Functional outcome and complications after surgical treatment of displaced low-energy femoral neck fractures in patients between 55 and 70 years

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Walking is a man`s best medicine

Hippocrates

Table of contest

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List of Abbreviations

AO	Arbeidsgemeinschaft für Osteosynthesefragen
AVN	Avascular Necrosis
ASA	American Society of Anaesthesiologists
BMD	Bone Mineral Density
BMI	Body Mass Index
CCI	Charlson Comorbidity Index
CI	Confidence Interval
DAIR	Debridement, Antibiotics and Implant Retention
DXA	Dual-energy X-ray Absorptiometry
EQ-5D-3L	Five-dimensional 3-level Scale of EuroQol
EQ-VAS	Visual Analogue Scale of EuroQol
FNF	Femoral Neck Fracture
HHS	Harris Hip Score
HOOS	Hip Disability and Osteoarthritis Outcome Score
IF	Internal Fixation
HA	Hemiarthroplasty
LMM	Linear Mixed Models
MCID	Minimal Clinically Important Difference
MDC	Minimal Detectable Change
MMRC	Modified Medical Research Council
N	Number
NAR	Norwegian Arthroplasty Register
NICE	National Institute for Health and Care Excellence
NHFR	Norwegian Hip Fracture Register

NPR	Norwegian Patient Register
NYHA	New York Heart Association
OR	Odds Ratio
PJI	Periprosthetic Joint Infection
PPF	Periprosthetic Fracture
PROMs	Patient-Reported Outcome Measurements
RCT	Randomized Controlled Trial
RR	Relative Risk
SD	Standard Deviation
THA	Total Hip Arthroplasty
VAS	Visual Analog Scale
WHO	World Health Organization

Papers included in the thesis

Paper I

High failure rate after internal fixation and beneficial outcome after arthroplasty in treatment of displaced femoral neck fractures in patients between 55 and 70 years.

An observational study of 2,713 patients reported to the Norwegian Hip Fracture Register.

Bartels S, Gjertsen JE, Frihagen F, Rogmark C, Utvåg SE

Acta Orthop. 2018 Feb;89(1):53-58. doi: 10.1080/17453674.2017.1376514.

Paper II

Low bone density and high morbidity in patients between 55 and 70 years with displaced femoral neck fractures: a case-control study of 50 patients vs 150 normal controls.

Bartels S, Gjertsen JE, Frihagen F, Rogmark C, Utvåg SE

BMC Musculoskelet Disord. 2019 Aug 14;20(1):371. doi: 10.1186/s12891-019-2732-8.

Paper III

Total hip arthroplasty leads to better results after low-energy displaced femoral neck fracture in patients aged 55 to 70 years. A randomized controlled multicenter trial comparing internal fixation and total hip arthroplasty.

Bartels S, Kristensen TB, Gjertsen JE, Frihagen F, Rogmark C, Dolotowski FC, Figved W, Benth JS, Utvåg SE

J Bone Joint Surg Am. 2022 Aug 3;104(15):1341-1351. doi: 10.2106/JBJS.21.01411.

Thesis Summary

A displaced femoral neck fracture (FNF) is a severe injury and will require hospitalization and surgery. The most common treatment options in Norway for FNFs are closed reduction and internal fixation (IF), hemiarthroplasty (HA) or total hip arthroplasty (THA). Patients with these fractures have a high risk of subsequent surgical complications, reduced function, hip pain, and reduced health-related quality of life. The literature on patients older than 70 years with displaced FNFs is extensive, and most studies have advocated arthroplasty as the treatment of choice. The middle-aged patient group aged 55-70 years is less well described and the treatment for displaced FNFs in this age group is still controversial. These patients are probably still working and demand a high level of activity and quality of life. The risk of persisting and serious problems after treatment and the health economic aspect are therefore a great challenge, even though the overall incidence of hip fractures has decreased in recent decades. A Norwegian study reported the overall annually hip fracture incidence in the particular age group 55-70 years to be 92 per 10.000 (53/10.000 women and 39/10.000 men) in the period 2009-2013. The average age for low-energy hip fractures is about 80 years, almost 70% are women. About 40% of all hip fractures are displaced FNFs. Most of these displaced FNFs are caused by a low-energy trauma, and the patients often have comorbidities, including osteoporosis, which may increase the risk of complications and the need for additional surgery.

Studies reporting bone mineral density at the time of fracture are rare and often describe a more geriatric population. For patients under 60 years of age, IF is usually recommended, as many surgeons endeavor to prevent replacement of the hip joint. Studies investigating outcomes after FNF in patients younger than 70 years have found a high risk of reoperation after IF due to mechanical failure, non-union or avascular necrosis. This may indicate that many hip fracture patients under 70 years of age are more osteoporotic and frailer than

individuals of the same age in the general population. Thus, it might be preferable to treat FNFs in this intermediate age group with an arthroplasty, as in patients older than 70 years.

In **paper I** we presented data on 2.713 patients reported to the national Norwegian Hip Fracture Register (NHFR) aged 55-70 years with displaced intracapsular femoral neck fractures in the period January 2005-December 2012. We found a high rate of reoperation for patients treated with IF (33%). Patients treated with HA or THA were significantly more satisfied and reported less pain. Although patients treated with HA were the frailest patient group with a crude one-year mortality of 15%, results were better for arthroplasty than in the IF group.

In **paper II**, we aimed to assess patient-related risk factors for low-energy displaced FNFs compared with sex- and age-matched controls. In this single center matched case-control study, we included 50 patients between 50-70 years of age with a low-energy displaced FNF and 150 participants randomly selected and matched by age and gender without a fracture from a normal population. We recorded patient baseline data, patient-reported outcome measurements (PROM), specific functional hip scores and performed Dual-energy X-ray Absorptiometry (DXA). We found more comorbidities assessed by Charlson comorbidity Score (CCI) and there were more patients with ASA class 2-3 in the fracture group. Patients in the fracture group had lower body mass index (BMI) and there were more smokers in this group.

In **paper III** we aimed to assess the effect of closed reduction and IF with cannulated screws versus THA for low-energy displaced FNFs in patients between 55 and 70 years according to PROMs, complications, and reoperations. In this multicenter randomized controlled trial, 102 patients were randomly allocated to either IF (51 pas.) or THA (51 pas.). The follow-up period was 24 months. ASA classification, CCI Score, NYHA, and mMRC Dyspnea scale were recorded to report comorbidity. The EQ-5D-3L index score, EQ-VAS, VAS pain, and

VAS satisfaction were accessed at each follow-up. Reoperations and complications were registered continuously. The primary outcome was the Harris Hip Score (HHS) at 12 months. Secondary outcomes were HHS at 4 and 24 months, Oxford Hip Score (OHS), and Hip Disability and Osteoarthritis Score (HOOS) at 4, 12, and 24 months after index surgery. We used the minimal clinically important differences (MCID) to determine clinical relevance.

Nine patients (18%) allocated to IF were converted to arthroplasty during index surgery because of unacceptable fracture reduction. Twenty-six patients (51%) in the IF group and two patients (3.9%) in the THA group had at least one major reoperation during the follow-up period.

The primary outcome, HHS at 12 months follow-up, was superior in the THA group (89.8 points) compared to IF (84.5). Although statistically significant, the mean difference of 5.3 points (95% CI 0.8 - 9.8, p=0.021) was smaller than the predefined MCID of 10 points. We found better results for the THA groups for all secondary outcomes.

In conclusion, patients with a low-energy displaced FNF between 55-70 years were more osteoporotic and frailer than their peers of a general population. Patients treated with IF had a high risk for reoperation. Compared to IF, treatment with THA leads to superior patient-reported functional outcome, more satisfaction, better quality of life, and less pain.

We suggest that low-energy displaced femoral neck fractures in patients between 55-70 years of age should preferably be treated with arthroplasty.

Thesis Summary in Norwegian

Et dislokert lårhalsbrudd er en alvorlig skade og vil føre til sykehusinnleggelse og operativ behandling. De mest brukte behandlingsalternativer i Norge er enten lukket reposisjon og fiksasjon (IF) av bruddet, hemiprotese (HA) eller totalprotese (THA). Pasienter med denne type brudd har en høy risiko for kirurgiske komplikasjoner og hoftesmerter, samt redusert funksjon og helserelatert livskvalitet. For eldre pasienter over 70 år med dislokert lårhalsbrudd er litteraturen omfattende, og de fleste studier anbefaler ledderstattende kirurgi med proteser som første valg. Den middelaldrende pasientgruppen mellom 55 og 70 år er mindre godt beskrevet og behandlingen for dislokerte lårhalsbrudd er fortsatt kontroversiell. Disse pasienter er ofte fortsatt yrkesaktive, har et høyt aktivitetsnivå og høye krav til livskvalitet. Risikoen for vedvarende og alvorlige problemer etter behandlingen er stor, med dertil følgende helseøkonomiske utfordringer, til tross at insidensen for hoftebrudd har blitt mindre over de siste 10 årene.

En norsk studie fra perioden 2009-2013 har vist en insidens for alle hoftebrudd i aldersgruppen mellom 55 og 70 år på 92 pasienter per 10.000 innbyggere (53/10.000 kvinner og 39 /10.000 menn). Gjennomsnittsalderen for hoftebrudd ligger på ca. 80 år, og neste 70% er kvinner. Om lag 40% av alle hoftebrudd er dislokerte lårhalsbrudd. De fleste hoftebruddene skyldes fall fra egen høyde, og disse pasienter har ofte andre sykdommer, inkludert benskjørhet, som øker risikoen for komplikasjoner og behov for ytterligere kirurgisk behandling. Studier som har sett på beintettheten ved bruddtidspunktet er sjeldne og beskriver ofte en mer geriatrisk populasjon. For pasienter under 60 år anbefales det som oftest reposisjon og osteosyntese (IF), i og med at mange kirurger prøver å forhindre ledderstattende kirurgi av hofteleddet. Studier som har undersøkt utfallet etter lårhalsbrudd for pasienter som er yngre enn 70 år, har funnet en høy risiko for reoperasjoner etter IF på grunn av mekanisk feil eller instabilitet, ikke tilhelet brudd eller avaskulær nekrose. Dette kan indikere at mange av hoftebruddpasienter under 70 år lider av osteoporose og er skrøpeligere enn personer av samme alder i den generelle befolkningen. Derav fremsettes hypotese om at disse pasienter med fordel bør behandles med ledderstattende kirurgi på lik linje med pasienter som er eldre enn 70 år.

I **artikkel I** la vi frem data fra 2.713 pasienter med dislokert lårhalsbrudd i aldersgruppen mellom 55 og 70 år som var registrert i det nasjonale norske hoftebruddregisteret fra januar 2005-desember 2012. Vi kunne påvise en høy andel av reoperasjoner for pasienter som var behandlet med IF (33%). Pasienter som var blitt behandlet med HA eller THA var signifikant mer fornøyde og hadde mindre smerter. Pasienter som fikk HA var i den skrøpeligste pasientgruppen med en ett-års dødelighet på 15% og selv hos disse var det bedre resultater med proteser sammenlignende med IF.

I **artikkel II** hadde vi som mål å vurdere pasientrelaterte risikofaktorer for lavenergetiske dislokerte lårhalsbrudd sammenlignet med en kjønns- og aldersjustert populasjon. I denne studien som ble gjennomført ved Akershus Universitetssykehus inkluderte vi 50 pasienter mellom 55 og 70 år med et lavenergetisk dislokerte lårhalsbrudd, og 150 tilfeldige deltakere fra den normale befolkningen uten brudd. Vi registrerte informasjon som alder, kjønn, vekt, høyde, pasients egen reporterte livskvalitet og funksjon, spesielle hoftefunksjonsscorer og resultater av en beintetthetsmåling. Vi fant sykere og skrøpeligere pasienter in bruddgruppen ved bruk av Charlson Comorbidity Index scoren (CCI), og det var flere pasienter i ASA kategori 2-3 i bruddpopulasjonen. Pasienter med brudd hadde en lavere body mass index (BMI), og vi fant at flere pasienter var røykere sammenlignet med kontrollgruppen.

I **artikkel III** hadde vi som mål å undersøke effekten av lukket reposisjon og IF sammenlignet med THA ved lavenergetiske dislokerte lårhalsbrudd hos pasienter mellom 55 og 70 år i forhold til pasients egen reporterte resultater, komplikasjoner og reoperasjoner. I denne multisenter RCT studien randomiserte vi 102 pasienter enten i IF gruppen (51 pas.)

eller i THA gruppen (51 pas.). Oppfølgingsperioden var 24 måneder. ASA klassifikasjon, CCI Score, NYHA og mMRC Dyspnea scale ble brukt til å registrere sykelighet. EQ-5D-3L index scores, EQ-VAS, VAS smerte og VAS fornøydhet ble registrert ved hvert oppfølgingstidspunkt. Reoperasjoner og komplikasjoner ble fortløpende registrert. Primære utfallmål var Harris Hip Score (HHS) ved 12 måneder. Sekundære utfallsmål var HHS ved 4 og 24 måneder, Oxford Hip Score (OHS), Hip Disability and Osteoarthritis Score (HOOS) ved 4, 12, og 24 måneder etter index operasjonen. Vi brukte «minimal clinically important differences» (MCID) til å bestemme målbare forskjeller.

Ni pasienter som opprinnelig skulle har vært behandlet med IF, ble allerede i løpet av index operasjonen konvertert til protese grunnet uakseptable reposisjonsresultat. Tjueseks pasienter (51%) i IF gruppen og 2 pasienter (3.9%) i THA gruppen hadde minst en stor reoperasjon i løpet av oppfølgingsperioden.

Primært endepunktet, HHS ved 12 måneders oppfølging, var bedre i THA gruppen (89.8 poeng) sammenlignet med IF (84.5). Selv om denne forskjellen på 5.3 poeng var statistisk signifikant (95% CI 0.8 - 9.8, p=0.021), var gjennomsnittlig forskjell mindre enn det på forhånd definerte MCID på 10 poeng. Vi kunne også påvise bedre resultater for alle sekundære utfallsmål i THA gruppen.

Vi konkluderte med at pasienter mellom 55 og 70 år med et lavenergetisk og dislokert lårhalsbrudd er skrøpeligere og har høyere forekomst av osteoporose enn en jevnaldrende normal befolkning. Pasienter som ble behandlet med IF hadde en høy risiko for reoperasjoner. Behandling med THA førte til signifikant bedre resultater i forhold til egen rapportert livskvalitet og funksjon, fornøydhet og smerte.

Vi anbefaler derfor at lavenergetiske dislokerte lårhalsbrudd hos pasienter mellom 55 og 70 år behandles med protesekirurgi.

Thesis at a glance

Paper	**Research question**	**Material**	**Main findings**
Paper I	What are the functional results and complications after low-energy displaced FNFs in patients between 55-70 years?	Observational study of 2.713 patients treated with IF, HA or THA reported to the Norwegian Hip Fracture Register	High rate of reoperations after IF and better PROMs after both THA and HA. Patients selected to HA represented a frailer group than patients treated with THA or IF
Paper II	Can we identify patient-related factors for low-energy displaced FNFs in patients between 55-70 years?	Case-control study of 50 patients with a displaced FNF versus a sex- and age-matched normal population of 150 persons without a fracture using DXA, comorbidity and hip function	Patients with displaced FNFs were significantly more osteoporotic, had higher comorbidities, and were more likely smokers. This patient group was frailer than expected and may benefit from a similar treatment as older patients over 70 years
Paper III	What is the better treatment option for low-energy displaced FNF in patients between 55-70 years?	Interventional randomized controlled multicenter trial including 51 patients treated with IF and 51 patients treated with THA	Better PROMs and hip function in patients treated with THA and a high rate of reoperations after IF

1. Introduction

1.1 Importance of topic and epidemiology

A displaced femoral neck fracture (FNF) is a severe injury that will require hospitalization and surgery (Fig.1) [1]. Patients with these fractures have a high risk of subsequent surgical complications, reduced function, hip pain and reduced health-related quality of life [2-8]. The literature on patients older than 70 years with displaced FNF is extensive and most studies have advocated arthroplasty as the treatment of choice [3, 8-14]. The middle-aged patient group aged 55-70 years has been less well described and the treatment for displaced FNFs in this group is still controversial [10-12]. These patients are probably still working and expect a high level of activity and quality of life. The risk of persistent and serious problems after treatment and the health economic aspect are therefore a great challenge, even though the overall incidence of hip fractures has decreased in recent decades [1, 15-21].

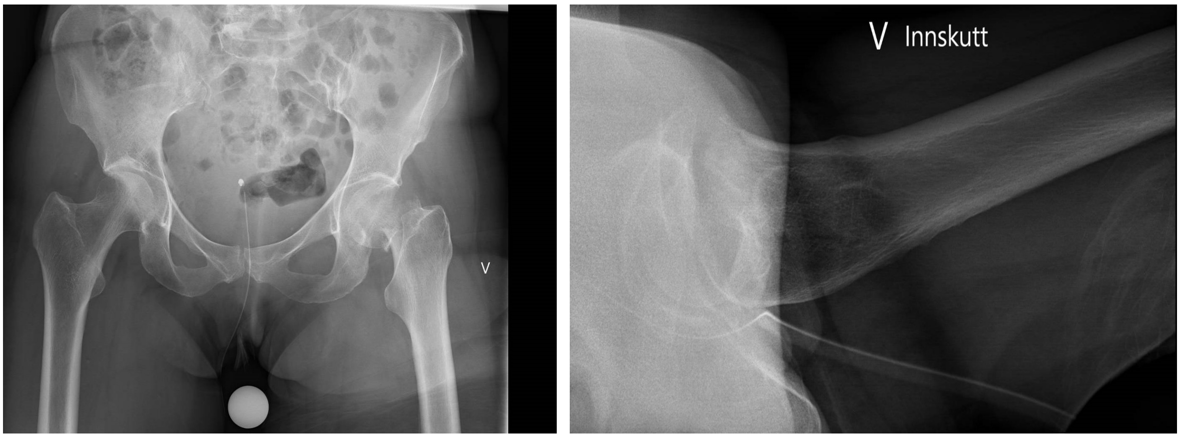


Fig.1: *X-rays of a displaced femoral neck fracture in the left hip on antero-posterior and lateral view*

Norway has one of the highest incidences of hip fractures in the world at approximately 8,500 cases annually (Fig.2) [22, 23]. All operations for fractures of the proximal femur are recorded by the Norwegian Hip Fracture Register (NHFR) or the Norwegian Arthroplasty Register (NAR).

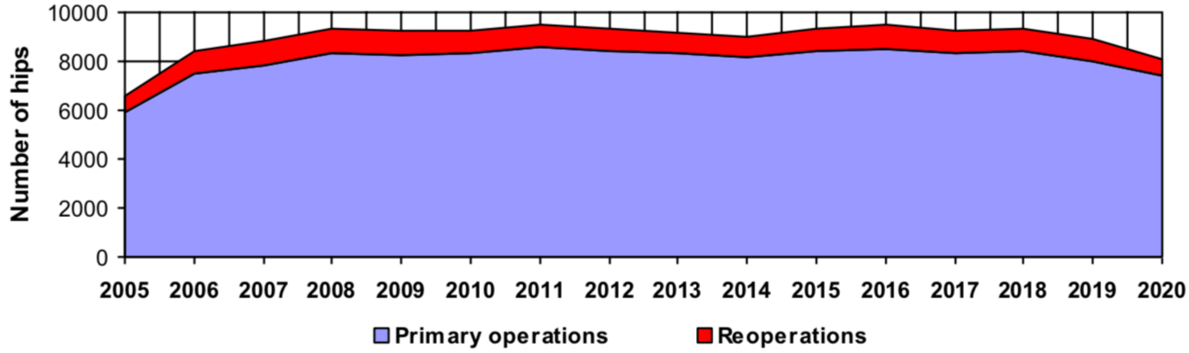


Fig.2: *Annual numbers of operations for hip fractures.*
From the Norwegian Hip Fracture Register`s Annual Report 2021 (reprinted with permission).

These patients are frail, and the five-year mortality has been reported to be up to 63% [23].

More than 60% of hip fractures patients have severe comorbidity (ASA class 3 or higher) (Fig.3).

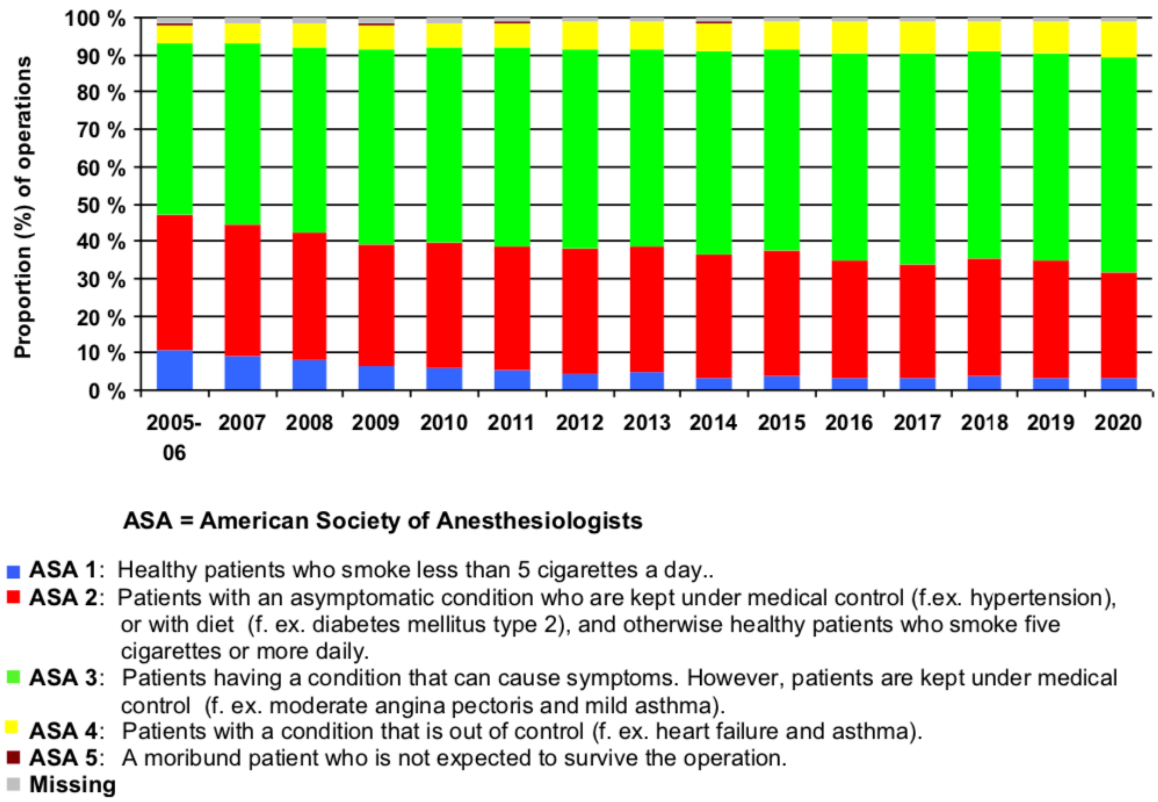
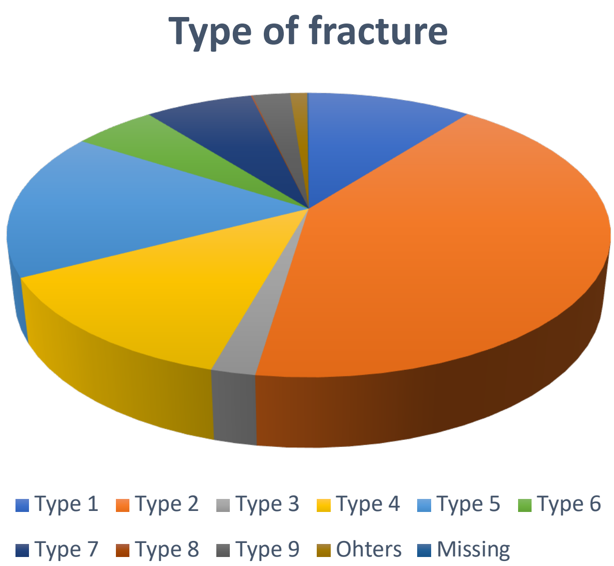


Fig.3: *Proportions (%) of patients/operations by ASA-classification.*
From the Norwegian Hip Fracture Register`s Annual Report 2021 (reprinted with permission).

The NHFR records all types of fractures in the proximal part of the femur, whereas total hip arthroplasties are recorded in the NAR. About 40% of all fractures are displaced FNFs (Type 2) (Fig.4).



Type 1: intracapsular fracture, undisplaced
Type 2: intracapsular fracture, displaced
Type 3: basocervical fracture
Type 4: trochanteric fracture (2 fragments) (AO/OTA A1)
Type 5: trochanteric fracture (multifragment) (AO/OTA A2)
Type 6: subtrochanteric fracture
Type 7: intracapsular fracture unspecified (from the NAR)
Type 8: trochanteric fracture unspecified (from the NAR)
Type 9: intertrochanteric fracture (AO/OTA A3)
Registration started in 2008

Fig.4: *Types of fractures and reasons for primary operations.*
Numbers and quantities from the Norwegian Hip Fracture Register`s Annual Report 2021 (reprinted with permission).

The average age for low-energy hip fractures is about 80 years, and almost 70% are women (Fig.5) [23].

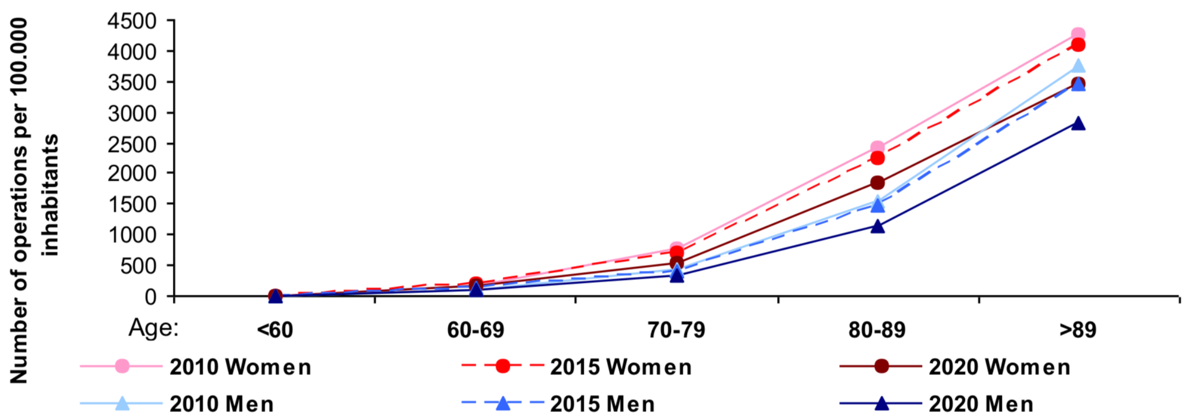


Fig.5: *Incidence of reported primary operations in different age groups (reported for 2010, 2015 and 2020). From the Norwegian Hip Fracture Register`s Annual Report 2021 (reprinted with permission).*

The overall hip fracture incidence in the age group between 55-70 years was reported to be 92 per 10.000 (53/10.000 women and 39/10.000 men) in a Norwegian study in the period 2009-2013 [20].

Most of these FNFs were caused by a low-energy trauma defined as a result of falling from standing height or less [24]. Patients were often frailer than expected and had other diseases and factors, that could increase the risk of fixation failure, complications and risk of reoperation [25-27]. Other factors that could influence functional outcome after hip fracture care might be medication (steroids, neuroleptic medication), alcohol consumption or osteoporosis. Studies describing trauma mechanism and bone mineral density at the time of fracture in the middle-aged population of 50-70 years are rare [25, 28]. Some studies have described a more geriatric population [29, 30]. Internal fixation (IF), with open or closed reduction is usually recommended for patients under 60 years of age [11, 12, 31]. Many surgeons try to prevent replacement of the hip joint as these patients often tolerate secondary interventions. For patients over 70 years with a displaced FNF, hemiarthroplasty (HA) with a cemented stem is usually recommended in Norway [3, 23]. Healthy and independent patients should be considered as suitable for total hip arthroplasty (THA), as these patients might benefit from this treatment option [6, 11].

Studies investigating outcome after FNF in patients younger than 70 years have found a high risk of reoperation after IF due to mechanical failure, non-union or avascular necrosis [31-34]. Rates of reoperation due to arthroplasty were much lower even for frailer patients with more comorbidities [31-34]. This may indicate that patients under 70 years of age with femoral neck fractures are frailer and more osteoporotic than expected and may benefit from arthroplasty in most cases.

This thesis focuses on the most common different types of treatment of displaced FNFs in patients between 55-70 years, aiming to find predisposing factors for good or inferior results after treatment and whether arthroplasty might be the better treatment alternative for this age group.

1.2 Anatomy and classification

Based on different types of fractures and principles of fracture treatment, the proximal femur can be divided into several parts (Fig.6) [2]. A classical FNF is defined as a fracture through the intracapsular part of the femoral neck (purple) and can be treated with either fixation of the fracture or with an arthroplasty.

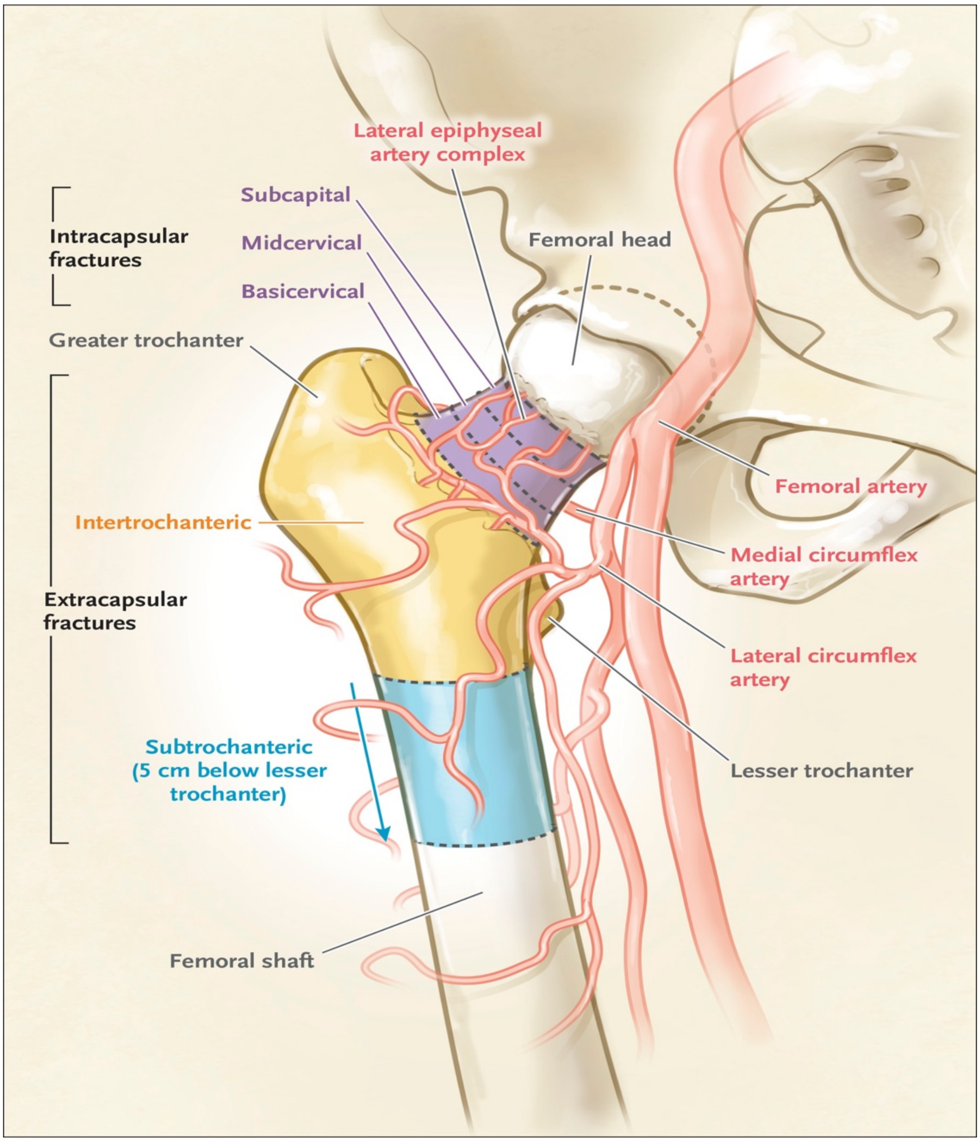


Fig.6: *Description of and blood supply to different parts of the proximal femur, reproduced with permission. From Bhandari and Swiontkowski. Management of Acute Hip Fracture. NEJM 2017. Copyright Massachusetts Medical Society [2].*

As displayed in Figure 6 the blood supply to the femoral head is mainly provided by anastomoses of vessels around the femoral neck arising from the medial and lateral circumflex artery. Fractures of the femoral neck may affect the blood supply in this area. Reduced blood supply can complicate the healing process or lead to secondary surgical interventions [2].

There are several different classifications of FNFs including the AO classification 31-B and the Pauwels classification, but the most commonly used one is the Garden classification (Fig.7), which is graduated from I to IV [35-37].

Due to problems with inter-observer reliability, the Garden classification has been simplified in daily practice, dividing FNFs into non-displaced and displaced fractures (Fig.7) [37-39].

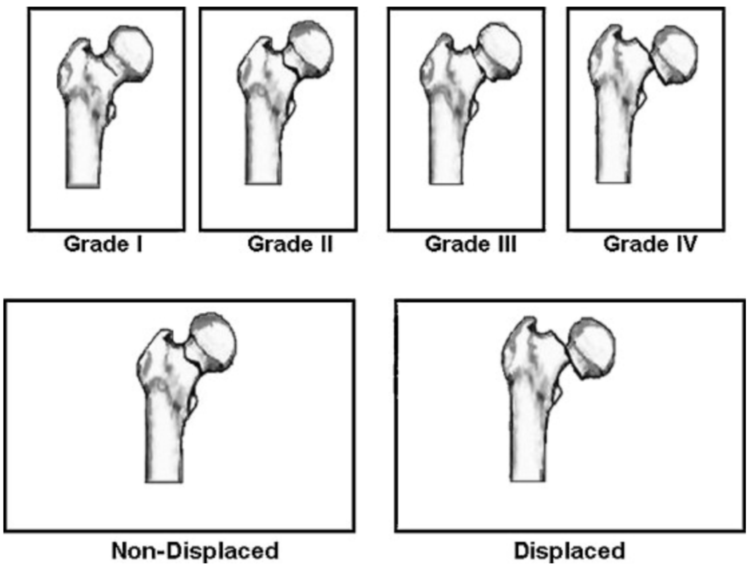


Fig.7: *Original and simplified Garden classification of FNFs Van Embden et al. 2012 (reprinted with permission)*, *published by Elsevier Masson SAS. All rights reserved [38].*

The Garden classification is based only on an anterior-posterior radiographic view without including a possible posterior tilt as displacement. In 2016, Dolatowski et al. were able to reproduce results and measurements from Palm et al., finding a posterior tilt of ≥ 20° to be an increased risk factor for osteosynthesis (fixation) failure in patients with non-displaced fractures (Garden I+II) [40, 41]. For this reason, measurement of the posterior tilt, where a tilt of ≥ 20° is defined as a displaced fracture, is often used in daily practice (Fig.8).

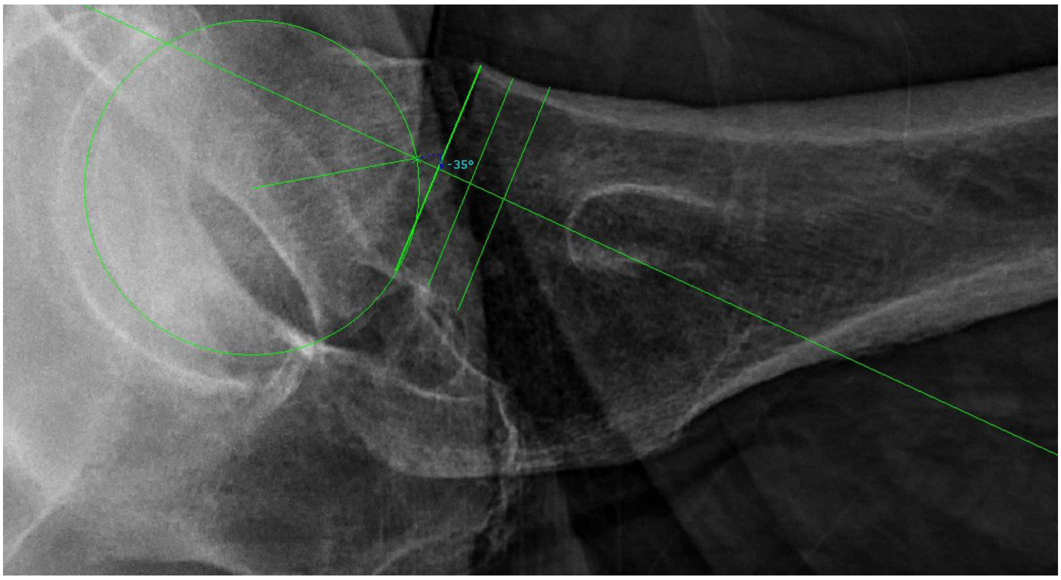


Fig.8: *X-ray of the posterior tilt of an FNF in a lateral view, from Max Temmesfeld (reprinted with permission)*

1.3 Treatment of femoral neck fractures

Regardless of age, a displaced FNF is a severe injury and will almost always require hospitalization and surgery (WHO) [1]. There is no requirement for non-operative treatment in daily practice [2, 42-44]. Non-operative treatment is associated with increased mortality compared to patients who undergo surgery and secondary dislocation of the fracture has been described as reaching 20% [45-48]. Additionally, non-operative treatment will cause unnecessary pain and prevent nursing care and mobilization. The most commonly used treatment options in Norway for FNFs are internal fixation (IF), hemiarthroplasty (HA) or total hip arthroplasty (THA) (Fig.9).

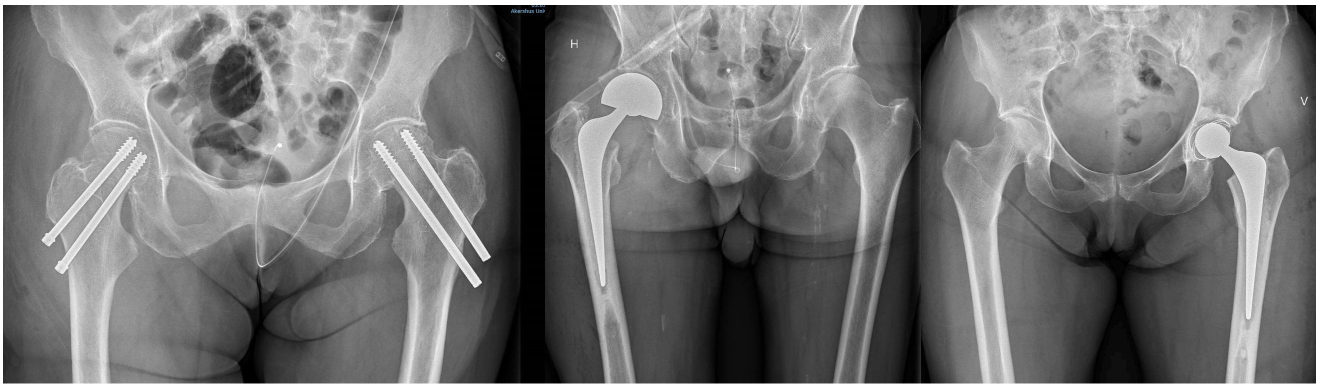


Fig.9: *X-rays of IF, HA and THA as possible treatment options for FNF*

1.3.1 Non-displaced femoral neck fractures

For non-displaced FNFs, treatment with IF is recommended in all age groups with acceptable functional results and assumed rates of non-union and avascular necrosis (AVN) of 5-15% [47, 49-53]. However, Dolatowski et al. presented a study in 2019 suggesting that treatment with HA in patients > 70 years improved mobility and reduced the risk of reoperation compared to treatment with IF [52].

1.3.2 Displaced femoral neck fractures

The treatment of displaced fractures varies, depending on patients` age, morbidity and bone quality. Treatments and outcomes in elderly and frail patients > 70 years have been extensively investigated, and arthroplasty is clearly recommended as the treatment of choice [3, 9-14]. The treatment of the young and middle-aged group < 70 years, however, is still controversial. Closed reduction and IF for patients under 60 years of age are usually recommended as many surgeons are reluctant to replace the native hip joint with an arthroplasty [7, 11, 12, 43, 47, 50]. IF is less invasive than prosthetic surgery, but the risk of reoperation due to mechanical failure, non-union or AVN is high [33, 51]. When an arthroplasty is performed due to failure of internal fixation, the risk of complications has been shown to be higher and both hip function and health-related quality of life might be inferior, compared to primary arthroplasty [54, 55]. In recent years, however, data in the NHFR have shown a shift from the use of internal fixation to arthroplasties, both hemiarthroplasty (HA) and total hip arthroplasty (THA) (Fig.10) [23].

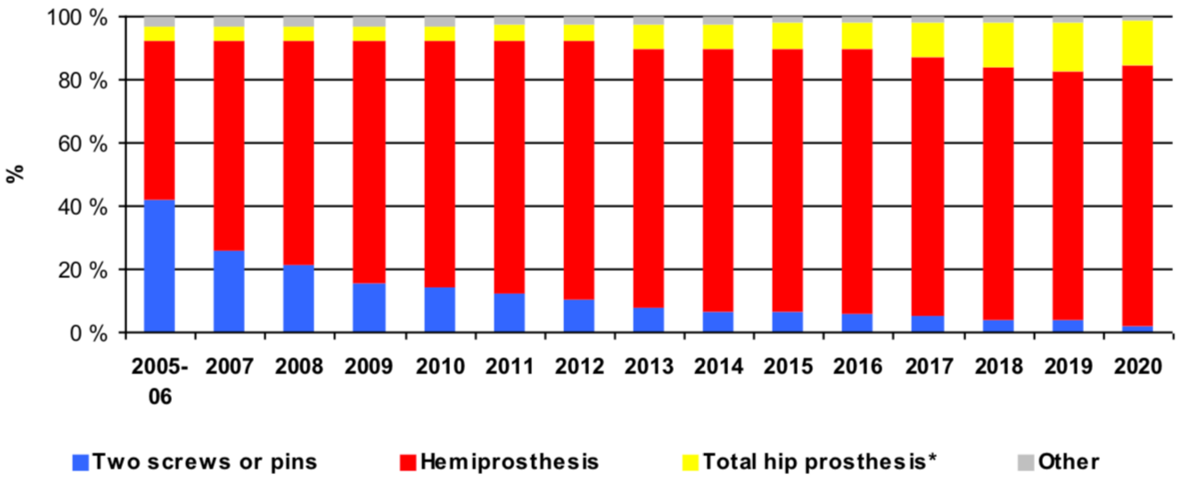
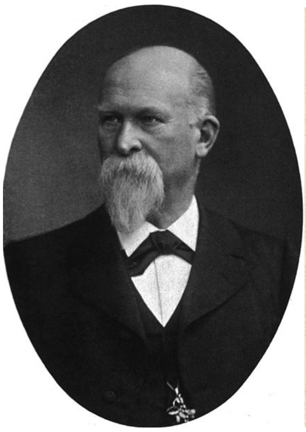


Fig.10: *Change of treatment over time for all displaced femoral neck fractures. From the Norwegian Hip Fracture Register`s Annual Report 2021 (reprinted with permission).*

1.4 History of treatment

The first internal fixation of an FNF was performed by the German surgeon Bernhard von Langenbeck (1810-1887) in 1858 with metal silver screws, but the patient died [56]. Franz König (1832-1910) performed the same operation successfully under antiseptic conditions in 1875 in Göttingen, Germany (Fig.11) [56, 57]. In 1894, Julius Nicolaysen (1831-1911), Professor of Surgery at the National Hospital (Rikshospitalet) in Oslo, performed his first operation with closed nailing of a fracture of the femoral neck (Fig.12) [56].



Franz König

Julius Nicolaysen

Fig.11: ***Franz König,*** *published in "Galerie hervorragender Ärzte und Naturforscher" (1911), by J.F. Lehmann, Munich*

Fig.12: ***Julius Nicolaysen,*** *Oslo Museum, c. 1870*

The history of hip replacement started in 1821 with Anthony White (1782-1849) from the Westminster Hospital in London performing the first excision arthroplasty [58]. In the 1950s the cemented Thompson and the uncemented Austin Moore prostheses were frequently used in treatment of different conditions of the hip, including fractures [58-61]. After that, the Christiansen prosthesis was the most commonly used prosthesis in Scandinavia in the 1970s but due to poor results it was replaced by the Charnley prosthesis [62, 63]. The Charnley prosthesis was developed by Sir John Charnley, who pioneered modern THA in the 1960s. The Charnley prosthesis with its further development was the most used prosthesis in Norway from 1987 to 2010 [23].

The success of the cemented Exeter prosthesis (Stryker) started in 1970, where Ling and Lee developed the first collarless, polished, and tapered hip stem [64]. Since then, the Exeter hip stem has been implanted in over two million patients globally with excellent long-term survivorship after nearly 22 years [65].

The cemented and anatomically shaped designs SP I and later SP II (Link) were developed and first established in 1978 by Hans-Herrmann Lubinus in Kiel, Germany [66]. It is one of the most frequently used and well documented anatomical implant in Norway [23].

The uncemented hydroxyapatite-coated Corail stem (DePuy/Synthes) was first implanted in 1986 by the ARTRO group in France and is the most used uncemented femoral stem in Norway [23, 67].

1.5 Contemporary surgery

1.5.1 Recommendations and general conditions

Displaced FNFs are normally treated surgically. Internal fixation has been recommended for patients under 60 years of age as these patients are considered to tolerate a secondary procedure if fracture fixation fails [7, 11, 12]. Fixation with two parallel cannulated screws is the most common method used in Scandinavia [23]. Outside Scandinavia sliding hip screws or multiple cancellous screws are recommended as standard treatment [2, 8, 23]. Internal fixation is less invasive than arthroplasty, but the risk of reoperation due to mechanical failure, non-union, or AVN is high [32, 33, 51, 68]. However, the risk of complications after secondary hip arthroplasty due to failed IF is higher, and hip function and quality of life might be inferior compared to primary hip arthroplasty [69]. For patients over 70 years, hemiarthroplasty or THA with cemented implants is recommended [11, 12, 23, 70-72]. Treatment with arthroplasty results in more blood loss and the duration of surgery is longer (Fig.13) [23, 73].

	Type of operations	Total	Mean duration of operations (minutes)	Standard deviation
*	Two screws or pins	22 378	26	14
	Three screws or pins	787	37	19
*	Bipolar hemiprosthesis	43 688	77	25
	Unipolar hemiprosthesis	301	74	20
	Hip compression screw and plate	22 837	56	27
	Hip compression screw with lateral support plate	9 191	75	34
	Short intramedullary nail without distal locking	368	49	21
	Short intramedullary nail with distal locking	10 297	53	26
	Long intramedullary nail without distal locking	133	82	43
	Long intramedullary nail with distal locking	6 797	96	48
*	Total hip prosthesis	4 547	94	32
	Other	2 222	68	39
	Missing	6	42	23

Fig.13: *Duration of surgery for different types of operations for the most used treatment options in Norway. The treatment options studied in this thesis are marked with *.*
From the Norwegian Hip Fracture Register`s Annual Report 2021 (reprinted with permission).

Early mobilization and full weight-bearing should be encouraged for both treatment principles. Both incidence of infection after hemiarthroplasty and time between admission and surgery are national measurement parameters in Norway [23, 70, 74]. Operations should preferably be performed within 24 hours and at the latest at 48 hours.

1.5.2 Internal fixation, reduction, and positioning of implants

Several different implants for IF in treatment of FNFs have been used in an attempt to achieve stability and avoid rotation and shortening of the fracture [51, 75]. There is little evidence as to which implant is best [8, 51, 75]. Further, the stability of two screws has been questioned, but there is little evidence supporting a reduced risk of fixation failure by adding one extra screw [76]. Internal fixation is usually performed under spinal anesthesia on a traction table by closed reduction with biplanar fluoroscopy and fixation with two parallel cannulated screws, which is also the most common method used in Scandinavia (Fig.14) [23].

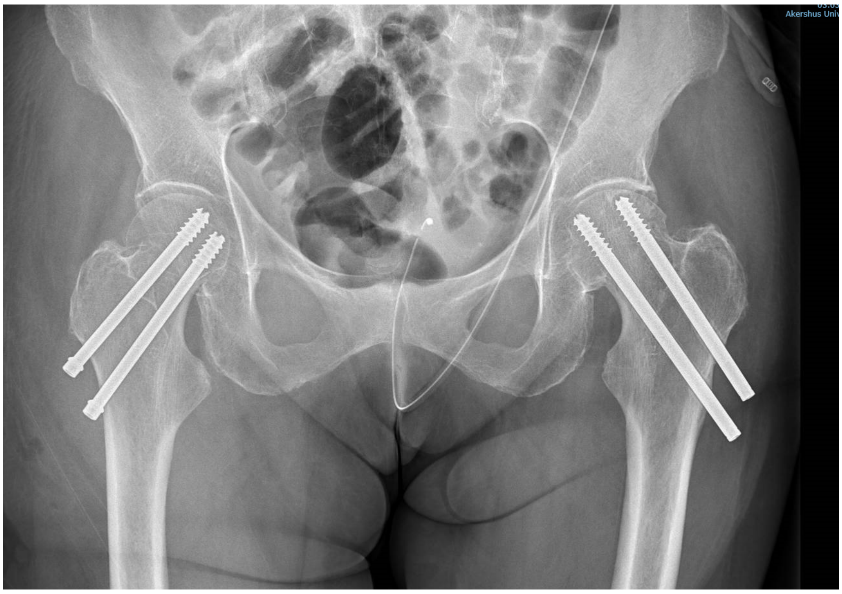


Fig.14: *Postoperative X-ray with two cannulated screws on the right hand side after femoral neck fracture*

After acceptable reduction with fluoroscopy, the distal screw should be positioned as close as possible to the medial cortex in the antero-posterior view and in the center of the femoral neck in the lateral view. The proximal screw should be positioned in the center of the femoral neck in the antero-posterior view and close to the posterior calcar in the lateral view. Both screws should be placed as deeply as possible into the subchondral bone of the femoral head. Patients treated with IF should receive perioperative single shot intravenous antibiotics and postoperative antithrombotic prophylaxis (5000 IU low-molecular-weight heparin once daily for two weeks) according to national recommendations [23, 70].

If closed reduction is unacceptable, the procedure should be converted to arthroplasty during the same anesthesia as suboptimal reduction might lead to an inferior outcome [2, 77].

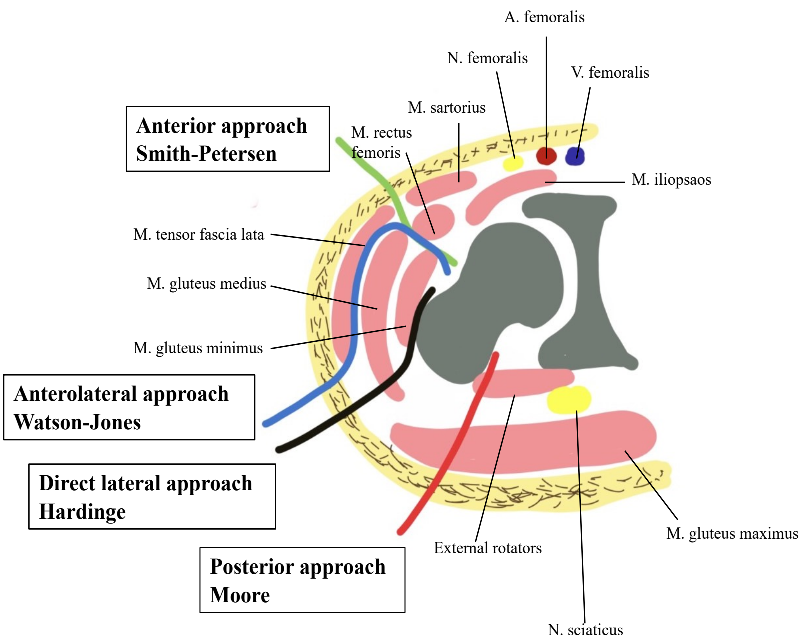
1.5.3 Arthroplasty

Hemiarthroplasty is recommended for patients with a displaced FNF who are older than 70 years [3, 4, 9, 11, 23]. Total hip arthroplasty should be performed with latest-generation hip implants with modular, mainly cemented implants/stems. Bone cement with antibiotics should be used [11, 70, 71, 78, 79]. To minimize the risk of postoperative dislocation, a prosthetic head size of at least 32 mm or dual mobility cups should be used [11, 23]. All patients should receive perioperative intravenous antibiotics (e.g. Cefalotine 2 g x 4, Cloxacillin 2 g + 1 g + 1 g + 1 g, or Clindamycin 600 mg x 3 in cases of penicillin allergy) and postoperative antithrombotic prophylaxis (5000 IU low-molecular-weight heparin once daily for two weeks), according to national recommendations [23, 70].

1.5.4 Surgical approaches for hip arthroplasty

There are several surgical approaches to the hip joint when arthroplasty due to FNF is performed (Fig.15).

Fig.15: *Simplified illustration of surgical approaches to the hip joint by Johanna Sævik Bartels, reprinted with permission*



These approaches are in use for both THA and HA. The most commonly used surgical approach to the hip joint in hemiarthroplasty in Norway, at almost 70%, is still the direct lateral approach, as described by Hardinge in 1982, followed by the posterior approach (Fig.16) [23, 80]. The anterior approach between the sartorius and tensor fascia lata muscles, described by Smith-Petersen, and the anterolateral approach between the gluteus medius and tensor fascia lata muscles, described by Watson-Jones, are less commonly used in treating FNFs with arthroplasty in Norway (Fig.16) [23, 81, 82].

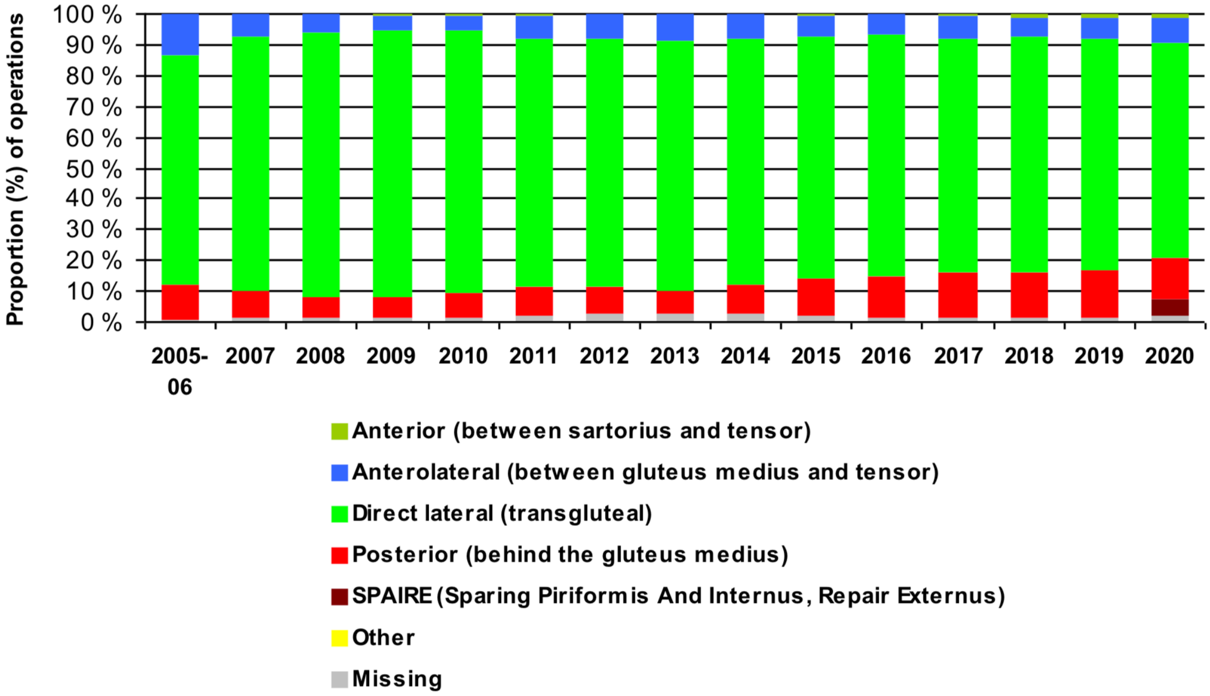


Fig.16: *Surgical approaches used in hemiarthroplasty.*
From the Norwegian Hip Fracture Register`s Annual Report 2021 (reprinted with permission).

When performing the direct lateral or transgluteal approach, a skin incision over the greater trochanter is made and the tensor fascia lata muscle is divided. Then the anterior portion of the gluteus medius and minimus muscules is released from the greater trochanter to expose the hip capsule. The posterior approach, as described by Moore in 1957, starts with a curved skin incision posterior to the lateral side of the greater trochanter [60]. After splitting the tensor fascia lata and gluteus maximus muscles, the short external rotators tendons are detached from the greater trochanter and secured with a holding suture for later repair. Reflection of the muscle/tendon bundle exposes the hip capsule. Surgeons should be aware of the location of the sciatic nerve to avoid iatrogenic injuries. Both the direct lateral and the posterior approach have disadvantages. The main concern in the direct lateral approach is the gluteus medius insufficiency after surgery, resulting in Trendelenburg sign and limping, as reported by several authors [83, 84]. A Norwegian study by Amlie et al. in 2014 reported inferior patient-reported outcome and more limping after the direct lateral approach than after the posterior approach in THA [85]. The main concern in the posterior approach is dislocation of the prosthesis, and several authors have shown a varying risk of reoperation using the posterior approach for hemiarthroplasty in elderly patients [86, 87]. Rogmark and Leonardsson published a review in 2016 where they recommended the direct lateral approach due to a lower rate of dislocation [71]. On the other hand, Parker (2015) found no significant differences in any of the outcome measurements, including mortality, degree of residual pain or regain of walking ability in a randomized trial of 216 patients [88].

1.5.5 Fixation of implants and recommendations

Most patients with an FNF belong to an older and fragile population (Figs.3+5). For patients under 70 years of age, little evidence exists. This group seemed to be frailer and more osteoporotic than expected and this might be taken into consideration [31-34]. Several studies have recommended cemented implants due to lower risk of reoperation, especially for hemiarthroplasty [71, 78, 89, 90]. National guidelines recommend cemented stems in arthroplasty due to FNF in the elderly population [11, 12, 70, 91]. Fortunately, the effect of these recommendations was demonstrated in the report of the NHFR in 2021 (Fig.17) [23].

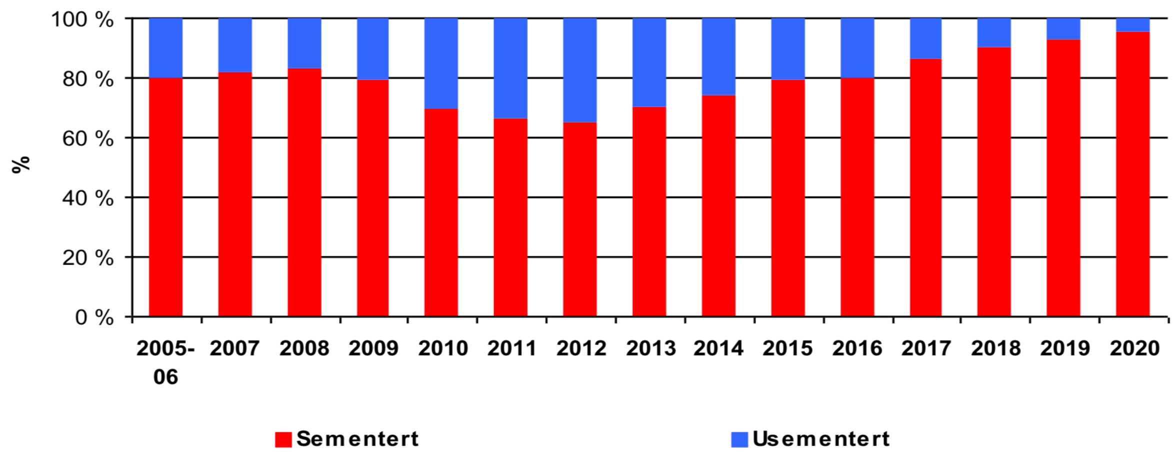


Fig.17: *Proportion of cemented and uncemented primary hemiarthroplasties used for FNFs. From the Norwegian Hip Fracture Register`s Annual Report 2021 (reprinted with permission).*

1.5.6 Cementation principles and stem design

There are two basic design principles for cemented femoral stems: taper slip and composite beam (Fig.18) [64, 92]. These consists of polished and tapered stems with subsidence and load bearing with the taper slip (e.g. the Exeter stem), and anatomical (e.g. the Lubinus SP II stem) or straight stems with matt or rough finish (e.g. the Charnley stem) using the composite beam with fixation in the cement mantle.

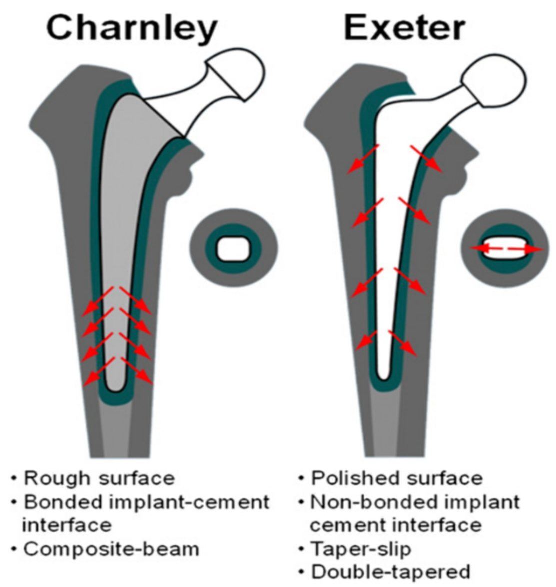


Fig.18: *Force transmission of the main basic design principles, reproduced with kind permission from JM Wilkinson [92].*

Different stem designs and cementation principles lead to different prosthesis survival, which should influence the choice of implants [23, 92-94].

1.6 Surgical complications

A displaced FNF in patients between 55 and 70 years almost always need operative treatment [7, 11, 12, 47]. The main goal of surgery is to regain the pre-fracture walking ability and quality of life with satisfactory, long-lasting treatment. However, some studies have reported a reoperation rate of 30% for IF and about 10% for THA [32, 50]. As mentioned above, there is little evidence regarding patients between 55 and 70 years with a low-energy FNF is rare. This is because most knowledge is based on studies of older patients or other diagnoses, such as osteoarthrosis in the case of THA.

1.6.1 Fixation failure and avascular necrosis after internal fixation

The main concerns after IF for femoral neck fractures are early or delayed fixation failure and avascular necrosis (AVN) of the femoral head (Fig.19).

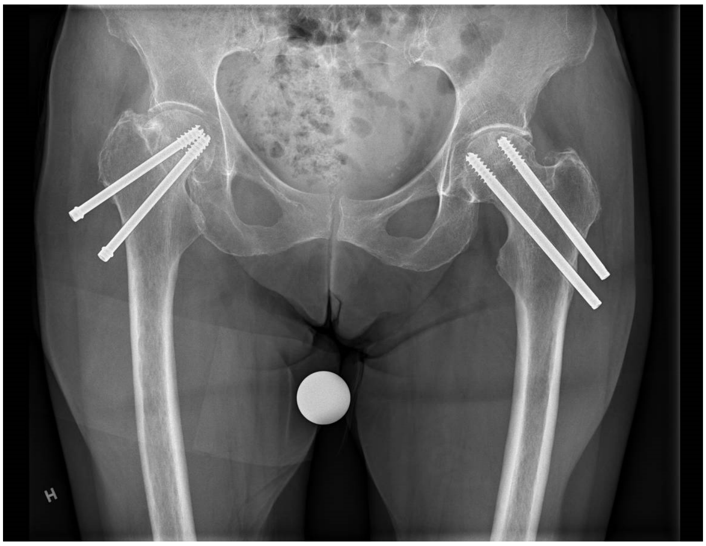


Fig.19: *X-ray of fixation failure after IF in the right hip*

The reoperation rate for IF has been reported to be as high as 44% in several studies [32, 95]. The rate of osteonecrosis of the femoral head, also referred to as AVN, reported in the literature ranges from 12 to 86%, with higher rates in young patients [96]. The reasons might be the disturbed vascularity associated with the trauma or the increased intraarticular pressure interrupting the blood supply to the femoral head (Fig.20) [97-99].

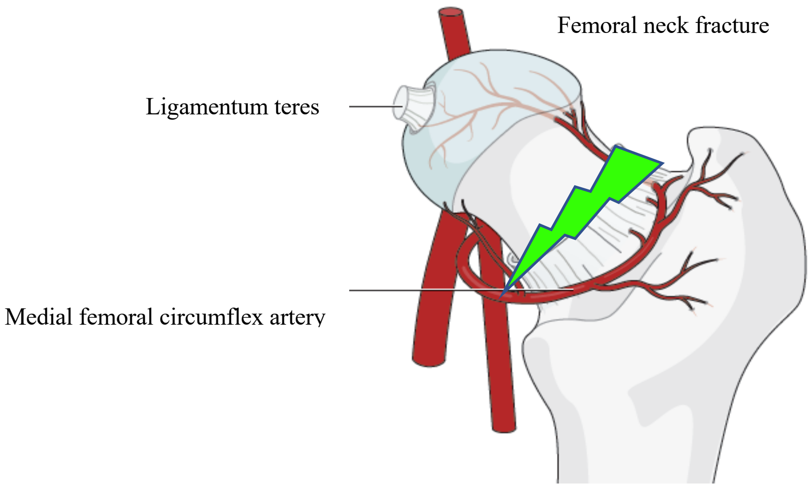


Fig.20: *Interrupted blood supply to femoral head. From the AO foundation (reprinted with permission)*

A meta-analysis including patients under 60 years of age found an AVN rate of 14.3% and a non-union rate of 9.3% [31]. The total incidence of malunion was reported to be 7.1%, implant failure was 9.7%, while surgical site infection was 5.1% [31]. The authors concluded that displaced fractures were more likely to need reoperation than non-displaced FNF. A more recent review article by Large et al. (2019) found no association between open and closed reduction or timing of treatment and rates of AVN [100].

1.6.2 Complications after arthroplasty

As mentioned above, THAs are less commonly used in the treatment of FNFs than hemiarthroplasties [23]. Studies of complications in these specific patients are rare and often small series. Long-term results and causes of reoperation are often based on reports from national arthroplasty registries (Fig.21) [23]. The most important complications of THA after displaced FNF are periprosthetic joint infections, dislocations, fractures around the implants (periprosthetic fractures), and loosening of implants.

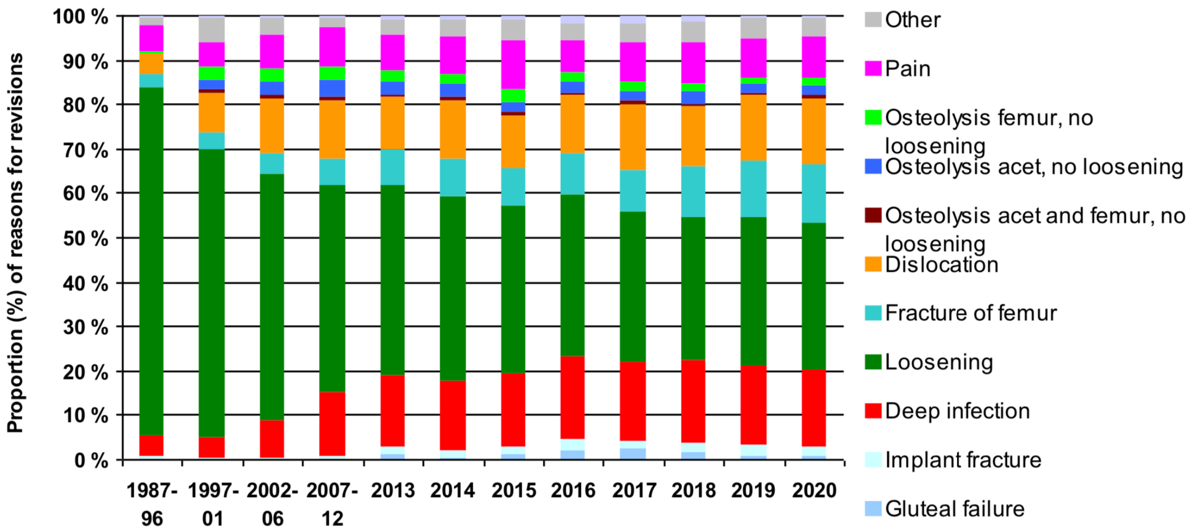


Fig.21: *Proportions (%) and causes for reoperations of THA.*
From the Norwegian Hip Fracture Register`s Annual Report 2021 (reprinted with permission).

1.6.2.1 Periprosthetic joint infection

One of the most catastrophic complications after prosthetic surgery is a periprosthetic joint infection (PJI), which is associated with high morbidity and often a need for complex and interdisciplinary cooperation (Fig.22) [101-103].

Fig.22: *Picture of clinically suspected deep infection of a hip arthroplasty 18 days after primary surgery*

In the group of elderly and frail patients treated with hemiarthroplasty, the rates of postoperative implant infections were described as being as high as 7-9 % and almost half of the patients had died after one year [104, 105]. A PJI usually requires secondary surgery and affects patients´ functional outcome and quality of life. PJI after arthroplasty ranges from 1-2% after surgery of primary osteoarthritis to 4.5% after FNF [106, 107]. The challenge in the management of PJI is the persistence of micro-organisms on the implant surface in the form of biofilm and there is often a need for biofilm-active antibiotics over a long period after surgical intervention [107, 108]. Debridement, antibiotics, and implant retention (DAIR) is usually recommended in early PJIs [106]. For late, chronic, or failed DAIR, a single or two-stage revision may be needed. A two-stage revision with removal of the implant and a temporary spacer (cemented with antibiotics) in the first operation and implantation of a revision prosthesis in a second procedure is the current gold standard treatment for PJI after THA with good results [109]. On the other hand, a single stage procedure may limit the burden with just a single operation with almost the same results [109].

1.6.2.2 Dislocation of the prosthesis

Dislocation of a THA after FNF is a serious problem and the rate could be as high as 10.7% (Fig.23) [110].

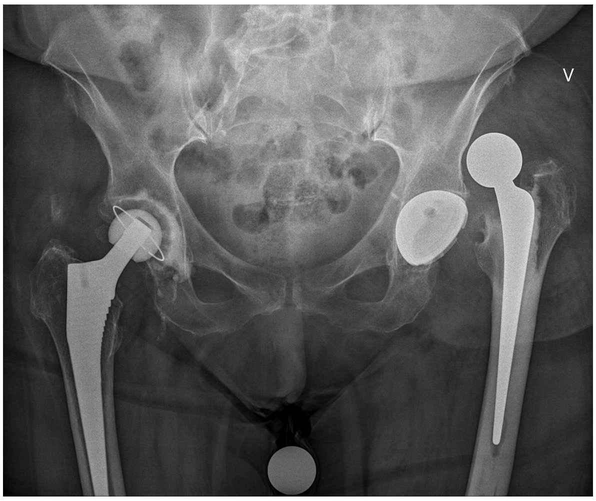


Fig.23: *X-ray of a dislocated total hip arthroplasty on the left hip*

There is a greater risk of revision for dislocation after FNF than in osteoarthritis (RR 2.03) [111]. Dislocation rates were 2-4% in two randomized trials comparing internal fixation with THA at 2 to 4 years follow-up [112, 113]. On the other hand, larger head size has been associated with lower rates of dislocation and 32 mm is probably the most preferred size [111, 114]. A newer concept is the use of dual mobility cups. These implants seemed to be a practical option to reduce dislocation rates for patients treated with THA [114-117]. On the other hand, Rogmark et al. (2022) did not find any reduced risk of revision for femoral neck fractures using dual mobility cups [118].

1.6.2.3 Periprosthetic fractures

A periprosthetic fracture (PPF) is a devastating complication after hip arthroplasty (THA + HA) and can affect the femur and/or the acetabulum (Fig.24). The femur is most commonly involved and the incidence of femoral periprosthetic fractures is estimated to be between 0.045% and 0.13% [119]. PPFs are commonly classified by the Vancouver classification (Fig.25) [119-121].

Fig.24: *X-ray of a periprosthetic fracture of femur on the right side (Vancouver Type B2)*

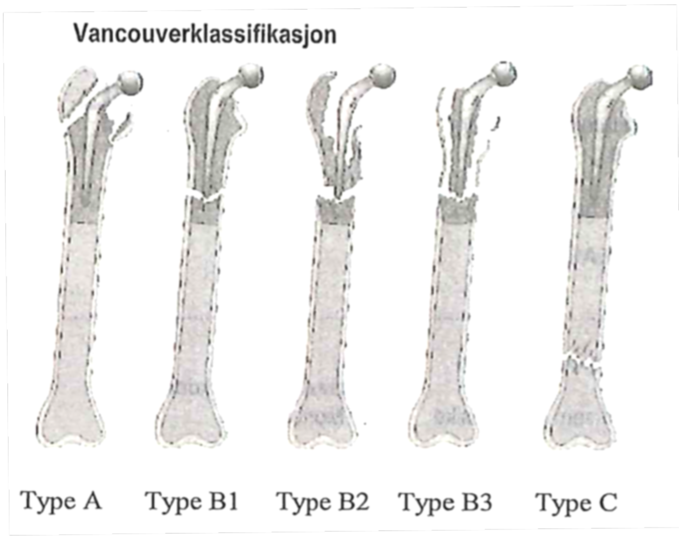


Fig.25: *Vancouver classification for periprosthetic femoral fractures according to Duncan and Masri. Illustration from the Norwegian Arthroplasty Register [121](reprinted with permission, Legeforlaget)*

Vancouver type A fractures involve the greater (A_G) or lesser (A_L) trochanter and can commonly be treated with cerclage, grip plates or non-operatively. Type B1 fractures with stable implants should be treated with internal fixation with open or closed reduction [119]. In type B2 a revision of the implant with a long stem prosthesis is recommended [119]. Type B3, where the implant is unstable, and the bone stock is insufficient, complex reconstruction of the prosthesis and the femur may be necessary [119]. A type C fracture occurs below the femoral stem and can usually be fixated with specific long plates. The treatment of PPFs is often extensive and associated with increased morbidity and mortality [119]. Additionally, a higher risk of PPFs for uncemented femoral stems has been reported [78, 90, 122, 123]. Another concern for the risk of periprosthetic fracture of the femur is the two different cementing principles for cemented stems (Fig.18) [124]. The Swedish Hip Arthroplasty Register recently published a study on THAs describing a tenfold higher risk of Vancouver Type B fractures for tapered, polished stems (e.g. Exeter) than for anatomical stems (e.g. Lubinus) [125].

1.6.2.4 Aseptic loosening of the prosthesis and implant survival

Most studies of femoral neck fractures treated with THA have short follow-up periods and trials with long-term follow-up for THA after acute FNF are rare [50].

Aseptic loosening is not a frequent complication with current modern implants in the case of hip fracture patients, especially in frail patients treated with HA. There is a more recent study by Johansson (2014) and some older studies reporting 10- and 20-years survival rates after FNF [126-128]. Lee reported 95% implant survival after 5 years, 94% after 10 years, 89% after 15 years and 84% after 20 years with the use of cemented implants [127]. Mabry reported 93% survival at 10 years and 76% after 20 years [128]. All these survival rates are worse than for THA after treatment for primary osteoarthritis, but still of high quality [50]. Patients with low-energy displaced FNF under 70 years are frailer and biologically older than expected, and aseptic loosening might not be an extraordinary problem [31-34].

1.7 The Norwegian Hip Fracture Register

The Norwegian Hip Fracture Register (NHFR) is part of the Norwegian National Advisory Unit on Arthroplasty and Hip Fractures. It is owned by the Norwegian Orthopedic Association. The NHFR is located in Bergen, Norway, and is operated by the Department of Orthopedic Surgery at Haukeland University Hospital in Bergen. The NHFR receives funding from the national health authority in Western Norway (Helse Vest). The register was established in autumn 2004 and started collecting data in January 2005 [129]. About 130.000 fractures of the proximal femur had been registered in the NHFR by 2020 [23]. The latest completeness analysis was performed in cooperation with the Norwegian Patient Register (NPR) for the period 2017-2018 and showed completeness of recording of primary osteosynthesis of 88%, of hemiarthroplasties of 94% and of total hip arthroplasties of 91% [23]. Until June 2021, patients included in the register signed an informed consent which was stored in their hospital medical record. The Norwegian Data Inspectorate has approved the recording of data. As is the case with the Norwegian Arthroplasty Register (NAR) Norwegian surgeons are familiar with the recording and the registration forms [130]. Following each surgery, operation, operation and patient data are recorded by the surgeons. All reoperations recorded are linked to the index operation due to unique identification number for each inhabitant in Norway. Primary operations and reoperations with THAs are recorded in the NAR and are added to the NHFR before analysis is performed. A reoperation is defined in the NHFR as any reoperation including closed reduction of dislocated HA, removal of fixation material, soft-tissue revision and revision and converting to HA or THA. Reoperations recorded in the NAR involve only removal or exchange of hardware. Closed reduction of a dislocated THA is not recorded in the NAR. In recent years, all reoperations should also be reported to the NAR. Cognitive impairment is only recorded in the NHFR. Patients receive questionnaires 4, 12 and 36 months postoperatively from the NHFR. This includes a VAS scale (visual analog scale) to measure the pain level in the operated hip, and the level of satisfaction with the operation. Patients also receive the Norwegian version of the EuroQol, evaluating health-related quality of life, including the EQ5-D-3L index score, and an EQ-VAS [9, 131].

Recorded data are available for all orthopedic surgeons in Norway [23]. The register distributes an annual report to all members of the Norwegian Orthopaedic Association, to the national health authorities, and all orthopedic departments performing surgery on fractures of the proximal femur [9]. Each participating hospital in Norway receives specific information about performance in hip fracture care, and particular survival analyses of fracture treatment and arthroplasties on an annual basis [129]. The NHFR presents a digital report annually, and each hospital can compare its own results with other hospitals relative to quality factors (www.kvalitetsregistre.no).

2. Aims of the study

2.1 Overall objective

The overall objective of this PhD thesis was to provide knowledge about treatment and functional outcome after surgery in patients between 55 and 70 years with a low-energy displaced femoral neck fracture and to identify risk factors influencing good and poor functional results.

2.2 Specific objectives

Paper I: to investigate functional results, reoperation risk, and mortality after low-energy displaced FNFs in patients between 55 and 70 years treated with cannulated screws, hemiarthroplasty or total hip arthroplasty by using data in the Norwegian Hip Fracture Register

Paper II: to assess patient-related risk factors for low-energy displaced FNF in patients between 55 and 70 years compared with a sex- and age-matched general population without a fracture

Paper III: to assess the effect of closed reduction and internal fixation with cannulated screws versus total hip arthroplasty of low-energy displaced FNFs in patients between 55 and 70 years according to patient-reported outcome measures, complications, and reoperations

3. Material and Methods

3.1 Study design and study population

3.1.1 Paper I

This prospective study included data on patients reported to the Norwegian Hip Fracture Register (NHFR) aged 55-70 years with displaced intracapsular femoral neck fractures from January 2005 to December 2012 [132]. The nationwide NHFR has collected data from all hip fracture operations performed in Norway since 2005 [129]. Compared to the Norwegian Patient Registry, the NHFR and the NAR had completeness of recording of primary operations of 93% and 97.5% [23]. The NHFR also presents annual individual hospital results (nrlweb.ihelse.net/eng/).

Hip fractures treated with primary THA and secondary THAs due to failure of the primary procedure were reported to the Norwegian Arthroplasty Register (NAR). Information from these operations and data on these patients were added to the dataset of the NHFR before analyses were performed.

Every Norwegian orthopedic surgeon reports patient and operative data to the registries after each operation, using a standard single page form. Comorbidities are reported as ASA (American Society of Anaesthesiologists) class and cognitive impairment is reported according to the clinical evaluation of the surgeon (yes, no, or uncertain) [129, 133]. Cognitive impairment is not recorded in the NAR. The definitions of reoperations differ between the NAR and the NHFR. In the NHFR, all types of reoperations should be reported, while reoperations in the NAR are defined as operations with exchange or removal of hardware or prosthetic components. Soft tissue debridement, only a DAIR, or closed reduction of a dislocated hip prosthesis will not be recorded in the NAR. Therefore, we concentrated on major reoperations as the most comparable outcome, defined as any reoperations including hardware, such as re-osteosynthesis, reoperations with secondary HA or THA, or the exchange or removal of prosthesis components. Removal of screws only after healed fracture or closed reduction of a dislocated prosthesis were defined as minor reoperations.

To access patient-reported outcomes, the NHFR sends questionnaires to all reported patients at 4 and 12 months after index surgery [129]. These forms contain a visual analog scale (VAS) examining the average level of pain from the operated hip within the past month (where 0 indicates no pain and 100 indicates unbearable pain) and a VAS measuring satisfaction with the result of the operation (0 indicates very satisfied and 100 indicates very dissatisfied). Additionally, the EQ-5D-3L (Norwegian translated version) and the visual analog scale EQ-VAS are included. The EQ-5D-3L has five dimensions (mobility, self-care, usual activities, pain or discomfort, anxiety or depression) and each item has three possible responses/levels (no problem, minor problems, major problems). An EQ-5D index score of 1 represents the best possible state of health, while 0 represents a health state similar to death. The EQ-VAS is a 20 cm long visual analog scale representing patients` health status, ranging from 0 (indicating the worst possible health) to 100 (indicating the best possible health).

As of December 31, 2012, 63.231 primary operations for hip fractures were registered in the NHFR. The primary inclusion criteria for this study were age 55-70 years and surgical treatment due to a displaced FNF. 2.805 patients reported to the NHFR fulfilled the inclusion criteria. Ninety-two patients treated with rarely used implants were excluded. Of the 2.713 remaining patients included in the study, 1.111 patients were treated with IF, 1.030 patients were treated with bipolar HA and 572 patients received THA. We had no information about displacement of FNFs treated with THA and thus reported to the NAR. We chose to rely heavily on these fractures being definable as displaced.

3.1.2 Paper II

In this pragmatic single center matched case-control study, we included 50 patients between

50-70 years of age with a low-energy displaced FNF from December 2013 to November 2017 [134]. As the control group we used 150 participants randomly selected and matched by age and sex without a fracture from the normal population in the same catchment area of Akershus University Hospital. The Department of Data and Analytics at Akershus University Hospital was responsible for the recruitment of this group using computer-generated randomization lists and both the National Population Register and the unique national identification number. All patients signed an informed consent and patients with cognitive impairment were not included. We used loose matching to match controls to the fracture group [135]. As suspected, most of the patients with an FNF were in the older part of the included population. Therefore, we divided patients in the fracture group into three different age groups for both genders (55-59, 60-64, and 65-69 years). The number of cases in the fracture group was used as a base before loose matching. To achieve statistical power, we used a tripling of the patients in the control group [136]. Information and data from patients with an FNF were accessed before discharge and a DXA (Dual-energy X-ray Absorptiometry) was performed postoperatively within six weeks after injury without any type of osteoporotic medication. Baseline data, PROMs, specific hip scores, and DXA for the control group were performed at a single outpatient appointment.

Baseline data such as age, sex, height and weight for the measurement of the Body Mass Index (BMI), current smoking status, Charlson comorbidity index (CCI), American Society of Anesthesiologists (ASA) score, and presence of diabetes were recorded [133, 137]. As PROMs and specific functional hip scores we used the Harris Hip Score (HHS), Oxford Hip Score (OHS), and the Hip Disability and Osteoarthritis Outcome Score (HOOS) [138-140]. A DXA scan was used to determine bone mineral density (BMD). DXA measurements were performed for all patients and participants by using the lumbar spine (L1-L4), total hip and femoral neck, including T-scores as a descriptive measurement [141].

3.1.3 Paper III

In this interventional superiority multicenter randomized controlled trial (RCT), treatment with IF using closed reduction and osteosynthesis with two cannulated screws and THA in patients aged 55-70 years with a displaced FNF were compared [142]. It was hypothesized that THA would lead to superior results compared to IF, as assessed by hip function, mobility, pain, health-related quality of life, patient satisfaction, and numbers of reoperations. This study was conducted at Akershus University Hospital, Lørenskog and Haukeland University Hospital, Bergen.

Patients between 55-70 years with a low-energy displaced femoral neck fracture were randomly allocated to treatment with IF or THA. From December 2013 to December 2018, we included 102 patients with a displaced FNF in this study. Eighty patients (41 IF and 39 THA) were recruited at Akershus University Hospital, Lørenskog, and 22 patients (10 IF and 12 THA) at Haukeland University Hospital in Bergen.

The simplified Garden classification was used to classify fractures as non-displaced or displaced [37]. In addition, Garden type I or II FNFs with a posterior tilt ≥ 20 degrees were graded as displaced [40, 41]. The surgeon on call classified fractures and the anesthesiologist on call classified the patient`s ASA grade. Before signing informed consent, all patients received written and oral information. Cognitively impaired patients were not included.

Patients were operatively treated using fast-track procedures and the triage systems of the trial centers. Operations were performed within 48 hours of admission to hospital [23, 70]. Internal fixation was performed under spinal anesthesia on a traction table by closed reduction with biplanar fluoroscopy and fixation with two parallel cannulated screws [8, 23, 143]. During closed fracture reduction, any varus malalignment or significant posterior tilt should be reduced, aiming at an anatomical reduction. Shortening of the femoral neck was accepted within only a few degrees. The distal screw was positioned as close as possible to the medial cortex in an antero-posterior view and in the center of the femoral neck in the lateral view. The proximal screw was positioned in the center of the femoral neck in the antero-posterior view and close to the posterior calcar in the lateral view. Both screws were placed as deeply as possible into the subchondral bone of the femoral head. If closed reduction was not acceptable, a consultant with ≥ 6 years` experience in hip fracture treatment was asked for help and attempted one additional closed reduction maneuver. If it was still not possible to reduce the fracture, the procedure was converted to arthroplasty immediately during the same anesthesia.

Total hip arthroplasty was performed with latest-generation hip implants with modular, mainly cemented implants. Optipac Refobacin (ZimmerBiomet) or Palacos R+G (Heraeus) bone cements were used for fixation. To minimize the risk of postoperative dislocation, prosthetic head size of at least 32 mm or dual mobility cups were used. Two different surgical approaches (67% lateral approach and 33% posterior approach) to the hip joint and different types of implants were used. Almost all patients were treated with cemented stems (94%) in line with established standard treatment at the trial centers. As recommended, all patients received perioperative intravenous antibiotics (Cefalotine 2 g x 4, Cloxacillin 2 g + 1 g + 1 g + 1 g, or Clindamycin 600 mg x 3 in the case of penicillin allergy) and postoperative antithrombotic prophylaxis (5000 IU low-molecular-weight heparin once daily for two weeks). Full weight-bearing was allowed and early mobilization was encouraged for all patients.

Harris Hip Score (HHS) assessed 12 months postoperatively was the primary outcome. Secondary outcomes were HHS at 4 and 24 months, Oxford Hip Score (OHS), Hip Disability and Osteoarthritis Outcome Score (HOOS), health-related quality of life (EQ-5D-3L index score and EQ-VAS), VAS pain, and VAS satisfaction at 4, 12, and 24 months. For comparable analyses the minimal clinically important differences (MCID) and/or the minimal detectable changes (MDC) for each PROM were defined. Complications and reoperations were monitored continuously.

3.2 Classification of femoral neck fractures

Fractures of the proximal femur includes the femoral neck (31B), trochanteric fractures (31A1+2) and subtrochanteric fractures (31A3) (Fig.26). For trochanteric and subtrochanteric fractures the AO-classification is the commonly used classification in Norway [23].

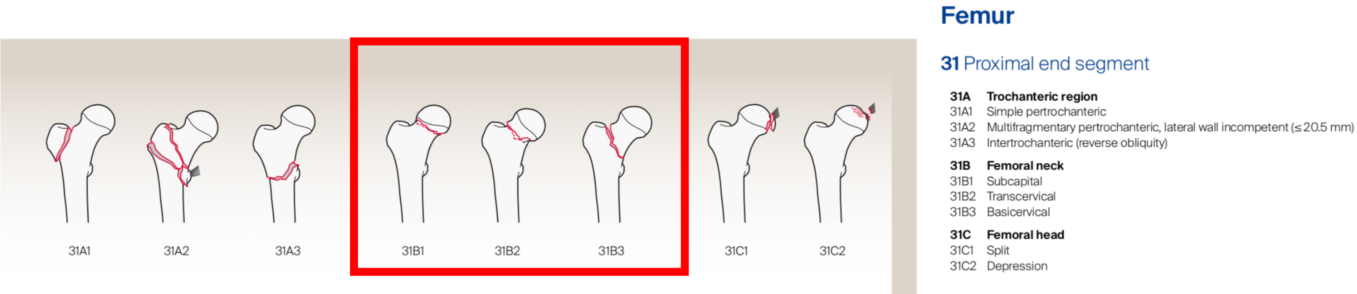


Fig.26: *AO fracture classification of the proximal femur. From the AO foundation (reprinted with permission)*

For fractures of the femoral neck, the Garden classification is the most commonly used and most preferred classification available [144]. It is based on 4 types of displacement in the X-ray anterior-posterior view [37]:

Garden Grade I: non-displaced and incomplete, including valgus impaction

Garden Grade II: non-displaced complete

Garden Grade III: displaced, complete fracture with incompletely displacement

Garden Grade IV: displaced, complete fracture with completely displacement

In daily clinical practice, the Garden classification is often simplified into non-displaced and displaced fractures. In **papers II + III**, we defined a posterior tilt with > 20° in the lateral view of X-rays as displacement and these fractures were classified and treated as displaced fractures [40, 41].

3.3 Outcome measures

We used several outcome measures in the three papers included in this thesis. In **paper I**, baseline data, as age, sex and cognitive impairment were recorded in the NHFR. We used EQ-5D-3L index score, generated by a European population, EQ-VAS, VAS pain and VAS satisfaction [131]. A visual analog scale (VAS) assessing the hip pain level (0 indicating no pain and 100 indicating unbearable pain) and a VAS of patients' satisfaction with the effect of surgery (0 indicating very satisfied and 100 indicating very unsatisfied) were assessed at follow-ups. Validated Norwegian versions of the EQ-5D-3L and the EQ-VAS (20 cm visual analog scale ranging from 0 indicating worst possible health to 100 indicating best possible health) were assessed at follow-ups [131]. Comorbidity was reported by ASA classification [133]. Additionally, types of implants, numbers of reoperations, baseline data and differences between responder, non-responder and non-receiver of questionnaires, and change of treatment over time were recorded. Due to different definitions of reoperations/ revisions in the NHFR and the NAR we divided reoperations into major and minor reoperations. Minor reoperations were defined as closed reduction of a dislocated HA or removal of screws only and we concentrated on major reoperations as the most comparable situation.

In **paper II,** we recorded age, sex, BMI, diabetes mellitus, smoking, ASA classification and the Charlson comorbidity index score (CCI) for comorbidities as baseline data [133, 137]. Specific hip scores as Harris Hip Score (HHS), Oxford Hip Score (OHS), and Hip Disability and Osteoarthritis Outcome Score (HOOS) were used as patient-reported outcome measurements [138-140]. Each participant in this study underwent a DXA measurement to determine bone mineral density (BMD) measured in the lumbar spine (L1-L4), total hip and the femoral neck. We used the World Health Organization (WHO) definition of osteoporosis, where a T-score ≥ -1 SD is defined as normal bone, a T-score > -2.5 - < -1 SD is osteopenia, and a T-score ≤ -2.5 SD is defined as established osteoporosis [141].

In **paper III**, we recorded age, sex, BMI, smoking and alcohol status, and osteoporosis status as baseline characteristics. Comorbidity was reported by ASA classification, Charlson comorbidity index score, NYHA, and mMRC Dyspnea scale [133, 137, 145, 146]. The EQ-5D-3L index scores used in this study was generated by a British study [147]. EQ-VAS, VAS pain and VAS satisfaction were accessed at each follow-up. Reoperations and complications were registered continuously. Outcome measurements were divided into primary and secondary outcomes. Primary outcome was HHS at 12 months. Secondary outcomes were HHS at 4 and 24 months, OHS, and HOOS at 4, 12, and 24 months after index surgery. We used minimal clinically important differences (MCIDs) or minimal detectable changes (MDCs) to determine clinical relevance. The values were defined according to clinical practice and previously published data (Fig.27) [3, 52, 142, 148-151].

Outcome Measure	Description of Measure	Score Interpretation	MCID or MDC*	Assessment Time Points	Assessor Blinding
HHS	Hip function (0-47 points), pain (0-44 points), range of motion (0-5 points), and deformity (0-4 points)	<70 = poor, 70-79 = fair, 80-89 = good, 90-100 = excellent	MCID 10	Prefracture and 4, 12, and 24 months	Surgeon and investigator unblinded
OHS	Hip function (0-48 points)	<27 = poor, 27-33 = fair, 34-41 = good, >41 = excellent	MCID 5.2	Prefracture and 4, 12, and 24 months	Surgeon and investigator unblinded
HOOS	5 subscales, measuring pain, symptoms, function in activity of daily living, function in sport and recreation, and quality of life, scored from 0 = worst to 100 = best	Each subscale is scored separately: <70 = poor, 70-79 = fair, 80-89 = good, 90-100 = excellent	MDC pain: 21.6, symptoms: 22.7, activities of daily living: 17.7, quality of life: 24.4	Prefracture and 4, 12, and 24 months	Surgeon and investigator unblinded
EQ-5D-3L	Quality of life, patient-reported, in 5 dimensions: mobility, self-care, usual activity, pain/discomfort, anxiety/depression; each dimension with 3 levels: no problems, some problems, and extreme problems	<0 = worse than death, 0 = death, 1 = highest quality of life	MCID 0.1	Postop. and 4, 12, and 24 months	Surgeon and investigator unblinded
EQ-VAS	Health related quality of life, patient-reported, Visual analogue scale, patient-reported), range 0-100	0 = worst imaginable health, 100 = best imaginable health	MCID 7	Postop. and 4, 12, and 24 months	Surgeon and investigator unblinded
VAS pain	Pain, patient-reported, range 0-100	0 = no pain, 100 = worst imaginable pain	MCID 10	Postop. and 4, 12, and 24 months	Surgeon and investigator unblinded
VAS patient satisfaction	Satisfaction, patient-reported, range 0-100	0 = maximally satisfied, 100 = maximally dissatisfied	MCID 10	Postop. and 4, 12, and 24 months	Surgeon and investigator unblinded

Fig.27: *Outcome measurements with predefined MCID and MDC according to published data and clinical practice [3, 52, 142, 148-151].*

3.4 Statistical analysis

The Pearson chi-square test was used for comparison of categorical variables and the Student´s t-test was used for continuous variables in independent groups. The Mann-Whitney U-test was used for non-parametric distributed outcomes in **paper II**.

Continuous variables were presented as mean values and standard deviations (SD). Categorical variables were summarized by the number of subjects and percentage in each category. All tests were two-sided, and continuous variables were normally presented with 95% confidence interval (CI). Results were considered statistically significant at the 5% level.

In **paper I**, we used Kaplan Meier analyses to calculate the one-year mortality. A Cox regression analysis with adjustment for age group, sex, and ASA grade was used to calculate relative risk (RR) for death within one year, and to calculate survival curves and hazard rate ratios for reoperations. Due to different definitions of reoperations in the NAR and the NHFR we included only major reoperations in the regression analyses.

In **paper II**, we used loose matching and tripling of the numbers in the control group to achieve statistical power. A logistic regression model with independent variables was used to identify several risk factors (smoking, CCI, and DXA) for a femoral neck fracture, reporting the odds ratios (OR).

In **paper III**, we used the independent samples t-test to assess the difference between the groups for the primary analysis, HHS score at 12 months. Linear mixed models with fixed effects for third-order time polynomial, groups, and the interaction between these were estimated to assess differences between groups in different outcome measurements at different time points. Random effects for patients were included in the linear mixed models to account for within-patient correlations due to repeated measurements. The possible clustering effect at the trial center level was assessed by intra-class correlation coefficient and was negligible. Nine patients allocated to the IF group were converted to THA in the same index operation due to unacceptable reduction of the fractures. These patients remained in the IF group according to the intention to treat principle. We discontinued inclusion after the allocation of 51 patients to each trial arm, since that the inclusion period was longer than expected and we found increasing reluctance by patients to consent, especially because they preferred THA. However, we had lower loss to follow-up than estimated, and hence retained the statistical power with lower recruitment.

3.5 Ethics

This project was approved by the South-Eastern Norway Regional Committees for Medical and Health Research Ethics (REK ref.: 2013/1023) and by the Data Protection Officer of Akershus University Hospital (PVO ref.: 13-065).

In **paper I**, only data from the NHFR were used. The NHFR has been approved as a national health registry and the Norwegian Data Inspectorate has approved the recording of data. All patients treated for hip fractures during the study period were to sign an informed consent form, which became part of their hospital medical record [129].

In **paper II**, inclusion was based on an informed and written consent and patients with cognitive impairment were not included. In this pragmatic sex- and age-matched case-control study, the intervention group consisted of 50 patients aged 50-70 years with a low-energy displaced FNF. The control group consisted of 150 participants without an FNF from the population in the same catchment area. The Department of Data and Analytics at Akershus University Hospital was responsible for the recruitment of the latter group, using computer-generated randomization lists and both the National Population Register and the unique national identification number assigned to each inhabitant in Norway.

In **paper III**, inclusion was based on an informed and written consent. All patients received information on the diagnosis, different treatment options, the range of possible of treatment-related complications and the expected prognosis following the two different types of treatment. Patients were informed about the rates of common complications, especially the risk of fixation failure for IF and the risk of deep infection and dislocation for THA. Patients who declined to participate received standard treatment based on local institutional procedures. Participants could withdraw their consent at any time without having to provide a reason. Patients who wished to leave in the study were treated and followed up by the trial center`s established treatment. Based on the knowledge at the time the study was planned, both treatment options were well documented and established in Norway and in the two departments. All implants used in the study had been thoroughly investigated by Scandinavian and international registries and the treatment options were recommended in international guidelines before the study was started. Additionally, the RCT reported **in paper III** was registered in an international database for randomized clinical trials (NCT:02085707), ClinicalTrials.gov.

4. Summary of results

4.1 Paper I

In cooperation with the NHFR, data from 2.713 patients aged 55-70 years with a low-energy displaced FNF were included. Of these, 1.111 patients were treated with IF, 1.030 patients received bipolar HA, and 572 were treated with THA. Patients treated with HA were older and had more comorbidities than those in the other two groups. Further, there were more patients with cognitive impairment in the HA group than in the IF group.

Olmed screws (DePuy/Synthes) were the most used implants in the IF group, while the cemented Exeter V40 prosthesis (Stryker) and the uncemented Corail (DePuy/Synthes) were the most used femoral stems in the HA and THA groups.

Three hundred and sixty-nine patients (33%) in the IF group and fifty-four patients (5.2%) in the HA group had at least one reoperation during the follow-up period. Sixteen patients (2.8%) in the THA group underwent a subsequent revision of the prosthesis with removal or exchange of prosthetic components. Due to different definitions of reoperations in the NHFR and the NAR we excluded minor reoperations, defined as removal of screws only or closed reduction of a prosthesis. The rate of major reoperation was 28% (306 out of 1.111 patients) for the IF patients, 4.3% (45/1.030) for the HA patients and 2.8% (16/572) for those treated with THA. When adjusting for age, sex, and ASA grade in a Cox regression model, HA had the same risk of reoperation as THA (RR, HA vs. THA, **0.85**, 95% CI: 0.45-1.6; p=0.627). IF had a greater risk of reoperation than THA (RR IF vs. THA, **11**, 95% CI: 6.7-18; p<0.001).

Furthermore, we analyzed PROM data from 549 patients who responded completely to questionnaires at 4 and 12 months. Responders were healthier than non-responders, according to the ASA classification. More patients treated with IF and fewer patients treated with arthroplasty responded to the questionnaires. Patients receiving HA or THA were more satisfied with the result of the operation and reported less pain after 4 and 12 months follow-up than patients treated with IF. THA patients reported significantly higher EQ-5D index scores at 4 and 12 months follow-up and a statistically significant higher EQ-VAS score after 4 months than patients in the IF group.

Crude one-year mortality was 6.3% (70/1.111) after IF, 15% (155/1.030) after HA, and 4.2% (24/572) after THA. With adjustment for age, sex and ASA classification, patients treated with HA had a higher one-year mortality than patients treated with a THA (RR 2.3, 95% CI: 1.5 - 5.5; p<0.001). No difference in one-year mortality was found between patients treated with IF and THA (RR 1.4, 95% CI: 0.85 - 2.2; p=0.195).

We detected a change over time in treatment for displaced femoral neck fractures. The percentage of patients treated with IF fell from 60% to 25% from 2005 to 2012. HA and THA increased from 24% to 45% and 16% to 29% respectively in the same period**.**

4.2 Paper II

In this sex- and age-matched study, we included 50 patients aged 50-70 years with a low-energy displaced FNF and a control group consisting of 150 participants from the population in the same catchment area without a fracture. Seventy-five percent of all participants were women. We found more comorbidities assessed by CCI score (2.64, 95% CI: 2.39 - 2.89 vs. 2.14, 95% CI: 2.04 - 2.24, p=0.001) and there were more patients with ASA class 2-3 in the fracture group than in the control group (ASA 2: 62% vs. 49.3%, ASA 3: 26% vs. 2%). Patients in the fracture group had lower BMI (24.2, 95% CI: 23.1 - 25.4 vs. 26.7, 95% CI: 26 - 27.4, p=0.001) and there were more smokers in this group.

We could not detect any significant differences in hip function using the OHS and the HOOS between the two groups, but the control group reported better HHS than the fracture group (97.1, 95% CI: 95.8 - 98.4 vs. 93.6, 95% CI: 91 - 96.3, p<0.001). We performed DXA measurements of lumbar spine, total hip, and the femoral neck for all participants in the control group. Five participants in the fracture group had implants in both hips, making measurements in this area impossible. There were more patients with osteopenia and osteoporotisis in the fracture group than in the control group. Furthermore, we performed a multivariate logistic regression analysis. We found statistically significant differences in the odds ratio for smoking (8.3, 95% CI: 3.8 - 17.9, p<0.001), presence of osteoporosis in the femoral neck (13.6, 95% CI: 4.1 - 45.3, p<0.001), and the CCI score (2.6, 95% CI: 1.6 - 4.1, p<0.001) for unadjusted variables. The adjusted odds ratio for a femoral neck fracture was 6.8 (95% CI: 2.8 - 16.1, p<0.001) for smokers compared to non-smokers, and 7.6 (95% CI: 2.1 - 27.9, p<0.001) for participants with osteoporosis compared to participants with normal bone mineral density.

4.3 Paper III

In this randomized controlled trial conducted at two Norwegian level III trauma hospitals, we compared the results after IF and THA in patients between 55 and 70 years with a displaced low-energy FNF. Fifty-one patients were allocated to IF and the same number to THA. The mean age of the trial population was 63.7 (SD 4.2) years, and 67.6% were women. Half of the patients (51.5%) belonged to the oldest age group (65-69 years). Compared to THA, a larger proportion of patients in the IF group were current smokers and diagnosed with osteoporosis. In the IF group, 8 mm cannulated, partially threaded screws were used in 42 patients (36 Hip Pins (Smith&Nephew) and 6 Olmed Hip Pins (DePuy/Synthes). In addition, nine patients were converted to arthroplasty during the index operation due to unacceptable reduction of the fracture. In the THA group the Exeter V40 (Stryker) (31 patients), Lubinus SP II (Link) (12 patients), CPT stem (ZimmerBiomet) (5 patients), and the uncemented Corail stem (DePuy/Synthes) (3 patients) were the stems used. The posterior approach was used in 17 patients, while 34 patients were treated with the direct lateral approach. Prosthetic head size of at least 32 mm or dual mobility cups were used in all patients in the THA group. Duration of surgery was longer, and intraoperative blood loss was higher, in the THA group. More patients in the THA group were treated by experienced surgeons. There were no differences in postoperative medical complications between the groups.

The primary outcome, HHS at 12 months follow-up, was superior in the THA group (89.8 points (SD 10.2)) to that of the IF group (84.5 (SD 11.6)). Although statistically significant, the mean difference of 5.3 points (95% CI 0.8 - 9.8, p=0.021) was smaller than the pre-defined MCID of 10 points. We found better results for the THA group for all secondary outcomes. All dimensions of the HOOS showed statistically significant differences for THA at all time points. HHS, OHS, hip pain (VAS), and patient satisfaction (VAS) were significantly different for THA after 4 and 12 months, but not after 24 months. There was a statistically significant difference between groups in mean EQ-5D index score in favor of THA at 4 months, but not at 12 or 24 months. The EQ-VAS showed statistically significant differences at 12 and 24 months.

Nine patients (18%) allocated to IF were converted to arthroplasty during index surgery because of unacceptable fracture reduction. Thirty-four patients (66.7%, 95% CI (0.52 - 0.79)) in the IF group and two patients (3.9%, 95% CI (0.005 - 0.13)) in the THA group had at least one reoperation during the follow-up period. Excluding minor reoperations, 26 patients in the IF group (51.0%, 95% CI (0.37-0.65)) underwent a major reoperation. Of those, 25 patients were treated with a secondary THA and one patient received a Girdlestone procedure (resection arthroplasty) due to a deep infection.

Two patients in the THA group underwent a reoperation, one required an exchange of the acetabular components due to malalignment, and one patient required removal of a bone cement leakage. There were no dislocations or infections in the THA group.

5. Discussion

5.1 Methodological considerations

5.1.1 Register studies and randomized controlled trials

Register studies and RCTs with their well-known limitations and advantages are both needed in scientific research; they are complementary and not necessarily in competition.

Randomized controlled trials are the “gold standard” with the highest level of evidence in medical scientific research [152]. In relation to the topic of this thesis, several randomized studies have investigated different types of treatment of displaced femoral neck fractures. An RCT is probably the best opportunity to compare two different types of treatment, with high internal validity and avoidance of selection bias and other possible confounding factors. Due to random allocation, the two groups should be nearly homogenous in baseline data, and both outcome measurements and follow-ups must be well controlled. However, RCTs have some limitations and disadvantages. As confirmed in this project, implementation and realization of a randomized controlled trial takes time and requires considerable work for the researchers and clinical departments. It might be necessary to include a large number of patients and have a long follow-up time to detect small differences between two different treatment groups. RCTs may only answer a small number of primary research questions and it might therefore be necessary to conduct several trials to draw conclusions in a hypothetical way about a specific treatment. Additionally, RCTs may have a lower external validity due to stricter inclusion criteria or lack of consent. Patients included may represent a healthier group than the general population.

On the other hand, register studies are considered less conclusive and thus have a lower level of evidence [152]. Register studies might offer a large number of included patients at lower costs and shorter time. It is possible to study rare events and it might be possible to explore questions that may be not ethical to investigate with other types of studies, e.g. waiting time from admission to final operative treatment in the case of hip fractures. Furthermore, register studies can provide epidemiological information, in our case incidence of a specific fracture in a rarely studied and atypical age group, several treatment options, and change of treatment over a period of time. The main disadvantages of register-based studies are the lack of data or other unknown confounders. The results may be influenced by undetected confounding factors. To avoid or minimize possible confounding, adjusted analyses, as in our case logistic regression models and Cox regression analysis, can be performed. The strengths, limitations and biases of register-based studies are important to acknowledge, and they should be highlighted in the presentation of the results [153]. Although these two types of studies represent different standards in the hierarchy of clinical research, they are complementary tools. Both RCTs and observational studies have their respectively strengths and limitations, but they complement each other and both contribute to scientific research.

5.1.2 Study design and study population

This project consists of different types of studies. The advantages and limitations of each study are discussed above. This project started with a nationwide register-based study, followed by an institutional observational study and finished with a randomized multicenter controlled trial, which complemented each other.

The register-based study, **paper I,** was sufficiently powered with 2.713 patients. A nationwide basis enabled us to investigate clinical outcome and complications for a large number of cases. In **paper II,** we investigated patient-related risk factors for low-energy displaced FNFs in patients between 55 and 70 years. The three-fold increase in controls compared to the 50 cases in this observational study enabled us to show statistical differences. In **paper III**, we assessed the effect of closed reduction and IF versus THA of low-energy displaced FNFs in patients between 55 and 70 years with an RCT. The two years of follow-up may have been too short to detect late complications. Concerns have been expressed for THA in particular, but RCTs with long-term follow-up identify no or very few late revisions of primary THA [126, 154]. In particular, a cemented femoral stem is associated with low long-term revision rates [4, 23, 33, 126, 155, 156]. A longer follow-up could also have highlighted the arthroplasty revision risk for patients starting with internal fixation and subsequently converted to arthroplasty.

We did not pre-define any thresholds, or specific criteria, for reoperations. We believed that a decision on reoperation must be taken in close cooperation with the patient, weighing subjective views of the clinical situation, which preludes strict criteria. Lack of pre-defined revision criteria could potentially lower the threshold for reoperation of IF, unlike revision of THA. The inclusion period was longer than expected and we found patients increasingly reluctant to consent, especially because they preferred THA. Thus, we decided to stop inclusion after allocation of 51 patients to each trial arm and partial ethical considerations due to the high rate of reoperations in the IF group. Additionally, it might have been better to use the same prosthesis and the same surgical approach to the hip joint in all patients allocated to THA. We used different implants and both the direct lateral and the posterior approach according to the two different established treatments at the two hospitals with patients in this study.

5.1.3 Classification of femoral neck fractures

We used the simplified Garden classification in **papers II + III** to divide the FNFs into non-displaced and displaced (Fig.7). Additionally, we defined FNFs with a posterior tilt ≥ 20° as displaced. The Garden classification used in the NHFR is the same simplified form, but without focusing on the posterior tilt **(paper I)**. The Garden classification is most commonly used and most orthopedic surgeons are familiar with the simplified classification [38]. Intra- and inter-observer variation has been shown to be acceptable in cases of non-displaced and displaced fractures of the femoral neck [39].

5.1.4 Outcome measurements

Patient-reported outcome measurements (PROM) have become more popular in recent decades and provide a unique source of information about patients` experiences in the treatment process. In this project, we assessed outcome by objective measurements and by PROMs. Results of the PROMs used in this project showed acceptable responsiveness and several studies have recommended the EQ-5D in hip fracture patients [157-160]. For hip specific PROMs, we used the Harris Hip Score (HHS) **(papers II + III)**, the Oxford Hip Score (OHS) **(papers II + III)** and the Hip Disability and Osteoarthritis Outcome Score (HOOS) **(papers II + III)** [138-140]. To assess patient-reported outcome and evaluate health-related quality of life, we used the Euro-Qol **(papers I + III)** [161]. The EQ-5D-3L index score generated from a large European population was used **(papers I + III)** [131]. Additionally, we used EQ-VAS, VAS satisfaction and VAS pain.

These different types of outcome measurements have strengths and limitations. Most of the specific hip assessment scores may not assess important outcome measurements such as mortality, pain resistance, regaining of pre-fracture QoL, mobility and independence [162]. Patients with hip fractures were frailer than expected and this must be taken into consideration when interpreting patient-reported outcomes. A Patient-Reported Outcome Measures Working Group has been established by the International Society of Arthroplasty Registries (ISAR) to convene, evaluate, and advise on best practice when assessing PROMs [163]. When using PROMs, the minimal clinically important difference (MCID) or the minimal detectable change (MDC) and patient acceptable symptomatic state (PASS) should be taken into account in describing a clinically measurable effect. Due to lack of consensus on MCID/MDC values for many specific hip measurement scores and different target populations, we defined MCID/MDC according to best clinical practice and previously published studies. The primary outcome in **paper III**, HHS, was initially established to assess data on post-traumatic arthritis following dislocation of the hip joint and acetabular fractures in young men with normal pre-injury hip function [138]. This may be inappropriate for a frail hip fracture population, as pain assessment is the main domain in the HHS [162]. Additionally, although the HHS is widely used in hip research, ceiling effects are known in its use, which may limit the validity of this specific score [164]. On the other hand, the HHS has been reported to perform well on response rate, discrimination ability and responsiveness in a population of patients with FNFs and it is often used in daily practice [3, 52, 165]. Additionally, the HOOS and the OHS are the most commonly used specific hip PROMs in arthroplasty registries [163].

The most commonly used generic questionnaire on health-related quality of life is the EuroQol 5-Dimension 3-Level (EQ-5D-3L), which measures non-disease specific health-related quality of life in five dimensions [163]. It is frequently used in hip fracture care, has been found to be easy to use for patients with FNFs, and good correlation between the EQ-5D index scores and other outcome measurements such as pain and independence has been reported [157]. We pre-defined an MCID of 0.1 points for the EQ-5D-3L based on our best knowledge, since there is little consensus on the MCID for the use of EQ-5D in this particular patient population aged 55-70 years [151, 166]. The weakness of assessment by patient questionnaires is that clinical outcome is reported by patients. Therefore, the results of the EQ-5D index score, EQ-VAS and VAS scales concerning pain and satisfaction should be interpreted with caution. Again, due to lack of consensus, we pre-defined the MCIDs on the numerical visual analogue scales of EQ-VAS (7 points), and VAS concerning pain (10 points) and satisfaction (10) to indicate measurable differences of clinical importance [148, 167, 168].

5.1.5 Completeness of data

In **paper I**, we used data from the Norwegian Hip Fracture Register. We have no precise information on the completeness of the reporting of the data. We are aware of some underreporting of primary outcome and reoperations; however, we have no reason to suspect that different treatment methods had different rates of reporting. The NHFR completed a coverage analysis (2017-2018), reporting completeness for primary treatment of osteosynthesis of 88%, for HA of 94% and for THA of 91% compared to data from the nationwide Norwegian Patient Register (NPR) [23]. Completeness analyses for reoperations showed 80% for osteosynthesis, 73% for HA and 84% for THA.

Since reoperations, revisions and secondary surgery are defined differently in the NHFR and NAR, we focused on major reoperations [169, 170]. We also used the same definition of reoperations and division into minor and major reoperations in **paper III**. The patients` self-reported questionnaires had a relatively low response rate and there were differences in outcome characteristics between responders and non-responders, and between receivers and non-receivers. Hence, the results of patient-reported outcomes in **paper I** should be interpreted with caution. Despite this, we are convinced of the unique source of information offered by PROM data in **paper I**.

5.2 Discussion of the main results

Treatment of displaced femoral neck fractures in patients between 55 and 70 years of age remains challenging. With an increased number of patients suffering from osteoporotic fractures and with an overall aging population, the numbers of displaced femoral neck fractures in this specific age group will also rise. This will considerably increase the economic burden of osteoporosis-related fractures [171, 172]. With one of the highest incidences of osteoporotic-related fractures in the world, Norway will face this problem extensively in the decades to come [25, 173]. The average age of hip fracture patients is described as 80 years and almost 70% are women [23]. For younger middle-aged hip fracture patients with a high demands of activity and quality of life, feasible treatment options are required. As a starting point, there are two different types of treatment options. The first option is to repair the fracture with reduction and internal fixation using various types of screws, plates, nails and other devices [51, 75].

The other possibility is to replace the fracture using arthroplasty, either HA or THA. Several studies favor THA over HA in active healthy elderly patients, but this remains still unclear [6, 72, 112, 156, 174-181].

5.2.1 Paper I

A total of 1.111 patients were treated with IF, 1.030 with HA and 572 with THA. Patients treated with IF and THA were the most comparable groups based on baseline characteristics. In accordance with other studies, mostly in elderly patients, the results in our study showed a preference for THA in this age group [175]. The fittest patients probably benefit from THA [179, 182]. Patients treated with HA were significantly frailer and had more comorbidities than the other groups. This fact has also been reported in several meta-analyses, recommending treatment with HA for patients with high comorbidities, increased physical restrictions and impaired condition [72, 183].

Patients treated with HA or THA reported less pain and were more satisfied than those receiving IF. In a Swedish study from 2013, patients older than 70 years treated with THA reported significantly less pain and higher satisfaction than patients treated with IF or HA, whereas in patients under 70 years the differences did not reach significance level [175]. This may indicate that surgeons divided patients into two different groups. Although patients in the HA group were frailer than in the IF group, results were better for arthroplasty. The use of HA for the frailest and “biologically old” patients in this particular age group of 55-70 years is supported by several studies recommending HA for institutionalized or cognitively impaired patients [72, 183]. The fittest, healthiest and independent patients may benefit from a THA [43, 178].

We found the rate of reoperation to be 33% after IF, 5.2% after HA and 2.8% after THA. The high number of reoperations in the IF group was in line with other studies [32, 47, 50, 51, 71, 126, 154, 181]. Relative to this high rate of reoperations, we had no exact data on the completeness of reporting of reoperations and we were aware of some underreporting [23]. On the other hand, there was no reason to believe that complications of different types of treatment may lead to different frequencies of reporting. We tried to compensate for the possibility of underreporting by focusing on major reoperations, as there are different definitions of reoperations or secondary procedures in the NAR and the NHFR [169, 170]. On the other hand, it is unlikely that different treatment options led to different rates of reporting. Nevertheless, we had a low rate of response of patient-reported outcomes (20% of the total study population). Responders were healthier than non-responders and non-receivers. The results should therefore be treated with caution, as other studies in the literature have reported response rates of up to 79% in a nationwide survey from the Swedish Hip Arthroplasty Register and the Swedish National Hip Fracture Register [175]. On the other hand, the nationwide collection of PROM data presented in **paper I** has provided a unique source of information.

During the period from 2005 to 2012, we found a change in the treatment of displaced FNFs. More patients were treated with arthroplasty at the end of the study period and there was a clear decline in treatment with IF. This trend has also been seen in the elderly population [155]. The reason for the increase of use of arthroplasty for displaced FNFs in the younger patient group could be increased knowledge about the beneficial outcome of HA for frailer patients [71].

The follow-up time was limited to one year in **paper I**, which might be too short to discover late complications of arthroplasty, such as aseptic loosening. As we and other authors have shown, this is probably not a significant problem when modern implants were used for HA and THA [122, 126, 154, 155, 169, 184].

5.2.2 Paper II

In **paper II**, we found significantly more patients with low bone mineral density in the fracture group compared with a normal population in the control group. Patients with low-energy hip fractures in this age group suffered from early osteoporosis [25, 27]. Additionally, we found more patients with more comorbidities in the fracture group, as comorbidities have been reported to be decisive factors in hip fracture patients [27]. We found a significantly higher number of smokers in the fracture group, a finding that has also been confirmed by a meta-analysis, identifying smoking as a correlated risk factor, especially in hip fractures [185]. Smoking and diabetes mellitus have been designated as the strongest independent impact factors for an increased hip fracture risk [186, 187]. Due to the limited numbers of participants in our study, we did not have sufficient power to confirm this. On the other hand, we found a lower BMI in the fracture group compared with the normal population in the control group. This could probably support the fact that a higher BMI has a protective effect on hip fracture risk [188]. We could not record reliable anamnestic information about alcohol consumption and drinking frequency in our study, while recognizing the association between alcohol consumption and hip fracture risk [189, 190].

We found more patients with lower BMD in the fracture group based on the total hip T-score and the femoral neck T-score. These findings have been confirmed by a Swedish study where 90% of a younger population with an FNF had a femoral neck BMD below the mean for the age group [28]. In the group age from 50 to 69, which was most comparable to our study population, more than half of their population in the Swedish study had osteopenia and 35%

had established osteoporosis. It might be difficult to claim that a low BMD was an important predominant factor for a low-energy displaced FNF in this specific age group and that this affects the number of reoperations. A Danish study could not demonstrate a significant association between low hip BMD and the numbers of fixation failures [30]. It is probably necessary to keep in mind that patients with low-energy hip fractures are frailer than their peers and could be treated with sufficiently mechanically stable implants, in an attempt to avoid a high number of reoperations and complications.

5.2.3 Paper III

In **paper III**, we demonstrated that THA had superior functional results in patients between 55 and 70 years with a low-energy displaced FNF, compared to those who received IF. Although the primary outcome, HHS at 12 months, was below the pre-defined MCID of 10 points, all secondary outcomes, including reoperations, showed better results for THA. The reasons for this might be that most patients in the IF group underwent a major reoperation during the follow-up period or were converted to THA due to unacceptable reduction already at index surgery. Especially at four months postoperatively, the mean differences were higher than the MCID/MDC for most secondary outcome measurements. A total of 34 patients (67%) in the IF group underwent a major reoperation during the follow-up period or a conversion to THA already at index surgery, compared to 4% major reoperations in the THA group. The duration of surgery was longer for THA and more operations in the THA group were performed by more experienced surgeons.

The most feared complications in the THA group are deep periprosthetic joint infections, periprosthetic fractures and dislocations of the prosthesis. Fortunately, we had none of these severe complications. Deep infections occur in about 4.5% of all cases and the fact that we had no dislocation of the prosthesis could be explained by the use of head size ≥ 32 mm or dual mobility heads only [112, 113].

THA was in our study performed by more experienced surgeons, perhaps specialized prosthetic surgeons, which could have influenced the rate of reoperation [191, 192]. The rate of reoperation was low, and we had no dislocations or PJIs of the THA. The rate of reoperation in the IF group was much higher than expected and has been reported in other comparable studies with approximately the same age group [32, 51, 77, 126, 132, 154, 193]. Additionally, surgeons' experience and the quality of reduction might also affect outcomes after IF in this group, including poor fracture healing, fixation failure, and the risk of AVN [51, 191, 192]. This was one of the reasons why we chose to concentrate mostly on secondary outcomes, as a larger number of patients in the IF group underwent either conversion at index procedure or received a major reoperation due to early failures. Additionally, the intention-to-treat principle could probably overestimate the real effects of IF at 12 months follow-up and may explain the small differences in primary outcome at 4 and 12 months shown in the IF group. This effect was also seen in a previously published Swedish study by Lagergren [156]. We used two cannulated screws and closed reduction for internal fixation, in line with Scandinavian practice [23]. These procedures have been questioned, but there is little evidence that open reduction and/or types of devices or numbers of additional screws would have affected the risk of reoperation or conversion to THA at index operation [2, 8, 51, 75, 76].

The follow-up time in our study was limited to two years. Some concern could be raised that this period was too short to detect late complications or reoperations, particularly in the THA group. Nevertheless, long-term results after treatment for displaced FNFs are rare and these studies have detected only a few or no late revisions following primary THA [126, 132, 154]. We preferred to use cemented stems preferably (94% of cases), as these stems have been associated with lower revision rates in long-term follow-up and are recommended for elderly patients by several national advisory units [11, 12, 23, 122, 132, 155]. The majority of patients included in this project were in the oldest age category, while the mean age was about 64 years. We therefore assume that our findings are most valid for patients aged 60 years and older.

Over the last decade, two international multicenter RCTs were conducted to evaluate the main surgical treatment strategies for displaced low-energy FNF [4, 8]. The HEALTH study investigated patients 50 years of age or older with a displaced FNF to be treated with HA or THA [4]. Patients were randomly allocated to THA (718 patients) or HA (723 patients). The mean age was around 79 years of age and about 70% of participants were female. The primary outcome was a secondary hip intervention within a two-year follow-up period. The authors concluded that there were no significant differences between the two treatment groups among non-institutionalized and independent patients and that THA provided an unimportant clinical improvement in function and QoL in the follow-up period compared to HA [4]. A sub-analysis explored the functional results in a subgroup containing the fittest part of the participants to determine wheter THA could be superior to HA in this group, but here too, the authors could not detect any differences between THA and HA [194]. They concluded that there were very few patients that would benefit more from THA than HA. These facts must be seen in the context of our study. In contrast to the HEALTH trial, all your patients were under the age of 70 years. We did not compare HA with THA, but concluded that THA led to superior functional outcome in the case of reoperations and patient-reported outcomes in comparison to IF. In light of the results of the HEALTH trial, HA might be the preferable treatment option until larger RCTs or register-based RCTs can indentify specific factors that favor THA or duo-mobility options [195].

The FAITH trial investigated reoperation rates after hip fracture surgery [8]. The study compared cancellous screws to sliding hip screws. The mean age of patients was 72 years and about 61% were females. Five hundred and forty-two patients were allocated to the sliding hip screw group, while five hundred and thirty-seven patients were included in the cancellous screw group. Thirty-two percent of the fractures were defined as displaced. The results showed no differences between the two groups in case of reoperations. The authors interpretated the data to argue that some groups of patients, such as smokers and those with displaced fractures could benefit from sliding hip screws.

In a comparison of these two trials, one study highlighted the differences [196]. The authors concluded that both studies reported results of femoral neck fractures, but in different study populations. In cases of displaced FNF, patients in the FAITH trial were significantly younger (66.9 years, SD 11.3 vs. 78.8 years, SD 8.4), healthier, more often male (55% vs. 30%) and had less well-established osteoporosis. These facts should be kept in mind when selecting patients for different treatment options, especially those under 70 years of age.

5.3 Summary of the main results

The incidence of low-energy displaced femoral neck fractures in patients between 55 and 70 years has decreased in the past decades and is still low [20, 25-27, 134]. Despite of the low incidence, these patients had increased demands for quality of life and a high activity level. In cooperation with the Norwegian Hip Fracture Register and the Norwegian Arthroplasty Register, we showed a high rate of reoperations after IF and better patient-reported outcome measurements after both THA and HA, including the three main operative treatment options in Norway. We recorded a change in treatment where fewer patients received IF and more patients treated with THA over time. Patients treated with HA represented a frailer group than patients treated with THA or IF.

We demonstrated that patients with displaced low-energy FNFs were more osteoporotic, had higher comorbidity and were more often smokers than a group of people without a fracture representing the normal population in the same area. Patients with femoral neck fractures were frailer than expected and should perhaps be compared with the population of elderly hip fracture patients.

Finally, in a multicenter randomized trial, comparing THA with IF, we showed that patients treated with THA reported better hip function and less hip pain. Although we could not detect the predetermined minimal clinically important difference in the primary outcome measurements, secondary outcomes were superior in the THA patient group. Patients treated with IF had a high number of reoperations. Hence, we decided to concentrate mostly on secondary outcomes, assuming that the MCID especially for the primary outcome of HHS at 12 months, was affected by the fact that many patients were either converted to arthroplasty at index operation or reoperated due to early fixation failure, using the intention-to-treat principle.

6. General conclusions

Paper I:

For patients between 55 and 70 years with displaced femoral neck fractures, treatment with closed reduction and internal fixation results in a higher number of reoperations than treatment with hemiarthroplasty or total hip arthroplasty. Although hemiarthroplasty patients had higher morbidity, results were better than for internal fixation.

With fewer reoperations, better patient satisfaction, less pain, and better quality of life, patients treated with THA had better results than those treated with IF at four and twelve months postoperatively. Patients receiving HA had better functional outcome than IF patients after four months, but not after twelve months. Nevertheless, with fewer reoperations HA might be a good alternative for the frailest patients. The results in paper I suggest that patients with displaced intracapsular femoral neck fractures between 55 and 70 years of age benefit from arthroplasty.

Paper II:

Patients between 55 and 70 years with a low-energy displaced femoral neck fracture were more osteoporotic, measured by DXA, and had more comorbidities than a comparable sex- and age-matched group from the general population without a femoral neck fracture. Our data indicate that patients with a displaced femoral neck fracture are frailer than expected and should probably not be compared with their age peers. From a clinical perspective, patients aged 55-70 years may benefit from similar treatment as those over 70 years, within a treatment algorithm considering biological age, individual factors, and medical challenges.

Paper III:

In patients between 55 and 70 years with low-energy displaced femoral neck fractures, total hip arthroplasty was superior to closed reduction and internal fixation. Although a minimal clinically important difference for the primary outcome could not be detected, all secondary outcomes demonstrated better results for THA. More than half of the patients allocated to IF underwent a major reoperation within two years of primary surgery. Patients treated with THA experienced better functional outcome and fewer reoperations than patients receiving closed reduction and IF.

7. Clinical implications

Patients between 55 and 70 years with low-energy displaced femoral neck fractures often have an increased biological aged and symptomatic comorbidities. These patients were more osteoporotic and frailer than their peers in a normal population. Comparing internal fixation and total hip arthroplasty for treatment of displaced femoral neck fractures, we could not detect any clinically important difference in the primary outcome of the Harris Hip Score between the two groups. For this reason, we focused on secondary outcomes, where all measurements showed superior results for total hip arthroplasty. Despite an age range of 55-70 years, the mean age of our study population was about 64 years and the majority of patients were in the oldest age category. Accordingly, we assume that our findings are most valid for patients aged 60 years and older.

With fewer reoperations and better patient-reported results, low-energy displaced femoral neck fractures in patients aged 55-70 years can beneficially be treated with arthroplasty.

8. Future perspectives

8.1 Mortality rates and implant survival after low-energy displaced FNF in long-term follow-up

Although several studies recommended THA over HA in mobile and independent patients, due to superior outcomes of THA, some other studies have stated that outcomes after THA or HA were quite similar and not of clinical importance [4, 5, 174, 176, 177, 193, 197]. There is a need for adequate long-term studies reporting reoperations and PROMs after 10-20 years for both treatment options, especially with a focus on dislocations and implant survival, as these are the most common concerns about THA [169]. In this case, dual mobility cups may provide increased benefit to avoid dislocations [114, 198-202].

We showed that patients with a low-energy displaced FNF are frailer than their peers in a normal population. It might be interesting to investigate mortality rates and implant survival in this particular group, since implant survival and patient morbidity and mortality over more than two years will influence the choice of treatment (fig.28) [126, 132].

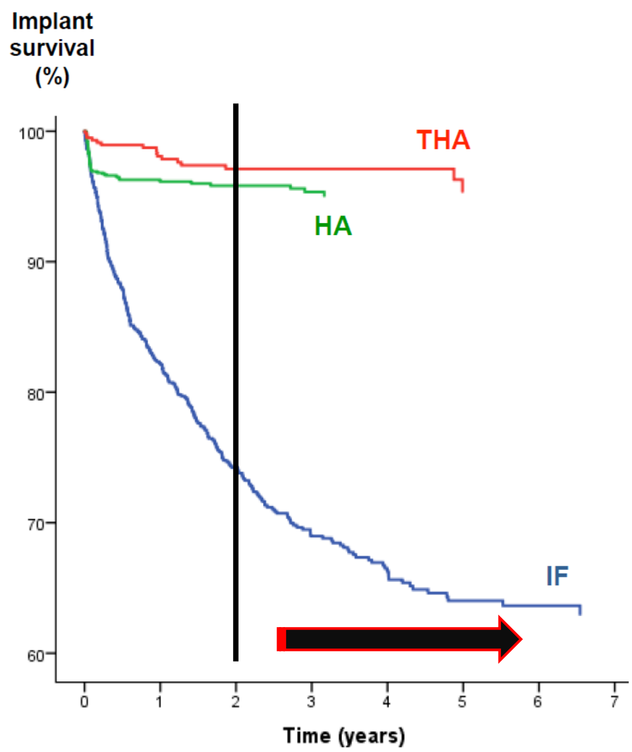


Fig.28: *Adjusted survival of implants for the different treatment groups with major reoperations as endpoint, distributed by primary treatment method. Cox regression analyses with adjustments for age, sex, and ASA classification [132].*
Marked with pillows for the period above two years

8.2 Economic considerations

Since it might be possible, based on weak or moderate evidence, to treat low-energy displaced FNF with hemiarthroplasty with similar outcomes as THA, there is a need for a precise basis for economic considerations, as THA is more expensive than HA, the duration of the operation is longer and the rates of dislocation and subsequent necessary treatment are higher. Several studies have shown that both THA and HA are more cost-effective treatments for elderly patients [21, 112, 203-208]. In cases of treatment with dual mobility cups, the implant costs are even higher. With an increased proportion of elderly people, the number of hip fractures will also increase.

8.3 Surgical approaches for arthroplasty in hip fracture care

As we may accept that THA results in more dislocations than HA and that the posterior approach has shown poor results, there is a need for studies that explore particular approaches to the hip joint when using HA as a possible treatment for displaced low-energy FNF. There are some ongoing studies with limited numbers of patients using a modified posterior approach "**s**ave **p**iriformis **a**nd **i**nternus, **r**epairing **e**xternus" (SPAIRE or hemi-spaire) and there is a need for high quality studies with large populations [23, 209, 210].

8.4 Treatment for patients with low-energy displaced FCF < 55 years of age

We concluded that patients with a low-energy displaced FNF aged 55-70 years are frailer than expected and could benefit from arthroplasty. There is limited evidence of treatment for these fractures in patients under 55 years, and there is a need for high volume studies, as the reoperation rate in this group is almost the same as in the older group [32, 33]. We are aware of the fact that fractures in younger individuals cause an increasinging number of high-energy injuries and that these patients may tolerate a secondary intervention better than older and frailer patients with more comorbidities and osteoporosis.

9. References

1. WHO, *Prevention and management of osteoporosis.* World Health Organ Tech Rep Ser, 2003. **921**: p. 1-164, back cover.
2. Bhandari, M. and Swiontkowski, M., *Management of Acute Hip Fracture.* N Engl J Med, 2017. **377**(21): p. 2053-2062.
3. Frihagen, F., Nordsletten, L., Madsen, JE., *Hemiarthroplasty or internal fixation for intracapsular displaced femoral neck fractures: randomised controlled trial.* BMJ, 2007. **335**(7632): p. 1251-4.
4. Bhandari, M., et al., *Total Hip Arthroplasty or Hemiarthroplasty for Hip Fracture.* N Engl J Med, 2019. **381**(23): p. 2199-2208.
5. Prestmo, A., et al., *Comprehensive geriatric care for patients with hip fractures: a prospective, randomised, controlled trial.* Lancet, 2015. **385**(9978): p. 1623-33.
6. Hopley, C., et al., *Primary total hip arthroplasty versus hemiarthroplasty for displaced intracapsular hip fractures in older patients: systematic review.* BMJ, 2010. **340**: p. c2332.
7. 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.
8. *Fracture fixation in the operative management of hip fractures (FAITH): an international, multicentre, randomised controlled trial.* Lancet, 2017. **389**(10078): p. 1519-1527.
9. 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.
10. Rogmark, C., et al., *Hip fractures in the non-elderly-Who, why and whither?* Injury, 2018. **49**(8): p. 1445-1450.
11. NICE, *Hip fracture: Management clinical guideline 124*. 2017, National Institute for Health and Care Excellence.: https://www.nice.org.uk/guidance/cg124.
12. Roberts, K.C. and Brox, W.T., *AAOS Clinical Practice Guideline: Management of Hip Fractures in the Elderly.* J Am Acad Orthop Surg, 2015. **23**(2): p. 138-40.
13. 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.
14. Li, X. and Luo, J., *Hemiarthroplasty compared to total hip arthroplasty for the treatment of femoral neck fractures: a systematic review and meta-analysis.* J Orthop Surg Res. 2021 Mar 3;**16**(1): p. 172.
15. Cooper, C., et al., *Secular trends in the incidence of hip and other osteoporotic fractures.* Osteoporos Int, 2011. **22**(5): p. 1277-88.
16. Johnell, O., Kanis, J.A., *An estimate of the worldwide prevalence and disability associated with osteoporotic fractures.* Osteoporos Int, 2006. **17**(12): p. 1726-33.
17. Støen, R.O., et al., *Hip fracture incidence is decreasing in the high incidence area of Oslo, Norway.* Osteoporos Int, 2012. **23**(10): p. 2527-34.
18. Omsland, T.K., et al., *Hip fractures in Norway 1999-2008: time trends in total incidence and second hip fracture rates: a NOREPOS study.* Eur J Epidemiol, 2012. **27**(10): p. 807-14.
19. Ahlborg, H.G., et al., *Prevalence of osteoporosis and incidence of hip fracture in women--secular trends over 30 years.* BMC Musculoskelet Disord, 2010. **11**: p. 48.
20. Søgaard, A.J., et al., *Continued decline in hip fracture incidence in Norway: a NOREPOS study.* Osteoporos Int, 2016. **27**(7): p. 2217-2222.

21. Zielinski, S.M., et al., *The societal costs of femoral neck fracture patients treated with internal fixation.* Osteoporos Int, 2014. **25**(3): p. 875-85.
22. 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.
23. Furnes, O., Hallan, G., et al., *Report 2021: Norwegian National Advisory Unit on Arthroplasty and Hip Fractures*, H.U.H. Bergen, Editor. 2021, National Hip Fracture and Arthroplasty Register: https://helse-bergen.no/seksjon/Nasjonal_kompetansetjeneste_leddproteser_hoftebrudd/Share%20point%20Documents/Rapport/Rapport%202021.pdf
24. Diamantopoulos, A.P., et al., *The epidemiology of low- and high-energy distal radius fracture in middle-aged and elderly men and women in Southern Norway.* PLoS One, 2012. **7**(8): p. e43367.
25. Lofthus, C.M., et al., *Young patients with hip fracture: a population-based study of bone mass and risk factors for osteoporosis.* Osteoporos Int, 2006. **17**(11): p. 1666-72.
26. Karantana, A., et al., *Epidemiology and outcome of fracture of the hip in women aged 65 years and under: a cohort study.* J Bone Joint Surg Br, 2011. **93**(5): p. 658-64.
27. Al-Ani, A.N., et al., *Risk factors for osteoporosis are common in young and middle-aged patients with femoral neck fractures regardless of trauma mechanism.* Acta Orthop, 2013. **84**(1): p. 54-9.
28. Al-Ani, A.N., et al., *Low bone mineral density and fat-free mass in younger patients with a femoral neck fracture.* Eur J Clin Invest, 2015. **45**(8): p. 800-6.
29. Heetveld, M.J., et al., *Femoral neck fractures: can physiologic status determine treatment choice?* Clin Orthop Relat Res, 2007. **461**: p. 203-12.
30. Viberg, B., et al., *Low bone mineral density is not related to failure in femoral neck fracture patients treated with internal fixation.* Acta Orthop, 2014. **85**(1): p. 60-5.
31. Slobogean, G.P., et al., *Complications following young femoral neck fractures.* Injury, 2015. **46**(3): p. 484-91.
32. Stockton, D.J., et al., *High rate of reoperation and conversion to total hip arthroplasty after internal fixation of young femoral neck fractures: a population-based study of 796 patients.* Acta Orthop, 2019. **90**(1): p. 21-25.
33. Upadhyay, A., et al., *Delayed internal fixation of fractures of the neck of the femur in young adults. A prospective, randomised study comparing closed and open reduction.* J Bone Joint Surg Br, 2004. **86**(7): p. 1035-40.
34. Damany, D.S., Parker, M.J., Chojnowski, A., *Complications after intracapsular hip fractures in young adults. A meta-analysis of 18 published studies involving 564 fractures.* Injury, 2005. **36**(1): p. 131-41.
35. Pauwels, F., *Atlas zur Biomechanik der gesunden und kranken Hüfte*. 1973: Springer Berlin, Heidelberg.
36. Shen, M., et al., *An update on the Pauwels classification.* J Orthop Surg Res, 2016. **11**(1): p. 161.
37. Garden, R., *Low-angle fixation in fractures of the femoral neck.* J Bone Joint Surg Br. , 1961. **Nov 1; 43(4)** p. 647-63.
38. 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.
39. 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.
40. Dolatowski, F.C., et al., *Preoperative posterior tilt of at least 20° increased the risk of fixation failure in Garden-I and -II femoral neck fractures.* Acta Orthop, 2016. **87**(3): p. 252-6.

41. 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.
42. Frihagen, F., *On the diagnosis and treatment of femoral neck fractures.* Acta Orthop Suppl, 2009. **80**(335): p. 1-26.
43. Parker, M., Johansen, A., *Hip fracture.* BMJ, 2006. **333**(7557): p. 27-30.
44. Hay, D., Parker, M.J., *Hip fracture in the immobile patient.* J Bone Joint Surg Br, 2003. **85**(7): p. 1037-9.
45. Tay, E., *Hip fractures in the elderly: operative versus nonoperative management.* Singapore Med J, 2016. **57**(4): p. 178-81.
46. Jain, R., Basinski, A., Kreder, H.J., *Nonoperative treatment of hip fractures.* Int Orthop, 2003. **27**(1): p. 11-7.
47. Frihagen, F., et al., *The treatment of femoral neck fractures.* Tidsskr Nor Laegeforen, 2010. **130**(16): p. 1614-7.
48. Prommik, P., et al., *Estonian hip fracture data from 2009 to 2017: high rates of non-operative management and high 1-year mortality.* Acta Orthop, 2019. **90**(2): p. 159-164.
49. Rogmark, C., Flensburg, L., Fredin, H., *Undisplaced femoral neck fractures--no problems? A consecutive study of 224 patients treated with internal fixation.* Injury, 2009. **40**(3): p. 274-6.
50. Heetveld, M.J., et al., *Internal fixation versus arthroplasty for displaced femoral neck fractures: what is the evidence?* J Orthop Trauma, 2009. **23**(6): p. 395-402.
51. Pauyo, T., et al., *Management of femoral neck fractures in the young patient: A critical analysis review.* World J Orthop, 2014. **5**(3): p. 204-17.
52. Dolatowski, F.C., et al., *Screw Fixation Versus Hemiarthroplasty for Nondisplaced Femoral Neck Fractures in Elderly Patients: A Multicenter Randomized Controlled Trial.* J Bone Joint Surg Am, 2019. **101**(2): p. 136-144.
53. Gjertsen, J.E., et al., *Clinical outcome after undisplaced femoral neck fractures.* Acta Orthop, 2011. **82**(3): p. 268-74.
54. 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.
55. Frihagen, F., et al., *Comparison of re-operation rates following primary and secondary hemiarthroplasty of the hip.* Injury, 2007. **38**(7): p. 815-9.
56. Dahl, H.K., *Surgical treatment of femoral neck fractures. The 100-year anniversary.* Tidsskr Nor Laegeforen, 1994. **114**(30): p. 3600-3.
57. Mei, J., *A brief history of internal fixation of femoral neck fracture.* Zhonghua Yi Shi Za Zhi, 2014. **44**(2): p. 101-5.
58. Gomez, P.F., Morcuende, J.A., *Early attempts at hip arthroplasty 1700s to 1950s.* Iowa Orthop J, 2005. **25**: p. 25-9.
59. Thompson, F.R., *Two and a half years' experience with a vitallium intramedullary hip prosthesis.* J Bone Joint Surg Am, 1954. **36-a**(3): p. 489-502.
60. Moore, A.T., *The self-locking metal hip prosthesis.* J Bone Joint Surg Am, 1957. **39-a**(4): p. 811-27.
61. Lestrange, N.R., *Bipolar arthroplasty for 496 hip fractures.* Clin Orthop Relat Res, 1990(251): p. 7-19.
62. Sudmann, E., et al., *The Charnley versus the Christiansen total hip arthroplasty. A comparative clinical study.* Acta Orthop Scand, 1983. **54**(4): p. 545-52.

63. Søreide, O., Mølster, A., Raugstad, T.S., *Replacement with the Christiansen endoprosthesis in acute femoral neck fractures. A 5 year follow-up study.* Acta Orthop Scand, 1980. **51**(1): p. 137-44.
64. Shen, G., *Femoral stem fixation. An engineering interpretation of the long-term outcome of Charnley and Exeter stems.* J Bone Joint Surg Br, 1998. **80**(5): p. 754-6.
65. Stryker. *Exeter femoral stem*. 2022.
66. Link. *SP II anatomical prosthesis*. 2022.
67. DePuy/Synthes. *Corail unsemented stem*. 2022.
68. Mahmoud, S.S., et al., *Outcomes of total hip arthroplasty, as a salvage procedure, following failed internal fixation of intracapsular fractures of the femoral neck: a systematic review and meta-analysis.* Bone Joint J, 2016. **98-b**(4): p. 452-60.
69. McKinley, J.C., Robinson, J.C., *Treatment of displaced intracapsular hip fractures with total hip arthroplasty: comparison of primary arthroplasty with early salvage arthroplasty after failed internal fixation.* J Bone Joint Surg Am, 2002. **84**(11): p. 2010-5.
70. *Norske retningslinjer for tverrfaglig behandling av hoftebrudd 2018*. 2018: https://www.legeforeningen.no/contentassets/7f4bec178c34464489d83240608fb9ee/norske-retningslinjer-for-tverrfaglig-behandling-av-hoftebrudd.pdf.
71. Rogmark, C., Leonardsson, O., *Hip arthroplasty for the treatment of displaced fractures of the femoral neck in elderly patients.* Bone Joint J, 2016. **98-b**(3): p. 291-7.
72. Rogmark, C., Johnell, O., *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.
73. Wilson, J.M., et al., *Fixation vs Arthroplasty for Femoral Neck Fracture in Patients Aged 40-59 Years: A Propensity-Score-Matched Analysis.* Arthroplast Today, 2022. **14**: p. 175-182.
74. FHI. *Norsk overvåkingssystem for antibiotikabruk og helsetjenesteassosierte infeksjoner (NOIS)*. 2022.
75. Parker, M.J., Stockton, G., *Internal fixation implants for intracapsular proximal femoral fractures in adults.* Cochrane Database Syst Rev, 2001. **2001**(4): p. Cd001467.
76. Nyholm, A.M., et al., *Osteosynthesis with Parallel Implants in the Treatment of Femoral Neck Fractures: Minimal Effect of Implant Position on Risk of Reoperation.* J Bone Joint Surg Am, 2018. **100**(19): p. 1682-1690.
77. Wang, C.T., et al., *Suboptimal outcomes after closed reduction and internal fixation of displaced femoral neck fractures in middle-aged patients: is internal fixation adequate in this age group?* BMC Musculoskelet Disord, 2018. **19**(1): p. 190.
78. 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.
79. Engesaeter, L.B., et al., *Antibiotic prophylaxis in total hip arthroplasty: effects of antibiotic prophylaxis systemically and in bone cement on the revision rate of 22,170 primary hip replacements followed 0-14 years in the Norwegian Arthroplasty Register.* Acta Orthop Scand, 2003. **74**(6): p. 644-51.
80. Hardinge, K., *The direct lateral approach to the hip.* J Bone Joint Surg Br, 1982. **64**(1): p. 17-9.
81. Smith-Petersen, M.N., *Approach to and exposure of the hip joint for mold arthroplasty.* J Bone Joint Surg Am, 1949. **31a**(1): p. 40-6.

82. Watson-Jones, R., Robinson, W.C., *Arthrodesis of the osteoarthritic hip joint.* J Bone Joint Surg Br, 1956. **38-b**(1): p. 353-77.
83. Sayed-Noor, A.S., et al., *Abductor Muscle Function and Trochanteric Tenderness After Hemiarthroplasty for Femoral Neck Fracture.* J Orthop Trauma, 2016. **30**(6): p. e194-200.
84. Hongisto, M.T., et al., *Lateral and Posterior Approaches in Hemiarthroplasty.* Scand J Surg, 2018. **107**(3): p. 260-268.
85. Amlie, E., et al., *Worse patient-reported outcome after lateral approach than after anterior and posterolateral approach in primary hip arthroplasty. A cross-sectional questionnaire study of 1,476 patients 1-3 years after surgery.* Acta Orthop, 2014. **85**(5): p. 463-9.
86. 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.
87. Kristensen, T.B., et al., *Posterior approach compared to direct lateral approach resulted in better patient-reported outcome after hemiarthroplasty for femoral neck fracture.* Acta Orthop, 2017. **88**(1): p. 29-34.
88. Parker, M.J., *Lateral versus posterior approach for insertion of hemiarthroplasties for hip fractures: A randomised trial of 216 patients.* Injury, 2015. **46**(6): p. 1023-7.
89. 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.
90. Kristensen, T.B., et al., *Cemented or Uncemented Hemiarthroplasty for Femoral Neck Fracture? Data from the Norwegian Hip Fracture Register.* Clin Orthop Relat Res, 2020. **478**(1): p. 90-100.
91. Parker, M.J., Gurusamy, K.S., Azegami, S., *Arthroplasties (with and without bone cement) for proximal femoral fractures in adults.* Cochrane Database Syst Rev, 2010(6): p. Cd001706.
92. Jayasuriya, R.L., et al., *Effect of sliding-taper compared with composite-beam cemented femoral prosthesis loading regime on proximal femoral bone remodeling: a randomized clinical trial.* J Bone Joint Surg Am, 2013. **95**(1): p. 19-27.
93. Carli, A.V., Negus, J.J., Haddad, F.S., *Periprosthetic femoral fractures and trying to avoid them: what is the contribution of femoral component design to the increased risk of periprosthetic femoral fracture?* Bone Joint J, 2017. **99-b**(1 Supple A): p. 50-59.
94. Kristensen, T.B., et al., *More reoperations for periprosthetic fracture after cemented hemiarthroplasty with polished taper-slip stems than after anatomical and straight stems in the treatment of hip fractures: a study from the Norwegian Hip Fracture Register 2005 to 2016.* Bone Joint J, 2018. **100-b**(12): p. 1565-1571.
95. Chang, C.H., et al., *Suboptimal outcomes after internal fixation for displaced intracapsular femoral neck fractures in 50- to 60-year-old patients.* Hip Int, 2020. **30**(4): p. 474-480.
96. Ly, T.V., Swiontkowski, M.F., *Treatment of femoral neck fractures in young adults.* J Bone Joint Surg Am, 2008. **90**(10): p. 2254-66.
97. Lazaro, L.E., et al., *Focal osteonecrosis in the femoral head following stable anatomic fixation of displaced femoral neck fractures.* Arch Orthop Trauma Surg, 2017. **137**(11): p. 1529-1538.
98. Ghayoumi, P., Kandemir, U., Morshed, S., *Evidence based update: open versus closed reduction.* Injury, 2015. **46**(3): p. 467-73.

99. Papakostidis, C., et al., *Timing of internal fixation of femoral neck fractures. A systematic review and meta-analysis of the final outcome.* Injury, 2015. **46**(3): p. 459-66.
100. Large, T.M., et al., *Posttraumatic Avascular Necrosis After Proximal Femur, Proximal Humerus, Talar Neck, and Scaphoid Fractures.* J Am Acad Orthop Surg, 2019. **27**(21): p. 794-805.
101. Guren, E., et al., *Prosthetic joint infection-a devastating complication of hemiarthroplasty for hip fracture.* Acta Orthop, 2017. **88**(4): p. 383-389.
102. Noailles, T., et al., *What are the risk factors for post-operative infection after hip hemiarthroplasty? Systematic review of literature.* Int Orthop, 2016. **40**(9): p. 1843-8.
103. Duckworth, A.D., et al., *Deep infection after hip fracture surgery: predictors of early mortality.* Injury, 2012. **43**(7): p. 1182-6.
104. Dale, H., et al., *Infection after primary hip arthroplasty: a comparison of 3 Norwegian health registers.* Acta Orthop, 2011. **82**(6): p. 646-54.
105. Westberg, M., Snorrason, F., Frihagen, F., *Preoperative waiting time increased the risk of periprosthetic infection in patients with femoral neck fracture.* Acta Orthop, 2013. **84**(2): p. 124-9.
106. Mellner, C., et al., *Early periprosthetic joint infection and debridement, antibiotics and implant retention in arthroplasty for femoral neck fracture.* Hip Int, 2017. **27**(4): p. 349-353.
107. Izakovicova, P., Borens, O., Trampuz, A., *Periprosthetic joint infection: current concepts and outlook.* EFORT Open Rev, 2019. **4**(7): p. 482-494.
108. Zimmerli, W., Trampuz, A., Ochsner, P.E., *Prosthetic-joint infections.* N Engl J Med, 2004. **351**(16): p. 1645-54.
109. Tirumala, V., et al., *Comparison of patient reported outcome measures after single versus two-stage revision for chronic infection of total hip arthroplasty: a retrospective propensity score matched cohort study.* Arch Orthop Trauma Surg, 2021. **141**(10): p. 1789-1796.
110. Iorio, R., et al., *Displaced femoral neck fractures in the elderly: outcomes and cost effectiveness.* Clin Orthop Relat Res, 2001(383): p. 229-42.
111. Conroy, J.L., et al., *Risk factors for revision for early dislocation in total hip arthroplasty.* J Arthroplasty, 2008. **23**(6): p. 867-72.
112. 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.
113. 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.
114. Tarasevicius, S., et al., *Dual mobility cup reduces dislocation rate after arthroplasty for femoral neck fracture.* BMC Musculoskelet Disord, 2010. **11**: p. 175.
115. Cha, Y.H., et al., *Dual mobility total hip arthroplasty in the treatment of femoral neck fractures.* Bone Joint J, 2020. **102-b**(11): p. 1457-1466.
116. Adam, P., et al., *Dual mobility cups hip arthroplasty as a treatment for displaced fracture of the femoral neck in the elderly. A prospective, systematic, multicenter study with specific focus on postoperative dislocation.* Orthop Traumatol Surg Res, 2012. **98**(3): p. 296-300.
117. Jobory, A., et al., *Reduced Revision Risk for Dual-Mobility Cup in Total Hip Replacement Due to Hip Fracture: A Matched-Pair Analysis of 9,040 Cases from the Nordic Arthroplasty Register Association (NARA).* J Bone Joint Surg Am, 2019. **101**(14): p. 1278-1285.

118. Rogmark, C., Nauclér, E., *Dual mobility cups do not reduce the revision risk for patients with acute femoral neck fracture: A matched cohort study from the Swedish Arthroplasty Register.* Injury, 2022. **53**(2): p. 620-625.
119. Yasen, A.T., Haddad, F.S., *Periprosthetic fractures: bespoke solutions.* Bone Joint J, 2014. **96-b**(11 Supple A): p. 48-55.
120. Brady, O.H., et al., *The reliability and validity of the Vancouver classification of femoral fractures after hip replacement.* J Arthroplasty, 2000. **15**(1): p. 59-62.
121. Duncan, C.P., Masri, B.A., *Fractures of the femur after hip replacement.* Instr Course Lect, 1995. **44**: p. 293-304.
122. 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.
123. Lin, F.F., et al., *Cemented versus uncemented hemiarthroplasty for displaced femoral neck fractures: A meta-analysis of randomized controlled trails.* Medicine (Baltimore), 2019. **98**(8): p. e14634.
124. Thien, T.M., et al., *Periprosthetic femoral fracture within two years after total hip replacement: analysis of 437,629 operations in the nordic arthroplasty register association database.* J Bone Joint Surg Am, 2014. **96**(19): p. e167.
125. Chatziagorou, G., Lindahl, H., Kärrholm, J., *The design of the cemented stem influences the risk of Vancouver type B fractures, but not of type C: an analysis of 82,837 Lubinus SPII and Exeter Polished stems.* Acta Orthop, 2019. **90**(2): p. 135-142.
126. 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.
127. Lee, B.P., et al., *Total hip arthroplasty for the treatment of an acute fracture of the femoral neck: long-term results.* J Bone Joint Surg Am, 1998. **80**(1): p. 70-5.
128. Mabry, T.M., et al., *Long-term results of total hip arthroplasty for femoral neck fracture nonunion.* J Bone Joint Surg Am, 2004. **86**(10): p. 2263-7.
129. Gjertsen, J.E., et al., *The Norwegian Hip Fracture Register: experiences after the first 2 years and 15,576 reported operations.* Acta Orthop, 2008. **79**(5): p. 583-93.
130. Havelin, L.I., *The Norwegian Joint Registry.* Bull Hosp Jt Dis, 1999. **58**(3): p. 139-47.
131. Greiner, W., et al., *A single European currency for EQ-5D health states. Results from a six-country study.* Eur J Health Econ, 2003. **4**(3): p. 222-31.
132. Bartels, S., et al., *High failure rate after internal fixation and beneficial outcome after arthroplasty in treatment of displaced femoral neck fractures in patients between 55 and 70 years.* Acta Orthop, 2018. **89**(1): p. 53-58.
133. Dripps, R., *New classification of physical status.* Anesthesiology, 1963. **24**: p. 111.
134. Bartels, S., et al., *Low bone density and high morbidity in patients between 55 and 70 years with displaced femoral neck fractures: a case-control study of 50 patients vs 150 normal controls.* BMC Musculoskelet Disord, 2019. **20**(1): p. 371.
135. Kuo, C.L., Duan, Y., Grady, J., *Unconditional or Conditional Logistic Regression Model for Age-Matched Case-Control Data?* Front Public Health, 2018. **6**: p. 57.
136. Hodge, S.E., et al., *Designing case-control studies: decisions about the controls.* Am J Psychiatry, 2012. **169**(8): p. 785-9.
137. Charlson, M.E., et al., *A new method of classifying prognostic comorbidity in longitudinal studies: development and validation.* J Chronic Dis, 1987. **40**(5): p. 373-83.

138. 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.
139. Dawson, J., et al., *Questionnaire on the perceptions of patients about total hip replacement.* J Bone Joint Surg Br, 1996. **78**(2): p. 185-90.
140. Nilsdotter, A.K., et al., *Hip disability and osteoarthritis outcome score (HOOS)--validity and responsiveness in total hip replacement.* BMC Musculoskelet Disord, 2003. **4**: p. 10.
141. Kanis, J.A., et al., *Standardising the descriptive epidemiology of osteoporosis: recommendations from the Epidemiology and Quality of Life Working Group of IOF.* Osteoporos Int, 2013. **24**(11): p. 2763-4.
142. Bartels, S., et al., *Total Hip Arthroplasty Leads to Better Results After Low-Energy Displaced Femoral Neck Fracture in Patients Aged 55 to 70 Years: A Randomized Controlled Multicenter Trial Comparing Internal Fixation and Total Hip Arthroplasty.* J Bone Joint Surg Am, 2022. **104**(15): p. 1341-1351.
143. Hoshino, C.M., O'Toole, R.V., *Fixed angle devices versus multiple cancellous screws: what does the evidence tell us?* Injury, 2015. **46**(3): p. 474-7.
144. 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.
145. Dolgin, M., *Nomenclature and Criteria for Diagnosis of Diseases of the Heart and Great vessels.* 9th ed. 1994, Boston, Massachusetts: Little, Brown & Co.
146. Mahler, D.A., Wells, C.K., *Evaluation of clinical methods for rating dyspnea.* Chest, 1988. **93**(3): p. 580-6.
147. Dolan, P., *Modeling valuations for EuroQol health states.* Med Care, 1997. **35**(11): p. 1095-108.
148. Ehrich, E.W., et al., *Minimal perceptible clinical improvement with the Western Ontario and McMaster Universities osteoarthritis index questionnaire and global assessments in patients with osteoarthritis.* J Rheumatol, 2000. **27**(11): p. 2635-41.
149. Naylor, J.M., et al., *Minimal detectable change for mobility and patient-reported tools in people with osteoarthritis awaiting arthroplasty.* BMC Musculoskelet Disord, 2014. **15**: p. 235.
150. Yeo, M.G.H., et al., *Are Oxford Hip Score and Western Ontario and McMaster Universities Osteoarthritis Index Useful Predictors of Clinical Meaningful Improvement and Satisfaction After Total Hip Arthroplasty?* J Arthroplasty, 2020. **35**(9): p. 2458-2464.
151. Walters, S.J., Brazier, J.E., *Comparison of the minimally important difference for two health state utility measures: EQ-5D and SF-6D.* Qual Life Res, 2005. **14**(6): p. 1523-32.
152. Concato, J., Shah, N., Horwitz, R.I., *Randomized, controlled trials, observational studies, and the hierarchy of research designs.* N Engl J Med, 2000. **342**(25): p. 1887-92.
153. Thygesen, L.C., Ersbøll, A.k., *When the entire population is the sample: strengths and limitations in register-based epidemiology.* Eur J Epidemiol, 2014. **29**(8): p. 551-8.
154. 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.

155. Støen, R., et al., *Randomized trial of hemiarthroplasty versus internal fixation for femoral neck fractures: no differences at 6 years.* Clin Orthop Relat Res, 2014. **472**(1): p. 360-7.
156. Lagergren, J., Möller, M., Rogmark, C., *Displaced femoral neck fractures in patients 60-69 years old - treatment and patient reported outcomes in a register cohort.* Injury, 2020. **51**(11): p. 2652-57
157. Tidermark, J., et al., *Femoral neck fractures in the elderly: functional outcome and quality of life according to EuroQol.* Qual Life Res, 2002. **11**(5): p. 473-81.
158. Tidermark, J., Bergström, G., *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.
159. Conner-Spady, B.L., et al., *Comparing the validity and responsiveness of the EQ-5D-5L to the Oxford hip and knee scores and SF-12 in osteoarthritis patients 1 year following total joint replacement.* Qual Life Res, 2018. **27**(5): p. 1311-1322.
160. Kang, S., *Assessing responsiveness of the EQ-5D-3L, the Oxford Hip Score, and the Oxford Knee Score in the NHS patient-reported outcome measures.* J Orthop Surg Res, 2021. **16**(1): p. 18.
161. Brooks, R., *EuroQol: the current state of play.* Health Policy, 1996. **37**(1): p. 53-72.
162. Bowers, T.M., Parker, M.J., *Assessment of outcome after hip fracture: development of a universal assessment system for hip fractures.* Sicot j, 2016. **2**: p. 27.
163. Rolfson, O., et al., *Patient-reported outcome measures in arthroplasty registries.* Acta Orthop, 2016. **87 Suppl 1**(Suppl 1): p. 3-8.
164. Wamper, K.E., et al., *The Harris hip score: Do ceiling effects limit its usefulness in orthopedics?* Acta Orthop, 2010. **81**(6): p. 703-7.
165. 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.
166. Coretti, S., Ruggeri, M., McNamee, P., *The minimum clinically important difference for EQ-5D index: a critical review.* Expert Rev Pharmacoecon Outcomes Res, 2014. **14**(2): p. 221-33.
167. Angst, F., Aeschlimann, A., Stucki, G., *Smallest detectable and minimal clinically important differences of rehabilitation intervention with their implications for required sample sizes using WOMAC and SF-36 quality of life measurement instruments in patients with osteoarthritis of the lower extremities.* Arthritis Rheum, 2001. **45**(4): p. 384-91.
168. Pickard, A.S., Neary, M.P., Cella, D., *Estimation of minimally important differences in EQ-5D utility and VAS scores in cancer.* Health Qual Life Outcomes, 2007. **5**: p. 70.
169. Gjertsen, J.E., et al., *Total hip replacement after femoral neck fractures in elderly patients : results of 8,577 fractures reported to the Norwegian Arthroplasty Register.* Acta Orthop, 2007. **78**(4): p. 491-7.
170. Gundtoft, P.H., et al., *Validation of the diagnosis 'prosthetic joint infection' in the Danish Hip Arthroplasty Register.* Bone Joint J, 2016. **98-b**(3): p. 320-5.
171. Svedbom, A., et al., *Osteoporosis in the European Union: a compendium of country-specific reports.* Arch Osteoporos, 2013. **8**(1): p. 137.
172. Borgström, F., et al., *Fragility fractures in Europe: burden, management and opportunities.* Arch Osteoporos, 2020. **15**(1): p. 59.
173. Lofthus, C.M., et al., *Epidemiology of distal forearm fractures in Oslo, Norway.* Osteoporos Int, 2008. **19**(6): p. 781-6.

174. 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.
175. 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.
176. Lewis, D.P., et al., *Hemiarthroplasty vs Total Hip Arthroplasty for the Management of Displaced Neck of Femur Fractures: A Systematic Review and Meta-Analysis.* J Arthroplasty, 2019. **34**(8): p. 1837-1843.e2.
177. Migliorini, F., et al., *Hemiarthroplasty versus total arthroplasty for displaced femoral neck fractures in the elderly: meta-analysis of randomized clinical trials.* Arch Orthop Trauma Surg, 2020. **140**(11): p. 1695-1704.
178. Liu, Y., et al., *Comparing total hip arthroplasty and hemiarthroplasty for the treatment of displaced femoral neck fracture in the active elderly over 75 years old: a systematic review and meta-analysis of randomized control trials.* J Orthop Surg Res, 2020. **15**(1): p. 215.
179. 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.
180. Ekhtiari, S., et al., *Total Hip Arthroplasty Versus Hemiarthroplasty for Displaced Femoral Neck Fracture: A Systematic Review and Meta-Analysis of Randomized Controlled Trials.* J Bone Joint Surg Am, 2020. **102**(18): p. 1638-1645.
181. 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.
182. Parker, M.J., Gurusamy, K., *Internal fixation versus arthroplasty for intracapsular proximal femoral fractures in adults.* Cochrane Database Syst Rev, 2006. **2006**(4): p. Cd001708.
183. He, J.H., et al., *Meta-analysis comparing total hip arthroplasty with hemiarthroplasty in the treatment of displaced femoral neck fractures in patients over 70 years old.* Chin J Traumatol, 2012. **15**(4): p. 195-200.
184. Figved, W., et al., *Radiostereometric analysis of hemiarthroplasties of the hip--a highly precise method for measurements of cartilage wear.* Osteoarthritis Cartilage, 2012. **20**(1): p. 36-42.
185. Kanis, J.A., et al., *Smoking and fracture risk: a meta-analysis.* Osteoporos Int, 2005. **16**(2): p. 155-62.
186. Holmberg, A.H., et al., *Risk factors for fragility fracture in middle age. A prospective population-based study of 33,000 men and women.* Osteoporos Int, 2006. **17**(7): p. 1065-77.
187. Pasoto, S.G., et al., *Osteoporotic hip fractures in non-elderly patients: relevance of associated co-morbidities.* Rheumatol Int, 2012. **32**(10): p. 3149-53.
188. Søgaard, A.J., et al., *Age and Sex Differences in Body Mass Index as a Predictor of Hip Fracture: A NOREPOS Study.* Am J Epidemiol, 2016. **184**(7): p. 510-519.
189. Søgaard, A.J., et al., *The association between alcohol consumption and risk of hip fracture differs by age and gender in Cohort of Norway: a NOREPOS study.* Osteoporos Int, 2018. **29**(11): p. 2457-2467.
190. Kanis, J.A., et al., *Alcohol intake as a risk factor for fracture.* Osteoporos Int, 2005. **16**(7): p. 737-42.

191. Authen, A.L., et al., *Surgeon's experience level and risk of reoperation after hip fracture surgery: an observational study on 30,945 patients in the Norwegian Hip Fracture Register 2011-2015.* Acta Orthop, 2018. **89**(5): p. 496-502.
192. Figved, W., et al., *Cemented versus uncemented hemiarthroplasty for displaced femoral neck fractures.* Clin Orthop Relat Res, 2009. **467**(9): p. 2426-35.
193. Sprague, S., et al., *Factors Associated With Revision Surgery After Internal Fixation of Hip Fractures.* J Orthop Trauma, 2018. **32**(5): p. 223-230.
194. Frihagen, F., et al., *Who, if anyone, may benefit from a total hip arthroplasty after a displaced femoral neck fracture?: a post hoc subgroup analysis of the HEALTH trial.* Bone Jt Open, 2022. **3**(8): p. 611-617.
195. Gjertsen, J.E., *Should Total Hip Arthroplasty Be Used for Hip Fracture?* N Engl J Med, 2019. **381**(23): p. 2261-2262.
196. Blankstein, M., et al., *The FAITH and HEALTH Trials: Are We Studying Different Hip Fracture Patient Populations?* J Orthop Trauma, 2020. **34 Suppl 3**: p. S1-s8.
197. Tang, X., et al., *The comparison between total hip arthroplasty and hemiarthroplasty in patients with femoral neck fractures: a systematic review and meta-analysis based on 25 randomized controlled trials.* J Orthop Surg Res, 2020. **15**(1): p. 596.
198. Farey, J.E., et al., *Bipolar Hemiarthroplasty Does Not Result in a Higher Risk of Revision Compared with Total Hip Arthroplasty for Displaced Femoral Neck Fractures: An Instrumental Variable Analysis of 36,118 Procedures from the Australian Orthopaedic Association National Joint Replacement Registry.* J Bone Joint Surg Am, 2022. **104**(10): p. 919-927.
199. You, D., et al., *Outcomes of total hip arthroplasty using dual mobility components in patients with a femoral neck fracture.* Bone Joint J, 2020. **102-b**(7): p. 811-821.
200. Darrith, B., Courtney, P.M., Della Valle, C.J., *Outcomes of dual mobility components in total hip arthroplasty: a systematic review of the literature.* Bone Joint J, 2018. **100-b**(1): p. 11-19.
201. Cnudde, P.H.J., et al., *Total, hemi, or dual-mobility arthroplasty for the treatment of femoral neck fractures in patients with neurological disease : analysis of 9,638 patients from the Swedish Hip Arthroplasty Register.* Bone Joint J, 2022. **104-b**(1): p. 134-141.
202. Ma, H.H., et al., *Outcomes of dual-mobility total hip arthroplasty versus bipolar hemiarthroplasty for patients with femoral neck fractures: a systematic review and meta-analysis.* J Orthop Surg Res, 2021. **16**(1): p. 152.
203. Rogmark, C., et al., *Costs of internal fixation and arthroplasty for displaced femoral neck fractures: a randomized study of 68 patients.* Acta Orthop Scand, 2003. **74**(3): p. 293-8.
204. Healy, W.L., Iorio, R., *Total hip arthroplasty: optimal treatment for displaced femoral neck fractures in elderly patients.* Clin Orthop Relat Res, 2004(429): p. 43-8.
205. Frihagen, F., et al., *The cost of hemiarthroplasty compared to that of internal fixation for femoral neck fractures. 2-year results involving 222 patients based on a randomized controlled trial.* Acta Orthop, 2010. **81**(4): p. 446-52.
206. Liu, H., et al., *Comparison of total costs between internal fixation and hemiarthroplasty for displaced femoral neck fractures.* J Orthop Sci, 2017. **22**(1): p. 75-80.
207. Axelrod, D., et al., *Is Total Hip Arthroplasty a Cost-Effective Option for Management of Displaced Femoral Neck Fractures? A Trial-Based Analysis of the HEALTH Study.* J Orthop Trauma, 2020. **34 Suppl 3**: p. S37-s41.

208. Swart, E., et al., *ORIF or Arthroplasty for Displaced Femoral Neck Fractures in Patients Younger Than 65 Years Old: An Economic Decision Analysis.* J Bone Joint Surg Am, 2017. **99**(1): p. 65-75.

209. Price, A., et al., *Effects of a modified muscle sparing posterior technique in hip hemiarthroplasty for displaced intracapsular fractures on postoperative function compared to a standard lateral approach (HemiSPAIRE): protocol for a randomised controlled trial.* BMJ Open, 2021. **11**(6): p. e045652.

210. Charity, J., Ball, S., Timperley, A.J., *The use of a modified posterior approach (SPAIRE) may be associated with an increase in return to pre-injury level of mobility compared to a standard lateral approach in hemiarthroplasty for displaced intracapsular hip fractures: a single-centre study of the first 285 cases over a period of 3.5 years.* Eur J Trauma Emerg Surg, 2023. **49**(1): p. 155-163

10. Appendices

Appendix I: Correspondence in Acta Orthopaedica 2019 regarding paper I

Appendix II: Supplementary data in Acta Orthopaedica 2018 Bartels S. et al. (paper I)

Paper I - III