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# TREATMENT OF DISPLACED FEMORAL NECK FRACTURES IN THE ELDERLY

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# Treatment of displaced femoral neck fractures in the elderly

THESIS FOR DOCTORAL DEGREE (Ph.D.)

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**To the memory of my beloved father and for my beloved family**

# ABSTRACT

Femoral neck fracture (FNF) in elderly patients is a common cause of suffering and premature death in individuals with osteoporotic bones. This fracture type is more common in women after menopause, and the associated patients are often osteoporotic, which contributes to a higher incidence of fractures. FNFs can be undisplaced or displaced, with the latter representing 70-75% of cases. The treatment of displaced FNF in the elderly is still controversial. Optimizing the treatment for improved outcomes and reducing the need for secondary surgery are mandatory for humanitarian and economic reasons. Various options for the surgical treatment of patients with FNF are available, including internal fixation (IF), hemiarthroplasty (HA) and total hip arthroplasty (THA). Each treatment has its advantages and disadvantages. IF is not controversial for the treatment of undisplaced FNF and represents the method of choice for displaced FNF in young patients (less than 65-70 years old) and the frailest elderly patients who are not medically fit for prosthesis surgery. HA is the most common surgical procedure in elderly patients with low functional demands, whereas THA is the preferred method for healthy, active and lucid elderly patients. HA is still the dominant procedure for the treatment of displaced FNF. In Sweden, 64% of all patients with displaced FNF are treated with HA, 22% are treated with THA and 14% are treated with internal fixation. The most common method of performing prosthesis fixation in elderly patients is with bone cement, although concerns over performing this method in older frail patients with multiple comorbidities have been noted. Bone cement implantation syndrome (BCIS) is more prevalent in cemented stems than uncemented stems in patients with FNF. Severe BCIS has a substantial impact on early and late mortality. Thus, the use of uncemented hydroxyapatite stems for this patient group may be justified. Recent reports on modern hydroxyapatite-coated femoral stems used in FNF patients have shown promising early results. However, a more direct comparison between uncemented and cemented stems is required because recent register data suggest a significant increased risk of reoperation with uncemented stems. The functional outcome and the rate of complications and reoperation after modern HA in patients with displaced FNF in combination with cognitive dysfunction are relatively unknown. This patient group has not been sufficiently analysed, and a few studies have recommended IF for this patient group. Moreover, some studies have reported improved post-operative functional outcomes and a lower rate of complications and

reoperation after cemented HA compared to IF, even in the presence of severe cognitive dysfunction.

The aim of this thesis was to define the optimal treatment for elderly patients with a displaced FNF with respect to their age, functional demands and cognitive function.

**Study I**: This study is a randomized controlled trial (RCT) of 100 patients ≥65 years of age with a displaced FNF, and it was designed to compare THA and IF. Follow-up evaluations were performed at three months and at one, two, four, eleven, and seventeen years. We found a higher Harris hip score and a lower rate of reoperations for patients who were treated with THA.

**Study II**: This study is a RCT of 69 patients aged 65-79 years with a displaced FNF, and it was designed to compare uncemented and cemented stems in patients treated with THA. The patients were followed up at three months and one and two years. Patients who were treated with the uncemented stems showed more complications than patients who were treated with the cemented stems without affecting the functional outcome.

**Study III**: This study is a RCT of 120 patients ≥80 years of age with a displaced FNF, and it was designed to compare THA and HA. The one-year results showed that THA did not present superior outcomes to those of HA.

**Study IV**: This study is a prospective observational cohort study of 160 patients with displaced FNFs, and it was designed to compare the results after HA in 100 patients aged ≥65 years with cognitive dysfunction with that of 60 patients aged ≥80 years without cognitive dysfunction. The patients were followed up at three months and one year. HA in patients with cognitive dysfunction was associated with higher mortality and a higher prevalence of the inability to walk. Patients with cognitive dysfunction who did not receive geriatric rehabilitation had worse patient-reported outcomes and were almost 9-times more likely to be confined to a wheelchair or bedridden.

**The main conclusions of this thesis are as follows:**

- THA is the treatment of choice for a displaced FNF in healthy and lucid elderly patients with good hip function preoperatively.
- Uncemented femoral stems should be avoided in patients older than 65 years with a displaced FNF.
- THA yields no benefits over HA in octa- and nonagenarians treated for a displaced FNF.
- HA is a safe option as a treatment for displaced FNF in patients with dementia or cognitive dysfunction.

# SAMMANFATTNING (SUMMARY IN SWEDISH)

Lårbenshalsfrakturer hos äldre patienter är en vanlig orsak till lidande och för tidig död i en åldrande befolkning med osteoporotiskt ben. Denna fraktur är vanligare hos kvinnor efter klimakteriet och patienterna är ofta osteoporotiska vilket kan bidra till en högre frakturförekomst. Lårbenshalsfrakturer kan vara med eller utan felställning, den förra är vanligast (70-75%). Behandlingen av felställda lårbenshalsfrakturer hos äldre är fortfarande kontroversiell. En optimering av behandlingen i syfte att minska behovet av sekundär kirurgi och erhålla ett bättre slutresultat är nödvändig både ur humanitära och ekonomiska skäl. Olika alternativ för kirurgisk behandling är tillgängliga, d.v.s. intern fixation, halvprotes och total höftprotes. Varje behandling har sina för- och nackdelar.

Intern fixation är okontroversiell vid behandling av icke felställda lårbenshalsfrakturer och är en standard metod för behandling hos unga patienter (under 65-70 år) och hos fragila äldre patienter som inte är medicinskt lämpade för protesoperation. Halvprotes är ett vanligt kirurgiskt ingrepp hos äldre över 80 år med låga funktionella krav, medan den totala höftprotesen är den föredragna metoden för en aktiv och klar patient under 80 år. Behandling med halvprotes är den dominerande proceduren för behandlingen av dessa frakturer. I Sverige behandlas 64% av patienterna med felställda lårbenshalsfrakturer med halvprotes, 22% med total höftprotes och 14% med intern fixation. Bencement är den vanligaste fixationsmetoden av proteskomponenter. Användandet av bencement hos äldre fragila patienter med multipla comorbiditeter innebär en ökad risk för tromboemoboliska komplikationer vilket kan leda till tidig död. Detta kan motivera användandet av ocementerade stammar i denna patientgrupp. Nya rapporter om moderna, hydroxapatitbelagda lårbenstammar som används hos patienter med lårbenshalsfrakturer har visat lovande tidiga resultat. Emellertid har nya registerdata visat en ökad risk för protesnära fraktur och därför krävs en direkt jämförelse mellan ocementerade och cementerade stammar.

Det funktionella utfallet och förekomsten av komplikationer hos patienter med felställda lårbenshalsfrakturer i kombination med kognitiv dysfunktion som behandlas med en modern halvprotes är relativt okänt. Dessa patienter har hög mortalitet efter en höftfraktur och låga funktionella krav samt en låg hälsorelaterad livskvalitet före frakturen jämfört med patienter utan kognitiv dysfunktion. Därför har intern fixation rekommenderats för denna patientgrupp. Å andra sidan finns rapporter vilka beskriver bättre postoperativ gångförmåga och funktionellt resultat efter halvprotes i närvaro av allvarlig kognitiv dysfunktion.

Syftet med denna avhandling var att definiera den optimala behandlingen för äldre patienter med felställd lårbenshalsfraktur med avseende på ålder, funktionella krav och kognitiv funktion.

**Studie I:** Detta är en RCT av 100 patienter ≥ 65 år med felställda lårbenshalsfrakturer som jämför total höftprotes och intern fixation. Uppföljningen utfördes på tre månader och 1, 2, 4, 11 och 17 år. Vi hittade högre Harris hip score och mindre omoperationer för patienter som behandlades med total höftprotes.

**Studie II:** Detta är en RCT av 69 patienter 65-79 år med felställda lårbenshalsfrakturer som jämför ocementerade och cementerade stammar i total höftprotes. Patienterna följdes upp vid 3, 12 och 24 månader. Den ocementerade stammen visade mer komplikationer än cementerad stam utan att påverka funktionella resultaten.

**Studie III:** Detta är en RCT av 120 patienter ≥80 år med felställda lårbenshalsfrakturer som jämför total höftprotes med halvprotes. 1 års resultat visar inget överlägset resultat vid utförande av total höftprotes över halvprotes.

**Studie IV:** Det här är en prospektiv observations kohortstudie av 160 patienter med felställda lårbenshalsfrakturer, jämför halvprotes hos100 patienter ≥ 65 år med kognitiv dysfunktion and hos 60 patienter ≥ 80år utan kognitiv dysfunktion. Patienterna följdes upp vid 3 och 12 månader. Halvprotes hos dementa och/eller patienter med kognitiv dysfunktion associeras med högre mortalitet och högre förekomst att bli icke gångare utan att påverka höftrelaterade komplikationer, reoperationer, hälsorelaterad livskvalitet och höftfunktion. De patienter med kognitiv dysfunktion som inte fick geriatrisk rehabilitering hade sämre patientrapporterade utfall och var nästan 9 gånger mer benägna att vara begränsade till rullstol eller sängliggande.

**De huvudsakliga slutsatserna i denna avhandling är följande:**

• Total höftprotes är den bästa behandlingen för en felställd lårbenshalsfraktur hos friska och kognitivt klara äldre patienter med god höftfunktion innan frakturen.

• Ocementerad stam bör undvikas hos patienter äldre än 65 år med en felställd lårbenshalsfraktur.

• Total höftprotes ger inga fördelar över halvprotes hos äldre äldre patienter behandlades för en felställd lårbenshalsfraktur.

• Halvprotes är ett säkert alternativ för behandling av felställda lårbenshalsfrakturer hos patienter med demens eller kognitiv dysfunktion

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# LIST OF SCIENTIFIC PAPERS

This thesis is based on the four following papers, which are indicated in the text by their Roman numerals (Studies I to IV)

I. Total Hip Replacement Versus Open Reduction and Internal Fixation of Displaced Femoral Neck Fractures: A Randomized Long-Term Follow-up Study.
Chammout G, Mukka S, Carlsson T, Neander G, Stark A, Sköldenberg
J Bone Joint Surg Am. 2012 Nov 7;94(21):1921-8

II. More Complications with Uncemented than Cemented Femoral Stems in Total Hip Replacement for Displaced Femoral Neck Fractures in the Elderly.
Chammout G, Muren O, Laurencikas E, Boden H, Kelly-Pettersson P, Sjöö H, Stark A, Sköldenberg O
Acta Orthop. 2017 April, 88(2):145-151.

III. Hemiarthroplasty Compared to Total Hip Arthroplasty for Displaced Femoral Neck Fractures in the Elderly: A Randomized Controlled Trial.
Chammout G, Kelly-Pettersson P, Hedbeck C-J Boden H, Stark Andre, Mukka S, Sköldenberg O.
Manuscript

IV. Primary Hemiarthroplasty for Displaced Femoral Neck Fractures in Elderly Patients with Cognitive Dysfunction
Chammout G, Kelly-Pettersson P, Hedbeck C-J Boden H, Stark Andre, Mukka S, Sköldenberg O
Manuscript submitted

# CONTENTS

# ABBREVIATIONS

| | |
|---|---|
| ADL | Activities of daily living |
| ASA | American Society of Anesthesiologists |
| BCIS | Bone cement implantation syndrome |
| EQ-5D | EuroQol5-dimension scale |
| EQ-5D index score | Quality of life score generated from the EQ-5D Questionnaire |
| FNF | Femoral neck fracture |
| HHS | Harris Hip Score |
| HRQoL | Health-related quality of life |
| HA | Hemiarthroplasty |
| PRO | Patient report outcome |
| PNRS | Pain numerical rating scale |
| SPMSQ | Short portable mental status questionnaire |
| RCT | Randomized controlled trial |
| THA | Total hip arthroplasty |
| THR | Total hip replacement |

# INTRODUCTION

## HISTORICAL BACKGROUND

Hip fractures affect the upper quarter of the femur and can involve the neck, trochanteric and subtrochanteric regions. Femoral neck fractures (FNFs) constitute approximately 50% of all hip fractures, and approximately 75% of all FNFs are displaced. Sir Astley Cooper (1768-1841) first described FNFs in 1822. Conservative treatment with bed rest or a spica-cast for abduction and internal rotation [1] represented the most common methods for many years. The first osteosynthesis is attributed to the German surgeon Von Langenbeck (1810-1887), who nailed a non-united FNF with a metal silver screw in 1858. However, the patient died because of infection. Loreta reported the first successful attempt of this procedure in 1888. In 1883, the American surgeon Nicholass Senn suggested that all FNFs should be treated surgically, although the proposition was not extensively accepted. Many sporadic attempts with limited success [2] were conducted with open reduction and temporary external or internal fixation until Smith-Petersen introduced the three-flanged nail in 1931 at the beginning of the era of internal fixation. The design was improved by the Swedish surgeon Sven Johansson (1932) and the American H. Heyward Wescott (1934). In 1941, the American Academy of Orthopedic Surgeons (AAOS) advocated the trifin nail technique for internal fixation. However, in 1976, the British Medical Research Council indicated that the trifin nail was not suitable for displaced FNFs. Asnis cannulated screws were developed in 1980, and they are still in use today.

In Sweden, Sven Johansson was the first person to improve the surgical technique for FNFs when he designed and used a nail to stabilize the fracture in 1932. In 1964, Nils Rydell at Sahlgrenska University Hospital designed a new spring-loaded nail with four flanges to prevent slipping after surgery. The Rydell nail predominated until Lars Ingvar Hansson introduced the hook pin, later called the Hansson pin, in 1982. In 1980, another orthopaedic surgeon named Sven Olerud invented the Olmed screw, which is currently the most used screw for FNFs in Sweden.

Despite the improvement in osteosynthesis, healing complication rates have been high; therefore, primary hip arthroplasty has been considered an alternative treatment. Endoprosthetic replacement has been used since the 1940s (Moore 1943). Originally only hemiarthroplasty (HA) was performed, although total hip arthroplasty (THA) was subsequently introduced as a primary treatment.

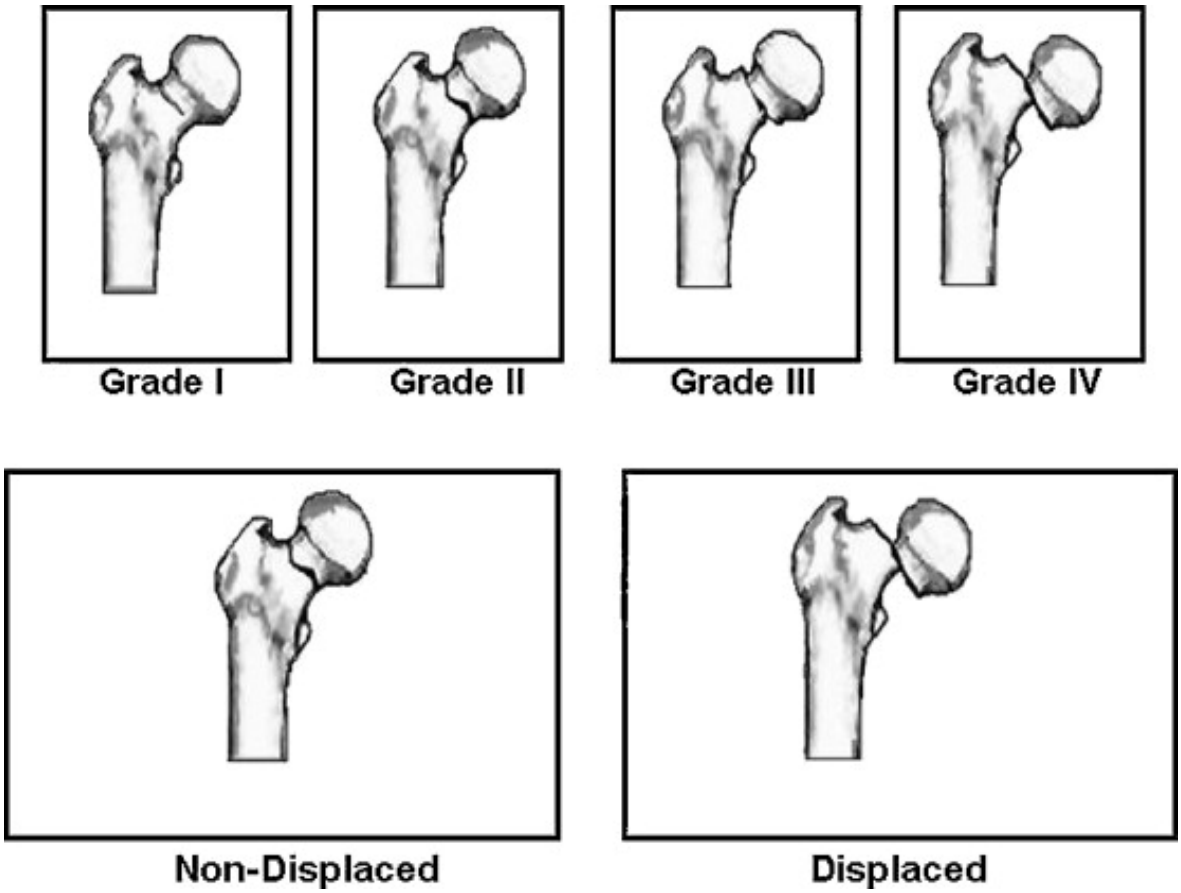
## EPIDEMIOLOGY

The estimated number of hip fractures worldwide is expected to rise to 1.7 million by 2025 and to 6.2 million by 2050 [3, 4]. The incidence of hip fractures is variable in different regions of the world. Scandinavian countries and the U.S. have been categorized as having a very high risk based on ten-year probabilities, whereas countries such as Turkey, Korea, Venezuela and Chile have been categorized a low-risk countries [5]. Improved osteoporosis prevention, healthier elderly populations, increased body mass index (BMI), improved functional ability and several fall preventive measures may have contributed to the decrease in the age-adjusted incidence of hip fractures [6-9]. The increase in the number of hip fractures despite the decrease in age-adjusted incidence is related to a growing ageing population worldwide, especially in the West. FNF in elderly patients is a common cause of suffering and premature death in individuals with osteoporotic bones. This type of fracture is more common in women after menopause, who are often osteoporotic, which contributes to a higher incidence of fractures. The mean age of hip fracture patients is approximately 80 years, and an exponential increase in incidence is observed with age [10, 11]. The incidence of hip fractures in Sweden is 18000 annually, which is expected to increase to 30,000 in 2050 as predicted by Rosengren et al. [12]. Sweden has one of the highest incidences of hip fractures worldwide [13], with 22 (men) and 34 (women) annual cases per 1000 persons aged 80 years and over as measured for 2013 [14]. The lifetime risk of hip fracture in Sweden is 11% for men and 20% for women [11]. Patients with hip fracture present a doubled risk of death during the first year compared with age-matched controls [15]. Risk factors associated with higher mortality are the American Society of Anesthesiologists (ASA) score, cognitive dysfunction and male gender [16, 17]. In particular, patients with a severe or incapacitating disease (ASA 3 – 4) combined with severe cognitive impairment (short portable mental status questionnaire (SPMSQ) 0 –2) have a higher mortality rate [17]. Other factors, such as a prolonged waiting time for surgery and a short length of stay in the hospital, have been suggested as risk factors [18-20]

## CLASSIFICATION

Although several classification systems are available for FNFs, none has been shown to be practical or have satisfactory and accurate predictive value. The first biomechanical classification was Pauwels' classification (1935), which is still frequently used in the literature and calculates the angle between the fracture line of the distal fragment and the horizontal line to determine the shearing stress and compressive force. Investigations of the reliability of Pauwels' classification [21, 22] have shown low interobserver agreement, thus demonstrating the unreliability of this classification. The AO (Arbeitsgemeinschaft für Osteosynthesefragen) classification has been difficult to use in practice and has shown low intraobserver and interobserver reliability [23]. The most commonly used classification method is likely that of Garden (1961), which consists of four groups and utilizes the degree of displacement or impaction as a discriminator. The Garden and AO classifications are more reliable than Pauwels' classification [24]. However, the reliability of the four-grade Garden classification shows poor reliability because of the difficult radiological distinction between different grades, especially I and II, and limited clinical relevance in terms of predicting the likelihood of mal-unions or avascular necrosis [25-32]. Several authors have recommended a simplified classification that divides FNFs into non-displaced and displaced fractures [28-32]. The reliability of the Garden classification improves when only the term non-displaced or displaced FNF is used [33]. Figure 1 shows the Garden classification.

Figure 1: Classification of femoral neck fracture according to Garden




**TREATMENT OF FEMORAL NECK FRACTURE**

The femoral head acquires its blood supply from three sources: (1) intramedullary vessels in the femoral neck, (2) ascending cervical vessels in the capsular retinaculum, and (3) round ligament vessels. The intramedullary supply is always interrupted by the fracture, and retinaculum vessels may also be disrupted if considerable displacement is observed. In elderly people, the remaining supply in the ligamentum teres is at best fairly meagre and non-existent in certain patients. Hence, a high incidence of avascular necrosis is observed in displaced FNFs. FNFs are, by definition, intracapsular, and they present a poor capacity for healing because (1) the injury deprives the head of its main supply by disruption of the capsular vessels; (2) intra-articular bone has only a flimsy periosteum and no contact with soft tissues, which could promote callus formation; and (3) synovial fluid prevents clotting of the fracture haematoma. Accurate apposition and impaction of bone fragments with closed or open reduction and internal fixation therefore present increased importance for fracture

healing. Operative treatment is almost mandatory. Displaced FNFs will not unite without internal fixation.

**Non-surgical treatment**

Non-surgical treatment of FNF is rarely performed, although it may be considered in frail or moribund patients for whom the risk of surgical intervention outweighs the benefit.

**Surgical treatment**

The choice of surgical procedure in elderly patients with FNFs is influenced by many elements, i.e., age, grade of fracture displacement, functional demands, cognitive functions, degree of physical fitness and surgeon preference and experience. The surgical procedure differs worldwide but mainly includes internal fixation and hip arthroplasty. Options for internal fixation include multiple screws or pins (2 or 3), and compression screw and a slide plate (Figure 2). Options for hip arthroplasty include HA and THA (Figure 3).

Figure 2: Option for internal fixation (IF)

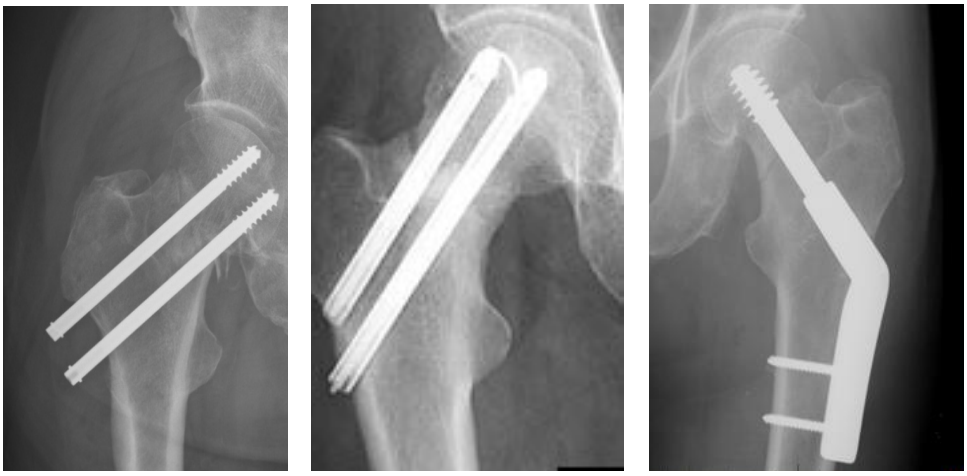
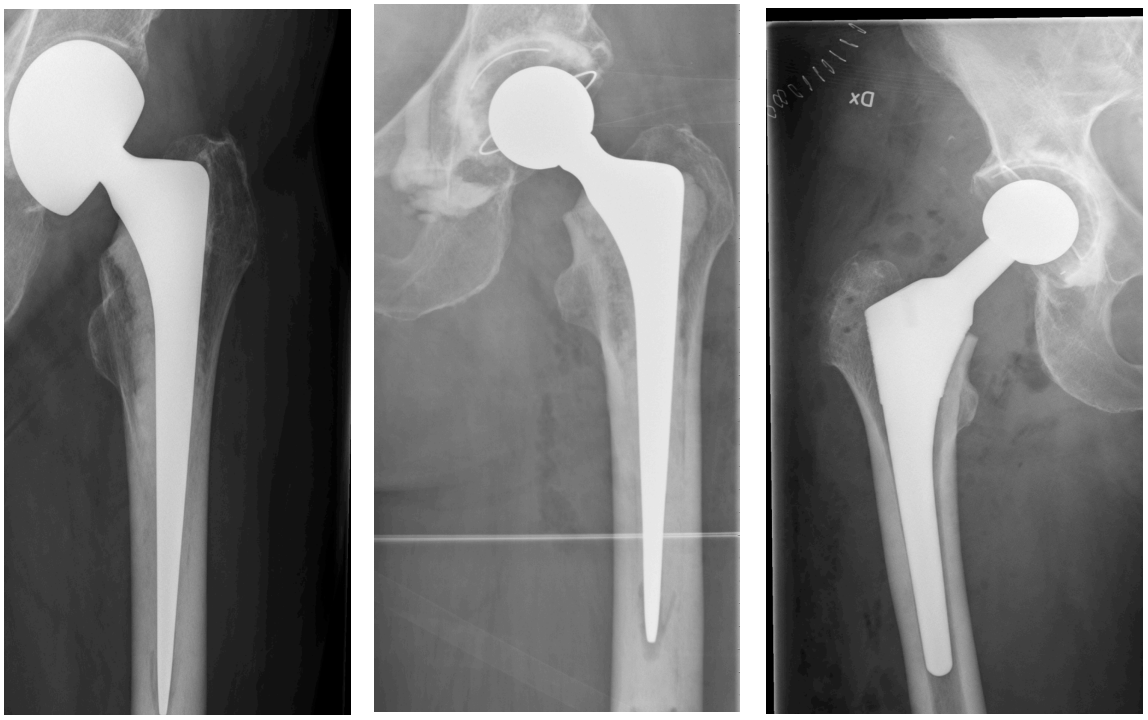


Figure 3: Options for arthroplasty



Cemented HA | THA with a cemented stem | THA with an uncemented stem

***Internal fixation (IF)***

Internal fixation (IF) was the dominant surgical procedure for all types of FNFs in Scandinavia until the beginning of the past decade. In Sweden, 87% of patients with displaced FNF were treated with IF in 1998, although this value decreased to 14% in 2015. IF is still the treatment of choice for undisplaced FNFs (Garden 1 - 2) despite a failure rate of up to 20% [34-39]. Most surgeons advocate IF as the treatment of choice for displaced FNF (Garden grade 3 - 4) in patients younger than 65-70 years of age to preserve the natural femoral head in young patients with high functional demands [40]. The failure rate in this patient group is lower than that in elderly patients [41]. Another cause of the preference for IF in this patient group is a longer life expectancy and a higher risk for revision surgery after arthroplasty. In the frailest elderly patients, IF is often the only possible solution. Avascular necrosis, non-union (pseudoarthrosis) and mechanical failure are the most frequent hip-related complications after a displaced FNF treated with IF. Of the patients treated with IF after a displaced FNF, 30-50% who suffer from these complications often require a reoperation with arthroplasty [42-44]; therefore, the method has been strongly questioned.

### *Hip arthroplasty*

A number of clinical studies with short-, intermediate- and long-term follow-up periods have demonstrated that arthroplasty is the treatment of choice for relatively healthy, active and lucid elderly patients with a displaced FNF compared with IF [42-56]. A significantly lower rate of reoperation for arthroplasty than for IF has been recognized in many randomized controlled trials (RCTs) with follow-up periods longer than 10 years [44, 55, 56]. The pain and functional outcomes of patients who underwent surgery using IF without healing complications was never better than in that of patients who had a successful primary arthroplasty procedure [44]. Arthroplasty as salvage for failed IF has been shown to result in a worse outcome than primary arthroplasty [57]. The optimal surgical procedure in elderly patients with displaced FNF and cognitive dysfunction remain controversial [58-62]. Previous direct comparisons have not identified obvious advantages of performing arthroplasty over IF in this patient group because of the poor results regardless of the surgical procedure [48, 58, 59]. However, studies using modern cemented HA showed good results in this patient population [60, 61]. Two types of arthroplasty have been used for displaced FNF: HA and THA. The implants in hip arthroplasty are fixed to the bone with or without bone cement (polymethyl methacrylate).

### **Hemiarthroplasty**

HA is the most commonly used treatment for displaced FNF and the preferred method in elderly patients with low functional demands [40, 44]. Treatment with HA consists of replacing the femoral head and leaving the acetabulum intact to articulate with a large metal head. There are three different types of HA prostheses: monoblock, modular unipolar and modular bipolar (Figure 4).

The monoblock HA prosthesis is manufactured in one segment; thus, the surgeon is unable to change the length of the neck or the offset. The higher complication rates and poor results have led to change to modular components. Currently, monoblock implants are regarded as outdated [63].

Modular unipolar HA prostheses are manufactured in two segments: the stem and the head. The metal head is solid and constructed to the same size as the measured original femoral head. The modular bipolar HA prosthesis has been developed to decrease the acetabular erosion caused by the friction between a large solid metal head and the acetabulum cartilage of the patient. The prosthesis has an inner spherical metal head that fits into a polyethylene shell, which in turn is enclosed by a metal cap that articulates with the acetabulum. This

design allows for movement not only between the acetabulum and the head but also between the inner head and the shell. The movement between the metal head and the shell theoretically reduces erosion. Many clinical trials have not observed improved surgical outcomes with the use of bipolar implants compared with those for unipolar implants [64-67], although less acetabular erosion has been observed [65, 67]. However, recent studies comparing the types of HA have shown a higher rate of dislocation and risk for reoperation in patients treated with bipolar HA than in those treated with unipolar HA [68, 69]. The use of bipolar HA has been reduced in Sweden as a result of these studies.

Figure 4: Types of hemiarthroplasty

Monoblock HA | Modular unipolar HA | Modular bipolar HA

**Total hip arthroplasty**

In THA, both the femoral head and acetabulum are replaced. THA is the preferred procedure for relatively healthy active and lucid elderly patients with displaced FNF rather than IF [42-56]. However, the type of arthroplasty, HA or THA, is still debated. Is there any advantage to replacing the healthy acetabulum with a prosthetic cup in the healthy, cognitive intact elderly patient? Most surgeons seem to prefer HA for elderly patients with low functional demands in the absence of arthritic changes in the hip. Many RCTs comparing HA with THA have not observed a functional difference and thus have not recommended THA as a standard treatment for displaced FNF in elderly patients [70, 71]. However, many RCTs have recommended THA over HA in healthy, cognitively lucid and relatively active patients [45, 72-76]. A large cohort study found that patients who were treated with THA had a lower level of pain and a higher level of satisfaction than patients who were treated with HA or IF [77]. The majority of the studies are conducted in a subgroup of patients who are active and living in their own homes and do not present cognitive alterations. The study settings are,

with few exceptions [71, 72, 75], composed of a relatively large population of patients less than 80 years of age. Surgeons favouring HA rely on the lower rate of dislocation, shorter operation times, less blood loss and less technically demanding surgery, whereas surgeons favouring THA rely on the tendency for improved hip function and quality of life. The longevity and level of activity of today's elderly increase the risk for protrusion of the femoral head in the acetabulum and, consequently, the need for revision surgery [73].

## CONSIDERATIONS RELATED TO THE TREATMENT

### Cemented or uncemented fixation

The fixation of a prosthesis to the bone can be performed with or without bone cement (polymethyl methacrylate (PMMA) [78]). PMMA was used first as a cement in dentistry, and Sir John Charnley popularized its use in orthopaedics whilst developing his low friction joint arthroplasty [79]. Mckee and Watson developed prostheses in the late 1940s and experimented with the dental acrylic cement PMMA for fixation. In cemented arthroplasty, the prosthesis is fixed to the bone by creating an interface between the bone and the prosthesis. The uncemented prosthesis was used earlier in time than the cemented prosthesis. Dr. Moore inserted the first uncemented prosthesis at John Hopkins Hospital in 1940 in a patient with a recurrent giant cell tumour [80]. Böhlman and Moore refined their implant, and in 1952, they described a model that featured a fenestrated stem, which allowed bone ingrowth. These implants were the first widely used hip arthroplasty products. In uncemented arthroplasty, the prosthesis is inserted by high contact with the bone and fixed via a press-fit procedure or using a taper-form prosthesis. The question of whether the prosthesis should be cemented in patients with FNF is widely debated but until now has not been resolved.

Comparisons between cemented and uncemented stems in hip arthroplasty for patients with a FNF have almost consistently favoured cemented fixation, which is mainly because of the superior outcomes regarding pain relief, walking ability, use of walking aids, and activities of daily living [81] as well as the a higher incidence of complications with uncemented stems, such as peri-prosthetic fracture [82]. However, recent reports on modern uncemented, hydroxyapatite-coated femoral stems used for this patient group have shown promising early results [83-85]. In addition, bone cement implantation syndrome (BCIS) is more prevalent in cemented stems than in uncemented stems and in patients with a FNFs [86]. BCIS is a well-described complication of cemented hip arthroplasty, and it is characterized by a number of systemic clinical features: drop in systolic blood pressure, hypoxemia, pulmonary hypertension, cardiac dysrhythmias, and occasionally cardiac arrest and death

[87, 88]. BCIS is classified into three grades according to Donaldson [89]. Grade 1: moderate hypoxia (SpO2<94%) or hypotension (fall in systolic blood pressure) (SBP>20%). Grade 2: severe hypoxia ($SpO_2$<88%), hypotension (fall in SBP >40%) or unexpected loss of consciousness. Grade 3: cardiovascular collapse requiring cardiopulmonary resuscitation. Severe BCIS has a substantial impact on early and late mortality [90]. The true incidence of BCIS in cemented arthroplasty for hip fractures is not known, which is mainly because an agreed upon standard definition has not been available until recently. In a study of 1016 patients who underwent cemented HA, Olsen et al. [90] found that 21% were grade 1, 5.1% were grade 2 and 1.7% were grade 3, and the early mortality was 9.3% in BCIS grade 1, 35% in grade 2 and 88% in grade 3. Thus, the use of uncemented hydroxyapatite stems for this patient group may still be justified.

**Cognitive dysfunction and femoral neck fractures**

Cognitive dysfunction is associated with an increased risk of sustaining a hip fracture, and the prevalence of impairment in cognitive function among hip fracture patients has been reported to reach 55% [91, 92]. Patients with cognitive dysfunction are plagued with a high mortality rate and a high rate of general and fracture-related complications [17, 48, 93, 94]. This subgroup of patients is often excluded in clinical trials, which has resulted in a failure to improve their outcomes and identify their risk factors of a poor prognosis [95]. The functional outcomes of patients with FNF and cognitive dysfunction treated with HA has been sparsely investigated, and evidence is lacking for the effect of post-operative rehabilitation in this subpopulation. Previous studies comparing HA and IF in this population have provided contradictory results [58-61].

**Surgical approach in hip arthroplasty**

Many surgical approaches to the hip joint have been mentioned in the literature. The four most commonly used in the clinical practice include anterior, anterolateral, direct lateral and posterior lateral approaches. The most frequently used approaches in hip arthroplasty are the direct and posterior lateral approaches [96-98]. In Sweden, 71% of hip fractures were operated using the direct lateral approach in 2016. The direct lateral approach is linked to increases in the prevalence of superior gluteal nerve damage, gluteus medius insufficiency and trochanter tenderness [99-102]. However, many authors have not observed clinically relevant effects [103, 104]. The posterior lateral approach is linked to an increased risk of reoperation because of prosthetic dislocation in patients who are treated for both osteoarthritis and FNF [105, 106]. The direct lateral approach has been proven to reduce the

dislocation rate after hip arthroplasty compared with the posterior lateral approach [68, 69, 107-109].

# OVERALL AIM OF THE THESIS

The overall aim of this thesis was to define the optimal treatment for elderly patients with displaced fractures of the femoral neck with consideration of the patients' age, functional demands and cognitive function.

# AIMS OF THE STUDIES

**STUDY I**

To compare the results of total hip replacement with those of IF in patients over 65 years of age with displaced FNF over a long-term follow-up period of seventeen years.

**STUDY II**

To compare the effectiveness and safety between a modern cemented and a modern uncemented hydroxyapatite-coated femoral stem in patients 65–79 years of age who were treated with THA for displaced FNF.

**STUDY III**

To compare the results of HA with those of THA in patients older than 80 years of age with a displaced FNF.

**STUDY IV**

To investigate the outcome after cemented HA for displaced FNF in elderly patients with cognitive dysfunction and to examine the impact of post-operative rehabilitation.

# HYPOTHESES OF THE STUDIES

**I.** THA in healthy elderly patients would yield significantly better functional results and fewer reoperations than IF over the long term.

**II.** An uncemented femoral stem used in THA for a displaced FNF would not be associated with more adverse peri-operative and post-operative events than a THA using a cemented stem, and the health-related quality of life (HRQoL) of the patients would be equivalent at 2 years.

**III.** THA could result in superior hip function, HRQoL and an absence of increasing rates of complications and reoperations compared with HA in cognitively intact elderly patients aged greater than 80 years treated for displaced FNF.

**IV.** Cemented HA with a direct lateral approach is an acceptable option and will not lead to more hip-related complications and reoperations in elderly patients with cognitive dysfunction or dementia than in patients who did not present cognitive dysfunction and were treated for a FNF.

# END POINTS

### STUDY I

The primary endpoint was hip function evaluated with the Harris hip score. Secondary end points included mortality, hip-related complications, reoperation, gait speed, pain in the involved hip and activities of daily living (ADL).

### STUDY II

The primary endpoints were the prevalence of all hip-related complications and HRQoL evaluated with the EuroQol-5D (EQ-5D) index up to 2 years after surgery. Secondary endpoints included overall mortality, hip function and general medical complications

### STUDY III

The primary endpoints were hip function and HRQoL evaluated with the Harris hip score and the EQ-5D index, respectively. Secondary endpoints included hip-related complications and reoperations, mortality, pain in the involved hip, ADL, surgery time, blood loss and general complications.

### STUDY IV

The main endpoints were the prevalence of all hip-related complications and the ability to return to previous walking status. Other outcomes included mortality, HRQoL (according to the EQ-5D index), hip function, ADL, pain numeric rating scale (PNRS) and adverse events during the study period.

# PATIENTS

All patients with a FNF who were admitted to the Orthopaedic Department at Danderyd Hospital between February 1990 and December 1994 (study I), between 2009 and 2014 (study II) and between 2009 and 2016 (studies III and IV) were screened for participation in the study during the inclusion period. We identified 1172 patients for study I and 1224 patients for studies II, III, and IV who were admitted because of a FNF.

The inclusion criteria were as follows.

- An acute displaced FNF (Garden III–IV) that had been sustained within the previous 36-48 hours.
- Ability to ambulate independently with or without walking aids.
- Age of 65 years or more in study I.
- Age of 65–79 years in study II.
- Age of 80 years or more in study III.
- Age of 65 years in the cognitive dysfunction group and 80 years and over in the control group in study IV.
- Admission from home, a healthy status or only mild systemic disease (ASA 1 or 2), ability to conduct all ADL (Katz index A) and a Harris hip score (HHS) of 100 points prior to the fracture in study I.
- Intact cognitive function, no diagnosis of dementia, lucidity and fully oriented in study I and at least 8 correct answers on a 10-item SPMSQ in studies II, III and in the control group in study IV. For patients with cognitive dysfunction in study IV, the condition was defined as a known diagnosis of dementia and/or a SPMSQ of ≤7.

Exclusion criteria included patients with osteoarthritis or rheumatoid arthritis in the fractured hip, pathologic fractures, inability to walk, concurrent joint disease or previous fracture in the lower extremities. We also excluded patients who were deemed unsuitable for an arthroplasty by the anaesthesiologist because of severe comorbidities and those who were unsuitable for participation in the study for any other reason.

In study IV, the differences in age in relation to mental status were related to the clinical routines at the Orthopaedic Department of Danderyd Hospital; a cemented HA is used for patients greater than 65 years with cognitive dysfunction and in those greater than 80 years without cognitive dysfunction. THA is used in relatively young (65-79 years) lucid patients.

The patients who fulfilled the inclusion criteria and agreed to participate in the study gave their oral and written informed consent to participate in the study. Consent for patients with cognitive dysfunction was obtained from relatives or significant others.

## Ethics

All studies were conducted in accordance with the Helsinki Declaration, and all protocols were approved by the local ethics committee. The patients in studies I, II, and III gave their informed consent to participate. In study IV, the patients or their caregivers gave oral and written informed consent to participate in the study.

# REGISTRATION

Studies I, II, III were registered and are publicly accessible at www.clinicaltrials.gov.

Study I: NCT01344772

Study II: NCT02247791

Study III: NCT022463

# MATERIAL

### INTERNAL FIXATION

The osteosynthesis device used in study I was two Olmed screws (Olmed; DePuy/Johnson & Johnson, Sollentuna, Sweden).

### HIP ARTHROPLASTY

In study I, all patients undergoing THA received a cemented, polished, tapered femoral stem manufactured from a titanium alloy (Ti-6Al-4V) (Bi-Metric; Biomet UK, Brigend, South Wales, United Kingdom) with a 28-mm chromium cobalt head. The acetabular component was a cemented polyethylene acetabular component (Müller; Biomet UK). The bone cement used was Optipac (Biomet, Malmö, Sweden).

An uncemented Bi-Metric stem (Biomet, Warsaw, Indiana, USA) was used in the uncemented group in study II. The Bi-Metric stem is a tapered, collarless, proximally coated (plasma-sprayed, commercially pure [CP]) titanium femoral stem. The modular collarless, polished, tapered femoral stem CPT (Zimmer, Warsaw, Indiana, USA) was used in study II and used up to 2014 in studies III and IV. After 2014, the hospital switched to a

cemented, matte, anatomical, collared femoral stem Lubinus SP II (Waldemar Link, Hamburg, Germany) according to a decision in our clinic. We used the 32-mm cobalt-chromium head in all patients in studies II, III and IV. For the acetabular component, we used a cemented highly crosslinked polyethylene acetabular component Marathon cup (DePuy, Warsaw, Indiana, USA) in all patients except three who obtained the uncemented Trilogy cup (Zimmer, Warsaw, Indiana, USA) according to the surgeon's preference.

A modular 32-mm cobalt chrome femoral head and a modular unipolar head Versys Endo (Zimmer, Warsaw, Indiana, USA) or unipolar head (Waldemar Link®, Hamburg, Germany) were used for THA patients and HA patients, respectively, in studies II, III and IV.

Bone cement (Palacos with gentamicin; Schering-Plough, Stockholm, Sweden) was used in all patients who received a cemented stem in studies II, III and IV.

# METHODS

## STUDY PROTOCOL

### Study I

A prospective RCT conducted between February 1990 and June 2010 (inclusion period February 1990 to December 1994). The randomization process for the first 20 patients was conducted using sealed opaque envelopes. No stratification was used. Because of hospital economic and logistic reasons related to a lack of operating theatre staff with THA experience during weekends, a change in allocation routines was implemented during the study. Thus, the following 80 patients were allocated according to the weekday they were admitted. Patients admitted on Monday to Thursday underwent THA, whereas patients admitted from Friday to Sunday underwent IF. The patients, surgeons and staff were not blinded to the choice of treatment. Follow-up examinations at 3 months and 1, 2, 4, 11 and 17 years were performed in the Orthopaedic Department at Danderyds Hospital, Sweden.

### Studies II and III

Single-centre, single-blinded RCTs were performed between 2009 and 2016 (study II (CHANCE trial); inclusion period, September 2009 through March 2014) and between 2009 and 2017 (study III (Hope-Trial); inclusion period, September 2009 to April 2016). The patients were block-randomized in groups of 10 at a 1:1 ratio to receive either a cemented or an uncemented stem in study II and either a HA or THA in study III. We used sealed envelopes, and randomization was stratified by sex to ensure that the sex distribution would be the same in both groups. The participants, who were the primary outcome assessors, were blinded to the choice of treatment, and they were not allowed to view their X-rays. To verify that the blinding was maintained during the study, the patients were asked whether they knew their assigned treatment at the 1-year follow up. The surgeons and staff were not blinded during the study. Follow-up examinations were performed at 3 months and 1 and 2 years for study II and at 3 months and 1 year for study III in the Orthopaedic Department at Danderyds Hospital.

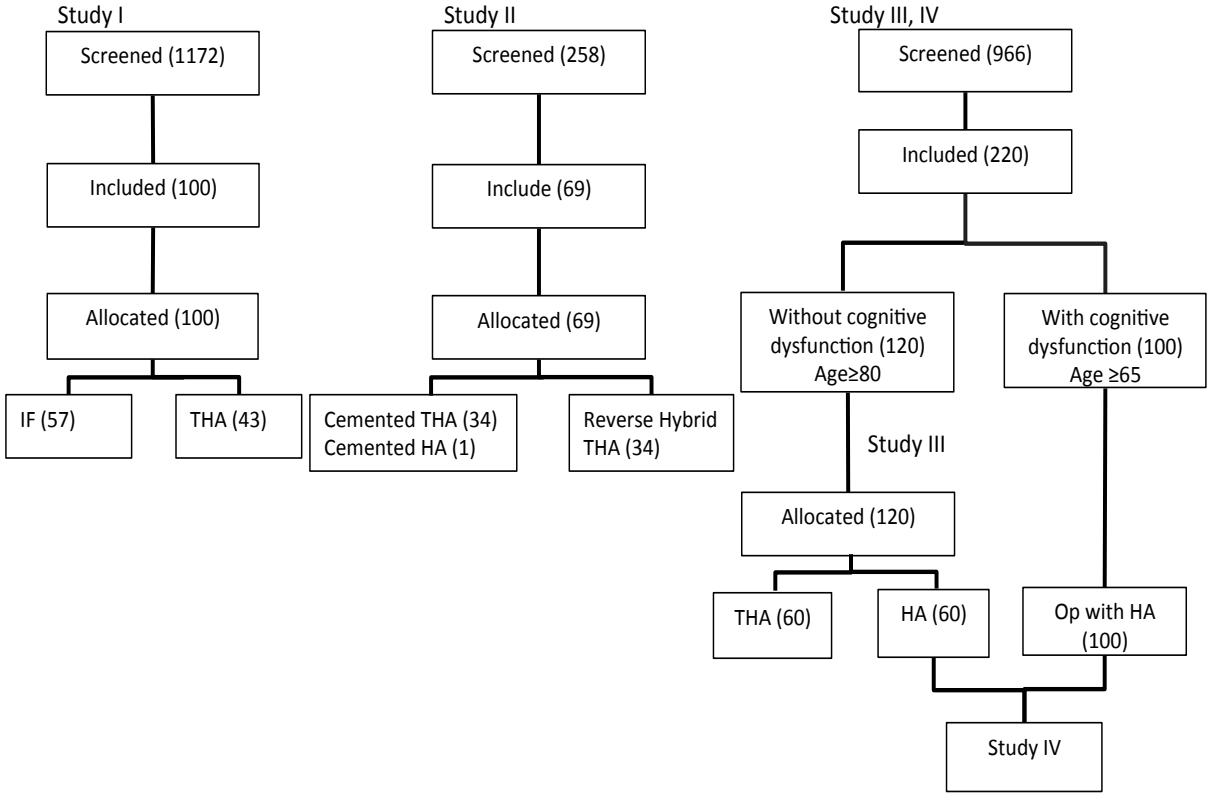
### Study IV

A single-centre, prospective, observational cohort study was conducted between September 2009 and March 2017 (inclusion period, September 2009 to March 2016). Patients with a displaced FNF treated with a HA using a direct lateral approach were included in the study. The cohort was divided into two groups: a cognitive dysfunction group, which was defined by a diagnosis of dementia and/or a SPMSQ of ≤7; and a control group, which was defined as

by absence of a diagnosis of dementia and with a SPMSQ ≥8, and these patients were recruited from the HA group of study III (HOPE-trial). We used a directed acyclic graph approach (Figure 5) to identify possible confounders [110]. Follow-up examinations at 3 months and 1 year were performed in the Orthopaedic Department at Danderyds Hospital. Figure 6 shows the flow diagram of the patients in this thesis.

Figure 5: Directed acyclic graph (DAG) for the statistical model. The variables shown in solid colours have been adjusted, and those that are shaded have not. The DAG is a tool that illustrates our interpretation of how the data are interconnected. Per definition, it is a simplification and a tool for the reader to better understand the underlying assumptions of the study.

**Figure 6: Flow diagram of patients in the thesis**



## FRACTURE CLASSIFICATION

All patients in the four studies had a displaced FNF classified as Garden III-IV except for certain patients for whom the fracture was classified as Garden I or II but was assessed as subcapital and not appropriate for IF because of the high risk of failure.

## ASA CLASSIFICATION AND ANAESTHESIOLOGICAL ASSESSMENT

The patient's general physical health status in all studies was assessed by an anaesthesiologist according to the ASA classification [111]. ASA 1 indicates a completely healthy person; ASA 2 indicates a person with mild systemic disease; ASA 3 indicates a person with severe systemic disease that is incapacitating; ASA 4 indicates a person with an incapacitating disease that is a constant threat to life; and ASA 5 indicates a moribund patient who is not expected to live 24 hours with or without surgery. In study I, only patients with ASA 1-2 were included. In the others studies in this thesis, patients with ASA 1, 2, 3 and 4 were included. All patients in the four studies were examined and cleared by an anaesthesiologist before inclusion. The assessment included a decision regarding whether the patient was healthy enough for both procedures in all studies.

## COGNITIVE FUNCTION

Cognitive function was assed using the SPMSQ [112]. The SPMSQ is a validated test with 10 questions, where 8–10 correct answers are classified as intact cognitive function, 3–7 correct answers are classified as an intermediate level (mild-moderate) of cognitive dysfunction and 0–2 correct answers are classified as a severe level of cognitive dysfunction (see appendix). The SPMSQ has shown good sensitivity and specificity for detecting cognitive dysfunction and has been validated for screening cognitive dysfunction in the elderly population [113, 114]. Cognitive function is a strong predictor of outcome after hip fracture surgery [17, 115]. The SPMSQ was used in studies II, III and IV. In studies II and III, only patients with at least 8 correct answers were included. In study IV, patients with fewer than 8 correct answers or with a diagnosis of dementia were included. In study I, we did not use any validated instrument for assessing cognitive function. However, the inclusion criteria included intact cognitive function (no diagnosis of dementia, with the patient being lucid and fully oriented).

## CHARNLEY CLASSIFICATION

The Charnley classification was used preoperatively in studies II, III and IV. This classification has a simple design with 3 classes: (A) 1 hip involved, (B) 2 hips involved but no other joints, and (C) some other factor contributing to a failure to achieve normal

locomotion, such as rheumatoid arthritis, senility, hemiplegia, or cardiovascular or respiratory disability [116] (please see the appendix).

## LIVING CONDITIONS

In study I, living conditions were categorized as independent for patients admitted from their own home, and only these patients were included in the study. In the other studies included in this thesis, living conditions were categorized as independent (i.e., living in own home, retirement community or block of service flats) or as institutionalized (i.e., care homes for demented patients or nursing homes). Patients were included in studies II, III, and IV regardless of their living conditions.

## HARRIS HIP SCORE (HHS)

Hip function was assessed in all studies in this thesis using the HHS [117]. The score was originally developed for hip function evaluations of arthroplasty after traumatic arthritis. This score has been widely used for evaluating hip function after THA and has been proven to be a valid and reliable score in patients after THA [118]. The HHS was originally surgeon-assessed but has been validated for self-reporting and outcomes after FNF [119, 120]. The total sum of all the points generates a maximum score of 100: pain (0–44 points); function (0–47 points); absence of deformity (0–4 points); and range of motion (0–5). A higher score corresponds to better hip function. Except for the range of motion dimension, the HHS is self-reported by the patient. In this thesis, the assessment of the HHS was performed via interviews, with the grading of pain and function accounting for a total of 91 points (see the appendix). The HHS was modified in this thesis for use as a patient self-reported questionnaire by excluding the clinical examination domain. This modification has previously been evaluated and found to be in accordance with the surgeon-assessed HHS [119]. The modified HHS is used in all studies in this thesis.

## GAIT VELOCITY AND WALKING ABILITY

Gait speed was measured as the time in seconds to walk 30 m with a comfortable velocity, and it was used in study I. The ability to return to previous walking ability and changes in the walking distance were assessed using question number 4 of the HHS. Walking ability was graded from 0 to 11 points, where 0 points equals non-walking ability, 2 points equals a walking distance less than 0.5 km or walking only indoors, 5 points equals a walking distance from 0.5-1 km, 8 points equals a walking distance from 1-2 km and 11 points equals a walking distance greater than 2 km.

**EQ-5D**

The quality of life was assessed with the EuroQol [121]. The EuroQol consist of 4 components: the health status part (EQ-5D), a visual analogue scale (EQ-VAS), the valuation part and the background data. The health status part (EQ-5D) was used in this thesis in studies II, III and IV. EQ-5D is widely used and has been translated into most major languages, including Swedish [121, 122]. The EQ-5D is a standardized non-disease specific instrument that measures quality of life using five dimensions: mobility, self-care, usual activity, pain/discomfort and anxiety/depression. Each dimension is divided into 3 levels: 1, no problems; 2, certain problems; and 3, extreme problems (see appendix). A unique health state is defined by combining 1 level from each of the dimensions, which results in 243 different health states. We used the preference scores ($EQ\text{-}5D_{index}$ scores) generated from a large population study in the United Kingdom [123] when calculating the scores for our patients. The states can be expressed as index scores ranging from -0.59 points (indicating the worst possible quality of life) to 1.0 (indicating the best possible quality of life), with 0 on the scale representing the state of being dead. Negative scores suggest that he corresponding health states are considered worse than being dead. The EQ-5D has been used in clinical trials in many different fields of medicine, including quality of life evaluations after hip fracture surgery [72, 124]. The responsiveness has been found to be adequate in patients with FNF [125, 126]. Preinjury EQ-5D was obtained using the recall principle, in which the patients were asked to recall their health status one week prior to injury. This method has been proven to be a valid measure [127]. In patients with cognitive dysfunction, the EQ-5D was obtained from the proxy, i.e., relatives or significant others. This method is also well documented [128, 129]

**ADL**

The status of the ADL index according to Katz et al. [130] was used in all studies in this thesis and is based on an evaluation of the functional independence or dependence of patients during bathing, dressing, going to the toilet, transferring, continence and feeding. ADL index A indicates independence in all six functions, index B indicates independence in all but one function, and indices C to G indicate dependence in bathing and in one to five other functions (see the appendix).

**PAIN NUMERIC RATING SCALE**

Pain in the involved hip was measured with the PNRS [131]. The PNRS is a 10-point (1-10) numerical rating scale that is easy to administer. A score of 0 indicates no pain, and score of 10 indicates the worst possible pain (See appendix). The PNRS was used in the four studies

in this thesis. Patients were asked to evaluate the level of pain they experienced in the operated hip during the previous week.

## SURGICAL TECHNIQUE

### Internal fixation (IF)

IF was used in study I, and it was conducted with the patient on a fracture table. The fracture was reduced closed, with the aid of an image intensifier, and it was fixed with two cannulated screws (Olmed; DePuy/Johnson & Johnson, Sollentuna, Sweden). Capsulotomy or joint aspiration was not performed. In the anteroposterior projection, the distal screw was aimed to the level of the lesser trochanter to rest on the medial inferior cortex of the femoral neck. The proximal screw was positioned parallel to and at least 1 cm from the distal screw. The screws were parallel and positioned in the central or posterior third of the femoral head and neck. All operations were performed on the day of admission or the following day.

### Hip arthroplasty

The posterior lateral approach without repair of the capsule or external rotational was used in study I [132]. The direct lateral approach was used in studies II, III, and IV [133]. The following surgical techniques and instrumentation were identical, regardless of the type of arthroplasty or approach. The femoral head was dislocated from the acetabulum, and resection of the femoral neck was performed. When performing a HA, the femoral head is measured and the head size is determined. When performing a THA, the acetabulum is prepared with reaming until the cartilage and cortical bone are removed. The acetabular component was positioned and fixated with bone cement. In the uncemented group in study II, the femur was reamed until cortical bone contact was obtained. The proximal femur was then prepared with broaches of increasing size until rotational stability was achieved. In the cemented stem, the proximal femur was reamed with 1 or 2 reams and then prepared with broaches of increasing size. The cement bed was cleaned with repeated high-pressure pulsatile lavage. A distal restrictor was used when cementing the femoral component.

As thromboprophylaxis, dextran (Macrodex; Meda, Sweden) was used one hour preoperatively and postoperatively daily for four days in study I, whereas low-molecular-weight heparin was used in studies II, III and IV postoperatively for at least 10 days. Antibiotic prophylaxis with cloxacillin (Ekvacillin; Meda, Sweden) (2 g) was administered preoperatively followed by 3 additional doses during the first 24 h.

Under the supervision of a physiotherapist, all patients were mobilized to full weight-bearing capacity on the first post-operative day. In the THA group in study I, the patients were

allowed to sit on a high chair and could stop using crutches at their own discretion. After six weeks, no restrictions were imposed. In studies II, III and IV, the patients were mobilized without any restrictions on the first post-operative day.

**RADIOLOGICAL ASSESSMENT**

In study I, an anteroposterior (AP) view of the pelvis and AP and lateral views of the hip were obtained pre- and postoperatively and at the follow-up visit. The plain radiograph was used. The positioning of the prosthetic components was evaluated and classified as follows.

- Good
    - minimum circumferential cement mantle around cup and stem, 2 mm;
    - abduction angle of the cup, 35°-55°;
    - anteversion angle of the cup, 10°-25°;
    - varus/valgus angle of the stem, below 3°;
    - post-operative limb-length difference, below 10 mm.
- Fair
    - at least four of the five categories graded as good.
- Poor
    - three categories or fewer graded as good.

In patients treated with IF, the reduction and position of the screws was categorized in accordance with the recommendations of Tidermark et al. [51] as follows

- Good (displacement <2 mm; Garden angel 160° to 175°; and posterior angulation <10$^{o}$);
- Fair (displacement <5 mm; Garden angel 160° to 175°; and posterior angulation <20°);
- Poor (displacement >5 mm; Garden angel <160° or > 175°; and posterior angulation >20°).

In the THA group, we examined the radiographs for radiolucent lines around the stem in the zones of Gruen et al. [134] and around the cup in the zones of DeLee and Charnley [135] Any circumferential radiolucent lines around the implants were defined as loosening.

In the IF group, healing of the fracture was defined as the presence of visible trabeculations across the fracture line and no signs of osteonecrosis. The absence of radiographically visible trabeculations across the fracture line and progressive or early displacement was

defined as a non-union.

In study II, an AP view of the pelvis and AP and lateral views of the hip were obtained pre- and postoperatively and also at 24 months, and these were reviewed by an independent radiologist. All femurs were classified preoperatively as type A, B, or C according to the Dorr classification [136]. Post-operative heterotopic ossification at 24 months was graded as described by Brooker et al. [137].

In studies III and IV, an AP view of the pelvis and AP and lateral views of the hip were obtained pre- and postoperatively. Radiological measurements at one year were not performed because one year is a relatively short time for any routine radiological change to occur. A digital radiograph was used in studies II, III and IV.

## STATISTICAL METHODS

In all studies, the statistical software SPSS Statistics 18.0-22.0 for Mac was used. Sample size calculations were performed using the software Sample Power 2.0. In all studies, P-values $\leq 0.05$ were considered significant.

### Sample size calculation

In study I, no formal power analysis was performed at the time of initiation of the study. An interim analysis (two-sided, p=0.05) after one year was performed on the primary end point, and we tested the null hypothesis that the mean HHS for the two groups would be equal. We assumed that a mean difference of 10 points (standard deviation 15 points) in the HHS was the smallest effect that would be clinically relevant. Taking into consideration the difference in the number of patients included in the two groups, we calculated that a total of 90 patients with a one-year follow-up period (40 in the THA group and 50 in the IF group) would provide a power of 87.5% to yield a significant result. A total of 100 patients (43 in the THA group and 57 in the IF group) were recruited to allow for any loss to follow up.

In study II, 60 patients in each group with a non-inferiority limit of 15% would be required to show non-inferiority at a power of 80% of the primary endpoint, all hip-related complications between the two groups with a total assumed complication rate of 20%. In addition, 40 patients in each group with a non-inferiority limit of 0.1 would be required to show non-inferiority at a power of 80% of the primary variable (HRQoL), which was measured via the EQ-5D and presented an assumed value of 0.73 (SD 0.18). Both calculations were performed with significance set to $p<0.025$ instead of $p<0.05$ to handle

multiplicity. Because this patient group has a 1-year mortality of 10%, 70 patients in each group (140 total) would be sufficient for the study.

In study III, prior to commencement of the study, a two-sided power analysis was performed. We wanted to test the null hypothesis assuming that the mean HHSs for the two groups will be equal. We assumed that a mean difference of 10 points (standard deviation, 15 points) [138] in the HHS is the smallest effect that will be clinically relevant. We calculated that a total of 80 patients (40 in each group) would have a power of 80% to yield a significant result.

This calculation also assumes that a sample of 40 patients in each group would be required to show to non-inferiority (non-difference) at a power of 80% of the second endpoint EQ-5D, which had an assumed value of 0.73 and a standard deviation of 0.18. The significance level was set at a conservative 2.5% ($p<0.025$) to handle multiplicity because two sample size calculations were included. We will include 60 patients in each group (120 total) to allow for loss to follow up.

In study IV, 50 patients in each group are required to show non-inferiority at a power of 80% of the primary variable complication rate between the two groups (patients included in study III versus patients with HA in study IV), with a total assumed complication rate of 30%. In addition, 40 patients in each group are required to show non-inferiority at a power of 80% of the secondary variable HRQoL as measured using the EQ-5D, with an assumed value of 0.73 (SD 0.18) one year after the surgery. Both calculations were conducted at $p<0.025$. Because this patient group with severe cognitive impairment has a high mortality rate, we will include 100 patients to allow for loss to follow up.

**Statistical analysis**

In studies I-III, analyses of the outcomes were based on the intention-to-treat principle, and all patients remained in the group to which they had been randomized regardless of any later surgical intervention. The data in all studies are presented with the mean differences and SDs, relative risk, odds ratios (ORs) and uncertainty estimation with 95% confidence intervals (CIs). A P-value <0.05 was considered statistically significant

In study I, patients with missing data at any of the follow-up evaluations were analysed with the last observation carried forward. For the clinical outcome variables (HHS, gait velocity, and VAS), we used a one-way repeated measure analysis of covariance (ANCOVA) to detect an overall difference between the two treatment arms throughout the study period using the estimated marginal means to adjust for the difference between the

two groups in terms of sample size. The Bonferroni correction was used to adjust for multiple comparisons. Kaplan-Meier curves with the log-rank test were used to analyse patient and implant survival.

In all studies, Student's t-test and Levene's test were performed to compare scaled variables, and Fisher's exact test was used to identify correlations between ordinal data. In study IV, a linear regression model was used to evaluate the HRQoL and hip function and a binary logistic regression was used to evaluate the risk of being unable to walk at the 1-year follow up. The factors used in the models were group (controls/cognitive dysfunction), geriatric rehabilitation after surgery (yes/no), pre-fracture function (EQ-5D/HHS and walking ability, respectively), age and sex. Two types of sensitivity analyses were performed to test the robustness of our models. First, because of the relatively large amounts of missing functional outcome score data at the 1-year follow up because of the high mortality rate, multiple imputation was used. Second, a competing risk analysis for hip complication outcome (according to Fine and Gray) with the exposure variable, age, sex, and ASA-class as the co-variates were used because of the higher mortality rate in the cognitive dysfunction group. We used SPSS 22 for Mac for the analyses.

# RESULTS

## STUDY I

### Patient flow and baseline data

In total, 1172 patients with FNF were admitted to the Orthopaedic Department at Danderyd Hospital, Stockholm, Sweden (flow of patients, Figure 7) during the study period. Of these, 100 patients met the inclusion criteria [mean age 78 years (range, 65-90 years, with 79 females)] and were recruited to participate in the study. All subjects received their allocated treatment. The characteristics of the two groups were similar at baseline (Table 1).

### Operative data

A total of 18 surgeons performed all the operations, and a greater proportion of IF was performed by the registrars (THA versus IF and consultants/registrars: 41/2 versus 47/10). The duration of surgery and blood loss were greater in the THA group. The THA was graded as good in 40 (93%) patients and fair in 3 (7%). In the IF group, closed reduction was categorized as good in 51 (89%) and fair in 6 (11%) patients. The positioning of the screws was considered good in 56 (98%) and fair in 1 (2%) patient. We found no correlation between the incidence of failed fracture healing and the reduction and positioning of the screws.

### Primary endpoint

The HHS was higher in the THA group, with a mean difference throughout the study period of 14.7 points (95% CI 9.2 to 20.1; $p<0.001$; ANCOVA), and the greatest difference between the groups was observed during the first 2 years (Figure 8).

### Mortality

Patient mortality was high regardless of the treatment. At 11 and 17 years, 34% and 14% patients were still living, respectively. The mortality rate did not differ between the groups over the study period.

### Hip complications and reoperations

Forty hips (40%) required at least one reoperation during the study period (Table 2), and 4 (9%) patients in the THA group and 22 (39%) in the IF group underwent a major reoperation (relative risk [RR] 0.24; 95% CI, 0.09 to 0.64; p=0.001) (Table 3). The overall rate of reoperation was 23% (10/43) in the THA and 53% (30/57) in the IF group (RR 0.44; 95% CI 0.24 to 0.80; p=0.003) (Table 3). The median time to first reoperation was 33 months (range, 0.5-114) in the THA group and 10 months (range, 0.5-47) in the IF group. Twelve patients underwent more than 1 surgical procedure (range 1-4), and 10 of these patients were in the IF

group. The most frequent complications in the THA group were dislocations (n=6), late-presenting peri-prosthetic fractures (n=2) and aseptic loosening (n=2). In the IF group, avascular necrosis (n=17) and non-union/mechanical failure (n=14) were the two most common hip complications. During the first two years after surgery, a large number of IF procedures failed, and 20 of the initially recruited 57 patients received a secondary THA. Patients who received primary THA underwent fewer reoperations (4 of 43 patients), which were performed at later time points (4 to 12 years after primary surgery) (Tables 2 and 3, Figure 9).

**Gait speed, pain and activities of daily living**

Gait speed was significantly faster in the THA group at 3 months (THA vs IF; 37 vs 50 seconds to walk 30 metres, p=0.005) but did not differ between the groups at later follow ups. Patients in the THA group had less pain in the operated hip throughout the study period. The mean difference was 1.2 points (95% CI 0.4 to 2.0; p<0.001, ANCOVA) out of 10 on the VAS. A greater proportion of patients in the THA group was fully independent in ADL during the 1st year of the study. At the later follow-up visits, differences were not observed between the groups (table 4).

**Figure 7: Flow of the patients in study I.**

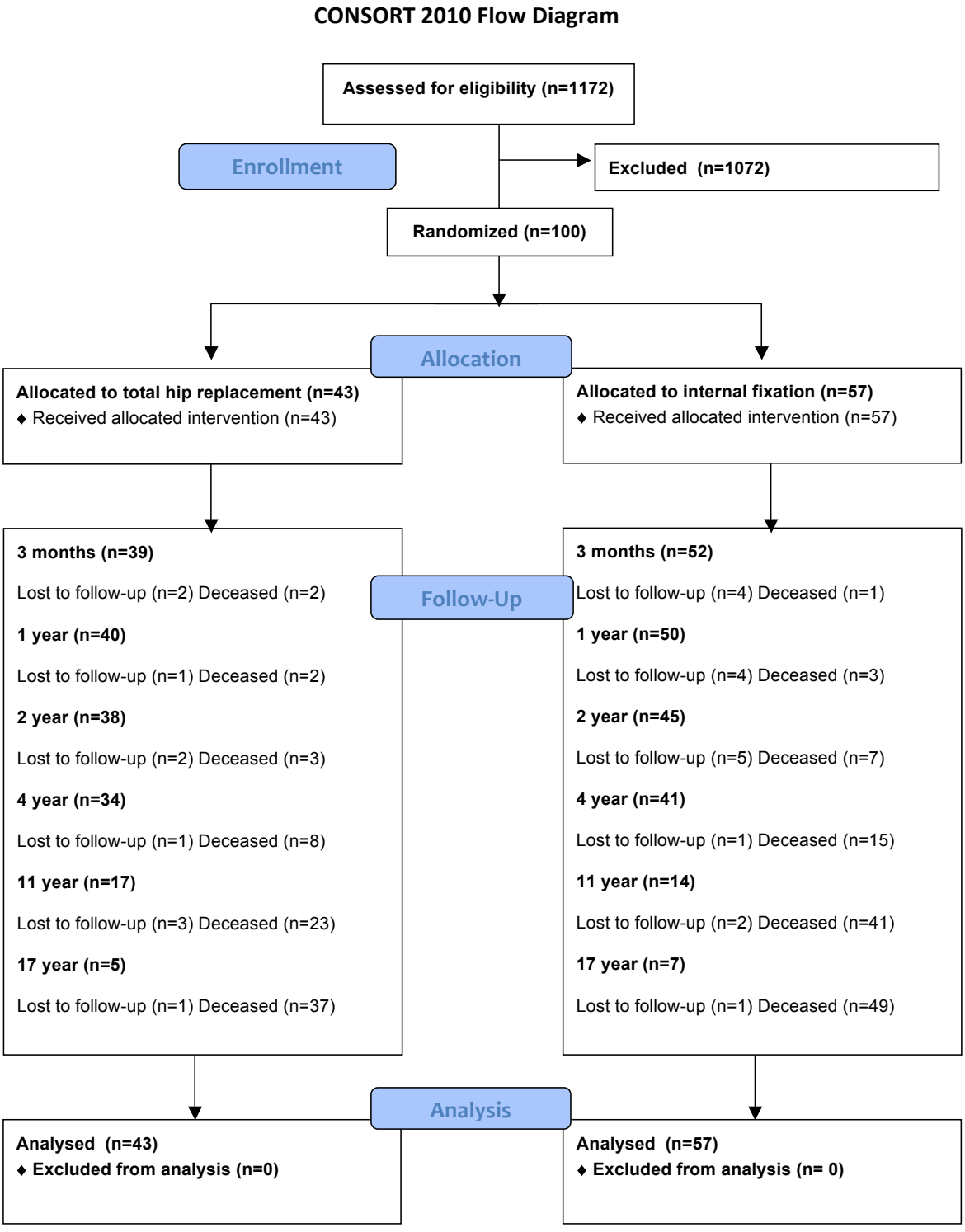


**Table 1:** Study population characteristics. Values indicate the number of patients or the mean, with percentages or ranges in parentheses.

| | THR (n=43) | IF (57) |
|---|---|---|
| **Sex** | | |
| Male | 5 (12%) | 16 (28%) |
| Female | 38 (88%) | 41 (72%) |
| **Age** | 78 (65-90) | 79 (66-90) |
| **Side** | | |
| Left | 20 (53%) | 26 (46%) |
| Right | 23 (47%) | 31(54%) |

**Figure 8:** Line graph illustrating the mean Harris hip score during the study period according to the treatment**.**

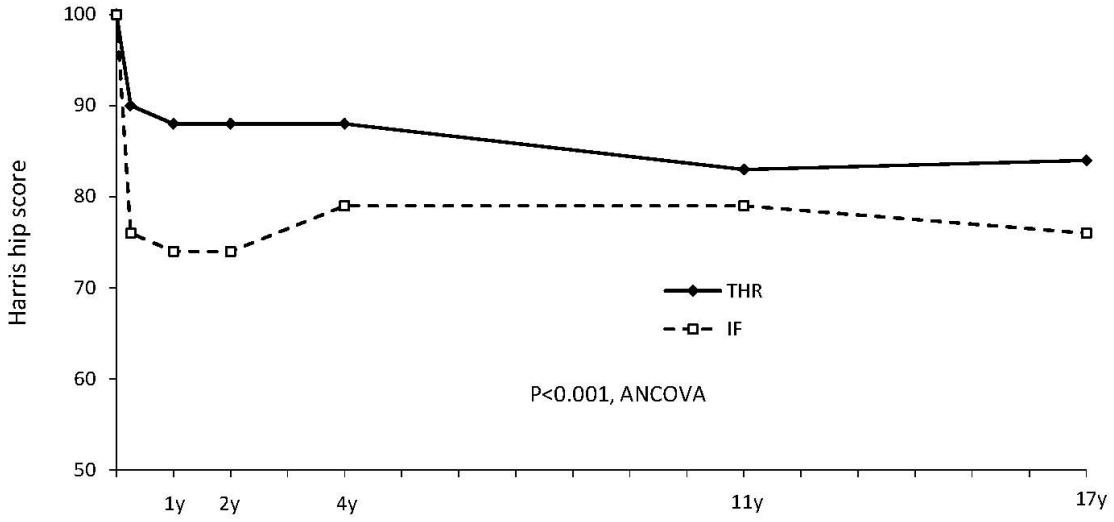


**Table 2:** All complications are counted; thus, more than one complication may apply for each each hip.

| **Hip complications** | **THR (n=43)** | **IF (n=57)** |
|---|---|---|
| Dislocation[a] | 9 | 1 |
| Pseudarthrosis/mechanical failure | 0 | 14 |
| Avascular necrosis | 0 | 17 |
| Deep infection | 0 | 2 |
| Lateral pain | 1 | 12 |
| Aseptic loosening | 2 | 1 |
| Peri-prosthetic fracture | 2 | 0 |
| ***Total number of hip complications*** | **14** | **47** |
| ***Number of hips with any complication***[b] | **11 (26%)** | **37 (65%)** |

No. (%) is presented

[a] One hip dislocated 4 times and 5 hips dislocated once in the total hip replacement group.

**Table 3:** Hip reoperations: All reoperations are counted; therefore, more than one reoperation may apply for each hip. [a] One hip dislocated 4 times and 5 hips dislocated once in the total hip replacement group.

| **Hip reoperations** | **THR (n=43)** | **IF (n=57)** |
|---|---|---|
| Closed reduction[a] | 9 | 1 |
| Screw removal | 0 | 14 |
| Excision arthroplasty (Girdlestone) | 0 | 2 |
| Hip arthroplasty as a secondary or tertiary procedure | 0 | 20 |
| Open reduction and internal fixation of peri-prosthetic fracture | 2 | 0 |
| Revision of total hip replacement because of aseptic loosening | 2 | 1 |
| Surgical debridement because of deep infection | 0 | 2 |
| ***Total number of hip reoperations*** | ***13*** | ***40*** |
| **Number of hips with any major reoperation** | **4 (9%)** | **22** |
| ***Number of hips with any reoperation*** | ***10 (23%)*** | ***30 (53%)*** |

No. (%) is presented

**Figure 9:** Line graph of the cumulative reoperation rate during the study period**.**

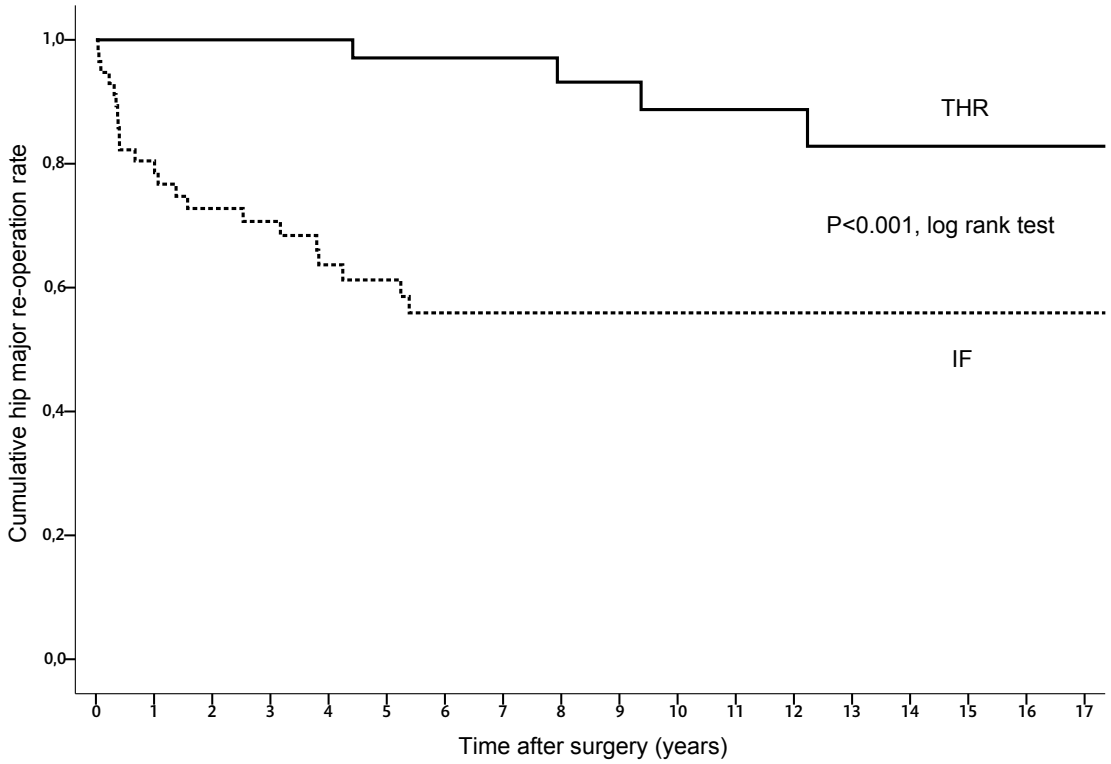



**Table 4:** Proportion of patients with fully independent activities of daily living according to the treatment.

| | **THA (n=43)** | **IF (n=57)** | **P-value** |
|---|---|---|---|
| **Baseline** | 100% (43/43) | 100% (57/57) | |
| **3 months** | 85% (33/39) | 64% (33/52) | 0.03 |
| **1 year** | 88% (35/40) | 70% (35/50) | 0.05 |
| **2 years** | 87% (33/38) | 78% (35/45) | 0.3 |
| **4 years** | 82% (28/34) | 73% (33/45) | 0.3 |
| **11 years** | 82% (14/17) | 79% (11/14) | 0.8 |
| **17 years** | 80% (4/5) | 71% (5/7) | 0.7 |

%. (No) is presented

## STUDY II

### Patient flow and baseline data

Sixty-nine patients were recruited to participate in the study (Figure 10). The mean age was 73 years, and 47 patients were female. There were twice as many patients with ASA 3–4 in the uncemented group (Table 5). All subjects received their allocated treatment except for 1 patient in the cemented group who received a cemented HA instead of a THA. Regarding hip complications and reoperations, all patients were available to follow up, including the 3 patients who refused to attend to their clinical follow-up visits.

When only half of the sample size had been reached (n=69), an interim analysis was performed, and the results showed that the incidence of hip complications was statistically significantly higher in the uncemented group; therefore, the study was stopped.

### Operative data

The mean surgery time was 13 minutes shorter in the uncemented group. The decrease in blood pressure during stem insertion did not (for any individual patient) reach the level that occurs in BCIS grade 1 according to Donaldson et al. [89]. Pulse oximetry decreased below 94% in 1 patient in each group and reached the level of BCIS grade 1. No deaths or cardiovascular collapse occurred during the cementing procedure. The operative data are presented in Table 6.

### Primary endpoints

Up to 2 years after surgery, 8 patients suffered at least 1 hip-related complication: 1 in the cemented group and 7 in the uncemented group (RR=7; 95% CI, 1–55; p=0.03, Fisher's exact test) (Table 7). Four patients in the uncemented group underwent a major reoperation, compared with 0 in the cemented group. The HRQoL EQ-5D was similar, and statistically significant or clinically significant differences were not observed between the groups during the study period (Table 8). The only complication that occurred in the cemented group was a dislocation of the prosthesis, which was treated with a closed reduction. In the uncemented group, 3 intra-operative peri-prosthetic fractures occurred. Two of these fractures were treated with cerclage wires, and the third was treated with a plate and screws. All fractures healed, but 1 stem had excessive migration, and the patient continued to experience pain. The stem was later revised to a cemented stem. One additional peri-prosthetic fracture (18 months postoperatively) was fixed with cerclage wires, and the stem was revised to a long uncemented stem. In the uncemented group, 3 patients sustained dislocations of the prosthesis. One of these dislocations occurred after a fall, and the second

was found to be dislocated on the first post-operative radiograph in a patient with an intra-operative peri-prosthetic fracture fixed with a plate and screws. This dislocation was treated with a change of the liner to an elevated rim. The third dislocation was caused by an undersized stem, which subsided and dislocated. This stem was revised to a cemented stem. One patient had a superficial infection, which was treated with antibiotics.

**Secondary endpoints**

*Mortality*

Four patients died during the study (2 in each group). No deaths occurred during the operation or within the first month postoperatively. Statistically or clinically relevant differences in the HHS and ADL were not observed between the groups throughout the study period. The mean PNRS was higher in the uncemented group during the first 3 months, and it was higher in the cemented group at 12 and 24 months. None of the differences were statistically significant (Table 8).

*General complications*

Four thrombotic events occurred in the cemented group during the study period: 2 patients suffered pulmonary embolisms during the primary hospital admission, and 1 patient had a pulmonary embolism between the 12-month and 24-month follow-up examinations. All pulmonary embolisms were temporary and treated with warfarin for 6 months. All 3 patients attended the 2-year follow-up visit. We found 1 deep-vein thrombosis at the 3-month follow up. No thrombotic events were found in the uncemented group (mean difference=0.15; 95% CI, −0.004 to 0.31; p=0.06). At the 3-month follow up, 2 patients in each group had suffered heart failure. One patient in each group had a cerebral vascular lesion prior to the 24-month follow-up visit. One patient in the uncemented group suffered an acute myocardial infarction before the 24-month follow-up visit. The CRP and D-dimer results were similar in both groups (Table 9). Most patients in the study had some degree of heterotopic ossification. Table 10 shows the radiological outcomes.

**Figure 10:** Flow of the patients in study II.

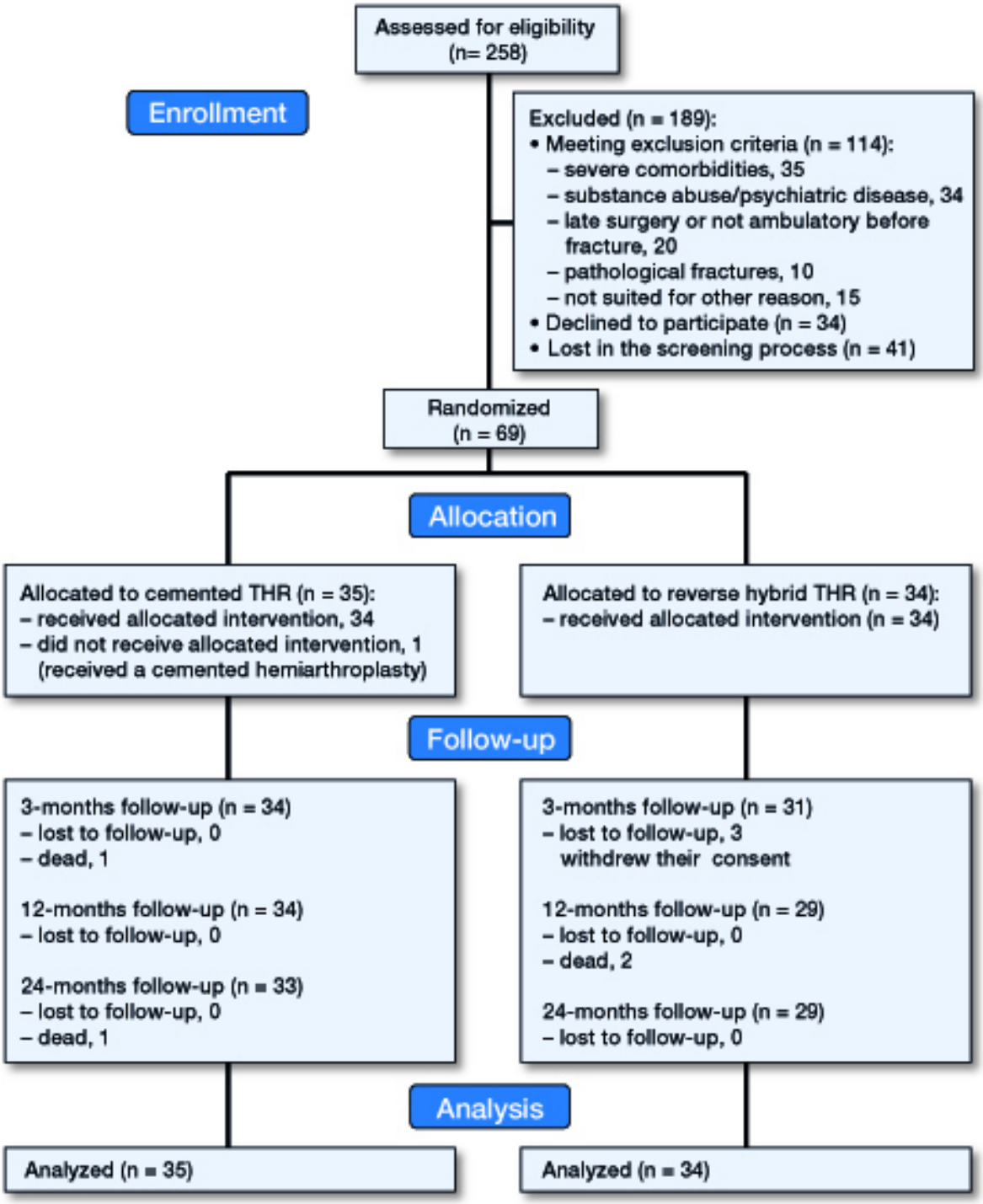


**Table 5:** Baseline data for all patients included in the study. Values indicate the number of patients or the mean, with standard deviations or ranges in parentheses.

| | **Cemented (n=35)** | **Uncemented (n=34)** |
|---|---|---|
| **Sex (n)** | | |
| Female | 22 | 25 |
| Male | 12 | 10 |
| **Age, mean (SD)** | 72 (4) | 73 (5) |
| **ASA (n)** | | |
| 1-2 | 26 | 17 |
| 3-4 | 9 | 17 |
| **BMI** | 23 (17-38) | 24 (20-34) |
| **Type of femur preoperatively (n)** | | |
| Dorr Type A | 12 | 5 |
| Dorr Type B | 19 | 27 |
| Dorr Type C | 4 | 2 |

**Table 6:** Operative data. Variables are presented as the mean, standard deviation and 95% confidence interval.

| **Outcome measure** | **Cemented (n=35)** | **Uncemented (n=34)** | **Mean difference** |
|---|---|---|---|
| Surgery time (min) | 111 (24) | 98 (20) | 13 (2 to 24) |
| Peri-operative bleeding (mL) | 453 (241) | 485 (287) | -32 (-169 to 104) |
| Change in systolic BP during stem insertion (mmHg) | -4 (8) | -3 (5) | -1 (-5 to 3) |
| Change in pulse oximetry (%) | 0 (2) | 0 (2) | 0 (-1 to 1) |

**Table 7:** Complications and reoperations. All complications and reoperations are counted; therefore, more than one complication or reoperation may apply for each hip.

| **Complications** | Cemented group (n=35) | Uncemented group (n=34) |
|---|---|---|
| Dislocation | 1 | 3 |
| Peri-prosthetic fracture intra-operative | 0 | 3 |
| Late Peri-prosthetic fracture | 0 | 1 |
| Superficial infection | 0 | 1 |
| Unstable stem | 0 | 1 |
| Total number of hip complications | 1 | 9 |
| Number of patients with any complication | 1 (3%) | 7 (21%) |
| **Additional treatment*/reoperation** | | |
| Plate fixation because of intra-operative peri-prosthetic fracture | 0 | 1 |
| Cerclage wires inserted because of intra-operative peri-prosthetic fracture | 0 | 2 |
| Closed reduction | 1 | 1 |
| Open reduction | 0 | 1 |
| Stem revision | 0 | 3 |
| Total number of hips requiring additional treatment during the primary surgery | 0 (0%) | 3 (9%) |
| Total number of hips with any major reoperation | 0 (0%) | 4 (12%) |

* Extra resources during the primary surgery because of some complication

No. (%) is presented

**Table 8:** Functional outcomes. Variables EQ-5D, HHS and PNRS are presented as the mean, standard deviation and 95% confidence interval. ADL is presented with proportion of patients with fully independent activities of daily living according to the treatment.

| Outcome measure | Cemented | Uncemented | Mean difference (95% CI) |
|---|---|---|---|
| **EQ-5D** | | | |
| Baseline | 0.8 (0.3) (n=35) | 0.8 (0.3) (n=32) | -0.00 (-0.2 to 0.1) |
| At 3 months | 0.7 (0.3) (n=34) | 0.7 (0.2) (n=30) | -0.00 (-0.2 to 0.1) |
| At 12 months | 0.8 (0.2) (n=33) | 0.8 (0.3) (n=29) | -0.00 (-0.2 to 0.9) |
| At 24 months | 0.7 (0.3) (n=30) | 0.8 (0.2) (n=26) | -0.03 (-0.2 to 0.1) |
| **HHS** | | | |
| Baseline | 93 (10) (n=35) | 91 (11) (n=32) | 2 (-3 to 7.1) |
| At 3 months | 73 (12) (n=34) | 72 (14) (n=31) | 1 (-6 to 7.2) |
| At 12 months | 79 (19) (n=34) | 82 (15) (n=31) | -3 (-11 to 5.7) |
| At 24 months | 80 (17) (n=34) | 81 (16) (n=30) | -1 (-9 to 10) |
| **ADL** | | | |
| Baseline | 100% (35/35) | 100% (34/34) | |
| At 3 months | 94% (32/34) | 94% (29/31) | |
| At 12 months | 90% (30/33) | 93% (28/30) | |
| At 24 months | 94% (29/31) | 93% (26/28) | |
| **PNRS** | | | |
| Baseline | 0.3 (1.5) (n=35) | 0.6 (1.6) (n=32) | -0.3 (-1 to 0.4) |
| At 3 months | 2.2 (1.0) (n=34) | 3.0 (2.4) (n=30) | -0.9 (-2 to 0.2) |
| At 12 months | 2.1 (2.4) (n=32) | 1.1 (1.5) (n=29) | 1 (-09 to 2) |
| At 24 months | 2.1 (2.3) (n=31) | 1.3 (1.9) (n=2) | 0.8 (-0.3 to 1.8) |

**Table 9**: Serological markers. Variables are presented as the mean, standard deviation and 95% confidence interval.

| Outcome measure | Cemented (n=35) | Uncemented (n=34) | Mean difference (95% CI) |
|---|---|---|---|
| **D-dimer** | | | |
| Preop | 3.9 (3.2) (n=29) | 3.4 (3) (n=27) | 0.5 (-1.1 to 2.2) |
| POD1* | 0.7 (0.84) (n=31) | 0.7 (.086) (n=31) | 0.03 (-0.4 to 0.5) |
| POD4* | 1.4 (4.9) (n=25) | 0.5 (0.18) (n=25) | 0.9 (-1 to 2.8) |
| At 3 months | 0.8 (0.7) (n=23) | 0.6 (0.3) (n=22) | 0.25 (-0.9 to 0.6) |
| **CRP** | | | |
| Preop | 14 (28) (n=35) | 29 (59) (n=33) | -16 ( -38 to 8) |
| POD1* | 120 (61) (n=32) | 122 (61) (n=31) | -2 (-33 to 28) |
| POD4* | 202 (88) (n=28) | 235 (64) (n=27) | -33 (-75 to 9) |
| At 3 months | 10 (23) (n=26) | 5 (6) (n=24) | 5 (-5- to 15) |

*POD: Post-operative day

**Table 10**: Radiological outcomes.

| Heterotopic Ossification at the 24-month follow up | Cemented (n=33) | Uncemented (n=28) |
|---|---|---|
| Grade 0 | 4 | 4 |
| Grade 1 | 16 | 13 |
| Grade 2 | 8 | 4 |
| Grade 3 | 2 | 7 |
| Grade 4 | 3 | 0 |

## STUDY III

### Patient flow and baseline data

Between September 2009 and March 2016, 966 patients with displaced FNF were admitted to the Orthopaedic Department at Danderyd Hospital. Of these, 120 patients met the inclusion criteria and were recruited to participate in the study (Figure 11). The study group included 90 women and 30 men with a mean age of 86 years (range, 80-94). 60 patients were randomized to the HA group and 60 were randomized to the THA group. All subjects received their allocated treatment except one subject who was allocated to THA but was operated with closed reduction and IF with 2 screws because of urosepsis. Regarding hip complications and reoperations, we could follow up all patients, including the 9 patients who refused to attend their clinical follow-up visits. The baseline data characteristics of the two groups are presented in Table 11, and differences are not observed with regard to sex, age, BMI and functional class according Charnley. However, two-thirds of the patients in the HA group presented ASA 3-4, whereas half of the patients in the THA group presented ASA 3-4.

### Operative data

The mean surgery time was 22 minutes shorter in the HA group, and this difference was statistically significant (p=0.001). Significant differences in preoperative bleeding were not observed. Table 11 shows the operative data. 26 patients in the HA group and 23 patients in the THA group were operated with the CPT stem. The remaining patients were operated with the SP2 stem.

### Primary endpoints

Differences in hip function or HRQoL were not observed between the groups up to one year after surgery (Table 12). The HHS significantly deteriorated in both groups, whereas the EQ-5D scores deteriorated only in the THA group, although this deterioration was not statistically significant.

### Secondary endpoints

Statistically significant differences were not observed in the prevalence of all hip-related complications and reoperations up to one year postoperatively. We found 4 complications in every group. In the HA group, one single dislocation and three deep peri-prosthetic infections were observed, whereas in the THA group, three superficial infections and one non-union were observed. The patient who was operated with closed reduction and IF developed non-union and underwent a major reoperation with THA. Two of three patients in the HA group

who suffered deep peri-prosthetic infection were treated surgically, whereas the third was treated conservatively with antibiotics for three months. The surgical procedure was the one–stage revision involving surgical debridement, removal of the prosthesis and re-cementing of a new implant. Table 13 shows the hip-related complications, reoperations and general complications during the study period. Differences in ADL and pain scores were not observed between the groups during the follow-up period. However, both of these scores deteriorated in both groups. No difference in mortality was found. Four patients, with 2 in each group, died during the study. No deaths occurred during surgery.

Two patients in each group were bedridden or wheelchair bound at the one-year follow-up visit. The ability to regain their previous walking function was diminished over the duration of the study period, with 47% (26/55) and 42% (24/57) of the patients in the HA and THA group able to regain their previous walking function, respectively. The mean deterioration in walking distance was statistically significant in both groups, and differences were not observed between the groups. The mean deterioration in walking distance according to the HHS was -2.2 (CI 95% -3.2 to -1.3; $p<0.001$) in the HA group and -2.4 (CI 95% -3.4 to -1.5; $p<0.001$) in the THA group.

**Figure 11:** Flow of the patients in study III.

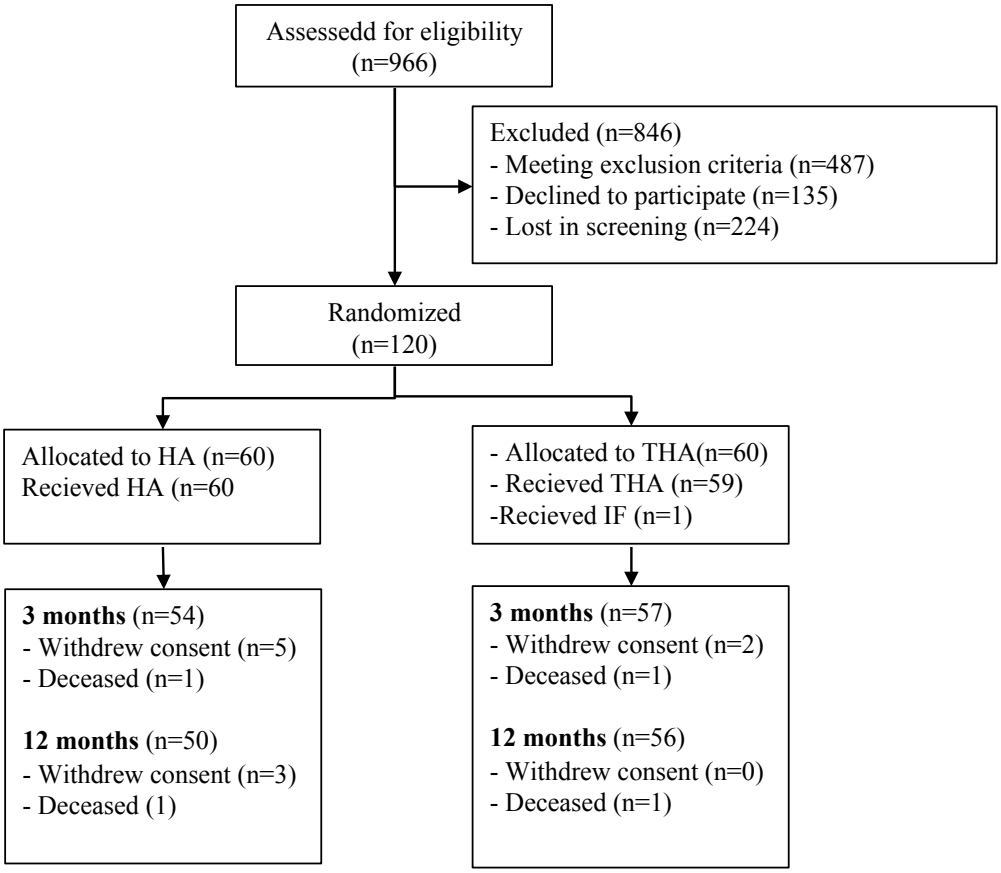


**Table 11:** Baseline data for all patients included in study III. Values indicate the number of patients or the mean and standard deviation with percentages in parentheses

| | HA (n=60) | THA (n=60) |
|---|---|---|
| **Sex (n)** | | |
| Female | 45 | 45 |
| Male | 15 | 15 |
| **Age** | 86±4 | 85±4 |
| **ASA** | | |
| 1-2 | 20 | 30 |
| 3-4 | 40 | 30 |
| **BMI** | 25±4 | 24±4 |
| **Functional class according to Charnley** | | |
| A | 50 | 46 |
| B | 4 | 9 |
| C | 6 | 5 |
| **Mobility:** No walking aid or just one stick (%) | 29 (48%) | 30 (50%) |
| **Living condition** | | |
| Independent living | 57 | 58 |
| Service buildings/senior housing | 3 | 2 |
| **Operative data** | | |
| Surgery time | 77±19 | 99±25 |
| Bleeding | 324±216 | 355±202 |
| **Discharged to geriatric ward** | 52 | 53 |

**Table 12:** Differences in functional outcomes between the two groups during the study period. Variables are presented as the mean, standard deviation 95% confidence interval. ADL is presented with proportion of patients with fully independent activities of daily living according to the treatment. P-values were derived from Student´s T-test for Variables EQ-5D, HHS, and PNRS, and from Chi-Square test for ADL variable.

| | **HA** (n=60) | **THA** (n=60) | **Mean difference (95% CI)** | **P-value** |
|---|---|---|---|---|
| **EO-5D** | | | | |
| Baseline | 0.67±0.34(n=59) | 0.75±0.26(60) | -0.08(-0.19 – 0.02) | 0.135 |
| At 3 months | 0.67±0.24(n=54) | 0.65±0.26(57) | 0.02(-0.07 – 0.11) | 0.664 |
| At 12 months | 0.66±0.27(n=50) | 0.68±0.30(56) | -0.0(-0.13 – 0.09) | 0.711 |
| **HHS** | | | | |
| Baseline | 88±12(n=59) | 89±10(60) | -1 (-5 – 3) | 0.648 |
| At 3 months | 69±14(n=54) | 70±13(57) | -1 (-6 – 4) | 0.718 |
| At 12 months | 71±16(n=50) | 74±16(56) | -3(-9 – 3) | 0.331 |
| **PNRS** | | | | |
| Baseline | 0.4±1.6(n=59) | 0.38±1.3(60) | -0.01(-0.54 – 0.52) | 0.969 |
| At 3 months | 2.3±1.9(n=54 | 1.9±1.7(57) | 0.33(-0.35 – 1) | 0.344 |
| At 12 months | 1.6±1.8(n=50) | 1.3±1.8(56) | 0.31(-0.39 – 1) | 0.310 |
| **ADL** | | | | |
| Baseline | 90%(53/59) | 93%(56/60) | | 0.440 |
| At 3 months | 69%(37/54) | 68%(39/57) | | 0.447 |
| At 12 months | 68%(34/50) | 64% (36/56) | | 0.626 |

**Table 13:** Complications and reoperation up to 1 year after surgery.

| **Complication** | **HA (n=60)** | **THA (n=60)** |
|---|---|---|
| Dislocation | 1 | 0 |
| Superficial infection | 0 | 3 |
| Deep peri-prosthetic infection | 3 | 0 |
| Non-healing fracture | 0 | 1 |
| Total number of hip complication | 4 | 4 |
| Number of patients with any hip complication | | |
| **Reoperation** | | |
| Closed reduction | 1 | 0 |
| Surgical debridement and one-stage revision | 2 | 0 |
| Another major reoperation | 0 | 1 |
| Total number of major reoperation | 2 | 1 |
| **General complications** | | |
| Pneumonia | 7 | 4 |
| Pulmonary embolism | 1 | 1 |
| Myocardial infarct | 1 | 2 |
| Cerebral vascular lesion (CVL) | 3 | 6 |
| Acute kidney failure | 0 | 1 |

## STUDY IV

### Patient flow and baseline data

A total of 966 patients were screened during the inclusion period, and 160 were recruited to participate in the study (Figure 12). The characteristics of the groups and the surgical data were similar at baseline, although the patients in the cognitive dysfunction group had lower functional outcome scores, a lower HRQoL and a shorter walking distance at baseline than the control group. Because the majority of patients in the cognitive dysfunction group were in nursing homes with staff available around the clock prior to the fracture, they were sent back to their nursing home. Only 38% of the patients in the cognitive dysfunction group received rehabilitation at a geriatric ward after surgery (Table 14).

### Hip complications and reoperations:

During the study period, twelve patients (8%) suffered at least one hip-related complication. Although the overall major reoperation rate was slightly higher in the cognitive dysfunction group than in the controls (6% versus 3%), this difference failed to reach statistical significance (Table 15). The results were unchanged after using of competing risk analysis. Two patients in the cognitive dysfunction group with recurrent dislocation were treated twice with closed reduction before revision surgery with a THA. Three peri-prosthetic fractures occurred in the cognitive dysfunction group in patients who had received a tapered CPT stem. All three were treated with open reduction and IF. Four patients, with three in the control group and one in the cognitive dysfunction group, suffered peri-prosthetic joint infections. Three were treated surgically, and one patient in the control group was treated conservatively with an antibiotic for three months. The surgical treatment was a one-stage revision involving surgical debridement, prosthesis removal and re-cementing a new implant.

### Walking ability

At the three-month follow-up after arthroplasty, 13% (10/75) of the surviving patients in the cognitive dysfunction group and 2% (1/54) in the control group were either confined to bed or in a wheelchair ($p=0.024$, Fisher's exact test). At one year, the proportion had increased to 31% (19/61) in the cognitive dysfunction group and 5% (2/50) in the control group (OR: 10.9; 95% CI: 2 to 49; $p<0.001$, Fisher's exact test). The capacity to return to preoperative walking ability was diminished over the study duration; 51% (37/73) of the patients in the cognitive dysfunction group and 47% (26/55) of patients in the control group returned to their previous walking ability ($p=0.86$, Fisher's exact test). Those patients in the cognitive dysfunction group who did not receive geriatric rehabilitation were almost nine times more

likely to be confined to a wheelchair or bedridden despite having no pain in the involved hip (OR: 8.8; 95% CI: 2.3 to 32.9; Table 16). The results were unchanged after the regression analysis and sensitivity analysis using multiple imputations. The geriatric rehabilitation programme and the presence of cognitive dysfunction (to a lesser extent) seemed to be the only two factors that influenced the loss of walking ability (Table 16).

**Mortality**

No sudden death related to cement implantation syndrome occurred during surgery. The cognitive dysfunction group had a higher mortality rate than the control group at one year at 35% (n=35) versus 4% (n=2), respectively.

**Functional outcomes**

All functional outcomes were better in the control group than the cognitive dysfunction group at baseline. The mean HRQoL remained unchanged from baseline throughout the study period in both groups, and the largest decline in HHS at one year occurred in the control group (Table 17, Figure 13). The mean PNRS increased significantly in the control group, and the initial significant difference between the groups was reduced during the study period (Table 17). The ADL deteriorated in both groups, and the initial difference in ADL between the two groups was maintained throughout the study period (Table 17). Those patients in the cognitive dysfunction group who did not receive geriatric rehabilitation had worse outcomes for HRQoL and hip function (Figure 14). The linear regression analysis shows that the presence of cognitive dysfunction, the status of geriatric rehabilitation and the pre-fracture value were the only factors that affected the HRQoL and hip function (Table 17).

**Adverse events**

Six patients (11%) in the control group and seven (7%) in the cognitive dysfunction group suffered pneumonia and required treatment during the study period. One patient (2%) in the control group and two (2%) in the cognitive dysfunction group suffered a pulmonary embolism and were treated with warfarin for six months. One patient in the control group suffered a myocardial heart infarct. During the study period, three (5%) patients in the control group and five (5%) in the cognitive dysfunction group suffered cerebral vascular lesion (CVL), and one patient in the cognitive dysfunction group had a DVT. No other general complications were identified during the study period.

**Figure 12: Flow of the patients in study IV**

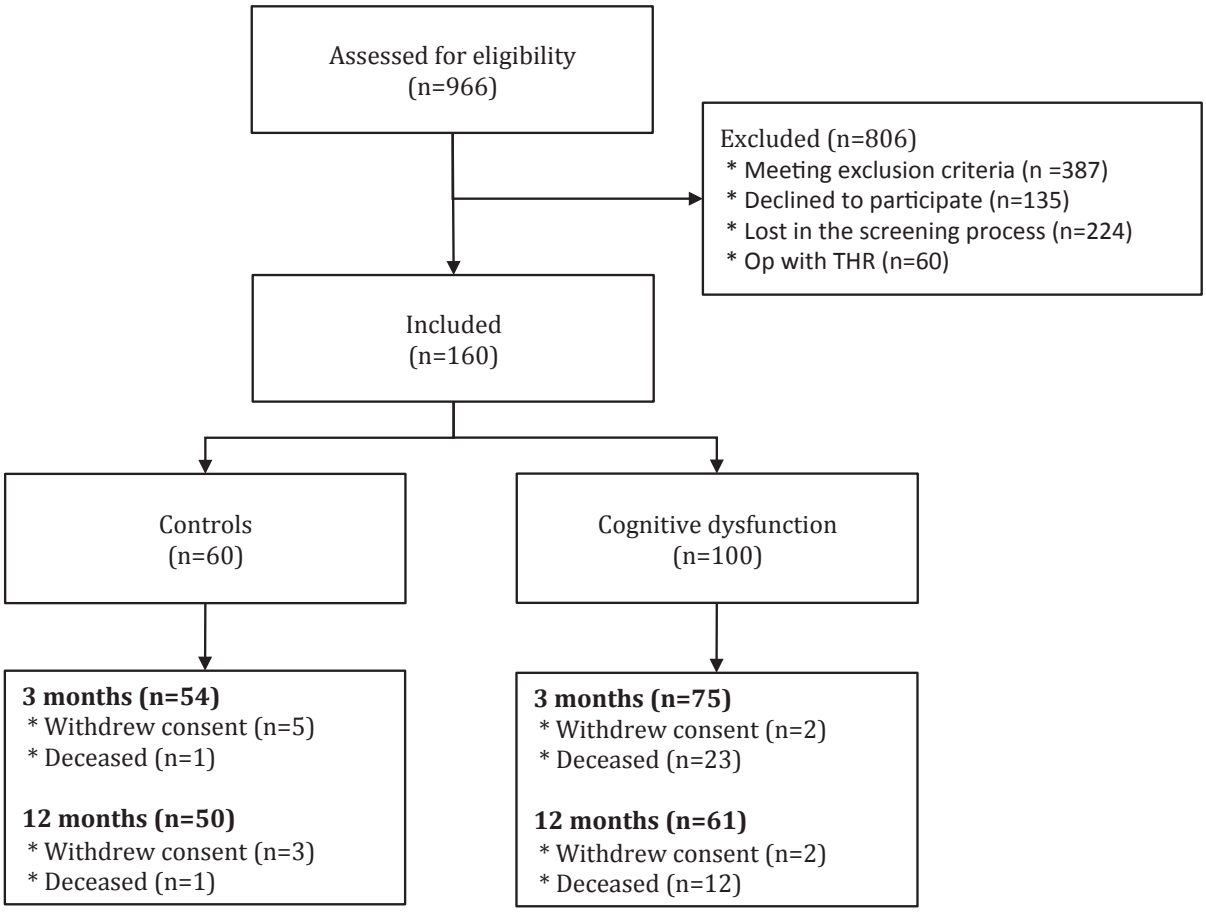


**Table 14**: Baseline data for all patients included in study IV. Numerical variables are presented as the mean and standard deviation, and categorical variables are presented as numbers with percentages.

| | Control group (n = 60) | Cognitive dysfunction group (n = 100) |
|---|---|---|
| Sex (n) | | |
| Female | 45 | 72 |
| Male | 15 | 28 |
| Age (years) | 86 ± 4 | 86 ± 6 |
| Cognitive status (SPMSQ) | | |
| Normal (8-10) | 60 | 0 |
| Mild-moderate dysfunction (3-7) | 0 | 10 |
| Severe cognitive dysfunction (0-2) | 0 | 90 |
| ASA (n) | | |
| 1-2 | 20 | 24 |
| 3-4 | 40 | 76 |
| BMI ($kg/m^2$) | 25 ± 4 | 23 ± 4 |
| Functional class according to Charnley (n) | | |
| A | 50 | 77 |
| B | 4 | 18 |
| C | 6 | 5 |
| Living conditions (n) | | |
| Independent living | 57 | 34 |
| Nursing home | 3 | 66 |
| Surgery time (min) | 77 ± 18 | 82 ± 22 |
| Bleeding (mL) | 329 ± 214 | 311 ± 140 |
| Discharged to geriatric ward (n) | 53 (88%) | 38 (38%) |
| Walking distance according to Harris Hip Score (Question 4; n) | | |
| Less than 0.5 km | 13 (22%) | 59 (61%) |
| 0.5-1 km | 8 (14%) | 22 (23%) |
| 1-2 km | 5 (8%) | 10 (10%) |
| More than 2 km | 33 (56%) | 6 (6%) |

**Table 15:** Complications and reoperation up to 1 year after surgery.

| **Complications** | **Control group (n=60)** | **Cognitive dysfunction group (n=100)** |
|---|---|---|
| Dislocation | 1 | 2 |
| Peri-prosthetic fracture | 0 | 3 |
| Superficial infection | 0 | 2 |
| Deep infection | 3 | 1 |
| Total number of hip complication | 4 | 8 |
| Number of patients with any hip Complication | 4 (7%) | 8 (8%) |
| **Reoperation** | | |
| Closed reduction of dislocation | 1 | 2 |
| Revision to total hip arthroplasty | 0 | 2 |
| Open reduction and internal of Peri-prosthetic fracture | 0 | 3 |
| Surgical debridement and one-stage revision | 2 | 1 |
| Total number of patients who underwent at least one reoperation | 3 | 6 |
| **Total number of any reoperation** | **3** | **10** |
| **Total number of major reoperation*** | **2 (3%)** | **6 (6%)** |

Complications: OR, 1.21 (95% CI, 0.35 to 4.2), p=1.00

Major reoperation: OR, 1.85 (95% CI, 0.36- to 9.5), p=0.71

Major reoperations were defined as the revision of total hip arthroplasty, open reduction and internal fixation and surgical debridement with one-stage revision

**Table 16:** Crude, adjusted and multiple imputation logistic and linear regression for outcomes at the 1-year follow-up visit. In the logistic regression model, the number of patients at risk and events at 1 year are presented for dichotomous variables. The models are adjusted by group, age, sex, and whether the patients were admitted to geriatric rehabilitation after surgery. All outcomes were also adjusted by their pre-fracture status, i.e., the pre-fracture HHS was used as a co-variate in the model for the Harris hip score at 1 year.

| | | | Crude | | Adjusted | | | Adjusted with MI | |
|---|---|---|---|---|---|---|---|---|---|
| **Variable** | **n** | **Event** | **Est.** | **95% CI** | **Est.** | **95% CI** | **P-** | **Est.** | **95% CI** |
| | | | | **Logistic regression (odds ratio)** | | | | | |
| **Confined to wheelchair/unable to walk 1 year** | | | | | | | | | |
| Group | | | | | | | | | |
| Controls | 50 | 2 (4%) | | Ref. | | Ref. | | | Ref. |
| Cognitive dysfunction | 61 | 19 (31%) | 10.1 | 2.4 – 49.3 | 4.2 | 0.7 – 23.0 | 0.1 | 3.3 | 0.5 – 8.1 |
| Geriatric rehab | | | | | | | | | |
| Yes | 73 | 4 (6%) | | Ref. | | Ref. | | | Ref. |
| No | 38 | 17 (45%) | 14.0 | 4.2 – 46.1 | 8.8 | 2.3 – 32.9 | 0.001 | 4.1 | 1.2 – 14.4 |
| Sex | | | | | | | | | |
| Female | 87 | 17 (20%) | | Ref. | | Ref. | | | Ref. |
| Male | 24 | 4 (17%) | 0.8 | 0.2 – 2.7 | 2.4 | 0.5 – 12.2 | 0.3 | 1.6 | 0.1 – 16.4 |
| Pre-fracture walking ability | | | 0.8 | 0.7 – 0.9 | 0.9 | 0.7 – 1.1 | 0.2 | | |
| Age | | | 1.0 | 0.9 – 1.1 | 0.9 | 0.8 – 1.1 | 0.3 | 0.9 | 0.9 – 1.1 |
| | | | | **Linear regression (units)** | | | | | |
| **Health-related quality of life (EQ-5D) index** | | | | | | | | | |
| Group | | | | | | | | | |
| Controls | | | | | | | | | |
| Cognitive dysfunction | | | -0.40 | -0.51 – -0.29 | -0.18 | -0.30 – -0.06 | 0.005 | -0.19 | -0.30 – -0.07 |
| Geriatric rehab | | | | | | | | | |
| No | | | | Ref. | Ref. | | | Ref. | |
| Yes | | | 0.42 | 0.31 – 0.55 | 0.25 | 0.13 – 0.37 | < 0.001 | 0.25 | 0.11 – 0.38 |
| Sex | | | | | | | | | |
| Female | | | Ref. | | Ref. | | | Ref. | |
| Male | | | -0.05 | -0.22 – 0.11 | 0.10 | -0.02 – 0.22 | 0.11 | 0.12 | 0.25 – 0.42 |
| Pre-fracture EQ-5D | | | 0.57 | 0.42 – 0.73 | 0.32 | 0.16 – 0.49 | < 0.001 | 0.30 | 0.08 – 0.51 |
| Age | | | -0.01 | -0.02 – 0.01 | -0.01 | -0.02 – 0.01 | 0.2 | -0.01 | -0.02 – 0.01 |
| **Hip function (HHS)** | | | | | | | | | |
| Group | | | | | | | | | |
| Controls | | | | Ref. | | Ref. | | | Ref. |
| Cognitive dysfunction | | | -2.5 | -8.5 – 3.5 | 6.2 | -0.2 – 12.5 | 0.06 | 4.7 | -1.3 – 10.7 |
| Geriatric rehab | | | | | | | | | |
| No | | | | Ref. | | Ref. | | | Ref. |
| Yes | | | 11.2 | 5.3 – 17.1 | 11.8 | 5.4 – 18.3 | < 0.001 | 7.7 | 1.4 – 13.9 |
| Sex | | | | | | | | | |
| Female | | | | Ref. | | Ref. | | | Ref. |
| Male | | | -4.2 | -11.4 – 3.0 | -0.4 | -7.2 – 6.4 | 0.9 | -1.3 | -8.4 – 5.8 |
| Pre-fracture HHS | | | 0.4 | 0.2 – 0.5 | 0.3 | 0.2 – 0.5 | 0.001 | 0.3 | 0.1 – 0.5 |
| Age | | | -0.3 | -1.0 – 0.3 | -0.1 | -0.6 – 0.5 | 0.9 | -0.1 | -0.9 – 0.6 |

**Table 17:** Functional outcomes during the study period. Variables are presented as the mean, standard deviation 95% confidence interval. ADL is presented with proportion of patients with fully independent activities of daily living according to the treatment. P-values were derived from Student´s T-test for Variables EQ-5D, HHS, and PNRS, and from Chi-Square test for ADL variable.

| Functional outcome | Control group (n=60) | Cognitive dysfunction group (n=100) | Mean difference (95% CI) | P-value |
|---|---|---|---|---|
| **EQ-5D** | | | | |
| Baseline | 0.67±0.34 (n=59) | 0.27±0.28 (n=96) | 0.4 (0.28-0.48) | <0.001 |
| At 3 months | 0.67±0.24 (n=54) | 0.24±0.3 (n=71) | 0.43 (0.33-0.53) | <0.001 |
| At 12 months | 0.66±0.27 (n=50) | 0.25±0.32 (n=57) | 0.41 (0.3-0.53) | <0.001 |
| **HHS** | | | | |
| Baseline | 88±12 (n=59) | 78±15.7 (n=97) | 10 (5 - 14) | <0.001 |
| At 3 months | 69±14 (n=54) | 61±17 (n=76) | 8 (2-13) | <0.007 |
| At 12 months | 71±16 (n=50) | 69±16 (n=61) | 2 (-4-8) | 0.528 |
| **PNRS** | | | | |
| Baseline | 0.4±1.6 (n=59) | 1.3±2.2 (n=93) | -0.9 (-1.5--0.3) | 0.004 |
| At 3 months | 2.3±1.9 (n=54) | 2.1±2.2 (n=69) | 0.2 (-0.6-0.9) | 0.711 |
| At 12 months | 1.6±1.8 (n=50) | 1.3±2 (n=57) | 0.3 (-0.5-1) | 0.46 |
| **ADL** | | | | |
| Baseline | 90% (53/59) | 13% (13/100) | | <0.001 |
| At 3 months | 69% (37/54) | 7% (5/73) | | <0.001 |
| At 12 months | 68% (34/50) | 7% (4/58) | | <0.001 |

**Figure 13.**

Line graph illustrating the mean (and 95% CI) hip function, health-related quality of life and pain scores during the study. Solid lines represent the control group, and dotted lines are the cognitive dysfunction group. HHS=Harris hip score. PNRS=Pain numerical rating scale. EQ-5D=European Quality of life five dimensions.

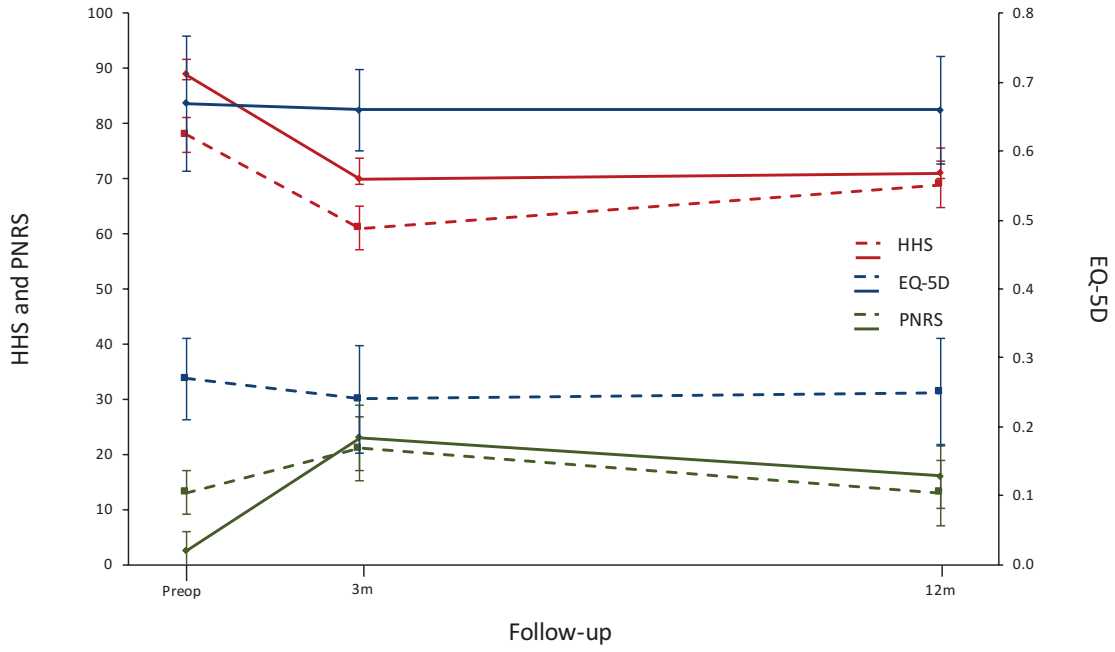
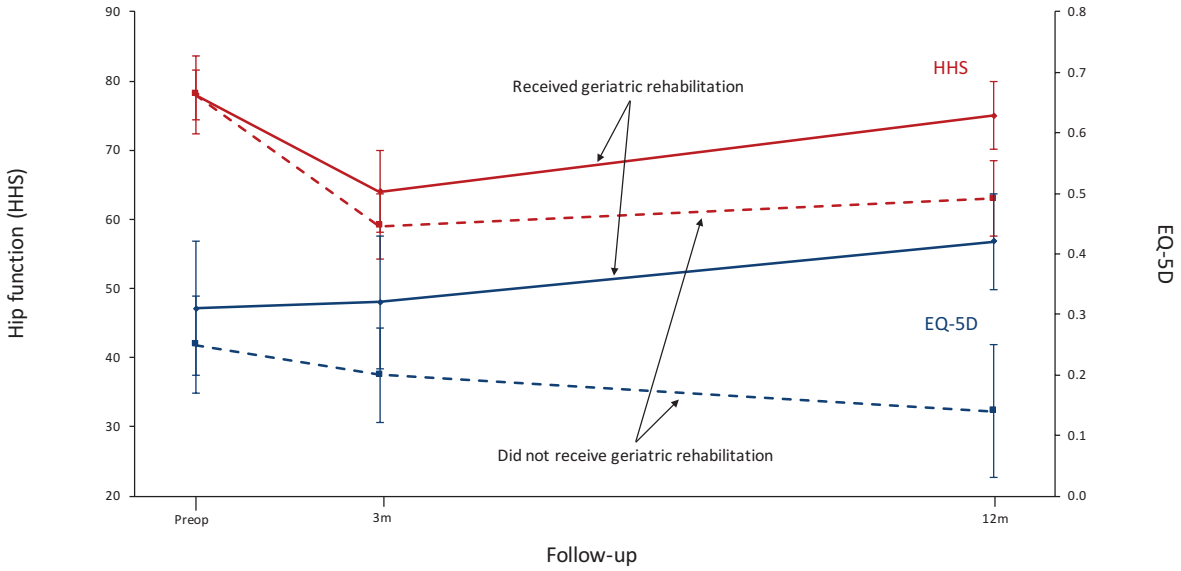


**Figure 14.**

Line graph illustrating the mean (and 95% confidence interval) hip function and health-related quality of life for patients in the cognitive dysfunction group who received and did not receive structured geriatric rehabilitation after surgery. HHS=Harris hip score. EQ-5D=European Quality of life five dimensions.



# GENERAL DISCUSSION

The overall purpose of this thesis was to define the optimal treatment for elderly patients with a displaced FNF with consideration of age, functional demands and cognitive function by investigating the clinical outcomes, which are based on the functional and surgical outcomes, after treatment of a displaced FNF with IF and hip arthroplasty. The results presented in this thesis indicate that cemented THA provides better hip function and significantly fewer complications and reoperations than IF in a group of healthy elderly patients with a displaced FNF over a long-term follow-up period of seventeen years. The results also indicate the occurrence of more complications with uncemented than with cemented stems in THA for a displaced FNF in elderly patients in the short-term follow up. The recent shift towards using cemented HA in elderly patients with a displaced FNF is reflected in the findings in this thesis, especially in studies III and IV.

## LONG-TERM RESULTS OF TOTAL HIP ARTHROPLASTY

During the first phase after the introduction of arthroplasty as a treatment option for displaced FNFs, the supporters of IF argued that the new method might lead to the need for additional revisions of arthroplasty over the long term because of aseptic loosening and peri-prosthetic fractures.

In study I, we evaluated the outcomes at eleven and seventeen years after enrolment, thus providing long-term data for fracture treatment that are rarely available, particularly in a randomized study design. The basic conclusion was that in active patients above 65 years of age, THA is superior to IF. This conclusion would have been ground-breaking and controversial in the early 1990s when this study began enrolling patients. This conclusion is now well known and accepted based on many studies published during the prolonged follow-up period of this study. Despite the early follow-up evidence that THA has fewer complications, clinicians remained concerned about this treatment because of the possibility of an increased incidence of late failure as a result of loosening and peri-prosthetic fracture compared with successful IF with a preserved native femoral head. This study addresses this concern by clearly showing that the high early failure rate after IF is not completely offset by late failures after THA and provides further strong evidence that THA is the best and most long-lasting option for the treatment of FNF in patients over sixty-five years of age with excellent pre-existing hip function. During the prolonged follow-up period of this study, three log-term follow-up studies have been published comparing THA with IF [44, 49, 56]. These studies included a greater number of patients than that in our study. Ravikumar and Marsh [49] evaluated hip function using the HHS and found that THR yielded a superior result over

IF at thirteen years. In a 10-years follow-up study, Leonardsson et al. [44] concluded that primary replacement provided reliable long-term results in patients with displaced fracture of the femoral neck. Johansson [56] did not use any patient-reported outcomes (PROs). In terms of complications and revision surgery, Ravikumar and Marsh, Leonardsson et al. and Johansson reported revision rates of 6.8%, 8.8%, and 5.0% for THA and 33%, 46.6% and 55% for IF, respectively. These results are consistent with our findings. The secondary outcome measurements favoured the group treated with THA, although a difference in mortality was not observed between the groups. Patients who were managed with THA also had less pain in the involved hip over the long term.

Since the early 1990s when this study was initiated, many improvements have been observed in total hip replacement that have increased the implant life span and reduced the risk of complications and need for revision surgery. The posterior lateral approach was used in this study without capsular repair. The posterior lateral approach has been linked to an increased risk for dislocation and revision surgery compared with the direct lateral approach [68, 69, 106-109]. The use of larger femoral head sizes (32-36 mm) has been shown to reduce the need for revision surgery because of dislocation [106]. A 28-mm head was used in this study.

The cemented, straight, polished and tapered femoral stem of the titanium alloy used in this study is a less-than-optimal cemented femoral component. Studies have shown superior results with a reduced incidence of aseptic loosening for cobalt-chromium stems compared with that of titanium alloy stems when used with bone cement [139, 140]. Two recent studies examining the prevalence of peri-prosthetic fractures in elderly patients who received stems similar to those used in our study indicated an increased risk of peri-prosthetic fracture [141, 142]. The cemented, straight, polished and tapered femoral stem of the titanium alloy used in this study is no longer used at our institution. However, the incidence of aseptic loosening of the prosthesis or peri-prosthetic fracture in this study did not exceed the rates in previously reported long-term studies of patients with osteoarthritis [143, 144]. The above-mentioned improvements have most certainly increased the differences in PRO and reoperation rates between primary THA and IF. The age limit of 65 years was used to differentiate young and elderly patient as well as the patients who underwent IF or THA in study I. This consideration was implemented in the early 1990s when study I began enrolling patients. As the longevity and level of activity of today's elderly increases, it is advisable to raise the age limit to 70 years.

## TREATMENT CHOICE

### Cemented or uncemented implants

The uncemented prosthesis was used earlier in time than the cemented prosthesis (Moore 1952). Previous comparisons in the treatment of FNFs have almost consistently favoured cemented fixation, which is mainly because of the better mobility, lower rates of peri-prosthetic fractures and revision, and reduced thigh pain, without increasing post-operative complications [81, 82]. Such results are based on studies comparing non-modular old-generation prostheses, such as Austin Moore and Thompson hip implants. Because good results have been achieved using modern hydroxyapatite-coated femoral stems in younger patients with osteoarthritis, the concept of inserting an uncemented femoral component in patients with displaced FNF has become popular for many surgeons [145]. The concern regarding intra-operative death caused by embolization of fat and bone marrow contents associated with cementation (BCIS) [146] is the principal argument for using uncemented implants.

In study II, we compared the effectiveness and safety between a modern cemented and a modern uncemented hydroxyapatite-coated femoral stem in patients 65–79 years of age who were treated with THA for displaced FNF. We found a higher risk of peri-prosthetic fractures and reoperations with the use of a reverse-hybrid THA than with the use of a cemented THA. Our trial did not have the statistical power to address the possible adverse effects of cement, and we did not find any indications of differences in mortality between the groups related to cementing. However, all thrombotic events occurred in the cemented group. The incidence of serious cement-related complications has been reported to be low [86], and a trial examining this would require several thousand patients. Despite this challenge, reports have indicated that peri-operative cardiovascular disturbances are more frequent in elderly patients with hip fracture when cemented rather than uncemented stems are used [147]. Previous investigations of outcomes after modern cemented and uncemented fracture-related arthroplasties are sparse, and several of the earlier trials are either of poor methodological quality or assess implants that are no longer frequently used [70, 148-150].

When we started this study, in addition to a pilot study in our clinic, on a modern hydroxyapatite-coated uncemented stem indicated that the uncemented stem could be used for elderly patients with osteoporotic fractures of the femoral neck without increasing the complication rate [84], only 12-month results were available from a RCT comparing HA using a modern modular cemented stem and HA using an uncemented hydroxyapatite-coated

stem for the treatment of FNF [83], and they did not show differences between the groups regarding complications, including peri-prosthetic fracture. Therefore, we found that it was justified to continue with this study. During the course of the study, results from six RCTs and one pilot study using modern cemented and uncemented stems have been reported. These studies detected few differences regarding function and HRQoL between the groups. Four studies with short-term results supported the use of cemented implants because of higher early implant-related complication rates in the uncemented group, which were mostly because of intra-operative peri-prosthetic fractures [151-154], whereas one RCT [155] showed no differences between the groups. For the late peri-prosthetic fractures, evidence from the Swedish Hip Arthroplasty Register [68, 156], from a 5-year follow up of a RCT [157] and a pilot study [158] indicated that uncemented stems constitute a risk factor for such complications in the long term. Data from the Norwegian Hip Fracture Register at the five-year follow up showed that uncemented HA had a 2.1-time increased risk for revision compared with cemented prostheses [159]. A Finnish database study found that uncemented HA was associated with more frequent mechanical complications and reoperations [160].

In study II, no difference in mortality between the groups was found. Neither RCT [83, 151-155, 157] showed any differences in mortality between patients treated with cemented or uncemented stems, which may have been because the study groups were underpowered to evaluate mortality.

A study based on the Australian Orthopaedic Association National Joint Replacement Registry showed a high risk of death in patients with cemented implants on the first post-operative day. However, the mortality risk was higher between the first week and first year post-fracture in the uncemented group [161]. One reason for the reversion of the early increased mortality risk after cemented HA could be that the patients with uncemented implants had more reoperations and thus ran the risk of new complications and death as a consequence of repeated surgery.

An analysis of the Norwegian Hip Fracture Register also found a higher risk of death on the day of surgery and the first post-operative day in patients who received cemented HA, although after day two, the mortality rate was equivalent [162]. A Finnish database study also observed higher mortality in the cemented group until day 4 after surgery [160]. The National Patient Safety Agency in the United Kingdom in 2009 highlighted the risk of using bone cement in patients with hip fracture and encouraged the use of mitigation measures, including patient assessments and anaesthetic and surgical techniques [163]

However, a subsequent study from the National Hip Fracture Database in the United Kingdom showed no increase in peri-operative mortality as a result of cementing of the femoral component in patients with hip fracture [164]. Concise guidelines have been recently published in the United Kingdom after a national collaboration to advise anaesthetists and surgeons on the measures for reducing the risk of BCIS [165]. The risk of BCIS can be reduced by many measures, including the identification of patients at risk (e.g., the presence of comorbidities, including cardiovascular and respiratory disease is well documented [86, 166-169]), modified anaesthetic techniques [170] and the use of a pressurized lavage and suction catheter to reduce the embolic load and the intramedullary pressure during insertion of the cement [86, 171]. A reduction in intramedullary pressure has been reported to lead to a three-fold reduction in the rate of intra-operative mortality [86]. If the canal is adequately cleaned and the patient is properly prepared and monitored during the procedure, pressurization of the cement appears to confer no disadvantage in terms of risk and improves fixation of the femoral component [172].

The risk of intra- and peri-operative death, which is low [86, 90], must be weighed against the risk of peri-prosthetic fracture and reoperations. A second fracture and subsequent surgical procedure represent serious setbacks for elderly patients [173, 174].

Based on our results and those of others, we do not recommend the use of uncemented stems for the treatment of displaced FNF in elderly patients. For patients with high risk factors for intra- and peri-operative death, a discussion with the anaesthesiologist must occur. If the risk for intra-and peri-operative death is assessed to be very high, a suitable uncemented stem may be used as an exception to avoid inevitable death. Because the studies that have shown high intra-operative and early post-operative complications have used a direct anterior approach, which was mentioned in the discussion section for study II (see the discussion of study II), I recommend a posterior approach when using an uncemented stem.

**Total hip arthroplasty or hemiarthroplasty**

The aim of any surgical procedure for elderly patients with a displaced FNF is to return the patient to their previous functional status as soon as possible or provide a satisfactory functional status with minimal morbidity and minimal risk for re-surgery. Surgeons favouring THA over HA rely on the tendency for improved hip function and quality of life. In study III in this thesis, differences between the groups in favour of the HA group were not observed except the operation time. The absence of better HRQoL and functional outcomes in the THA group in study III compared with that of other studies [45, 72-76] may be explained by the

older age, lower mobility and limited demands for patients in study III compared with the healthy and relatively active patients in those studies.

Several reports have suggested that a higher risk of dislocation occurs with THA [71, 81, 175, 176], whereas others have found similar risks for both HA and THA [45, 74]. This inconsistency may be influenced by other factors, such as the surgical approach. The posterior lateral approach is linked to an increased risk of reoperation because of prosthetic dislocation in patients treated for osteoarthritis and FNF [105, 106]. The direct lateral approach has been proven to reduce the dislocation rate after hip arthroplasty compared with the posterior lateral approach [68, 69, 107, 108]. Dislocation was not observed in the THA group in study IV where the direct lateral approach was used. However, in study I in this thesis and in study [71], the posterior lateral approach was used.

The long-term wear of acetabular cartilage and the subsequent need for conversion of HAs to THAs is another reason why THA should be used in lucid healthy active elderly patients [73]. In study III, radiological measurements of erosion of the acetabular cartilage in patients treated with HA was not performed because we believe that 1 year is a short time for erosion to occur. We did not identify any erosion in the HA group because of increased pain in any hip during the one-year follow-up examination. This result is inconsistent with the study by Baker et al. [73], who found significantly lower hip function and a shorter self-reported walking distance in the HA group than the THA group. At the 3-year follow up, 66% (20/32) of patients in the HA group had radiographic evidence of acetabular erosion. Only two hips were revised to THA, and three additional hips had acetabular erosion that was sufficiently severe to indicate revision. The inclusion of only healthy, relatively younger (mean age of 75 years) active patients with good walking ability may have contributed to the higher rate of acetabular erosion and the poor outcomes following HA.

In a four-year follow up of a RCT, Hedbeck et al. [74] found 14% acetabular erosion at grade 1 (narrowing of the articular cartilage, with no bone erosion) in the bipolar HA group. However, significant differences in pain or functioning were not observed between the patients with and without erosion, and no revision to THA was recorded. The mean age in the study by Hedbeck was 80 years when the patients were included. The absence of revision in the HA group in our study and in the study by Hedbeck may be attributed to the limited activity in patients above 80 years of age and insufficient time for the appearance of clinical erosion.

In accordance with our results, many short-, intermediate- and long-term follow-up trials did not show significant differences between HA and THA and did not recommend THA for elderly patients with a displaced fracture of the femoral neck [70, 71, 76, 177, 178]

In conclusion, over a short-term follow-up period, differences were not observed in the outcomes after treatment with either HA or THA in elderly patients with a mean age of 85.5 years with a displaced FNF. I recommend HA for patients aged 80 years and above with a displaced femoral fracture.

Our four-year follow-up period of this study will elucidate whether elderly patient above 80 years of age with a displaced FNF will show greater benefits from THA relative to HA.

**Hemiarthroplasty for patients with cognitive dysfunction**

Historically, patients with cognitive dysfunction were regarded as contraindicated for arthroplasty because of the high risk of complications, such as infection, dislocation, and peri-prosthetic fracture, and the high rate of mortality and general complications [17, 48, 58, 59, 93, 94]. In addition, these patients may feel better in their own environment and will not receive benefits from rehabilitation. Therefore, these patients are discharged early to their own accommodation without any rehabilitation. Because IF is a simple surgical procedure that presents less trauma and is less demanding than arthroplasty procedures and because of the above-mentioned factors, many surgeons prefer this procedure instead of arthroplasty for this patient group.

The results for patients with FNF and cognitive dysfunction treated with HA have been sparsely investigated, and limited evidence is available for the effect of post-operative rehabilitation in this subpopulation; moreover, whether the results differ in comparison with patients without cognitive dysfunction is unclear. In study IV in this thesis, patients with and without cognitive dysfunction who received cemented HA using a direct lateral approach after displaced FNF were examined, and we found a slightly higher but not statistically significant prevalence of hip-related complications and reoperations in the cognitive dysfunction group. Changes in the EQ-5D were not observed over time. A higher rate of mortality and a higher prevalence of being unable to walk were observed in the cognitive dysfunction group than in the control group; however, the capacity to return to previous walking ability was poor in both groups. The cognitive dysfunction patients who did not receive geriatric rehabilitation had a worse patient-reported outcome and were almost nine times more likely to be confined to a wheelchair or bedridden than those who received geriatric rehabilitation.

The findings of this study regarding hip-related complications and reoperation are inconsistent with previous findings showing that this patients group has a significantly higher risk for complications. In a subgroup analysis, Johansson et al. [48] found that patients with cognitive dysfunction who received THA had a dislocation rate of 32% while patients with normal cognitive function who received THA had a dislocation rate of 12%. However, the posterior lateral approach, which is linked to an increased risk of reoperation because of prosthetic dislocation in patients treated for osteoarthritis and FNF [105, 106], was used in this study. In addition, the study had a limited number of patients with cognitive dysfunction who were received THA (22 patients). However, the use of THA in elderly patients with FNF, even those with normal cognitive function, is still debated, and until now, many RCTs [70, 71, 76, 177, 178] have not recommended THA for elderly patients with FNF. Therefore, patients with cognitive dysfunction who usually have limited activity and high mortality after hip fracture operation are not eligible for an extensive surgical procedure, such as THA.

Two previous RCTs [58, 59] conducted in patients with cognitive dysfunction reported a lower HRQoL and higher rate of reoperations in the HA group than in the IF group. The prevalence of being unable to walk was high (65%) in both studies, regardless of the surgical procedure. The authors in both studies did not recommend HA for patients with cognitive dysfunction. However, the prosthesis used in both studies was non-modular and older generation and is now outdated. In addition, the sample size in both studies may not have been sufficiently large.

The rate of hip-related complications and reoperations in the cognitive dysfunction group in study IV in this thesis was markedly lower than that of patients who received THA and HA in previous analyses [48, 58, 59] and slightly higher than that of patients without cognitive dysfunction, but this latter difference was not statistically significant.

The deterioration in HRQoL and functional outcomes in study IV did not differ between patients with or without cognitive dysfunction. The incidence of being unable to walk in study IV was 31% in the cognitive function group and 65% in previous studies [58, 59], which may reflect the lower rate of complications and reoperations in our study and the effect of rehabilitation because 38% of patients with cognitive dysfunction were discharged to a geriatric ward.

The high incidence of being unable to walk among patients with cognitive dysfunction likely reflects the natural process of dementia and cognitive impairment or the difficulty assimilating rehabilitation regimes in these patients. The high incidence could also indicate a

lack of rehabilitation resources for this patient group. Many patients with dementia or cognitive dysfunction live in nursing homes and often become discharged early from the hospital without receiving adequate rehabilitation. In our study, patients with cognitive dysfunction who did not receive geriatric rehabilitation had worse outcomes for HRQoL and hip function and were almost nine times more likely to be confined to a wheelchair or bedridden despite not having pain in the involved hip than those patients in the same group who received adequate rehabilitation. This finding confirms the results of other studies [179-182] showing that patients with cognitive dysfunction can benefit from participation in rehabilitation programmes and regain their pre-fracture function after rehabilitation.

Surgeons should be aware that the lack of structured rehabilitation after surgery leads to significant deterioration in walking ability regardless of a mechanically well-functioning prosthetic joint.

# IMPLICATIONS FOR FUTURE RESEARCH

- The results of study I show that THA is the treatment of choice for a displaced FNF in healthy and lucid elderly patients with good hip function preoperatively. The posterior lateral approach was used in this study, and it is still the most common approach in hip arthroplasty. This approach, which was used in study 1, is linked to an increased risk of dislocation rate after FNF compared with the direct lateral approach, which was used in studies II and III. However, the direct lateral approach is more traumatic and associated with post-operative limping. Limping may not be important problem in elderly patients with limited walking ability, although it may represent a problem in younger and more active patients. Dual mobility cups have showed promising results for decreasing the frequency of dislocation [183]. It would be interesting to perform a multicentre RCT for FNF patients to compare the direct lateral approach using the ordinary cup with the posterior lateral approach using a dual mobility cup in terms of complications, reoperations, HRQoL and hip function.
- The use of bone cement in the elderly and frail populations can cause serious cardiopulmonary complications and sudden death during cementation or the early peri-operative period. In study II, we found a higher risk of peri-prosthetic fractures and reoperations with the use of uncemented stem in patients with FNF; therefore, the uncemented stem was not recommend for patients with FNF. However, for frail patients with a higher risk for bone implantation syndrome, a modern uncemented stem may be indicated to avoid inevitable death. Future research should investigate the advantages and disadvantages of using a modern uncemented prosthesis in patients with a higher risk for BCIS compared with a cemented stem using mitigation measures to reduce the risk for BCIS.
- HA is the most common procedure for patients with a displaced FNF. In Sweden, 64% of patients with a displaced FNF receive HA. When we started study III, limited evidence was available showing that THA produced better HRQoL or functional outcomes than HA in elderly patients with a displaced FNF. As the study progressed, many RCTs with short, intermediate and long follow-up periods showed no differences between THA and HA. This inconsistency may be influenced by other factors, such as the surgical approach and patient age, activity and mental status. Because of this inconsistency between studies, I recommend further multicentre

RCTs with a large sample size that consider the surgical approach and patient age, activity and mental status.

- The results of study IV show that cemented HA with a direct lateral approach is a good option for elderly patients with a displaced FNF and cognitive dysfunction. The results are generally consistent with those of patients without cognitive dysfunction regarding the complications, reoperations, HRQoL and hip function. This study also showed that patients with cognitive dysfunction can benefit from participation in rehabilitation programmes and can regain their pre-fracture function after rehabilitation. This finding is inconsistent with previous assumptions. However, only 38% of patients in study IV were discharged to a geriatric ward. Because of the positive findings between rehabilitation and opportunities to restore walking ability in this patient group, a large cohort study to further address this finding is justified.

# MAIN CONCLUSIONS OF THIS THESIS

- THA is the treatment of choice for a displaced FNF in healthy and lucid elderly patients with good hip function preoperatively;
- Uncemented femoral stems should be avoided in patients older than 65 years with a displaced FNF;
- THA yields no benefit compared with HA in octogenarians treated for a displaced FNF;
- HA is a safe option as a treatment for displaced FNF in patients with dementia or cognitive dysfunction

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# REFERENCES


1. Whitman, R., *The Abduction Treatment of Fracture of the Neck of the Femur: An Account of the Evolution of a Method Adequate to Apply Surgical Principles and Therefore the Exponent of Radical Reform of Conventional Teaching and Practice.* Ann Surg, 1925. **81**(1): p. 374-91.
2. Freeman, L., *X. The Union of Ununited Fractures of the Neck of the Femur by Open Operation.* Ann Surg, 1904. **40**(4): p. 561-70.
3. Gullberg, B., O. Johnell, and J.A. Kanis, *World-wide projections for hip fracture.* Osteoporos Int, 1997. **7**(5): p. 407-13.
4. Dennison, E., M.A. Mohamed, and C. Cooper, *Epidemiology of osteoporosis.* Rheum Dis Clin North Am, 2006. **32**(4): p. 617-29.
5. Kanis, J.A., et al., *International variations in hip fracture probabilities: implications for risk assessment.* J Bone Miner Res, 2002. **17**(7): p. 1237-44.
6. Rogmark, C., et al., *Incidence of hip fractures in Malmo, Sweden, 1992-1995. A trend-break.* Acta Orthop Scand, 1999. **70**(1): p. 19-22.
7. Jaglal, S.B., et al., *Population trends in BMD testing, treatment, and hip and wrist fracture rates: are the hip fracture projections wrong?* J Bone Miner Res, 2005. **20**(6): p. 898-905.
8. Kannus, P., et al., *Nationwide decline in incidence of hip fracture.* J Bone Miner Res, 2006. **21**(12): p. 1836-8.
9. Abrahamsen, B. and P. Vestergaard, *Declining incidence of hip fractures and the extent of use of anti-osteoporotic therapy in Denmark 1997-2006.* Osteoporos Int, 2010. **21**(3): p. 373-80.
10. Chevalley, T., et al., *[Incidence of hip fracture: reversal of a secular trend].* Rev Med Suisse, 2007. **3**(115): p. 1528-30, 1532-3.
11. Karampampa, K., et al., *Declining incidence trends for hip fractures have not been accompanied by improvements in lifetime risk or post-fracture survival--A nationwide study of the Swedish population 60 years and older.* Bone, 2015. **78**: p. 55-61.
12. Rosengren, B.E. and M.K. Karlsson, *The annual number of hip fractures in Sweden will double from year 2002 to 2050: projections based on local and nationwide data.* Acta Orthop, 2014. **85**(3): p. 234-7.
13. Kanis, J.A., et al., *A systematic review of hip fracture incidence and probability of fracture worldwide.* Osteoporos Int, 2012. **23**(9): p. 2239-56.
14. Nilson, F., et al., *Trends in hip fracture incidence rates among the elderly in Sweden 1987-2009.* J Public Health (Oxf), 2013. **35**(1): p. 125-31.
15. Abrahamsen, B., et al., *Excess mortality following hip fracture: a systematic epidemiological review.* Osteoporos Int, 2009. **20**(10): p. 1633-50.
16. Johnell, O., et al., *Mortality after osteoporotic fractures.* Osteoporos Int, 2004. **15**(1): p. 38-42.

17. Soderqvist, A., et al., *Prediction of mortality in elderly patients with hip fractures: a two-year prospective study of 1,944 patients.* Gerontology, 2009. **55**(5): p. 496-504.

18. Al-Ani, A.N., et al., *Early operation on patients with a hip fracture improved the ability to return to independent living. A prospective study of 850 patients.* J Bone Joint Surg Am, 2008. **90**(7): p. 1436-42.

19. Nordstrom, P., et al., *Length of hospital stay after hip fracture and short term risk of death after discharge: a total cohort study in Sweden.* BMJ, 2015. **350**: p. h696.

20. Bretherton, C.P. and M.J. Parker, *Early surgery for patients with a fracture of the hip decreases 30-day mortality.* Bone Joint J, 2015. **97-B**(1): p. 104-8.

21. van Embden, D., et al., *The Pauwels classification for intracapsular hip fractures: is it reliable?* Injury, 2011. **42**(11): p. 1238-40.

22. Gaspar, D., et al., *AO group, AO subgroup, Garden and Pauwels classification systems of femoral neck fractures: are they reliable and reproducible?* Med Glas (Zenica), 2012. **9**(2): p. 243-7.

23. Blundell, C.M., et al., *Assessment of the AO classification of intracapsular fractures of the proximal femur.* J Bone Joint Surg Br, 1998. **80**(4): p. 679-83.

24. Turgut, A., et al., *Is surgeons' experience important on intra- and inter-observer reliability of classifications used for adult femoral neck fracture?* Acta Orthop Traumatol Turc, 2016. **50**(6): p. 601-605.

25. Frandsen, P.A., et al., *Garden's classification of femoral neck fractures. An assessment of inter-observer variation.* J Bone Joint Surg Br, 1988. **70**(4): p. 588-90.

26. Thomsen, N.O., et al., *Observer variation in the radiographic classification of fractures of the neck of the femur using Garden's system.* Int Orthop, 1996. **20**(5): p. 326-9.

27. Barnes, R., et al., *Subcapital fractures of the femur. A prospective review.* J Bone Joint Surg Br, 1976. **58**(1): p. 2-24.

28. Eliasson, P., L.I. Hansson, and J. Karrholm, *Displacement in femoral neck fractures. A numerical analysis of 200 fractures.* Acta Orthop Scand, 1988. **59**(4): p. 361-4.

29. Beimers, L., et al., *Subcapital hip fractures: the Garden classification should be replaced, not collapsed.* Can J Surg, 2002. **45**(6): p. 411-4.

30. Parker, M.J., *Garden grading of intracapsular fractures: meaningful or misleading?* Injury, 1993. **24**(4): p. 241-2.

31. Parker, M.J., *Prediction of fracture union after internal fixation of intracapsular femoral neck fractures.* Injury, 1994. **25 Suppl 2**: p. B3-6.

32. Zlowodzki, M., et al., *Perception of Garden's classification for femoral neck fractures: an international survey of 298 orthopaedic trauma surgeons.* Arch Orthop Trauma Surg, 2005. **125**(7): p. 503-5.

33. Van Embden, D., et al., *The reliability of a simplified Garden classification for intracapsular hip fractures.* Orthop Traumatol Surg Res, 2012. **98**(4): p. 405-8.

34. Parker, M.J., A. White, and A. Boyle, *Fixation versus hemiarthroplasty for undisplaced intracapsular hip fractures.* Injury, 2008. **39**(7): p. 791-5.

35. Palm, H., et al., *A new measurement for posterior tilt predicts reoperation in undisplaced femoral neck fractures: 113 consecutive patients treated by internal fixation and followed for 1 year.* Acta Orthop, 2009. **80**(3): p. 303-7.

36. Rogmark, C., L. Flensburg, and H. Fredin, *Undisplaced femoral neck fractures--no problems? A consecutive study of 224 patients treated with internal fixation.* Injury, 2009. **40**(3): p. 274-6.

37. Gjertsen, J.E., et al., *Clinical outcome after undisplaced femoral neck fractures.* Acta Orthop, 2011. **82**(3): p. 268-74.

38. Lapidus, L.J., et al., *Internal fixation of garden I and II femoral neck fractures: posterior tilt did not influence the reoperation rate in 382 consecutive hips followed for a minimum of 5 years.* J Orthop Trauma, 2013. **27**(7): p. 386-90; discussion 390-1.

39. Kim, J.W., S.E. Byun, and J.S. Chang, *The clinical outcomes of early internal fixation for undisplaced femoral neck fractures and early full weight-bearing in elderly patients.* Arch Orthop Trauma Surg, 2014. **134**(7): p. 941-6.

40. Bhandari, M., et al., *Operative management of displaced femoral neck fractures in elderly patients. An international survey.* J Bone Joint Surg Am, 2005. **87**(9): p. 2122-30.

41. Gray, A.J. and M.J. Parker, *Intracapsular fractures of the femoral neck in young patients.* Injury, 1994. **25**(10): p. 667-9.

42. Bhandari, M., et al., *Internal fixation compared with arthroplasty for displaced fractures of the femoral neck. A meta-analysis.* J Bone Joint Surg Am, 2003. **85-A**(9): p. 1673-81.

43. Rogmark, C., et al., *A prospective randomised trial of internal fixation versus arthroplasty for displaced fractures of the neck of the femur. Functional outcome for 450 patients at two years.* J Bone Joint Surg Br, 2002. **84**(2): p. 183-8.

44. Leonardsson, O., et al., *Long-term follow-up of replacement compared with internal fixation for displaced femoral neck fractures: results at ten years in a randomised study of 450 patients.* J Bone Joint Surg Br, 2010. **92**(3): p. 406-12.

45. Keating, J.F., et al., *Randomized comparison of reduction and fixation, bipolar hemiarthroplasty, and total hip arthroplasty. Treatment of displaced intracapsular hip fractures in healthy older patients.* J Bone Joint Surg Am, 2006. **88**(2): p. 249-60.

46. Gao, H., et al., *Which is the best alternative for displaced femoral neck fractures in the elderly?: A meta-analysis.* Clin Orthop Relat Res, 2012. **470**(6): p. 1782-91.

47. Lu-Yao, G.L., et al., *Outcomes after displaced fractures of the femoral neck. A meta-analysis of one hundred and six published reports.* J Bone Joint Surg Am, 1994. **76**(1): p. 15-25.

48. Johansson, T., et al., *Internal fixation versus total hip arthroplasty in the treatment of displaced femoral neck fractures: a prospective randomized study of 100 hips.* Acta Orthop Scand, 2000. **71**(6): p. 597-602.

49. Ravikumar, K.J. and G. Marsh, *Internal fixation versus hemiarthroplasty versus total hip arthroplasty for displaced subcapital fractures of femur--13 year results of a prospective randomised study.* Injury, 2000. **31**(10): p. 793-7.

50. Rogmark, C. and O. Johnell, *Primary arthroplasty is better than internal fixation of displaced femoral neck fractures: a meta-analysis of 14 randomized studies with 2,289 patients.* Acta Orthop, 2006. **77**(3): p. 359-67.

51. Tidermark, J., et al., *Internal fixation compared with total hip replacement for displaced femoral neck fractures in the elderly. A randomised, controlled trial.* J Bone Joint Surg Br, 2003. **85**(3): p. 380-8.

52. Parker, M.J., et al., *Hemiarthroplasty versus internal fixation for displaced intracapsular hip fractures in the elderly. A randomised trial of 455 patients.* J Bone Joint Surg Br, 2002. **84**(8): p. 1150-5.

53. Blomfeldt, R., et al., *Comparison of internal fixation with total hip replacement for displaced femoral neck fractures. Randomized, controlled trial performed at four years.* J Bone Joint Surg Am, 2005. **87**(8): p. 1680-8.

54. Frihagen, F., L. Nordsletten, and J.E. Madsen, *Hemiarthroplasty or internal fixation for intracapsular displaced femoral neck fractures: randomised controlled trial.* BMJ, 2007. **335**(7632): p. 1251-4.

55. Parker, M.J., G. Pryor, and K. Gurusamy, *Hemiarthroplasty versus internal fixation for displaced intracapsular hip fractures: a long-term follow-up of a randomised trial.* Injury, 2010. **41**(4): p. 370-3.

56. Johansson, T., *Internal fixation compared with total hip replacement for displaced femoral neck fractures: a minimum fifteen-year follow-up study of a previously reported randomized trial.* J Bone Joint Surg Am, 2014. **96**(6): p. e46.

57. Blomfeldt, R., et al., *Displaced femoral neck fracture: comparison of primary total hip replacement with secondary replacement after failed internal fixation: a 2-year follow-up of 84 patients.* Acta Orthop, 2006. **77**(4): p. 638-43.

58. van Dortmont, L.M., et al., *Cannulated screws versus hemiarthroplasty for displaced intracapsular femoral neck fractures in demented patients.* Ann Chir Gynaecol, 2000. **89**(2): p. 132-7.

59. Blomfeldt, R., et al., *Internal fixation versus hemiarthroplasty for displaced fractures of the femoral neck in elderly patients with severe cognitive impairment.* J Bone Joint Surg Br, 2005. **87**(4): p. 523-9.

60. Hedbeck, C.J., et al., *Internal fixation versus cemented hemiarthroplasty for displaced femoral neck fractures in patients with severe cognitive dysfunction: a randomized controlled trial.* J Orthop Trauma, 2013. **27**(12): p. 690-5.

61. Rogmark, C., et al., *Primary hemiarthroplasty in old patients with displaced femoral neck fracture: a 1-year follow-up of 103 patients aged 80 years or more.* Acta Orthop Scand, 2002. **73**(6): p. 605-10.

62. Gjertsen, J.E., et al., *Internal screw fixation compared with bipolar hemiarthroplasty for treatment of displaced femoral neck fractures in elderly patients.* J Bone Joint Surg Am, 2010. **92**(3): p. 619-28.

63. Rogmark, C., et al., *Monoblock hemiarthroplasties for femoral neck fractures--a part of orthopaedic history? Analysis of national registration of hemiarthroplasties 2005-2009.* Injury, 2012. **43**(6): p. 946-9.

64. Enocson, A., et al., *Unipolar versus bipolar Exeter hip hemiarthroplasty: a prospective cohort study on 830 consecutive hips in patients with femoral neck fractures.* Int Orthop, 2012. **36**(4): p. 711-7.

65. Hedbeck, C.J., et al., *Unipolar hemiarthroplasty versus bipolar hemiarthroplasty in the most elderly patients with displaced femoral neck fractures: a randomised, controlled trial.* Int Orthop, 2011. **35**(11): p. 1703-11.

66. Zhou, Z., et al., *Unipolar Versus Bipolar Hemiarthroplasty for Displaced Femoral Neck Fractures in Elderly Patients.* Orthopedics, 2015. **38**(11): p. 697-702.

67. Jia, Z., et al., *Unipolar versus bipolar hemiarthroplasty for displaced femoral neck fractures: a systematic review and meta-analysis of randomized controlled trials.* J Orthop Surg Res, 2015. **10**: p. 8.

68. Leonardsson, O., et al., *Higher risk of reoperation for bipolar and uncemented hemiarthroplasty.* Acta Orthop, 2012. **83**(5): p. 459-66.

69. Rogmark, C., et al., *Posterior approach and uncemented stems increases the risk of reoperation after hemiarthroplasties in elderly hip fracture patients.* Acta Orthop, 2014. **85**(1): p. 18-25.

70. Dorr, L.D., et al., *Treatment of femoral neck fractures with total hip replacement versus cemented and noncemented hemiarthroplasty.* J Arthroplasty, 1986. **1**(1): p. 21-8.

71. van den Bekerom, M.P., et al., *A comparison of hemiarthroplasty with total hip replacement for displaced intracapsular fracture of the femoral neck: a randomised controlled multicentre trial in patients aged 70 years and over.* J Bone Joint Surg Br, 2010. **92**(10): p. 1422-8.

72. Blomfeldt, R., et al., *A randomised controlled trial comparing bipolar hemiarthroplasty with total hip replacement for displaced intracapsular fractures of the femoral neck in elderly patients.* J Bone Joint Surg Br, 2007. **89**(2): p. 160-5.

73. Baker, R.P., et al., *Total hip arthroplasty and hemiarthroplasty in mobile, independent patients with a displaced intracapsular fracture of the femoral neck. A randomized, controlled trial.* J Bone Joint Surg Am, 2006. **88**(12): p. 2583-9.

74. Hedbeck, C.J., et al., *Comparison of bipolar hemiarthroplasty with total hip arthroplasty for displaced femoral neck fractures: a concise four-year follow-up of a randomized trial.* J Bone Joint Surg Am, 2011. **93**(5): p. 445-50.

75. Macaulay, W., et al., *Prospective randomized clinical trial comparing hemiarthroplasty to total hip arthroplasty in the treatment of displaced femoral neck fractures: winner of the Dorr Award.* J Arthroplasty, 2008. **23**(6 Suppl 1): p. 2-8.

76. Avery, P.P., et al., *Total hip replacement and hemiarthroplasty in mobile, independent patients with a displaced intracapsular fracture of the femoral neck: a seven- to ten-year follow-up report of a prospective randomised controlled trial.* J Bone Joint Surg Br, 2011. **93**(8): p. 1045-8.

77. Leonardsson, O., et al., *Patient-reported outcome after displaced femoral neck fracture: a national survey of 4467 patients.* J Bone Joint Surg Am, 2013. **95**(18): p. 1693-9.

78. Pauwels, R., et al., *Reduction of scatter-induced image noise in cone beam computed tomography: effect of field of view size and position.* Oral Surg Oral Med Oral Pathol Oral Radiol, 2016. **121**(2): p. 188-95.

79. Charnley, J., *Total hip replacement by low-friction arthroplasty.* Clin Orthop Relat Res, 1970. **72**: p. 7-21.

80. Moore, A.T. and H.R. Bohlman, *Metal hip joint: a case report. 1942.* Clin Orthop Relat Res, 2006. **453**: p. 22-4.

81. Parker, M.J., K.S. Gurusamy, and S. Azegami, *Arthroplasties (with and without bone cement) for proximal femoral fractures in adults.* Cochrane Database Syst Rev, 2010(6): p. CD001706.

82. Khan, R.J., et al., *Cemented or uncemented hemiarthroplasty for displaced intracapsular femoral neck fractures.* Int Orthop, 2002. **26**(4): p. 229-32.

83. Figved, W., et al., *Cemented versus uncemented hemiarthroplasty for displaced femoral neck fractures.* Clin Orthop Relat Res, 2009. **467**(9): p. 2426-35.

84. Skoldenberg, O.G., et al., *A new uncemented hydroxyapatite-coated femoral component for the treatment of femoral neck fractures: two-year radiostereometric and bone densitometric evaluation in 50 hips.* J Bone Joint Surg Br, 2011. **93**(5): p. 665-77.

85. Kim, Y.H. and J.H. Oh, *A comparison of a conventional versus a short, anatomical metaphyseal-fitting cementless femoral stem in the treatment of patients with a fracture of the femoral neck.* J Bone Joint Surg Br, 2012. **94**(6): p. 774-81.

86. Parvizi, J., et al., *The Frank Stinchfield Award. Sudden death during primary hip arthroplasty.* Clin Orthop Relat Res, 1999(369): p. 39-48.

87. Rinecker, H., *New clinico-pathophysiological studies on the bone cement implantation syndrome.* Archives of orthopaedic and traumatic surgery, 1980. **97**(4): p. 263-274.

88. Orsini, E.C., et al., *Cardiopulmonary function and pulmonary microemboli during arthroplasty using cemented or non-cemented components. The role of intramedullary pressure.* J Bone Joint Surg Am, 1987. **69**(6): p. 822-32.

89. Donaldson, A.J., et al., *Bone cement implantation syndrome.* Br J Anaesth, 2009. **102**(1): p. 12-22.

90. Olsen, F., et al., *Bone cement implantation syndrome in cemented hemiarthroplasty for femoral neck fracture: incidence, risk factors, and effect on outcome.* Br J Anaesth, 2014. **113**(5): p. 800-6.

91. Holmes, J. and A. House, *Psychiatric illness predicts poor outcome after surgery for hip fracture: a prospective cohort study.* Psychol Med, 2000. **30**(4): p. 921-9.

92. Samuelsson, B., et al., *Gender differences and cognitive aspects on functional outcome after hip fracture--a 2 years' follow-up of 2,134 patients.* Age Ageing, 2009. **38**(6): p. 686-92.

93. Stromberg, L., et al., *The appearance and disappearance of cognitive impairment in elderly patients during treatment for hip fracture.* Scand J Caring Sci, 1997. **11**(3): p. 167-75.

94. Marottoli, R.A., et al., *Predictors of mortality and institutionalization after hip fracture: the New Haven EPESE cohort. Established Populations for Epidemiologic Studies of the Elderly.* Am J Public Health, 1994. **84**(11): p. 1807-12.

95. Mundi, S., H. Chaudhry, and M. Bhandari, *Systematic review on the inclusion of patients with cognitive impairment in hip fracture trials: a missed opportunity?* Can J Surg, 2014. **57**(4): p. E141-5.

96. Jolles, B.M. and E.R. Bogoch, *Posterior versus lateral surgical approach for total hip arthroplasty in adults with osteoarthritis.* Cochrane Database Syst Rev, 2006(3): p. CD003828.

97. Havelin, L.I., et al., *The Nordic Arthroplasty Register Association: a unique collaboration between 3 national hip arthroplasty registries with 280,201 THRs.* Acta Orthop, 2009. **80**(4): p. 393-401.

98. Chechik, O., et al., *Surgical approach and prosthesis fixation in hip arthroplasty world wide.* Arch Orthop Trauma Surg, 2013. **133**(11): p. 1595-600.

99. Baker, A.S. and V.C. Bitounis, *Abductor function after total hip replacement. An electromyographic and clinical review.* J Bone Joint Surg Br, 1989. **71**(1): p. 47-50.

100. Ramesh, M., et al., *Damage to the superior gluteal nerve after the Hardinge approach to the hip.* J Bone Joint Surg Br, 1996. **78**(6): p. 903-6.

101. Picado, C.H., F.L. Garcia, and W. Marques, Jr., *Damage to the superior gluteal nerve after direct lateral approach to the hip.* Clin Orthop Relat Res, 2007. **455**: p. 209-11.

102. Berstock, J.R., A.W. Blom, and A.D. Beswick, *A systematic review and meta-analysis of complications following the posterior and lateral surgical approaches to total hip arthroplasty.* Ann R Coll Surg Engl, 2015. **97**(1): p. 11-6.

103. Downing, N.D., et al., *Hip abductor strength following total hip arthroplasty: a prospective comparison of the posterior and lateral approach in 100 patients.* Acta Orthop Scand, 2001. **72**(3): p. 215-20.

104. Chomiak, J., et al., *Lesion of gluteal nerves and muscles in total hip arthroplasty through 3 surgical approaches. An electromyographically controlled study.* Hip Int, 2015. **25**(2): p. 176-83.

105. Lindgren, V., et al., *The type of surgical approach influences the risk of revision in total hip arthroplasty: a study from the Swedish Hip Arthroplasty Register of 90,662 total hipreplacements with 3 different cemented prostheses.* Acta Orthop, 2012. **83**(6): p. 559-65.

106. Hailer, N.P., et al., *The risk of revision due to dislocation after total hip arthroplasty depends on surgical approach, femoral head size, sex, and primary diagnosis. An analysis of 78,098 operations in the Swedish Hip Arthroplasty Register.* Acta Orthop, 2012. **83**(5): p. 442-8.

107. Enocson, A., et al., *Dislocation of hemiarthroplasty after femoral neck fracture: better outcome after the anterolateral approach in a prospective cohort study on 739 consecutive hips.* Acta Orthop, 2008. **79**(2): p. 211-7.

108. Skoldenberg, O., et al., *Reduced dislocation rate after hip arthroplasty for femoral neck fractures when changing from posterolateral to anterolateral approach.* Acta Orthop, 2010. **81**(5): p. 583-7.

109. Cebatorius, A., et al., *Choice of approach, but not femoral head size, affects revision rate due to dislocations in THA after femoral neck fracture: results from the Lithuanian Arthroplasty Register.* Int Orthop, 2015. **39**(6): p. 1073-6.

110. Shrier, I. and R.W. Platt, *Reducing bias through directed acyclic graphs.* BMC Med Res Methodol, 2008. **8**: p. 70.

111. Owens, W.D., J.A. Felts, and E.L. Spitznagel, *ASA PHYSICAL STATUS CLASSIFICATIONS - STUDY OF CONSISTENCY OF RATINGS.* Anesthesiology, 1978. **49**(4): p. 239-243.

112. Pfeiffer, E., *A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients.* J Am Geriatr Soc, 1975. **23**(10): p. 433-41.

113. Erkinjuntti, T., et al., *Short Portable Mental Status Questionnaire as a screening test for dementia and delirium among the elderly.* J Am Geriatr Soc, 1987. **35**(5): p. 412-6.

114. Smith, M.J., W.S. Breitbart, and M.M. Platt, *A critique of instruments and methods to detect, diagnose, and rate delirium.* J Pain Symptom Manage, 1995. **10**(1): p. 35-77.

115. Givens, J.L., T.B. Sanft, and E.R. Marcantonio, *Functional recovery after hip fracture: the combined effects of depressive symptoms, cognitive impairment, and delirium.* J Am Geriatr Soc, 2008. **56**(6): p. 1075-9.

116. Charnley, J., *The long-term results of low-friction arthroplasty of the hip performed as a primary intervention.* J Bone Joint Surg Br, 1972. **54**(1): p. 61-76.

117. Harris, W.H., *Traumatic arthritis of the hip after dislocation and acetabular fractures: treatment by mold arthroplasty. An end-result study using a new method of result evaluation.* J Bone Joint Surg Am, 1969. **51**(4): p. 737-55.

118. Soderman, P. and H. Malchau, *Is the Harris hip score system useful to study the outcome of total hip replacement?* Clin Orthop Relat Res, 2001(384): p. 189-97.

119. Mahomed, N.N., et al., *The Harris hip score: comparison of patient self-report with surgeon assessment.* J Arthroplasty, 2001. **16**(5): p. 575-80.

120. Frihagen, F., et al., *Outcome after femoral neck fractures: a comparison of Harris Hip Score, Eq-5d and Barthel Index.* Injury, 2008. **39**(10): p. 1147-56.

121. Brooks, R., *EuroQol: the current state of play.* Health Policy, 1996. **37**(1): p. 53-72.

122. Burstrom, K., M. Johannesson, and F. Diderichsen, *Swedish population health-related quality of life results using the EQ-5D.* Qual Life Res, 2001. **10**(7): p. 621-35.

123. Dolan, P., et al., *The time trade-off method: results from a general population study.* Health Econ, 1996. **5**(2): p. 141-54.

124. Tidermark, J., *Quality of life and femoral neck fractures.* Acta Orthop Scand Suppl, 2003. **74**(309): p. 1-42.

125. Tidermark, J., et al., *Responsiveness of the EuroQol (EQ 5-D) and the SF-36 in elderly patients with displaced femoral neck fractures.* Qual Life Res, 2003. **12**(8): p. 1069-79.

126. Tidermark, J. and G. Bergstrom, *Responsiveness of the EuroQol (EQ-5D) and the Nottingham Health Profile (NHP) in elderly patients with femoral neck fractures.* Qual Life Res, 2007. **16**(2): p. 321-30.

127. Marsh, J., D. Bryant, and S.J. MacDonald, *Older patients can accurately recall their preoperative health status six weeks following total hip arthroplasty.* J Bone Joint Surg Am, 2009. **91**(12): p. 2827-37.

128. Coucill, W., et al., *EQ-5D in patients with dementia: an investigation of inter-rater agreement.* Med Care, 2001. **39**(8): p. 760-71.

129. Selai, C., *Assessing quality of life in dementia.* Med Care, 2001. **39**(8): p. 753-5.

130. Katz, S., et al., *Studies of Illness in the Aged. The Index of Adl: A Standardized Measure of Biological and Psychosocial Function.* JAMA, 1963. **185**: p. 914-9.

131. Downie, W.W., et al., *Studies with pain rating scales.* Ann Rheum Dis, 1978. **37**(4): p. 378-81.

132. Moore, A.T., *The self-locking metal hip prosthesis.* J Bone Joint Surg Am, 1957. **39-A**(4): p. 811-27.

133. Gammer, W., *A modified lateroanterior approach in operations for hip arthroplasty.* Clin Orthop Relat Res, 1985(199): p. 169-72.

134. Gruen, T.A., G.M. McNeice, and H.C. Amstutz, *"Modes of failure" of cemented stem-type femoral components: a radiographic analysis of loosening.* Clin Orthop Relat Res, 1979(141): p. 17-27.

135. DeLee, J.G. and J. Charnley, *Radiological demarcation of cemented sockets in total hip replacement.* Clin Orthop Relat Res, 1976(121): p. 20-32.

136. Dorr, L.D., et al., *Structural and cellular assessment of bone quality of proximal femur.* Bone, 1993. **14**(3): p. 231-42.

137. Brooker, A.F., et al., *Ectopic ossification following total hip replacement. Incidence and a method of classification.* J Bone Joint Surg Am, 1973. **55**(8): p. 1629-32.

138. Chammout, G.K., et al., *Total hip replacement versus open reduction and internal fixation of displaced femoral neck fractures: a randomized long-term follow-up study.* J Bone Joint Surg Am, 2012. **94**(21): p. 1921-8.

139. Maurer, T.B., et al., *Increased loosening of cemented straight stem prostheses made from titanium alloys. An analysis and comparison with prostheses made of cobalt-chromium-nickel alloy.* Int Orthop, 2001. **25**(2): p. 77-80.

140. Kovac, S., et al., *Long-term survival of a cemented titanium-aluminium-vanadium alloy straight-stem femoral component.* J Bone Joint Surg Br, 2006. **88**(12): p. 1567-73.

141. Inngul, C. and A. Enocson, *Postoperative periprosthetic fractures in patients with an Exeter stem due to a femoral neck fracture: cumulative incidence and surgical outcome.* Int Orthop, 2015. **39**(9): p. 1683-8.

142. Broden, C., et al., *High risk of early periprosthetic fractures after primary hip arthroplasty in elderly patients using a cemented, tapered, polished stem.* Acta Orthop, 2015. **86**(2): p. 169-74.

143. Lucht, U., *The Danish Hip Arthroplasty Register.* Acta Orthop Scand, 2000. **71**(5): p. 433-9.

144. Malchau, H., et al., *The Swedish Total Hip Replacement Register.* J Bone Joint Surg Am, 2002. **84-A Suppl 2**: p. 2-20.

145. Keisu, K.S., et al., *Primary cementless total hip arthroplasty in octogenarians. Two to eleven-year follow-up.* J Bone Joint Surg Am, 2001. **83-A**(3): p. 359-63.

146. Christie, J., et al., *Echocardiography of transatrial embolism during cemented and uncemented hemiarthroplasty of the hip.* J Bone Joint Surg Br, 1994. **76**(3): p. 409-12.

147. Yli-Kyyny, T., et al., *Perioperative complications after cemented or uncemented hemiarthroplasty in hip fracture patients.* Scand J Surg, 2013. **102**(2): p. 124-8.

148. Sonne-Holm, S., S. Walter, and J.S. Jensen, *Moore hemi-arthroplasty with and without bone cement in femoral neck fractures. A clinical controlled trial.* Acta Orthop Scand, 1982. **53**(6): p. 953-6.

149. Emery, R.J., et al., *Bipolar hemiarthroplasty for subcapital fracture of the femoral neck. A prospective randomised trial of cemented Thompson and uncemented Moore stems.* J Bone Joint Surg Br, 1991. **73**(2): p. 322-4.

150. Parker, M.I., G. Pryor, and K. Gurusamy, *Cemented versus uncemented hemiarthroplasty for intracapsular hip fractures: A randomised controlled trial in 400 patients.* J Bone Joint Surg Br, 2010. **92**(1): p. 116-22.

151. Taylor, F., M. Wright, and M. Zhu, *Hemiarthroplasty of the hip with and without cement: a randomized clinical trial.* J Bone Joint Surg Am, 2012. **94**(7): p. 577-83.

152. Talsnes, O., et al., *No difference in mortality between cemented and uncemented hemiprosthesis for elderly patients with cervical hip fracture. A prospective randomized study on 334 patients over 75 years.* Arch Orthop Trauma Surg, 2013. **133**(6): p. 805-9.

153. Inngul, C., et al., *Cemented versus uncemented arthroplasty in patients with a displaced fracture of the femoral neck: a randomised controlled trial.* Bone Joint J, 2015. **97-B**(11): p. 1475-80.

154. Moerman, S., et al., *More complications in uncemented compared to cemented hemiarthroplasty for displaced femoral neck fractures: a randomized controlled trial of 201 patients, with one year follow-up.* BMC Musculoskelet Disord, 2017. **18**(1): p. 169.

155. Deangelis, J.P., et al., *Cemented versus uncemented hemiarthroplasty for displaced femoral neck fractures: a prospective randomized trial with early follow-up.* J Orthop Trauma, 2012. **26**(3): p. 135-40.

156. Rogmark, C., et al., *Posterior approach and uncemented stems increases the risk of reoperation after hemiarthroplasties in elderly hip fracture patients: An analysis of 33,205 procedures in the Norwegian and Swedish national registries.* Acta Orthopaedica, 2014. **85**(1): p. 18-25.

157. Langslet, E., et al., *Cemented versus uncemented hemiarthroplasty for displaced femoral neck fractures: 5-year followup of a randomized trial.* Clin Orthop Relat Res, 2014. **472**(4): p. 1291-9.

158. Sköldenberg, O.G., et al., *Good stability but high periprosthetic bone mineral loss and late-occurring periprosthetic fractures with use of uncemented tapered femoral stems in patients with a femoral neck fracture.* Acta Orthopaedica, 2014. **85**(4): p. 396-402.

159. Gjertsen, J.E., et al., *More re-operations after uncemented than cemented hemiarthroplasty used in the treatment of displaced fractures of the femoral neck: an*

*observational study of 11,116 hemiarthroplasties from a national register.* J Bone Joint Surg Br, 2012. **94**(8): p. 1113-9.

160. Yli-Kyyny, T., et al., *Cemented or uncemented hemiarthroplasty for the treatment of femoral neck fractures?* Acta Orthop, 2014. **85**(1): p. 49-53.

161. Costain, D.J., et al., *Perioperative mortality after hemiarthroplasty related to fixation method.* Acta Orthop, 2011. **82**(3): p. 275-81.

162. Talsnes, O., et al., *Perioperative mortality in hip fracture patients treated with cemented and uncemented hemiprosthesis: a register study of 11,210 patients.* Int Orthop, 2013. **37**(6): p. 1135-40.

163. NPSA/2009/RRR001.), C.K.M.s.r.i.p.u.h.a.f.f.o.t.p.f.N.P.S.R. *Mitigating surgical risk in patients undergoing hip arthroplasty for fractures of the proximal femur. National Patient Safety Report NPSA/2009/RRR001.)*. 2009.

164. Costa, M.L., et al., *Does cementing the femoral component increase the risk of peri-operative mortality for patients having replacement surgery for a fracture of the neck of femur? Data from the National Hip Fracture Database.* J Bone Joint Surg Br, 2011. **93**(10): p. 1405-10.

165. Membership of Working, P., et al., *Safety guideline: reducing the risk from cemented hemiarthroplasty for hip fracture 2015: Association of Anaesthetists of Great Britain and Ireland British Orthopaedic Association British Geriatric Society.* Anaesthesia, 2015. **70**(5): p. 623-6.

166. Dearborn, J.T. and W.H. Harris, *Postoperative mortality after total hip arthroplasty. An analysis of deaths after two thousand seven hundred and thirty-six procedures.* J Bone Joint Surg Am, 1998. **80**(9): p. 1291-4.

167. Parvizi, J., et al., *Thirty-day mortality after elective total hip arthroplasty.* J Bone Joint Surg Am, 2001. **83-A**(10): p. 1524-8.

168. Parvizi, J., M.H. Ereth, and D.G. Lewallen, *Thirty-day mortality following hip arthroplasty for acute fracture.* J Bone Joint Surg Am, 2004. **86-A**(9): p. 1983-8.

169. Zhan, C., et al., *Incidence and short-term outcomes of primary and revision hip replacement in the United States.* J Bone Joint Surg Am, 2007. **89**(3): p. 526-33.

170. Sinclair, S., S. James, and M. Singer, *Intraoperative intravascular volume optimisation and length of hospital stay after repair of proximal femoral fracture: randomised controlled trial.* BMJ, 1997. **315**(7113): p. 909-12.

171. Breusch, S.J., et al., *[Cemented hip prosthesis implantation--decreasing the rate of fat embolism with pulsed pressure lavage].* Orthopade, 2000. **29**(6): p. 578-86.

172. Sierra, R.J., J.A. Timperley, and G.A. Gie, *Contemporary cementing technique and mortality during and after Exeter total hip arthroplasty.* J Arthroplasty, 2009. **24**(3): p. 325-32.

173. Lindahl, H., et al., *The excess mortality due to periprosthetic femur fracture. A study from the Swedish national hip arthroplasty register.* Bone, 2007. **40**(5): p. 1294-8.

174. Bhattacharyya, T., et al., *Mortality after periprosthetic fracture of the femur.* J Bone Joint Surg Am, 2007. **89**(12): p. 2658-62.

175. Carroll, C., et al., *Hemiarthroplasty and total hip arthroplasty for treating primary intracapsular fracture of the hip: a systematic review and cost-effectiveness analysis.* Health Technol Assess, 2011. **15**(36): p. 1-74.

176. Burgers, P.T., et al., *Total hip arthroplasty versus hemiarthroplasty for displaced femoral neck fractures in the healthy elderly: a meta-analysis and systematic review of randomized trials.* Int Orthop, 2012. **36**(8): p. 1549-60.

177. Tol, M.C., et al., *Hemiarthroplasty or total hip arthroplasty for the treatment of a displaced intracapsular fracture in active elderly patients: 12-year follow-up of randomised trial.* Bone Joint J, 2017. **99-B**(2): p. 250-254.

178. Mouzopoulos, G., et al., *The four-year functional result after a displaced subcapital hip fracture treated with three different surgical options.* Int Orthop, 2008. **32**(3): p. 367-73.

179. Huusko, T.M., et al., *Randomised, clinically controlled trial of intensive geriatric rehabilitation in patients with hip fracture: subgroup analysis of patients with dementia.* BMJ, 2000. **321**(7269): p. 1107-11.

180. Rolland, Y., et al., *Rehabilitation outcome of elderly patients with hip fracture and cognitive impairment.* Disabil Rehabil, 2004. **26**(7): p. 425-31.

181. Beloosesky, Y., et al., *Functional gain of hip fracture patients in different cognitive and functional groups.* Clin Rehabil, 2002. **16**(3): p. 321-8.

182. Al-Ani, A.N., et al., *Does rehabilitation matter in patients with femoral neck fracture and cognitive impairment? A prospective study of 246 patients.* Arch Phys Med Rehabil, 2010. **91**(1): p. 51-7.

183. Caton, J.H., et al., *A comparative and retrospective study of three hundred and twenty primary Charnley type hip replacements with a minimum follow up of ten years to assess whether a dual mobility cup has a decreased dislocation risk.* Int Orthop, 2014. **38**(6): p. 1125-9.

# APPENDIX

SPMSQ - Short Portable Mental State Questionnaire

Fråga:

1. Vad är det för datum i dag? Rätt/Fel
2. Vilken veckodag är det? Rätt/Fel
3. Vad heter detta sjukhus? Rätt/Fel
4. Vilken adress har du? Rätt/Fel
5. Hur gammal är du? Rätt/Fel
6. När föddes Du (år, månad, dag)? Rätt/Fel
7. Vad heter nuvarande statsminister? Rätt/Fel
8. Vad hette den förre statsministern? Rätt/Fel
9. Vad var din mors flicknamn? Rätt/Fel
10. Dra 3 från 20 och fortsätt hela vägen ner. Antal rätta svar. Rätt/Fel

**Function classification according Charnley**

(A) - En höft sjuk - för övrigt väsentligen frisk

(B) - Bilat höfter sjuka - för övrigt väsentligen frisk

(C) -Flera leder påverkade/annat gånghandikapp

**Harris Hip Score**

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**1. Beskriv om du har någon smärta i den opererade höften?**

A. Ingen

B. Lätt smärta, ingen begränsning i aktivitet, känner av höften vid enstaka tillfällen

C. Lindrig, ej påverkan i dagliga aktiviteter, smärta vid större ansträngning, ibland smärtstillande läkemedel

D. Måttlig smärta, begränsad i dagliga aktiviteter, regelbundet smärtstillande läkemedel

E. Uttalad smärta, stark begränsning i dagliga aktiviteter, regelbundet starka smärtstillande läkemedel

F. Invalidiserande smärta, vilosmärtor

**2. Använder du något gånghjälpmedel?**

A. Inget

B. Käpp vid långa promenader

C. Nästan alltid käpp

D. 1 Krycka eller rollator

E. 2 Käppar

F. 2 Kryckor eller gångbord G. Går inte alls

**3. Har du hälta på den opererade sidan efter promenad med det gånghjälpmedel du använder?**

A. Ingen hälta

B. Lätt hälta

C. Måttlig hälta

D. Uttalad hälta

**4. Hur långt kan du gå med det gånghjälpmedel du använder?**

A. Över 2 kilometer

B. 1-2 kilometer

C. 0,5 – 1 kilometer

D. Mindre än 0,5 kilometer eller endast inomhus

E. Kan inte gå

**5. Trappor**

A. Jag går i trappa utan stöd

B. Jag använder ledstång eller räcke vid trappgång

C. Jag går i trappa med stora svårigheter

E. Jag kan inte gå i trappa

**6. Ta på skor och strumpor på opererade sidan**

A. Utan svårighet

B. Med svårighet

C. Jag kan inte ta på mig skor och strumpor själv

**7. Sitta**

A. Jag kan sitta bekvämt på en vanlig stol

B. Jag sitter endast bekvämt i en hög stol, jag kan endast sitta bekvämt i en halvtimme

C. Jag kan inte sitta bekvämt i en halvtimme på grund av höftsmärta

**8. Tunnelbana/Buss**

A. Jag kan åka tunnelbana eller buss

B. Jag kan inte åka tunnelbana eller buss

**Formulär EQ-5D**

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Rörlighet

1. Jag går utan svårigheter

2. Jag kan gå men med viss svårighet

3. Jag är sängliggande

Hygien

1. Jag behöver ingen hjälp med min dagliga hygien, mat eller påklädning

2. Jag har vissa problem att tvätta eller klä mig själv

3. Jag kan inte tvätta eller klä mig själv

Huvudsakliga aktiviteter (t ex arbete, studier, hushållssysslor, familje- och fritidsaktiviteter)

1. Jag klarar av mina huvudsakliga aktiviteter

2. Jag har vissa problem med att klara av mina huvudsakliga aktiviteter

3. Jag klarar inte av mina huvudsakliga aktiviteter

Smärtor/besvär

1. Jag har varken smärtor eller besvär

2. Jag har måttliga smärtor eller besvär

3. Jag har svåra smärtor eller besvär

Oro/nedstämdhet

1. Jag är inte orolig eller nedstämd

2. Jag är orolig eller nedstämd i viss utsträckning

**ADL**

- Oberoende i alla nedanstående funktioner
- ○ Hjälp med bad/dusch
- ○ Hjälp med påklädning
- ○ Hjälp med toabesök
- ○ Hjälp att komma i/ur säng
- ○ Inkontinent
- ○ Hjälp med att äta

**Smärt nummreringsskala (NRS)**

Ringa in det nummer som bäst motsvarar din GENOMSNITTLIGA nivå för din höft/bensmärta i den opererade benet under de sju senaste dagarna

1 – Ingen smärta

2

3

4

5

6

7

8

9

10 – Värsta tänkbara smärta