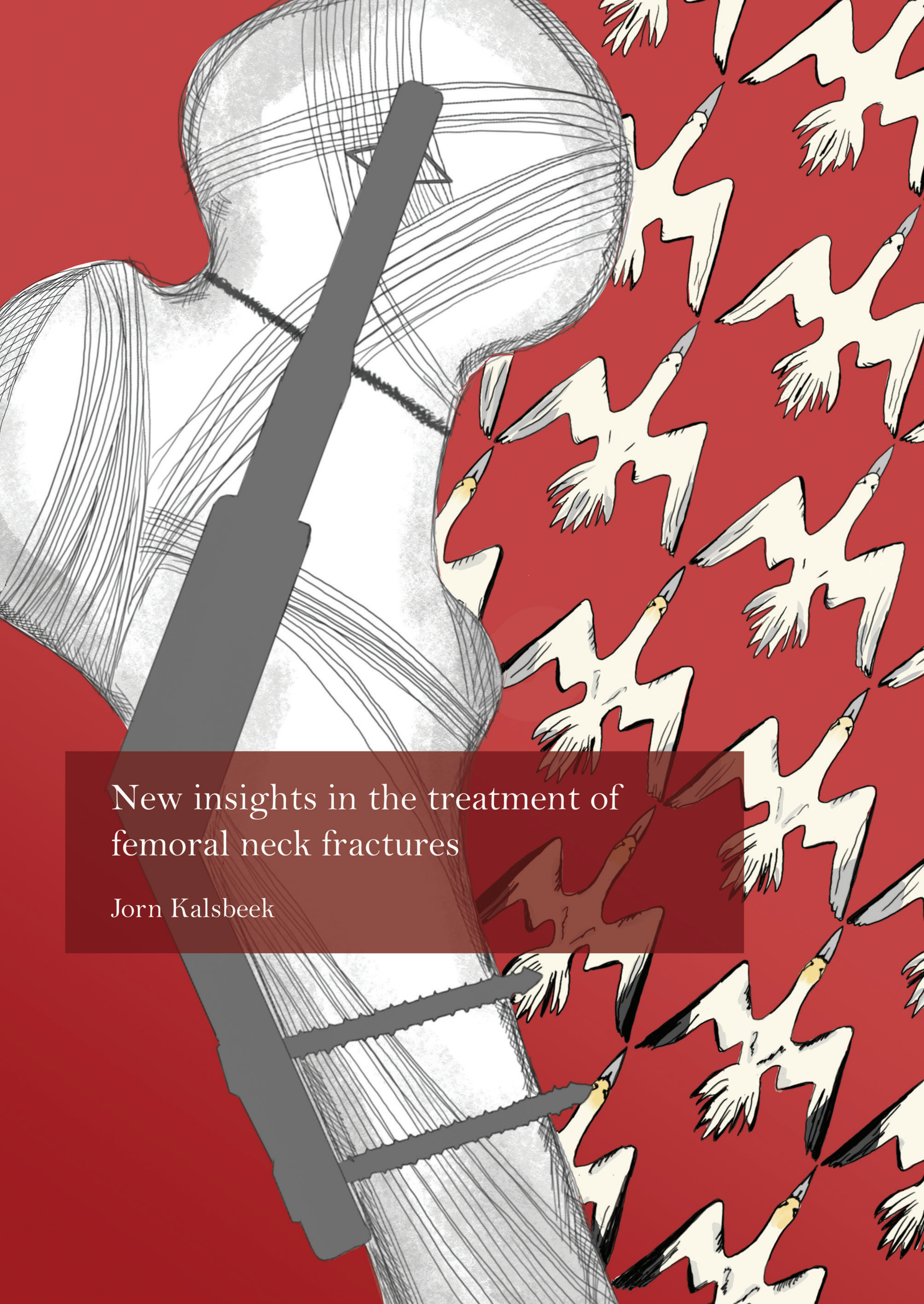
New insights in the treatment of femoral neck fractures
Kalsbeek, J.H.



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Jorn Kalsbeek

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J.H. Kalsbeek

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New insights in the treatment of femoral neck fractures

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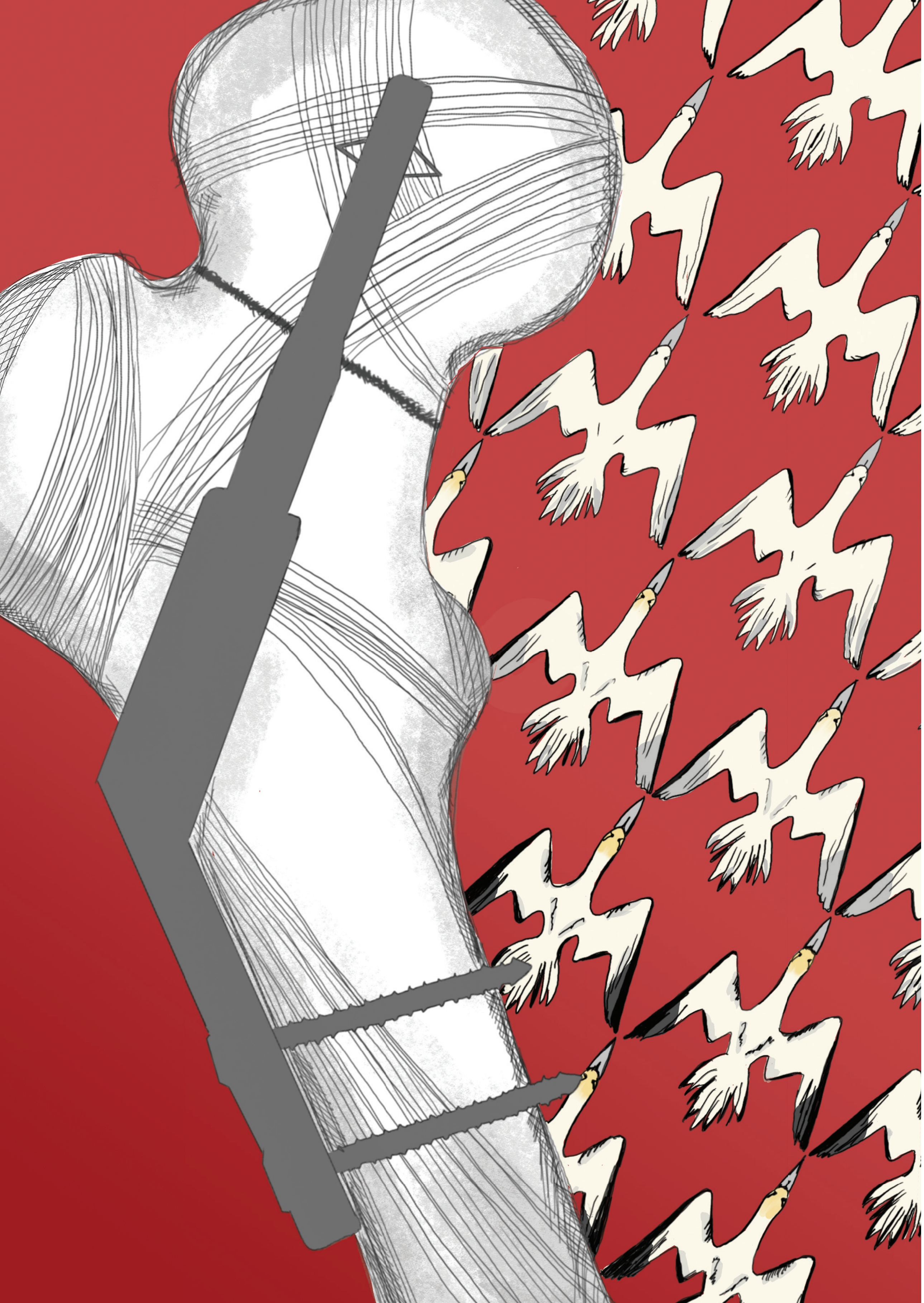

Chapter 1

Introduction and outline of this thesis

INTRODUCTION, AIM AND OUTLINE OF THIS THESIS

In the period 2000–2019, 224,307 patients with a femoral neck fracture (FNF) were admitted to the hospitals in the Netherlands. That is on average 61 patients with a FNF every day. The related cost is estimated to be 21,495 euro per patient.[1] The majority of patients undergo surgical treatment,[2] but despite these enormous numbers of patients with FNFs that are operated on daily bases, and the numerous related scientific publications, the outcome of FNF treatment can still be improved.

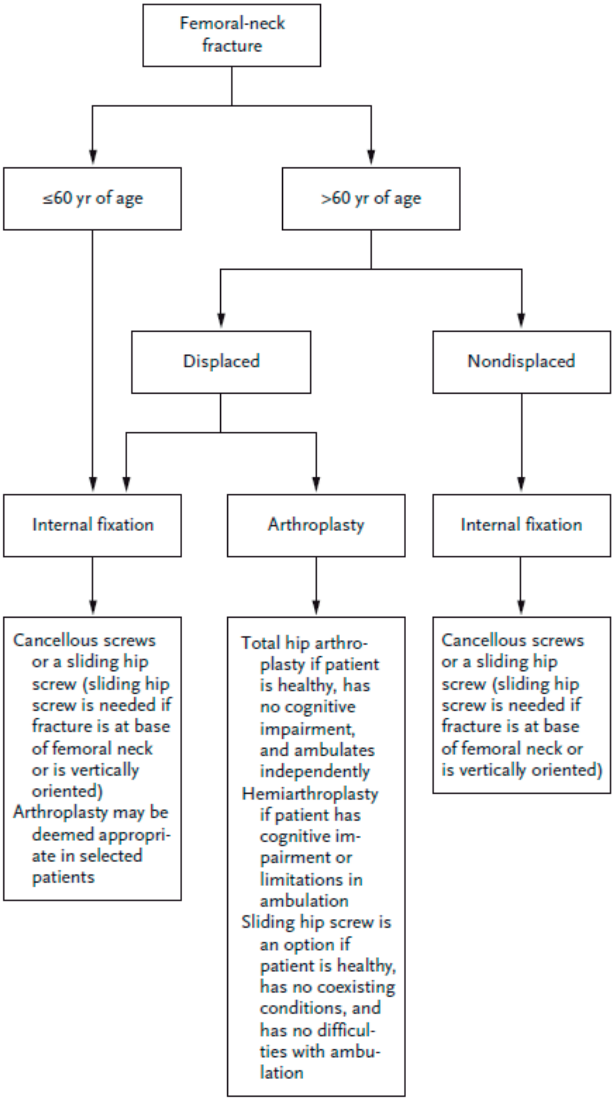

Figure 1. Recommended Management of Femoral Neck Fractures by Bhandari et al. [3]

The preferred surgical treatment strategy for an FNF is predominantly based upon the amount of displacement of the fracture and age of the patient, amongst other patient related characteristics. Patients with undisplaced FNFs (uFNF) can be treated with internal fixation (IF). Younger patients, aged ≤60 years, with displaced FNFs (dFNF) may also be treated with IF, whereas elderly patients are treated with total or hemiarthroplasty (Figure 1).[3] The Dutch guideline for proximal femur fractures advices all uFNFs are to be treated with IF, just like international literature. DFNFs in patients of 18–80 years of age may be treated with IF after 'shared decision making' provided that the patient is healthy (ASA 1–2), has good renal function (eGFR ≥60 ml/min/1.73 m), the risk of revision surgery is expected to be 'acceptable' and an adequate reduction and fixation can be acquired (Figure 2). Patients older than 60 years not suitable for IF should be treated with (hemi)arthroplasty.[4] Both IF and arthroplasty have possible disadvantages and complications. Whereas internal fixation is associated with high revision rates (10–48.8%) due to non-union (9.3–18.5%), avascular necrosis (AVN) (9.7–14.3%) of the femoral head and cut-out of the implant[5-7], arthroplasty of the hip is associated with pulmonary embolism, cement induced syndrome, severe morbidity due to infection, dislocation of the prothesis and limited implant survival.[8,9] To

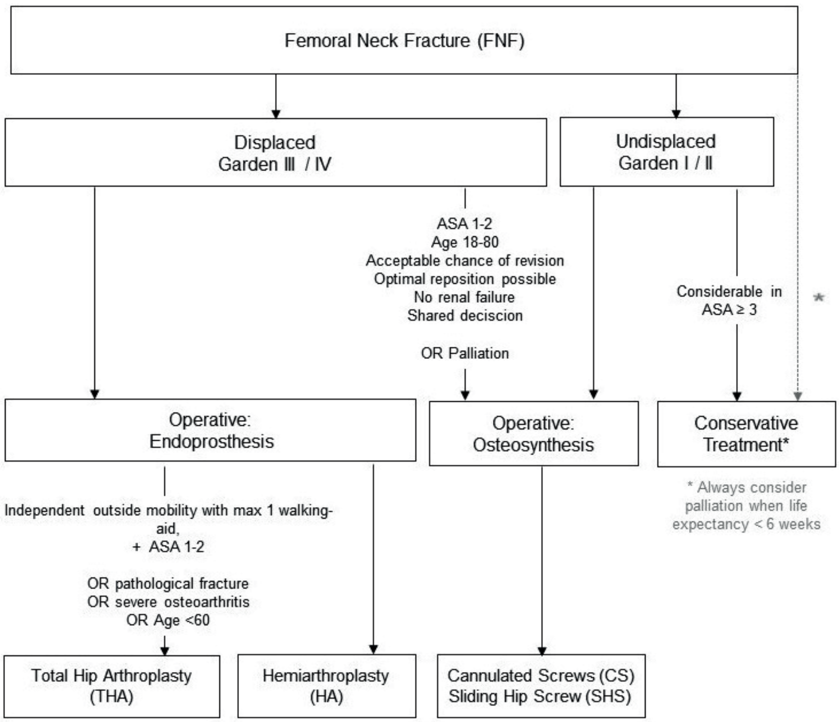

Figure 2. Recommend treatment strategy for Femoral Neck Fractures according to the Dutch Guideline for proximal femur fractures.[4,34]

understand why treatment of FNFs with IF has such high failure rates, knowledge of hip anatomy, biomechanics and biological characteristics of the FNF is prerequisite.

There are several aspects of the femoral neck that determine if the fracture heals. The femoral neck relies on primary (direct) bone healing as it lacks a cambium layer in its fibrous covering to participate in external callus formation (secondary, indirect bone healing). Therefore, achieving perfect anatomical reduction and stable fixation is crucial for facilitating direct remodelling of the Haversian system.[10] Additionally, FNFs can have a devastating impact on the vascular supply of the femoral head and neck. Blood supply of the femoral head comes from medial and lateral circumflex artery, the foveal artery and metaphyseal vessels. The retinacular vessels (ascending cervical arteries), originating from the circumflex arteries supply the majority of the blood to the femoral head (Figure 3).[11,12] Following a fracture of the femoral neck, these vessels can be torn or kinked and to preserve remaining and restore blood supply, again, an anatomical reduction and stable fixation is essential.[13]

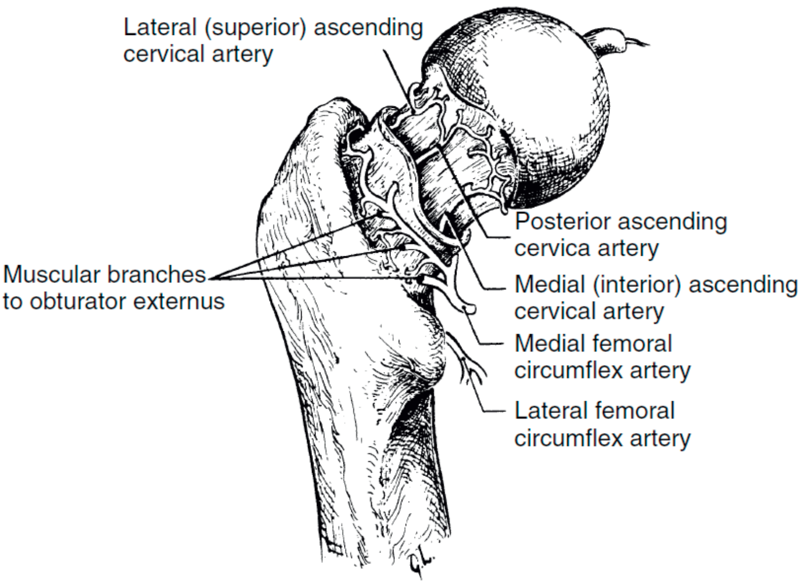

Figure 3. Arterial blood supply to the head and neck of the posterior aspect of the left proximal femur.[11]

Considering this biology, displacement of the femoral head is a substantial factor in determining the optimal treatment strategy for a FNF. Displacement of the femoral head has a devastating effect on vascular supply, and achieving anatomical repositioning poses a challenge, leading to a much higher failure rate of fracture healing in dFNFs compared to uFNFs, respectively 21–49% [5,14,15] versus 11–19% [16,17]. The global standard for determining displacement of FNFs is the Garden Classification, where Garden types I and II represent uFNF and types III and IV represent dFNF.[18] However, this classification is solely based upon the anteriorposterior(AP) radiographs. Displacement of the femoral head in posterior direction is not included in this classification. But this posterior tilt may also influence vascularization and stability, and therefore outcome of treatment, as much as varus angulation, as measured in the AP view, does. Yet posterior tilt is not included in conventional classifications (i.e. Garden, Pauwels or AO/OTA classification).[18-20]

As described, adequate reduction and stable fixation is essential for a successful treatment with internal fixation. DFNF are recommended to be reduced using a closed technique by traction and internal rotation.[21] A good reduction of the fracture lies entirely with the surgeon. For fixation of the fracture there are multiple implants available, from which the Dynamic Hip Screw (DHS) and multiple cannulated screws (CS) are most commonly used. Cadaveric studies have shown fixed angle devices to have an advantage over CS in terms of stabilizing the fracture.[22,23] The DHS also has a slight advantage in clinical practice over CS in treatment of patients with displaced FNF.[6] Yet, reoperation rates still run up to 24% after treatment with the DHS and 34% after CS in patients with dFNFs. To improve treatment outcome of FNFs, two decades ago, a trauma surgeon in the East of the Netherlands, dr. Ariaan van Walsum, developed a new implant for the fixation of FNFs. A suitable implant, in his opinion, should have the following characteristics: good angular and rotational stability, firm femoral head fixation, a small frontal area and low implant volume and the possibility of applying dynamic compression over the fracture. After years of development and successful laboratory tests showing improved stability over DHS and the Twinhook, the Dynamic Locking Blade Plate (DLBP), nicknamed The Gannet, was born (Figure 4).[24] It showed good results in a small pilot study with 25 patients with a failure rate of 8% at two-year follow-up and a 4% failure rate in a prospective cohort of 172 patients with uFNFs at one year follow-up.[25,26]

Besides fracture related (displacement and posterior tilt of the femoral head) or operation related factors (dexterity of the surgeon, reduction of the fracture and implant choice) that influence the outcome of a FNF, various patient related factors affect the outcome of a treatment. After all, it is the physiology of the patient that heals the fracture. Numerous pre-operative, patient related predictors have been examined in literature. For example smoking influences (re)vascularisation of the fracture site, osteoporosis influences bone healing and alcohol consumption affects bone metabolism, contributes to malnutrition and comorbidities and therefore increases NU and AVN.[27-29] The Dutch treatment guideline for hip fractures exclusively incorporates renal failure as a predictive factor for treatment failure in femoral neck fractures.[4] However, they assert that it remains unclear which category of patients would benefit more from IF as opposed to prosthesis in the treatment of dFNFs.

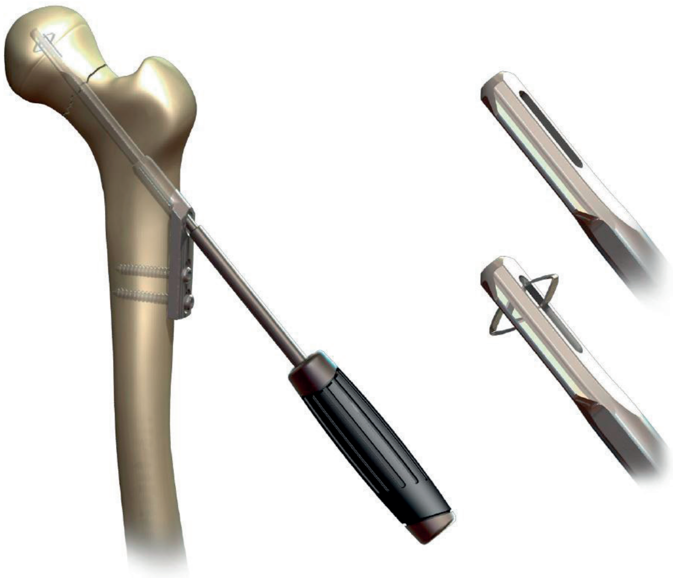

Figure 4. Illustration of the Dynamic Locking Blade Plate also known as the Gannet.

After more than a century of research on FNFs it can be concluded that a definitive solution for the treatment of this challenging fracture remains elusive. A complex mix of patient, fracture and intervention related factors determine the outcome of treatment.

The overall aim of this thesis is to improve treatment outcome of FNF surgery by identifying and, if possible, improving factors that influence FNF healing. This objective is pursued by systematically reviewing the current literature, evaluating and analysing the results of the DLBP, and devising and planning new studies to ensure further development of the DLBP. Eventually this thesis may assist surgeons in selecting the optimal treatment for patients with FNFs and substantiate future algorithms and guidelines for treatment of FNF.

OUTLINE OF THIS THESIS

Identifying factors that influence outcome of treatment of femoral neck fractures

Identifying patient, fracture and treatment related factors of importance for the outcome of FNF surgery is the first step in determination of the preferred treatment. To help surgeons to select the right patient with a dFNF that is suitable for IF, **Chapter 2** describes the results of a systematic review and meta-analysis that provide a comprehensive overview of possible predictors that increase the risk over revision surgery of dFNF that were treated with IF.

We identified three patient related predictors and two operation related predictors that increase the risk of revision surgery and quantify their risk of fixation failure. In the next two chapters we examine one fracture related factor that influences the outcome of treatment of uFNF. In **Chapter 3** we evaluated the influence of posterior tilt of the femoral head on the outcome of treatment of uFNFs. Preoperative posterior tilt was measured in a prospective documented cohort with 193 patients with uFNFs and correlation with revision surgery and posterior tilt was analysed in order to update the globally used Garden classification. Next, we validated two methods to measure posterior tilt. The Lateral Garden Angle[30] and the new Posterior Tilt Measurement according to Palm[31] were tested for inter and intra observer reliability in **Chapter 4,** using fifty X-rays and four observers.

Improving the treatment of femoral neck fracture surgery

The second aim of this thesis was to investigate the clinical outcome of FNFs after treatment with the DLBP. In **Chapter 5** we present the results of a prospective documented multicentre cohort of 106 young patients with a dFNF treated with the DLBP with a follow up of one year. Patients of 18–60 years were included to ensure IF was the correct indication according to literature.[32,33] The primary outcome parameter was failure in fracture healing due to non-union, avascular necrosis or implant failure requiring revision surgery. The results were promising, yet high level evidence to prove the DLBP has better treatment outcome than globally used internal fixation devices, was still needed. We therefore designed the DEFENDD trial. The aim of the DEFENDD trial is to test if the favourable results with the DLBP persist in a randomized controlled trial (RCT) for patient aged 65 years or younger with initially displaced FNFs. In **Chapter 6** we present the study protocol for the DEFENDD trial, a multicentre RCT comparing the results of the DLBP with the DHS. The primary outcome parameter is the incidence of revision surgery after 1 year. Secondary study parameters are the incidence of avascular necrosis, non-union, (implant related) complications, functional outcome, elective removal of the implant and health-related quality of life and costs. The follow-up of the earlier published studies was limited to one year, because most of the complications occur within one year. Yet some FNFs are still revised after one year. That is why we examined the long-term outcome of patients that were treated with the DLBP in **Chapter 7**. We analysed a prospective registered database of 468 patients treated with the DLBP. The primary outcome parameter after a minimal follow-up of seven years was revision surgery. Complications, elective removal of the implant, the indication for revision surgery and mortality were secondary outcome parameters. Because of the large numbers in the cohort and the long follow-up we were able to present survival analyses of the implant and multivariate regression analyses of potential predictors for failures.

In **Chapter 8** we discuss the clinical implications and future perspectives related to the studies in this thesis. A summary of this thesis is presented in **Chapter 9** and, in Dutch, **Chapter 10.**

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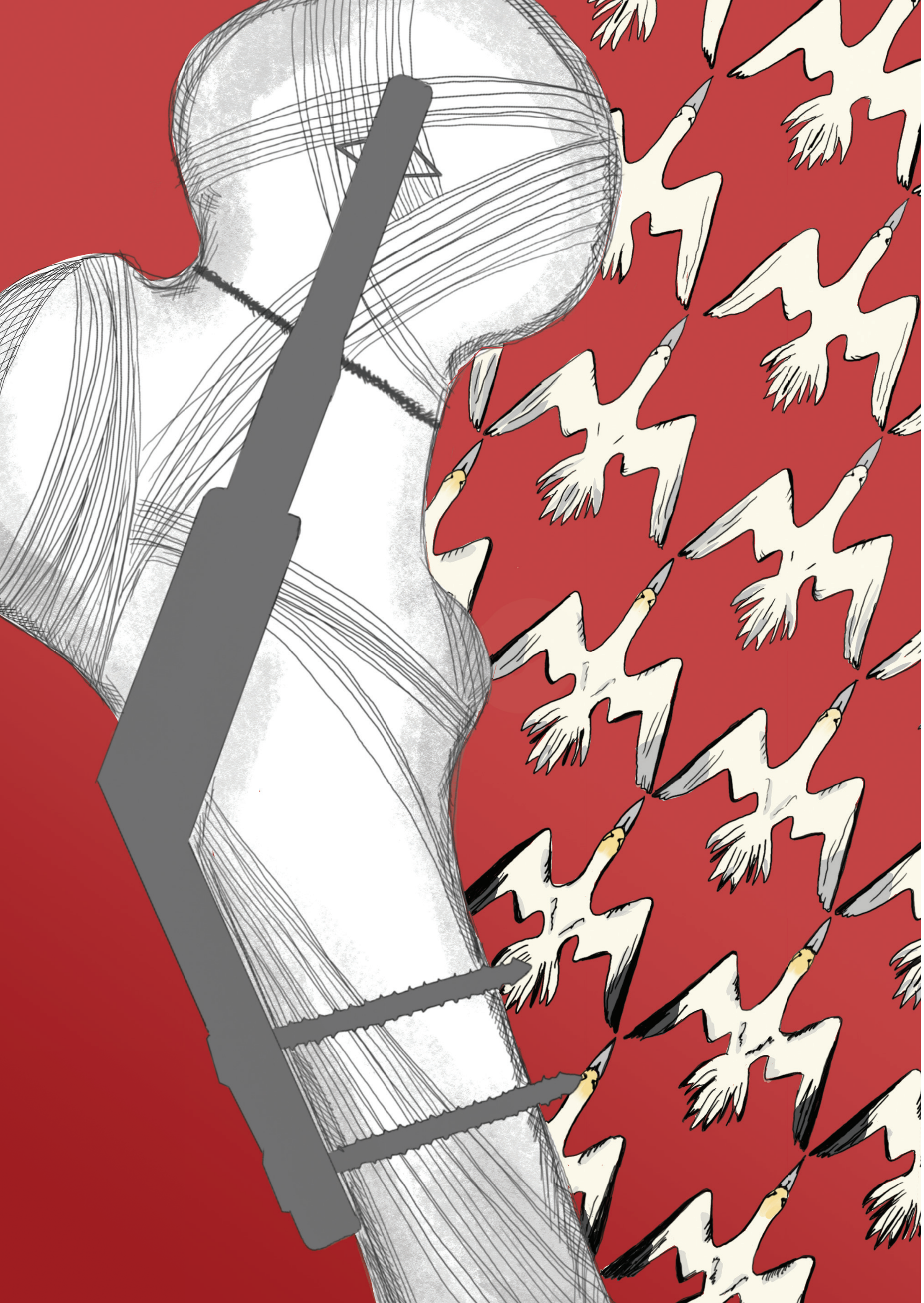

Chapter 2

What makes fixation of femoral neck fractures fail? A systematic review and meta-analysis of risk factors

J.H. Kalsbeek, M.F. van Donkelaar, P. Krijnen, W.H. Roerdink,
R. de Groot, I.B. Schipper

Injury. February 2023;54:652-60.

ABSTRACT

Introduction

This systematic review aims to provide an overview of predictors for failure of treatment of displaced femoral neck fracture (dFNF) with internal fixation and quantify their risk of fixation failure in a meta-analysis.

Patients and Methods

PubMed, Embase, Web of Science, Cochrane Library, and EMCare were searched for original studies published from January 2000, including adult patients with an internally fixated dFNF, that reported data on predictors for fixation failure defined as revision surgery due to non-union, avascular femoral head necrosis or cut-out of implant. RevMan version 5 software was used to pool univariable Odds Ratio's (OR) for predictors of fixation failure by means of a random effects model.

Results

This review included 16 articles (15 articles cohort studies and one randomised trial). Twenty-four predictors for fixation failure were identified and analysed, 16 of which were evaluated in just one study. Data of 7 predictors were pooled in a meta-analysis. Female sex (OR 1.78, 95% confidence interval [CI] 1.26–2.52), smoking (OR 3.64, 95% CI 1.68–7.91), age >50 years (OR 3.64, 95% CI 1.68–7.91), inadequate fracture reduction (OR 2.28, 95% CI 1.62–3.22), fixation with cannulated screws (CS) or pins compared to fixed angle devices (OR 2.16, 95% CI 1.03–4.54) were identified as significant predictors for fixation failure.

Conclusion

This study can help surgeons to choose the preferred treatment for patients with a dFNF and substantiate future algorithms and guidelines for treatment of FNF.

2

INTRODUCTION

Treatment of displaced femoral neck fractures (dFNF) remains challenging.[1] DFNF are treated with either reposition and internal fixation (IF) or (hemi)arthroplasty. Considering the pros and cons of these two treatment modalities, (hemi)arthroplasty is known to be associated with a higher infection rate than IF and can be complicated by hip dislocation.[2] Also peri-prosthetic fractures may occur with devastating consequences. Furthermore, most prostheses need revision surgery after around 25 years.[3,4] Alternatively, treatment with IF may lead to avascular necrosis (AVN) of the femoral head, resulting in non-union of the fracture or cut-out of the implant.[5] These complications result in more reoperations than treatment with a prosthesis.[2,6,7] Failure rates of dFNF treated with IF up to 48% have been reported.[2] Despite countless publications on FNF treatment, it is still unclear which patients with a dFNF have an high risk of unsuccessful treatment with IF and may be better off with a prosthesis. Today treatment algorithms for dFNF are mainly based on age[8,9] stating that younger patients are preferably treated with fracture reduction and IF, whereas older patients are preferably treated with (hemi)arthroplasty. There is no clear consensus from what age patients with a dFNF would better be treated with a prosthesis.[8-10] The treatment outcome with IF is influenced by many factors. Predictors for failure of treatment with IF are mentioned in literature.[11-15] Some predictors are patient-related (gender, osteoporosis, smoking, comorbidities), while others are fracture-related (displacement, posterior cortex comminution) or operation-related (reposition of the fracture, choice and position of the implant).

To our knowledge there is no overview in literature of all known potential predictors of failure of treatment of dFNF with IF. An overview of predictors and the substantiation of their role in treatment failure may help surgeons choose the preferred treatment strategy for patients with a dFNF. This systematic review of the literature aims to provide an overview of predictors for failure of treatment of dFNF with IF and quantify their risk of fixation failure in a meta-analysis.

METHODS

This review and meta-analysis were conducted and reported in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement.[16] The review protocol was registered in the international prospective register of systematic reviews PROSPERO (protocol number CRD42020210914).

Eligibility criteria

We selected all types of original studies, available in English, German or Dutch, published from January 2000, including patients of 18 years or older with a dFNF treated with any form of IF, that reported the odds ratios (ORs) of predictors of failure of treatment (defined as any revision surgery such as conversion to arthroplasty, girdle stone, core decompression, vascular fibular graft, valgus (intertrochanteric) osteotomy due to non-union, avascular femoral head necrosis or cut out of implant) or that provided sufficient information to calculate the ORs. No minimal duration of follow up was required.

Exclusion criteria

Studies of which the full text was not available, were excluded. Reviews, surveys, current (management) concepts, editorials, commentaries, animal studies or cadaveric studies, meeting abstracts, conference proceedings, case studies and case series (N<20) were also excluded.

Search strategy and selection process

A systematic search was conducted in PubMed, Embase, Web of Science, Cochrane Library, and EMCare on August 21, 2020, which was updated on November 11, 2021 and July 19, 2022. The search strategy was developed with help of an experienced medical librarian and adjusted for each specific database. The search terms included 'displaced femoral neck fractures', 'internal fixation', 'revision surgery/re-operation', 'predictors for failure' and their synonyms. The search strategy was validated by confirming that 4 predefined relevant articles were identified using the search terms.[17-20] Details of the search strategy are provided in Supplementary Material 1. After removal of duplicates, title and abstract of the identified records were independently screened by two reviewers (JHK and MFD) and documented in Rayyan Systems Inc[21], using the predetermined eligibility criteria and exclusion criteria. Excluded articles were classified according to the reason of exclusion. Disagreements were discussed with a third author (WHR or IBS). Next, the full texts of the selected articles were assessed for eligibility using the same criteria. The reference lists of the included articles were searched by hand to identify relevant publications that were missed in the search.

Data extraction and quality of evidence assessment

Data-extraction from the full-text articles was done by two independent reviewers (JHK and MFD) using a previously designed data extraction form. Any disagreements were discussed with a third author (PK). Information of the following study characteristics were extracted: first author's name, year of publication, study design, number of patients included for analysis, patients' mean age, exclusion criteria, type of implant used for fracture fixation, mean follow up, number and percentage of patients with and without the investigated potential predictors for failure, in the groups with and without fixation failure (reoperation).

The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach was used to determine certainty in the pooled estimates of association between prognostic factors and future outcome for 5 domains including risk of bias, imprecision, inconsistency of results across studies, indirectness, and publication bias.[22] Risk of bias in the individual studies was assessed using the Quality in Prognostic Studies (QUIPS) tool (supplementary data 2).[23] Inconsistency of results across studies was assessed by analysing the Forest Plots and by the amount of statistical heterogeneity in results (I^2) between the studies included in the meta-analysis. Imprecision of the estimates was based on whether the 95% confidence interval (CI) excluded an OR of 1 and the width of the CI. Indirectness evaluates whether the study population and outcome were comparable between studies. The probability of publication bias was visually assessed using funnel plots.

Data synthesis

RevMan version 5 software[24] was used to pool univariable OR's for predictors of fixation failure by means of a random effects model. The I^2 statistic, indicating the percentage of variation across studies due to statistical heterogeneity, was used to measure the inconsistency of the studies' outcomes, and was qualified as follows: 0% to 40% (might not be important); 30% to 60% (may represent moderate heterogeneity); 50% to 90% (may represent substantial heterogeneity); 75% to 100% (considerable heterogeneity).[25] Sensitivity analysis was done by leaving out individual studies from the analysis to assess their effect on the overall results.

RESULTS

Study identification and selection

The literature search, including the update, yielded a total of 2348 regular references (1040unique records). The selection process with reasons for exclusion of studies is presented in Figure 1. A total of 16 articles were included for analysis.[19,20,26-39]

Study characteristics

The characteristics of the included studies with the definitions of the investigated predictors are outlined in Table 1. All studies but one were prospective or retrospective cohort studies. One study comprised a randomised controlled trial. The studies were conducted in China (1), Denmark (1), Israel (2), the Netherlands (4), Scotland (1), Sweden (2), Taiwan (1), and the USA (4). Together, the 16 studies included a total of 2409 patients. Of these, 1874 patients (1875 dFNFs) met the review's inclusion criteria and were eligible for analysis. Although the inclusion criteria for the patients in the studies were similar, there was a wide range of exclusion criteria. In total 31 different exclusion criteria were used, 18 of which were only mentioned in one study (Table 1). The mean age of the patients in the included studies ranged from 38–84 years old. In four of the 16 studies the patients' mean age was above 60 (n=778). All studies had a mean follow up of at least 12 months (range 12–150 months). The overall reoperation rate was 24.3% (455 of 1875 dFNFs), ranging from 6.7–40.5%.

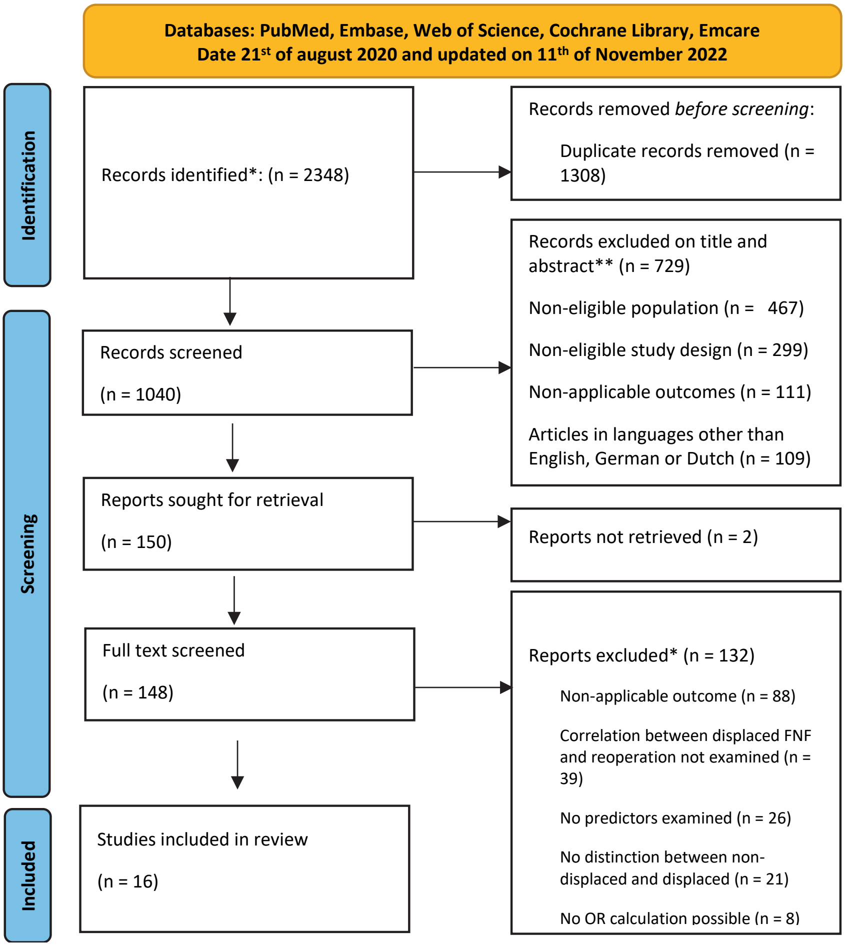

Figure 1. PRISMA 2020 flow diagram for systematic reviews. FNF, Femoral neck fracture. OR, Odds ratio. *Details of the search strategy are reported in Supplementary Material 1.
* Some studies were excluded due to multiple reasons.

Risk of bias and quality of evidence assessment

The risk of bias within the studies was moderate to high (supplementary material 2). Risk of bias due to confounding was assessed highest, because only a few potentially important confounders were accounted for in the analysis in the individual studies. Yet as stated in our introduction there is a wide range of factors that potentially influence the reoperation rate.

Table 1. Study characteristics and predictors for reoperation

Study details	Study design	Patients (n) included	Mean age (years)	Exclusion criteria	Treatment	Mean follow up (months)	Reoperations	Predictors investigated + cut off values	Significance predictors (p<0.05)
Campenfeldt 2018	Prospective cohort	120	58 (range 20-69)	Unable to walk Not living independently Psychotic disease Severe cognitive impairment Chronic renal failure Hyperparathyroidism Simultaneous fracture of the lower extremity Fracture older than 48 h before admission Patients with previous pathology in the fractured hip	CRIF Two CS (Olmed)	24	28% (33/120)	Age (50-69 / 20-49 years) Gender (female/male) ASA score (3-4/1-2) [a1] Alcohol (AUDIT high/low) [a2] Smoking (yes/no) Mechanism of injury (high / low energy) Fracture reduction (fair-poor/good) [a3] Position of screws (not good/good) [a4] BMD femoral neck (low/ normal) [a5]	Not significant (univariate model) Not significant (univariate model) Not significant (univariate model) Significant (multivariate model) Not significant (univariate model) Not significant (univariate model) Not significant (univariate model) Not significant (univariate model) Significant (multivariate model)
Gardner 2014	Retrospective cohort	69	43 (SD 13)	< 6 months follow up Pathologic fracture Fracture involving either trochanter or extending beyond the intertrochanteric line Femoral head fracture Acetabulum fracture	CRIF and ORIF CS with 6.5 mm or 7.3 mm cannulated partially threaded CS (Synthes. West Chester, PA) or SHS (Synthes. West Chester, PA).	18	28% (19/69)	Implants (CS/SHS) Smoking (yes/no) Fracture reduction (excellent/good-fair)[b1] Diabetes (yes/no)[nd] Alcohol abuse (yes/no)[nd] End stage renal disease(yes/ no)[nd] Steroids (yes/no)[nd] Weight bearing status (as tolerated/protected)[nd] Gender(female/male)	Not significant (multivariate model) Not significant (multivariate model) Significant (multivariate model) Not significant (univariate model) Not significant (univariate model) Not significant (univariate model) Not significant (univariate model) Not significant (univariate model) Not significant (univariate model)

Table 1. *Continued*

Study details	Study design	Patients (n) included	Mean age (years)	Exclusion criteria	Treatment	Mean follow up (months)	Reoperations	Predictors investigated + cut off values	Significance predictors (p<0.05)
Heetveld 2006	Retrospective analysis of a prospective cohort	102	77	FNF > 48 hours old Advanced arthrosis of the ipsilateral hip Established rheumatoid arthritis Pathologic fracture	CRIF/ORIF DHS, DHS with anti rotational screw, 3 CS	24	38% (39/102)	Fracture reduction (inadequate/adequate)[c2] Implant positioning (inadequate/adequate)[c3] Overall operation technique (inadequate/adequate)[c4]	Significant (multivariate model) Not significant (multivariate model) Not significant (multivariate model)
Heetveld 2005	Prospective cohort	111	77	FNF > 48 hours old Advanced arthrosis of the ipsilateral hip Established rheumatoid arthritis Pathologic fracture	DHS, DHS with anti rotational screw, CS	24	41% (45/111)	Osteoporosis measured using the femoral neck (osteoporosis/osteopenia+normal)[d1]	Not significant (univariate model)
Hoshino 2016	Retrospective cohort	62	39 (SD 12)	Treated with parallel screw configurations, proximal femoral locking plates or cephalomedullary nails < 6 months follow-up	ORIF and CRIF (<5%) The dynamic hip screw (DHS) and the dynamic helical hip system (DHHS) (DePuy Synthes, Inc., West Chester, PA) Pauwel screw; either a solid 4.5-mm or cannulated 7.3-mm lag screw	17	30% (19/63)	Implants (pauwel screws/ fixed angle device)	Significant (univariate model)

Table 1. *Continued*

Study details	Study design	Patients (n) included	Mean age (years)	Exclusion criteria	Treatment	Mean follow up (months)	Reoperations	Predictors investigated + cut off values	Significance predictors (p<0.05)
Huang 2010	Retrospective cohort	104	47	Inadequate reduction Bilateral hip fracture Open fracture Previous fracture Symptomatic osteoarthritis of the hip before injury Rheumatoid arthritis Pathologic fracture and a malignant disease No complete sets of preoperative, postoperative and follow-up radiographs	CRIF Percutaneous fixation with parallel CS(7.0 mm in diameter, Synthes)	57	30% (31/104)	Posterior wall disruption (yes/no)[e1]	Significant (univariate model)
Kalland 2019	Prospective RCT	114	ND for dFNF	Fracture of the contralateral hip	Pinloc or 2 Hansson Pin System	12	22% (25/114)	Implants (Hansson Pins/ Pinloc) Age (≥70/50-69)	Not significant (univariate model) Not significant (univariate model)
Kalsbeek 2018	Prospective cohort	106	52 (range 23-60)	Any implant other than DLBP Pathological fracture Concomitant fractures of the lower limb Symptomatic arthritis Local infection or inflammation Inadequate local tissue coverage Any mental or neuromuscular disorder, which would create an unacceptable risk of fixation failure, complications or evaluation postoperatively.	Dynamic locking blade plate	12	13% (14/106)	Gender (female/male) Tip Apex Distance (>25mm/≤25mm)[f1] Reposition (malreduction/ good reduction)[f2]	Not significant (univariate model) Not significant (univariate model) Not significant (univariate model)
Kenan 2015	Retrospective cohort	27	44 (range 23–59)	none	CRIF/ORIF Three 7.3 mm CS	150 (range 96–204)	14.8% (4/27)	Age (50-60/<50)	Significant (univariate model)

Table 1. *Continued*

Study details	Study design	Patients (n) included	Mean age (years)	Exclusion criteria	Treatment	Mean follow up (months)	Reoperations	Predictors investigated + cut off values	Significance predictors (p<0.05)
Marchand 2022	Retrospective cohort	77	38 (range 18-59)	Severe osteoarthritis Bone metabolism disorders Fractures associated with a fracture to the ipsilateral acetabulum	DHS or DHHS	12	19.5%(15/77)	Implants (DHS/DHHS)	Not significant (univariate model)
Nyholm 2020	Retrospective cohort	537 (deceased patients excluded)	69 (range 21–102)	Foreign citizens Incorrect date of surgery in DFDB Alternative surgical technique Dead prior to postoperative radiography New fracture of the hip before postoperative radiography Quality of radiographs did not allow evaluation Radiographs not available Postoperative radiographs taken > 5 days after surgery Previous fracture of the hip Bilateral fractures of the hip at time of surgery Maldeveloped caput	8.0-mm Olmed screws and 6.5 or 7.3-mm Cannulated screws, DePuy-Synthes, Johnson & Johnson MD&D; 8.0-mm Asnis Screws, Stryker; or 6.5-mm Hansson Pins, Swemac Orthopaedics	12	23% (124/537)	Age (≤60/>60) Gender(female/male) Time to surgery (<24h/>24h) Severe displacement (mildly/severely displaced)[g1] Insufficient reduction(partly-not/fully reduced)[g2] Protrusion of an implant (yes/no)[g3] Bone quality (CTI) (≤0.5/>0.5)[g4] Angulation of implants (≤125°/>125°)[g5]	Not significant (multivariate model) Significant (multivariate model) Significant (multivariate model) Significant (multivariate model) Significant (multivariate model) Significant (multivariate model) Not significant (multivariate model) Not significant (multivariate model)
Patterson 2020	Retroscpective cohort	234	45 (18-65)	Pathologic FNF Ipsilateral acetabular, femoral head, shaft, or supracondylar femur fracture Less than minimum 6-month follow-up	CRIF, ORIF with sliding hip screw or cephalomedullary nail or CS	18 (range 6–130)	26% (55/212)	Reduction technique (ORIF/CRIF)	Significant (univariate model)
Stearns 2009	Retrospective cohort	78	56 (range 18-65)	Incomplete records	SHS and CS	43	6,7% (4/59)	Alcohol abuse (alchohol abuse/no abuse)[h1]	Not significant (univariate model)

Table 1. *Continued*

Study details	Study design	Patients (n) included	Mean age (years)	Exclusion criteria	Treatment	Mean follow up (months)	Reoperations	Predictors investigated + cut off values	Significance predictors (p<0.05)
Thein 2014	Retrospective cohort	78	54 (SD 16)	Pathological fractures Previous surgery on the ipsilateral hip or femur Failure to complete 1 year of follow-up.	CRIF Targon FN or multiple CS.	28,7	25,6% (20/78)	Implant (CS/Targon FN)	Significant (univariate model)
van Dortmont 2000	Randomized controlled trial	28	84 (range 72-92)	ND	CRIF Three cannulated AO/ASIF screws.	14 (range 0.5-60)	14% (4/28)	Reduction (Inadequate/adequate) [i1]	Not significant (univariate model)
Xiong 2019	Retrospective cohort	46	50 (range 19–60)	Pathological fracture Malignant disease Open fracture Previous fracture Symptomatic osteoarthritis of the hip before injury Rheumatoid arthritis No complete sets of preoperative, postoperative, and follow-up radiographs	Closed reduction and fixation with multiple cannulated screws (6.5mm in diameter) in inverted triangle or diamond configuration	22 (range 12–36)	9% (4/46)	Inferior calcar buttress reduction pattern[i1] (non-anatomical/anatomical)	Not significant (univariate model)

AP: anteriorposterior; AVN: avascular necrosis; CRIF: closed reduction and internal fixation; CS: Cannulated screws; DFDB: Danish Fracture Database; dFNF: displaced femoral neck fracture; DHHS: dynamic helical hip system; FNF: femoral neck fracture; IF: internal fixation; ISS: injury severity score; ND: not described; ORIF: open reduction and internal fixation; OTA: Orthopaedic Trauma Association; SFFN: stress fracture of the femoral neck; SHS: sliding hip screw.

a1: American Society of Anesthesiologists classification (ASA score).

a2: Alcohol Use disorder Identification Test (AUDIT) A total score of 8 or more in men or 5 in women indicates a strong likelihood of hazardous or harmful high alcohol consumption.

a3: Good reduction was a displacement of < 2 mm, a posterior angulation of <10 between the femoral head/neck compared to the femoral shaft on a lateral radiograph and a Garden angle of 160° to 175°.

a4: The screw position was considered as optimal when the distal screw was positioned on the femoral calcar and introduced at the level of the lesser trochanter. The tip of both screws should be less than 5 mm from the subchondral bone and the proximal screw should be parallel positioned (< 10°) and at least 2 cm apart from the distal screw. On the lateral projection the screws should lie on the central or posterior third of the femoral head and neck and be parallel. The position was considered as suboptimal if one or more of these criteria were not fulfilled.

a5: BMD: Bone Mass Density; T-scores of femoral neck were calculated for patients between 50–69 years and Z-scores in patients 20–49 years of age according to the recommendation by the International Society of Clinical Densitometry. A T-score > -1 SD (standard deviation) was considered a normal BMD, osteopenia if T-score of -1 to -2.49 SD and osteoporosis if T-score <-2.5 SD. In patients (20–49 years), a Z -score <-2 SD was considered as a low BMD. Low BMD was defined as osteopenia/osteoporosis in patients between 50–69 years or Z -score <-2 SD in patients 20–49 years old.

b1: Excellent (<2 mm displacement and/or <5 degrees of angulation), good (2-5mm displacement and/or 5-10 degrees of angulation), fair (5-10 mm displacement and/or 10-20 degrees of angulation) or poor (>10 mm displacement and/or >20 degrees of angulation).

c1: PSS: Physiologic Status Score; high PSS is defined as mobile with no or one walking aid outside the home, living independently at home or partial dependence on social services/relatives, good cognitive function and ASA 1-2.
c2: Adequate reduction: on anteroposterior view within 160 to 180 degrees (Garden index). In the lateral view 10 degrees of anteversion or retroversion is acceptable.
c3: Implant positioning: CS had to be inserted according to the following criteria: (1) two screw positions within 3 mm of the inferior and posterior cortices of the femoral neck calcar, (2) parallelism of the inserted screws to within 10°, (3) screw tips to within 5 mm of the subchondral bone in the femoral head, (4) minimal screw diameter of 6.5 mm, and (5) screws should be inserted in a manner to lag and not across the fracture site. A SHS had to be inserted according to the following criteria: (1) screw tip on anteroposterior and lateral views of the hip are less than 25 mm from the apex of the femoral head (tip apex distance) and not anterior or superior in the femoral head, (2) screw in the central or dorsal part of the femoral head and not crossing the fracture line on the lateral view, and (3) two- (preferable) or four-hole side-plates were acceptable.
c4: Adequate reduction and implant positioning combined.
d1: Osteoporosis is a T score of below -2.5 SD (standard deviation).
e1: The posterior wall of the femoral neck was considered to be disrupted if a fragment was observed on the antero-posterior or lateral plain radiograph of the affected hip or on an antero-posterior radiograph of the pelvis.
f1: Tip-apex distance: 25mm is the cut off value.
f2: The Garden Alignment Index was used. The acceptable range of reduction is a 160 to 180° angle.
g1: Mildly displaced=Garden II with > 20° posterior tilt or Garden III type fracture. Severely displaced=Garden type IV FNF.
g2: Fully reduced = Non-displaced in anteroposterior (AP) view, < 10° posterior tilt (PT). Partly/not reduced = Non-displaced in AP view, ≥ 10° PT or displaced in AP view.
g3: Implant protrusion into the joint (evaluated by eye).
g4: Cortical thickness index (CTI) measured as the part of the diameter of the femoral shaft that consisted of cortex measured 10 cm below the tip of the trochanter minor.
g5: Angle of implants to the lateral cortex of the femoral shaft in anteroposterior view.
h1: Alcohol abuse = self-admitted chronic alcohol abuse (> 40 units per week) or documented evidence of complications of long-term abuse (such as Korsakoff's Syndrome or alcoholic liver disease).
i1: Adequate fixation is a Gardens angle within 170-179°, a lateral Gardens angle not exceeding 20° and a Western infirmary Glasgow angle within 140-149°.
j1: Anatomic cortical apposition with smooth inferior cortex apposition vs positive cortical apposition obtained calcar support. The proximal head-neck fragment is slightly superiorly displaced intentionally (less than one cortex thickness or 4 mm) to the distal fragment, so that the inferior cortex of the proximal head-neck fragment can be buttressed by the calcar cortex of the distal neck fragment.

Table 2. Quality of evidence using the GRADE approach*

Predictor	Risk of bias	Inconsis-tency	Impreci-sion	Indirect-ness	Publication bias	Certainty of estimates
Gender	Moderate	High	Moderate	High	High	High
Smoking	Moderate	High	Moderate	High	High	High
Alcohol abuse	Moderate	Low	Low	High	High	Moderate
Fracture reduction	Moderate	High	High	High	High	High
Bone quality	Low	Low	Low	Moderate	High	Moderate
Cannulated screws vs Fixed angle devices	Moderate	Low	Moderate	High	High	Moderate
Age (>50y, <50y)	Moderate	Moderate	High	High	High	High
Screw/implant position	Low	Very low	Moderate	High	High	Moderate
Posterior wall disruption	Very low	NA	Low	High	NA	Low
ASA classification	Very low	NA	Very low	High	NA	Very low
Mechanism of injury	Very low	NA	Very low	High	NA	Very low
Diabetes	Very low	NA	Very low	High	NA	Very low
End stage renal disease	Very low	NA	Very low	High	NA	Very low
Steroid use	Very low	NA	Very low	High	NA	Very low
Weight bearing status	Very low	NA	Very low	High	NA	Very low
Overall operation technique	Very low	NA	Low	Moderate	NA	Low
Tip Apex Distance	Very low	NA	Very low	High	NA	Very low
DHS vs DHHS	Very low	NA	Very low	High	NA	Very low
Time to surgery	Low	NA	Low	High	NA	Low
Displacement	Low	NA	Moderate	High	NA	Low
Protrusion of an implant	Low	NA	Low	High	NA	Low
Angulation of implant	Low	NA	Low	High	NA	Low
Closed or open reduction	Very low	NA	Low	High	NA	Low
Non-anatomic cortical buttress reduction technique	Very low	NA	Very low	High	NA	Very low

***Certainty in the estimates was graded as previously described by Foroutan et al.**[22]**:**
High: We are very confident that the variation in risk associated with the prognostic factor (probability of future events in those with/without the prognostic factor) lies close to that of the estimate.
Moderate: We are moderately confident that the variation in risk associated with the prognostic factor (probability of future events in those with/without the prognostic factor) is likely to be close to the estimate, but there is a possibility that it is substantially different.
Low: Our certainty in the estimate is limited: the variation in risk associated with the prognostic factor (probability of future events in those with/without the prognostic factor) may be substantially different from the estimate.
Very low: We have very little certainty in the estimate: the variation in risk associated with the prognostic factor (probability of future events in those with/without the prognostic factor) is likely to be substantially different from the estimate.
NA: Not assessed because evaluated in just one study.

Also in some studies the potential predicators were poorly defined. No publication bias was found by the visual distribution of funnel plots (supplementary material 3).

Overall, the quality of evidence for the prognostic factors included in de meta-analysis were assessed as moderate to high (Table 2). The prognostic factors that were evaluated in one study were rated low to very low. For predictors evaluated by only one study inconsistency and publication bias could not be assessed. We are certain of the study population and outcome were comparable between studies due to our strict eligibly criteria so indirectness was rated high for almost all predictors.

Predictors for reoperation after fixation of dFNF

Twenty-four predictors for treatment failure (reoperation) were identified and analysed, 16 of which were evaluated in just one study (supplementary material 4). Definitions of the predictors in the individual studies are shown in Table 1. We were able to pool the data of 7 predictors in a meta-analysis. Regarding the patient characteristics, higher risk of reoperation was found for female patients compared to male patients (OR 1.78, 95% CI 1.26–2.52; Figure 2), for age >50 years compared to age ≤50 years (OR 3.64, 95% CI 1.68–7.91; Figure 3), and for smoking compared to no smoking (OR 2.27, 95% CI 1.12–4.62; Figure 4). Alcohol abuse (Figure 5) and bone quality (Figure 6) were not found to be statistically significant risk factors for re-operation. Regarding treatment-related factors, higher risk of reoperation was found for inadequate fracture reduction (OR 2.28, 95% CI 1.62–3.22; Figure 7), and for cannulated screws (CS) or pins compared to fixed angle devices (OR 2.16, 95% CI 1.03–4.54; Figure 8).

For the predictors bone quality and type of implant there was moderate statistical heterogeneity, respectively 32 and 46%. For bone quality, the heterogeneity seemed mainly due to the definition of good and lesser bone quality, which differed in all three studies (Table 1).[20,26,32] Therefore no sensitivity analysis was performed. Considering the predictor 'type of implant', heterogeneity may have been caused by the fact that all studies used slightly different CS and fixed angle devices.[28,30,34,37] Only Kalland used cannulated pins instead of CS as intervention technique.[30] If Kalland was left out of the analysis, the statistical heterogeneity decreased from 46 to 37% and the OR of CS versus fixed angle devices increased to 2.84 (95% CI 1.21–6.66).

Fifteen predictors were investigated in only one study and one predictor (adequate position of the implant) was evaluated in two studies that could not be combined due to heterogeneity of the implant material. Four of these sixteen predictors were statistically significant in the individual studies: presence of posterior wall disruption (OR 4.50; 95% CI 1.84–10.98)[29], adequate overall operation technique (OR 4.17; 95% CI 1.61–10.81)[27], displacement of the femoral head (OR 2.77; 95% CI 1.83–4.22)[32], angulation of the CS to the lateral cortex (OR

2.37; 95% CI 1.04–5.42)[32] (supplementary material 4). In the study by Camperfeldt et al. no association with reoperation was found for ASA classification and mechanism of trauma.[26] In the study by Gardner reoperation was not associated with diabetes, end-stage renal disease, steroid use and weight-bearing status.[37] In the study by Nyholm no association with reoperation was found for time to surgery and protrusion of the implant.[32] Reoperation was also not related to the tip-apex distance[20], closed reduction[38], and non-anatomic cortical buttress reduction[36]. Marchand et al. did not find any difference in reoperation between two fixed angle devices (the dynamic hip screw (DHS) and the dynamic helical hip system (DHHS)).[39] Adequate position of the implant was no statistically significant predictor in the studies by Camperfeldt and Heetveld.[26,27]

Study or Subgroup	Female Events	Female Total	Male Events	Male Total	Weight	Odds Ratio M-H, Random, 95% CI
Campenfeldt 2018	18	61	15	59	18.7%	1.23 [0.55, 2.74]
Gardner 2014	11	31	8	38	10.5%	2.06 [0.71, 6.03]
Kalsbeek 2018	9	49	5	57	8.9%	2.34 [0.73, 7.53]
Nyholm 2020	84	237	40	176	61.9%	1.87 [1.20, 2.90]
Total (95% CI)		**378**		**330**	**100.0%**	**1.78 [1.26, 2.52]**
Total events	122		68			

Heterogeneity: Tau² = 0.00; Chi² = 1.15, df = 3 (P = 0.77); I² = 0%
Test for overall effect: Z = 3.25 (P = 0.001)

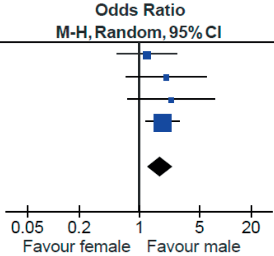

Figure 2. Forest plot of the comparison of female versus male.

Study or Subgroup	>50 years Events	>50 years Total	≤50 years Events	≤50 years Total	Weight	Odds Ratio M-H, Random, 95% CI
Campenfeldt 2018	31	101	2	19	25.9%	3.76 [0.82, 17.30]
Kenan 2015	4	14	0	17	6.6%	15.00 [0.73, 307.45]
Nyholm 2020	119	484	5	53	67.5%	3.13 [1.22, 8.04]
Total (95% CI)		**599**		**89**	**100.0%**	**3.64 [1.68, 7.91]**
Total events	154		7			

Heterogeneity: Tau² = 0.00; Chi² = 0.95, df = 2 (P = 0.62); I² = 0%
Test for overall effect: Z = 3.26 (P = 0.001)

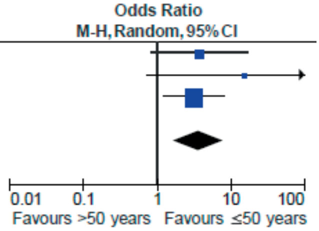

Figure 3. Forest plot of the comparison of age >50 years old versus ≤50 years old.

Study or Subgroup	Smoking Events	Smoking Total	Non smoking Events	Non smoking Total	Weight	Odds Ratio M-H, Random, 95% CI
Campenfeldt 2018	16	45	17	75	75.8%	1.88 [0.83, 4.25]
Gardner 2014	5	9	14	60	24.2%	4.11 [0.97, 17.41]
Total (95% CI)		**54**		**135**	**100.0%**	**2.27 [1.12, 4.62]**
Total events	21		31			

Heterogeneity: Tau² = 0.00; Chi² = 0.85, df = 1 (P = 0.36); I² = 0%
Test for overall effect: Z = 2.27 (P = 0.02)

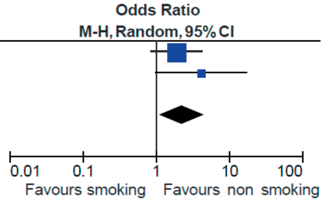

Figure 4. Forest plot of the comparison of smoking versus non-smoking.

Study or Subgroup	Alcohol abuse Events	Alcohol abuse Total	No alcohol abuse Events	No alcohol abuse Total	Weight	Odds Ratio M-H, Random, 95% CI
Campenfeldt 2018	14	32	19	86	70.2%	2.74 [1.16, 6.51]
Gardner 2014	0	4	19	64	11.7%	0.26 [0.01, 5.05]
Stearns 2009	3	28	1	31	18.1%	3.60 [0.35, 36.80]
Total (95% CI)		**64**		**181**	**100.0%**	**2.18 [0.75, 6.35]**
Total events	17		39			

Heterogeneity: Tau² = 0.23; Chi² = 2.45, df = 2 (P = 0.29); I² = 18%
Test for overall effect: Z = 1.44 (P = 0.15)

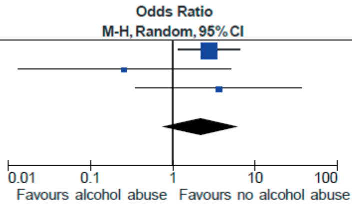

Figure 5. Forest plot of the comparison of alcohol abuse versus no alcohol abuse.

Study or Subgroup	Lesser bone quality Events	Lesser bone quality Total	Good bone quality Events	Good bone quality Total	Weight	Odds Ratio M-H, Random, 95% CI
Campenfeldt 2018	25	80	2	23	10.6%	4.77 [1.04, 21.94]
Heetveld 2005	16	38	29	73	29.9%	1.10 [0.50, 2.45]
Nyholm 2020	62	249	56	275	59.5%	1.30 [0.86, 1.96]
Total (95% CI)		**367**		**371**	**100.0%**	**1.42 [0.84, 2.41]**
Total events	103		87			

Heterogeneity: Tau² = 0.08; Chi² = 2.95, df = 2 (P = 0.23); I² = 32%
Test for overall effect: Z = 1.30 (P = 0.19)

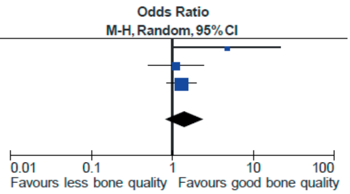

Figure 6. Forest plot of the comparison of good bone quality versus lesser bone quality.

Study or Subgroup	No adequate reduction Events	No adequate reduction Total	Adequate reduction Events	Adequate reduction Total	Weight	Odds Ratio M-H, Random, 95% CI
Campenfeldt 2018	10	26	23	94	14.1%	1.93 [0.77, 4.84]
Gardner 2014	15	43	2	20	4.7%	4.82 [0.98, 23.64]
Heetveld 2006	16	26	23	76	13.8%	3.69 [1.46, 9.34]
Kalsbeek 2018	2	13	12	93	4.5%	1.23 [0.24, 6.23]
Nyholm 2020	91	329	33	207	60.6%	2.02 [1.29, 3.14]
van Dortmont 2000	2	5	2	23	2.2%	7.00 [0.70, 70.05]
Total (95% CI)		**442**		**513**	**100.0%**	**2.28 [1.62, 3.22]**
Total events	136		95			

Heterogeneity: Tau² = 0.00; Chi² = 3.77, df = 5 (P = 0.58); I² = 0%
Test for overall effect: Z = 4.68 (P < 0.00001)

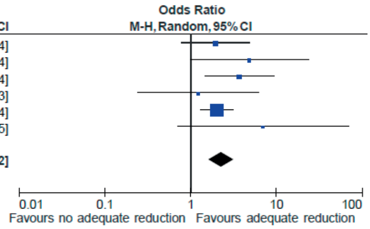

Figure 7. Forest plot of the comparison of adequate reduction versus no adequate reduction of the femoral neck fracture.

Study or Subgroup	CS(pins) Events	CS(pins) Total	FA devices Events	FA devices Total	Weight	Odds Ratio M-H, Random, 95% CI
Gardner 2014	9	29	10	40	25.8%	1.35 [0.47, 3.91]
Hoshino 2016	9	15	10	48	21.6%	5.70 [1.64, 19.81]
Kalland 2019	12	54	12	60	30.3%	1.14 [0.46, 2.81]
Thein 2014	16	47	4	31	22.3%	3.48 [1.04, 11.70]
Total (95% CI)		**145**		**179**	**100.0%**	**2.16 [1.03, 4.54]**
Total events	46		36			

Heterogeneity: Tau² = 0.26; Chi² = 5.53, df = 3 (P = 0.14); I² = 46%
Test for overall effect: Z = 2.04 (P = 0.04)

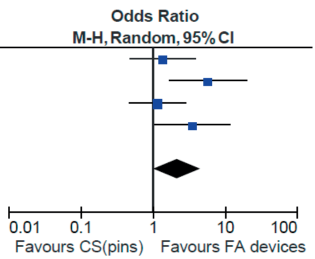

Figure 8. Forest plot of the comparison of cannulated screws (CS) or pins versus a fixed angle

DISCUSSION

In this systematic review and meta-analysis we identified predictors for failure of treatment with IF for dFNF. The results of the meta-analysis show five risk factors for reoperation: female gender, age >50 years, smoking, inadequate fracture reduction, fixation with cannulated screws or pins. Another four predictors were identified in single studies: presence of posterior wall disruption, adequate overall operation technique, displacement of the femoral head, and angulation of the CS to the lateral cortex.

Four articles were included in our meta-analysis that investigated the effect of gender on treatment failure (Figure 2).[19,26,32,37] We found that female patients appear to have a higher risk to be reoperated than men (OR 1.78, 95% CI 1.26–2.52). This might be explained because the femoral neck shaft angle is lower in women compared to men.[40] This results in a larger moment arm which leads to more downward force on the collum femoris. In theory, this could lead to an earlier cut-out. Yet, other authors deny the existence of this anatomic difference between men and women.[41] Another explanation could be that bone quality in postmenopausal women is inferior compared to men.[42] However, the three studies in our meta-analysis for bone quality did not show an effect of bone quality on the failure rate (Figure 6).[20,26,32] Age was also identified as a predictor for reoperation (OR 3.64, 95% CI 1.68–7.91). In this meta-analysis we used 50 years of age as a cut-off point because then we could combine the results of three studies. With increasing age bone quality declines and the incidence of other comorbidities rises.[42] In literature the cut-off point for age for fixating dFNF with IF usually lies between 60–70 years old.[8,9] We believe there is not an exact age above which arthroplasty can be advised as age is just one of many factors that is affect the reoperation rate of patients with dFNF treated with IF.

Two studies investigated smoking as a predictor for reoperation.[26,37] Although the association was not statistically significant in these individual studies, smoking became a statistically significant predictor of treatment failure after we combined the data of these studies. Smoking causes peripheral artery disease.[43] Thus, smoking may compromise the vascularisation of the femoral neck and head, which we believe to be one of the most important factors for union and viability of the femoral head. Also smoking is associated with slower healing and non-union of fractures.[44]

Fracture reduction was one of the most investigated predictors in this review.[19,26,27,32,35,37] All studies accepted fracture reduction with a maximum malalignment of around 10–20 degrees in the anteriorposterior plane and 10 degrees in the lateral plane. Combining the results of these studies in our meta-analysis showed a statistically significant association between an inadequate reduction and reoperation. An adequate reduction in combination with stable fixation will provide the most optimal conditions for (re)vascularisation of the femoral head.

It could be that CS provide less stability after adequate reduction. Earlier biomechanical and cadaver studies support the finding that fixed-angle devices are superior to CS in stabilizing FNF.[45,46] The results of four studies comparing CS or pins with a fixed-angle device are in line with those findings.[28,30,34,37] The meta-analysis of these four studies showed a favourable outcome for the fixed angle devices, which may provide better stability.

Besides type of implant the adequate placement of the implant is also important. Two studies investigated placement of implants[26,27], but were not combined in a meta-analysis due to differences in study design. Both studies investigated the placement of CS, yet Campenfeldt investigated fixation with 2 CS and Heetveld with 3 CS. Also, both studies used different definitions of adequate screw placement (Table 1). Furthermore, Heetveld also looked at the placement of the sliding hip screw and its relation to reoperation. The data of CS and the sliding hip screw in this study was combined. Despite these differences, implant positioning in both studies did not affect the reoperation rate. Another recently published study also showed that the position of a sliding hip screw in the femur does not influence the revision rate.[47] The position of three cannulated screws on the other hand does affect the revision rate of FNF according to Schottel et al.[47]

We found a significant association between initial angle of the CS to the lateral cortex using the data of Nyholm.[32] Although Nyholm et al. also found a similar result in their univariable Cox regression analysis, the association was no longer statistically significant in their multivariable analysis. We could not find any literature that substantiates the supposed association between the angulation of CS to the latter cortex.

One study stated that the overall operation technique is also of significant influence on the outcome of treatment of dFNF and should therefore not be delegated to inexperienced surgeons.[27] The results in that study are difficult reproduce due to a complex and extensive definition of a good overall operation technique (Table 1). Although these results are difficult to compare with other literature, the importance of adequate reduction and placement of the implant essential for proper stability and therefore a successful treatment.[48-50]

Presence of posterior wall disruption was identified as a predictor of revision surgery in a study by Huang et al.[29] Due to posterior comminution, a disrupted posterior cortex will remain after reduction, which could lead to more instability.[51,52] Some authors even advocate the use of a fibular graft to buttress the posterior cortex.[53]

Nyholm stated that severe displacement of the femoral head (Garden type IV) is also associated with a higher reoperation rate.[32] In another, slightly older study, the 4-grade Garden system did not predict an unfavorable outcome (defined as change of position of the screws, collapse of the fracture by more than 20 mm, perforation of the femoral head by screw(s), or salvage with arthroplasty).[54] We could not find other studies that compared the reoperation rate of Garden type III and IV FNF.

Conclusion

In conclusion, our systematic review and meta-analysis identified female gender, age above 50 years old, smoking, inadequate fracture reduction and treatment with cannulated screws as predictors for reoperation of patients with dFNF treated with IF. Female patients with a dFNF above 50 years of age that smoke have a high risk of failure of treatment. Furthermore if a dFNF cannot be properly repositioned the surgeon might consider to convert to an arthroplasty at a low threshold and if the dFNF is adequately repositioned it should preferably be fixated with a fixed angle device. This study can help surgeons to choose the preferred treatment for patients with a dFNF and substantiate future treatment algorithms and guidelines for treatment of FNF.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi: 10.1016/j.injury.2022.11.042 .

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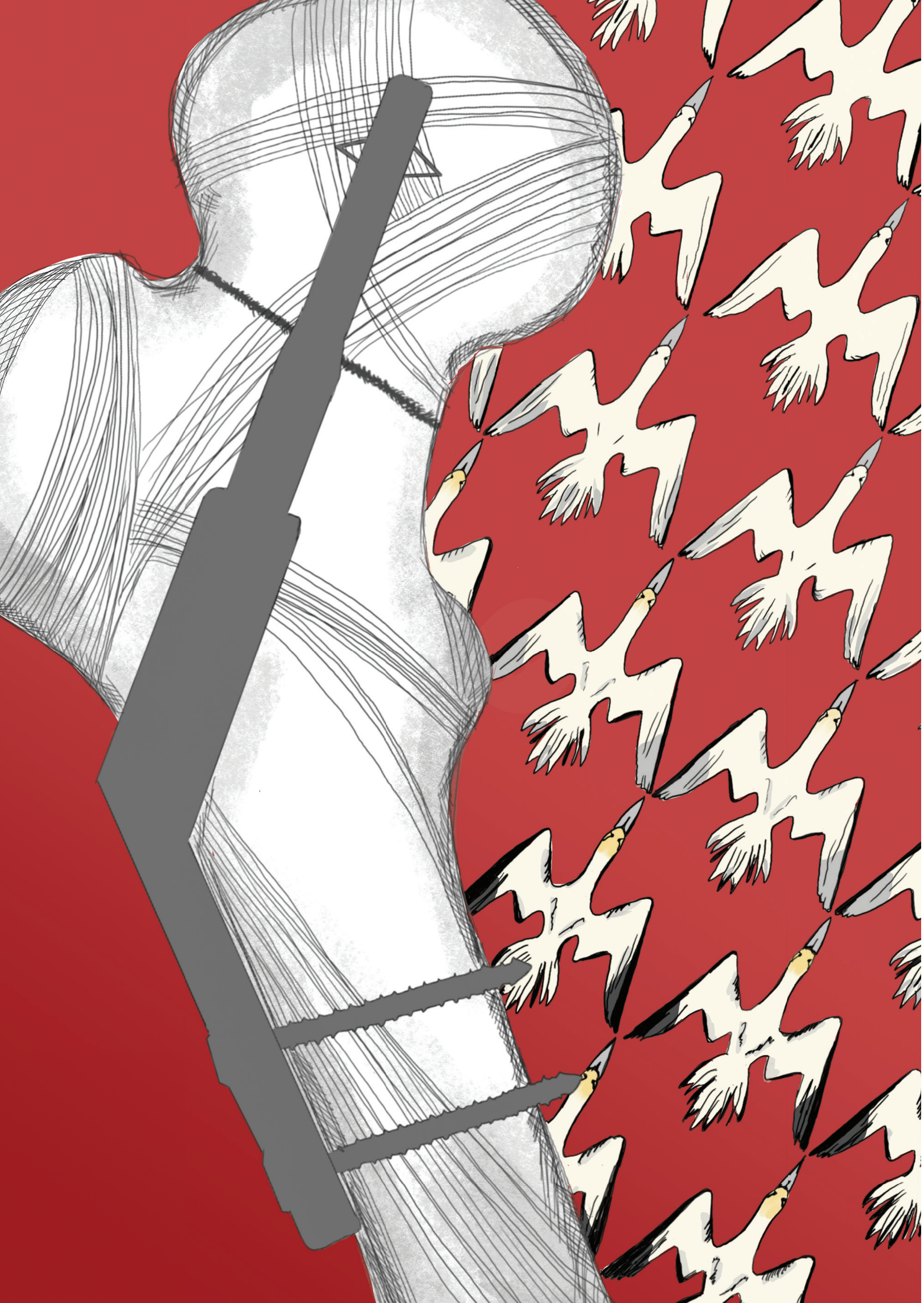

Chapter 3

More than 20° posterior tilt of the femoral head in undisplaced femoral neck fractures results in a four times higher risk of treatment failure

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ABSTRACT

Purpose

In this study, we aimed to determine the correlation between the preoperative posterior tilt of the femoral head and treatment failure in patients with a Garden type I & II femoral neck fracture (FNF) treated with the Dynamic Locking Blade Plate (DLBP).

Methods

Preoperative posterior tilt was measured in a prospective documented cohort of 193 patients with a Garden type I and II FNF treated with the DLBP. The correlation between preoperative posterior tilt and failure, defined as revision surgery because of avascular necrosis, non-union, or cut-out, was analyzed.

Results

Patients with failed fracture treatment (5.5%) had a higher degree of posterior tilt on the initial radiograph than the patients with uneventful healed fractures: 21.4° and 13.8°, respectively (p=0.03). The failure rate was 3.2% for Garden type I & II FNF with a posterior tilt <20° and 12.5% if the preoperative posterior tilt was ≥20°. A posterior tilt of ≥20° was associated with an odds ratio of 4.24 (95% CI, 1.09–16.83; p = 0.04).

Conclusion

Garden type I & II FNFs with a significant preoperative posterior tilt (≥20°) seem to behave like unstable fractures and have a four times higher risk of failure. Preoperative posterior tilt ≥20° of the femoral head should be considered as a significant predictor for failure of treatment in Garden type I & II FNFs treated with the DLBP.

INTRODUCTION

The Garden classification is most commonly used to describe displacement of femoral neck fractures (FNF).[1] Garden types I & II are relatively undisplaced or stable FNFs whereas Garden types III & IV are displaced or unstable fractures. This classification is based solely on the review of anteroposterior (AP) radiographs.[2] The preoperative tilt of the femoral head in the anterior and posterior directions is not included in this classification. A posterior tilt may be of consequence for the stability of the fracture. Most of the studies describing the clinical relevance of a posterior tilt show that it influences the outcome of treatment, with osteosynthesis of undisplaced FNFs.[3-9] However, the correlation between posterior tilt and treatment failure is not always clear and undisputed.[10,11] Several researchers have used 20° as the cut-off point above which posterior tilt is assumed to be relevant to the clinical outcome; however, this value is only founded by a few authors.[4,7,9] Most fixations used in these studies concerned cannulated screws or sliding hip screws. Little is known about the influence of posterior tilt when other implants are used. The Dynamic Locking Blade Plate (DLBP) is a relatively new implant with demonstrated increased fracture-implant construct stability. It has been used for fixation of displaced and undisplaced FNFs since 2010.[12-14]

In this study, we aimed to determine the correlation between the preoperative posterior tilt of the femoral head and the treatment failure rate in patients with a Garden type I & II FNF treated with the DLBP.

PATIENTS AND METHODS

Set up

Five hospitals in the Netherlands that all used the Dynamic Locking Blade Plate (DLBP, Baat Medical, Hengelo, Netherlands) as a standard of care for fixation of FNFs prospectively collected data on patients with hip fractures who had been treated with the DLBP. Patients in these hospitals were treated according to “the Dutch guideline for the treatment of proximal femoral fractures” with the use of the DLBP for internal fixation for the fracture.[15] These data were retrospectively analyzed.

The measurements and analysis were in line with earlier performed studies within a research program that had been assessed by the Medical Research Ethics Committee (MREC). The MREC concluded that the studies do not meet the criteria to be evaluated by a MREC and can consequently be performed without official MREC approval.

Patients

All patients with a FNF who were treated between January 8, 2010 and January 1, 2015 with the Dynamic Locking Blade Plate were identified. Patients with a Garden I or II FNF were included for further analysis. Patients with pathological fractures, concomitant fractures of the lower extremity, symptomatic arthritis, local infection or inflammation, open fractures, morbid obesity classified as a body mass index of ≥35 kg/m^2, and a mental or neurological disorder that could impair successful healing of the fracture were excluded.

Data acquisition and outcome

The data on the following were collected by the treating trauma surgeons: Sex, age, 4-grade Garden classification, time to surgery, operation time, pre-reduction posterior tilt, quality of reduction (an angle between 155–180° on the anteroposterior (AP) and lateral X-rays was considered to be a good reduction)[16] and tip-apex distance (TAD).[17] The mean follow up was 1 year and the range for follow up was also 1 year. Appointments for follow up and postoperative X-rays were made directly postoperatively, at 6 weeks, 3 months, 6 months, and 1 year or until the primary endpoint was reached. The primary outcome was failed treatment in terms of avascular necrosis of the femoral head (AVN), non-union, implant cut-out, with the need for revision surgery. Non-union was defined as persistent pain in the hip or inability to bear weight in combination with a visible fracture line or absence of cortical bridging or bridging trabeculae over the fracture site on the AP and lateral radiographs at least 4 months postoperative, which led to revision surgery.

Avascular necrosis was defined as persistent pain in the hip or inability to bear weight in combination with at least stage 2 AVN according to the Steinberg classification.[18] The Steinberg classification uses the AP and lateral radiographs to assess AVN wherein stage 2 is defined as an abnormal radiograph which shows “cystic” and sclerotic changes in the femoral head. Cut-out of the implant was defined as breakage or cut-out of the blade, plate, or screws; inadequate expansion/malfunction of the anchors; or any malfunction of the implant that led to revision surgery.

Fracture classification and posterior tilt measurement

For the X-rays patients were positioned in supine position, the contralateral leg positioned with both hip and knee in 90° flexion. If needed the foot was supported. The injured leg was positioned in its natural position with slight exorotation of the foot. The X-ray generator was positioned horizontally perpendicular to the detector, and the detector was positioned parallel to the femoral neck at the lateral side of the pelvis. Fractures were classified as Garden type I & II or Garden type III & IV by the treating surgeon and re-classified by the first author (JHK) to avoid single observer bias. In case of any discrepancy in the classification or measurement between the first author and the treating surgeon, the case was reviewed and discussed with the second author (ADPW). In all Garden type I & II fractures, the preopera-

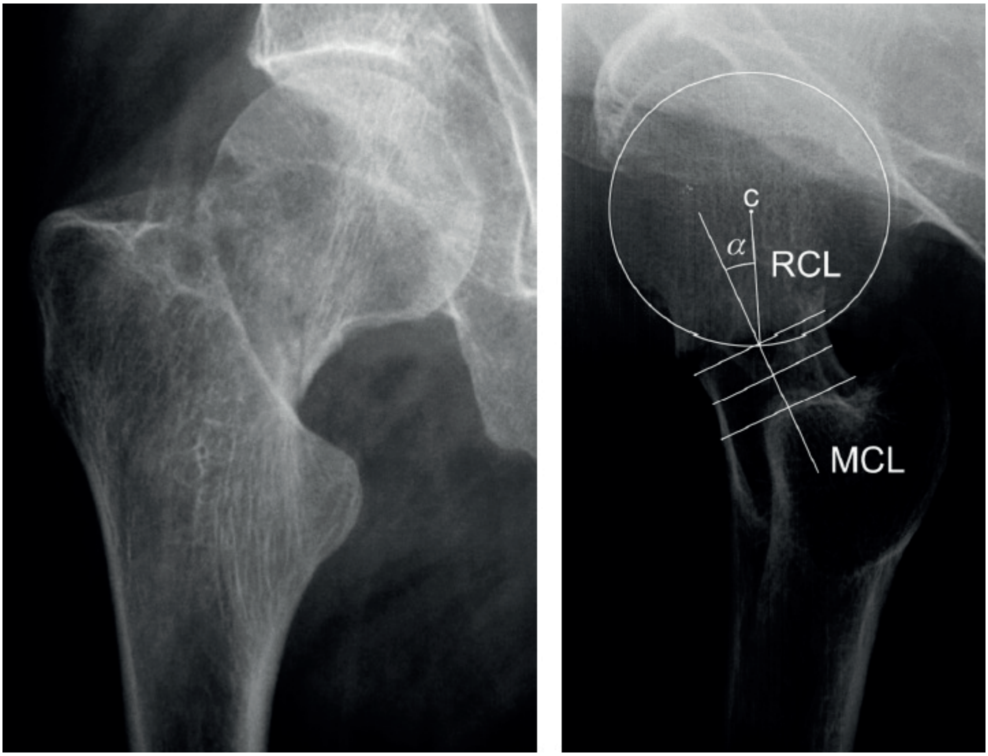

Figure 1. The posterior tilt measurement (PTM) according to Palm[4] is the angle (α) between the mid-collum line (MCL) and the radius collum line (RCL).

tive posterior tilt on the lateral view was measured by the first author (JHK) according to the Posterior Tilt Measurement (PTM).[4] The degree of posterior tilt of the femoral head was determined by the angle between two lines, the mid-collum line (MCL) and the radius collum line (RCL) (Figure 1). The middle of the femoral neck was determined by drawing three perpendicular lines across the narrowest part of the collum, with 5 mm between each line. The RCL was drawn from the middle of the femoral head to the intersection of the MCL and the caput circle.[4]

Surgical treatment

Reduction was performed using a closed technique for all the fractures. The FNFs of all included patients were fixated with the DLBP. The DLBP is a barreled side-plate combined with a cannulated locking blade (Figure 2).[13,14] Perioperative care was given according to the local hospital protocols, including pre-operative antibiotic prophylaxis, direct full–weight-bearing of the operated hip after surgery according to patients' pain perception and functional capacities, and antithrombotic prophylaxis.

Figure 2. Dynamic Locking Blade Plate.

Statistics

Statistical analysis was performed with SPSS v. 2 software (IBM Corp., Armonk, New York) for Windows 7 (Microsoft, Redmond, Washington). Baseline characteristics are displayed as mean with SD or median range for continuous variables. Categorical variables are displayed as numbers with corresponding percentages. Differences in baseline characteristics between healed and failed fractures were tested with an independent *t*-test or Mann-Whitney U test depending on the distribution of the continuous data. For categorical data, the chi-square test was used. Several cut-off points for posterior tilt that are highly associated with failure are described in literature.[4,5,7] To find a cut-off point with the highest clinical relevance, the data were also classified in groups with a posterior tilt either less than or greater than/equal to 10°, 15°, 20°, and 25°. To test the association between dichotomized posterior tilt and failure, a univariate logistic regression analysis was performed. Potential confounders from Table 1 that were associated with posterior tilt and with failure ($p<0.15$) were taken into account in the multivariate logistic regression analyses. P-values less than or equal to 0.05 were considered to be statistically significant.

RESULTS

Patients

There were 456 patients with a hip fracture who were treated with DLBP. The flowchart is shown in Figure 3. In 46 of the 456 cases there was discrepancy between the initial and second classification. Consensus was reached in all of the cases after review by a third party [ADPW].

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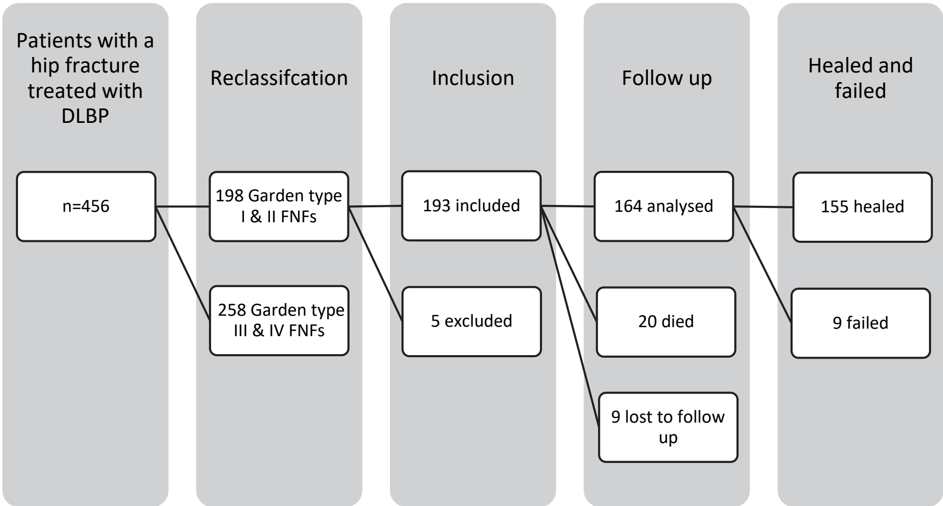

Figure 3. Flowchart of patient inclusion and follow up. DLBP, Dynamic Locking Blade Plate; FNF, femoral neck fracture.

Of the 456 patients, 198 had Garden type I & II and 258 Garden type III & IV FNFs. Two patients with a Garden type I & II FNF had concomitant fractures of the lower extremity, and three patients had a mental and/or neurologic disorder. In this study, 193 patients were included for analysis. Twenty of these patients died during follow up. None of these patients died as a result of the operation or a related complication. Eight patients were lost to follow up (moved abroad or had follow up in hospitals not participating in this study), and for one patient, no preoperative X-rays could be obtained.

The mean age of the 164 patients with a Garden type I & II FNF was 68.5 years (range 35–101) and 61.6% were female. The time (or delay) until operation was registered as either within 24 h or after 24 h. Of the 164 patients, 21% (n=36) were not treated within 24 h. There was no statistical difference between the healed and failed group in terms of delay to surgery.

Failure of treatment

In total, the treatment failed in nine of the 164 patients (5.5%). These nine patients all needed revision surgery. Three patients had AVN diagnosed on X-ray, two patients had non-union of the fracture, one patient had non-union with clinical suspicion for AVN but not seen on the X-ray, and three patients had cut-out of the implant. In 12 patients the femoral head had not been properly reduced and posterior tilt persisted. Treatment failed in two of these patients.

Posterior tilt of the femoral head

Table 1 shows the demographics of the patient groups with healed fractures versus failed fractures. The mean posterior tilt was 14.2° (SD=10.6). Patients with failed fracture treatment had more posterior tilt on the initial radiograph than the patients with healed fractures, 21.4° versus 13.8° (p=0.03). Failure of treatment tended to be associated with an older age, a greater TAD, and malreduction, but the associations were not statistically significant.

Table 1. Demographics and outcome measurements for healed versus failed fractures

	Healed FNF n=155	Failed FNF treatment n=9	p-value
Mean age in years (SD)	68.3 (14.2)	73.7 (9.3)	0.13
Female, n (%)	94 (60.6)	7 (77.8)	0.48
Mean TAD in millimeters (SD)	21.0 (6.4)	24.2 (7.7)	0.15
Malreduction, n (%)	10 (6.5)	2 (22.2)	0.13
Mean PTM in degrees (SD)	13.8 (10.4)	21.4 (11.1)	0.03
Operation time in minutes (SD)	42 (18.4)	46 (19.1)	0.49

FNF, femoral neck fracture; *SD*, standard deviation; *TAD,* tip-apex distance; *PTM,* posterior tilt measurement.

After classification into groups with the posterior tilt of the femoral head less than or greater than/equal to 10°, 15°, 20°, and 25°, no differences were found between the patients with healed and failed fractures in the groups 10°, 15°, and 25° (Table 2). If posterior tilt angles were divided into <20°and ≥20° groups, we did find statistically significant differences between these groups, as shown in Table 3 (p=0.04).

Table 2. Odds ratios of dichotomized PTM into groups < and ≥ than 10°, 15°, 20° and 25° posterior tilt of the femoral head related to healed and failed fractures

Group	Odds ratio	p-value	95% confidence interval
PTM > 10°	5.9	0.08	0.72–48.60
PTM > 15°	3.5	0.08	0.85–14.69
PTM > 20°	4.2	0.04	1.09–16.83
PTM > 25°	3.8	0.09	0.88–16.56

PTM, posterior tilt measurement.

Posterior tilt of ≥20° was associated with an OR of 4.24 (95% CI, 1.09–16.83; p=0.04). No differences were found between patients with a posterior tilt <20° and ≥20° in terms of gender (p=0.20), TAD (p=0.37), and malreduction (p=0.73). Patients with a posterior tilt ≥20° were on average 5.4 years younger (mean <20° = 69.9, mean ≥20° = 64.5) than patients with a posterior tilt <20° (p=0.033). If we corrected the odds ratio (OR) of the posterior tilt angle ≥20° for age, the OR increased to 5.36 (95% CI, 1.30–22.11; p=0.02).

Table 3. Crosstab of dichotomized PTM into <20° and ≥20° posterior tilt of the femoral head related to healed and failed fractures

	Healed FNF	Failed FNF treatment	Total
PTM ≥20°	35 (87.5%)	5 (12.5%)	40
PTM <20°	120 (96.8%)	4 (3.2%)	124
Total	155 (94.5%)	9 (5.5%)	164

PTM, posterior tilt measurement; *FNF*, femoral neck fracture. Odds ratio = 4.24 (95% CI, 1.09–16.83; p=0.04).

DISCUSSION

This study aimed to determine the correlation between the preoperative posterior tilt of the femoral head on the initial radiograph and the treatment failure rate in patients with a Garden type I & II FNF after fixation with the Dynamic Locking Blade Plate (DLBP). A larger posterior tilt was associated with treatment failure. A posterior tilt of ≥20° was associated with a four times higher failure rate.

It is well known that the displacement of the femoral head caused by a FNF potentially compromises the vascularization of the femoral head. Most of the blood supply to the femoral head originates from the fragile lateral epiphyseal arteries that originate from the retinacular or subsynovial arteries that form an intracapsular ring in the hip joint.[19] After displacement of the femoral head these vessels can be torn or kinked and this may result in an impaired blood flow, which can be devastating for the vitality of the femoral head. This impaired blood flow may also occur in FNFs with varus angulation on the AP X-ray and posterior tilt on the lateral X-ray. Posterior tilt of the femoral head could result from posterior comminution of the femoral neck (Figure 1), and posterior comminution is associated with non-union and AVN.[20,21] After reduction of the fracture, a gap remains in the posterior cortex, which results in an unstable posterior border despite optimal reduction. In case of insufficient bone stock or inadequate fixation, this posterior instability may lead to an early collapse of the femoral head and treatment failure. This underpins the importance of optimal visualization of the fracture for classification purposes. Subsequently, the lateral X-ray has to be included in the assessment of the fracture and the fracture classification. An FNF with posterior tilt needs to be recognized preoperatively and has to be treated as a fracture that is presumably unstable, even when the AP classification shows a Garden type 1 or 2 fracture.

Several researchers have published articles on the influence of posterior tilt. Alho et al. were the first to describe the correlation between posterior tilt and failure of treatment in 1992.[10] Their study, however, included only 13 undisplaced FNFs, which did not allow for any definitive conclusions. In a retrospective analysis of 375 undisplaced FNFs, Conn and Parker demonstrated an association between a larger posterior tilt and non-union but no association between posterior tilt and AVN.[3] In 2013 Clement et al. concluded that posterior tilt was a significant predictor of fixation failure.[5] Clement et al. defined a posterior tilt as a Lateral Garden Angle (LGA) of <170°. No substantiation was given for the number of degrees. Following these findings in literature, we did an additional analysis in which we categorized our data into a posterior tilt <10° and ≥10°, but this did not demonstrate any significant correlation between posterior tilt and failure in our data. Clement et al. used the LGA to measure posterior tilt of the femoral head. We believe the LGA is a reliable method to measure however it is inferior to the PTM of Palm et al., which has a better interobserver reliability.[22]

Palm et al. showed in a retrospective analysis that a posterior tilt of ≥20° is a significant predicator for failure of non-displaced FNF treated with cannulated screws.[4] Dolatowski et al. also found an increased risk of fixation failure with a hazard ratio (HR) of 2.4 (95% CI, 1.1–5.4); p=0.03) for posterior tilt ≥20° after dichotomization of the angle.[7] In 2019 Dolatowski et al. did another analysis on the influence of posterior tilt. In 111 patients treated with internal fixation, an increased HR of 2.2 for healing-related complications was found (95% CI, 1.2–4.0); p=0.008) in patients with a posterior tilt of ≥20°.[23] In 2019 Sjöholm et al. did a retrospective analysis of 417 patients with an undisplaced FNF and found an HR of 1.5 (95% CI, 1.2–2.0) for posterior tilt ≥20°.[9] They also found an increased risk for failure for anterior tilt of more than 10° (HR 2.9; 95% CI,1.4–6.3). We did not analyze anterior tilt in this cohort because the anterior tilt was not measured in any of the patients.

Sjöholm et al. analyzed the influence of 30° and 40° posterior tilt.[9] Posterior tilt of 30° and 40° show an HR of 3.3 (95% CI, 1.7–6.4) and 7.0 (95% CI, 2.4–21), respectively. We could not find a significant difference in odds ratios for higher or smaller cut-off points of posterior tilt. This was probably because of the small number of failures in our study. Okike et al. did a secondary analysis of 555 patients with a undisplaced FNF treated with internal fixation which showed an HR of 2.2 (95% CI, 1.2–4.0; *p*=0.008) if posterior tilt was higher than 20°.[8] In 2013, Lapidus et al. performed the only large study that contradicted the influence of posterior tilt on failure in Garden type I and II FNF treatment.[11] They measured the posterior tilt in 382 Garden type I and II FNFs. Their results conflict with current literature and the results in our study.

3

Despite varying results, different outcome parameters, different implants, and heterogeneity of study populations, posterior tilt seems to be a predisposing factor for failure in treatment with internal fixation in Garden type I & II FNF. This is confirmed in a recently published systematic review and meta-analysis by Nielsen et al.[24]

The indications for fracture fixation with a DLBP were the same as those for other internal fixation devices such as the dynamic hip screw or cannulated screws, and the hospitals followed the recommendations stated in the Dutch Guideline for treatment of proximal femoral fractures.[15] In this national guideline and the current guideline for treatment of proximal femoral fractures, the lateral X-ray is not included in assessing the characteristics of the fracture and determining the stability and angulation of the FNF.[25]

To analyze the position of the blade of the DLBP in the femoral head we measured the TAD. In our study an increased TAD was not associated with a higher failure rate. We also tested the TAD as a potential confounder. The odds ratio of ≥20° posterior tilt did not significantly change when corrected for the TAD (p = 0.37). A possible explanation for the limited influence of the head load carrier position may be the high stability of the DLBP-blade compared to femoral head screw of other implants used for fixating FNF.[26]

Our results show failure rates of 3.2% for the Garden type I & II FNF with a posterior tilt <20° and 12.5% if the posterior tilt is ≥20°. These numbers are similar to the failure rates that we found for displaced (Garden III and IV) FNFs in patients age 60 and younger treated with the DLBP.[14] It seems that "stable," undisplaced, Garden type I & II FNF with significant posterior tilt (≥20°) in fact behave like unstable fractures. Therefore, despite the use of the original Garden classification for decades, we suggest a modified Garden classification wherein Garden type I & II FNFs with a posterior tilt of <20° are classified as undisplaced fractures and Garden type I & II with posterior tilt of ≥20° and type III & IV as displaced fractures (Figure 4). Palm et al. already included posterior tilt into a new algorithm in 2012, but they also incorporated vertical fractures into the algorithm.[27] We think that vertical fractures

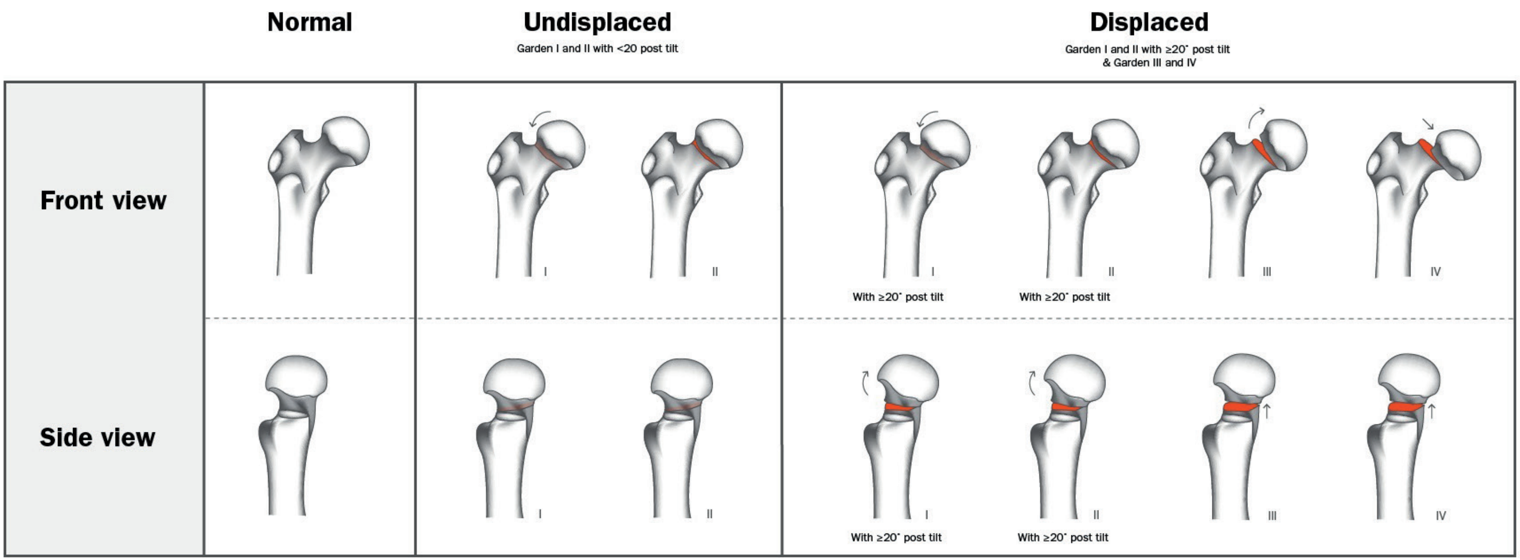

Figure 4. Proposed modified Garden classification of undisplaced and displaced femoral neck fractures, taking into account the amount of initial posterior tilt (displacement).

according to the Pauwels classification should not be incorporated in a treatment algorithm, since the reliability of the Pauwels classification is limited and has low predictive value with regard to outcome.[28,29] However, we do believe the proposed modified Garden classification could influence the treatment strategy that we use today. We expect that the treatment strategy for FNFs in elderly patients with a Garden type I & II fracture will shift from fracture fixation to hip replacement when the posterior tilt of the femoral head is greater than 20°.

A strength of this study is the fact that there was no missing data of patients treated with the DLBP because of the prospective documentation of the outcome parameters. However, this study also has some limitations. The most important one is the small number of patients with failed treatment. A consequence was that we, due to the small numbers after dichotomization, could not find significant differences in odds ratios for higher or smaller cut-off points of posterior tilt. Therefore, we could not assess if posterior tilt <20° also significantly influences the treatment. Another limitation was posed by the inability to perform a multivariate analysis to correct for the case mix of all patient-related parameters. As a result, we could not determine the influence of the specific variables and their relevance, nor could we confirm the association found after univariable analysis of posterior tilt as a predictor of treatment failure. However, after correction for age, one of the probably dominant variables of influence, the OR for failure related to posterior tilt, increased.

CONCLUSION

The results of this study show that posterior tilt of 20° or more was associated with a four times higher failure rate in Garden type I & II FNFs treated with the DLBP. It seems that "stable" undisplaced, Garden type I & II FNF with a significant posterior tilt (≥20°) in fact behave like unstable fractures. Therefore, a preoperative posterior tilt ≥20° of the femoral head should be considered as a significant predictor for failure of treatment in FNF treated with the DLBP. An adapted Garden classification that includes the posterior tilt for Garden type I and II fractures may prove helpful in future choices of treatment and subsequent prevention of failure of treatment with osteosynthesis.

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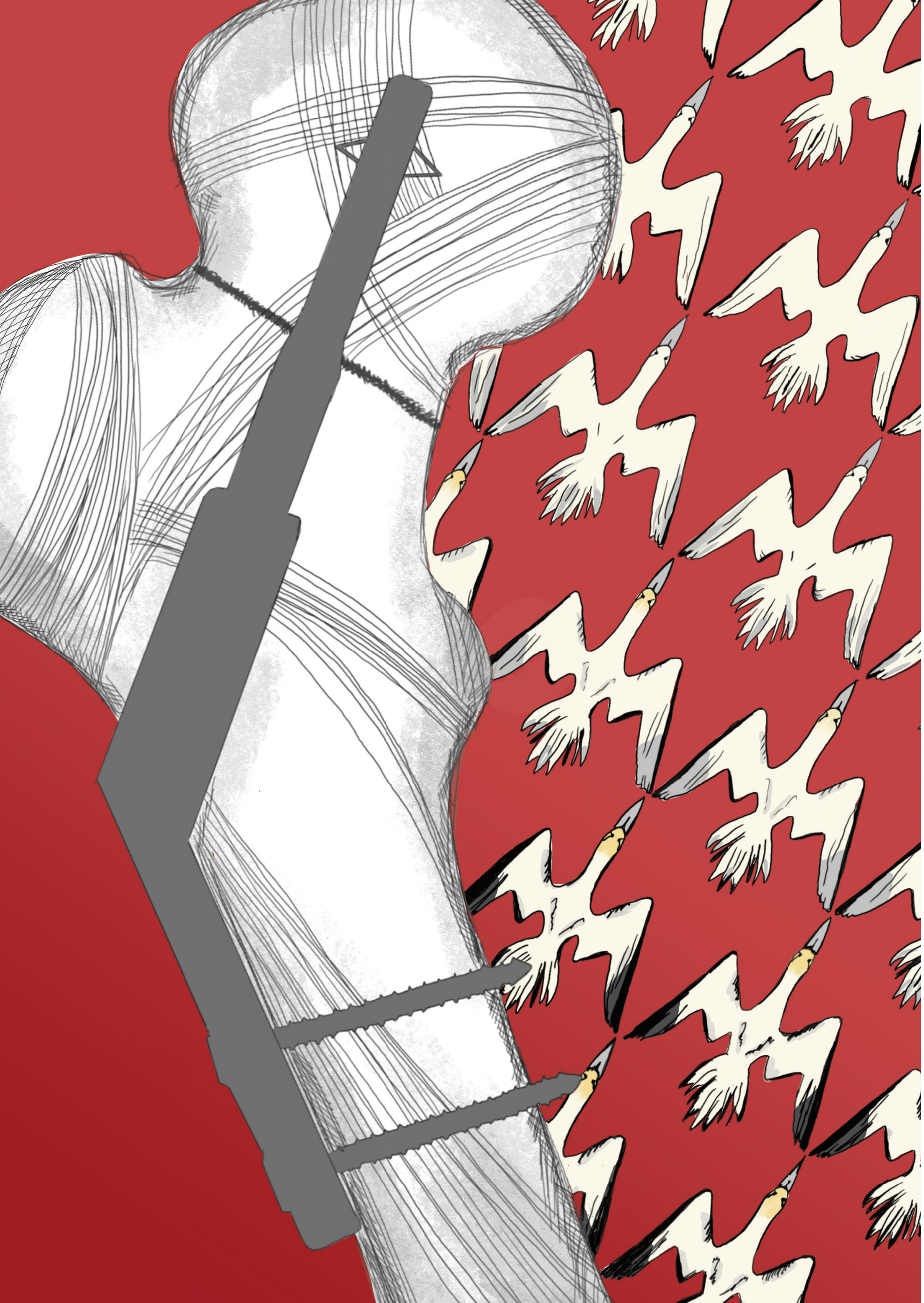

Chapter 4

Validation of two methods to measure posterior tilt in femoral neck fractures

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ABSTRACT

Introduction

Posterior tilt of the femoral head in femoral neck fractures (FNF) may influence stability of the fracture and may therefore affect the treatment outcome. Posterior tilt can be measured with different methods. The Lateral Garden Angle (LGA) has been used for this purpose for decades and more recently the Posterior Tilt Measurement (PTM) was introduced. Despite the fact that both methods (LGA and PTM) are used in multiple studies, they have never been compared for reliability in a direct study. The aim of this study is to analyze the intra and inter observer variability of the LGA described by Garden and the PTM according to Palm.

Methods

Four observers measured the posterior tilt on the radiographs of 50 FNF two times with both methods. Intra and inter observer reliability were determined for the LGA and the PTM.

Results

The intra observer reliability for both methods is substantial with an intra class coefficient of 0.75. The inter observer reliability of the PTM is also substantial with an intra class coefficient of 0.75 compared to a moderate reliability of the LGA with an intraclass coefficient of 0.60.

Conclusion

Based on our results we believe the LGA and the PTM are both reliable methods to measure posterior tilt. Yet the Posterior Tilt Measurement seems to have a better inter observer reliability and therefore has a slight preference over the Lateral Garden Angle.

INTRODUCTION

Posterior tilt, also known as retroversion or anterior angulation of the femoral head, is diagnosed on the lateral radiograph of the hip. If there is displacement in the transverse plane, it often concerns posterior tilt of the femoral head due to the mechanism of the trauma and the anatomy of the hip. FNF are usually classified using the Garden Classification.[1] This classification is solely based upon the AP radiographs. Consequently the tilting of the femoral head in the anterior and posterior direction is not included in this classification.[2] Over the years several authors described the influence of pre-operative posterior tilt on the risk of reoperation rate, avascular necrosis or non-union of femoral neck fractures (FNF).[3-11]

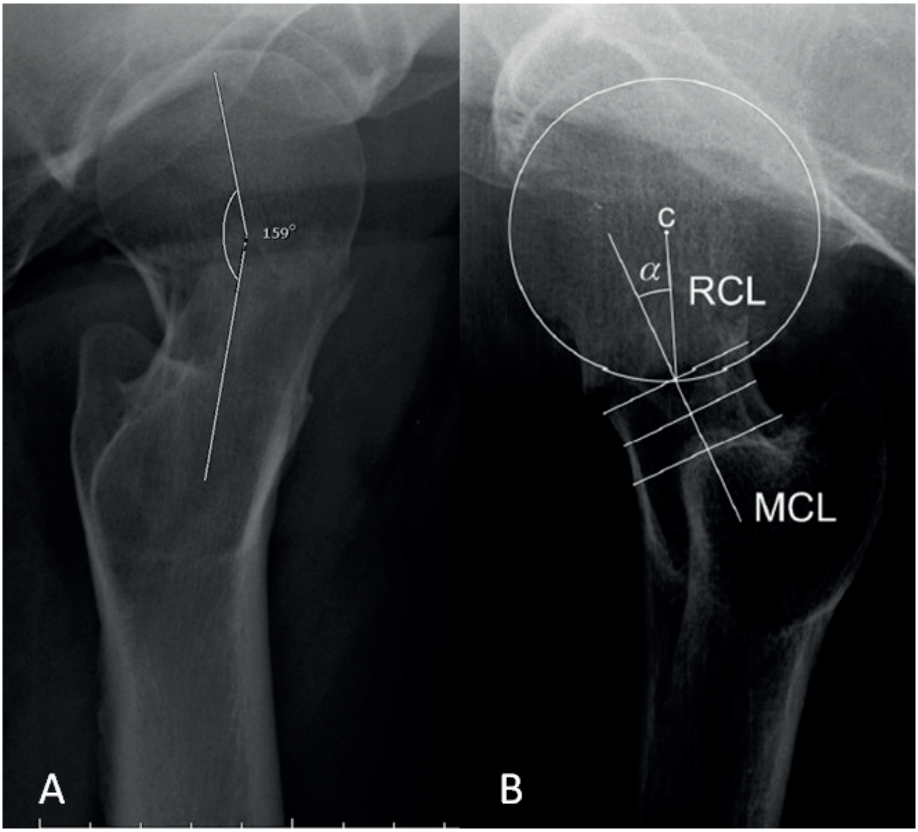

Figure 1. A. Lateral Garden Angle (LGA) is measured according to Gardens description using the trabeculae on the lateral view of the X-ray. The central axes of the femoral head and the neck normally lie in a straight line 180°.[2,12] **B.** The posterior tilt of the femoral head is determined by the angle between two lines, the mid-collum line (MCL) and the radius collum line (RCL). The middle of the collum (femoral neck) is determined by drawing three perpendicular lines across the narrowest part of the collum, with 5 mm between each line. The RCL is drawn from the middle of the femoral head to the intersection of the MCL and the caput circle.[7]

There are several ways to measure posterior tilt. Most used is the Lateral Garden Angle (LGA), which originates from the Garden Alignment Index (GAI) that was introduced by Garden to determine the position of the femoral head after reduction (Figure 1A).[2,12] This index describes the anteriorposterior fracture angle(APA) and the Lateral Garden Angle (LGA) of the femur. The LGA is used by several authors for measuring posterior tilt.[3-5]

In 2009 Palm et al. suggested a new method to measure posterior tilt, the Posterior Tilt Measurement (PTM) (Figure 1B). He stated the LGA to be a too unreliable method.[7] Yet literature provides no evidence regarding the reliability of the LGA. The PTM is also widely used.[6,8-11,13] According to some authors this new way of measuring posterior tilt has an excellent inter and intra observer reliability. The interclass coefficient varies between 0.77–0.94 and the intraclass coefficient varies between 0.77–0.97.[6,7,13]

However, despite the fact that both methods (LGA and PTM) are used in multiple studies, they have never been compared for reliability in a direct study. The aim of this study is to analyse the intra and inter observer variability of the LGA described by Garden and the PTM according to Palm.

METHODS

Fifty radiographs of pre-operative undisplaced FNFs were collected from a database of undisplaced FNFs.[14] The radiographs were randomly selected, using SPSS to generate a random sample from the database. No radiographs were excluded because of 'inadequate quality' to avoid selection bias and to create a realistic setting of clinical practice. All radiographs were collected from one hospital, anonymized and all saved in random order, varying per CD-ROM, on four different CD-ROMs. The posterior tilt angle of all 50 FNF radiographs was assessed four times by four different observers (JHK, ADPW, ABV, EK). The observers were three trauma surgeons (two senior consultants (ADPW, ABV) and one junior consultant (EK), and a last year medical student (JHK) specifically trained for the purpose). The measurements were performed according to the schedule in Table 1: Each observer measured every two weeks 1 CD-ROM with the same 50 radiographs in different order, alternating the LGA and the PTM measurements for all 50 radiographs on one CR-ROM, both two times. All observers were familiar with the LGA, still the description was given. The PTM was explained to all the observers individually and the observers were allowed to practice the PTM on 10 separate radiographs before they participated in the study. Also all the observers were obliged to read the article of Palm.[7]

Table 1. Design of the intra and inter observer measurements

Time	Week 1	Week 3	Week 5	Week 7
Observer 1	cd 1	cd 4	cd 3	cd 2
Observer 2	cd 2	cd 1	cd 4	cd 3
Observer 3	cd 3	cd 2	cd 1	cd 4
Observer 4	cd 4	cd 3	cd 2	cd 1
Method	*LGA*	*PTM*	*LGA*	*PTM*

cd= CD-ROM

Position of the patient

All radiographs were taken in one hospital using a standard positioning technique according to the hospital protocol for hip fractures: Patients were positioned in supine position, the contralateral leg positioned with both hip and knee in ninety degrees flexion. If needed the foot was supported. The injured leg was positioned in its natural position, showing slight exorotation of the foot. The X ray generator was positioned horizontal, perpendicular to the detector and the detector was positioned parallel to the femoral neck at the lateral side of the pelvis.

Measurements

Lateral Garden Angle: This angle is measured according to Gardens description using the trabeculae on the lateral view of the X-ray. The central axes of the femoral head and the neck normally lie in a straight line 180°.[2,12]

Posterior Tilt Measurement: The posterior tilt of the femoral head is determined by the angle between two lines, the mid-collum line (MCL) and the radius collum line (RCL). The middle of the collum (femoral neck) is determined by drawing three perpendicular lines across the narrowest part of the collum, with 5 mm between each line. The RCL is drawn from the middle of the femoral head to the intersection of the MCL and the caput circle.[7]

Statistics

We determined inter observer and intra observer reliability of both measurement tools by comparison of the measurement results of the four observers. Statistical analysis were performed using SPSS v. 21 ((IBM Corp., Armonk, NY, USA) for Windows 7. The intra class coefficients were calculated to assess intra and inter observer reliability using a two-way random effects model with absolute agreement. The intra class coefficients were interpreted according to the method of Landis & Koch: <0.00 reflects poor, 0.00–0.20 'slight', 0.21–0.40 'fair', 0.41–0.60 'moderate', 0.61–0.80 'substantial' and 0.80–1.00 'almost perfect'.[15] P-values less than 0.05 were considered to be statistically significant.

Ethics

The measurements and analysis are in line with earlier performed studies in this research line which were assessed by the regional Medical Research Ethics Committee (MREC). The MREC approved of this study and decided that no written informed consents were required.

RESULTS

Intra and inter observer reliability were determined for the LGA and the PTM. The results demonstrate a substantial intra observer reliability for the LGA as well for the PTM with an intraclass coefficient of 0.75 (95% CI 0.60–0.85) for the LGA and also 0.75 (95% CI 0.60–0.85) for the PTM. Yet the inter observer reliability for the PTM seems better with an intra class coefficient of 0.75 (95% CI 0.64–0.83) compared to 0.60 (95% CI 0.47–0.73) of the LGA (Table 2). A complete overview of the results of the different observers is shown in Table 2. The measured angles were also divided into 2 categories (<20° and ≥20°) according to both measurements methods to evaluate clinical validity for both measurement methods. Yet no reliable analyses could be achieved due to too few fractures with an angle of ≥20° within the 50 fractures measured by the observers.

Table 2.1. Intra- and inter rater reliability of the **Lateral Garden Angle (LGA)**

Intra rater reliability LGA	Intra class coefficient	95% CI	Agreement
Observer 1	0.77	0.62-0.86	Substantial
Observer 2	0.76	0.61-0.86	Substantial
Observer 3	0.71	0.54-0.83	Substantial
Observer 4	0.76	0.61-0.86	Substantial
Mean observer 1/2/3/4	**0.75**	0.60-0.85	**Substantial**
Inter rater reliability LGA			
Observer 1/Observer 2	0.74	0.57-0.84	Substantial
Observer 1/Observer 3	0.53	0.29-0.70	Moderate
Observer 1/Observer 4	0.63	0.41-0.77	Substantial
Observer 2/Observer 3	0.59	0.37-0.75	Moderate
Observer 2/Observer 4	0.66	0.46-0.79	Substantial
Observer 3/Observer 4	0.54	0.31-0.71	Moderate
Observer 1/2/3/4	**0.60**	0.47-0.73	**Moderate**

Intra class coefficient was interpreted as follows: <0.00 ‘poor’, 0.00-0.20 ‘slight’, 0.21–0.40 ‘fair’, 0.41–0.60 ‘moderate’, 0.61–0.8 ‘substantial’ and 0.80–1.00 ‘almost perfect’.[15]

Table 2.2. Intra- and inter rater reliability of the **Posterior Tilt Measurement (PTM*)***

Intra rater reliability PTM	Intra class coefficient	95% CI	Agreement
Observer 1	0.79	0.65-0.88	Substantial
Observer 2	0.61	0.40-0.76	Substantial
Observer 3	0.72	0.55-0.83	Substantial
Observer 4	0.89	0.81-0.94	Almost perfect
Mean observer 1/2/3/4	**0.75**	0.60-0.85	**Substantial**
Inter rater reliability PTM			
Observer 1/Observer 2	0.71	0.53-0.83	Substantial
Observer 1/Observer 3	0.76	0.60-0.86	Substantial
Observer 1/Observer 4	0.80	0.67-0.88	Almost perfect
Observer 2/Observer 3	0.72	0.55-0.83	Substantial
Observer 2/Observer 4	0.75	0.59-0.85	Substantial
Observer 3/Observer 4	0.76	0.61-0.86	Substantial
Observer 1/2/3/4	**0.75**	0.64-0.83	**Substantial**

Intra class coefficient was interpreted as follows: <0.00 'poor', 0.00–0.20 'slight', 0.21–0.40 'fair', 0.41–0.60 'moderate', 0.61–0.80 'substantial' and 0.80–1.00 'almost perfect'.[15]

4

DISCUSSION

Our results show a substantial intra and inter observer reliability for both the LGA and the PTM. The intra observer reliability (0.75) is the same for both methods; the inter observer reliability (0.75 vs. 0.60) seems to be slightly better using the PTM.

Last decade several authors preferred to use the PTM in their studies despite the lack of evidence on the superiority of the PTM over the LGA.[6-11] Several studies published an intra observer reliability ranging from 0.77–0.97 for the PTM and an inter observer reliability ranging from 0.77–0.94.[6,7,13] We could not reproduce these results. In our study three of the observers had no experience with the PTM apart from the 10 radiographs to practice on. In studies in which the observers had experience with the PTM the reliability was higher. An intra observer reliability of 0.95–0.97 and an inter observer reliability of 0.90–0.94 is seen in studies with experienced observers.[6,7] Yet an intra observer reliability of 0.77 and an inter observer reliability of 0.77 was published in a study with inexperienced observers.[13] These studies, including our study, show a tendency towards a learning curve which might improve the reliability of the PTM if it is used over a longer period of time. All our observers used the LGA in their clinical practice. Still the inter observer reliability of the PTM seems superior to that of the LGA.

One of the factors that may have affected our results and those of previous studies on the reliability of the posterior tilt measurements in hip fractures, is the fact that the lateral view of the hip is often difficult to obtain and even more difficult to standardize. Many lateral images are actual oblique views. This influences the way the trabeculae are projected and therefore effects the LGA measurement because the LGA, officially, is measured using the trabeculae. Furthermore the three perpendicular lines, used to measure the PTM, often cannot be drawn due to the oblique view in which the major trochanter blocks the view of the narrowest part of the femoral neck. Hoelsbrekken investigated the influence of the position of the hip on the PTM.[16] He used a 3D-printer generated hip with an undisplaced FNF from which lateral view radiographs were taken in different positions. His study showed that the PTMs can differ 3.8°–9.8° if the hip is positioned from 10° internal rotation to 40° external rotation and 0° to 30° flexion. They concluded that different positions of the hip result in rather similar PTM values and that the difference in PTMs induced by non-standardized positioning is negligible in clinical practice. We feel differently about this aspect of the PTM. The minimal detectable change in study of Hoelsbrekken was lower than the difference in measurements in one of the observers (7.2 versus 9.8), so the position of the hip can induce a valid change in measurements. Moreover, a dispersion of almost 10° can make a big difference in clinical practice and treatment related strategies. FNF treatment decisions are based on the amount of displacement of the femoral head. Garden type III and IV fracture are usually treated with an arthroplasty. Whereas patients with an undisplaced FNF, Garden type I and II FNFs will according to the current guidelines mostly be treated with cannulated hip screws or a sliding hip screw device. Yet the posterior tilt is not included in the Garden classification. Several studies suggest 20° posterior tilt in Garden type I&II FNF as a cut-off point to discriminate between non displaced and displaced FNF at the axial view radiograph.[6,17] We believe the posterior tilt should be measured in daily practice and should be included in the treatment decision plan.

The PTM and the LGA are used for measurements on pre- and postoperative radiographs. Yet during the intra operative reduction of the fracture no objective measurement methods are used to determine if the fracture is adequately reduced. The surgeon uses the compass in his eye to determine whether the reduction is adequate or not and this could have consequences for the treatment. If the fracture cannot be properly reduced during the operation the surgeon may choose to convert the operation from internal fixation to a prothesis. Yet, do surgeons measure the same posterior tilt angles using a simple morphological classification? We could not find any literature on using posterior angular measurements during surgery. Dolatowski did include a morphological classification for preoperative radiographs in his reliability study.[6] For this morphological classification the observers described the FNF on the lateral radiograph as undisplaced or displaced without measuring the posterior tilt angle. The inter observer reliability for PTM was 0.90 (95% CI 0.87–0.92) versus 0.68 (95% CI 0.60–0.76) for the morphologic classification. Based on this study the PTM seems superior to a morphologic classification however this is never tested intra operatively. Further research should be conducted regarding the reliability of the PTM and a morphologic classification during surgery. Also the feasibility of angular measurements during the operation in day to day practice should be evaluated.

The results of this study are limited by the fact that three of the four observers had no experience using the PTM, but were experienced with the LGA. If the observers had already been familiar with the use of the PTM, the ICCs might have been higher and the difference in inter observer reliability might have been more outspoken as compared to that of the LGA.

Several studies describe a cut off point for the significance of posterior tilt.[6-8,10] We could not perform reliable subgroup analyses for radiographs of fractures in a posterior tilt of <20° and ≥20°. Therefore, no conclusion could be drawn about the observer reliability for a cut-off point for the LGA and the PTM.

CONCLUSION AND RECOMMENDATIONS

Based on our results we believe both the Lateral Garden Angle and the Posterior Tilt Measurements are reliable methods to measure posterior tilt in preoperative radiographs of femoral neck fractures. Yet the Posterior Tilt Measurement seems to have a better inter observer reliability and therefore has a slight preference over the Lateral Garden Angle.

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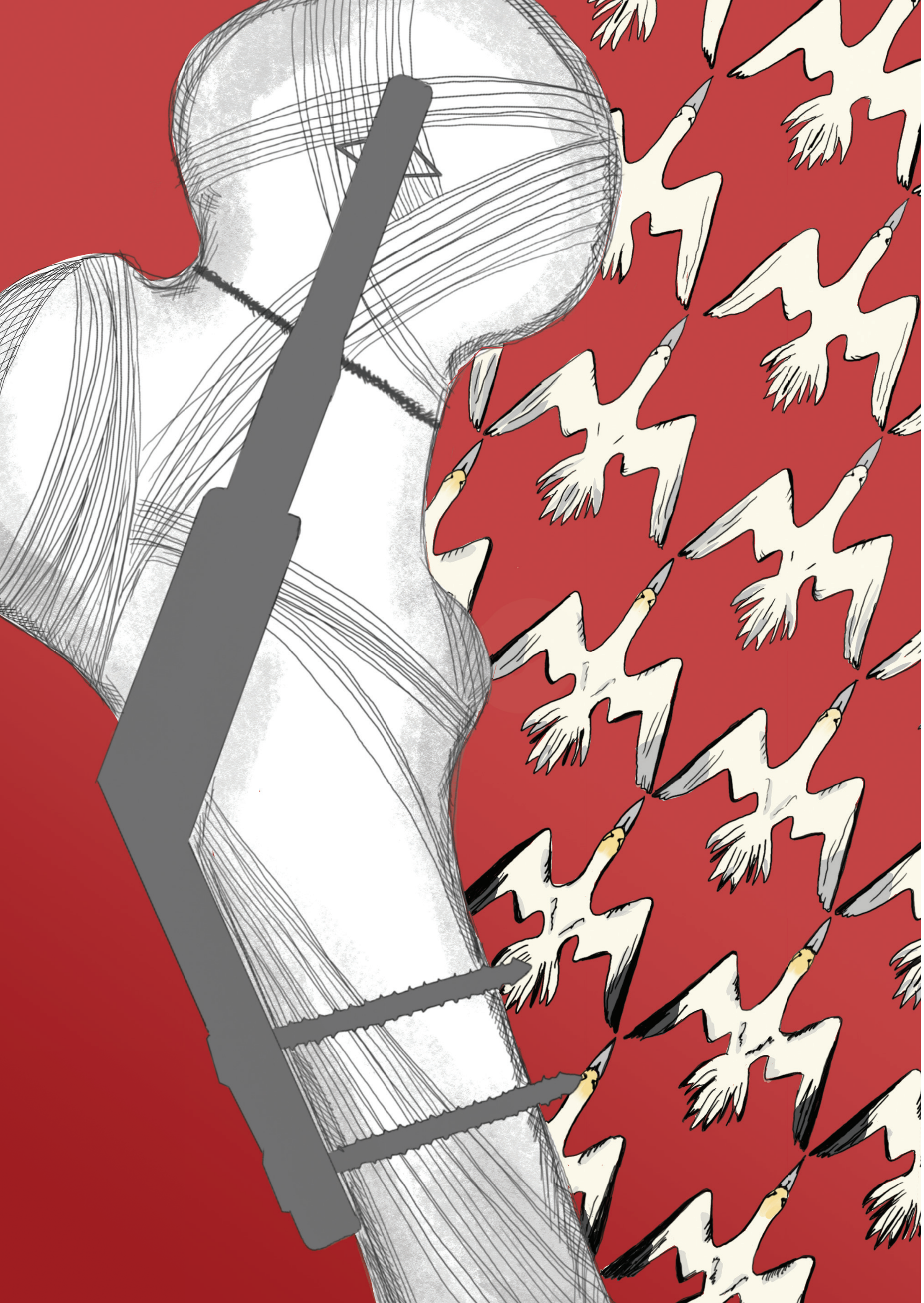

Chapter 5

Displaced femoral neck fractures in patients 60 years of age or younger; results of internal fixation with the Dynamic Locking Blade Plate

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J.T. Winkelhorst, B.P. Bertelink, W.H. Roerdink

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ABSTRACT

Aims

The objective of this study was to investigate bone healing after internal fixation of displaced femoral neck fractures (FNFs) with the Dynamic Locking Blade Plate (DLBP) in a young patient population treated by various orthopaedic (trauma) surgeons.

Patients and methods

We present a multicentre prospective case series with a follow-up of 1 year. All patients aged ≤60 years with a displaced FNF treated with the DLBP were included. Patients with pathological fractures, concomitant fractures of the lower extremity, symptomatic arthritis, local infection or inflammation, inadequate local tissue coverage, or any mental or neuro-muscular disorder were also excluded. Primary outcome measure was failure in fracture healing due to non-union, avascular necrosis or implant failure requiring revision surgery.

Results

In total, 106 consecutive patients (mean age 52 years, range 23–60; 46% [49/106] female) were included. The failure rate was 14 of 106 patients (13.2%, CI 7.1–19.9%). Avascular necrosis occurred in 11 patients (10.4%), non-union in six (5.6%) and loss of fixation in two (1.9%).

Conclusion

The rate of fracture healing after DLBP fixation of displaced femoral neck fracture in young patients is promising.

INTRODUCTION

The biology of the fracture healing of femoral neck fractures (FNF) is characterised by its specific the type of bone healing and the vascularity of the femoral neck and head. These biologic features place the FNF apart from most other fractures, including the intertrochanteric hip fractures. Awareness of the biological characteristics of the femoral neck fractures is prerequisite in the operative treatment of FNF.

The viability of the femoral head after FNF is dependent on preservation of the remaining vascular supply and on revascularisation and repair of the necrotic areas before collapse of the necrotic bone segment can occur.[1-4] To preserve the remaining blood supply to the displaced femoral head, accurate reduction and stable fixation is critical in any attempt to salvage the femoral head.[1] An important source of revascularisation is the vascular ingrowth across the uniting fracture line.[2] The transverse shear and the rotational interfragmentary movement (IFM) caused by poor fracture stabilisation are deleterious to revascularisation as they disrupt angiogenesis in the femoral head.[3] Kumar et al stated that decreased or absent vascularity of the femoral head is seen in approximately 75% of FNFs whereas 80% of femoral heads with initial vascular compromise seem to regain blood flow within 6 weeks.[4] The (re)vascularisation of the femoral head is further compromised when using implants with larger volumes as this may increase the incidence of AVN.[5,6]

Bone healing of FNF is determined by the anatomical fact that the intracapsular portion of the neck has essentially no cambium layer in its fibrous covering to participate in external callus formation.[7] The cells in the cambium layer of the periosteum are highly proliferative and osteogenic, and respond to mechanical stimulation.[8] Unlike diaphyseal but similar to scaphoid fractures, FNFs cannot heal by periosteal (external) callus formation; hence, healing is by primary osteonal reconstruction.[9,10] Primary bone healing requires anatomical reduction and a stable fixation. In the context of fixation of FNF the term 'stable' means that the transverse shear- and rotational IFM are minimalized within the strain tolerance of 2% while allowing controlled axial IFM.[11]

The consensus is that young patients with displaced FNF are treated by internal fixation, whereas elderly patients are treated by total or hemi-arthroplasty (Figure 1).[12-14] Generally, patients aged <60 years are considered to be young patients.[15] However, treatment of a displaced FNF by internal fixation remains controversial because of the high failure rate encountered after internal fixation. Overall, the literature gives an incidence of 30–33% for non-union and 10–16% for AVN in displaced fractures.[16-19] The data received from the FAITH trial show 11.1% non-union and 6.3% AVN and an overall revision rate of 22.3% for displaced FNF.[20] Revision rates of 35%[18] and up to 48%[19] for displaced fractures were reported in two large meta-analyses. More recently, Parker reported a revision rate of 20.7% in patients with displaced FNF treated with the Targon Femoral Neck plate.[21] A 2015 meta-analysis on the results of internal fixation in patients <60 years old with a displaced FNF reported a revision rate of almost 18%.[15]

Fig. 1a

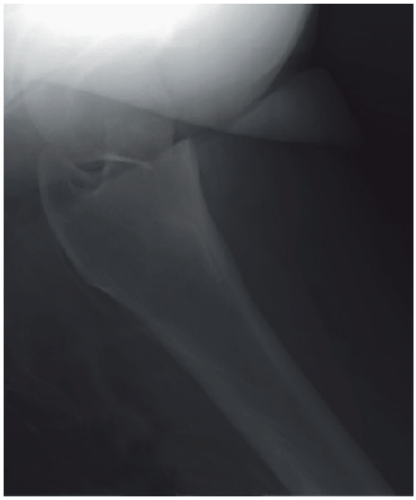

Fig. 1b

Figure 1. a) Anteroposterior and **b)** lateral radiograph of displaced femoral neck fracture in a 57-year-old woman.

The most commonly used implants are multiple parallel (cannulated) screws or sliding hip screw (SHS) devices.[22] It is obvious that not all factors contributing to the failure rate of the FNF are implant-related. Other factors such as primary displacement, posterior comminution, fracture reduction and implant positioning are even more important than implant choice.[23-25]

However, triggered by the poor results of internal fixation achieved with the current implants, we analysed the possible biological, surgical and implant-related factors contributing to the high failure rate, and formulated features of a new implant tailored to the fixation of FNF. We then developed this new implant with the working name 'Dynamic Locking Blade Plate' (DLBP). It is characterised by a low implant volume combined with rotational and angular stability while allowing controlled axial compression (Figure 2).

The DLBP was initially tested by two surgeons who participated in the development of the implant. This earlier small pilot study with a follow-up of 2 years reported a failure rate of 8% in 25 patients (mean age 60 years; range 39–75) with undisplaced or displaced FNF.[26] A larger prospective multicentre study of the DLBP with a follow-up of 1 year demonstrated a failure rate of 4% among 149 patients (mean age 69 years, range 35–101) with an undisplaced FNF.[27] The primary objective of the present study was to determine the failure rate of the DLBP in a larger general population of patients aged <60 years of age with a displaced FNF and treated by various orthopaedic (trauma) surgeons and surgical trainees. Secondary objectives were to determine complication rates, radiographic outcome and mobilisation after surgery, and compare these between groups.

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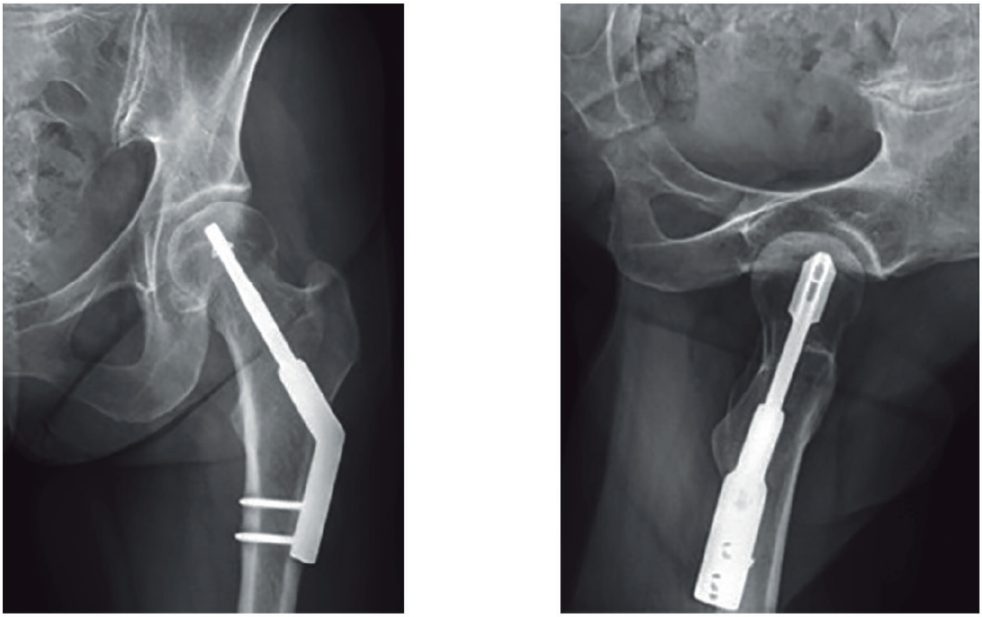

Fig. 2a Fig. 2b

Figure 2. a) Anteroposterior and **b)** lateral radiograph of the patient in Figure 1 following treatment using the dynamic locking blade plate with union of the fracture line.

PATIENTS AND METHODS

Design and cohort

This was a multicentre prospective case series. All patients aged ≤60 years admitted to the participating hospitals with a displaced FNF were treated by internal fixation with a DLBP. In cases where the on-call surgeon was unfamiliar with the DLBP or the patient chose otherwise following informed consent, patients were treated with an arthroplasty or an implant other than the DLBP (e.g. cannulated hip screws or SHS). All patients aged ≤60 years of age or younger treated by the DLBP were included, while all patients treated with an arthroplasty or any implant other than the DLBP were excluded. Pathological fractures, concomitant fractures of the lower extremity, symptomatic arthritis, local infection or inflammation, inadequate local tissue coverage, or any mental or neuromuscular disorder, which would create an unacceptable risk of fixation failure or complications in postoperative care, were excluded. A displaced FNF was defined as a grade 3 or 4 fracture according to the conventional Garden classification. Following surgery, patients were mobilised by permissive weight-bearing according to pain.

Implant

The DLBP was developed by Baat Medical Engineering in Hengelo, the Netherlands and is now marketed as the 'Gannet'. The DLBP consists of a two-hole standard 135° barrelled side-plate combined with a low-volume cannulated locking blade (Figure 3). The side plate provides angular stability and allows controlled dynamic axial compression of the fracture. Two side wings at the tip of the blade provide rotationally stable fixation of the locking blade in the femoral head. The expandable impaction anchors lock the blade in the femoral head and prevent perforation and backing out of the implant and further augment the rotational

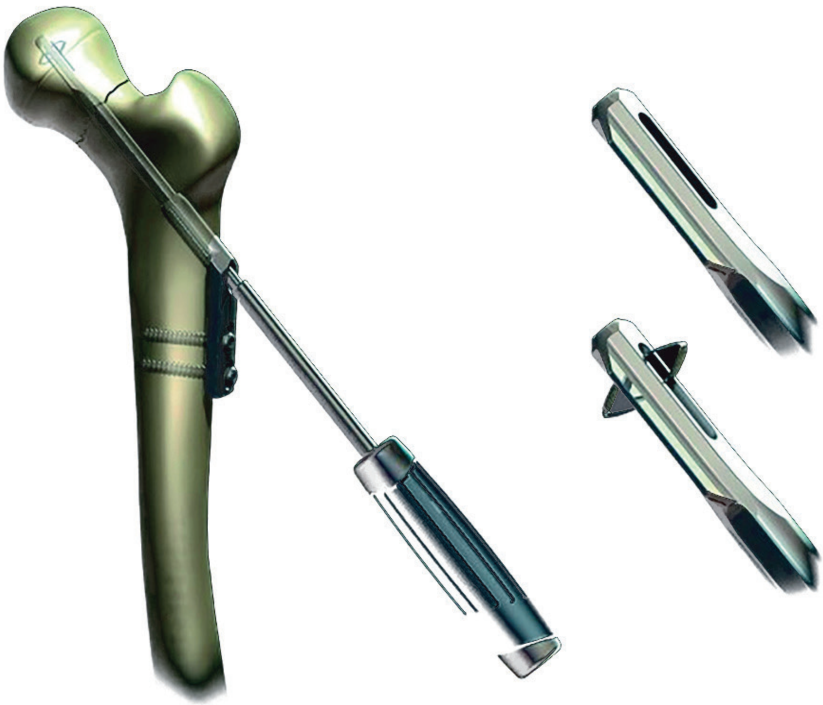

Figure 3. The Dynamic Locking Blade Plate also known as the Gannet Implant.

stability.[28] The volume of the DLBP inserted 50 mm into the head is 1800 mm^3. The volumes of the DHS and 3 cannulated screws are respectively 2700 mm^3 and 2520 mm^3.[29] Surgery was undertaken by general orthopaedic- and trauma (orthopaedic) surgeons. All participating surgeons were trained in the use of the DLBP, and the first surgical procedure was undertaken under the supervision of a surgeon with wide experience with the DLBP. Trainee surgeons were always supervised by a senior consultant. Reduction was performed using closed technique for all the fractures. The surgical technique is described in an earlier published study.[28,30]

5

Outcomes measurements

Anteriorposterior (AP) and lateral X-rays were assessed by a radiologist and by the treating surgeon for fracture healing and complications. The radiographs were standardized for projection and also for rotation within the pain limits. Follow-up was performed by the authors at 6 weeks, 3 months and 1 year. The primary outcome measure, failure of fixation, is defined as the need for revision surgery because of non-union, AVN or cut out of the implant. Union was defined by an absence of visible margins in the fracture. Non-union was identified by either displacement of the fracture or clearly visible margins of the fracture 1 year postoperatively. AVN was defined according to the Steinberg classification from stage 2 and upward.[31] The Garden Alignment Index was used to evaluate the fracture reduction on the first postoperative X-ray.[32,33] As reported previously, the acceptable range of reduction is a 160–180° angle.[34,35] The impaction at the fracture site was assessed by measuring the degree of telescoping of the lag screw with correction for magnification in millimetres. The position of the locking blade in the femoral head, as a predictor of implant cut-out, was assessed by the corrected tip–apex distance (TAD) on the first postoperative X-rays; TAD >25 mm is predictive of a higher extrusion rate.[23] The measurements were performed by the authors. Before and 1 year after surgery mobility was assessed by need for walking aids: no walking aids, one crutch, two crutches or a walker.

Statistical analysis

Statistical analysis was performed using SPSS v. 21 (IBM Corp., Armonk, NY, USA) for Windows 7. The primary analysis was descriptive. Frequencies and percentages are reported for categorical data, and means and ranges for continuous data are presented. Mean differences between groups (healed versus failed) were compared using Student's t-test and chi-squared test. Statistical significance was defined as $p<0.05$.

RESULTS

One level 1 community trauma centre and four level 2 community teaching hospitals participated in the study. Between 1 August 2010 and 31 December 2014, 135 consecutive patients aged ≤60 years with a displaced FNF were admitted to these hospitals. Of these, 21 patients were treated by devices other than the DLBP: eight chose a hemi- or total hip arthroplasty following informed consent, and 13 were treated by other implants than the DLBP because the on-call surgeon was unfamiliar with the DLBP. The remaining 114 patients were treated with the DLBP, and of these five were excluded: two had a mental disorder, two had known neuromuscular disease and one had concomitant fractures of the lower extremity. The fracture healed in four of these five patients. Thus, of the 135 patients with a displaced FNF, 109 were included in the study. None of the patients died within the follow-up period and only three were lost to follow-up (Figure 4). Seven patients did not have a radiograph after one year. Follow-up after one year through interview by telephone revealed that none of the seven patients underwent revision surgery.

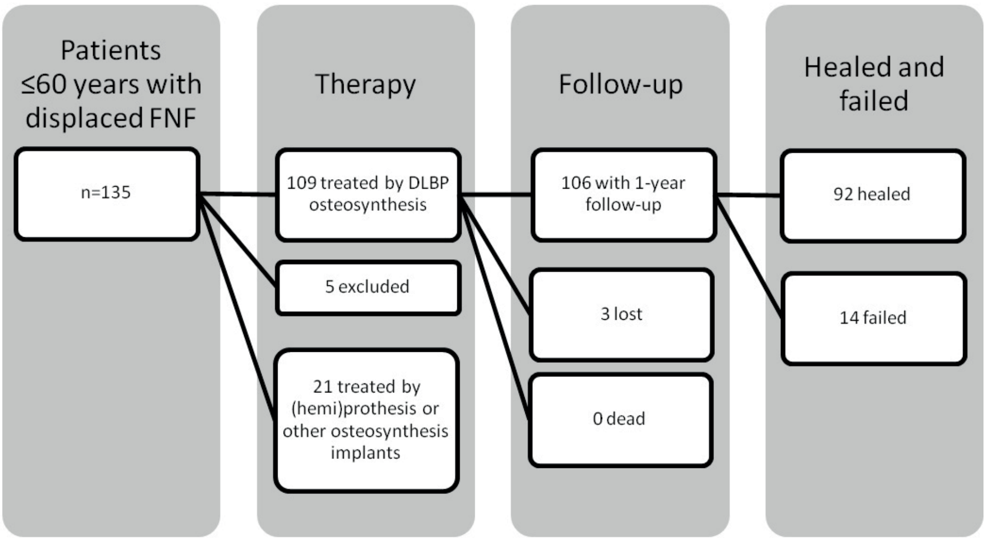

Figure 4. Flowchart of patient population. *DLBP*, dynamic locking blade plate; *FNF*, femoral neck fracture.

Surgery was undertaken by (orthopaedic) trauma surgeons (86%) and trainee surgeons (14%). Follow-up for all included patients was at least 1 year. Mean patient age was 52 years (range 23–60) and 46% (49/106) were female. Of the treated patients, 85% (90/106) were operated within 24 hours and 97% (103/106) within 48 hours. Mean operating time was 44 min (range 15–102). One patient developed a local complication of a deep infection.

One implant-related complication, no expansion of the impaction anchors, was noted in five patients. In one case, the insufficient expansion of the anchors was accompanied by a high TAD of 29 mm, resulting in implant extrusion and loss of fixation. Loss of fixation was not seen in any of the other four cases. There were no perforations or backing out of the implant, and no breakage of blades, plates or screws occurred. Overall mean TAD was 22.0 mm (range 9.0–40.0 mm) and mean impaction was 7.1 mm (0–23 mm).

Failure rate for the displaced femoral neck fixated by the DLBP was 14 of 106 patients (13.2%; 95% CI 7.1–19.9%). There were no statistical differences between the healed and failed group in terms of sex, age or TAD. In the group of healed fractures, 11 (12.0%) fractures were inadequately reduced, while there were two (14.3%) malreductions in the failed patient group (Table 1).

Table 1. Variable characteristics divided in healed and failed fractures

	Healed	Failed	p-value
Female (%)	40 (43.5)	9 (64.3)	0.163*
Mean age (SD)	51.5 (8.4)	53.1 (6.1)	0.474†
TAD > 25 mm (%)	22 (23.9)	4 (28.6)	0.742†
Malreduction (%)	11 (12.0)	2 (14.3)	0.681*

*Chi-squared test
†Students *t*-test
TAD, tip–apex distance

AVN was the most common complication. In the 14 failed fractures, bone healing was complicated by: AVN in 11 patients (10.4%), non-union in six (5.6%) and loss of fixation in two (1.9%). Four patients had a combination of complications. Three of the six non-unions were combined with AVN and one patient suffered a combination of non-union, AVN and cut-out. In all of the 14 failed cases, revision surgery was performed by total hip arthroplasty. All patients were free of walking aids before surgery, except one who used a walker. Only five patients did not recover to the pre-existent mobility grade. Elective implant removal after fracture healing, due to possible implant related complaints or on patient’s request, was performed in 17%.

DISCUSSION

The goals of surgical treatment for displaced FNF are 1) to do no further vascular harm, 2) provide the stability necessary for revascularisation of the femoral head and 3) provide the stability necessary for primary bone healing. The DLBP was designed to be compatible with FNF biology, and is a low-volume, dynamic implant providing angular and rotational stability. In this study, DLBP fixation of displaced FNF led to failure caused by AVN in 10.4 % of patients. The viability and stability of the DLBP is also apparent from the low degree of fracture impaction with a mean of 7.1 mm after 1 year, while the literature gives an incidence of 14.7–22.5% of AVN in young patients and mean impaction of 9.3 mm.[15,17,36-38]

Other possible implant-related factors contributing to the high failure rate of the common implants are the insufficient intrinsic angular and rotational stability.[39,40] The stability of multiple screws is fully dependent on the three-point fixation principle based on precise screw placement and is consequently surgeon-dependent.[40] As the most common implants fail to provide adequate rotational stability, the clinical importance of the prevention of rotational IFM seems to be underestimated.[29] Biomechanical testing demonstrated that a de-centralized position of a lag screw by only 3 mm in the femoral head can result in rotation of the femoral head around the lag screw as the physiologic load torque could outrun resistance of the cancellous bone around the implant.[39] This rotation initiates a reaction whereby the stability of cancellous bone fails rapidly after the first trabeculae are fractured and that may lead to a cut out of the implant.[41] Resistance of the bone–implant interface depends on the design of the implant. Biomechanical analysis showed that the rotational stability of the DLBP proved to be three times higher than that of SHS.[29] The counter-clockwise rotational stability of a lag screw is negligible.[42] Unlike the SHS devices, no torque force at all is exerted on the femoral head on insertion of the DLBP, and therefore it is unnecessary to insert an extra pin or screw in the femoral head to prevent rotation.

Jenkins et al demonstrated by micro-computed tomography that greatest density and trabecular thickness was found in the centre of the head and the weakest area was the apex and peripheral areas of the head.[43] The DLBP provides stability by using one single implant in the biomechanical most optimal, rotation-neutral, centre-centre position in the femoral head.[39,43] This contrary to other implants where two, three or even four screws/pins are placed in suboptimal peripheral positions. It was also shown that two or more parallel angular stable screws may be complicated by the so called 'Z effect' (or reverse Z effect), in which the lag screws migrate in opposite directions during physiological loading, which can lead to perforation.[44,45]

Irrespective of the implant used, the single most important step in surgical treatment of displaced FNF is fracture reduction. Surprisingly, in this study, there was almost no difference in failure rates between reduced and malreduced FNFs, indicating that either the number of malreduced fractures was too low or that the DLBP is capable of stabilising malreduced FNF. It has to be mentioned that the reduction was measured by one observer and an inter- and intra observer variation has to be taken into account. The second most important technical step is the central and deep positioning of the implant in the femoral head. If the insertion into the femoral head is too shallow and/or too decentralised, the holding power of the implant is reduced.[23] However, in this study, a TAD >25 mm did not contribute to failure by cut-out. Again, this could be due to the study being underpowered or to the improved holding strength of the DLBP. The stability of the DLBP was demonstrated by a low rate of non-union (5.6% versus 6–11% in the literature), and cut-out (1.9% versus 9–13.1% in literature) and not a single case of perforation of the femoral head.[15,20,24,36,37] The overall failure rate in 106 young patients (23–60 years old) was 13.2%. These results compare favourably with the literature and with recently published results of new implants.[21]

The strength of this study is its prospective design and the well-defined patient population (young patients with displaced FNF). Despite this specific patient population we had a relatively large patient cohort. The contribution of a variety of (orthopaedic) trauma surgeons from five different hospitals also advocates for treatment by DLBP in general hospitals. Limitations of this study include its relative short follow-up of 1 year and lack of an official mobility score.

CONCLUSION

The DLBP has been developed specifically for the fixation of FNFs and is characterised by a combination of dynamic compression, angular and rotational stability, and low implant volume within the femoral head. Despite the participation of various surgeons in this multicentre study, the DLBP held up its performance as demonstrated in an earlier pilot study. The failure rate of the DLBP for displaced femoral neck fractures (13.2%) in young patients is promising and warrants a randomised controlled trial comparing the DLBP with contemporary implants.

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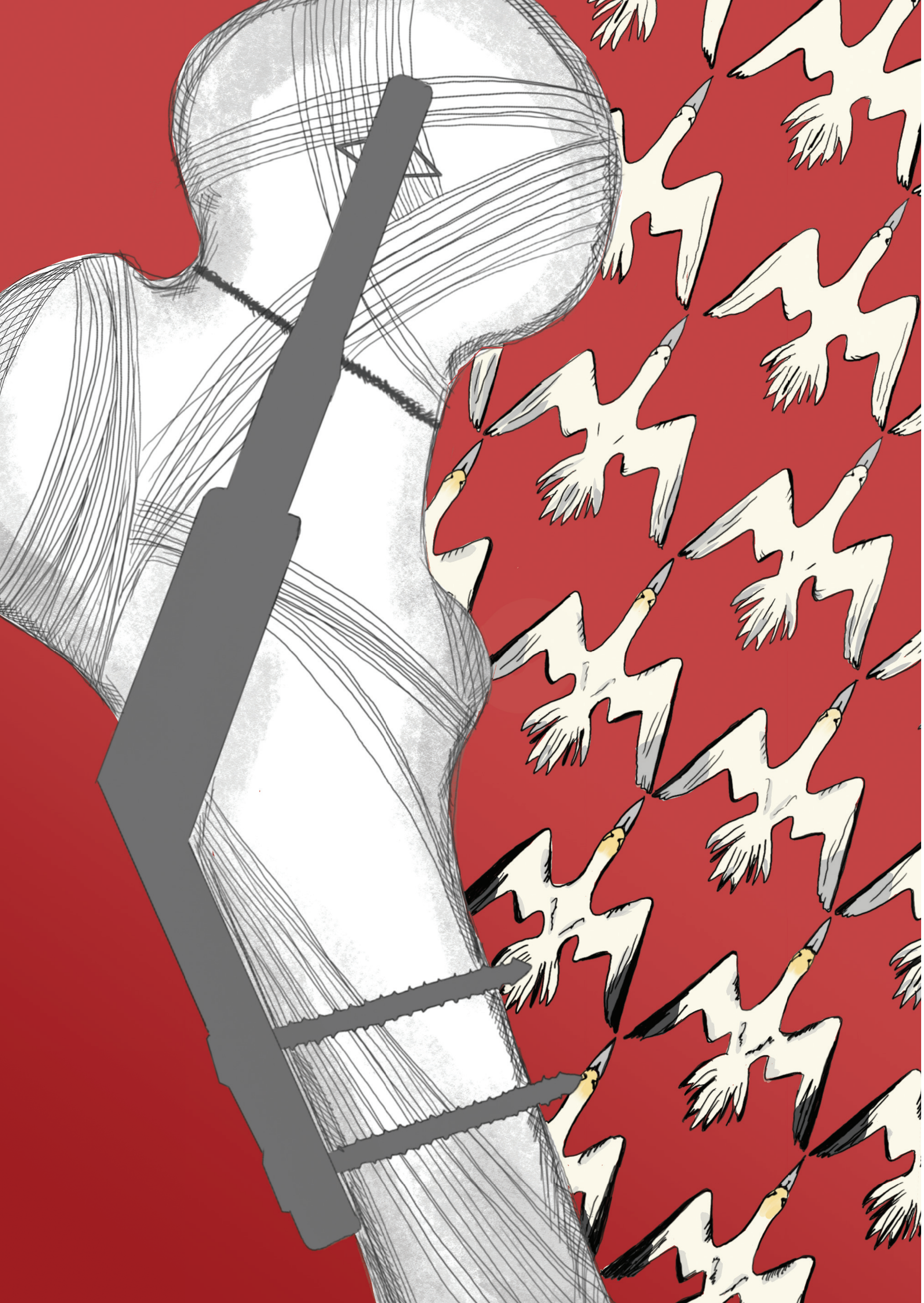

Chapter 6

The Dynamic Locking Blade Plate: Seven-year follow-up results of 389 patients with a femoral neck fracture

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ABSTRACT

Purpose

This study aimed to investigate the long-term outcomes of patients with a femoral neck fracture (FNF), treated with the Dynamic Locking Blade Plate (DLBP).

Methods

Retrospective analysis of prospectively collected data of a multicentre cohort of hip fracture patients was conducted, regarding the long-term incidence of revision surgery after DLBP. Implant failure was evaluated using Kaplan-Meier and Cox regression analysis. Secondary outcomes were the indication for revision surgery, complications, time to revision surgery, rate of elective removal of the implant, potential predictors for revision surgery and mortality.

Results

Median follow-up of 389 included patients was 98 months; 20.6% underwent revision surgery; 28.8% after treatment of a displaced FNF (dFNF) and 10.0% with a undisplaced FNF (uFNF). 5.7% (n=22) of the patients had operation related complications and 32.9% (n=128) deceased during follow-up. Median time to revision surgery was 13 (dFNF) and 18 months (uFNF). 15.7% of the DLBPs were electively removed. In the multivariate Cox regression analysis, female gender (hazard ratio 2.1, 95% CI 1.2–3.7) and a TAD >25mm (hazard ratio 2.9, 95% CI 1.7–5) were significant predictors for revision surgery in patients with dFNF.

Conclusion

This study is the first long-term follow-up study on the outcome of the DLBP. The DLBP demonstrated positive long-term results in the treatment of FNF.

INTRODUCTION

The treatment of femoral neck fractures (FNFs) has been discussed extensively for many decades. The two main surgical treatment options are internal fixation and (hemi) arthroplasty. However, both treatments know potential disadvantages and complications. Arthroplasty of the hip is associated with dislocation, pulmonary embolism, cement induced syndrome, limited implant survival and severe morbidity due to infection[1,2], Internal fixation is associated with high failure rates (10–49%) due to non-union, avascular necrosis (AVN) of the femoral head and cut-out of the implant.[3]

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To improve the outcome of head preserving treatment of FNFs, the Dynamic Locking Blade Plate (DLBP) was developed, a fixed angle device characterized by its excellent rotation stability, low implant volume and simple operation technique.[4-6] The DLBP demonstrated good results in treatment of FNF, with 4% failure rate at one year in a prospective multicentre cohort study of 172 patients with undisplaced FNFs (uFNF).[5] Another prospective cohort study of 106 young patients with displaced FNFs (dFNF) demonstrated a failure rate of 13.2% after one year.[6] A randomised controlled trial comparing the DLBP with the Dynamic Hip Screw is ongoing at this moment.[7]

The follow-up of these studies was limited because most of the complication occur within one year. Yet some FNFs are still revised after one year.[8,9] Kelly et al. found a mean time to revision of 1.3 years (range 73 days – 4.9 years) within a cohort of FNFs treated with a sliding hip screw with a mean follow-up time of 8.2 years (range 6.7–10.1).[10] Mean time to AVN varies between 16–18.8 months with a total range of 3–60 months.[11-13] Patients may also suffer from posttraumatic osteoarthritis (PTOA) which can present years after the initial trauma. In 35% of patients treated for FNF, PTOA is found to be the indication for subsequent total hip arthroplasty.[14]

The aim of this study was to investigate the long-term outcomes of patients with an FNF, treated with the DLBP. More specifically, the need for and type of revision surgery were evaluated, as were complication and mortality rates in patients with a minimum of seven years follow-up.

PATIENTS AND METHODS

Design and cohort

Retrospective analysis of prospectively documented data of a multicentre cohort including 468 adult patients treated with the DLBP between 2010–2014 was conducted. In this cohort all consecutive patients of any age with a uFNF, patients with a dFNF of ≤65 years and patients between 65 and 75 years who were not dependent on walking aids and who were not admitted in a nursing home prior to the fracture were included. Their prospectively registered data including clinical outcomes up to one year have been published previously.[5, 6] For the present study, all patients with an FNF from this cohort with a minimum follow-up of seven years, or shorter if the endpoint (revision surgery or death) was reached before seven years of follow up, were eligible. Patients who met any of the following criteria were excluded in this study:

- Pathological fracture
- Ipsilateral or contralateral fracture(s) of the lower extremity
- Symptomatic osteoarthritis or radiographic osteoarthritis grade III or IV[15]
- Previous surgery of the ipsilateral hip
- Patients who were wheelchair-bound in their pre-injury situation
- Patients who were not mentally competent to take a survey

Study outcome parameters

The main study outcome parameter was the incidence of revision surgery, defined as any reoperation due to failure of treatment (cut-out of the implant, AVN, non-union, or PTOA), such as conversion to (total) hip arthroplasty, girdle stone, core decompression, vascular fibular graft, valgus (intertrochanteric) osteotomy. Elective removal of the DLBP after union of the fracture was not considered as revision surgery.

Secondary outcome parameters were the indications for revision surgery (AVN, non-union, cut-out of the implant, PTOA), operation related complications such as bleeding or infection and general hospital complications such as delirium and pneumonia, time to revision surgery, elective removal of the DLBP, and mortality. AVN was defined as stage 2 necrosis and upward, according to the Steinberg classification.[16] Our definition of non-union was based on the Radiographic Union Score for Hip (RUSH).[17] Non-union was defined as a visible fracture line on the radiograph, absence of cortical bridging or bridging trabeculae over the fracture site in combination with persisting pain in the hip or the inability to bear weight for at least 9 months after surgery or sooner if revision surgery was performed because it was no longer expected that fracture healing would occur. PTOA was defined as having symptoms of OA including pain, stiffness of the joint with or without radiologic findings of OA in absence of AVN, non-union or cut-out of the implant.

Other data registered in the database were age, gender, fracture displacement, posterior tilt of the femoral head, time to surgery, operation time, reduction of the fracture, Tip-Apex-Distance (TAD), postoperative complications, mortality and revision rate and indication for revision at one year. Fracture displacement was assessed according to the Garden classification with uFNF defined as Garden type 1 & 2 and dFNF as Garden type 3 & 4.[18] The Garden

Alignment Index was used to evaluate the fracture reduction on the first postoperative radiograph.[19] The acceptable range of reduction is a 160 to 180° angle.[20,21] Posterior tilt was measured using the posterior tilt measurement according to Palm et al.[22]

Study procedure

If patients were eligible for the present study, outcome data additional to their one-year follow-up data were collected from the medical records. If information on the presence or absence of revision surgery during at least seven years, and if applicable peri-operative information of the revision surgery, could not be found in the records, the patient was contacted by telephone. If information on the primary outcome could not be retrieved the patient was excluded. Seven years follow-up was chosen because time between implantation of a DLBP in the last included patient and the start of data collection was seven years.

Statistical analysis

Statistical analysis was performed using SPSS Statistics 28 software (IBM Corp., Armonk, New York) for Windows 10 Home (Microsoft, Redmond, Washington). The data was analysed in subgroups of patients with uFNF and dFNF. Results are presented as frequency and percentage for categorical data and mean (standard deviation) or median (range) for continuous data. Difference in revision rate between the groups with uFNF and dFNF was evaluated using Kaplan-Meier survival curves and compared with the log-rank test. Kaplan-Meier analysis was also used to compare revision surgery rates between subgroups of patients with various indications for revision surgery (AVN, non-union, cut-out of the implant, posttraumatic OA). Potential predictors for revision surgery (female gender, operation performed by a surgical resident, TAD>25mm, age>65 years, inadequate reduction for dFNF and posterior tilt >20° in uFNF were assessed using univariable and multivariable Cox proportional hazards regression analysis, separately for the uFNF and dFNF groups. Statistical significance was set at $p<0.05$.

Ethical approval

This study was conducted in compliance with the declaration of Helsinki (2008) and the principles of good clinical practice (GCP). According to the institutional Medical Research Ethics Committee, this study did not meet the criteria of the Dutch Medical Research Involving Human Subjects Act (WMO), so that ethical approval was not needed.

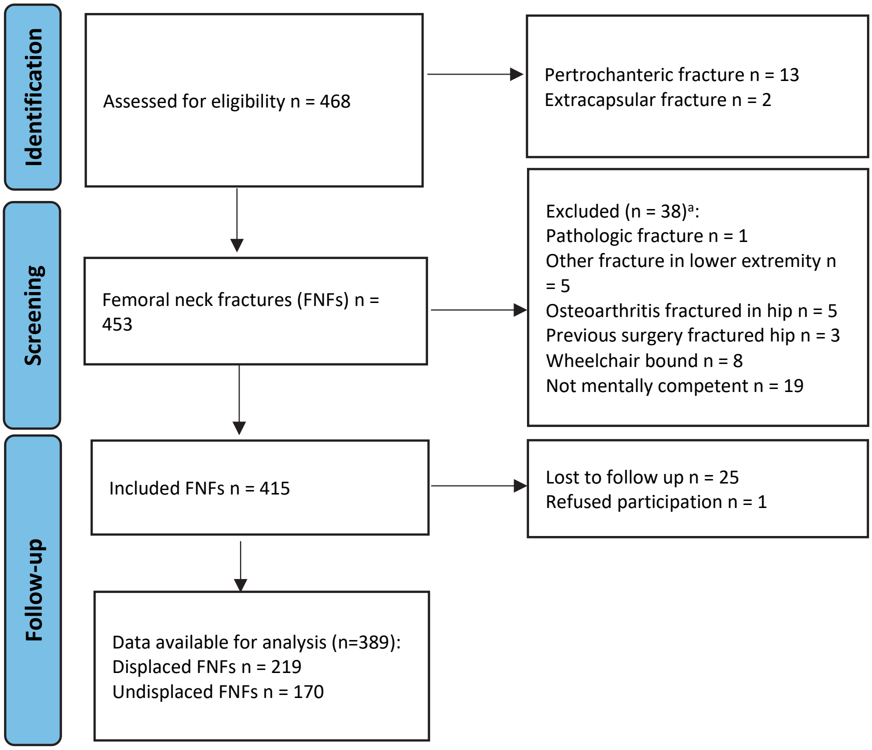

Figure 1. STROBE flow diagram

[a] Some patients met multiple exclusion criteria

RESULTS

Seventy-nine of the 468 patients in the cohort were excluded, leaving 389 patients eligible for analysis (219 with dFNF and 170 with uFNF). Reasons for exclusion are presented in Figure 1. The characteristics of the study population are presented in Table 1. Median follow-up was 98 months (range 0–150) and similar in both dFNF and uFNF. Of the 389 patients, 80 patients (20.6%) underwent revision surgery, 63 of the 219 patients with a dFNF (28.8%) and 17 of the 170 patients with a uFNF (10.0%). The rate of revision surgery was higher for the dFNF group than for the uFNF group (Figure 2; log-rank test p<0.001).

Twenty-two patients (5.7%) had an operation related complications and 41 patients (10.5%) had one or more general hospital complications. Detailed information about complications can be found in Tables 2 and 3. Almost one third of all patients (n=128, 32.9%) died during follow up. There were three instances of in-hospital deaths; one patient died after a cardiac event, another patient experienced a fatal pneumonia and the third patient expired due to heart failure secondary to a pneumonia.

Table 1. Demographic and clinical characteristics of 389 included patients

Variable	**Total n=389**	**Displaced FNF n=219**	**Undisplaced FNF n=170**
Mean age, in years (SD)	65.8 (13.3)	62.8 (12.2)	69.7 (13.7)
Male, n (%)	169 (43.4)	106 (48.4)	63 (37.1)
Mean operation time, in minutes (SD)[a]	43.1 (18.7)	43.9 (19.5)	42.0 (17.7)
Operating physician, n (%)[b]			
Surgeon	328 (84.8)	183 (83.6)	145 (86.3)
Surgical resident	59 (15.2)	36 (16.4)	23 (13.7)
Time to surgery, n (%)			
within 24 hours	321 (82.9)	187 (85.8)	134 (79.3)
within 48 hours	362 (93.5)	206 (94.5)	156 (92.3)
Mean TAD, in mm (SD)[c]	21.4 (6.9)	21.6 (7.2)	20.1(6.5)
Mean posterior tilt, in degrees (SD)	13.8 (9.8)	N/A	13.8 (9.8)
Inadequate reduction, n (%)	48 (12.9)	29 (13.8)	19 (11.8)
Median follow-up, in months (range)	98 (0–150)	99 (0–150)	98 (0–150)

[a] N=9 missing.
[b] N=2 missing.
[c] N=21 missing.
FNF = femoral neck fracture; SD = standard deviation; TAD = Tip-Apex-Distance; N/A= not applicable.

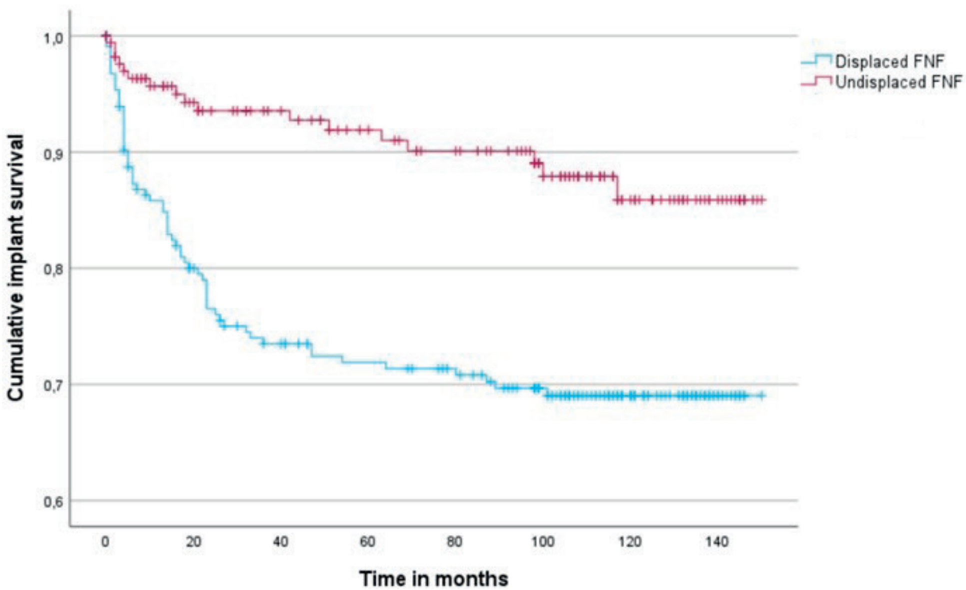

Figure 2. Kaplan–Meier curves for time to revision surgery in patients with displaced FNF and undisplaced FNF. Log-rank test, p<0.001.

Table 2. General complications in 389 femoral neck fracture patients

Complication	n
Urinary retention	4
Urinary tract infection	2
Delirium	19
Pneumonia	7
Ileus	2
Hypertension	1
Electrolyte disturbance	2
Decubitus	1
Cardiac event	6
Anaemia	1
Alcohol withdrawal seizure	1
Renal dysfunction	1
Heart failure	1
Total	48

Table 3. Perioperative complications in 389 femoral neck fracture patients

Complications	n
Wings of implant did not expand (partially)	9
Piece of drill head remained in femoral head	1
Fracture Related Infection	3
Gauze remained in wound	1
Device malfunction	1
Postoperative bleeding	6
Blade measured too short and was revised in a second operation	1
Total	22

The type and indications for revision surgery for dFNF and uFNF are presented in Table 4. Although the difference in indications for revision surgery did not reach statistical significance, dFNFs seemed to be more often revised due to AVN than uFNFs (46.0% vs. 29.4% p=0.22), while uFNFs seemed to more often need revision due to PTOA (47.1% vs. 25.4%, p=0.08). Figure 3 shows the Kaplan Meier curve for time to revision surgery per indication for revision for dFNF and uFNF together. Median time to revision for PTOA was 32 months and respectively 1, 4 and 14 months for cut-out, non-union and AVN (log rank test, p<0.001). In three patients treatment failed (two cut-out, one AVN), yet no revision was performed because the patients could not be operated; two patients had severe lung disease and one patient was 90 years old and had a poor clinical condition. Sixty-one (15.7%) DLBPs were electively removed after union.

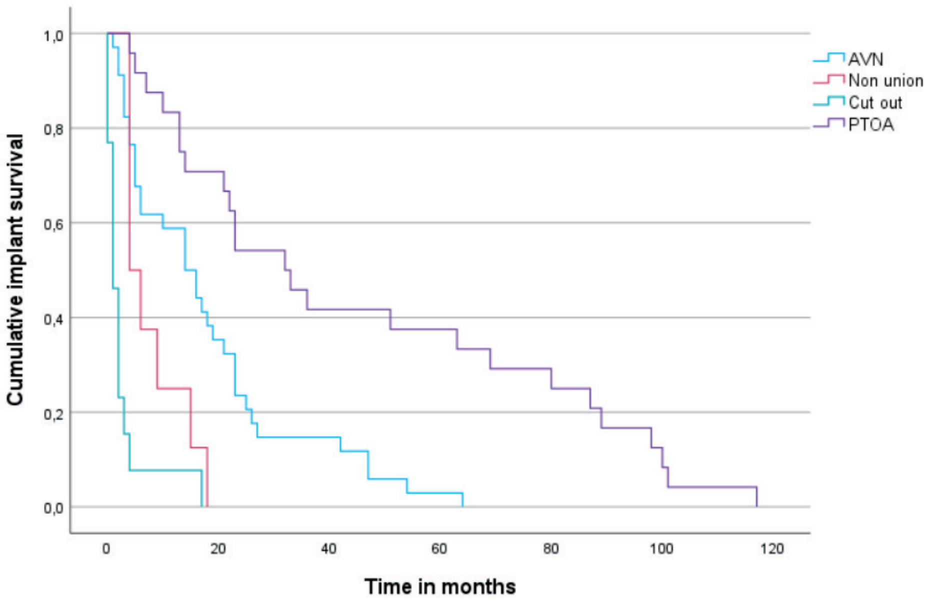

Figure 3. Kaplan–Meier curves for time to revision surgery by indication for revision. Log-rank p<0.001. AVN=avascular necrosis, PTOA=Posttraumatic osteoarthritis.

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Table 4. Type and indication for revision surgery after treatment with the Dynamic Locking Blade Plate

Revision type	Total n=80	Displaced FNF n=63	Undisplaced FNF n=17	p-value
Total hip arthroplasty, n (%)	74 (92.5)	58 (92.1)	16 (94.1)	0.78
Hemiarthroplasty, n (%)	6 (7.5)	5 (7.9)	1 (5.9)	
Indication				
Avascular necrosis, n (%)	34 (42.5)	29 (46.0)	5 (29.4)	0.22
Non-union, n (%)	8 (10.0)	7 (11.1)	1 (5.9)	0.52
Cut out, n (%)	13 (16.3)	10 (15.9)	3 (17.6)	0.86
Posttraumatic osteoarthritis, n (%)	24 (30.0)	16 (25.4)	8 (47.1)	0.08

[a] One patient in the displaced FNF group was revised abroad, the indication for revision could not be determined.
FNF = femoral neck fracture

The multivariable Cox proportional hazards regression analysis did not identify any predictors for revision surgery in the uFNF group (Table 5). Female gender (hazard ratio 1.99, 95% CI 1.14–3.49) and a TAD >25 mm (hazard ratio 2.66, 95% CI 1.52–4.67) were statistically significant predictors for revision surgery in patients with dFNF. Notable was that fracture reduction was not a significant predictor for revision surgery in the dFNF group. Yet in a multivariate analysis, fracture reduction was a significant predictor for AVN after dFNF (HR 2.90, CI 95% 1.20–7.01, Table 6). None of the other characteristics were predictors for AVN.

Table 5 Predictors for revision surgery of femoral neck fractures (FNF) treated with the Dynamic Locking Blade Plate: uni- and multi-variable Cox regression analyses

		Univariable analysis		**Multivariable analysis**	
Displaced FNF		*Hazard ratio (95% CI)*	*p-value*	*Hazard ratio*	*p-value*
Gender	Male	Reference			
	Female	1.70 (1.02–2.83)	0.04	1.99 (1.14–3.49)	0.02
Surgeon	Surgeon	Reference			
	Surgical resident	1.06 (0.55–2.02)	0.87	1.04 (0.53–2.04)	0.91
TAD	≤25 mm	Reference			
	>25 mm	2.20 (1.31–3.69)	0.03	2.66 (1.52–4.67)	<0.001
Age	≤65 years	Reference			
	66–75 years	1.50 (0.89–2.57)	0.13	1.33 (0.76–2.33)	0.32
	>75 years	1.28 (0.56–2.90)	0.56	1.47 (0.64–3.38)	0.36
Reduction	Adequate reduction	Reference			
	Inadequate reduction	1.75 (0.93–3.29)	0.83	1.53	0.22
Undisplaced FNF					
Gender	Male	Reference			
	Female	2.71 (0.78–9.44)	0.12	2.79 (0.78–10.02)	0.12
Surgeon	Surgeon	Reference			
	Surgical resident	2.76 (0.97–7.87)	0.06	2.30 (0.76–6.95)	0.14
TAD	<25 mm	Reference			
	≥25 mm	1.16 (0.38–3.54)	0.80	1.64 (0.51–5.23)	0.41
Age	≤65 years	Reference			
	66–75 years	2.08 (0.67–6.49)	0.21	1.85 (0.58–5.97)	0.30
	>75 years	1.40 (0.42–4.68)	0.59	1.45 (0.43–4.91)	0.55
Posterior tilt	≤20°	Reference			
	>20°	1.80 (0.68–4.72)	0.24	1.87 (0.70–5.01)	0.22

DISCUSSION

In this study we evaluated the revision rate of FNF treated with the DLBP during a minimum follow-up of seven years. The revision rate was 10.0% in uFNF and 28.8% in dFNF. Long-term results of large prospective multicentre cohorts of patients with FNF are rare in literature. There are only few studies investigating outcomes of more than 100 patients with FNFs treated with IF, with a follow-up of at least five years.[23-27] All of these studies concerned treatment with cannulated screws or pins. The rates of revision surgery presented in these studies range from similar to our results to much higher percentages, 31.3–45.6% in dFNF and 10.7–19.0% in uFNF. We have not been able to find any large, long-term studies of

Table 6. Independent predictors for avascular necrosis of the femoral head (AVN) of patients with displaced femoral neck fractures (FNF) treated with the Dynamic Locking Blade Plate: uni- and multivariable Cox regressions

		Univariable analysis		**Multivariable analysis**	
Displaced FNF		*Hazard ratio (95% CI)*	*p-value*	*Hazard ratio*	*p-value*
Gender	Male	Reference			
	Female	1.50 (0.72–3.15)	0.28	1.45 (0.64–3.28)	0.38
Surgeon	Surgeon	Reference			
	Surgical resident	1.30 (0.53–3.19)	0.57	1.44 (0.56–3.74)	0.45
TAD	≤25 mm	Reference			
	>25 mm	1.73 (0.78–3.82)	0.18	1.77 (0.75–4.20)	0.20
Age	≤65 years	Reference			
	66–75 years	1.01 (0.44–2.34)	0.98	0.85 (0.35–2.10)	0.72
	>75 years	1.44 (0.48–4.30)	0.51	1.79 (0.58–5.50)	0.31
Reduction	Adequate reduction	Reference			
	Inadequate reduction	2.89 (1.27–6.55)	0.01	2.90 (1.20–7.01)	0.02

FNF treated with a DHS. However, studies with a short (i.e. 12 to 24-month) follow-up have shown revision rates of 24–41% in dFNF and 9.8–16.3%.[9, 28-29] Low implant volume and high angular and rotational stability may attribute to improved stability of the fracture-implant complex and subsequent lower revision rates. However, it also could be that these five studies included predominantly older people, with an average age of 77–82 years for patients with a dFNF and 79–81 years for patients with a uFNF, compared to 63 and 70 years respectively in our study.[23-27] These age differences render comparison of results and interpretation of findings of these studies difficult.

In concordance with earlier findings in literature, dFNFs were revised more often than uFNFs (28.8% vs 10.0%). These numbers are higher than previously reported revision rates of the DLBP with a follow-up of one year.[5,6] In our cohort the median time to revision surgery was 13 months for dFNF and 18 for uFNF. Other studies also found a median time to revision surgery of more than one year.[10-13] Figure 2 demonstrates dFNF were revised more often in the first 24 months. This might be due to the specific indications for revision. We found that 46% of the dFNFs needed revision surgery because of AVN, in comparison to 29.4% of uFNF. UFNFs were more often revised because of PTOA (25.4% vs 47.1%). Although this difference is not significant, probably because of the low rate of revisions in the uFNF group, the results present a trend regarding the different indications for revision surgery in dFNFs and uFNFs. Figure 3 shows that AVN was revised at an earlier stage than PTOA. Median time until revision for AVN was 14 months and 32 months for PTOA. Thirty percent of all revisions were due to PTOA. These numbers are corresponding with the 35–38% described in literature.[14,30] However, there is no other literature describing time to PTOA and overall incidence of PTOA after FNF.

We could not find any independent predictors for revision surgery in uFNFs. This might be due to a lack of statistical power with only 17 revisions in the undisplaced fracture group of 170 patients. The inherent stability of an undisplaced fracture and the preservation of a significant portion of vascularization in these fractures will probably be the main factors that attribute to low revision rates. Female gender and a TAD >25 mm showed to be independent predictors for revision surgery in displaced hip fractures and increased the risk respectively 2.0 and 2.7 times. A recent meta-analysis provided an overview of predictors for revision of internally fixated dFNFs and also identified female gender as a predictor for revision surgery (OR 1.78, 95% CI 1.26–2.52).[31] TAD was not associated with a higher risk of revision surgery in this systematic review. However only one included study in this review described TAD as a possible predictor and interestingly, this study utilized the same population as the current study with one year follow-up.[6] TAD is widely described as a predictor for failure after fixated extracapsular fractures but not for intracapsular FNFs.[32] On the other hand, reduction of the fracture has been widely described in literature as a predictor for revision surgery after internal fixation of FNFs.[31] However, based on our data, fracture reduction did not emerge as a significant predictor. Fracture reduction has a large influence on the vascularisation of the femoral head and therefore on the risk of AVN. Due to the long follow-up of this study a rather large amount of patients with dFNFs were revised because of PTOA (25.4%). The follow-up in the studies included in the meta-analysis of Kalsbeek et al. was 24 months at most versus a median follow-up of 98 months in this study. Possibly these patients are mainly revised due to AVN and therefore reduction has more influence on the revision rate. We could not retrieve information on the proportion of FNFs that needed revision because of AVN in the studies included in the meta-analysis. To test the hypothesis that reduction of the fracture is a predictor for AVN we performed a multivariable Cox regression analysis on our data (Table 6). Fracture reduction was a predictor for AVN in dFNF (HR 2.90, CI 95% 1.20–7.01). This indicates that reduction of the fracture is essential to ensure viable vascularisation to the femoral head and prevent AVN.

PTOA may occur due to the fact that a fractured hip, even with optimal reduction, will never fully regain its original anatomical integrity. Due to these (little) biomechanical changes the load distribution through the hip differs and accelerates decline of joint cartilage. Furthermore, a decreased vascularisation of the femoral head and cartilage after an FNF in elderly patients could impair the ability to slow this increased degeneration.

Strengths of this study are its large cohort, its prospective inclusion of the patients, long follow-up and the small percentage of patients lost to follow-up. A small part of the data was collected retrospectively. This causes limitations inherent to a retrospective set-up. Furthermore, we studied a young population with FNFs whereas most other studies will show a higher average age of their study population. This age difference renders comparison between groups difficult. Other limitations are the absence of a valid functional outcome and the lack of registration of more possible predictors for revision surgery, such as smoking [31].

CONCLUSION

This study is the first long-term follow-up study on the outcome of the DLBP and first large long-term cohort study of FNFs with a relatively young population. Although study populations differ throughout literature and are not exactly comparable to our patients cohort, the DLBP demonstrated positive long-term results in the treatment of FNFs, with an overall 7-year revision rate of 20.6%, a revision rate of 28.8% for dFNF, and 10.0% for uFNF. Our study identified female gender and a TAD >25 mm as predictors for revision in dFNF.

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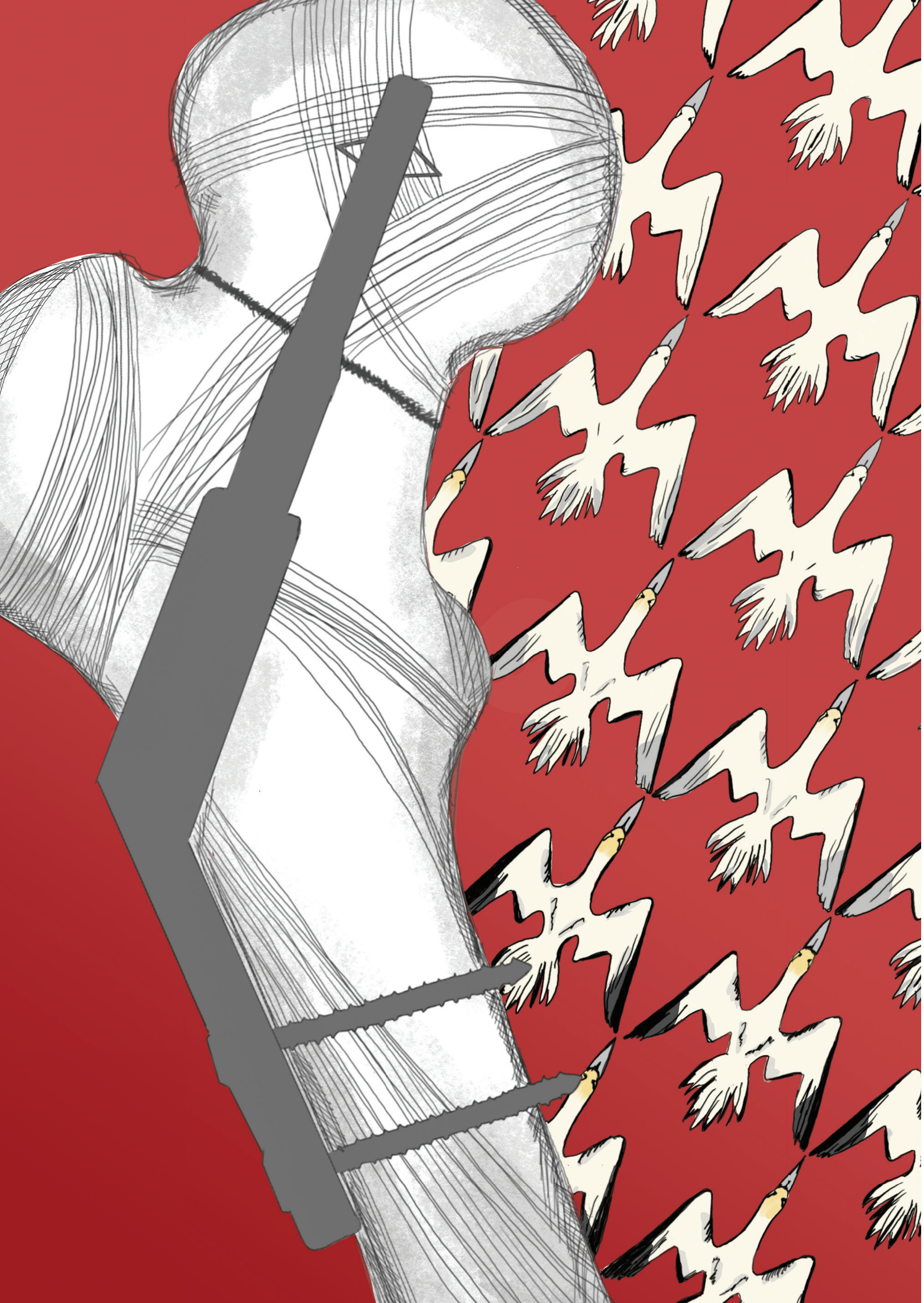

Chapter 7

Study protocol for the DEFENDD trial: an RCT on the Dynamic Locking Blade Plate versus the Dynamic Hip Screw for displaced femoral neck fractures in patients 65 years and younger

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BMC Musculoskeletal Disorders. March 2020;21(1):139-x.

ABSTRACT

Background

The Dynamic Locking Blade Plate (DLBP) was recently introduced for fixation of displaced femoral neck fractures (FNF) and has been well received. Although the results of this implant in young patients are promising, the DLBP has not yet been compared to a standard device such as the Dynamic Hip Screw (DHS). The aim of this study is to compare the clinical outcome and costs of displaced FNF treated with internal fixation by means of either the DLBP or the DHS in patients up to 65 years of age. We hypothesize that the DLBP is superior compared to the DHS in terms of revision surgery rate, union rate, incidence of avascular necrosis and implant related failure.

Methods

The DEFENDD trial is a multicentre randomized controlled trial that includes 266 patients of 18–65 years with a displaced FNF. Patients will be randomized to receive either a DLBP or a DHS with a 1:1 allocation using a random block size, stratified for centre. Clinical follow up will last one year and questionnaires will be obtained up to two years. The main outcome parameter is the incidence of revision surgery within one year, due to either non-union, avascular necrosis (AVN) or cut out of the implant. Secondary study parameters are the incidence of avascular necrosis, non-union, (implant related) complications, functional outcome, elective removal of the implant and health-related quality of life and costs.

Discussion

The outcome of the DEFENDD trial will provide high-level evidence of which implant is favourable for the treatment of femoral neck fractures in young patients (≤65 years).

Trial registration

Netherlands Trial Register, NL7300 Registration date 25-09-2018.

BACKGROUND

In 1990 an estimated 1.66 million patients sustained a hip fracture worldwide. This number has increased over time and is estimated to be around 6 million in 2050 worldwide.[1] Despite these numbers the optimal treatment of hip fractures is still under debate and subsequently evolving. This especially applies to the treatment of displaced femoral neck fractures (FNFs), which differs considerably worldwide. A general consensus is that young patients (up to 65 years of age) should be treated with fracture reduction and internal fixation.[2,3] Patients above 75 years of age are in majority treated with arthroplasty. The treatment of FNFs in young elderly (between 65 and 75 years old) is still under debate and is therefore referred to as the 'unsolved fracture'.[4-6]

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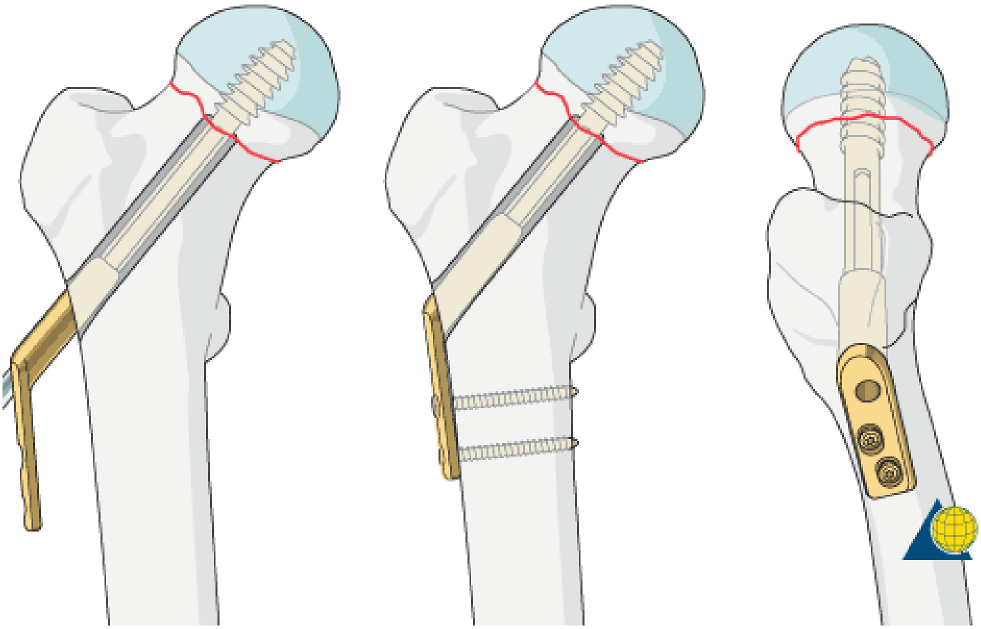

Figure 1. The Dynamic Hip Screw (DHS).[24]

Nowadays, the most commonly used implants for fixation of FNFs are multiple cannulated parallel screws and the Dynamic Hip Screw (DHS) (Figure 1). The DHS has a small advantage over multiple parallel screws in displaced FNFs, in that it is known to have a lower reoperation rate.[7] Despite the frequent use of both these implants the failure rate of displaced FNFs is still high, with a non-union rate of 30–33% and an incidence of avascular necrosis (AVN) of 10–16%.[3,8-10] The reoperation rate, as a result of non-union and AVN is between the 18–48%.[3,10,11] The Dynamic Locking Blade Plate (DLBP) (Figure 2), otherwise called 'The

Gannet', is specifically designed for the surgical fixation of intracapsular hip fractures though small metal 'wings'. The characteristics of the DLBP are its low implant volume, rotational stability, angular stability and its simple instrumentation and surgical technique. In a prospective multicentre cohort study in the Netherlands 172 patients with an undisplaced FNF were treated with the DLBP. The results of this study showed a failure rate of 4%.[12] Another recent prospective cohort study of 106 patients of 60 years and younger with displaced FNF demonstrated a DLBP related failure rate of 13.2%.[13]

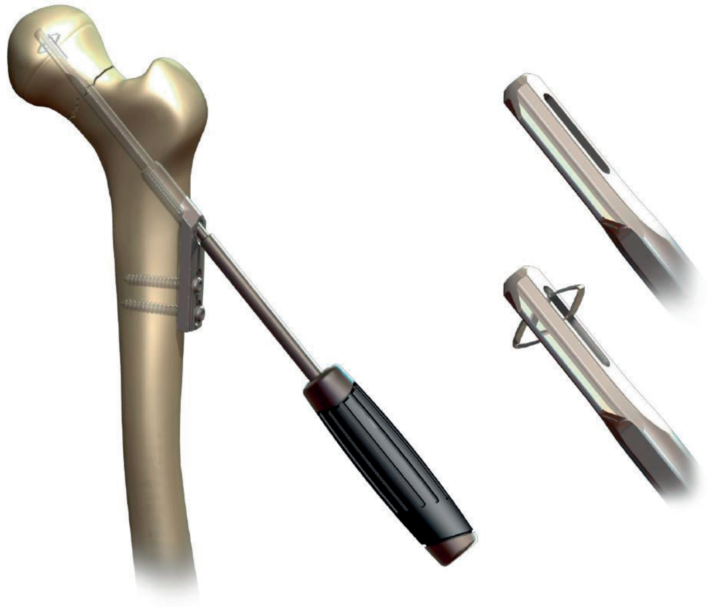

Figure 2. The Dynamic Locking Blade Plate with impaction anchors.

The aim of the current study is to test if these favourable results with the DLBP persist in a multicentre randomized controlled trial for patients aged 65 years or younger with initially displaced FNFs. We hypothesize that the DLBP is superior compared to the DHS in terms of revision surgery rate, union rate, incidence of avascular necrosis and implant related failure. Also, the cost-effectiveness of the DLBP versus DHS will be assessed.

METHOD/DESIGN

Primary and secondary objectives

The primary objective is to test if the incidence of revision surgery (primary endpoint) is lower in patients ≤65 years with an initially displaced FNF treated with the DLBP in comparison to treatment with DHS. Secondary objectives are to determine the incidence of AVN, non-union, implant related complications, non-implant related complications and elective removal after fixation with the DLBP or DHS. Also, we compare operating time, functional outcome and cost-effectiveness of DLBP and the DHS.

Study design

This is a multicentre unblinded randomized controlled trial with a superiority design comparing two implants. One group will be treated with the DLBP. The other group will be treated with DHS (control group). The study will be performed in six trauma centres in the Netherlands. Data will be registered in Castor EDC, an online data capture program.

Eligibility criteria

All consecutive patients between 18 and 65 years with a displaced FNF, Garden type III or IV according to the Garden classification, admitted to the participating hospitals are eligible for the study.[14]

Exclusion criteria

- Pathological fracture.
- Ipsilateral or contralateral fracture(s) of the lower extremity.
- Injury Severity Score (ISS) of ≥16.
- Local infection or inflammation at time of operation.
- Symptomatic arthritis, diagnosed by a rheumatologist.
- Symptomatic osteoarthritis or radiographic osteoarthritis grade III or IV.[15]
- Previous surgery of the ipsilateral hip.
- Open fracture.
- Morbid obesity (BMI ≥35).
- Patients who were wheelchair-bound in their pre-injury situation.
- Patients who were, at the time of trauma, admitted to a nursing home.
- Patients who are not mentally competent

Randomization

After obtaining written informed consent patients are randomized with a 1:1 allocation using a random block size, stratified for centre. Variable block sizes will be determined by the estimated inclusion number of each centre. An online randomization module is used for treatment allocation.

Sample size calculation

The failure rate or revision rate of the DHS in patients ≤65 years with displaced FNFs described in today's literature is 32–44%.[7,16] The failure rate of the DLBP in patients of 60 years and younger with a displaced FNF in a previous cohort study was 13.2%.[13] Analysis of our data showed a failure rate of 15% for the DLBP in patients of 65 years and younger (non-published data). For the determination of the sample size we assumed a 30% failure rate for the DHS and 15% failure rate for the DLBP. For a power of 80% we need 121 patients per group to prove the superiority of the DLBP regarding the primary outcome (need for revision surgery) with alpha of 5% in a two-sided test. Taking into account that up to 10% of the patients may be lost to follow up, 266 patients need to be included for adequate statistical power, i.e. 133 patients per group.

Study interventions

This trial will be performed in six trauma centres in the Netherlands. In three of the centres the DLBP will be introduced before starting this trial. In the other three participating centres the DLBP is already used. A learning curve is taken into account. The first three DLBP's in each participating centre will be implanted under supervision of an instructor from the manufacturer or an experienced surgeon who has implanted three or more DLBP's. The first DLBP's of a surgeon can be included, provided that they are implanted under supervision.

Dynamic Locking Blade Plate

The Dynamic Locking Blade Plate consists of a 2-hole standard 135° side-plate combined with a low-volume cannulated dynamic locking blade (Figure 2). The side plate provides angular stability combined with dynamic axial compression of the fracture. Two side wings at the tip of the blade provide rotational stable fixation of the locking blade in the femoral head combined with a high weight-bearing surface. The expandable impaction anchors lock the blade in the femoral head and prevent perforation and backing out of the implant and further augment the rotational stability. The DLBP is now marketed as the Gannet.[12]

Dynamic Hip Screw

The control group will be treated with the Dynamic Hip Screw, a stainless steel lag screw in the femoral neck and head that is fixated to the femur shaft with a compression plate using two-four 4.5 mm cortical screws (Figure 1). The DHS is used globally and is provided by a wide range of commercial producers in various sizes. It can be implanted with or without an additional cannulated antirotational screw. The type of DHS used in the control group is at the discretion of the surgeon. The trauma and orthopaedic surgeons in participating trauma centres have a wide experience with internal fixation of FNF by means of DHS.

Direct post-operative care

Both groups receive standard care including direct mobilization after surgery. Mobilization therapy will be given by a physiotherapist according to the hospital protocol for hip fracture after care. All patients receive low-molecular-weight heparin anticoagulation therapy during their stay in the hospital.

Study procedures

A time schedule of procedures and measurements is presented in Table 1. The selection of eligible patients will take place in the emergency department (ED). According to standard care, X-ray examinations of the pelvis and hip are made on admission and assessed by the radiologist and trauma surgeon. Eligible patients will receive oral and written information about the study from the physician in the ED. The patients have at least six hours to consider participation in the study and will be given the opportunity to ask questions about the study. Written informed consent will be obtained by the surgical resident or the surgeon after admission to the ward. Randomization will be done by the treating surgeon. After inclusion the patient will be allocated to one of the two study groups (DLBP or DHS) using an online randomization program. The baseline parameters will be registered by a nurse upon arrival on the surgical ward before surgery. The perioperative care will be the same for all included patients.

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Table 1. Time schedule for study procedures and measurements

	Emergency department	Admission	Post-op visit (≤5 days)	6 weeks follow-up	3 months follow-up	6 months follow-up	12 months follow-up	24 months follow-up*
Informed consent		x						
Baseline characteristics		x						
Radiography	x		x	x	x		x	
Questionnaires		x		x	x	x	x	x
Complications registration		x	x	x	x		x	x

* Contact by telephone

Surgery will be performed by an (orthopaedic) trauma surgeon or by an (orthopaedic) trauma resident under the direct supervision of an (orthopaedic) trauma surgeon. The aim is to operate within 24–36 hours based on the Dutch guidelines for treatment of FNFs.[17] After surgery, details about the surgery will be documented. After discharge patients are scheduled for outpatient visits after 6 weeks, 3 and 12 months. Conventional radiographs will be taken and assessed during these visits (Table 1). The patients need to fill out a questionnaire before follow up visits and 6 months after discharge. Also, the patient will be contacted by telephone 24 months after enrolment in the study for additional questionnaires about mobility and complication registration.

Primary outcome parameter

The primary outcome is the incidence of revision surgery after fixation of an initially displaced FNF treated with DLBP or DHS due to non-union, AVN or cut out of the implant. This will be monitored during one year of follow up after surgery.

Secondary outcome parameters

Incidence of avascular necrosis: AVN is defined as hip pain in combination with radiographical signs for AVN as described by Steinberg.[18] According to the Steinberg classification AVN is present from stage 2 and upward. AVN will be assessed by the treating surgeon. As is customary in the Netherlands, all radiographs are also assessed by a radiologist.

Incidence of non-union: there is no consensus in the literature regarding to the definition of (non-)union.[19] Our definition of non-union is based on the Radiographic Union Score for Hip (RUSH).[20] Non-union is a visible fracture line on the radiograph, absence of cortical bridging or bridging trabeculae over the fracture site in combination with persisting pain in the hip and the inability to bear weight at least 9 months post-operative or sooner if revision surgery was performed because it was no longer expected that fracture healing would occur. Non-union will be assessed by the treating surgeon.

Incidence of implant related complications: an implant related complication is defined as breakage or cut-out of the plate or screws, inadequate expansion/malfunction of the anchors or any malfunction of the implant which may or may not lead to revision surgery. Implant related failure will be monitored during one year of follow up.

Post-operative complications: post-operative complication is defined as any unanticipated event other than the above mentioned, for which operative treatment or medical treatment is required, e.g. wound infection, bleeding or pneumonia. Every complication occurring during the hospital stay of the patient will be recorded.

Rate of elective implant removal after union: Elective implant removal after union will be recorded during one year of follow up after surgery. Reasons for elective removal will be described.

Functional outcome: patient-reported post-surgical function will be scored using the validated Dutch version of the International Hip Outcome Tool (iHOT-12NL).[21] The iHOT-12NL is a patient-reported questionnaire that measures health-related quality of life and physical function in younger, active patients with hip disorders. Scores on the iHOT-12NL range between 0–100 (worst – best possible function). This questionnaire will be filled out by the patient during admission and at 6 weeks, 3, 6 and 12 months follow up.

Operation time: the operation time is recorded in the surgical report.

Baseline parameters: Additional parameters that will be recorded are: sex, date of birth, general health score (using the ASA classification), fracture type and side, trauma surgeon or orthopaedic trauma surgeon, type of anaesthesia, Body Mass Index. These parameters will be assessed during admission as a baseline measure.

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Costs: Costs will be assessed from a societal perspective. Cost of (revision) surgery will be calculated using a bottom-up approach. Using a questionnaire the patients will report other health care use such as physiotherapy, rehabilitation care or nursing home care, visits to the general practitioners and medical specialists and medication, and non-medical care (domestic help and absenteeism). This questionnaire will be filled out by the patient at 6 weeks, 3, 6 and 12 months follow up. Health care use will be valued using Dutch reference prices.[22]

Health related quality of life: the EuroQol (EQ-5D-5L) questionnaire measures five dimensions (mobility, self-care, daily activities, pain/discomfort, anxiety/depression), on a five-point scale (no, some, moderate, much or extreme problems). For each health state described by the patients, a utility score can be calculated that reflects society's valuation of that health state.[23] In addition, patients rate their overall health-related quality of life on a Visual Analogue scale (VAS). This questionnaire will be filled out by the patient during admission and at 6 weeks, 3, 6 and 12 months follow up. The utility scores obtained by the descriptive system and the VAS will be used in the cost-effectiveness analysis.

Statistical analysis

Statistical analysis will be performed using SPSS (IBM Corp., Armonk, NY, USA). Primary analysis will be done according to the intention-to-treat principle. If patients are not treated according their allocated treatment a per-protocol analysis will be conducted to confirm the intention-to-treat analysis. Baseline characteristics of the treatment groups will be presented as mean with SD or as median and range for continuous variables and as number and percentage for categorical variables.

The primary outcome parameter, the incidence of revision surgery after one year, will be compared between the treatment groups using logistic regression analysis, including study centre as a covariate, since some study sites have used the DLBP for several years and whereas in other medical centres the DLBP has only been introduced recently. In literature there is no clear evidence of other covariates that have a strong or moderate association with the primary outcome. The secondary parameters: the incidence of AVN, non-union, implant-related complications, post-operative complications, and elective implant removal after one year will be analysed in the same manner as the primary outcome parameter. Operation time will be compared between the treatment groups using the independent samples t-test or the Mann-Whitney test, as appropriate. Functional outcome at the specified follow-up moments will be compared between the treatment groups using an independent samples t-test. In addition, the course of functional recovery over time will be compared using a linear mixed model with time, treatment and baseline characteristics as fixed effects, and patient as random effect. Missing data will be imputed using multiple imputation before testing the differences in the outcome parameters. P-values less than 0.05 will be considered statistically significant.

The economic evaluation will compare differences in societal costs, as described in the paragraph 'Study parameters', to differences in quality adjusted life years (QALYs). Utilities obtained from the EQ-5D-5L will be used to determine QALYs. The QALYs will be calculated from the area under the curve in a utility-time figure. The duration of the trial will be taken as the time-horizon. Group averages will be statistically compared using non-paired t-test and a net-benefit analysis will be used to compare costs to patient outcome. Results will be presented in a cost-effectiveness acceptability curve.

Monitoring

Patient data will be handled confidentially and in compliance with the Dutch Personal Data Protection Act. Collected data will be stored in Castor EDC, an electronic data capture program. Stored data will be coded, using a unique combination for centre and successive study number. The key to the code will be accessible by the local investigators and the coordinating investigators. Study data will be kept for 15 years and destroyed afterwards. The local investigators will have access to the link between code and personal data of the patients of only his centre. The coordinating and the principal investigator have access to all the data. The co-investigators will have access to the coded data of all patients.

The coordinating investigators will report all adverse events to the accredited Medical Research Ethics Committee (MREC) that approved the protocol. No data safety managing board is installed. The investigator will submit a summary of the progress of the trial to the accredited METC once a year. Information will be provided on the date of inclusion of the first subject, numbers of subjects included and numbers of subjects that have completed the trial, serious adverse events/ serious adverse reactions, other problems, and amendments. No planned interim analyses will be conducted.

DISCUSSION

In this paper we present the rationale and design of a randomized controlled trial that compares the clinical outcomes of the DLBP and the DHS. The DHS is a globally accepted osteosynthesis and it has been for decades. Yet the failure rate is high. The DLBP is a new implant that is on the market since 2010. Today's evidence for this implant is not as wide-spread as for the DHS, but the results from earlier studies are promising. The outcome of the DEFENDD trial will provide high-level evidence of which implant is favourable for the treatment of femoral neck fractures in young patients (≤65 years). The results of this trial will be published in peer-reviewed international journal.

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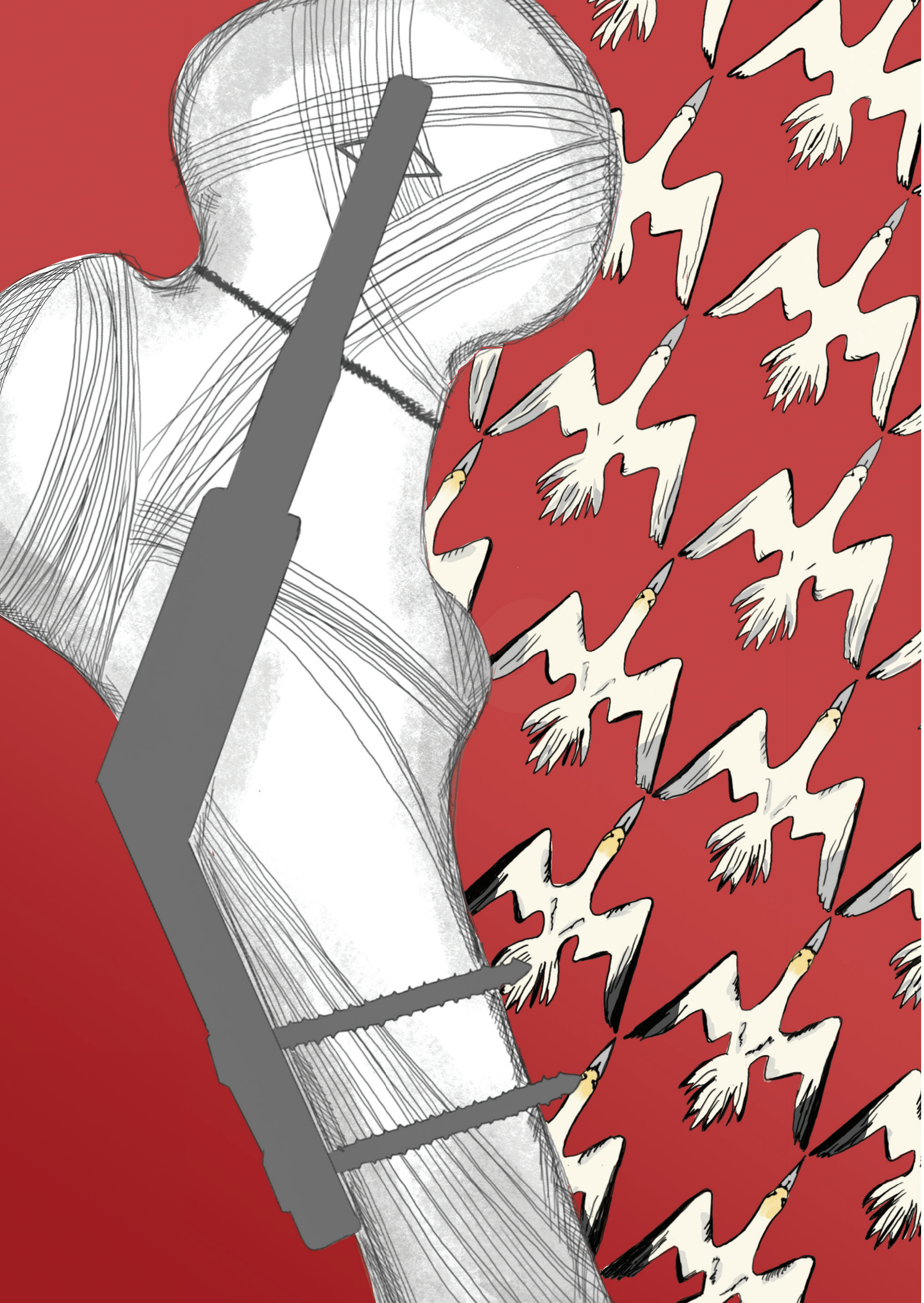

Chapter 8

Discussion, clinical implications, and future perspectives

This thesis does not provide a simple answer on how to treat patients with Femoral Neck Fractures (FNFs). Treatment of a patient with an FNF requires a proper assessment of, and a good conversation with the patient. Successful fracture treatment depends on various factors. Some factors are related to the patient characteristics, others depend on the type of fracture, and again other factors are controlled by the treating surgeon and the treatment of choice. We have to know and recognize these factors, weigh them properly and discuss the treatment options with the patient for the optimal individualised care for each of the FNF patients.

FRACTURE RELATED FACTORS

Almost a century ago, Gathorne Girdlestone stated: '*For a bone is a plant, with its roots in the soft tissues and, when its vascular connections are damaged, it often requires not the technique of a cabinet-maker, but the patient care of a gardener.*'[1] This is particularly applicable to the intracapsular FNF, due to its unique biological features. Displacement of the femoral head is the most crucial factor affecting treatment outcome.[2,3] As described in the introduction of this thesis the healing of the FNF depends on primary bone healing. Primary bone healing requires anatomical alignment of the femoral neck to ensure direct osteonal reconstruction in absence of callus formation. In undisplaced FNF (uFNF) this anatomical alignment and the vascular supply is not significantly disturbed.[4] Undisplaced, stable FNFs are defined as Garden classification type 1 and 2 fractures on the anteriorposterior radiograph.

In **Chapters 3 and 4**, based on the results of the studies, we propose posterior tilt to be included in the assessment of displacement of the FNF (Figure 1). Posterior tilt of ≥20° increases the risk of reoperation fourfold. This significant posterior tilt of the femoral head renders the FNF an unstable fracture. Due to the small number of patients with failed treatment, our conclusion on posterior tilt in **Chapter 3** could not yet been tested in a multivariate regression analysis, which limits the generalisability of the conclusion. But it is supported by the results of a recently published systematic review and meta-analysis.[5] They state that the reoperation rate of uFNFs with a posterior tilt of ≥20° increases from 10.3% to 24.5% (overall risk ratio of 0.11 (95% confidence interval; 0.04–0.18)) compared to uFNF with a posterior tilt of <20°. In that perspective it is interesting that the current Dutch guideline for proximal femur fractures states the Garden type I and II are uFNFs based on the AP view, without considering the lateral radiograph and thus the posterior tilt as an indicator for displacement.[6]

Following our results and conclusions of **Chapters 3 and 4** we recommend, also for the future Dutch guideline, to use the 'Modified Garden Classification' to determine the stability of a FNF (Figure 2).[7] This classification adds posterior tilt to the original Garden classification. The posterior tilt should be measured using the Posterior Tilt Measurement (PTM) according to Palm[8] (Figure 3), because in **Chapter 4** we showed that the PTM is more reliable than the Lateral Garden Angle[9], or any morphological measurement. Displacement in posterior direction influences anatomical alignment and vascular blood supply, just like varus angulation in the coronal plane, but posterior tilt is also often accompanied by posterior comminution (Figure 1). In **Chapter 2,** one of the included studies for our systematic review identified posterior comminution as a predictor for reoperation.[10] It may influence the postoperative stability of the fracture because a gap in the posterior cortex could remain after reduction of the fracture. However, the lack of a good definition of posterior comminution, and solid scientific evidence on the predictive value of posterior wall comminution, prevents a substantiated answer on the question if posterior wall comminution influences the revision rate of FNFs treated with internal fixation (IF).[10-13]

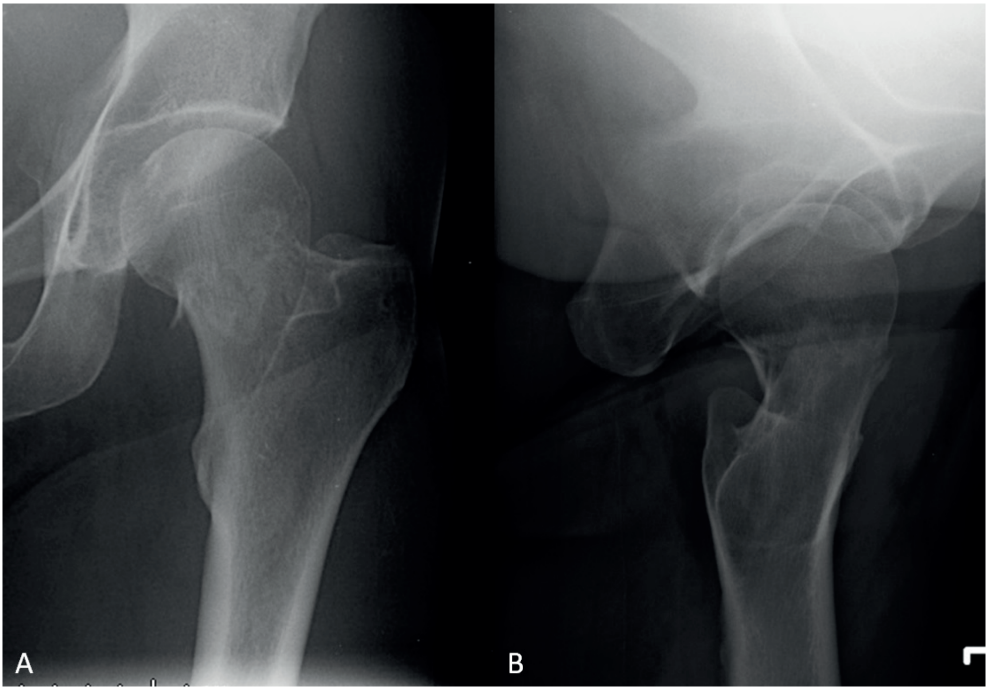

Figure 1. A: Anteriorposterior radiograph of a 'non-displaced' FNF. **B:** Lateral radiograph of a FNF with posterior tilt of the femoral head and comminution of the posterior cortex.
FNF: Femoral Neck Fracture

PATIENT RELATED FACTORS

The phrase: *'There is a fracture. I need to fix it!'* is well-known within the orthopaedic trauma community. Although the discussion in this cartoon about administering anaesthesia to a deceased 97-year-old with a femur fracture is an exaggeration, it holds valuable lessons.[14] With over three-quarters of the proximal femur fractures occurring in patients older than 75 years of age, the comorbidity in most patients with a FNF is high.[15] Undoubtedly, the surgeon must assess the patient thoroughly before he or she chooses if and how to fix the fracture. It is still debated which of the many patient characteristics influence the healing of FNF and to what extent. The Dutch guideline for treatment of patients with proximal femur fractures only identifies renal failure (CKD eGFR <60 ml/min/1.73 m^2) as a strong predictor for reoperation in patients with a FNF.[6] However, their recommendation is based on the review of only four studies.[16-19] This limited overview of literature made us conduct a systematic review and meta-analysis in **Chapter 2** in a search for factors that might be of influence on failure of FNF healing. We screened 2348 studies and identified female gender, age above 50, smoking, inadequate fracture reduction and treatment with cannulated screws as predictors for revision surgery in displaced FNFs (dFNFs), treated with IF. Notably, renal failure was not found to be a predictor for revision surgery. Moreover, we did not even include the two studies mentioned in the Dutch guideline. This was because the primary endpoint in our analysis was revision surgery, and Duckworth et al. also included patients in their analysis that sustained non-union or avascular necrosis of the femoral head (AVN) without revision surgery. Kuo et al. included both non-displaced and displaced FNFs in their analysis and our review focussed solely on dFNFs. We specifically defined our endpoint the way we did as revision surgery due to non-union, cut-out or AVN is a clearly defined and objective endpoint. Other outcome parameters, like the diagnosis non-union, cut-out or AVN are often subjective and debatable. For example, there is no consensus on a uniform definition of non-union.[20] Furthermore, the diagnosis of AVN is mainly based on plain radiographs and can easily be missed at early stages.[21] The explicit outcome 'revision surgery', however, may have one drawback, since it might have led to the exclusion of papers describing potential predictors for failure of FNF healing, defined by other endpoints. Nevertheless, in our analysis 24 factors potentially influencing the risk of revision surgery were identified, from which several patient characteristics were quantified as strong predictors for revision surgery. Therefore, when deciding on the treatment strategy and planning for IF or arthroplasty for a patient with a dFNF, it is important to consider factors such as female gender, age above 50, and smoking.

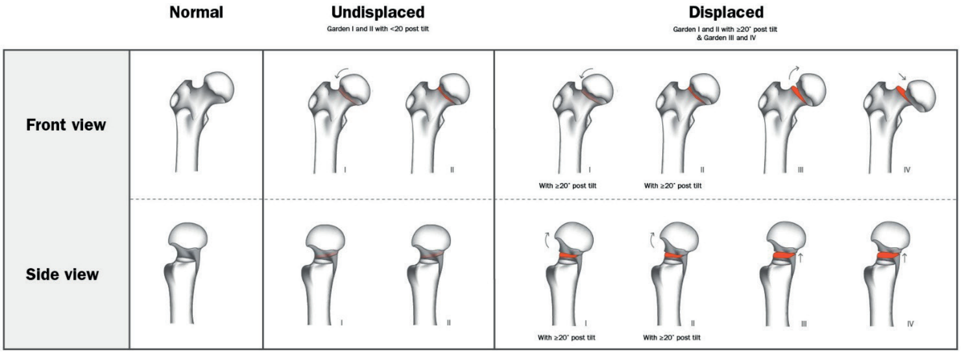

Figure 2. Modified Garden Classification including posterior tilt of the femoral head.[7]

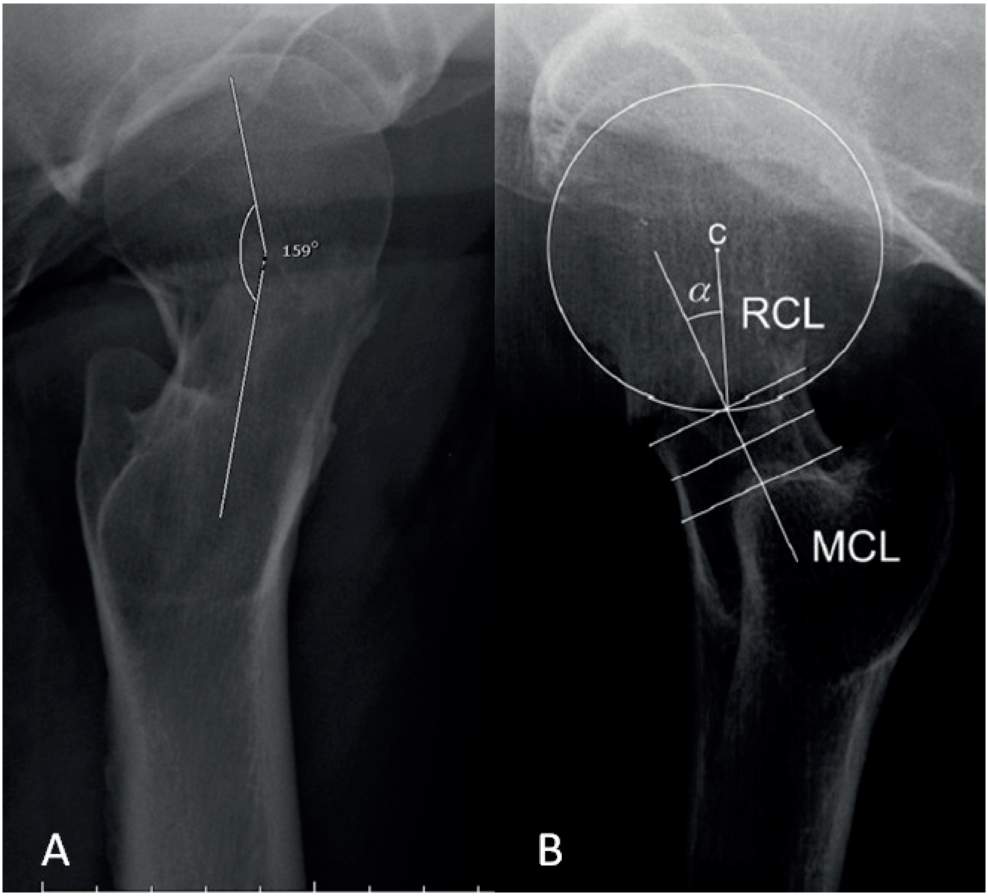

Figure 3. A: Lateral Garden Angle according to Keller.[9] B: Posterior Tilt Measurement according to Palm.[8]

OPERATION RELATED FACTORS

'We are not only justified but warranted in asserting that the only cause for nonunion in the case of intracapsular fractures is to be found in our inability to maintain perfect coaptation and immobilization of the fragments during the time required for bony union to take place – Senn, 1883' [22] Nicholas Senn already told us: the operation procedure is essential in the successful treatment of the FNF. As we described in previous chapters, reduction is the most important step of the procedure. Dislocation of the fracture may not only disrupt the retinacular vessels, the vessels may also become kinked or entrapped.[23] Therefore, early anatomic reduction allows vascularisation to restore. We showed in **Chapter 2** that inadequate reduction may double the risk of revision surgery (odds ratio (OR) 2.28, 95% CI 1.62–3.22) and may increase the risk of AVN in patients treated with the dynamic locking blade plate (DLBP) by almost three times (hazard ratio (HR) 2.90, 95% CI 1.20–7.01) as presented in **Chapter 6**. We did not find any evidence that argues for open reduction of the fracture, it is even associated with a greater risk of reoperation.[24] If adequate reduction (i.e. an acceptable range of 160–180° on AP and no more than 10° posterior tilt on the lateral X-ray) cannot be achieved during the operation the surgeon should consider converting to a prothesis. This may present logistical obstacles, as not all surgeons who perform IF are able to perform total hip arthroplasty. However, it may prevent the need for secondary surgery in the future.

After a good reduction a suitable devise has to be implanted for fixation of the fracture. Cannulated screws (CS) and the Dynamic Hip Screw (DHS), also known as the sliding hip screw, are globally the most used devises for internal fixation of FNFs.[25] In the Netherlands, the DHS is used more frequently than CS to fixate hip fractures, with rates of 13.1% and 5.3%, respectively.[26] In 2017, the FAITH trial, a large international randomized controlled trial (RCT), showed a slight advantage of the DHS over CS in dFNFs.[3] Additionally, as shown in **Chapter 2**, fixed-angle devices are superior to CS in terms of revision surgery (OR 2.16, 95% CI 1.03–4.54). This can be well explained, as fixed-angle devices have been shown to provide better angular and rotational stability, as discussed in **Chapter 5**. The argument that CS are less invasive might be true for the skin incisions, three/four stab incisions versus a small 5 cm incision for the fixed-angle device, but the total implant load is at least as invasive in the femoral neck and head as the DHS, as is described in **Chapter 5**. Taking this into account, a fixed-angle device is preferred over CS for fixation of FNFs.[27] Yet, are we satisfied with the results of the fixed-angle devices, like the DHS, that we have been using for decades? And is (biomechanical) implant improvement a necessary and realistic option?

THE DYNAMIC LOCKING BLADE PLATE

The Gannet, a seabird with streamlined wings that can reach up to two meters in length. The name ‘Gannet’ is derived from Old English ‘ganot’ meaning strong. This applies perfectly to the Gannet implant, also called the Dynamic Locking Blade Plate (DLBP) (Figure 4, 5). The idea of the Gannet originated twenty years ago from the lack of a strong and stable fixation for the FNF. Earlier biomechanical studies provided evidence that the DLBP offers a three times better rotational stability compared to the DHS.[28] This is achieved by a smaller implant volume compared to the DHS and CS, which have volumes of 2700 mm^3 and 2520 mm^3 respectively. The DLBP has a volume of only 1800 mm^3, making it a less invasive option.[29] Moreover, the frontal area of the DHS is 133 mm^2 and 31 mm^2 for the DLBP which has a lower impact on the small femoral neck, yet a higher load bearing surface of respectively 221 mm^2 versus 338 mm^2.[28] The operation technique of the DLBP is simple and straightforward and it does not require anti-rotation screws or k-wires during or after implantation.[30] Because the DLBP has to be tapped in and not screwed in like the DHS, the femoral head will not rotate during insertion which can be devastating for the remaining vascular supply. Although the biomechanical rationale and tests were favourable for the DLBP, it was unknown if this would actually result in less revision surgery in the clinical situation. The first large multicentre study of the DLBP showed promising results with a 4% revision rate in 149 uFNF in patients (mean age 69 years, range 35–101 years) compared to 8–14% described in literature.[31-33]

Figure 4. The Dynamic Locking Blade Plate, also know as the Gannet.

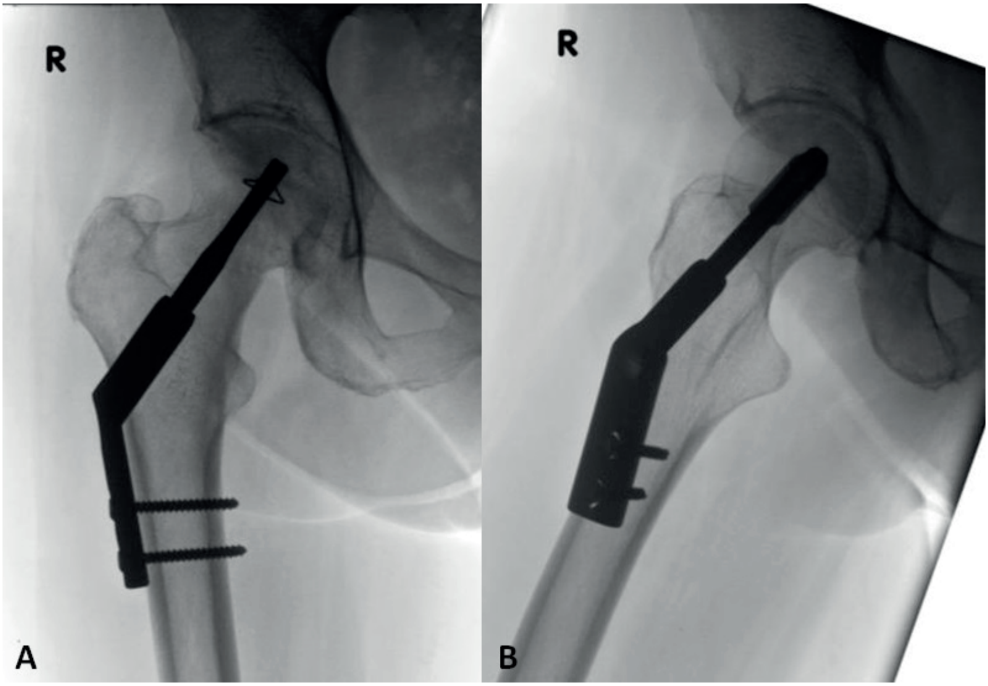

Figure 5. Intraoperative radiograph of the Dynamic Locking Blade Plate fixating a Femoral Neck Fracture.

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In **Chapter 5** we present the results of the second large cohort of 106 young patients with dFNFs treated with a DLBP. They showed a failure rate of 13.2% compared to 32–44% in literature for the DHS and other IF devices.[3,34] We do emphasize that prevention of revision surgery is one aspect of a successful treatment. Functional outcome, patient experience and patient satisfaction are other clinical outcome parameters that are at least as important as successful fracture healing. In **Chapter 5** we assessed functional outcome based on the need for walking aids.[29,31] This simple assessment is not sufficient for representation of the clinical situation as it does not consider factors such as pain or discomfort or assessment of activities of daily living. For example, femoral neck shortening (FNS) is a less familiar complication that may occur after IF of FNFs. FNS can significantly impair gait velocity, gait symmetry, physical function and quality of life.[35,36] The mean FNS after dFNFs treated with the DLBP was 7.1 mm, compared to 9.3–11.0 mm in literature.[35,37] The increased stability of the DLBP may reduce FNS and improve functional outcomes after FNF treatment. The lack of these functional outcome parameters poses a considerable limitation to the aforementioned two large prospective cohorts.

Literature states that most complications and reoperations will occur within two years, yet large cohorts with long-term follow-up of FNFs treated with IF are scarce.[38,39] To provide long-term follow-up insights for the DLBP we retrospectively analysed our first cohorts seven years after treatment of the first patient. In **Chapter 6** we present that revision rates of patients treated with the DLBP doubled within the seven years following their initial one-year follow-up. Revision surgery after two years was mainly because of posttraumatic osteoarthritis (PTOA), defined as having symptoms of osteoarthritis including pain, stiffness of the joint with or without radiologic findings of osteoarthritis in absence of AVN, non-union or cut-out of the implant. It is important to note that a proportion of the 389 patients in our study would also have had a hip replacement for osteoarthritis had they not fractured their hip. The 5-year incidence rate of total hip replacement for osteoarthritis in patients aged 69 years and younger is 1.9–5.6%.[40] The revision rate due to PTOA in our study was 6.2% (24 out of 389 patients). It is debatable whether it is always a failure of treatment if patients treated with the DLBP are revised after a longer period, after union of the fracture and due to PTOA.

Chapter 6 also demonstrated female gender and a Tip-Apex-Distance (TAD) of more than 25 mm as significant indicators for revision surgery of dFNFs treated with the DLBP. This higher revision rate in female patients is consistent with the findings in our meta-analysis presented in **Chapter 2**. TAD >25 mm did not emerge as a significant predictor in our review, as almost all studies on TAD and failure of fracture healing are described in patients with extracapsular and not intracapsular femoral fractures. The results of the DLBP are good compared to current literature. Revision rates are lower after treatment with de DLBP compared to cannulated screws or pins, 10.0% versus 10.7–19% in uFNF and 28.8% versus 31.3–45.6% in dFNF.[41-45] We have not been able to find any large, long-term studies of FNFs treated with a DHS. The DEFENDD trial in **Chapter 7** was designed to answer the question if the DLBP is superior to the DHS in treatment of dFNFs in all aspects of clinical practice. A population with dFNFs was chosen because, as described in the introduction of this thesis, displacement of the femoral head leads to instability of the fracture and high failure rates. Therefore, there is more to gain with a biomechanically stable implant in dFNFs than in uFNFs. Revision operation due to non-union, AVN or cut-out is the primary outcome parameter in this trial. Patients-reported outcome measures (PROMs) are also being acquired. Pre- and postoperative function and health-related quality of life questionnaires will be filled out by the patients up to one year postoperative. The DHS has been used globally for multiple decades and is provided by a wide range of commercial producers, making it a more cost-effective option compared to the DLBP. However, if the DBLP proves superior in terms of revision surgery and operation time, it may ultimately result in lower treatment costs. A cost-effectiveness analysis will provide these results.

Overlooking the evidence that is produced regarding the DLBP, we can state that the implant has improved the results of FNF treatment in terms of revision surgery. Level 1 evidence and PROMs are still to be provided by the DEFENDD trial.

CLINICAL IMPLICATIONS OF THIS THESIS

'Everything should be made as simple as possible, but not simpler' – Albert Einstein. Over the past decade, we strived to develop a treatment algorithm for FNFs, incorporating the DLBP, based on our own data and the most recent literature. However, this endeavour has proven to be more challenging than anticipated. Treatment of the FNF does not lend itself for a simple algorithm. As again shown in this thesis, the determination of the optimal treatment for FNFs depends on many factors and, most importantly, is a shared decision.

Despite the absence of a new treatment algorithm for the FNF, as a result of this thesis, the studies in this thesis still contribute to current knowledge on the topic in several ways:

- The original Garden classification requires modification as the lateral or axial radiograph should be incorporated in the Garden classification.
- If posterior tilt of the femoral head exceeds 20°, the related FNF should be considered a displaced and instable fracture, and should be treated accordingly.
- Posterior tilt should be measured using the Posterior Tilt Measurement according to Palm.[8]
- Patients with a dFNF should be treated with a fixed-angle device, preferably the DLBP and not with cannulated screws or pins.
- Patients with uFNFs of all ages can be treated with the DLBP. Female patients with a dFNF, age over 50 years and/or smoke, have a higher risk of revision surgery and therefore may be better treated with arthroplasty.
- If the surgeon is unable to achieve adequate reduction of the FNF they should consider converting to (hemi)arthroplasty.

This knowledge can assist surgeons in their daily practice, and it can complement future guidelines for the treatment of FNF.

FUTURE PERSPECTIVES

'*As for the future, your task is not to foresee it, but to enable it*.' – *Antoine de Saint Exupery*. Since 2023, the term "artificial intelligence" (AI) has emerged as the single most important concept in relation to future perspectives. The use of AI in FNF treatment may also be a potential avenue for future research. As previously discussed in **Chapters 2, 4 and 6**, the failure rate may double or triple if the fracture is inadequately reduced. However, the surgeon's decision regarding the adequacy of reduction is based on visual assessment alone, which resulted in almost 13% of inadequately reduced fractures. By employing artificial intelligence and machine learning, an intraoperative assistant can be developed to provide real-time, accurate assessments of femoral neck fracture reductions, that might significantly improve quality of reduction and treatment outcome.

Although a universal algorithm for the treatment of FNFs could not be produced, several treatment algorithms have been developed in the past.[46-48] These algorithms are based on the healing of the fracture and take patient and fracture-related factors like age, displacement of the fracture, comorbidity, cognitive impairment, limitations in ambulation or delay, into account. Yet none of these algorithms include patients' preferences or have conservative therapy as a treatment option. To successfully treat FNFs, it is important to identify the primary outcome parameter(s) based on the patients' preferences. This could be reluctance towards a prothesis, achieving full functional recovery or only attaining independence in activities of daily living, absence of any pain or the need for a minimal invasive procedure or one definitive operation. Even conservative treatment is a viable treatment option for frail patients with limited life expectancy.[49] Future research should compare PROMs for different therapies and determine the factors that influence these outcomes, such as FNS, rather than focusing on creating a comprehensive treatment algorithm for FNFs. Functional outcome and patient experiences after treatment with the DLBP should be compared to treatment with DHS or total hip replacement in a randomized controlled trial.

Additionally, it is necessary to aid both junior and senior physicians in discussing treatment options and outcomes with the patients. Especially in vital patients under the age of 70 with a dFNF, since the treatment strategy for these patient group is not definite. The development of a patient decision aid could be beneficial for doctors and patients. After all, a successful treatment is determined not only by union of the bone, but foremost by patient satisfaction.

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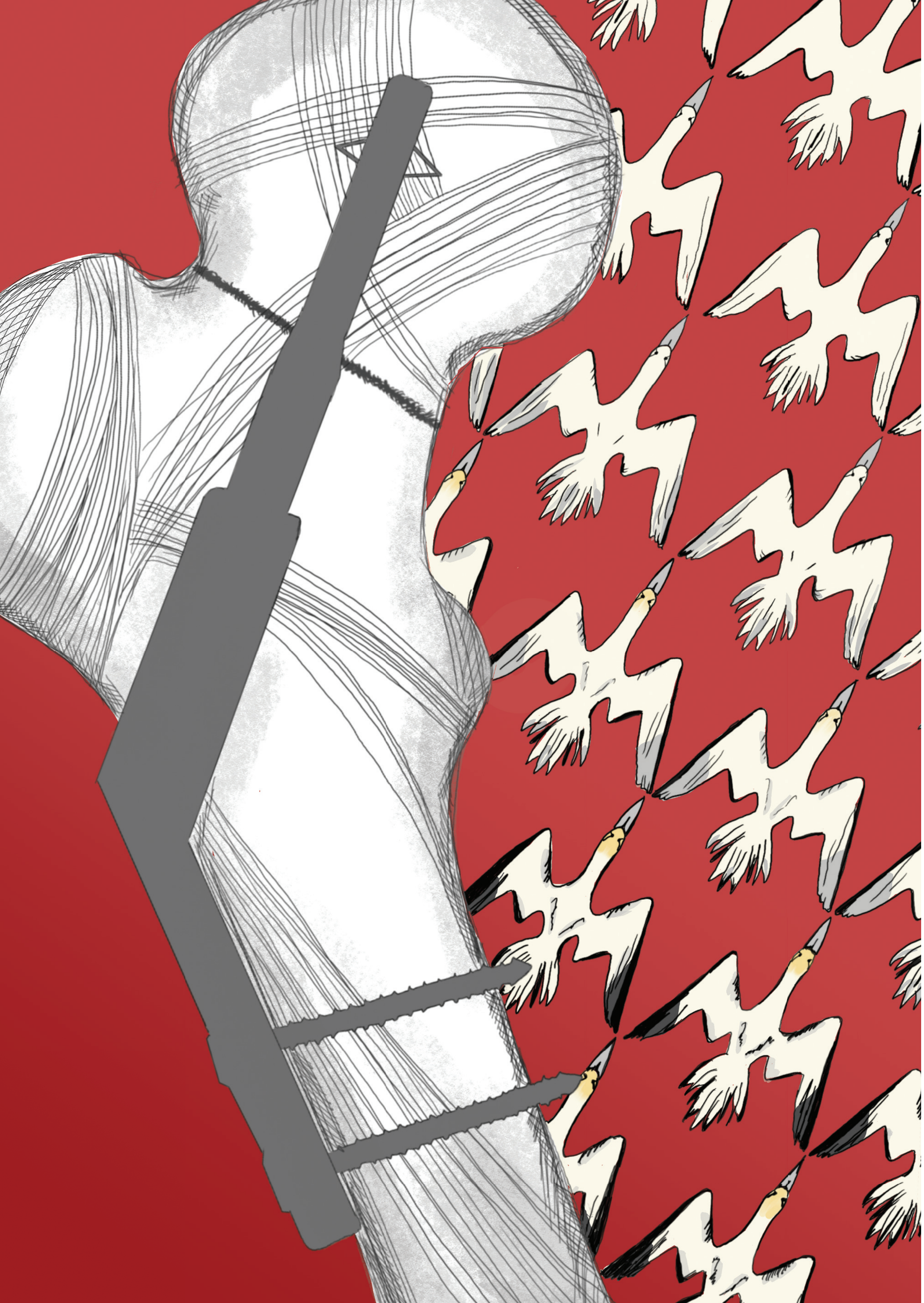


Chapter 9

Summary

The optimal treatment of Femoral Neck Fractures (FNFs) has been subject of debate for decades. A complex mix of patient, fracture and intervention-related factors determine the outcome of treatment. The overall aim of this thesis is to improve the treatment outcome of FNF surgery by identifying and, if possible, improving the factors that influence FNF healing.

IDENTIFY FACTORS THAT INFLUENCE OUTCOME OF TREATMENT OF FEMORAL NECK FRACTURES

Chapter 2 presents a systematic review that aims to provide an overview of predictors for failure of treatment of displaced FNFs (dFNFs) that were treated with internal fixation and quantify the risk of fixation failure in a meta-analysis. PubMed, Embase, Web of Science, Cochrane Library, and EMCare were searched for original studies published from January 2000, that included adult patients with an internally fixated dFNF and reported data on predictors for revision surgery due to non-union, avascular femoral head necrosis or cut-out of the implant. Univariable odds ratios (OR) for predictors of revision surgery were pooled using a random effects model. A total of 2348 articles were analysed resulting in the inclusion of 16 articles that met the inclusion criteria. These studies identified 24 potential predictors for revision surgery. Female sex (OR 1.78, 95% confidence interval (CI) 1.26–2.52), smoking (OR 3.64, 95% CI 1.68–7.91), age >50 years (OR 3.64, 95% CI 1.68–7.91), inadequate fracture reduction (OR 2.28, 95% CI 1.62–3.22), fixation with cannulated screws (CS) or pins compared to fixed angle devices (OR 2.16, 95% CI 1.03–4.54) were significant predictors for fixation failure. These factors have to be taken into consideration when deciding on the optimal treatment strategy.

One potential predictor for revision surgery in is thoroughly examined in **Chapters 3 and 4.** In **Chapter 3** we examined the correlation between the preoperative posterior tilt of the femoral head and revision surgery in patients with undisplaced FNFs (uFNFs). Posterior tilt was measured in 193 patients with a Garden type 1 and 2 FNF treated with the Dynamic Locking Blade Plate (DLBP). Results showed that patients that underwent revision surgery within the first year after the initial operation had a higher degree of posterior tilt prior to the surgical reduction and fixation compared to patients who had uneventful treatment: 21.4° and 13.8° of posterior tilt, respectively (p=0.03). The failure rate was 3.2% for uFNFs with a posterior tilt of less than 20° but increased to 12.5% for those with a posterior tilt of 20° or more. A posterior tilt of ≥ 20°was associated with an OR of 4.24 (95% CI 1.09–16.83; p=0.04). It appears that "stable" undisplaced, Garden type I and II FNFs with a significant posterior tilt (≥20°) in fact behave like unstable fractures. Therefore, posterior tilt ≥20° of the femoral head is a significant predictor for revision surgery of uFNFs treated with the DLBP. This finding suggests that a modified Garden Classification should be used to determine FNF displacement, incorporating posterior tilt as a factor.

To substantiate our results in **Chapter 3** we compared two measurements methods for posterior tilt of the femoral head for intra and inter observer reliability in **Chapter 4**. The Lateral Garden Angle (LGA) and the newer Posterior Tilt Measurement (PTM) were used to measure posterior tilt. Four observers measured the posterior tilt on the radiographs of 50 FNFs twice using both methods. The intra observer reliability for both methods is substantial, with an intra class coefficient of 0.75. The inter observer reliability of the PTM is substantial with an intra class coefficient of 0.75 compared to a moderate reliability of the LGA with an intraclass coefficient of 0.60. Based on these results, the PTM has a slight preference over the LGA for measuring the posterior tilt of the femoral head in uFNFs.

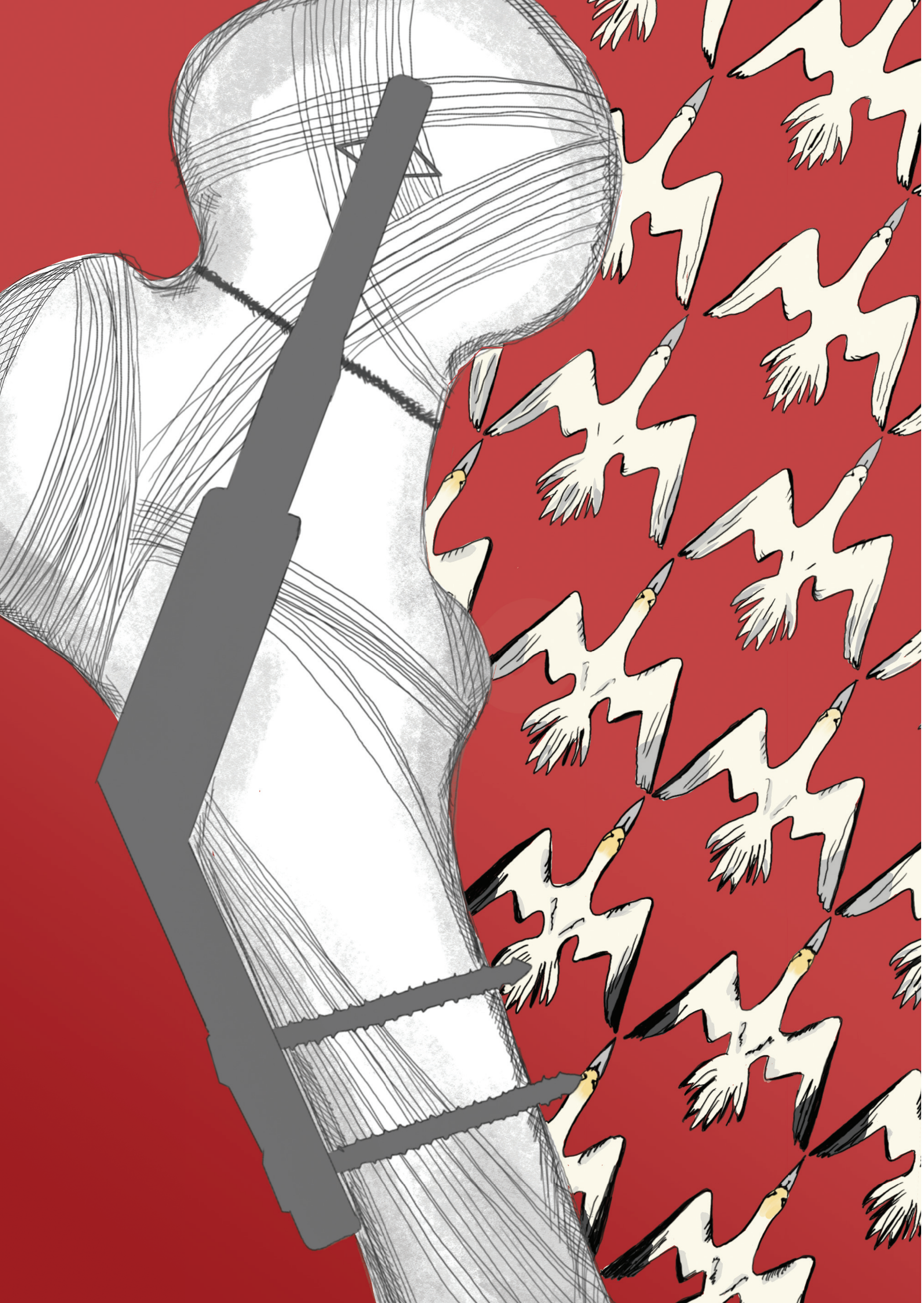
IMPROVING THE TREATMENT OF FEMORAL NECK FRACTURE SURGERY

The Dynamic Locking Blade Plate (DLBP), also known as 'the Gannet', has been used in Dutch hospitals for over a decade. The results of a small pilot study with 25 patients with an FNF treated with the DLBP were promising, with a failure rate of 8% at the two-year follow-up. In a prospective cohort of 172 patients with uFNFs, the failure rate was 4% at one-year follow-up. **Chapter 5** presents the first results of the DLBP in dFNFs in young patients. A multicentre prospective case series was conducted, including patients aged ≤ 60 years with a dFNF treated with the DLBP, with a follow-up of one year. The primary outcome parameter was revision surgery due to non-union, avascular necrosis of the femoral head (AVN) or cut-out of the implant. Out of the 106 consecutive included patients, 14 required revision surgery, resulting in a revision rate of 13.2% (95% CI 7.1–19.9). When compared to other implants in the literature, that show revision rates ranging from 18–48%, the DLBP appears to be the more favourable implant.

In **Chapter 6** we analysed the long-term results of the DLBP. A retrospective analysis was done of earlier collected prospective data. Revision surgery due to cut-out of the implant, AVN, non-union, or posttraumatic osteoarthritis (PTOA) was the main outcome parameter. Secondary outcome parameters were the indication for revision surgery, complications, time to revision surgery, rate of elective removal of the implant, potential predictors for revision surgery and mortality. The median follow-up of 389 patients included in the study was 98 months; 20.6% underwent revision surgery; 28.8% after treatment of a dFNF and 10.0% after a uFNF. Postoperative complications were observed in 10.5% (n=41) of the patients, and 32.9% (n=128) deceased during follow-up. The median time to revision surgery was 13 months for dFNFs and 18 months for uFNFs. 15.7% of the DLBPs were removed electively. In the multivariate Cox regression analysis, female gender (hazard ratio 2.1, 95% CI 1.2–3.7) and a Tip-Apex-Distance greater than 25 mm (hazard ratio 2.9, 95% CI 1.7–5) were significant predictors for revision surgery in patients with dFNFs. Although study populations differ throughout literature and are not exactly comparable to our patients cohort, the DLBP demonstrated positive long-term results in the treatment of FNF compared to other implants, with an overall revision rate of 28.8% versus 31.3–45.6% for dFNF, and 10.0% versus 10.7–19% for uFNF.

To prove this hypothesis the DEFENDD trial was designed. The study protocol is presented in **Chapter 7.** The aim of the DEFENDD trial is to compare the clinical outcomes and costs of dFNFs treated with internal fixation using either the DLBP or the Dynamic Hip Screw (DHS) in patients up to 65 years of age. The hypothesis is that the DLBP is superior compared to the DHS in terms of revision surgery rate, union rate, incidence of avascular necrosis and implant-related failure. This multicentre randomised controlled trial has a clinical follow-up of one year and questionnaires will be obtained for up to two years. The main outcome parameter is the incidence of revision surgery within one year, due to either non-union, avascular necrosis (AVN) or cut-out of the implant. Secondary study parameters include the incidence of avascular necrosis, non-union, (implant-related) complications, functional outcome, health-related quality of life, elective removal of the implant and treatment-related costs. The DEFENDD trial will provide high-level evidence on which implant is favourable for the treating dFNFs in young patients.

In **Chapter 8** the clinical implications are presented and discussed. The results in this thesis may assist surgeons in their daily practice and complement future treatment guidelines for FNFs. Further research should focus on the functional outcome of the DLBP, as well as factors that influence patient-related outcome measures. Additionally, decision aids should be developed to assist surgeons and patients in choosing the most optimal treatment for the patient with a femoral neck fracture.



Chapter 10

Nederlandse samenvatting

De optimale behandeling van collumfracturen is al tientallen jaren onderwerp van discussie. Een complexe mix van patiënt, fractuur en interventie gerelateerde factoren bepaalt het resultaat van de behandeling. Het doel van dit proefschrift is het verbeteren van de uitkomsten na behandeling van collumfracturen door het identificeren en indien mogelijk, verbeteren van de factoren die de genezing van de collumfractuur beïnvloeden.

IDENTIFICEREN VAN UITKOMST BEPALENDE FACTOREN VOOR DE BEHANDELING VAN COLLUMFRACTUREN

In **Hoofdstuk 2** wordt een systematische review van de huidige literatuur beschreven met als doel een overzicht te geven van voorspellers voor het falen van de behandeling van gedisloceerde collumfracturen die behandeld zijn middels interne fixatie. Het risico op het falen van de behandeling is vervolgens gekwantificeerd in een meta-analyse. PubMed, Embase, Web of Science, Cochrane Library en EMCare werden geraadpleegd om originele studies te vinden gepubliceerd vanaf januari 2000. De studies moesten volwassen patiënten includeren met gedisloceerde collumfracturen die behandeld waren middels interne fixatie. Daarnaast moesten gegevens worden gepresenteerd over voorspellers voor revisiechirurgie als gevolg van non-union, avasculaire femurkop necrose (AVN) of cut-out van het implantaat. Univariabele odds ratio's (OR) voor voorspellers van revisiechirurgie werden gepoold met behulp van een random-effects model. In totaal werden 2348 artikelen gescreend, wat resulteerde in de inclusie van 16 artikelen die voldeden aan de inclusiecriteria. Deze studies identificeerden 24 potentiële voorspellers voor revisiechirurgie. Significante voorspellers voor revisie chirurgie waren: het vrouwelijk geslacht (OR 1,78, 95% betrouwbaarheidsinterval (CI) 1,26–2,52), roken (OR 3,64, 95% CI 1,68–7,91), leeftijd >50 jaar (OR 3,64, 95% CI 1,68–7,91), inadequate fractuur repositie (OR 2,28, 95% CI 1,62–3,22), fixatie met gecannuleerde schroeven (CS) of pennen ten opzichte van implantaten met pen en een plaat (OR 2,16, 95% CI 1,03–4,54). Met deze factoren moet rekening worden gehouden bij het bepalen van de optimale behandelstrategie voor collumfracturen.

Eén potentiële voorspeller voor revisiechirurgie wordt uitgebreider onderzocht in de **Hoofdstukken 3 en 4.** In **Hoofdstuk 3** wordt de correlatie onderzocht tussen preoperatieve posterieure kanteling van de femurkop en revisiechirurgie bij patiënten met een niet-gedisloceerde collumfractuur. De posterieure kanteling werd gemeten bij 193 patiënten met een Garden type 1 of 2 collumfractuur die zijn gefixeerd met de Dynamic Locking Blade Plate (DLBP). De resultaten tonen dat patiënten die binnen een jaar na de initiële operatie zijn gereviseerd meer posterieure kanteling van de femurkop hadden in vergelijking met patiënten die niet zijn gereviseerd: respectievelijk 21,4° en 13,8° (p=0,03). Het percentage revisie chirurgie nam toe van 3,2% naar 12,5% indien de posterieure kanteling 20° of meer betrof in vergelijking met fracturen waarbij de kanteling minder dan 20° was. Een posterieure kanteling van ≥20° is geassocieerd met een OR van 4,24 (95% CI 1,09–16,83; p=0,04). Het lijkt erop dat "stabiele" niet-gedisloceerde collumfracturen, Garden type I en II, met een significante posterieure kanteling (≥20°) zich gedragen als instabiele fracturen. Daarom is posterieure kanteling van ≥20° van de femurkop een significante voorspeller voor revisiechirurgie van niet-gedisloceerde collumfracturen die zijn behandeld met de DLBP. De resultaten van dit onderzoek ondersteunen de gepresenteerde 'Modified Garden Classification', waarbij de posterieure kanteling van de femurkop wordt meegenomen in het bepalen van de stabiliteit van een collumfractuur.

In **Hoofdstuk 4** hebben we twee meetmethodes om de posterieure kanteling van de femurkop vergeleken op betrouwbaarheid binnen en tussen beoordelaars. De Lateral Garden Angle (LGA) en de nieuwere Posterior Tilt Measurement (PTM) werden gebruikt om de posterieure kanteling te meten. Vier beoordelaars hebben de posterieure kanteling van de femurkop na een collumfractuur op 50 röntgenfoto's twee keer met beide meetmethodes gemeten. De intrabeoordelaarsbetrouwbaarheid is voor beide methodes 'substantieel' met een intraclass-coefficient van 0,75. De interbeoordelaarsbetrouwbaarheid van de PTM is eveneens 'substantieel', wederom met een intraclass-coefficient van 0,75. De interbeoordelaarsbetrouwbaarheid van de LGA is daarentegen 'middelmatig' met een intraclass-coefficient van 0,6. Op basis van deze resultaten heeft de PTM een voorkeur boven de LGA voor het meten van posterieure kanteling van de femurkop bij niet-gedisloceerde collumfracturen.

VERBETEREN VAN DE BEHANDELING VAN COLLUMFRACTUREN

The Dynamic Locking Blade Plate (DLBP), beter bekend als 'de Gannet', wordt al meer dan tien jaar gebruikt in Nederlandse ziekenhuizen. De resultaten van een kleine pilotstudie met 25 patiënten met een collumfractuur die behandeld werden met de DLBP waren veelbelovend, met een revisie percentage van 8% na twee jaar follow-up. In een prospectief cohort van 172 patiënten met een niet-gedisloceerde collumfractuur was het revisie percentage 4% na één jaar follow-up. **Hoofdstuk 5** beschrijft de eerste resultaten van de DLBP als behandeling voor gedisloceerde collumfracturen bij patiënten van ≤60 jaar in een multicenter prospectieve case-serie met een follow-up van één jaar. De primaire uitkomstparameter was revisiechirurgie vanwege non-union, AVN of cut-out van het implantaat. Van de 106 geïncludeerde patiënten ondergingen 14 patiënten revisiechirurgie, wat resulteerde in een revisiepercentage van 13,2% (95% CI 7,1–19,9). In vergelijking met andere implantaten in de literatuur, met revisiepercentages variërend van 18–48%, lijkt de DLBP een beter implantaat te zijn.

In **Hoofdstuk 6** analyseerden we de lange-termijn resultaten van de DLBP. Er werd een retrospectieve analyse uitgevoerd van prospectief verzamelde data. Revisiechirurgie vanwege non-union, AVN, cut-out van het implantaat of posttraumatische artrose (PTOA) was de primaire uitkomstparameter. Secundaire uitkomstparameters waren de incidentie van indicaties voor revisiechirurgie zoals hierboven beschreven, (operatie gerelateerde) complicaties, tijd tot revisiechirurgie, percentage electief verwijderde DLBPs, potentiële voorspellers voor revisiechirurgie en mortaliteit. De mediane follow-up van 389 geïncludeerde patiënten was 98 maanden. 20,6% onderging een revisie operatie; 28,8% na behandeling van een gedisloceerde collumfractuur en 10,0% na een niet-gedisloceerde collumfractuur. Postoperatieve complicaties kwamen voor in 10,5% (n=41) van de patiënten en 32,9% (n=128) overleed tijdens de follow-up. De mediane tijd tot revisie was 13 maanden bij een gedisloceerde en 18 maanden bij een niet-gedisloceerde collumfracturen. 15,7% van de DLBPs werden electief verwijderd. In een multivariate Cox regressieanalyse waren het vrouwelijk geslacht (hazard ratio 2,1, 95% CI 1,2–3,7) en een Tip-Apex-Distance van groter dan 25 mm (hazard ratio 2,9, 95% CI 1,7–5) significante voorspellers voor revisiechirurgie bij patiënten met gedisloceerde collumfracturen. Hoewel de onderzoekspopulaties in de literatuur verschillen en niet precies vergelijkbaar zijn met ons patiënten cohort, toonde de DLBP goede lange-termijnresultaten voor de behandeling van collumfracturen in vergelijking met bestaande implantaten, met een revisiepercentage van 28,8% versus 31,3–45,6% voor gedisloceerde collumfracturen en 10,0% versus 10,7–19% voor niet-gedisloceerde collumfracturen.

Om deze hypothese te bewijzen is de DEFENDD trial opgezet en het protocol van de studie wordt gepresenteerd in **Hoofdstuk 7.** Het doel van de DEFENDD studie is het vergelijken van de klinische uitkomsten en kosten van de DLBP en de Dynamische Heup Schroef (DHS) als behandeling voor gedisloceerde collumfracturen bij patiënten tot en met 65 jaar. De hypothese is dat de DLBP superieur is in vergelijking met de DHS wat betreft het aantal revisie operaties, union percentage, de incidentie AVN en implantaat gerelateerd falen van de behandeling. Deze multicenter gerandomiseerde trial heeft een klinische follow-up van één jaar en er zullen tot twee jaar na de operatie vragenlijsten worden afgenomen. De primaire uitkomstparameter is de incidentie van revisiechirurgie vanwege non-union, AVN of cut-out van het implantaat binnen één jaar. Secundaire uitkomstparameters zijn de incidentie van AVN, non-union, (implantaat gerelateerde) complicaties, functionele uitkomsten, gezondheid gerelateerd kwaliteit van leven, electieve verwijdering van het implantaat en behandeling gerelateerde kosten. De DEFENDD trial zal hoogwaardig bewijs leveren voor welk implantaat beter is voor de behandeling van gedisloceerde collumfracturen bij jonge patiënten.

In **Hoofdstuk 8** staan de klinische implicaties van het proefschrift. De resultaten van de studies in dit proefschrift dragen bij aan de kennis over de behandeling van collumfracturen en kan chirurgen helpen bij het maken van keuzes omtrent behandelstrategieën van de collumfractuur. Daarnaast kan dit proefschrift een bijdrage leveren aan toekomstige richtlijnen omtrent de behandeling van de collumfractuur. Verder onderzoek zou zich moeten richten op functionele uitkomsten van de DLBP en op factoren die patiënt specifieke uitkomsten beïnvloeden. Daarnaast zou een keuzehulp zowel chirurgen als patiënten kunnen helpen bij het kiezen van de optimale behandeling voor de patiënt met een collumfractuur.

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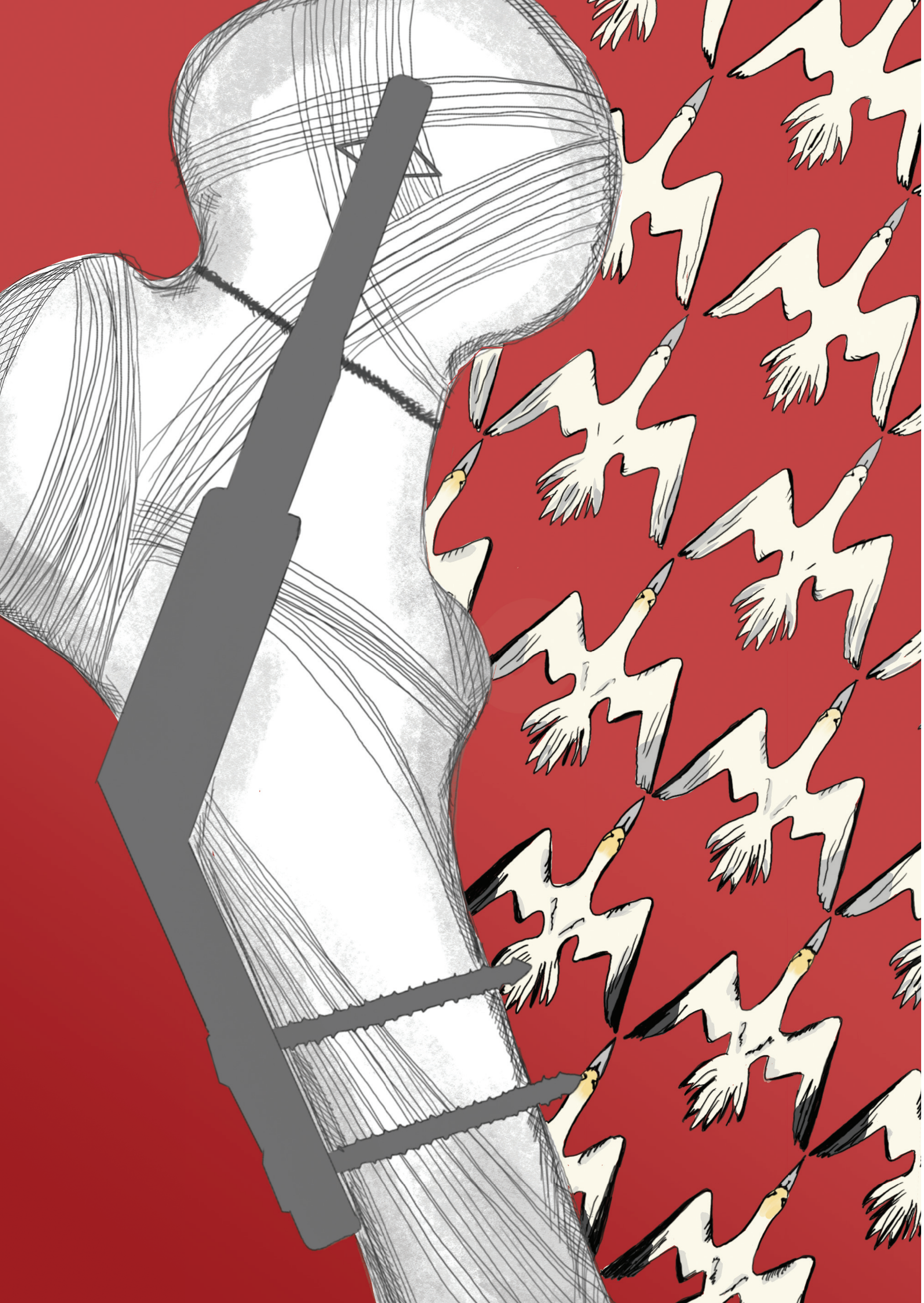

Chapter 11

Appendices

LIST OF PUBLICATIONS

van Walsum ADP, Vroemen J, Janzing HMJ, Winkelhorst T, **Kalsbeek J,** Roerdink WH. Low failure rate by means of DLBP fixation of undisplaced femoral neck fractures. *Eur J Trauma Emerg Surg* 2017;43:475-80.

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CURRICULUM VITAE AUCTORIS

Jorn Kalsbeek was born on 30th of April 1990 in Heerenveen, the Netherlands. After completing the gymnasium on the Bornego College he moved to Groningen to study medicine in 2008. He completed the majority of his internships at Ziekenhuisgroep Twente in Almelo. During this period, he collaborated with Ariaan van Walsum and Herbert Roerdink on a research project examining the clinical results of the Dynamic Locking Blade Plate. After completing the mandatory internships, he undertook a facultative internship of three months on the trauma unit at Groote Schuur Hospital in Cape Town. Back in the Netherlands he did his last internship at the surgical ward at Medisch Spectrum Twente and wrote his thesis: 'The influence of posterior tilt of the femoral head on the failure rate of femoral neck fractures. An analysis of 164 undisplaced femoral neck fractures treated by Gannet osteosynthesis.' He graduated in 2016 and started working as a resident at Deventer Ziekenhuis. Since 2017, Prof. Dr. I.B. Schipper has been one of his supervisors, during which time they established the DEFENDD trial. In 2018, he became an official PhD candidate at the University of Leiden. After working at Medisch Spectrum Twente in 2019, he started his surgical training at Universitair Medisch Centrum Groningen in 2020. Since 2021 he is working at Medisch Spectrum Twente as a surgical resident. He lives in Deventer with his wife Inge and two daughters, Jinte en Djoeke.

DANKWOORD

In de afgelopen jaren hebben veel mensen een bijdrage geleverd aan het tot stand komen van mijn proefschrift. Bij enkelen wil ik even stilstaan.

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