Clinical results after hip fracture - with special focus on hip arthroplasty

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Abstract

Hip fractures are of major concern worldwide, but even if literature is abundant, there are still gaps to fill. The global outcome needs to be better understood, including patient-reported outcome. Many studies focus on improving surgical outcome, with less focus on medical complications. The true number of adverse events after hip fracture surgery is unknown. Femoral neck fractures (FNFs), constituting half of all hip fractures, are commonly treated with arthroplasty, but evidence on whether to use hemiarthroplasty (HA) or total hip arthroplasty (THA) is unclear.

Paper I is a retrospective cohort study of all patients with hip fracture at our hospital during one year, examining complications and patient-reported outcome. Absence of medical and hip complications correlated to improved satisfaction and pain. Medical complications alone correlated to loss of function. One-third regained pre-fracture mobility and one-third received enough rehabilitation.

Paper II is an observational cohort study comparing two matched groups of patients with THA or HA as treatment for FNF. THA had significantly reduced risk of revision and reoperation, and was associated with reduced mortality.

Papers III and IV are observational cohort studies on patients treated with THA or HA for FNF, with adjustment for comorbidity and socioeconomic background. A majority suffered an adverse event, one-third suffered a medical complication and one-fifth a hip complication. THA was associated with fewer medical complications and lower mortality but more hip complications, even after matching according to comorbidity and socioeconomic variables.

In conclusion, complications are important for outcome and improving the overall care of hip fracture patients is as important as the choice of surgical treatment. THA may perform better than HA in some aspects in selected patients, but an unbiased comparison between the two types of arthroplasties is difficult to achieve.

Key words
hip fracture, femoral neck fracture, arthroplasty, complications, adverse events, PROM, rehabilitation

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Det till synes omöjliga är möjligt.

- Hans Rosling

Contents

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List of papers

This thesis is based on the following papers, in the text referred to by their Roman numerals.

I. **Complications and patient-reported outcome after hip fracture - A consecutive annual cohort study of 664 patients.**
Susanne Hansson, Ola Rolfson, Kristina Åkesson, Szilard Nemes, Olof Leonardsson, Cecilia Rogmark.
Injury. 2015 Nov;46(11):2206-11.

II. **Reduced risk of reoperation after treatment of femoral neck fractures with total hip arthroplasty: A matched pair analysis.**
Susanne Hansson, Szilard Nemes, Johan Kärrholm, Cecilia Rogmark.
Acta Orthopaedica. 2017;88(5):500–4.

III. **Adverse events are common after hip fracture arthroplasty. A national study of 34 441 patients.**
Susanne Hansson, Szilard Nemes, Kristina Åkesson, Johan Kärrholm, Cecilia Rogmark. *In manuscript.*

IV. **More hip complications after total hip arthroplasty than after hemiarthroplasty as primary hip fracture treatment. Analysis of 5 815 matched pairs in the Swedish Hip Arthroplasty Register**.
Susanne Hansson, Erik Bülow, Anne Garland, Johan Kärrholm, Cecilia Rogmark. *In manuscript.*

Abbreviations

AE	Adverse event
ASA	American Society of Anesthesiologists
BMI	Body mass index
CCI	Charlson comorbidity index
FNF	Femoral neck fracture
HA	Hemiarthroplasty
ICD-10	International Statistical Classification of Diseases and Related Health Problems -Tenth Revision
IF	Internal fixation
NPR	National Patient Register
PIN	Personal identity number
RCT	Randomized controlled trial
SHAR	Swedish Hip Arthroplasty Register
THA	Total hip arthroplasty
VAS	Visual analogue scale

Populärvetenskaplig sammanfattning

Höftfrakturer är ett stort problem för människor över hela världen. Ändå vet vi inte tillräckligt om hur det går för de patienter som fått en höftfraktur, särskilt inte vad patienterna själva tycker. Många studier har fokuserat på att studera det kirurgiska resultatet och mindre vikt har lagts vid att granska medicinska komplikationer, t ex lunginflammation eller hjärtinfarkt, som kan drabba patienterna efter operationen. Den verkliga förekomsten av komplikationer efter en höftfrakturoperation är inte tillräckligt väl studerad.

Det finns flera olika typer av höftfrakturer, där brott på lårbenshalsen (eng. femoral neck fracture, FNF) utgör hälften. FNF behandlas oftast med någon form av konstgjord höftled (höftprotes). Detta eftersom blodcirkulationen till lårbenshuvudet ofta skadas av frakturen vilket hindrar skelettet från att läka när frakturen bara fixeras med spikar eller skruvar. Höftprotesen kan vara en halvprotes (eng. hemiarthroplasty, HA), där endast lårbenshalsen och lårbenshuvudet tas bort och byts ut mot en metallstam och -kula, eller en totalprotes (eng. total hip arthroplasty, THA) där även en skål (cup) sätts in i ledskålen i bäckenet, mot vilken proteshuvudet ledar. Fördelen med HA är att de har ett större huvud än THA och därför inte hoppar ur led lika lätt (luxation). Operationstiden är också kortare och innebär mindre blodförlust än för THA. Däremot ledar huvudet på HA direkt mot patientens egen ledskål vilken riskerar att slitas ner, ett potentiellt smärtsamt tillstånd som kallas erosion. THA har i vissa studier visats ge bättre rörlighet och gångförmåga (funktion) än HA och patienterna som fått THA har varit mer nöjda, medan andra studier inte har visat någon skillnad.

Det råder oenighet bland ortopeder, både i Sverige och internationellt, om vilken höftprotes som är ”bäst”, eftersom för- och nackdelarna är svåra att väga mot varandra. Däremot är man relativt ense om att THA huvudsakligen ska användas till friskare och aktiva äldre med felställd FNF, medan HA är förstahandsval till de som är sjukliga och mycket gamla. Hur vital personen är avgör alltså valet av höftprotes.

Denna avhandling baseras på fyra studier. I första studien studerades patienter som genomgått operation för höftfraktur, oavsett typ, i Malmö under ett år. Från journalerna samlades information in om medicinska

komplikationer inom 6 månader efter operationen och höftkomplikationer (t.ex. infektioner eller luxationer) inom det första året. En enkät skickades ut till patienterna ett år efter operationen för att få information om patienternas upplevelse av resultatet. I genomsnitt rapporterade patienterna att de var nöjda med resultatet efter ett år, men att de fortfarande hade måttlig smärta i höften. Bara en tredjedel ansåg att de hade fått tillräcklig rehabilitering och bara en tredjedel uppgav att de hade återfått den funktion de hade före höftfrakturen, trots att sjukvården har som mål att samtliga patienter med höftfraktur ska återfå sin tidigare funktion. Risken att ha kvarstående smärta efter ett år och att vara mindre nöjd med operationsresultatet var större hos de patienter som drabbats av någon form av komplikation. Endast förekomsten av medicinska komplikationer, inte ålder eller hur svår frakturen var, var kopplat till sämre funktion efter ett år.

I de tre övriga studierna hämtades information från Svenska Höftprotesregistret (SHPR), ett nationellt register som samlar in information om de höftproteser som opereras in i Sverige. 97 % av alla höftproteser som sätts in p.g.a. höftfraktur fångas upp av registret. I studie III och IV samkördes informationen i SHPR med Patientregistret och Statistiska centralbyrån (SCB). Genom att leta efter specifika diagnoskoder och åtgärdskoder i Patientregistret kunde vi få en mera heltäckande bild av hur vanliga komplikationer efter höftprotesoperation var. Från SCB hämtade vi information om inkomst, utbildning och civilstånd för att kunna göra en bättre jämförelse av patienterna, eftersom det är känt att skillnad i socioekonomiska faktorer kan påverka resultatet efter operation.

I studie II-IV jämfördes THA och HA enligt olika modeller. Patienterna med THA hade lägre risk för omoperation och medicinska komplikationer men högre risk för höftkomplikationer. THA-patienterna hade även lägre dödlighet. Att THA ger högre risk för höftkomplikation kan förklaras av den högre risken för luxation. Patienterna som får HA är oftast äldre och skörare, och trots att vi använt statistiska metoder som tar hänsyn till patientgruppernas olikheter bedömer vi att skillnaden i medicinska komplikationer och risken att dö i förtid beror på att THA-patienterna är mer vitala. Vitalitet (en ungefärlig motsats till det engelska begreppet ”frailty”) är ett mångfacetterat begrepp och är svårt att mäta i ett register med begränsade variabler, men är ofta uppenbart för läkaren som träffar patienten och bedömer vilken typ av protes som är lämpligast för henne eller honom.

Hälften av alla patienter i studie III hade drabbats av någon form av komplikation. En tredjedel drabbades av en medicinsk komplikation och en femtedel av höftkomplikation. Samma patient kunde drabbas av flera

komplikationer. De vanligaste medicinska komplikationerna var hjärt-kärlsjukdom, lunginflammation och urinvägsinfektion. De vanligaste höftkomplikationerna var fraktur på lårbenet, infektion i höften och luxation.

Sammanfattningsvis verkar THA fungera bättre än HA som behandling för höftfraktur, men en rättvisande jämförelse av proteserna är svår att åstadkomma. Vi har inte funnit några övertygande bevis för att så många fler personer med höftfraktur ska opereras med THA i framtiden. HA verkar fungera bra när man ser till den något lägre risken för höftkomplikationer. Att drabbas av en komplikation i efterförloppet efter höftfraktur spelar stor roll för resultatet. Därför är det minst lika viktigt att förbättra det generella omhändertagandet av patienter med höftfraktur som att optimera valet av behandlingsmetod.

Introduction

Hip fractures, also termed proximal femoral fractures, are of major concern for all populations worldwide. In 1990, the estimated incidence of hip fractures globally was 1.6 million[43] and is predicted to rise to 6.3 million by the year 2050[15]. In Sweden, approximately 17 000 individuals each year suffer a hip fracture[37] and the number is expected to increase to 30 000 in 2050[76]. Hip fractures most often occur in frail elderly people after low-energy trauma, e.g. falling from standing[16]. Three out of four hip fractures occur in women, due to lower bone mineral density and longer life-expectancy[72]. Not only is hip fracture a common injury among older people, it is also much feared. When asking women above 75 years of age to choose between death and sustaining a "bad" hip fracture, 80% would rather be dead[78].

Classification

Hip fractures are traditionally classified as intracapsular or extracapsular, due to the blood supply of the femoral head, and the different prerequisites for fracture healing depending on the anatomic region in which the fracture occurs[85] (Figure 1). Most of the intracapsular fractures are femoral neck fractures (FNFs). Because of the anatomy of the blood vessels supplying the femoral head, fractures of the femoral neck risk damaging the blood supply to the head, resulting in healing problems (avascular necrosis or nonunion)[102]. FNFs are further classified as non-displaced or displaced, as the degree of displacement influences the healing potential and thereby decides how the fracture should be treated[45]. In Sweden 2017, 13% of all hip fractures were non-displaced FNF and 40% displaced FNF[37]. But the younger the patient, the more fractures are non-displaced[91].

Trochanteric (or intertrochanteric) and subtrochanteric fractures are classified as extracapsular. Trochanteric fractures are located at the well-vascularized metaphyseal bone between the greater and lesser trochanters. These fractures do not normally affect the blood supply of the proximal femur and are not associated with the same healing problems as FNFs[102]. Subtrochanteric fractures are located within 5 cm distal to the lesser trochanter[85]. Trochanteric fractures constitutes 35% of all hip fractures in Sweden, and subtrochanteric fractures 8%[37].

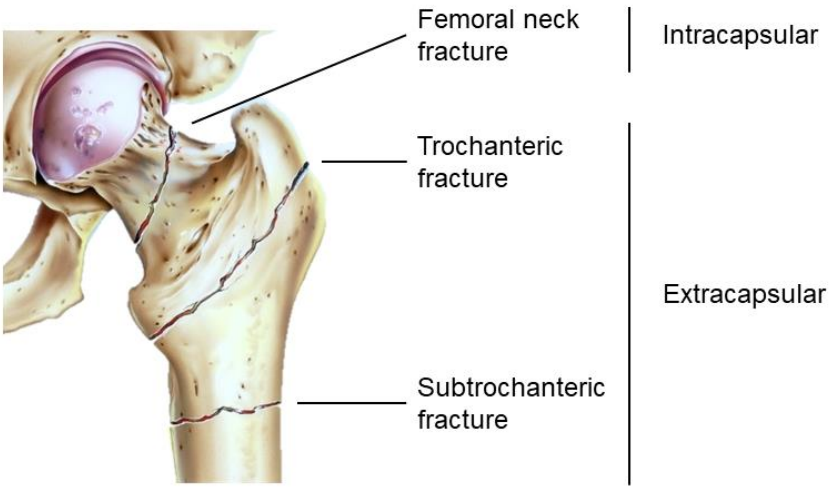

Figure 1.
Classification of hip fractures.

Treatment

FNFs can be treated with either reduction and internal fixation (IF), or arthroplasty. IF consists of two or more pins or screws fixating the fracture. IF is often used for non-displaced fractures in all patients or displaced fractures in young and middle aged individuals[7]. The benefit of IF is that it is a short procedure with minimal blood loss, and the patient's own femoral head is preserved. Displaced FNFs treated with IF have a reoperation rate of 30-50% due to disturbance in blood supply and subsequent healing complications[12,25,42,50]. Instead, the preferred treatment for displaced FNFs in

the elderly is arthroplasty, due to lower reoperation rates and the benefit of a stable hip joint allowing immediate postoperative mobility[25]. Extracapsular fractures are treated with reduction and either sliding hip screw and lateral femoral plate, or intramedullary nailing[66].

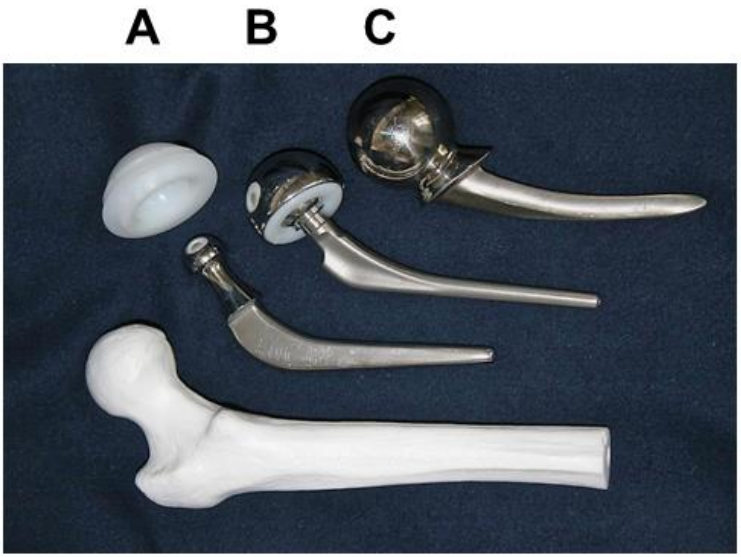

Figure 2.
A:Total hip artroplasty. B: Hemiartroplasty. C: Monoblock prosthesis, no longer used in Sweden and not part of this thesis.

Arthroplasty

In Sweden, during the last 20 years, treatment of FNF has shifted from IF to arthroplasty. Arthroplasty is currently the most common treatment for FNF, being used as primary treatment already in patients in their fifties and older [75,91]. In hip arthroplasty, the patient's femoral head and neck is removed and is replaced with a metal stem inserted in the femoral canal. The fixation of the stem can be with bone cement or uncemented with stems allowing for ingrowth of bone. If only the head and neck of femur is replaced, the arthroplasty is called hemiarthroplasty (HA). If also a cup is inserted in the acetabulum to which the head articulates, it is termed total hip arthroplasty (THA). HA has a

much larger head than THA, reducing the risk of dislocation[74,100]. However, because the head articulates directly against the cartilage, HA may cause acetabular erosion, which in early stages might be a silent condition only diagnosed radiologically. Erosion can also give pain, in particular when walking. HAs can be unipolar with only one large head. Bipolar HAs were developed to reduce the risk of erosion, consisting of a smaller head articulating against a larger mobile head, which in turn articulates against the acetabular cartilage[3,97]. As no clear differences between uni- and bipolar hemiarthroplasties can be shown in the long run[41], this thesis consider modern, modular hemiarthroplasties as one group.

THA results in longer surgery and more intra-operative blood loss than HA[5,8]. Still, pooling of results from randomized controlled trials (RCTs) did not show higher mortality after THA compared to HA[100]. Some randomized studies show THA to result in better function and health-related quality of life[4,47,56] while others found no difference[5,20].

There is a discrepancy in the use of mainly HA or mainly THA in elderly patients with displaced FNF. Even if the UK national guidelines (NICE)[63] say that THA should be offered to patients without cognitive impairment, with ability to walk independently outdoors and who are medically fit for anesthesia and the procedure, the use of THA for FNF varies from 1 to 60% in hospitals in the UK[69].

Other surgical aspects than implant type influences the clinical outcome. Arthroplasties inserted without bone cement are associated with increased risk of periprosthetic fracture compared to cemented ones[74]. Only 2-3% of the fracture arthroplasties in Sweden are cementless[46], and therefore arthroplasties with this type of fixation were excluded from the studies in this thesis. Inserting an arthroplasty via a posterior approach increases the risk of dislocation, compared to the direct lateral approach[74]. In Sweden, approximately one third of the arthroplasties are inserting by posterior approach and two-thirds by lateral approach[46]. Approach is not studied specifically in this thesis.

National registers

Since 1947, all individuals who reside permanently in Sweden will be given a unique personal identity number (PIN)[55], by which the person can be identified in national registers and medical records. Through the use of PIN, the information in several national registers can be cross-matched and each individual identified in all the registers. This gives a great opportunity for researchers to collect data on a large number of individuals and include those individuals normally difficult to include in clinical trials, e.g. elderly patients with cognitive impairment. The Swedish Knee Arthroplasty Register, founded in 1975 by Göran Bauer, was the first national quality register in Sweden. Currently, there are 96 national registers in Sweden with some degree of governmental financial support[90].

Swedish Hip Arthroplasty Register

The Swedish Hip Arthroplasty Register (SHAR), founded in 1979 by Peter Herberts and Gunnar Andersson, registers hip arthroplasty surgeries performed in Sweden, with a coverage of 100% for both public and private hospitals. Procedure-related data (i.e. date of procedure, type of surgery, diagnosis, laterality, hospital, type of implant) is recorded as well as patient-related information (i.e. personal identity number, age, sex, body mass index (BMI), and American Society of Anaesthesiologists (ASA) classification). The completeness of registration of emergency procedures is approximately 97% during the last decade. Reoperations are recorded continuously, revisions as well as any other subsequent open procedure affecting the hip (dislocation, infection, periprosthetic fracture, and other complications). The completeness of revision surgery is 93%. Hemiarthroplasties are recorded in the register since 2005. BMI and ASA are recorded routinely since 2008. Dementia is only recorded for hemiarthroplasties[46].

National Patient Register

The National Patient Register (NPR, in Swedish: Patientregistret) covers all inpatient care, outpatient visits and psychiatric care involving contact with a physician in Sweden from both private and public caregivers, excluding primary care. The register was founded in 1964, since 1987 information from private hospitals is registered, and since 2001 outpatient visits are included. Coverage of inpatient care is almost 100%, while coverage of hospital-based outpatient care is only about 80%, due to missing data from private caregivers. Coverage of outpatient data from public caregivers is 100%. The NPR consists of patient-related data (sex, age, county of residence etc.), data about the caregiver, administrative data about the admission, and medical data about diagnoses. Main diagnosis, secondary diagnosis and external cause of injury are registered through ICD-10 codes (International Statistical Classification of Diseases and Related Health Problems)[99] and procedures are registered through NOMESCO codes (in Swedish: KVÅ-koder)[65]. Main diagnosis is registered in 99% of all hospital discharges[5492].

Statistics Sweden

Statistics Sweden (in Swedish: Statistiska Centralbyrån, SCB) is responsible for developing, producing and distributing official statistics for Sweden. For example, Statistics Sweden contains information on socioeconomic data such as income, education and marital status[89].

Measures of comorbidity

Comorbidity is defined as the patients' total burden of illnesses unrelated to the principal diagnosis[38]. In observational studies, comorbidity may act as a confounder and needs to be adjusted for. Several comorbidity indices have been developed to classify the overall burden of comorbidity. Two of the most commonly used indices are Charlson comorbidity index and Elixhauser comorbidity index, both based on the diagnostic coding system of ICD-9 or ICD-10. The American Society of Anesthesiologists (ASA) classification is designed to assess perioperative risk. ASA classification has subsequently been used as a comorbidity index, although it is not developed as such.

American Society of Anesthesiologists classification

The ASA classification was developed as a tool for classifying physical status of surgical patients[77]. Later, it was expanded to include a sixth category for organ donors (Table 1). It is widely used in clinical practice, simple and easily applied. However, it has a large interobserver variability. Postoperative morbidity and mortality increases with increasing ASA class[83,95].

Charlson comorbidity index

The Charlson comorbidity index (CCI)[13] is the most widely used comorbidity index and has been validated for several surgical procedures. It was developed in 1984 by chart review of 559 patients admitted to a hospital in New York and an index was created by assessing the association of the patients' comorbidities with one-year mortality. The index has been validated in numerous studies. The CCI consists of 19 conditions, each condition given the weight of 1, 2, 3 or 6, depending on the relative risk of one-year mortality. A total score is calculated from the sum of the weighted scores. The index has been updated several times with translation to the ICD-10 system by Deyo in 1992[18] and modification of the weights by Quan in 2011[70](Table 2).

Elixhauser comorbidity index

The Elixhauser comorbidity index[22] was developed in 1998 as an index comprising 30 comorbidities defined by ICD-9 codes from administrative data. It has later been updated for use with ICD-10 codes[71]. In the original version, each comorbidity represents a dichotomous variable without a weighting system. Van Walraven et al.[96] updated the index in 2009 by developing a weighting algorithm, based on the association between comorbidity and death (Table 3).

Comparison of comorbidity indices

ASA score seems to be a better predictor than CCI score for readmission after hip fracture[1]. Both higher ASA score and higher CCI score are proven to be indicators of mortality after hip fracture[87]. When compared with CCI, EI is better in predicting readmissions, in-hospital and 1-year mortality [59,88]. However, both CCI and Elixhauser are poor predictors of postoperative mortality after THA, but Elixhauser seems to be the least bad choice[10].

Tabel 1.
The American Society of Anesthesiologists (ASA) classification

ASA CLASS	PHYSICAL STATUS
ASA 1	A normal healthy patient.
ASA 2	A patient with a mild systemic disease.
ASA 3	A patient with a severe systemic disease that is not life-threatening.
ASA 4	A patient with a severe systemic disease that is a constant threat to life.
ASA 5	A moribund patient who is not expected to survive without the operation.
ASA 6	A brain-dead patient whose organs are being removed for donation.

Tabel 2.
The Charlson comorbidity index including modification by Quan

COMORBIDITY	CHARLSON/DEYO	QUAN
Myocardial infarction	1	0
Congestive heart failure	1	2
Peripheral vascular disease	1	0
Cerebrovascular disease	1	0
Dementia	1	2
Chronic pulmonary disease	1	1
Rheumatologic disease	1	1
Peptic ulcer disease	1	0
Mild liver disease	1	2
Diabetes without chronic complications	1	0
Diabetes with chronic complications	2	1
Hemiplegia or paraplegia	2	2
Renal disease	2	1
Any malignancy, including leukemia and lymphoma	2	2
Moderate or severe liver disease	3	4
Metastatic solid tumor	6	6
AIDS/HIV	6	4
Maximum comorbidity score	**29**	**24**

Tabel 3.
The Elixhauser comorbidity index according to van Walraven

COMORBIDITY	POINTS
Drug abuse	-7
Obesity	-4
Depression	-3
Blood loss/anaemia	-2
Deficiency/anaemia	-2
Valvular heart disease	-1
Alcohol abuse	0
Diabetes complicated	0
Diabetes uncomplicated	0
HIV/AIDS	0
Hypertension	0
Hypothyroidism	0
Peptic ulcer disease (excluding bleeding)	0
Psychosis	0
Rheumatoid disorders	0
Peripheral vascular disease	2
Chronic pulmonary disease	3
Coagulopathy	3
Pulmonary circulation disorders	4
Solid tumour without metastasis	4
Cardiac arrhythmias	5
Fluid and electrolyte disorders	5
Renal failure	5
Neurodegenerative disorders	6
Weight loss	6
Congestive heart failure	7
Paralysis	7
Lymphoma	9
Liver disease	11
Metastatic cancer	12

Frailty

Chronological age is an exact measure and has a strong association with mortality and adverse events. But even for patients of the same chronological age, a substantial difference in comorbidity and overall health status may exist, often referred to as difference in biological age. The term frailty has been introduced to describe and quantity this difference. Frailty describes a multifaceted syndrome of loss of energy, physical ability, cognition, and health. To be able account for frailty in clinical and scientific practise, several frailty indices have been developed, but no gold standard exist[67,82]. A higher frailty index is associated with higher mortality after femoral neck fracture. Between age and frailty, there was only a weak correlation [67]. Retrieving information on frailty from registries is difficult due to the complex nature of the condition, consisting of characteristics difficult to quantify and record.

Measures of clinical outcome

Patient-reported outcome measures

Traditionally, the outcomes studied after hip fracture have been mortality, radiological appearance and surgical outcome. Nowadays, patient-reported outcome measures (PROMs) are regarded as more or less mandatory, to also capture the patient's perspective of the result after hip fracture. PROMs can be generic, often named health-related quality-of-life instruments (EQ-5D or SF-36) [23,98] or organ/disease-specific. For hip patients, Harris Hip Score (HHS), Hip Disability and Osteoarthritis Outcome Score (HOOS) and Oxford Hip Score (OHS) are the most commonly used[64].

In paper 1, we used EQ-5D 3L[24,23] to assess the patients' health-related quality of life after hip fracture. EQ-5D is a standardized instrument consisting of five questions evaluating different dimensions of health (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and a visual analogue scale (EQ VAS). In EQ-5D 3L, each dimension has three levels ("no problems", "some problems", and "extreme problems"). With EQ VAS, patients are asked to rate their health on a vertical scale, ranging from "best imaginable health state" to "worst imaginable health state". In paper I, we instead used two VAS to evaluate pain and satisfaction after hip fracture, as in the routine PROM follow-up of osteoarthritis patients in SHAR[46]. At the point of study design, EQ VAS was not used in the SHAR.

Pre-intervention patient-reported outcome is relatively easily collected in patients undergoing elective surgery, in contrast to those who suffer a fracture. In emergency patients, the technique of recall pre-fracture PROM may lead to some uncertainty, as well as the fact that many suffer from impaired cognitive function and need a proxy to answer the questions[49].

Reoperation and revision

In SHAR, reoperation after arthroplasty is defined as any kind of subsequent open surgical procedure related to the inserted arthroplasty, no matter if the arthroplasty, or any of its parts, is replaced, extracted or left untouched. Revision after arthroplasty is defined as a subsequent procedure where at least one part of the prosthesis is exchanged, added or extracted. All revisions are also classified as reoperations, but not all reoperations are revisions[46]. Other national hip fracture and arthroplasty register may however use more or less different definitions.

Adverse events

An adverse event (AE) is defined as an unintended injury or complication resulting in temporary or permanent disability, death or prolonged hospital stay, and is caused by healthcare management rather than by the natural disease process[9]. AE is a wider term including both medical complications and hip complications as well as mortality. Although the rates of AEs often are used as quality indicators after surgery, no consensus exist in what defines AEs and how long the follow-up period should be[19,35]. There is also no consensus on the best way of reporting AEs[19,93].

Conditions considered as medical complications are usually acute or newly diagnosed diseases affecting the patient in the postoperative period. Aggravation of an existing chronic disease also ought to be regarded. Medical complications are for example cardiac complications, thromboembolic events, pulmonary disease or urinary tract infections. Surgical complications after hip fracture are complications affecting the operated hip, i.e. dislocations, periprosthetic fractures and surgical site infections.

A consensus meeting with orthopedic surgeons, trauma surgeons and geriatricians suggested medical complications after hip fracture to be measured at discharge from the hospital, and at 30-days after admission. The follow-up for surgical complications is suggested to occur at time of discharge, 30 days and one year after the admission for hip fracture[51]. SHAR reports on adverse

events within 90 days after surgery[46] and the follow-up period of medical complications varies extensively in different studies, ranging from the period of in-hospital stay[48], 30 days[80], 4 months[21] to 6 months[57] after surgery.

Mortality

Mortality is a common and important outcome measure after hip fracture surgery. Compared to an aged-matched population, individuals suffering osteoporotic fractures of the hip, shoulder or spine have increased mortality[51]. One-year mortality for hip fracture patients also differs between studies, but is usually around 20%[61] and is significantly higher than in a matched control population[31,33,44]. To some degree, the excess mortality is caused by the fracture itself, but comorbidities and frailty associated with fracture risk explain most of the risk. Time frame for mortality differs between studies and most commonly varies between in-hospital mortality, 30 days and one year. Comparison of in-hospital mortality between studies is difficult as lengths of stay differs substantially between different health care models[51]. Some studies show decreasing mortality rates for hip fracture patients[27,68], while another found no change in mortality during thirteen years[40]. Simultaneously, the prevalence of comorbidities is increasing while mortality is declining or at least remains unchanged, suggesting an improvement in the overall care of hip fracture patients.

Aim of this thesis

The overall aim was to examine treatment of hip fractures, with focus on femoral neck fractures treated with arthroplasty, to be able to give clinical recommendations on the optimal treatment for these patients.

Specific aims, papers I-IV

I. To examine which surgical and patient-related factors influence complication rates and patient-reported outcome after hip fracture surgery, including the effect of a fast-track system for hip fractures, and also explore the patients' perception on rehabilitation and return of function.

II. To examine the difference in outcome between THA and HA as treatment for femoral neck fracture, with focus on reoperations, revisions and mortality.

III. To assess the number of adverse events after hip fracture arthroplasty, with emphasis on medical complications, and examine if there was an association between adverse events and type of arthroplasty.

IV. To examine the difference in outcome between THA and HA as treatment for femoral neck fracture, with focus on adverse events, including both medical and hip complications as well as mortality.

Patients and methods

A majority of the studies in this thesis (study II-IV) are register-based, whereas the first study (study I) is based on a cohort of patients treated at Skåne University Hospital in Malmö. Studies II-IV include patients with femoral neck fracture treated with hip arthroplasty, while study I includes patients with any kind of hip fracture, regardless of surgical treatment.

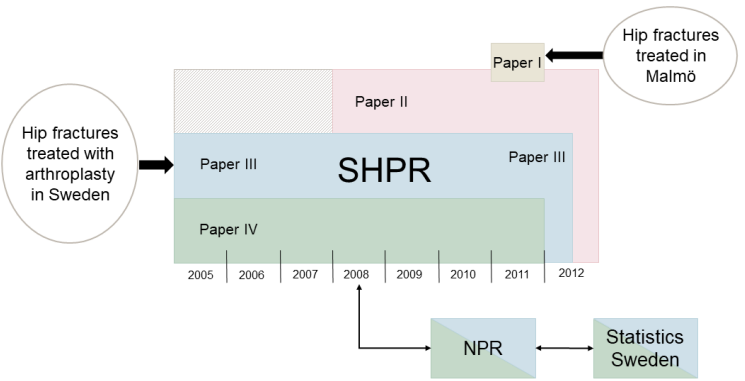

Figure 3.
Timeline of papers I-IV.

Paper I

Paper I is a retrospective cohort study of all patients above 20 years having surgery for acute hip fracture at Skåne University Hospital in Malmö in the year 2011. Pathologic fractures (except osteoporotic fractures) and patients living outside of the catchment area of the hospital were excluded. In patients with more than one hip fracture within this year, only the first fracture was included. 664 patients were included in the study. To facilitate the statistical

calculations, some variables describing patient or fracture characteristics were grouped. Patients with impaired mobility, diagnosed with dementia or receiving daily assistance were classified as nonautonomous. Dislocated FNFs treated with internal fixation, unstable trochanteric fractures and subtrochanteric fractures were classified as severe fractures.

From the medical records, information was gathered on the patients' pre-fracture conditions (place of residence, dependency in activities of daily living, walking ability, cognitive impairment and previous hip fracture) and information about the hip fracture treatment (type of fracture, surgical details, length of stay and whether the patient entered the hospital through the fast-track system). Medical records were scrutinized for general complications within six months after the hip fracture surgery, and for local complications within one year (Table 7). A questionnaire was sent by post to all patients still alive after one year, comprising questions on health-related quality of life (EQ-5D), visual analogue scales (VAS) for pain and satisfaction and multiple-choice questions regarding mobility and rehabilitation (Appendix 1).

Paper II

Paper II is a register-based observational study collecting data from SHAR on patients treated with hip arthroplasty after acute femoral neck fracture during 2008-2012. BMI and ASA classification was not recorded routinely in SHAR until 2008 and this time frame was chosen in order to be able to match the patients according to BMI and ASA classification. Uncemented arthroplasties are uncommon in Sweden as treatment for hip fracture and only constituted 2% of the surgeries in the dataset, and was therefore excluded. For patients with more than one hip fracture treated with arthroplasty during the study period, only the first surgery was included. Moribund patients (ASA 5 or those who died during surgery) were also excluded. This resulted in 11 253 patients (Figure 4). The outcomes studied were revisions, reoperations and mortality.

Since patients treated with HA generally are older and have more comorbidities than patients treated with THA, a comparison of the patients straight off will be misleading. In order to create two comparable groups, propensity score matching was used. All patients with THA was matched with an equal number of HA patients with type of arthroplasty as outcome and age, sex, ASA classification, and BMI as independent variables. This resulted in two groups with 2 902 patients in each. 114 patients, all treated with THA, were not able to match.

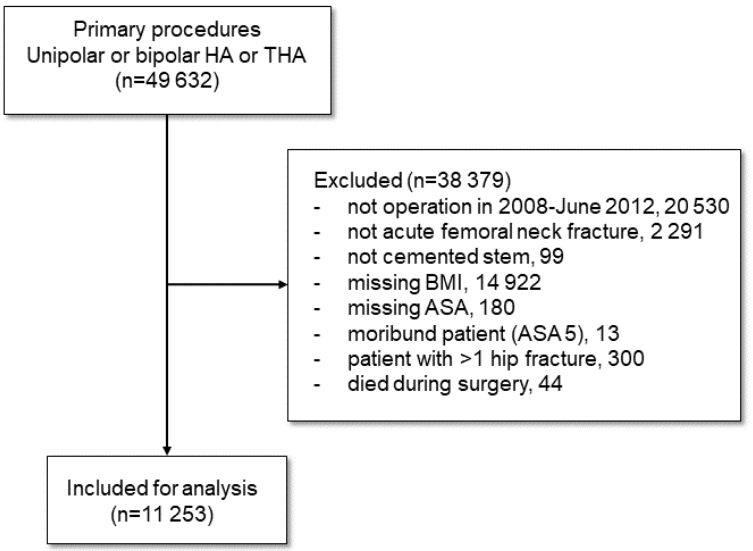

Figure 4.
Flowchart of included and excluded patients in Paper II.

Paper III

Papers III and IV are based on the same dataset of patients, containing cross-matched data from SHAR, NPR, and Statistics Sweden. Each patient was identified in all the registers through their unique personal identity number given to all Swedish residents. The dataset contained patients having surgery with hip fracture arthroplasty during 1999-2012. Patients treated with THA or HA for acute hip fracture during 1 January 2005 to 30 June 2012 were included. This time frame was chosen to enable a follow-up of six months after surgery. Hemiarthroplasties are recorded in SHAR routinely since 2005, why studies on earlier years will not be relevant. Uncemented procedures were excluded, as well as the second surgery in patients treated with more than one hip arthroplasty during the study period.

From NPR, information was gathered on ICD-10 codes and NOMESCO codes representing medical complications within 180 days after hip fracture surgery, or hip complications within the study period (Appendix 2). From the

ICD-10 codes, Elixhauser comorbidity index was generated. From Statistics Sweden, information on marital status, education and income was gathered, as these may be potential confounders. 34 441 patients were included in the study (Figure 5).

The outcomes studied were mortality, adverse events in general, and medical complications and hip complications specifically. Outcome was compared between THA and HA to examine if there was a difference in adverse events depending on type of arthroplasty.

The outcomes studied were the incidence of any adverse event, medical complications, hip complications and death for all patients. The outcome was also compared to see if there was a difference depending on type of arthroplasty.

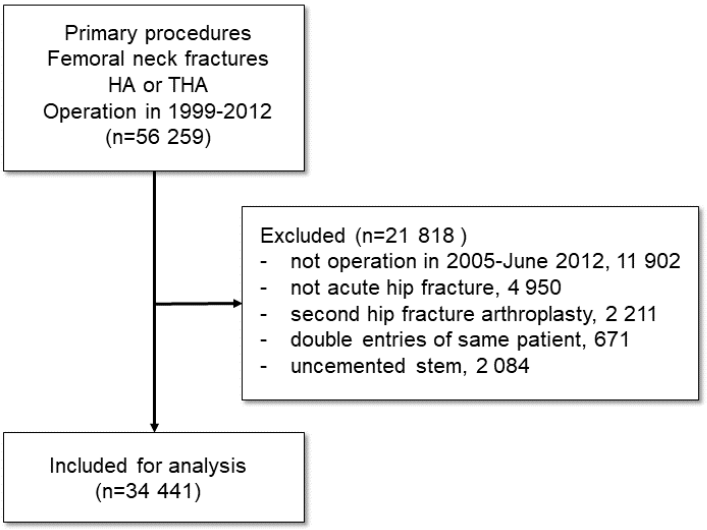

Figure 5.
Flowchart of included and excluded patients in Paper III.

Paper IV

In paper IV, the same dataset as in paper III was used, with cross-matched data from SHAR, NPR and Statistics Swede. To enable a follow-up period of at least one year, only patients with surgery between 2005 and 2011 was included. Due to difficulty in matching, patients below 60 years or above 95 years of age were excluded. A total of 30 953 patients treated with cemented THA or HA were included (Figure 6).

To enable better comparison of the two diverse groups of patients treated with THA and HA, the patients were matched by propensity score matching with type of arthroplasty as outcome and age, sex, income, education, marital status and Elixhauser index as independent variables. This generated two groups with 5 815 patients in each group. The outcomes studied were medical complications within 180 days, hip complications within the study period and death within one year.

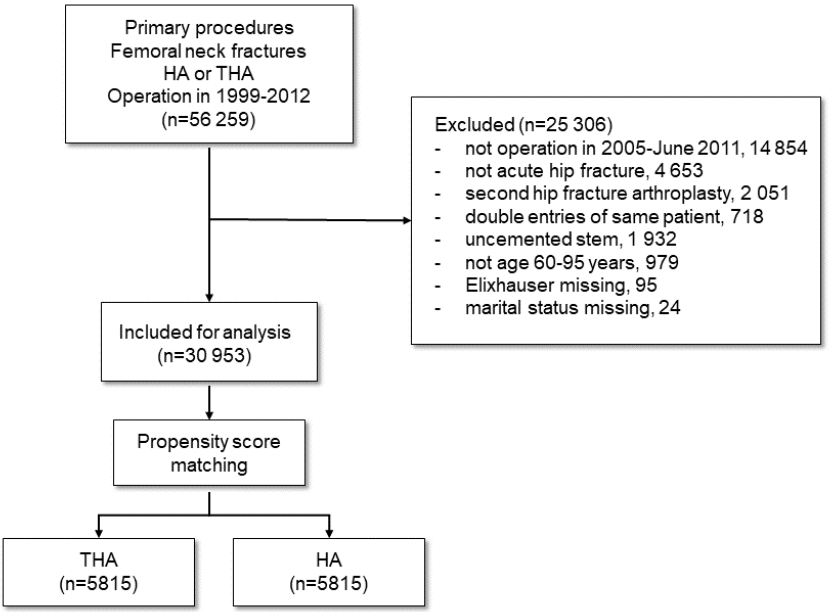

Figure 6.
Flowchart of included and excluded patients in Paper IV.

Statistics

Statistical calculations were performed using IBM SPSS Statistics and R. In papers II and IV, the studies were designed together with statisticians working at SHAR, and the statistical calculations were performed by statisticians. In papers I and III, the statisticians acted as advisors during the process of the study.

The frequency of complications and death in paper I and III are reported as absolute numbers and percentages. The mean values of EQ-5D-index and VAS values for pain and satisfaction in paper I are compared with t-test. Continuous outcome variables in paper I are compared with linear regression. Logistic regression models were used in paper I, III and IV to analyze ordinal outcome variables and enable adjustment for potential confounders. In paper I, the model included the variables age, sex, severe fracture, autonomy, dementia, fast-track system, surgery within 24 hours, general complications and local complications. In paper III, the model included type of arthroplasty, age, sex, level of education, marital status and Elixhauser comorbidity index. In paper IV, the model included type of arthroplasty, age, sex, income, education, marital status, Elixhauser index and year of surgery.

In paper II, patient demographics and survival times were compared with t-test for continuous data and chi-square test for categorical data. Kaplan-Meier curves were generated to compare the outcomes studied. Competing risks survival regression was used to calculate the absolute risk of the outcomes studied. In papers II and IV, propensity score matching was used to be able to compare the patients treated with THA and HA. In paper II, the matching was performed based on age, sex, BMI, and ASA classification. In paper IV, more covariates were available through the cross-matching with other registers. The matching was based on age, sex, education, income, marital status, and Elixhauser comorbidity index.

Ethical considerations

Study I was approved by the Regional Ethical Review Board in Lund (ref. 2012/213). Studies II, III and IV were approved by the Regional Ethical Review Board in Gothenburg (ref. 024-15 and 271-14).

Data from SHAR was collected without any contact between the study subjects and the researcher. All data from SHAR, NPR and Statistics Sweden was presented to the researcher without information of name or personal identity number of the participants. The patients included in SHAR are informed in writing before registration. Participation is optional and all patients are free to be withdrawn from the register at any time.

Results

Patient-reported outcome and fast-track system (Paper I)

76% (384 of 503) of the patients still alive one year after hip fracture surgery answered the postal questionnaire. Mean EQ-5D-index was 0.47 (SD 0.38), mean VAS for pain was 24 (SD 22) and mean VAS for satisfaction was 28 (25). 111 patients (29%) reported to have regained their previous function in the injured hip and 114 (30%) reported to have received enough rehabilitation.

Female patients, nonautonomous patients, patients with dementia and patients suffering a medical complication reported significantly lower mean values on EQ-5D-index. General and local complications were correlated with less satisfaction. Suffering general or local complications or having a severe fracture was correlated with higher pain score. Dementia was correlated with lower pain score. General complications correlated with loss of function and older age correlated with inadequate rehabilitation (Table 5).

441 patients (66%) were included in the fast-track system, 163 (25%) were excluded correctly, usually due to serious illness or head trauma. 60 patients (9%) never entered the fast-track system. The only significant effect of the fast-track system was reduced waiting-time to surgery. 78% (342 of 441) of the patients included in the fast-track system had surgery within 24 hours, compared to 62% (138 of 223) among the others ($p < 0.001$). No difference was found in length of hospital stay or incidence of complications between the patients included in the fast-track system and those not included.

Table 5.
Patient characteristics correlated to satisfaction and pain VAS by linear regression and to function and rehabilitation by proportional odds model.

PROM	OUTCOME	β/OR[a]	(95% CI)[b]
Satisfaction (VAS)	General complications	10.061	(2.968-17.154)
	Local complications	15.005	(5.581-24.430)
Pain (VAS)	General complications	9.521	(3.336-15.707)
	Local complications	8.863	(0.6444-17.081)
	Severe fracture	6.346	(1.565-11.127)
	Dementia	-7.950	(-15.876 --0.0250)
Loss of function	General complications	2.129	(1.064-4.613)
Inadequate rehabilitation	Age	1.022	(1.001-1.043)

[a] β-coefficient for continuous variabels, Odds Ratio for categorical variabels
[b] CI = Confidence Interval

Revision and reoperation with mortality as competing risk (Paper II)

When comparing the unmatched group of patients, THA performed better than HA in terms of revision and reoperation and was associated with lower mortality. There was no association between age, sex, ASA classification or BMI and risk of reoperation or revision (Table 6).

The same results were found when the analyses were repeated on the matched data. THA had a lower risk of revision (absolute risk reduction 0.51; 95% CI 0.37–0.71) and reoperation (0.63; 0.48–0.84) and was associated with lower mortality when death was a competing risk for revision (0.59; 0.54–0.65) and reoperation (0.58; 0.53–0.64).

Table 6.
Risk of revision and reoperation with death as competing risk, unmatched patients.
Absolute risk reduction (95% CI).

	REVISION		DEATH		REOPERATION		DEATH	
THA	0.51	(0.37-0.71)	0.59	(0.54-0.65)	0.63	(0.48-0.84)	0.58	(0.53-0.64)
Age	0.97	(0.95-0.98)	1.03	(1.02-1.03)	0.97	(0.96-0.99)	1.03	(1.02-1.03)
Female	0.81	(0.65-1.02)	0.69	(0.66-0.72)	0.82	(0.67-1.01)	0.69	(0.66-0.73)
ASA 2	0.93	(0.54-1.60)	1.7	(1.3-2.2)	1.2	(0.73-2.0)	1.7	(1.3-2.2)
ASA 3	1.01	(0.58-1.8)	2.6	(2.0-3.3)	1.3	(0.79-2.2)	2.5	(1.99-3.2)
ASA 4	0.99	(0.50-2.0)	3.5	(2.7-4.5)	1.2	(0.66-2.3)	3.5	(2.7-4.5)
BMI	1.01	(0.98-1.04)	0.96	(0.95-0.96)	1.02	(1.0-1.05)	0.96	(0.95-0.96)

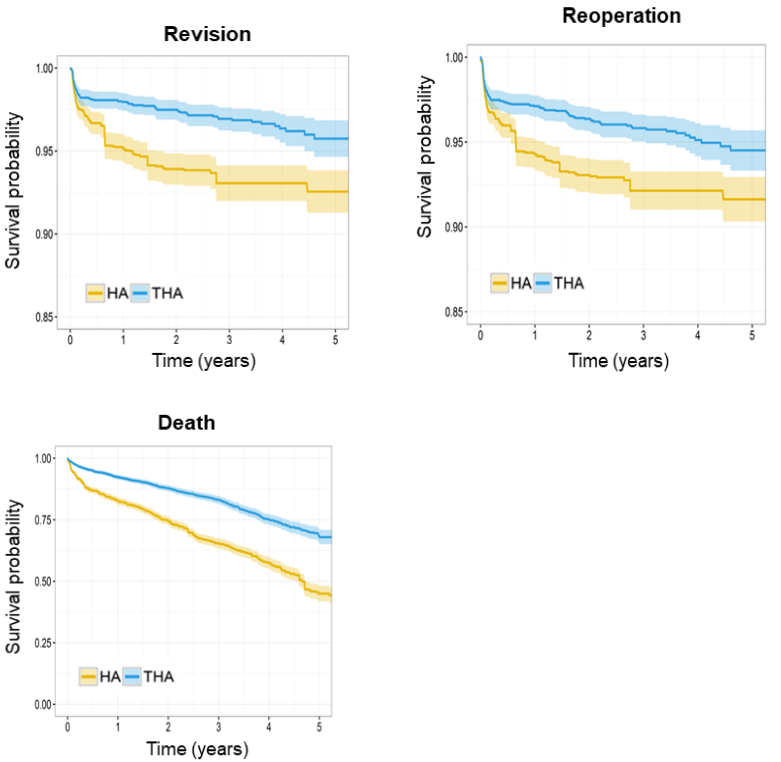

Figure 7.
Kaplan-Meier survival curves (± 95% confidence interval) with revision, reoperation and death as end-point.

Adverse events including mortality (Papers I, III and IV)

The most common general complications within six months after hip fracture surgery in paper I were additional fall, pneumonia, and additional fracture. The one-year mortality was 24%. The most common local complications within one year after surgery were wound infection, deep infection, and nonunion. The reoperation rate was 7% (Table 7).

Paper III showed that 53% (n=18 208) of the patients treated with hip fracture arthroplasty suffered an adverse event within 180 days after surgery. 32% (n=11 034) suffered a medical complication within 180 days and 21% (n=7 047) suffered a hip complication within the study period. Mortality within 180 days was 17% (n=5 823) for all patients, 6% (n=384) for THA and 20% (n=5 439) for HA. The most common medical complications were cardiovascular, pneumonia and urinary tract infection (Table 8). 7.9% of the patients had been registered with a diagnostic code representing fracture surgery on femur at any time post-operatively. 5.3% had suffered an infection in the hip, and the dislocation rate was 5.3% (Table 9). Dislocations were more common among the THA patients. There was no clear difference in the distribution of complications between the two patient groups.

In paper III the patients with THA and HA were unmatched. When compared with logistic regression and adjusted for potential confounders, THA was associated with fewer medical complication within 6 months post-surgery but with more hip complications. THA was also associated with lower mortality. The odds of suffering any adverse event (any medical or hip complication or death) was lower for the THA patients (Table 10).

Paper IV showed similar results as paper III when the THA and HA patients were matched with propensity score matching and compared through logistic regression. Also in this study, THA was associated with fewer medical complications and more hip complications. In this study, one-year mortality was examined. THA was associated with lower mortality than HA (Table 10).

Table 7.
Frequency of general complications and local complications in Paper I.

GENERAL COMPLICATIONS	N	(%)	LOCAL COMPLICATIONS	N	(%)
Additional fall	97	(15)	Wound infection	27	(4)
Additional fracture	76	(11)	Deep infection	14	(2)
Pneumonia	41	(6)	Nonunion	13	(2)
Dementia (diagnosed post-fracture)	24	(4)	Periprosthetic fracture	5	(1)
Myocardial infarction	13	(2)	Dislocation	3	(0.5)
Stroke	11	(2)	Other hip related complications (e.g. persistent pain, avascular necrosis)	37	(6)
Pulmonary embolism	12	(2)			
Deep vein thrombosis	8	(1)			
Death (within 1 year)	161	(24)	Reoperation	47	(7)

Table 8.
Frequency of medical complications in paper III, n (%).

	ALL		THA		HA	
Cardiovascular	7 016	(20)	848	(13)	6 168	(22)
Pneumonia	2 098	(6)	215	(3)	1 883	(9)
Urinary tract infection	1 925	(6)	225	(3)	1 700	(6)
Cerebrovascular	1 165	(3)	156	(2)	1 009	(4)
Thromboembolic	888	(3)	221	(3)	667	(2)
Urinary retention	692	(2)	97	(2)	595	(2)
Renal failure	406	(1)	52	(1)	353	(1)
Stomach ulcer	367	(1)	64	(1)	303	(1)
Pressure wound	372	(1)	53	(1)	319	(1)

Table 9.
Frequency of hip complications in paper III, n (%).

	ALL		THA		HA	
Fracture surgery on femur	2 734	(8)	545	(8)	2 189	(8)
Infection	1 822	(5)	410	(6)	1 412	(5)
Dislocation	1 826	(5)	539	(8)	1 287	(5)
Problems with wound healing	833	(2)	204	(3)	629	(2)
Any reoperation	1 739	(5)	336	(5)	1 403	(5)

Table 10.
Odds ratio for THA patients suffering an adverse event 6 months post-surgery compared to HA patients. Odds ratio (95% confidence interval).

	PAPER III	PAPER IV
Medical complication	0.79 (0.72-0.85)	0.83 (0.76-0.91)
Hip complication	1.41 (1.29-1.53)	1.31 (1.20-1.43)
Any medical and/or hip complication	1.00 (0.92-1.07)	
Mortality[a]	0.44 (0.38-0.50)	0.42 (0.38-0.48)
Any adverse event incl. death	0.84 (0.78-0.90)	

[a] Death within six months in paper III, within one year in paper IV

Discussion

Many studies have been published on improving the outcome after hip fracture, both in general aspects and regarding surgical technique. When studying different implants, two discords are ongoing: Between intra- and extramedullary implants in extracapsular fractures, and between total and hemiarthroplasties in displaced femoral neck fractures. This thesis focus on clinical outcome in general, and on the comparison of THA and HA in particular.

For displaced FNF, the best choice of surgical treatment is still not known. Most studies are too small and only include a selection of the hip fracture population, often excluding the oldest patients and those with cognitive impairment. The strength of register-based studies is the large study population, and that patients of all ages, health statuses and cognitive function can be included. However, the observational design carries the problem of not being able to control for all confounding factors. RCTs eliminate this problem, but has the limitation of smaller sample sizes and the inability to include all kinds of patients, thus limiting their generalizability.

Patient-reported outcome and function

Paper I focused on general outcome and examined factors influencing patient-reported outcome one year after hip fracture surgery. The main finding was that the occurrence of medical complications or hip complications affected the outcome. Both medical and hip complications were associated with worse outcome in terms of both pain and satisfaction one year after the fracture. Suffering a medical complication was the only factor associated with not regaining pre-fracture function. No association was found between age, having a severe fracture or dementia and loss of function. Hence, this study was not able to answer the questions of what patients to pay special attention to when admitted with hip fracture, but rather emphasized the need of optimizing the post-operative care to reduce the risk of complications. A model known to successfully reduce the rate of complications, improve function and lower

mortality after hip fracture is the use of an orthogeriatric care models[29,30,58]. One clinical perspective on the results found in paper I is the need for a continued collaboration between orthopedic surgeons and geriatricians. The thought-provoking finding that "only" medical complications were associated with functional decline reminds us to design future studies properly, with meticulous reporting of adverse events.

Guidelines state that for every patient with hip fracture, the goal is for the patient to regain the same function as before the injury. But even though this is written in the journal of every hip fracture patient in our clinic, less than one-third of the patients in paper I had reached this goal. Previous studies have found rates of functional recovery varying from thirty-five percent[17], similar to our findings, to more encouraging numbers of seventy-four to eighty percent[2,86]. Less than one-third of the patients in paper I considered the rehabilitation provided to be sufficient. Although we did not study the association between insufficient rehabilitation and loss of function, it is likely to assume that one exists. This is also supported in a previous study, where patients with hip fracture who received rehabilitation within three months after discharge had improved functional outcome[2]. Hence, more efforts need to be put in optimizing rehabilitation after hip fracture.

Studying the mean values of VAS for pain and satisfaction, we found that the hip fracture patients on average had moderate pain in their hip one year after the injury, but also reported that they were satisfied with the result of the surgery, implying that patients with hip fracture will not automatically complain if complications arise. The health care should be careful in assuming that patients with hip fracture will give alert when all is not well, but rather have other methods for finding these patients.

Reoperation and revision

In paper II, the risk of revision and reoperation for THA and HA was examined. THA performed better than HA in terms of both revision and reoperation. In contrast, the Dutch national arthroplasty register (LROI) reported, based on revisions reported to LROI, a higher revision rate after THA[60]. The result may be biased by more posterior approach, uncemented stems, and younger, healthier patients in the THA group. In addition, HAs performed by trauma surgeons were not included. The authors concluded that revision rates for both HA and THA were "considerable".

A third suggestion came from a study based on an administrative database in England, that there was no difference in revision rates between THA and

HA, but found significantly higher rates of dislocation for THA[39]. They used procedure codes for closed reduction of dislocations in theatre, whereas in our study, data on dislocations were not available. An RCT with seven to ten years follow-up showed a revision rate of 2.5% for THA, in contrast to 20% for HA, mainly illustrating the role of patient selection. This study comprised only healthy and active individuals, and reported a very high rate of acetabulum erosion[3]. A recent meta-analysis found ten RCTs reporting on revision surgery, and a slightly lower revision rate after THA. The pooled revision rate was 8.3% after HA and 5.3% after THA[100].

A difference in frailty may still exist between THA and HA patients, even though the patients in paper II were matched in an attempt to eliminate such differences. The abstract concept of frailty cannot be defined by register data, but will be apparent to the surgeon assessing the patient preoperatively, and influence the choice of arthroplasty. In fact, a short visual estimation may be enough for health care staff to accurately predict a patients frailty and risk of future fractures and death[26]. The higher risk of revision and reoperation after treatment with HA could be explained by this selection bias, as frail patients are more likely to suffer deep infections and periprosthetic fractures.

The reasons for revision and reoperation was not studied specifically in paper II. There are several reasons for subjecting a patient with arthroplasty to reoperation or revision, some more pressing than others. Whether or not the patient is considered fit enough for a subsequent surgery will also influence the decision. Except for moribund patients, a periprosthetic fracture distal to the trochanter major will most certainly imply major surgical treatment. Since HA patients generally are more frail than THA patients, they are more likely to suffer periprosthetic fractures, explaining some of the difference in reoperation and revision rates between the arthroplasties. A fulminant deep infection of a hip treated with arthroplasty will in the majority of patients entail a reoperation according to the ”DAIR” concept (debridement, antibiotics, irrigation, retention) and in some cases a revision exchanging parts of the prosthesis. Although, in the most frail elderly patients with infections able to suppress with lifelong antibiotics, this might be the preferred treatment instead of exposing the patient for a strenuous surgical procedure. Thus, in these cases, frailty will imply less risk of secondary surgery.

Although the risk of dislocation is higher for THA, a hemiarthroplasty with frequent dislocations is easier to convert to a total hip arthroplasty by inserting an acetabular cup than to revise a THA with more or less well-positioned implant parts. Non-ambulatory patients with a THA with frequent dislocations may simply be left untreated with a permanently dislocated prosthesis. A less

potential reason for the higher revision rates of HA is acetabular erosion, which does not exist in THA. This is not a common complication with the current patient selection[46]. Revision can also be performed due to aseptic loosening, which ought to apply for both THA and HA. Finally, complication rates are higher for surgeons with a lower annual volume of arthroplasties[53,73,84]. One can assume that HAs more often are performed by less experienced surgeons, this could also be part of the explanation for higher revision and reoperation rates in HA.

Medical complications and adverse events in general

As frailty is not only defined by age and comorbidity but, depending on definition, also by socioeconomic factors and psychological health, the information available in SHAR will not give the full picture. To be able to make a better comparison of the THA and HA patients, comorbidity and socioeconomic factors were included as confounding factors in the analyses in papers III and IV.

In paper III, we examined the incidence of adverse events, especially medical complications, within six months after hip fracture arthroplasty. We found that adverse events were common, fifty-three percent of the patients were affected. Thirty-two percent of the patients suffered a medical complication; cardiovascular events, pneumonia and urinary tract infection being most common. In paper I, the most common medical complication was additional fall, followed by pneumonia and additional fracture. The difference in distribution of medical complications is most likely not due to a difference in study population, but rather in the different methods of data collection in the studies. The design of paper I permitted us to gather AEs from the running text in medical record, whereas paper II was based on ICD-10 and NOMESCO codes. Thus, the event of a fall will not be traceable by the collection of ICD codes.

Other studies have found complication rates after hip fracture of twenty[32,81] to fifty percent[21,34,57]. We found an incidence of cardiac complications of twenty percent, similar to another Swedish study which reported fifteen percent cardiac complications [21], but much higher than other studies reporting only one to two percent cardiac complications [32,79]. The definition of cardiac complications and the length of the follow-up differed considerably between the studies, probably explaining most of the differences.

Retrieving information on complications through retrospective record review is a sensitive but time-consuming process[14,62,94]. Collecting information

on complication rates through a large register-based study by the use of diagnostic codes enables examination of a much larger study population, but with the risk of including too many or two few events, depending on the selected codes. Today, there is no consensus on what diagnoses to classify as adverse events after surgery, although incidence of adverse events often is used as a quality indicator for many caregivers. These differences in defining and collecting information on adverse events which exist between studies, make the comparison of our results with previous studies difficult.

Since the surgery of THA is longer and entails more blood loss than HA[5,8], it is likely to assume that THA would be associated with more medical complications than HA. In paper III, the outcome of medical complications was compared between THA and HA, with adjustment for potential confounders (i. e. age and sex, comorbidity, and socioeconomic factors). In paper IV a similar comparison was made, but the THA and HA patients were matched based on these confounding variables. Most likely, the implant itself does not affect the risk of medical complications. The lower risk of medical complications for THA rather implies that despite adjusting for confounding factors and matching the patients in order to create comparable groups, a difference in frailty between the patients still exist. This residual confounding is difficult to control in studies based on registers alone. However, since THA was not associated with more medical complications than HA, the procedure does not seem to be so strenuous as to affect the risk of medical complications.

Hip complications

In paper III, we also aimed to examine the incidence of hip complications after hip fracture surgery through the use of diagnostic codes. We found that twenty-one percent of the patients in our material had suffered a hip complication. In paper I, we found a rate of hip complications of fifteen percent when using the method of record review. However, the total number of complications was not examined specifically but rather the frequency of every single complication. Therefore, the number is an approximate. Previous studies report varying rates of hip complications after hip fracture, differing between five[8] and thirteen percent[6]. The reported rate will differ due to type of fracture, the patients included and due to the definition of hip complications used.

To distinguish what kind of hip complication the diagnostic codes represented was more difficult than classifying the medical complications. A large number of NOMESCO codes exists, and many different codes can be chosen for the same kind of procedure by different surgeons. In paper III, we

found eight percent of the patients to be diagnosed with any code that represents fracture surgery on femur after the initial hip fracture surgery. Since laterality is not registered in NPR, it is not possible to distinguish if the fracture was located to the same side as the hip fracture or to the opposite leg. However, the patient suffering the complication would probably be just as troubled no matter what leg was involved, and may suffer adversely of having an additional fracture in any circumstance. In paper I, only one percent of the patients suffered a periprosthetic fracture. Since the information was collected by record review, laterality was not an issue, but the follow-up period was only one year. Hence, the results are not comparable between the papers. In paper I, we found a frequency of infection in the hip, both wound infection and deep infection, of six percent, comparable to paper III, in which five percent was diagnosed with infection.

The dislocation rate in paper I was only one-half percent, while we in paper III found dislocation in five percent of the patients. The difference in dislocation rate between the studies is most likely due to the use of different approaches. In study I, direct lateral approach was used; in the other studies, posterior approach was used in half of the patients. Posterior approach carries a higher risk of dislocation[74]. To some extent, the different lengths of follow-up play a role. During the first years of study III, femoral heads with a diameter of 28 mm dominated in Sweden, but were gradually replaced with 32 and 36 mm heads. Since larger head sizes are associated with lower risk of dislocation[11], this might also be part of the explanation. Neither of the studies contained information on head size.

In papers III and IV, the association between hip complications and type of arthroplasty was also examined. THA was found to be associated with more hip complications than HA, even after adjusting for potential confounders (paper III and IV) and after matching of the patients (paper IV). The higher risk of hip complications with THA may be due to a higher risk of dislocation. A previous meta-analysis comparing THA with HA, found THA to be associated with more hip complications[100]. However, only dislocation and infection was studied. This study did not find any difference in risk of infection. Other studies have not found a difference in hip complications between THA and HA[4,36], possibly due to smaller studies. Since our studies included a large number of patients and a wide range of codes representing hip complications, the risk of missing any adverse events after hip fracture is reduced.

Mortality

The one-year mortality rate in paper I was twenty-four percent, which is in line with other studies[28,61]. Since THA is a more strenuous procedure than THA, it is reasonable to assume THA to be associated with higher mortality than HA. In papers II, III and IV, mortality was compared between THA and HA, and in all the studies THA was associated with lower mortality. Possibly, the explanation for this is the same kind of selection bias as discussed for medical complications, namely that there still exists a difference in comorbidity or frailty between the patients, which we were not able to control for completely. Since THA is recommended for active and healthy patients, the lack of information on pre-fracture functional level may add to the residual confounding. However, our results impliy that THA is not strenuous enough to entail higher mortality. Most likely, the choice of THA or HA per se will not affect the mortality after hip fracture surgery.

Limitations

This thesis contains two kind of studies - one local retrospective cohort study, and three national observational studies with and without cross-matching to other registers. The main limitation for both types is the risk of residual confounding, as addressed above. Another limitation is that primary care is not included in NPR, from where the information on ICD- and NOMESCO-codes was gathered. This will imply a risk of underestimating complications, but ought not to affect the comparison between HA and THA, as undetected adverse events are assumed to be distributed similarly between the groups. Codes from administrative registers are relatively blunt tools as discussed above. In addition, ICD-10 codes are also used for economical purposes, leading to so called DRG creep, when codes are chosen strategically to get a higher reimbursement[101].

The strength of paper II and III is the large population, covering nearly all hip fracture arthroplasties in Sweden during the study periods, thus reflecting the results of standard-of-care in a Western-world country. Paper I may have lesser external validity, as it is based on one hospital only. Further limitations are the lack of PROMs in Paper II-IV, and the risk of underreporting of reoperations to SHAR. In particular, infection-related reoperations and periprosthetic fracture surgeries are shown to be underreported[46,52]. On the other hand, completeness of revision surgery in SHAR is satisfactory. By the addition of information from NPR in paper III and IV, we aimed to overcome this limitation.

Conclusions

- Avoiding complications, medical as well as hip-related, are important to improve patient-reported outcome after hip fracture. Medical complications alone affect the functional outcome after one year.
- A majority of patients with hip fracture do not receive enough rehabilitation, and only one-third reach the goal of regaining pre-fracture function.
- The only advantage of a fast-track for hip fractures possible to measure seems to be shorter waiting-time to surgery.
- THA has a lower risk of revision and reoperation compared to HA as treatment for femoral neck fractures.
- THA is associated with lower mortality compared to HA.
- Adverse events are common after hip fracture, affecting half of the patients. One-third suffer a medical complication and one in five a hip complication.
- THA is associated with less medical complications but more hip complications than HA.

Clinical perspective

Even though THA seems to perform better than HA in some aspects, an unbiased comparison between the two types of arthroplasties is difficult to achieve. Since complications play such an important role for patient-reported outcome, improving the overall care of hip fracture patients is at least equally important as the choice of surgical treatment.

This thesis, based on national data, shows that THA as treatment for hip fracture is associated with both fewer reoperations and more hip complications, when compared to HA. The contradictory nature of our findings may be explained by different thresholds to perform a reoperation in the event of a complication. The degree of patient frailty inherent in the choice of implant, will influence both the risk of some complications, and the surgeon's readiness to perform secondary surgery. Some technical features, such as THA head size, might tilt our results. Still, we consider hip complications a better endpoint than reoperations or revisions, given that not all complications lead to secondary surgery. Thereby, this thesis questions an uncritical increase in the use of THA in elderly hip fracture patients. The higher risk of hip complications may overshadow the aim to gain the functional benefits of THA shown in some, but not all, randomized trials on the topic.

In addition, also shown in this thesis, only one-third of the patient actually received what they deemed as enough rehabilitation. Thereby, these theoretical functional benefits of THA may not be achieved in reality. Organizational issues, such as access to qualified surgeons outside of office hours, and health care cost, must also be considered. Since complications play such an important role for patient-reported outcome, as shown in the thesis, improving the overall care of hip fracture patients is at least equally important as the choice of surgical treatment.

Future research

Hip fracture research stands at a cross road, where we can choose to continue to do comparative studies on implants with more or less similar design, or accept that most modern and established implants are “good enough”, and therefore focus on other issues. A parallel transition has taken place in the field of elective arthroplasty surgery, where focus has shifted from implant survival to risk factors for inferior outcome in other, more holistic aspects.

If we continue to compare implants, where we already know the differences to be small, power calculations will tell us to include thousands of individuals in clinical trials. The alternative - observational studies based on, for example, national registers - is somewhat easier to conduct, but limited by residual confounding. As several steps of the care pathway for hip fracture patients still are suboptimal, it may be a signal to us that other research and quality improvement efforts are more pressing.

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Appendix

Appendix 1.

Questionnaire sent to patients in Paper I one year after hip fracture surgery. Translated from Swedish.

Mark your answer to the questions below by placing a tick in one of the boxes (like this ☒):

Do you have symptoms from **the other** hip? ☐ Yes ☐ No

Do you have **another** condition impairing your ability to walk?
(e.g. pain from other joints, back pain, angina) ☐ Yes ☐ No

By placing a tick in one box in each group below (like this ☒), please indicate which statements best describe your own **health state** today (not only concerning the injured hip).

Mobility
I have no problems in walking about ☐
I have some problems in walking about ☐
I am confined to bed ☐

Self-care
I have no problems with self-care ☐
I have some problems washing or dressing myself ☐
I am unable to wash or dress myself ☐

Usual activities *(e.g. work, study, housework, family or leisure activities)*
I have no problems with performing my usual activities ☐
I have some problems with performing my usual activities ☐
I am unable to perform my usual activities ☐

Pain/discomfort
I have no pain or discomfort ☐
I have moderate pain or discomfort ☐
I have extreme pain or discomfort ☐

Anxiety/depression
I am not anxious or depressed ☐
I am moderately anxious or depressed ☐
I am extremely anxious or depressed ☐

Pain: Place **a cross** on the line which you think represent your average perception of pain from the injured hip during the last month:

No pain — Worst possible pain

mild — moderate — intolerable

Satisfaction: Place **a cross** on the line which you think represent how satisfied you are with the result of the surgery:

Very satisfied — Unsatisfied

very satisfied — satisfied — moderate — doubtful — unsatisfied

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(only mark one box per question)

Compared to **before** the injury, my mobility and walking ability today is:

- Better ☐
- The same ☐
- A little worse ☐
- Much worse ☐

I have received help with rehabilitation after the injury:

- Yes, enough ☐
- Yes, but in a limited amount ☐
- No, not enough rehabilitation ☐
- No, no rehabilitation at all ☐

Who answered the questions?

- I have answered the questions personally (some practical assistance is acceptable) ☐
- A relative/health professional has answered the question according to their knowledge of me ☐

Appendix 2.

Categorization of ICD-10 and NOMESCO codes representing medical and hip complications within 180 days after surgery.

CATEGORY OF COMPLICATION	ICD-10 AND NOMESCO CODES
Medical complications	
Cardiovascular	I11.x-I13.x, I20.x-I24.x, I25.3, I25.4, I25.6, I30.x-I33.x, I38.9, I39.8, I40.x-I41.x, I44.x-I50.x, I51.1-I51.4, I51.6-I51.9, I52.x, I70.2-I70.9, I71.0, I71.1, I71.3, I71.5, I71.8, I72.x, I73.9x, I77.0-I77.2, I77.6-I77.9, I79.x, I97.8, I97.9, I98.1, I98.8, I99.9, J81.9, T81.0, T81.1, T81.7
Pneumonia	J12.x-J22.x
Urinary tract infection	N30.0, N30.9, N39.0
Cerebrovascular	I60.x-I66.x, I67.6, I67.8, I67.9, I68.1-I68.8, I81.9, I82.0-I82.3
Thromboembolic	I26.x, I28.x, I80.x, I82.8, I82.9, I87.0
Urinary retention	R33.9
Renal failure	I12.0, I13.x, N17.x, N99.0
Stomach ulcer	K25.x, K26.x, K27.x, K29.8, K29.9
Pressure ulcer	L89.x
Hip complications	
Fracture surgery femur	M966F, NFJx
Infection	M00.0, M00.0F, M00.1, M00.2, M00.2F, M00.8, M00.8F, M00.9, M00.9F, M86.0F, M86.1F, M86.6, M86.6F, NFSx, T81.4, T84.5, T84.5F, T84.5X, T84.7, TNF05, TNF10
Dislocation	M24.3-4, M24.4F, NFH0-NFH30, NFH4x, NFH7-9, S73.0, T93.3
Any reoperation	NFA00-22, NFA31-32, NFCx, NFF01-12, NFF22, NFF32, NFF92, NFL09-19, NFL39-49, NFL69-99, NFM09-29, NFM49, NFM79-99, NFTx, NFWx
Girdlestone, arthrodesis	NFG09-49, NFG99, NFQ09
Extraction of prothesis or implant	NFUx
Other hip complication	M24.0, M24.5-6, M25.6, T84.0, T84.0F, T84.0X, T84.3, T84.4, T84.8, T88.8
Problems with wound healing	QDBx, QDE35, QDG30, T81.3
Other surgical complication	G57.0, G57.2-4, G57.8-9, M96.8-9, S34.2, S74.x, T81.2, T81.5-6, T81.8, T81.8W, T81.9, T88.9