of the women had a harmful alcohol consumption, and the Swedish average is suggested to be 11% [19]. The corresponding number for men was 31% in the study, and population data suggest 18 to 23% in Sweden and Denmark [19, 35]. In other observational studies, the presence of alcohol use disorder varies from 15 to 38% [2, 9, 10, 36, 37]. A cohort from Scotland, described by Stearns et al., exhibit extreme use of alcohol and tobacco, 47 and 67%, but is characterized as a "largely very deprived population" [38].

On the DUDIT questionnaire, 8% of the study cohort presented a result indicating a drug-related problem, which is close to 3 times higher than previously reported from the Swedish population [20]. To the best of our knowledge, no earlier studies on patients with hip fractures have used DUDIT to estimate substance use disorder; wherefore, comparison is not possible. Still, the majority of the fracture patients did not have alcohol or substance use disorder, which is otherwise a perfunctory explanation often heard—that younger patients with hip fractures are "addicts". This suggests that other associated factors may be present as well in young and middle-aged patients with hip fractures.

Medical history

In terms of comorbidity, our cohort was divided into thirds, with either none, one, or several comorbidities. The third of the patients with multiple comorbidities carried 78% of the total disease burden. Previous diseases potentially associated with hip fracture were found in 48% of the patients. Other studies on young hip fracture patients have noted comorbidities in 9 to 55%, suggesting different types of populations between the studies [7, 10, 36, 38–41].

Previous medication

Proton pump inhibitors and selective serotonin reuptake inhibitors were consumed by 9 and 8% of the patients, respectively. Corticosteroids, a known mediator of poor bone health [13], were used by 5%, and previous studies have reported on 1 to 9% [10, 42].

Blood sample results

Pathological values for calcium, vitamin D, and albumin were common. This may reflect predisposal for poor bone health and general frailty. Also the findings of low sex hormones could be associated with low BMD, but these tests were taken post-operatively and after opioids were given, which may lower the level of testosterone [43].

DXA results

Analysis of bone mineral density at the time of the hip fracture showed a high prevalence of osteopenia and osteoporosis, only 1 in 8 had a normal DXA result. Patients with a hip fracture due to a higher than low-energy trauma mechanism had slightly better DXA results, but still only 1 in 6 had a normal T-score. Remarkably, no normal results were found in patients younger than age 40. Mean T-scores for women and men from the HFU-60 cohort were lower than NHANES III in all age groups and were all categorized as osteopenia. These findings state that bone quality should be suspected to be abnormal in young and middle-aged patients with hip fractures. Furthermore, we were not able to distinguish any subgroups with no or low risk of low bone mass, why all young and middle-aged patients with hip fractures may be considered at risk of low bone mass, and should be investigated accordingly [44].

In comparison, normative DXA data from a populationbased sample of 25-year-old women from Malmö, Sweden, reported a much lower prevalence of osteopenia and osteoporosis [45]. Thus, osteopenia in either femoral neck, total hip, or lumbar spine was seen only in 4.5–9.3% of the cases and osteoporosis in 0–0.3%.

In a population-based sample of women and men aged 30–60 years, from Tromsø, Norway, the prevalence of osteoporosis in femoral neck or total hip is reported to be between 0 and 5% depending on age and sex, i.e. considerably lower than our findings [46].

That our cohort of patients with hip fractures under the age of 60—regardless of trauma mechanism—have inferior bone health is supported by the similarity between our results and Al-Ani et al., who found osteopenia in 54% and osteoporosis in 35% in their somewhat older group with hip fractures from Stockholm, Sweden [12].

Limitations

Our study has some limitations; the legislation on personal privacy prohibits us to perform a drop-out analysis of eligible patients not included in the study; therefore, we cannot estimate the influence of selection bias.

An upper age limit of 60 years could be considered both too high and too low for a study focusing on non-elderly hip fracture patients. There is no consensus regarding the cut-off between non-elderly and elderly patients; a range from 40 to 70 years have been used in earlier studies [12, 39]. We chose 60 years as the upper age limit of our cohort, partly due to the clinical guidelines at the department of origin of the study, where 60 years of age has been the divide for arthroplasty, rather than osteosynthesis, as the treatment of choice for displaced femoral neck fractures. The proportion of non-elderly individuals of all hip fracture patients is 2-13% according to previous reports [4, 6], the proportion in our material is 6% which corresponds well considering the variation in age limits in previous studies.

One could argue that there are few very young patients in our cohort, 91% of the patients are aged 40 to 59 years, but this is coherent with a Danish register study where 90% of hip fractures in patients under 65 years of age are found in patients aged 40 to 65 [4]. In a Swedish register study on patients with hip fractures younger than 50 years, the median age was 42 [47]. When excluding patients aged 50–59, our cohort show a corresponding median age of 44; hence, we consider our sample sufficiently representative.

Strengths

We consider our study to have important strengths; three quarters of the eligible cases were included in this multicenter prospective study. The patients were thoroughly investigated regarding demographics, trauma mechanism, lifestyle factors, comorbidity, and medication as well as by blood samples and DXA, providing an extensive description of the patient group. The participating hospitals served both urban and rural catchment areas and provided care for all fracture cases regardless of trauma or patient type. Care given at low or no cost for the patients ensures that no one abstains from seeking hospital care. Thereby, we regard our study population to reflect the entire, heterogenous group of individuals suffering hip fractures in young and middle age. This is in contrast to studies performed at Level I trauma centers or health care systems were socially deprived individuals have little access to hospital care, leading to selection bias [7]. Our results are generalizable to many highincome countries, whilst other parts of the world may face more traffic or occupational injuries and a different case mix [8, 41].

We believe that DXA performed at the time of hip fracture in contrast to years after, more accurately describes the pre-fracture condition. Al-Ani et al. [12] have presented similar DXA results adjacent to the fracture, but in a smaller and older patient group. To put our DXA results in relation to normative data, we have compared our findings to 1047

reference populations regarding different ages and sex, both internationally used reference data (NHANES III) [25] and locally collected normative DXA result data [45, 46]. The comparisons support the argument that the bone health of young and middle-aged patients with hip fractures is inferior to what could be expected in the general population of the same ages.

Conclusion

Our cohort of patients with hip fractures under the age of 60 is heterogenous; the patients present a wide range of demographics and lifestyle factors as well as previous fractures and comorbidities. Based on our findings, young and middle-aged patients with hip fractures show signs of vitality and health, yet primarily—and more concerning—there is a high degree of frailty and risk factors for osteoporosis and fractures are numerous. We also found a high prevalence of osteopenia and osteoporosis compared to the general population, only one in eight had a normal DXA result.

Clinical perspective

The majority of the patients had previous medical conditions and abnormal blood sample results as well as inferior bone quality on BMD assessment by DXA. We suggest that all young and middle-aged patients with hip fractures should undergo a thorough health investigation including DXA, a non-invasive and relatively easily accessible procedure that previously have been reported to be performed in only less than half of young patients with hip fractures [1].

The variation in patient characteristics and physical abilities at the time of the hip fracture suggests that these patients have different needs regarding rehabilitation to reach their pre-fracture functional level and demands. Other rehabilitation pathways tailored to the needs of these patients, not only standard geriatric hip fracture rehabilitation, are assumingly needed. This will be analyzed further in future studies within the HFU-60 project.

Appendix

Table 5 Definition of recorded variables

Variable	Data source	Method of assessment (measurement)
Demographics		
Age	Personal number ^a	Age at fracture according to birth date
Sex	Personal number ^a	Sex as defined by personal number
Occupation	Patient interview	Pre-defined category selected by patient
Household circumstances	Patient interview	Pre-defined category selected by patient
BMI	Patient interview and medical charts	Weight divided by squared length (kg/m ²)
The injury		
Trauma mechanism	Patient interview and medical charts	Defined as low-energy or not low-energy
Fracture type	Radiographs	Classified by orthopaedic surgeon
Lifestyle factors		
Smoking	Patient interview	Pre-defined category selected by patient
Pack years	Patient interview	Average number of cigarettes/day x years smoking
Diet	Patient interview	Pre-defined category selected by patient
AUDIT [19]	Patient questionnaire	Score according to questionnaire instructions
DUDIT [20]	Patient questionnaire	Score according to questionnaire instructions
Physical activity level score (BHW-PA [15])	Patient interview	Score according to questionnaire instructions
Hand grip strength	Functional test by physiotherapist	Measured in kg by dynamometer
Medical history		
Any previous disease	Patient interview and medical charts	Presence of previous disease
Potentially hip fracture associated previous disease	Patient interview and medical charts	Presence of pre-specified previous disease
Hospital admission within 1 year prior to hip fracture	Patient interview and medical charts	Defined as yes or no
ASA classification [14]	Medical charts	Assessed by anesthesiologist
Previous hip fracture	Patient interview and medical charts	Defined as yes or no
Previous other fracture (after 20 years of age)	Patient interview and medical charts	Defined as yes or no
Fragility fracture in first-hand relative	Patient interview and medical charts	Defined as yes or no
Previous medication	Patient interview and medical charts	Presence of pre-specified medical treatments
Blood sample result	Medical charts	Defined as normal or below/above reference
DXA result	DXA investigation	Result defined according to WHO definitions

^aThe personal number is a national identification number including information on birth date and sex, unique to every individual, used nationally in both Denmark and Sweden

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diseases ated with		Women $n = 91$	Men $n = 127$	Total $n = 218$
hip fracture Numbe	er of patients with disease(s) potentially associated hip fracture	52 (57%)	53 (42%)	105 (48%)
Neopla	isms			
ICD-1	0 chapter 2, code C00-D49			
Maligr	nant disease	2 (2%)	3 (2%)	5 (2%)
	rine, nutritional and metabolic diseases 0 chapter 4, code E–			
Diabet	es	10 (11%)	13 (10%)	23 (11%)
Hypert	hyreosis	1 (1%)	0	1 (0.5%)
Hypoth	nyreosis (treated w. substitution)	8 (9%)	1 (1%)	9 (4%)
Hyper	parathyroidism	1 (1%)	1 (1%)	2 (1%)
Mb Cu	shing	1 (1%)	0	1 (0.5%)
Нурор	hosphatemia	0	1 (1%)	1 (0.5%)
Hypog	onadism in men	-	1 (1%)	1 (1%)
Prolon	ged amenorrhea in women of fertile age	2 (2%)	-	2 (2%)
Mental	l, Behavioral and Neurodevelopmental disorders			
Icd-10	chapter 5, code F-			
Anorez	xia	3 (3%)	0	3 (1%)
Psychi	atric disease and disability	8 (9%)	12 (9%)	20 (9%)
(e.g. de	epression, psychosis, dementia, retardation)			
Diseas	es of the nervous system			
ICD-1	0 chapter 6, code G–			
Status	post stroke	5 (6%)	2 (2%)	7 (3%)
Other	neurological disease	18 (20%)	15 (12%)	33 (15%)
(e.g. p	olyneuropathy, paresis)			
Diseas	es of the respiratory system			
ICD-1	0 chapter 10, code J–			
Chroni	c obstructive pulmonary disease	10 (11%)	6 (5%)	16 (7%)
Diseas	es of the digestive system			
ICD-1	0 chapter 11, code K–			
Inflam	matory bowel disease (e.g. Mb Crohn)	3 (3%)	1 (1%)	4 (2%)
	sorption owel resection, coeliac disease)	5 (6%)	1 (1%)	6 (3%)
Diseas	es of the musculoskeletal system and connective tissue			
ICD-1	0 chapter 13, code M–			
Rheum	natoid arthritis and other rheumatic conditions	9 (10%)	4 (3%)	13 (6%)
Childh	ood hip disease	1 (1%)	1 (1%)	2 (1%)
	ysplasia, Mb Legg-Calvé-Perthes)			
Osteop		13 (14%)	4 (3%)	17 (8%)
-	es of the genitourinary system,			
	0 chapter 14, code N–			
	insufficiency	1 (1%)	5 (4%)	6 (3%)
	diagnosis that impairs walking ability	8 (9%)	8 (6%)	16 (7%)

			Women $n = 91$	Men $n = 127$	Total $n = 218$	
Previous use of potentially hip	fracture associated medication		34 (37%)	36 (29%)	70 (32%)	
ATC code	Example of use/diagnosis	Example of medication name				
A02BC Proton pump inhibitors	Peptic ulcer, gastro-oesopha- geal reflux disease	Omeprazole, pantoprazole, lansoprazole	12 (13%)	7 (6%)	19 (9%)	
N06AB Selective serotonin reuptake inhibitors	Antidepressants	Citalopram, sertraline, fluox- etine	10 (11%)	8 (6%)	18 (8%)	
N02A Opioids	Pain	Morphine, methadone, fentanyl	8 (9%)	7 (6%)	15 (7%)	
H02AB Glucocorticoids	Systemic corticosteroids	Prednisolone, betamethasone, hydrocortisone	6 (7%)	6 (5%)	12 (6%)	
B01A Antithrombotic agents	Antithrombotic therapy	Heparin, dalteparin, warfarin	4 (4%)	8 (6%)	12 (6%)	
N03AF Carboxamide derivates	Antiepileptics	Carbamazepine, oxcarbazepine, rufinamide	5 (5%)	5 (4%)	10 (5%)	
C03CA Loop-diuretics	Hypertension, heart failure	Furosemide	5 (5%)	4 (3%)	9 (4%)	
M01A NSAID	RA, osteoarthrosis, pain	Diclofenac, ibuprofen	4 (4%)	5 (4%)	9 (4%)	
H03AA Thyroid hormones	Hypothyreosis	Levothyroxine, liothyronine	7 (8%)	1 (1%)	8 (4%)	
M05B Bisphosphonates	Osteoporosis	Aledronic acid, zoledronic acid	3 (3%)	4 (3%)	7 (3%)	
G03 Sex hormones	Hormonal therapy	Androgens, estrogens	3 (3%)	2 (2%)	5 (2%)	
L01, L04 Antineoplastic and immu- nomodulating agents	Cancer, rheumatoid arthritis	Cyklophosphamide, busulfan, methotrexate	2 (2%)	2 (2%)	4 (2%)	
L02BG Aromatase inhibitors	Cancer (breast, endometrial, prostatic)	Anastrozole, letrozole, exemes- tane	1 (1%)	0	1 (0.5%)	
G03AC06 Progestogens	Contraceptive	Medroxyprogesterone	1 (1%)	0	1 (0.5%)	

 Table 7
 Previous potentially hip fracture associated medication

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Table 8 Blood sample results

	No. of san	nples	Below reference		Normal		Above reference	
	Women	Men	Women	Men	Women	Men	Women	Men
Pre-operative								
Hemoglobin	90	127	40 (44%)	41 (32%)	50 (56%)	84 (66%)	0	2 (2%)
Leucocytes	89	124	1 (1%)	0	23 (26%)	29 (23%)	65 (73%)	95 (77%)
Platelet count	72	93	9 (13%)	7 (8%)	57 (79%)	80 (86%)	6 (8%)	6 (7%)
CRP	90	124	N/A	N/A	72 (80%)	77 (62%)	18 (20%)	47 (38%)
Sodium (Na+)	90	127	24 (27%)	28 (22%)	63 (70%)	98 (77%)	3 (3%)	1 (1%)
Potassium (K+)	90	127	14 (16%)	11 (9%)	71 (79%)	100 (79%)	5 (6%)	16 (13%)
Creatinine	89	127	33 (37%)	18 (14%)	52 (58%)	91 (72%)	4 (5%)	18 (14%)
INR	83	112	N/A	N/A	73 (88%)	100 (89%)	10 (12%)	12 (11%)
Post-operative								
Calcium-P	77	112	24 (31%)	31 (28%)	53 (69%)	80 (71%)	0	1 (1%)
Albumin	69	101	40 (58%)	37 (37%)	29 (42%)	64 (63%)	0	0
25-hydroxyvitamin D	74	104	34 (46%)	59 (57%)	40 (54%)	45 (43%)	N/A	N/A
Alkaline phosphatase	84	107	1 (1%)	3 (3%)	68 (81%)	83 (78%)	15 (18%)	21 (20%)
PTH	79	114	0	3 (3%)	71 (90%)	96 (84%)	8 (10%)	15 (13%)
TSH	77	115	5 (7%)	0	69 (87%)	107 (93%)	3 (4%)	8 (7%)
T3	24	26	6 (25%)	1 (4%)	17 (71%)	24 (92%)	1 (4%)	1 (4%)
T4	26	33	0	0	26 (100%)	30 (91%)	0	3 (9%)
P-Testosterone	-	108	_	65 (60%)	-	43 (40%)	_	0
Estradiol	72	_	61 (85%)	-	11 (15%)	-	0	-
Tissue transglutaminase antibody	75	109	N/A	N/A	74 (99%)	109 (100%)	1 (1%)	0

	Women		Men		
	Low DXA T-score $< -1 n = 67$	Normal DXA T-score $\geq -1 n = 9$	Low DXA T-score $< -1 n = 95$	Normal DXA T-score $\geq -1 \ n = 13$	
Age median (IQR)	54 (51–57)	56 (50–58.5)	51 (44–56)	49 (45–56.5)	
Smoking*	n = 66		n=94		
Non-smoker	24 (36%)	5 (56%)	41 (44%)	9 (69%)	
Previous smoker	13 (20%)	1 (11%)	13 (14%)	2 (15%)	
Current smoker	29 (44%)	3 (33%)	40 (43%)	2 (15%)	
Pack years*	n = 40	n=4	n=47	n=4	
Min–max	0.3-54	6.8–47	0.9-107.5	10-52.5	
Median (IQR)	25 (13-37)	34 (11-47)	30 (18-44)	26 (11-49)	
AUDIT*	n = 58	n=8	n = 90		
High AUDIT	15 (26%)	2 (25%)	28 (31%)	3 (23%)	
Min-max	0-40	0-13	0-36	0-24	
Median (IQR)	4 (1-6)	4.5 (1.5-5.8)	5 (3–9)	3 (0.5–7.5)	
DUDIT*	n=61	n = 7	n = 83	n = 12	
High DUDIT	3 (5%)	1 (14%)	10 (12%)	0	
Min-max	0–5	0-8	0-36	0-0	
BMI*			n=91		
Min–max	16.7-33.9	23.1-36	15.8-35.8	21.7-34.6	
Mean (SD)	22.8 (4)	28.4 (4.4)	24.1 (3.7)	26.4 (3.3)	
Trauma mechanism					
Low-energy trauma	50 (75%)	7 (78%)	58 (61%)	5 (39%)	
Not low-energy trauma	17 (25%)	2 (22%)	37 (39%)	8 (62%)	
Any disease	47 (70%)	5 (56%)	56 (59%)	11 (85%)	
Potentially hip fracture associated disease	40 (60%)	2 (22%)	37 (39%)	6 (46%)	
Other disease(s)	34 (51%)	4 (44%)	34 (36%)	8 (62%)	
Hospital admission within last year*	16 (24%)	2 (22%)	19(20%) n = 94	4 (31%)	
ASA classification					
Mean (SD)	2.09 (0.71)	2.11 (0.93)	1.95 (0.86)	1.85 (0.69)	
ASA I	14 (21%)	2 (22%)	35 (37%)	4 (31%)	
ASA II	33 (49%)	5 (56%)	32 (34%)	7 (54%)	
ASA III	20 (30%)	1 (11%)	26 (27%)	2 (15%)	
ASA IV	0	1 (11%)	2 (2%)	0	
Comorbidity calculation		. ,			
Min–max	0–7	0–7	0–7	0–5	
Mean (SD)	1.82 (1.8)	1.33 (2.3)	1.09 (1.3)	1.69 (1.4)	
Any previous fracture*	34 (51%)	2 (22%)	37 (40%) n = 93	11 (85%)	
Fragility fracture in the family*	19(30%) n = 64	1 (11%)	13 (14%) n = 92	0	
Previous potentially hip fracture associated medication	26 (39%)	3 (33%)	28 (30%)	4 (31%)	
Blood samples below reference*					
Calcium	18 (31%) n=59	2(29%) n = 7	23 (26%) $n = 86$	4(36%) n = 11	
Albumin	29(55%) n = 53	4(67%) n=6	26(34%) n = 76	4 (44%) n = 9	
Vitamin D	26(46%) n = 56	1(17%) n=6	46(59%) n = 78	4(36%) n = 11	
Testosterone	_	-	47(57%) n = 82	9(75%) n = 12	
Estradiol	46 (85%) <i>n</i> =54	5(71%) n = 7	_	_	

Table 9 Patient characteristics according to DXA result, focusing on risk factors for osteoporosis

*Variables with missing data, the number of observations for each variable is indicated for each cell with missing data

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Paper II

Trauma mechanism and bone mineral density did not impact hip fracture type – a multicenter cohort of 218 patients under 60 years of age

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ABSTRACT

Background

Young and middle-aged adults constitute 5-10% of the total hip fracture population, and it has been suggested that trauma mechanism and bone quality might be associated with fracture type and degree of displacement. We aimed to describe the fracture classification in our cohort, and further to analyze associations between trauma mechanism, DXA result, and fracture type.

Methods

In a prospective, multicenter, cohort study of patients under 60 we descriptively analyzed hip fracture classification and associations to trauma mechanism and DXA result at the time of the fracture.

Results

The cohort consisted of 218 patients, of whom 184 were investigated with DXA at the time of the fracture. Median age for the full cohort was 53 years (IQR 47-57), 127 were men (58%), 54% had a normal body mass index, and 67% were classified ASA I-II. Most fractures were intracapsular (63%), unstable/displaced (66%), and primarily due to low-energy trauma (68%). Analyses of the associations between fracture type and trauma mechanism (n=218), DXA result (n=184), and a combination of trauma mechanism and DXA result (n=184) did not show statistically significant results. However, clinically important findings were noted: low-energy trauma (57%) (p=0.06); non low-energy trauma resulted in proportionally more intracapsular fractures (71%) compared to low-energy trauma (59%) (p=0.07).

Conclusion

In our cohort of adults under 60 years, most hip fractures were unstable/displaced, the anatomical location was mainly intracapsular, and most fractures resulted from low-energy trauma. The trauma mechanism or bone mineral density, by itself or in combination, did not significantly impact the hip fracture type.

Introduction

Young and middle-aged adults constitute approximately 5-10% of the population sustaining a hip fracture (1–5). High-energy trauma has previously been suggested as the main cause of hip fractures in non-elderly adults and it is a common belief that their risk of osteopenia or osteoporosis is low (6–8).

Young and middle-aged adults differ from older patients regarding the distribution of hip fracture types, where lower bone quality in the elderly have been proposed as a reason for a shift toward more unstable fractures (3). A common notion is also that fracture type, and especially degree of displacement, is associated to trauma mechanism – that higher energy trauma would induce a displaced or more unstable fracture pattern. However, to the best of our knowledge, this has not been shown in previous reports. We believe such an investigation to be of importance for a better understanding of hip fractures and the characteristics of the patients who suffer them in younger age.

From a prospectively collected cohort of adults, we recently reported that 2/3 of their hip fractures occurred due to low-energy trauma, with only 1 in 8 having a normal dual-energy x-ray absorptiometry (DXA) result at the time of the fracture (4). The aim of the present study was to describe the fracture classification in our cohort, and further to analyze associations between trauma mechanism, bone mineral density (BMD), and fracture type.

Methods

Study design

The current study is a secondary analysis of a cohort of young and middle-aged patients with hip fractures – Hip Fractures in adults Under 60 years of age (HFU-60). HFU-60 is a prospective, multicenter, cohort study and the demography and epidemiology, lifestyle factors, comorbidity, and general health in the cohort together with analysis of DXA results has previously been described in detail (4). This current study analyzes the fracture classification and its associations to trauma mechanism and DXA result. The STROBE guidelines were considered in the reporting of the study (9).

Setting & Participants

Adults under the age of 60 with hip fractures, treated at the participating departments in Denmark (Lillebælt Hospital Kolding, Odense University Hospital, Copenhagen University

Hospital Hvidovre) and Sweden (Skåne University Hospital Malmö) were eligible to participate in the study. All patients living in the catchment area, with any type of acute hip fracture apart from pathological fractures (i.e., tumor or metastases), were eligible for inclusion regardless of prior medical, cognitive or functional level. Concurrent other injuries were not a reason for exclusion from the study. Informed consent was provided by all patients before study inclusion. The inclusion started in Malmö in July 2015, followed by the other centers in 2016, and study inclusion was closed at all departments in December 2018.

Hip fracture classification

Fractures were classified according to a predefined protocol, according to the 2007 revision of the AO/OTA Fracture and Dislocation Classification Compendium (10). Fractures were classified as: undisplaced femoral neck (Garden 1-2, AO 31-B1), displaced femoral neck (Garden 3-4, AO 31-B3), basicervical (AO 31-B2), stable pertrochanteric (AO 31-A1 + A2.1), unstable pertrochanteric (AO 31-A2.2-3 + A3), or subtrochanteric (AO 32 until 3cm below lower border of lesser trochanter) (10,11). Fracture classifications were performed by orthopedic surgeons associated to the study project (SSR, BV, HP, CFM, CR). Classification of hip fractures according to AO/OTA classification by orthopedic surgeons has previously been found to be accurate and highly consistent (12). For the interpretation and classification, pre-operative antero-posterior (AP) and lateral X-rays of the hip and AP pelvis, intra-operative fluoroscopy imaging, as well as information from operative reports were available.

Fracture types were grouped according to anatomical site into intracapsular (femoral neck and basicervical) and extracapsular (pertrochanteric and subtrochanteric). Fractures were also grouped according to the fracture pattern into stable/undisplaced (undisplaced femoral neck, stable pertrochanteric) and unstable/displaced (displaced femoral neck, basicervical, unstable pertrochanteric, subtrochanteric). Basicervical fractures were considered intracapsular and unstable in accordance with AO/OTA definition and due to inherent rotational instability (13). The categorization of fracture types as less or more stable depending on the fracture pattern was coherent with existing classification systems (10,11,14).

Trauma mechanism

The trauma mechanism was defined as low-energy trauma if a same level fall from standing or sitting position. Any other trauma was classified as non low-energy trauma, thus not distinguishing intermediate trauma mechanisms from true high-energy trauma (e.g., high speed

traffic accidents or falls from a height). The trauma mechanism was categorized based on information from medical charts and structured patient interviews.

Bone mineral density

DXA investigations were performed at the participating hospitals, according to local clinical regimens (4). DXA measurements were classified by T-scores in accordance with recommendations from the International Osteoporosis Foundation when investigating younger individuals, and classified according to WHO definitions (normal \geq -1, osteopenia -2.5 to -1, and osteoporosis \leq -2.5) (15). DXA measurements were available from the lumbar spine and the unfractured contralateral hip as total hip and femoral neck, the lowest T-score from any location was used in the analyses.

Descriptive variables

Body mass index (BMI) was calculated (kg/m^2) and categorized as underweight (<18.5), normal (18.5-24.9), overweight (25-29.9) and obese (>30) (16). American Society of Anesthesiologists (ASA) classification was categorized by the attending anesthesiologist pre-operatively, and collected from medical charts (17).

Bias

The patients were included consecutively, but a few potentially eligible patients were not assessed for inclusion (due to researchers not available). In addition some declined participation in the HFU-60 study (4). By legislation on personal privacy, we were prohibited to perform a drop-out analysis on patients eligible but not included in the study. This might introduce a selection bias; the potential impact could not be estimated.

Ethical considerations

The study was conducted in accordance with the Helsinki Declaration and registered at ClinicalTrials.gov (NCT03848195). HFU-60 was approved by ethical review boards in Sweden (Regionala etikprövningsnämnden Lund (Diarienummer: 2015/28)) and Denmark (Videnskabsetisk Komité for Region Syddanmark (Projekt ID: s-20150137)).

Statistical methods

Collected data was stored online using Research Electronic Data Capture (REDCap) (projectredcap.org). Age was not normally distributed and is presented as median with

interquartile range (IQR), other presented variables are categorical. Associations between trauma mechanism, DXA result, and fracture classification were analyzed using Chi-square tests. We also analyzed the associations between fracture type and low- or non low-energy trauma in combination with (< -2.5) and without osteoporotic T-score (> -2.5). Data analysis was performed using IBM SPSS version 26, a p-value of <0.05 was considered statistically significant.

Results

The cohort consisted of 218 patients, of whom 184 were investigated with DXA at the time of the fracture (Figure 1). Median age for the entire cohort was 53 years (IQR 47-57), 127 were men (58%), 1/2 of the patients had a normal body mass index, 2/3 were classified ASA I-II, and a low-energy trauma caused 2/3 of the hip fractures (Supplementary Table 1). Patients investigated with DXA also had a median age of 53 (47–57) (Table 1), compared to a median age of 55 (48–57) for the 34 patients (19 men, 41% normal BMI, 41% ASA I-II, 82% low-energy trauma) who were excluded from the analysis, due to DXA > 3 months post-fracture (n=8) or no available DXA investigation (n=26).

Femoral neck fractures constituted 58% (2/3 were displaced), pertrochanteric fractures 34% (2/3 were unstable). Remaining fractures were basicervical (5%) and subtrochanteric (4%), i.e. intracapsular fractures, 63%, were more common than extracapsular (Figure 2). In 7 patients (5 low-energy, 2 non low-energy trauma), other concurrent fractures were seen; in the spine, ribs, the contralateral lower extremity, or in the upper extremities.

Analyses of the associations between trauma mechanism and fracture classification did not differ significantly statistically, but clinically important findings were seen. Non low-energy trauma led to an intracapsular fracture more often (71%) than an extracapsular (29%) (Table 2). Furthermore, a trend was seen towards a larger proportion of intracapsular compared to extracapsular fractures being due to non low-energy trauma, 50/137 (37%) vs 20/81 (27%) (p=0.07). Low-energy trauma resulted in unstable/displaced fractures more often (70%) than non low-energy trauma (57%), though not statistically significant (p=0.06) (Table 3).

On DXA investigation, normal T-score was found in 12%, osteopenic in 57%, and osteoporotic in 31% (Table 1). Associations between DXA result and fracture types were not statistically significant, and a similar distribution was seen regarding intra-/extracapsular fractures (Table

2). A normal T-score was associated with a tendency towards a lower rate of unstable/displaced fractures (59%), compared to osteopenic (69%) and osteoporotic T-scores (68%), though not statistically significant (Table 3).

Analyses of associations between the combination of trauma mechanism and osteoporotic DXA results with fracture classification were not statistically significant, although clinically important findings were seen. In the low-energy trauma group, 43/120(36%) had osteoporotic T-scores (< -2.5), compared to 14/64 (22%) in the non low-energy group (p=0.05). The distribution of intra- vs. extracapsular fracture types by trauma mechanism combined with DXA result was similar (Table 2), as it was regarding stability (Table 3).

Discussion

Intracapsular hip fractures were most common in our cohort of patients aged under 60, and most patients fractured their hip due to a low-energy trauma. Analyses on the associations between fracture type, trauma mechanism, and DXA result did not reach statistical significance, though clinically important findings were seen.

Hip fracture classification

Our finding of 63% of the fractures being intracapsular is comparable to previous studies, who reported a distribution of approximately 3:2 in younger patients (7,18–20), and the distribution of the specific fracture classification among the intracapsular fractures were also comparable to previous reports (7,13).

In extracapsular fractures, previous studies have reported higher proportions of subtrochanteric fractures (25-38%) compared to our 10% (7,19,20). However, they did not report using the AO/OTA classification, nor whether pertrochanteric fractures were considered stable or unstable, making comparisons uncertain.

Trauma mechanism

Most fractures in our cohort were due to low-energy trauma, and similar to the 71% reported in a register cohort of patients \leq 60 years with femoral neck fractures (13). Contrarily to what could be expected – that a higher energy trauma mechanism would result in a more severe fracture type – our findings suggest that an unstable/displaced fracture was more common after low-energy trauma. This probably indicates that factors beyond trauma mechanism are implicated in fracture stability. We used a definition of trauma mechanism that distinguished same level falls from any other trauma mechanisms. As a dichotomization into either low- and high-energy trauma is frequently used in the literature, one could expect uniform definitions to be present. But consensus regards low-energy trauma only (21). There is no clear definition of high-energy trauma. It often includes high-speed traffic accidents and falls from a height (e.g., >3m or more) (1,6,7,22). Triage of patients to dedicated trauma centers can be based on similar definitions. For example, the Swedish National Trauma Alert Criteria specifies car accident >50 km/h without seatbelt and falls >5m (23). The energy in such a trauma might by far supersede the force needed to break even a healthy bone.

A definition of an intermediate trauma mechanism is lacking, where a fracture could be expected, but not necessarily associated with complicating large soft tissue damage or injury to multiple organ systems. This grey zone between same level falls and potentially life-threatening high-energy traumas will also include many sports injuries. An addition of an intermediate trauma mechanism would add finer granularity to future studies to differentiate hip fracture types and the association with trauma mechanism.

Bone mineral density

Most patients had osteopenia or osteoporosis on DXA investigation. Regardless of trauma mechanism, the prevalence of osteoporosis was higher than in previous population-based samples where a prevalence of osteoporosis lower than 5% were reported (24,25). We found 36% osteoporotic T-score in the low-energy and 22% in the non low-energy trauma group. The latter possibly reflects that there is some truth to the popular belief that these fractures are less related to osteoporosis. However, osteoporosis will assumingly be a silent, unknown disease for a young or middle-aged individual, and thereby not a reason to abstain from situations involving a risk of forceful trauma. Furthermore, the trauma mechanism itself does not protect against osteoporosis – as osteoporosis does not protect against higher energy trauma mechanisms – a rather obvious syllogism also supported by a previous study (26). Therefore, it is important to consider investigation of bone health also in patients who suffer hip fractures through forceful trauma mechanisms.

Trauma mechanism in combination with bone mineral density

Inferior bone quality did not by itself explain a more severe hip fracture pattern, which has also been shown for distal radius fractures (27). Although we found a somewhat lower rate of unstable/displaced fractures in those with normal bone quality compared to osteopenic and

osteoporotic bone, the association was not strong enough to be statistically significant. After non low-energy trauma was combined with an osteoporotic T-score, a higher rate of unstable fracture patterns was found compared to with higher T-scores, which may indicate that bone quality can be implicated in the fracture pattern. In contrast, unstable fractures were least common in low-energy trauma in combination with osteoporosis. An explanation could be that other biomechanical factors and properties of bone (e.g., microarchitecture, elasticity, the proportion of cancellous vs cortical bone, etc.) probably are involved in the upcoming of different fracture types and patterns, not only trauma mechanism and BMD.

Limitations & Strengths

Our study has some limitations, firstly, 24% of the eligible patients were not included in the HFU-60 study (4). Unfortunately, we cannot estimate the potential selection bias this introduces to our study as we were legally prohibited to perform a drop-out analysis. The patients excluded from the analyses of DXA investigations might also introduce a selection bias. However, this probably did not lead to an overestimation of the prevalence of osteoporotic T-scores, since their characteristics were also associated with low BMD (i.e. higher median age, lower proportion of normal BMI and ASA I-II, and higher rate of low-energy trauma in relation to patients included in the analyses). Compared to other clinical studies on patients of corresponding age, our cohort is one of the largest. Still, our sample size may limit the statistical power of our findings. The participants were interviewed within a few days after the accident by a researcher at each hospital, nevertheless there may have been cases of recall bias or misunderstanding about the nature of the reported trauma. Fractures were classified by orthopedic surgeons at the participating centers, no analysis of intra- or interobserver variability was performed which could be a possible limitation; however, fracture classification according to AO/OTA by orthopedic surgeons have previously been found to be highly accurate (12). The study also has strengths. The participating public hospitals serve both urban and rural areas, and provide care for all fracture cases in their catchment areas, regardless of patient or trauma type. Thereby we consider our cohort to be a representative sample of the hip fracture population under age 60, which is also supported by the similar fracture patterns described in the 2020 Swedish Fracture Register report (3). Our findings support those from earlier studies,

with the novel strengths of using stringent fracture classification, timely DXA measurements and an analysis of associations between fracture classification, trauma mechanism, and bone mineral density.

Conclusion

In our cohort of adults under 60 years, most hip fractures were unstable/displaced and the anatomical location was mainly intracapsular. Most fractures resulted from low-energy trauma. There were no statistically significant associations between fracture classification and trauma mechanism, bone mineral density, or trauma mechanism in combination with osteoporotic T-score. Our finding of a high prevalence of low bone mineral density in patients with hip fractures due to both low- and non low-energy trauma calls for awareness of the risk of osteoporosis associated with hip fractures regardless of age and trauma type.

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None of the authors has potential conflicts of interest related to the study.

Data supporting the findings of this study are available upon reasonable request to the corresponding author.

All authors were involved in the study design and critically reviewed and approved the manuscript. SSR performed analyses and wrote the first draft. CR initiated the HFU-60 study project and supervised SSR.

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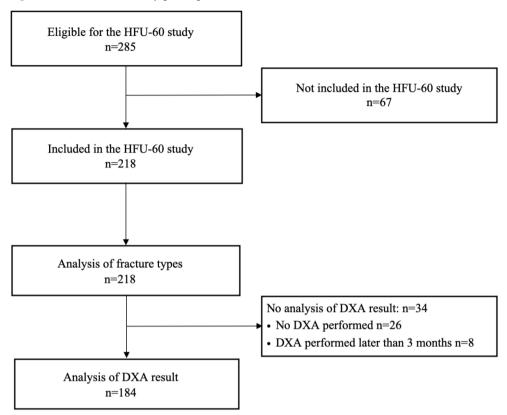
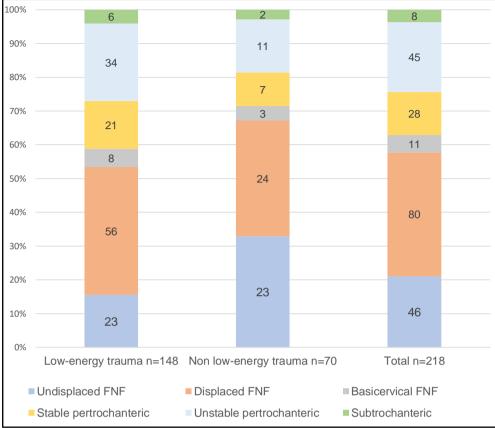


Figure 1 Flow chart of study participants

Figure 1 Flow chart of study inclusion and analysis of fracture types and DXA result. For details regarding inclusion in the HFU-60 study, please refer to Strøm Rönnquist et al, 2022 (4).



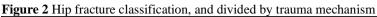


Figure 2 Hip fracture classification distribution fractioned by percentage, and divided by trauma mechanism. FNF: femoral neck fracture. Hip fractures were classified according to the 2007 revision of AO/OTA classifications (10): undisplaced FNF 31-B1; displaced FNF 31-B3; basicervical FNF 31-B2; stable pertrochanteric 31-A1 & 31-A2.1; unstable pertrochanteric 31-A2.2-3 & 31-A3, subtrochanteric 32.

					-		
	Total		Women		Men		
	184	(100%)	76	(41%)	108	(59%)	
Age							
Median (IQR)	53	(47-57)	54.5	(51-57)	51	(44-56)	
Min-max	28-59		30-59		28-59		
BMI *							
Underweight (<18.5)	11	(6)	8	(11)	3	(3)	
Normal (18.5-24.9)	101	(55)	37	(49)	64	(59)	
Overweight (25-29.9)	57	(31)	25	(33)	32	(30)	
Obese (>30)	11	(6)	6	(8)	5	(5)	
ASA classification							
ASA I	55	(30)	16	(21)	39	(36)	
ASA II	77	(42)	38	(50)	39	(36)	
ASA III	49	(27)	21	(28)	28	(26)	
ASA IV	3	(2)	1	(1)	2	(2)	
Trauma mechanism							
Low-energy	120	(65)	57	(75)	63	(58)	
Non low-energy	64	(35)	19	(25)	45	(42)	
T-score							
Normal (>-1)	22	(12)	9	(12)	13	(12)	
Osteopenia (-1 to -2.5)	105	(57)	41	(54)	64	(59)	
Osteoporosis (<-2.5)	57	(31)	26	(34)	31	(29)	
of contralateral hip	22		10		12		
of lumbar spine	9		5		4		
of both hip and spine	26		11		15		

Table 1 Participant characteristics for patients investigated by DXA, and divided by sex.

Table 1 Characteristics for patients investigated by DXA, and divided by sex, n (%) if not otherwise specified. IQR: inter quartile range, BMI: body mass index, ASA: American Society of Anesthesiologists, DXA: dual energy x-ray absorptiometry. * BMI missing 4 men.

	Intracapsular		Extracapsular		p-value
	n (%)		n (%)		
Trauma mechanism n=218					p=0.071
Low-energy	87	(59)	61	(41)	
Non low-energy	50	(71)	20	(29)	
T-score n=184					p=0.665
Normal (> -1)	16	(73)	6	(27)	
Osteopenia (-1 to -2.5)	72	(69)	33	(31)	
Osteoporosis (< -2.5)	36	(63)	21	(37)	
Low-energy trauma & T-score n=120)				p=0.527
Low-energy with osteoporotic T-score (< -2.5)	26	(60)	17	(40)	
Low-energy with T-score \geq -2.5	51	(66)	26	(34)	
Non low-energy trauma & T-score na	=64				p=0.847
Non low-energy with osteoporotic T-score (< -2.5)	10	(71)	4	(29)	
Non low-energy with T-score \geq -2.5	37	(74)	13	(26)	

Table 2 Anatomical fracture type by trauma mechanism, T-score, and a combination of trauma mechanism and T-score.

Table 2 Anatomical fracture type defined as intracapsular (femoral neck and basicervical) or extracapsular (pertrochanteric and subtrochanteric). Trauma mechanism was defined as low-energy trauma if a same level fall from standing or sitting position, other trauma was classified as non low-energy trauma. Of the full cohort (n=218), 184 patients were DXA-investigated, where an osteoporotic T-score was defined as < -2.5 in either the lumbar spine or the contralateral hip (total hip or femoral neck).

	Stable/undisplaced		Unstable/	p-value		
	n (n (%)		n (%)		
Trauma mechanism n=218					p=0.056	
Low-energy	44	(30)	104	(70)		
Non low-energy	30	(43)	40	(57)		
T-score n=184					p=0.676	
Normal (> -1)	9	(41)	13	(59)		
Osteopenia (-1 to -2.5)	33	(31)	72	(69)		
Osteoporosis (< -2.5)	18	(32)	39	(68)		
Low-energy trauma & T-score	e n=120				p=0.354	
Low-energy with osteoporotic T-score (< -2.5)		(33)	29	(67)		
Low-energy with T-score \geq -2.5	19	(25)	58	(75)		
Non low-energy trauma & T-s	score n=64				p=0.243	
Non low-energy with osteoporotic T-score (< -2.5)	4	(29)	10	(71)		
Non low-energy with T-score ≥ -2.5	23	(46)	27	(54)		

Table 3 Fracture type based on stability by trauma mechanism, T-score, and a combination of trauma mechanism and T-score.

Table 3 Fractures were categorized as stable/undisplaced (undisplaced femoral neck, stablepertrochanteric) or unstable/displaced (displaced femoral neck, basicervical, unstablepertrochanteric, subtrochanteric). Trauma mechanism was defined as low-energy trauma if asame level fall from standing or sitting position, other trauma was classified as non low-energy trauma. Of the full cohort (n=218), 184 patients were DXA-investigated, where anosteoporotic T-score was defined as < -2.5 in either the lumbar spine or the contralateral hip</td>(total hip or femoral neck).

	Study population		Low-energy		Non low-energy	
			trauma		trauma	
	218	(100%)	148	(68%)	70	(32%)
Age						
Median (IQR)	53	(47-57)	54	(49-57)	51	(45-56)
Min-max	23-59		23-59		28-59	
BMI *						
Underweight (<18.5)	21	(10)	17	(12)	4	(6)
Normal (18.5-24.9)	115	(54)	75	(51)	40	(57)
Overweight (25-29.9)	65	(31)	44	(30)	21	(30)
Obese (>30)	11	(5)	8	(5)	3	(4)
ASA classification						
ASA I	60	(28)	29	(20)	31	(44)
ASA II	86	(39)	57	(39)	29	(41)
ASA III	66	(30)	56	(38)	10	(14)
ASA IV	6	(3)	6	(4)	0	
Fracture type, intracapsular:						
Undisplaced FNF	46	(21)	23	(16)	23	(33)
Displaced FNF	80	(37)	56	(38)	24	(34)
Basicervical FNF	11	(5)	8	(5)	3	(4)
Fracture type, extracapsular:						
Stable pertrochanteric	28	(13)	21	(14)	7	(10)
Unstable pertrochanteric	45	(21)	34	(23)	11	(16)
Subtrochanteric	8	(4)	6	(4)	2	(3)

Supplementary Table 1 Participant characteristics for the full cohort (n=218) and divided by trauma mechanism.

Supplementary table 1 Participant characteristics for the full cohort, and divided by trauma mechanism, n (%) if not otherwise specified. Hip fractures were classified according to the 2007 revision of AO/OTA classifications (10): undisplaced FNF 31-B1; displaced FNF 31-B3; basicervical FNF 31-B2; stable pertrochanteric 31-A1 & 31-A2.1; unstable pertrochanteric 31-A2.2-3 & 31-A3. IQR: inter quartile range, BMI: body mass index, ASA: American Society of Anesthesiologists, FNF: femoral neck fracture. *BMI missing 6 patients.

Paper III

Lingering challenges in everyday life for younger patients with hip fractures – a qualitative study of the lived experience during the first three years

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ABSTRACT

Purpose

The aim was to illuminate the lived experience of recovery from a hip fracture in adults under age 60 in order to guide future healthcare services.

Methods

Participants were purposively sampled from a prospective multicenter cohort study in Sweden and Denmark, and narrative interviews were conducted with 19 individuals 0.7-3.5 years after the fracture. We used a phenomenological hermeneutic method to describe the participants' expressed essential meaning.

Results

The experience of sustaining a hip fracture was expressed as a painful and protracted process of regaining self-confidence, function, and independence. It also implied a sense of growing old from one day to the next, the body being feebler, and being looked upon as a burden by coworkers. Participants were afraid of new falls and fractures, resulting in an increased wariness.

When expressing fears and persisting symptoms, participants described being neglected and marginalized by the healthcare system, which was perceived as non-receptive and routinely driven by a notion that hip fractures affect only the elderly. Rehabilitation targeted towards needs different from those of elderly individuals was requested.

Conclusion

The lived experience of sustaining a hip fracture in individuals under 60 includes substantial challenges in everyday life, even up to 3.5 years after the injury. Rehabilitation pathways tailored to the needs of these patients are requested.

Background

A patient with a hip fracture is typically seen as old and frail, and is assumed to have a fracture caused by low-energy trauma [1]. Incurring a hip fracture at an older age is associated with an increased risk of functional deficit, persisting pain, increased fear of falling, decreased health-related quality of life and death [1–3]. Strategies such as remaining active, managing expectations and maintaining participation in activities have been described as essential to maintain function and quality-of-life [4]. Is this also the case for young and middle-aged adults sustaining hip fractures? This more heterogeneous group constitutes approximately one tenth of all hip fractures [5–10]. While some are healthy, others are predisposed to fractures due to lifestyle factors, functional limitations, hormonal deficiency or diseases [6, 11, 12]. Among the elderly, we know that empowerment of patients was not adequately achieved in the hip fracture pathways [13]. However, there is a lack of knowledge regarding younger patients' perspectives. The need for increased awareness of their experiences, in order to design better fracture management and rehabilitation, led us to conduct this study. Our aim was to illuminate the lived experiences and the path of recovery for adults sustaining a hip fracture before the age of 60. A clinical perspective was to involve patients' experiences in future healthcare management to ensure that their needs are effectively addressed.

Methods

Study design

The present work is a qualitative study using a phenomenological hermeneutic method described by Lindseth and Norberg [14]. This qualitative method was chosen to build a deeper understanding of the expressed lived experiences of individuals sustaining hip fractures before the age of 60 based on their narratives. In the reporting of this study, the Standards for Reporting Qualitative Research [15] were considered.

Setting and sampling

Participants were purposively sampled from the prospective, multicenter cohort study, *Hip fractures in adults under the age of 60 years (HFU-60)*, which analyzes the epidemiology, treatment and outcome of hip fractures in this group [12]. From the total cohort of 218 participants in the HFU-60 study, 30 participants with a variety of characteristics were selected and invited. Inclusion criteria

were as follows: speaking Swedish or Danish, being able to individually partake in the interview, minimum 6 months' time since the hip fracture and New Mobility Score \geq 3 pre-fracture [16]. Of the invited individuals, 19 agreed to participate.

Ethical considerations

The study was conducted in accordance with the Helsinki Declaration, and all participants provided informed written consent. Approval was obtained from ethical review boards in Sweden (Regionala etikprövningsnämnden Lund (dnr: 2015/28)) and Denmark (the Regional Health Service and University Research Ethics Committee and the Danish Data Agency (S-20150137) (case approval no 15/51398)). Data was pseudonymized and stored in a secure database. All quotations from participants were included with permission. Data will be made available upon reasonable request to the corresponding author.

Data collection

Participants in the present study were interviewed in either their homes or a hospital setting, based on preference. The interviews were conducted from April to August 2019 and lasted between 35 and 71 minutes, resulting in a rich and extensive dataset. Data collection continued until data saturation was obtained; i.e., no new aspects or experiences presented themselves in the interviews. Basic demographic data (age, marital status, occupation, comorbidity, previous fractures) and history of the present hip fracture incident were collected before the interviews. The interviews were initiated with an open-ended question: "Could you tell me about when you sustained your hip fracture and how you have experienced the time after as well as your recovery?". A complementary interview guide was used by the interviewer, with follow-up questions such as, "How was the first time-period when you came home from the hospital?", "Do you have any symptoms from your hip today?", "Can you describe your feelings toward your fracture?", and "What is your opinion of the care that you received both at the hospital but also once you were discharged?". The follow-up questions were intended to keep the interviewee within the aim of the study.

Researcher characteristics and reflexivity

The research team represented different fields within both qualitative and quantitative areas of research. The interviews were conducted by two experienced qualitative researchers, HKS and CMJ, in the interviewers' and the respondents' native language (Swedish and Danish, respectively). The interviewers were not involved in the fracture treatment, hospital care or rehabilitation. The recorded data material was transcribed by the interviewer in the language in which the interview was conducted. For a joint analysis on both datasets, we performed triangulation continuously during data collection through comparisons by the bilingual author SSR, who evaluated whether the two national data collections were conducted in a comparable way. Trustworthiness was established by demonstrating reflexivity, credibility, transferability, and dependability according to Koch's [17] criteria (Table 1).

Data analysis

The interpretation using the method of phenomenological hermeneutics was conducted on 3 levels [14, 18].

1. Naïve reading involved reading the text several times as openly as possible to obtain a general understanding of the meaning behind the words, rather than what the participants said. Each interviewer constructed a naïve understanding of their interview data, which were translated into English early on. In the comparison of naïve readings, we found that findings in the Swedish and Danish interviews were echoed in one another, enabling a joint analysis of data. This superficial deduction provided direction for the next level of interpretation.

2. Thematic structural analysis, in which the text was reflected upon. Units of meaning were identified based on "what is said". Through further interpretation, units of significance were identified and finally, in a dialectic movement, themes emerged to fulfill a deeper understanding.

3. Comprehensive understanding, which comprised a critical interpretation and discussion to reach a further understanding of the text. Through critical reflection, and in relation to relevant literature, the emergent themes were discussed to gain new knowledge and understanding of participants' experiences. Any discrepancies during the 3 levels of analysis were resolved through consensus.

Results

13 women and 6 men were interviewed at 0.7 to 3.5 years (median 1.5 (IQR 1.3-3)) post-fracture. Characteristics for the participants are presented in Table 2.

Naïve reading and understanding

The apprehension that healthcare and rehabilitation for younger and elderly patients with hip fractures are conducted according to the same standard care plan made the younger participants feel anxious and old from one day to another. Moreover, they felt incapable of actively taking part in their own care and rehabilitation plan. Being forced to act as one's own health advocate, navigating within a routine-driven and non-receptive healthcare organization, was also described.

Participants described a sense of being treated with ignorance by professional caregivers with perceived limited knowledge when they articulated fears and perceptible symptoms. They felt abandoned by those responsible for guiding them on their path of recovery. For our participants, who were all of working age with demands on their physical ability, it was important to receive information on which symptoms were concerning or normal after a hip fracture, and on how they could create optimal conditions for rehabilitation based on their remaining capabilities.

Fear of falling made participants cautious, hesitant, and limited in their surroundings, as well as in social gatherings and new settings, even up to 3.5 years following the hip fracture. Where a participant would once have pushed their limits, restraint was now demanded to listen to the body's signals and degree of stamina, but also to anticipate any risks that could cause a new fall and potential damage to the operated hip or aggravation of symptoms.

To overcome a hip fracture at a young age required intrinsic motivation to accept any forthcoming physical setbacks, but also to view improvements as a step in the right direction towards regaining their previous abilities and pre-fracture independence. Patients created strategies to motivate themselves to continue the rehabilitation and other activities – to challenge themselves and to prove, not only to themselves but also to friends and family, that they were motivated and had momentum. Attentive and responsive support from healthcare staff was perceived as a vital and decisive factor with potentially significant impact on their path of recovery and residual symptoms, but most participants felt they lacked this advantage.

Structural analysis

The structural analysis of the interviews revealed that the recovery experience was a painful and protracted process of regaining function, independence, and self-confidence. The fracture brought the participant's everyday life to a stand-still, creating feelings of weakness, disability, and inability. The interviews revealed different approaches to defying these difficulties and feelings of despair, remaining hopeful and generating motivation for recovery strategies to obtain the pre-fracture level of function. The emerged themes are summarized in Table 3, together with examples of quotes from the interviews.

Growing old overnight

The participants described a sense of growing old overnight due to the type of fracture they had sustained, especially as friends and family members called their injury an "old people's fracture". Similarly, the provided care was executed according to a standard protocol developed from the experience of hip fractures in the older population. Much of the information regarding the fracture and prognosis was given while participants were under the influence of analgesics, leading to problems remembering later during the recovery process. The participants said that upon expressing symptoms, they were ignored and disregarded, receiving contradictory information about the causes of the symptoms and possible methods of relief. The participants' narrations also depicted the care and rehabilitation as mechanical and numb to the specific rehabilitation needed. They were also told that thanks to their young age, they would heal faster and could expect fewer difficulties during their rehabilitation. The rehabilitation was planned and executed without the involvement of the participants were prescribed sedative analgesics when discharged, which made them indistinct and non-coherent when returning home and created difficulties in returning to normal routines and relationships with family and friends.

During their hospital stay, participants witnessed the medical staff's efforts to explain how the fracture would affect their everyday life. The information received from physicians and nurses was perceived as adapted to elderly patients and sometimes as contradictory. Participants were guided by a physiotherapist in how to move and what to avoid; however, these appointments were brief and left unanswered questions. Deficient communication left participants in doubt regarding what was valid information. Upon discharge, the participants described an obvious lack of awareness of, and interest

in, their home situation and everyday life – for example, how they lived, their ability to receive support with daily chores, how they would manage obligations toward work, family members or close friends, as well as socializing. Participants' need for transportation was a crucial issue to enable and maintain effective daily routines, but this need was not discussed. Participants were also in consensus regarding the sensation of being abandoned to pursue further rehabilitation on their own, either through municipal care or private caregivers, creating a sense of being forced to act as their own advocate to receive any further rehabilitation without support or assistance with referral from the hospital.

A person lacking capability

The customization of the participant's home by the municipal caregivers to permit activities of daily life (removal of thresholds and carpets, elevating the toilet, etc.) further increased the feeling of insignificance and inability to manage on one's own. Participants found themselves without the capabilities typical of their age group. Inner age (self-perceived) and outer age (chronological or perceived by others) did not reflect one another. Participants living alone were forced to ask friends or relatives to make daily purchases, which was attended by feelings of self-doubt, shame and inability to cope. The experience of increased load, stiffness and pain from the hip, groin, and surgery incision led participants to feel both discomfort in their limited life, and thankfulness for the support they received. This duality was described as a conflict between needed support and diminished and limited integrity, autonomy, and capability, where participants resisted accepting their need for help.

Inconsistent emotions and subsequent consequences

Participants described experiencing strong emotions and struggling to confidently believe in a future where they achieved a full recovery from the hip fracture. The path was filled with challenges they had to overcome. Some defined this part of the process as being two individuals: one overly positive and one feeling depressed and hopeless. The participants likewise presented two different personae: one facade that they displayed in front of friends and significant others expressing confidence, and another when they were alone with their thoughts about an insecure and unpredictable future. This latter persona was preoccupied by fear of falling and suffering another fracture, feelings of sadness and entrapment, self-imposed isolation but also external exclusion, as well as frustration and anger towards those feelings of helplessness, weakness, dependence, and frailty.

Pain was explicitly described by most participants, in some cases experienced daily and in others more seldom and less intense. The pain was described as a constant reminder of the fracture, leading to more cautious movements, exhaustion, and dark thoughts of a future with pain and stiffness as fellow passengers. Regardless of incidence or intensity of hip pain, participants described varying levels of fear of falling and doubt in their own body. This led them to create more margins in their life, planning ahead and thinking about what might or might not occur in order to avoid aggravating lingering symptoms. Fear of falling also had negative effects in social contexts, through avoidance of crowds and new, unfamiliar environments, but also of familiar contexts where certain roles and expectations might involve exposure to possible risks. Participants also struggled with the unanswered question of why they broke their hip.

To maintain as much normalcy as possible in everyday life during the process of recovery, participants described being forced to overcome adversities and handle reactions from others. The symptoms of the fracture were disguised so as not to be apparent to anyone other than significant others. People around them had difficulty believing in the severity of the symptoms and therefore questioned the participants' credibility and the seriousness of their limitations. This in turn created shame over the insinuation of over-reacting, leading participants to force themselves to act as others expected them to. Recurrent feelings of growing old, frail, fragile and incapable, which in turn damaged integrity, pride, self-image, and self-worth, were presented in the participants' narrations. Feeling broken and unmotivated and worrying that the function in their injured leg would never fully return was also expressed.

Total standstill in midlife

To sustain a hip fracture meant a total standstill in the middle of life. Many participants recounted physical limitations such as fatigue, weak muscles, inability to sit down, stiffness, back pain, and radiating pain from the groin and hip. Ordinary chores were difficult and time consuming due to fear of falling, loss of physical strength, limited leg function, and participants' mistrust of their own bodies. As a result, some chores were put off to the future. Reduced work capability affected some of the participants, which meant prolonged sick leave or reassignment to other work duties. This in turn created decreased income, a noticeable change and worry for the participant.

Other psychological effects were reduced well-being and feeling depressed, a strong lack of confidence, and uncertainty. Variation in the intensity of the physical symptoms from one day to the next was one of the main factors affecting the participants' frame of mind.

Defy despair

Participants had painted a dark and murky picture of the path to recovery with several hindrances, both physical and psychological. However, some experiences also fueled their motivation and reinforced the will to regain their former condition and bodily constitution. Several aspects in the narrations could qualify as methods to fight the sense of despair and thereby avoid letting stiffness, pain and fear govern their lives.

Participants described actions to strengthen their autonomy and gradually increase the intensity of the rehabilitation without overly burdening the affected hip. These small steps helped them strengthen both internal and external assets, which in turn strengthened their ambition to fully recover. Hope was a crucial ingredient in the recovery process. Setting short- and long-term goals for their rehabilitation amplified this sensation. Some participants recounted several strategies to generate the strength to complete the exercise sessions. Decisive factors in completing the rehabilitation were, according to the participants, early mobilization and the use of aids in their home to preserve strength to be able to attend rehabilitation sessions. Additional strategies to maintain progress included stopping to rest when feeling overexerted, keeping a positive attitude and maintaining physical activities at home between exercise sessions. Changing routines could also significantly help reduce stress and increase the sense of autonomy.

Returning to normal

Continuous rehabilitation required motivation to persist. Belief in improvement, strength, and endurance to actively partake in scheduled activities or meetings with physiotherapists were expressed as crucial for the participants. Some recognized procrastination and used excuses to avert the exertion, avoiding the overwhelming reality of the lengthy path to full recovery. Some participants explained that they had the will, but their body refused. Others told themselves that rehabilitation must work, which increased their motivation to continue fighting and not give up. Participants emphasized the need to find methods to increase the motivation for recovery, even when the path felt dark. Some maintained social networks and pointed to this as an important part of their rehabilitation pathway. More objective determining factors to preserve motivation were housing, civil status, understanding employers and continuous feedback from physiotherapists with a program based on the person's abilities and strength. Good physical shape before the accident determined the level of motivation and odds of a successful recovery by contributing better capacity and ingenuity of finding ways forward. Additionally, the perceived level of competence and professionalism of the physiotherapist made a major difference for the participants, as did increased trust in their own body and their immediate surroundings' understanding of the long rehabilitation process.

Comprehensive understanding and discussion

The main finding is that the participants experienced significant challenges in their daily lives, even up to 3.5 years after the fracture. They also expressed a desire for individually targeted rehabilitation and support of their needs, and some described feeling neglected by the healthcare system.

Healthcare staff-imposed challenges in recovery immediately after injury

Encounters with healthcare staff matter to patients. Our participants disclosed a sense of growing old overnight, due in part to the type of fracture but first and foremost due to the way the staff treated them. The feeling of standardized and mechanical care and rehabilitation without patient involvement, and the fact that participants felt ignored, disregarded and that they received contradictory information, support previous suggestions that awareness of younger patients' specific needs for recovery must be acknowledged [19].

Lingering challenges

Pain was explicitly described by most participants. Lingering pain years after the hip fracture in younger patients was previously described by Swiontkowski at al. [20] almost four decades ago. This suggests that outcomes have not improved sufficiently with time, despite other improvements in healthcare services.

Fear of falling was a prominent reality for our participants, as previously reported among younger patients [19]. In the elderly, associations with poorer functional recovery and lower quality of life have been found [21–23]. Fear of falling is an important factor to address during the care and rehabilitation after hip fractures, and awareness is a prerequisite for prevention of any negative effects.

A general wish among the participants was to return to their normal, pre-fracture state. Several studies of elderly patients described sustaining a hip fracture as a "lifebreaking event" because of the multidimensional consequences the injury has on their everyday life, both psychological and social [13, 24].

Recurrent feelings of becoming old, frail, fragile and incapable were presented, which in turn damaged integrity, pride, self-image, and self-worth. A previous qualitative study on patients under age 60 with hip fractures reported psycho-social impact to be present up to 10 years following the fracture [25], supporting our finding of lingering implications and highlighting the need for long-term follow-up of results.

The hip fracture was described as bringing life to a total standstill. Some of the participants could not satisfactorily perform their work obligations, which meant prolonged sick leave or modified tasks. This supports previous suggestions of potential economic implications due to a hip fracture in individuals of working age [26].

Factors influencing recovery

Standardized plans for care and rehabilitation after hip fractures are based on scientific evidence but were regarded by our participants as rigid and not individually customized. The ideal care might also involve a more holistic view of the patients as individuals, with their specific needs being met. Participants in our study reported that individually targeted rehabilitation and support of needs contributed greatly towards their recovery, and those who did not receive it expressed a lack of it. Similar needs were identified by a study on the elderly that found less than one third of those with hip fractures considered their rehabilitation to be adequate [27]. This indicates that there is obvious room for improvement regarding support of recovery.

Other factors we found to encourage recovery were hope and belief in improvement, support from family and friends and understanding employers. It appears that social support is equally important

to our younger participants as it is to the elderly after hip fracture [28]. Difficulty appreciating the severity of lingering symptoms and limitations by the outside world has also been reported in the UK [25]. Our study participants emphasized the need to find ways to increase and maintain motivation.

Evaluation of outcome

Traditionally, reports of the outcome of orthopedic interventions as successful or failure have been determined by surgeons, focusing on complications or re-operation rates [29]. These outcomes are important and quantifiable, but absence of complications or re-operation does not necessarily equal a successful recovery from a patient's perspective [30, 31].

Recommendations on reporting hip fracture outcomes important to patients include radiographic, clinical and functional outcomes [32]. Additionally, a more patient-centered core outcome data set, including presence of hip-related pain and limping; level of return to daily life activities, work, sports and leisure activities; and assessment of health-related quality-of-life and objective functional performance have been suggested [11].

Through the present study, we add the explicitly patient-centered outcome of the individual's experience of sustaining a hip fracture by illuminating physical, psychological and social perspectives. Adding a psycho-social assessment might be of value in future evaluation of outcomes following hip fracture.

Future support in recovery after hip fractures

The findings of lingering physical and psychological implications suggest a need for continuous long-term support of patients sustaining a hip fracture. The physical and psychosocial factors enabling recovery are similar in both elderly and younger patients [19]. Our participants expressed the same thoughts on recovery as those reported in a qualitative systematic review of hip fracture recovery in elderly patients [33]. This indicates that chronological age might be a poor measure to predict recovery or guide healthcare support of recovery. On the other hand, it has been proposed that the higher demands of a younger and more active individual, e.g., at work or in physical leisure activities, can be harder to fulfil [11, 32]. Full return to a pre-injury state of mobility and function seems difficult to reach for all patients, and psychosocial implications affect patients years after injury [1, 11, 25, 27, 34].

Perhaps recovery from injury should not be defined as a return to the previous self-perceived definition of oneself, as for some this appears to be an impossible target. In a qualitative study of patients who survived life-threatening accidents, it was reported that a redefinition of oneself was crucial to self-preservation [35]. This redefinition may also be of value for patients who have suffered hip fractures – taking previous and recent experiences and the abruptly developed new life situation after injury into account – focusing on expectations, aspirations and aims from both physical and psychosocial perspectives, with support from health care services.

Patients must be informed of the lengthy rehabilitation process, and rehabilitation should be tailored to the individual [36, 37]. This study, as well as other studies, have identified that this individualized care is lacking [38, 39].

Our results suggest provision of tailored and alternative pathways of rehabilitation, including support of the patient's redefinition of self after suffering a hip fracture. Healthcare services should be equipped to provide adequate support for the recovery of all patients, not only standard geriatric hip fracture rehabilitation. From the point of view of both the patient and society, future research must identify the subgroups of patients with hip fractures who do and do not recover, to better understand what can be expected after the injury.

Limitations and strengths

Our participants were purposively sampled from a larger cohort and are thus not representative of the whole group, which one could consider a limitation. However, we aimed to illuminate patients' experiences after sustaining a hip fracture, not to provide a complete documentation of all patients' experiences. Nevertheless, our participants represent a broad sampling of characteristics (Table 2). As a sample of experiences, our participants' contributions are valid, highlighting aspects of recovery that matter to patients.

We explored the participants' experiences through interviews, in which they expressed their notions of what was important for their recovery. The qualitative method enabled an improved understanding of aspects of recovery after hip fracture that are significant to patients. Our results add to – and support – a small but emerging body of knowledge, suggesting that our findings have external validity to patients with hip fractures in other high- and middle-income countries.

The collection and analysis of data were performed in accordance with the method of phenomenological hermeneutics, following three well-described methodological abstraction levels, which strengthens the trustworthiness of the study in reproducibility (Table 1) [14].

Conclusion

The lived experience of sustaining a hip fracture in patients under 60 years includes challenges in everyday life, even years after the injury. Lingering pain and feelings of weakness, disability and physical inability were expressed by participants. The provided care and rehabilitation were perceived as adapted to elderly patients, not to the needs of younger individuals. In perspective, other pathways of care and rehabilitation, including improved information, are suggested in order to meet the diverse demands of all patients with hip fractures.

Author contributions

All authors were involved in the study design and approved the final manuscript. SSR compared the two national datasets, curated quantitative data, wrote, and reviewed the manuscript. HKS interviewed participants, performed qualitative analysis, wrote, and reviewed the manuscript. CMJ interviewed participants, performed qualitative analysis, wrote, and reviewed the manuscript. SO initiated the study and critically reviewed the manuscript. CR initiated the study, wrote, and reviewed the manuscript.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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44]	
Trustworthiness criteria	Fulfilment of criteria
Reflexivity	Data, themes, sub-themes and saturation of findings were continuously discussed amongst the analyzing authors. The analyzing authors were also responsible for the interviews and collection of data, adding tacit knowledge and a more profound understanding.
	To understand the impact of and on our pre-understanding of the narratives, as well as to grasp potential decisive parts of the narration, participants were asked elaborating questions. Field notes regarding context, thoughts, and description of the location were collected to give the narration a contextualized frame.
Credibility	Findings were based on participants' narratives. Both interviewers and a bilingual author were involved in the process of analysis to establish consistency and researcher triangulation in the interpretation of the data.
Transferability	By using a purposive sampling frame and recruiting participants representing different demographic characteristics in form of marital status, level of education, employment, comorbidity and cause of hip fracture, the experiences from a broad spectrum of patients were enlightened.
Dependability	Findings were continuously evaluated and challenged in iterative processes, by holding regular team meetings throughout the data collection and analysis periods.

Table 1 Demonstrating trustworthiness in the qualitative data collection and analysis [17, 40–44]

Table 2 Participant characteristics

Characteristics	Number of participants =19		
Ago at fracturo			
Age at fracture Min-max	32-59 years		
Median (IQR)	56 (51-58)		
	50 (51-58)		
Marital status			
Single	5 (26%)		
Cohabiting	2 (11%)		
Married	12 (63%)		
	()		
Level of education			
Elementary	2 (11%)		
Secondary education	11 (58%)		
College / University	6 (32%)		
Employment			
Yes	15 (79%)		
No	4 (21%)		
Comorbidity			
Yes	9 (47%)		
No	10 (53%)		
Prior fracture			
Yes	10 (53%)		
No	9 (47%)		
Cause for hip fracture			
Simple fall / same level fall	8 (42%)		
Sports accident	7 (37%)		
Fall from height	2 (11%)		
Traffic accident	1 (5%)		
Work accident	1 (5%)		

Themes	Examples of quotes
Growing old overnight	"We are all different, you cannot give me the same instructions as an eighty-year-old."
A person lacking capability	"Feeling tired all the time because I do not get the sleep I need because of the pain"
Inconsistent emotions and subsequent consequences	"A low energy trauma hip fracture is an old peoples' disease – so why me?"
Total standstill in midlife	"My neighbor could walk nicely one month after the operation. I am now one YEAR after the operation and I still have problems even though I am younger. This is embarrassing!"
Defy despair	"I want to be exactly the same as before the operation but then I understand, I do not have that strength in the leg because it has taken quite a lot of damage. But I want to return to who I was before. I have so many beautiful shoes to use, ones with really high heels. They have been my motivation to get better (laughs), because I decided I will use them again (laughs)."
Returning to normal	"I think it has taken a long time to get back to normal. And, well, I am not quite sure that I actually am fully back to normal But now is maybe the new normal."

Table 3: Emerged themes, including exemplar quotes from participant interviews

Paper IV

Rate of conversion to secondary arthroplasty after femoral neck fractures in 796 younger patients treated with internal fixation: a Swedish national register-based study



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Background and purpose — In younger patients with a femoral neck fracture (FNF), internal fixation is the recommended treatment regardless of displacement. Healing complications are often treated with arthroplasty. We determined the rate of conversion to arthroplasty up to 5 years after fixation of either undisplaced FNFs (uFNFs) or displaced FNFs (dFNFs).

Patients and methods — The study was based on prospectively collected data from the Swedish Fracture Register (SFR) and the Swedish Arthroplasty Register (SAR). FNFs in patients aged < 60 treated with parallel pins/screws or sliding hip screws (SHS) registered in SFR 2012–2018 were cross-referenced with conversions to arthroplasty registered in SAR until 2019. The cumulative conversion and mortality rates were determined by Kaplan–Meier analyses and patient- and surgery-dependent risk factors for conversion by Cox regression analyses.

Results — We included 407 uFNFs and 389 dFNFs (median age 52, 59% men). The 1-year conversion rate was 3% (95% CI 1–5) for uFNFs and 9% (CI 6–12) for dFNFs. Corresponding results at 5 years were 8% (CI 5–11) and 25% (CI 20–30). Besides a displaced fracture, age 50–59 was associated with an increased rate of conversion in uFNFs. This older group also had a higher mortality rate, compared with patients aged < 50. There was no sex difference for mortality.

Interpretation — Adults aged under 60 with uFNFs and dFNFs face an 8–25% risk, respectively, of conversion to arthroplasty within 5 years after internal fixation. This is new and pertinent information for surgeons as well as patients.

In younger individuals with femoral neck fractures (FNF), internal fixation (IF) is the recommended treatment alternative (1). Nevertheless, the risk of healing complications has to be acknowledged; osteonecrosis of the femoral head and non-union are the most common but the actual rate of conversion to arthroplasty is insufficiently described in younger patients. A population-based study on 796 individuals aged under 50 years found a conversion rate of 14%, but did not distinguish fracture displacement (2). A smaller case series (n = 122) presented a conversion rate of 22% for displaced FNFs (dFNF) (3). Besides the obvious need to give correct information on prognosis to younger patients, detailed knowledge on conversion rate is mandatory to underpin a sound treatment strategy. The debate focuses on where to draw the line between internal fixation and hip replacement as primary treatment of a dFNF. Different age limits are proposed, even as low as 45 years has been suggested (4). Traditions and surgical preferences vary internationally; the Scandinavian countries have had a higher age limit for primary arthroplasty as treatment for FNFs but have gradually shifted from 70 to approximately 60 years (5,6). Also, for undisplaced FNFs (uFNF), primary arthroplasty has recently been put forward as an alternative, at least in elderly patients (7.8). We designed a national register-based study to determine the rate of conversion to arthroplasty from IF due to uFNFs and dFNFs in patients under the age of 60. Furthermore, we descriptively analyzed mortality and the relationship between conversion rate and sex, age, trauma mechanism, and surgeon's experience.

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Patients and methods

Study design

This longitudinal cohort study is based on 2 Swedish national registries with prospectively collected data: the Swedish Fracture Register (SFR) and the Swedish Arthroplasty Register (SAR). We followed the STROBE guidelines for reporting the study.

Setting

The SFR started in 2011 and during the study period (2012–2018) the coverage for hip fractures increased from 18% to 86% due to an increased number of hospitals reporting to the register (9,10). By 2021 all orthopedic departments in Sweden participated, i.e., coverage of 100%, in the register, which comprised 645,000 fractures at the end of 2021. The completeness of the register has been validated and in 2018 the completeness for femoral fractures was 55% (11,12). FNFs are classified in the SFR according to the 2007 AO/OTA classification as undisplaced subcapital (31-B1), transcervical/basicervical (31-B2), and displaced subcapital (31-B3) (13). The accuracy of the fracture classification in the SFR has been validated, and was found to be substantial (14). The injury, fracture classification, and treatment are registered by a physician through individual log-in on the SFR webpage.

SAR is the national quality register for hip and knee replacement surgery in Sweden. SAR has a coverage of 100% for all departments performing hip replacement surgery, both public and private. For the years of the current study, the completeness was approximately 98% for total hip arthroplasty (THA), 96% for hemiarthroplasties (HA), and 92% regarding revisions of both THA and HA (15). By regular co-processing with the population register (the Swedish Tax Agency) any date of death is noted in both register databases.

Participants

Data for all patients aged 18 to 59 years registered with a hip fracture (defined by the ICD codes \$72.00, \$72.10 and S72.20) in SFR from 2012 to 2018 was extracted and crossreferenced with available data from SAR for each individual from the date of the index fracture until December 31, 2019. The unique individual personal number of each Swedish citizen ensures a reliable match between registers and subsequent surgeries and/or death. Only the 1st registered hip fracture was included in the study; contralateral and subsequent ipsilateral fractures and duplicate registrations were excluded. The uFNFs (AO/OTA 31-B1, Garden 1-2) and dFNFs (AO/ OTA 31-B3, Garden 3-4) were further examined for eligibility; other fracture types were excluded (13). We identified all available FNFs in the SFR, but the data search did not include any concurrent fractures. As they are specified in the reporting procedure, and identified by their ICD-10 diagnose codes (M84.4, M84.8, M84.3), pathological, spontaneous, and stress fractures were excluded from the analysis together with peri-

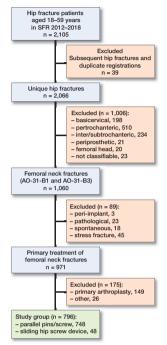


Figure 1. Flowchart of inclusion

implant fractures. Based on the primary treatment, fractures treated with IF (parallel pins/screws or sliding hip screw devices [SHS]) were identified, and we excluded patients treated with primary arthroplasty, intramedullary nail, other types of plate fixation, or non-surgically from further analysis on conversion rate (Figure 1).

Study variables

We analyzed basic demographic and epidemiological variables (i.e., sex, age, and trauma mechanism) and data on the primary fracture treatment from SFR (i.e., type of IF used and surgeon's experience defined as performed by either a resident or a specialist), together with the rate of conversion to hip arthroplasty registered in SAR and mortality. Trauma mechanism was defined according to the definition used in SFR: low-energy trauma is same-level falls and high-energy trauma is caused by truly high level of energy, such as traffic accidents or falls from a height. Length of follow-up was defined as time from injury date to date of death or end of study period on December 31, 2019.

Study outcomes

The main aim was to determine rates of conversion to arthroplasty after IF of uFNFs and dFNFs at 1, 2, and 5 years. FurTable 1. Patient characteristics. Values are count (%) unless otherwise specified

Characteristics	uFNF AO-31-B1 n = 407	dFNF AO-31-B3 n = 389	Total n = 796
Median age (IQR)	53 (48–57)	52 (45–56)	52 (46–57)
Age < 50	133	159	292 (37)
Age 50–59	274	230	504 (63)
Sex distribution ($p = 0.008$)			. ,
Men	222 (55)	248 (64)	470 (59)
Women	185 (46)	141 (36)	326 (41)
Trauma mechanism (p = 0.005	5)	. ,	. ,
High-energy trauma	44 (11)	72 (19)	116 (15)
Low-energy trauma	321 (79)	293 (75)	614 (77)
Missing	43 (11)	25 (6)	66 (8)
Primary treatment (p = 0.5)			
Parallel pins/screws	385 (95)	363 (93)	748 (94)
Sliding hip screw	22 (5)	26 (7)	48 (6)
Surgeon's experience (p = 0.0			
Resident surgeon	139 (34)	95 (24)	234 (29)
Specialist surgeon	254 (62)	278 (71)	532 (67)
Missing	14 (3)	16 (4)	30 (4)
Mean follow-up, years, (SD)	3.5 (1.7)	3.5 (1.7)	3.5 (1.7)

uFNF: undisplaced femoral neck fracture.

dFNF: displaced femoral neck fracture.

thermore, analyses were performed on mortality and associations between conversion to arthroplasty and sex, age, trauma mechanism, and surgeon's experience in the study group.

Statistics

Observations were grouped according to fracture classification (i.e., uFNF or dFNF), sex, and age < 50 or 50-59. Data on continuous variables were assessed for normality and presented as mean or median, depending on normal distribution. We analyzed associations between categorical variables using a chi-square test. Kaplan-Meier analysis was used to determine the rate of conversion to secondary arthroplasty as cumulative reoperation rate (CRR) with 95% confidence interval (CI) at 1, 2, and 5 years after the injury and to estimate mortality rates. We used a Cox proportional hazards regression model to determine hazard ratios (HR) between risk factors for secondary arthroplasty, where female sex, age 50-59, high-energy trauma mechanism, and resident surgeon previously have been described to have increased risk of reoperation and were assumed to be associated with a higher HR (4,16-18). Participants with missing data for a variable were excluded from analysis of that specific variable. Analysis of data was performed in IBM SPSS version 26 (IBM Corp, Armonk, NY, USA) and R version 4.0.2 (R Foundation for Statistical Computing, Vienna, Austria).

Ethics, data sharing, funding, and potential conflicts of interests

The study was conducted in accordance with the Helsinki Declaration and was approved by the Swedish national ethi-

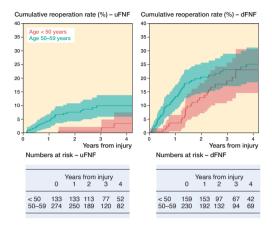


Figure 2. Cumulative reoperation rate with 95% confidence intervals presented by age classification and fracture type. uFNF: undisplaced femoral neck fracture. dFNF: displaced femoral neck fracture.

cal review board (Etikprövningsnämnden: Dnr 2019-05024). Data was pseudonymized before extraction from the registries and subsequent analysis. The data supporting the findings of this study is available upon reasonable request to the corresponding author. The study was supported by grants from the Research and Development Council of Region Skåne and a grant from the Swedish Research Council funding for clinical research in medicine. The authors declare no conflicts of interest related to the study.

Results

2105 hip fractures were identified in the SFR. After exclusion, 407 uFNFs and 389 dFNFs treated with internal fixation with parallel pins/screws or SHS were analyzed (Figure 1).

Patients were aged 20 to 59 years at the time of the fracture, 59% of the fractures occurred in men, and 77% were due to low-energy trauma. Fractures due to high-energy trauma were more prevalent in dFNFs compared with uFNFs. The distribution of parallel pins/screws and SHS was similar in uFNFs and dFNFs. Specialists performed 2/3 of all operations due to FNFs (Table 1).

108 of the 796 participants underwent a conversion to arthroplasty, 28 after IF of uFNFs, and 80 after dFNFs. There were 2 conversions to HA, all others to THA. In an implant survival analysis, the conversion rates after 1, 2, and 5 years for dFNFs were 9% (95% CI 6–12), 17% (CI 13–21), and 25% (CI 20–30), which were higher than for uFNFs, which demonstrated 3% (CI 1–5), 5% (CI 3–8), and 8% (CI 5–11) (Table 2, see Supplementary data).

Table 3. Cox proportional hazard ratios and 95% confidence intervals for conversion to arthroplasty

	HR (CI)	p-value
Undisplaced femoral neck fracture Female sex Age (50–59) High-energy trauma Resident surgeon Displaced femoral neck fracture Female sex	1.2 (0.5–2.7) 5.2 (1.4–20) 2.9 (0.8–11) 1.5 (0.6–3.3) 1.5 (0.9–2.4)	0.7 0.02 0.1 0.4 0.1
Age (50–59) High-energy trauma Resident surgeon	0.8 (0.5–1.3) 1.1 (0.6–2.0) 1.7 (1.0–2.8)	0.3 0.7 0.06

HR (CI): hazard ratio with 95% confidence interval.

Age 50–59 was associated with an increased rate of conversion to arthroplasty for uFNFs but not for dFNFs (Figure 2). When analyzing risk factors for conversion, age 50–59 had an HR of 5.2 (CI 1.4–20) compared with age < 50 years in the uFNF groups. No other risk factors could be identified (Table 3).

The exclusion of 149 patients treated with primary arthroplasty theoretically reduced the number of FNFs at risk of conversion to arthroplasty (Figure 1). Median age (IQR) for patients treated with primary arthroplasty was 56 (54–58). 9% were aged < 50, 56% were women, and 89% low-energy trauma (n = 14, 84 and 133 respectively).

The mortality rates were similar between uFNFs and dFNFs and between men and women (Figures 3 and 4). At 1 year, 20 individuals had died and at 5 years, 62. The 1- and 5-year cumulative mortality rate of individuals aged 50–59 at the time of the fracture was 4% (CI 2–6) and 16% (CI 11–20) compared with 0% and 5% (CI 2–7) for those aged < 50 (Table 4, see Supplementary data).

Discussion

A considerable proportion of young and middle-aged individuals with an FNF can expect a conversion to hip arthroplasty within 5 years post-fracture, 1 in 4 for displaced fractures and 1 in 12 for undisplaced fractures.

Our rates of conversion to arthroplasty were comparable to previous reports on younger patients (2,3). Stockton et al. (2) considered their conversion rate to be high and called for improvement in the treatment of FNFs in younger patients. Our results for uFNFs are in close proximity, but we regard the conversion rate to be acceptable and believe it confirms IF as the gold standard for uFNFs in this age group. For patients with dFNFs on the other hand, outcome after IF is poorer. In our 50–59-year group, there is an immediate and steady increase in the rate of conversion during the entire follow-up, showing a readiness of the surgeons to perform secondary surgery. Surgeons may feel at ease, as other patients in the same

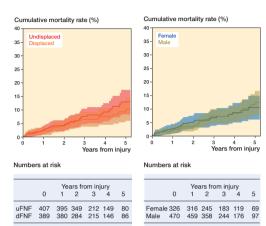


Figure 3. Cumulative mortality rate with 95% confidence intervals presented by fracture type.

Figure 4. Cumulative mortality rate with 95% confidence intervals presented by sex.

age span with symptomatic osteoarthritis are routinely given a hip replacement nowadays, as we know better the good longterm prognosis for the arthroplasty. Remarkably, the youngest group with dFNF also ended up with a 23% conversion rate at 5 years, albeit their rate was modest during the earliest years, maybe reflecting a more guarded attitude towards arthroplasty in this age group. On the other hand, when 3 of 4 with dFNFs still had their native hip at 5 years, the result in terms of conversion to arthroplasty can be said to be acceptable or even good. Future endeavors should focus on improving the clinical pathway for this group of young patients, for whom this fracture is still unsolved (19).

In elderly patients, the degree of displacement of the FNF, including both posterior and anterior tilt, and fracture comminution, have been found to predict failure of IF (20-22). Our results confirm that displacement according to Garden is a risk factor for failure leading to conversion arthroplasty in younger patients also. Nevertheless, our conversion rate is much lower than in geriatric patients treated with internal fixation of their dFNFs, where major secondary surgery can be expected in approximately 40% (23,24).

Should we lower the age limit for primary arthroplasty? The rationale for treating younger patients with internal fixation, even if their fracture is displaced, is the theoretical benefits of preserving the femoral head and a fear of multiple revisions of an arthroplasty during a long remaining life span. But if we consider long-term results from RCTs on patients aged over 60, those initially treated with IF never reached superior functional results compared with those treated with arthroplasty (22,25). When considering risk of revision of the primary arthroplasty, one should bear in mind that conversion arthroplastes are associated with inferior outcome compared with

primary arthroplasties for FNFs (26,27). Ideally, those with an inherently higher risk of fixation failure should be identified preoperatively and selected for primary arthroplasty. Otherwise, a focus on realistic expectations and readiness for swift conversion arthroplasty when needed would also be acceptable in the future, given that most young patients' fractures actually do heal.

Notably, there was no difference between men and women regarding mortality, although elderly males with hip fractures have a higher risk of dying (28), and younger women have been reported to have more comorbidities (29). The 5-year mortality of 16% for those 50–59 years old is noteworthy, and the 1-year mortality of 4% was 10-fold higher compared with the mean mortality rate for the same ages in the general Swedish population during the years of the study (30,31). They may in this aspect resemble the elderly, which could speak in favor of a primary arthroplasty rather than internal fixation in those of advanced biological age and an expected shorter survival. This is supported by an analysis of cost-effectiveness where the lowest age proposed for THA as primary treatment of FNFs was 45 years in patients with multiple comorbidities whereas it was 54 for healthy patients (4).

Limitations

That some individuals in the older age span with dFNF were initially selected for primary arthroplasty may affect the conversion rates reported in our study. Assuming that these patients were identified as at particularly high risk of fixation failure, our estimates of the conversion rates are potentially underestimated by this selection bias.

The number of parallel implants varies internationally. In line with Scandinavian tradition, 2 pins or screws are used almost exclusively in this cohort. There is little support in the literature that adding extra screws will reduce the risk of redislocation or non-union (16). That only 6% received an SHS hindered us from testing the suggestion made by the FAITH study (32), i.e., that SHS could have some benefits in those with displaced fractures.

We lack data on whether an open reduction has been performed, but the Swedish tradition is to rely on closed reduction only. Also, the literature has so far not been able to show any clear benefits of open reduction (33,34).

Indices depicting comorbidities and biological age/frailty would have been desirable variables to analyze, but unfortunately the registers do not include these potentially important risk factors for conversion to arthroplasty. Those selected for primary arthroplasty in our material may represent such a subgroup of frailer individuals.

Strengths

Our study is the largest to date analyzing conversion rate after IF due to uFNFs and dFNFs. We believe our result to have good external validity as it reflects everyday practice in non-selected patients and surgeons. We consider conversion to arthroplasty as a marker of a major hip complication. Naturally, other outcomes are valuable and patient-reported outcome is always preferrable. Any kind of reoperation could be relevant to report, but in Sweden valgus osteotomy, core decompression, or vascular grafts are very seldom utilized. Implant removal is a common reoperation, but the severity of the underlying situation is difficult to grade. It can span from routine procedures with no or little discomfort experienced by the patients to major complications such as deep infection or fracture collapse. We also chose our outcome due to the SAR's high completeness and national coverage, leading to a reliable result.

Conclusion

After IF in patients aged < 60, the rate of conversion to arthroplasty for dFNFs was significantly higher than for uFNFs during the entire follow-up. At 5 years, 25% and 8%, respectively, had undergone a conversion to hip arthroplasty.

In dFNFs, the conversion rates were similar in all ages. For uFNFs the conversion rates in patients aged 50–59 were significantly higher than for younger patients. No other risk factors for conversion to arthroplasty could be identified in our material. Mortality rates were markedly higher for patients aged 50–59 but did not differ between men and women or between uFNFs and dFNFs.

In perspective, both surgeons and patients should be aware of the risk of conversion to arthroplasty at the time of initial treatment. A clinical implication would be a long-term followup scheme and readiness for swift conversion when needed.

All authors were involved in the study design and approved the final manuscript. SSR initiated the study, curated data, performed statistical analysis, wrote, and reviewed the manuscript. LL critically reviewed the manuscript. BV contributed expert knowledge, wrote, and reviewed the manuscript. CR initiated the study, supervised SSR, wrote, and reviewed the manuscript.

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Supplementary data

Table 2a. Cumulative reoperation rate with 95% confidence intervals presented by fracture type

Fracture type Time, years	No. at risk	Cumulative events	CRR (95% CI)			
Undisplaced fer	Undisplaced femoral neck fracture (n = 407)					
1	383	12	3.0 (1.3–4.6)			
2	302	21	5.4 (3.1-7.7)			
3	197	25	6.9 (4.2–9.5)			
4	134	27	8.0 (4.9–11)			
5	73	27	8.0 (4.9–11)			
Displaced femoral neck fracture ($n = 389$)						
1	345	35	9.2 (6.2–12)			
2	229	63	17 (13–21)			
3	161	73	22 (17–26)			
4	111	78	24 (19–29)			
5	64	79	25 (20-30)			
5	04	79	23 (20-30)			

CRR: cumulative reoperation rate.

Table 4. Cumulative mortality rate with 95% confidence intervals by age classification

Age group Time, years	No. at risk	Cumulative events	CMR (95% CI)			
< 50 years (n =	< 50 years (n = 292)					
1	292	0	0 (0-0)			
2	228	4	1.5 (0.0-3.0)			
3	165	9	3.8 (1.3-6.2)			
4	108	10	4.5 (1.7-7.3)			
5	60	10	4.5 (1.7-7.3)			
50-59 years (n = 504)						
1	483	20	4.0 (2.3-5.7)			
2	375	28	5.7 (3.6-7.7)			
3	262	40	9.1 (6.3–12)			
4	187	44	11 (7.6–14)			
5	106	52	16 (11–20)			

CMR: cumulative mortality rate.

Table 2b. Cumulative reoperation rate with 95% confidence intervals presented by age classification and fracture type

Age group				
Fracture type	No. at	Cumulative		
Time, years	risk	events	CRI	R (95% CI)
< 50 years				
Undisplaced fer	noral neo	ck fracture (n =	133))
1	133	0	0	(0–0)
2	113	1	0.8	(0.0-2.4)
3	77	1		(0.0-2.4)
4	52	3		(0.0-7.7)
5	32	3		(0.0-7.7)
Displaced femo		-		(0.0 7.17)
1	153	6		(0.8-6.7)
2	97	19	13	(7.3–18)
3	67	25	19	(12–26)
4	42	28	23	(15-31)
5	20	28	23	(15-31)
50-59 years				(
Undisplaced fer	noral neo	ck fracture (n =	274)
1	250	12		(2.0-6.9)
2	189	20		(4.4-11)
3	120	24	10	(6.1–14)
4	82	24	10	(6.1–14)
5	41	24	10	(6.1–14)
Displaced femo	ral neck	fracture (n = 23	30)	· /
1	192	29	13	(8.5–17)
2	132	44	21	(15-26)
3	94	48	23	(17–29)
4	69	50	25	(19–31)
5	44	51	26	(20–33)

CRR: cumulative reoperation rate.

On hip fractures in adults under the age of 60



Sebastian Strøm Rönnquist, born in 1982, studied medicine at Umeå University and graduated in 2011. After an internship in Copenhagen and receiving his license to practice medicine, he commenced specialist training in orthopedic surgery at Skåne University Hospital Malmö/Lund. As a specialist in orthopedic surgery since 2018, he works clinically in pediatric orthopedics.

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