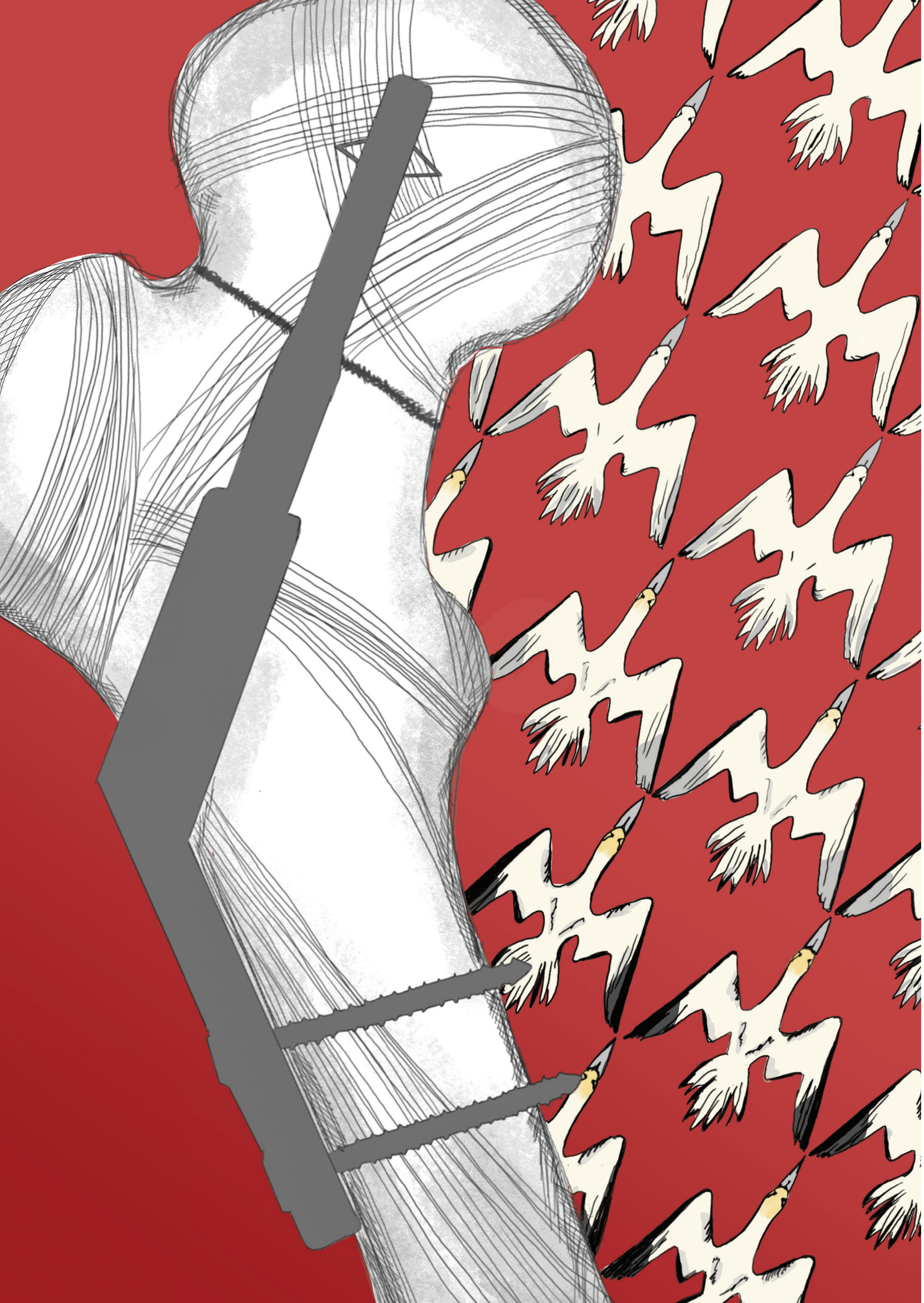
New insights in the treatment of femoral neck fractures
Kalsbeek, J.H.



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.

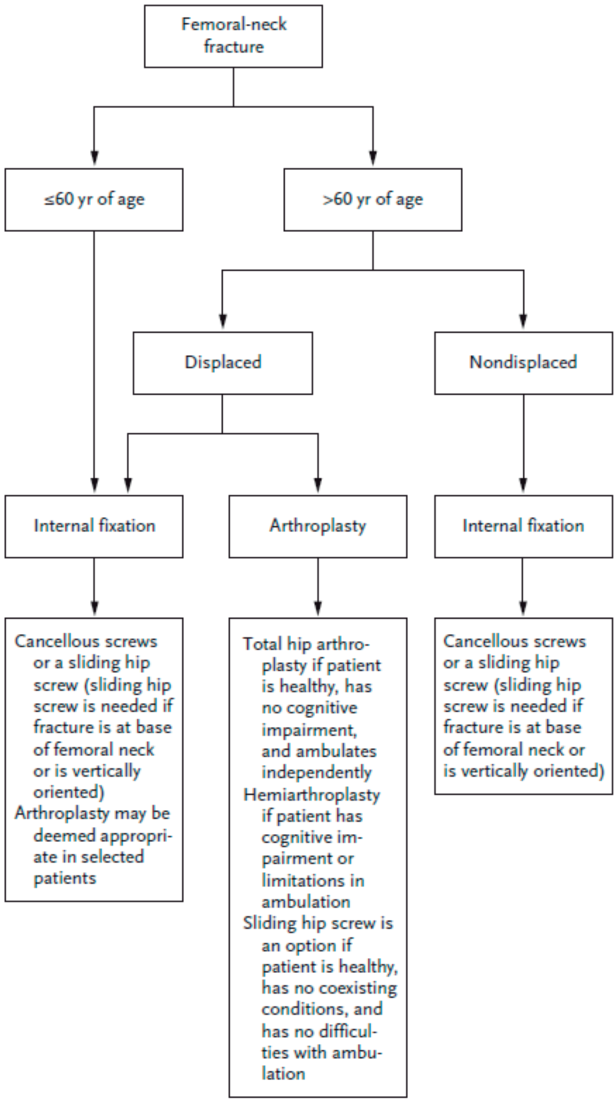


Figure 1. Recommended Management of Femoral Neck Fractures by Bhandari et al. [3]

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

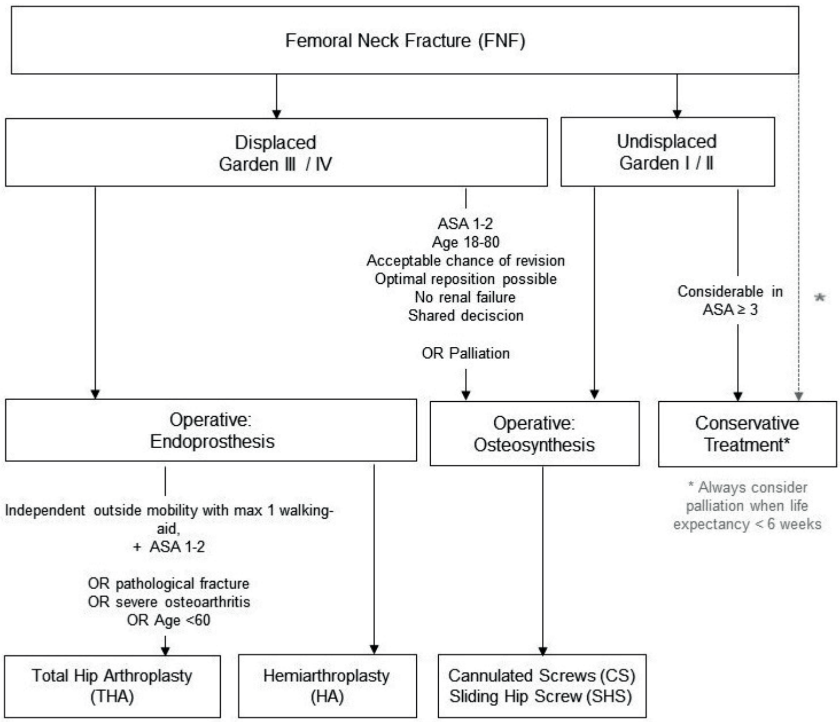


Figure 2. Recommend treatment strategy for Femoral Neck Fractures according to the Dutch Guideline for proximal femur fractures.[4,34]

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]

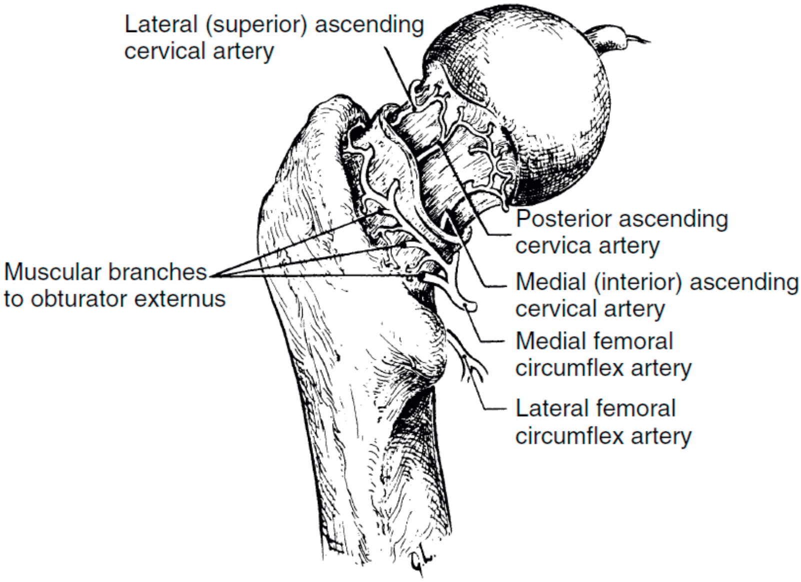


Figure 3. Arterial blood supply to the head and neck of the posterior aspect of the left proximal femur.[11]

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.

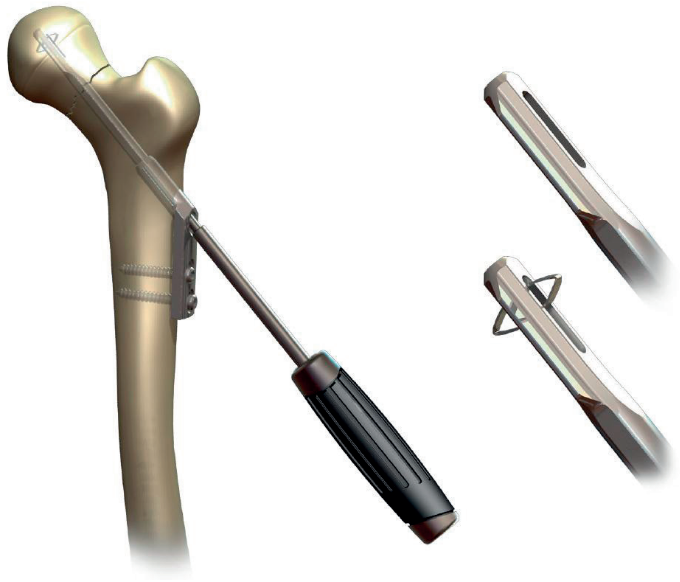


Figure 4. Illustration of the Dynamic Locking Blade Plate also known as the Gannet.

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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