Distal femur fracture in the elderly patient

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Cover Painting: Far, far away, Soria Moria Palace shimmered like Gold. Theodor Kittelsen (1900)

Soria Moria Palace (*Soria Moria slott*) is a Norwegian folk tale that was written down in the *"Norske Folkeeventyr"* by Peter Christen Asbjørnsen and Jørgen Moe (1843).

Legend has it that Soria Moria is an imaginary palace that cannot be reached by any road. The journey to get there is solitary because everyone is different and must find their own way. The Ash Lad is a humble character who overcomes obstacles and ultimately succeeds.

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“In the middle of difficulty lies opportunity”

Albert Einstein

1. Abstract

Studies on the epidemiology of distal femur fractures show a vast increase in low-energy trauma-associated fractures in older ages. Age-related changes in bones lead to loss of bone matrix and increased porosity, which entails an increased risk for fractures and different fracture patterns than in younger individuals. Corresponding age-related changes also occur in muscles, resulting in decreased muscle mass and strength, which impairs the ability to recuperate after a fracture.

To reduce the risk of surgical complications, it is common practice to limit weight-bearing on the fractured leg after surgical fixation of distal femur fractures. Typically, patients are restricted to bear no more than 30% of their body weight on the affected leg. There is, however, a lack of knowledge on how a period of restricted weight-bearing affects the long-term outcome in elderly patients with distal femur fractures.

This thesis aimed to evaluate how the patient's everyday function, surgical fixation and ability to recover were affected by eight weeks of restricted weight-bearing. The thesis also aimed to assess fracture demographics and design a new fracture classification adapted to the characteristics of distal femur fracture in elderly patients.

A randomised controlled trial compared restricted weight-bearing for eight weeks after surgery with full immediate weight-bearing. The primary outcome was patient-reported everyday living function. Secondary outcomes were postoperative fracture alignment, secondary displacement of the fractures during healing, weight-bearing ability, and gait recovery assessed during a one-year follow-up.

There was no difference in patient-reported function between groups. The use of a traction table facilitated an excellent postoperative fracture alignment. All fractures were fixated with a long plate applied with a minimally-invasive technique, and there was no non-union or plate breakage within the one-year follow-up. However, there was a significant fracture subsidence of 4.9 ± 4.2 mm in mean of the femur. The restricted weight-bearing group showed a small but significant increase in secondary displacement. Five of six major secondary displacements and mechanical adverse events also occurred in this group.

Only one-third of the patients in the restricted weight-bearing group managed to comply with the recommended loading of 30% of the body weight. Despite this, the restricted group had a significantly lower gait speed at 16 weeks and one year.

A survey of fracture demographics of 342 patients 65 years or older showed a dominance of spiral fractures of the distal shaft, which increased with advancing age. Two-thirds of patients had peri-implant fractures associated with knee and hip replacements or previous fracture fixation devices. A new fracture classification for distal femur fractures in elderly patients was developed. Reliability tests of the new classification showed substantial agreement.

Concluding the results of the thesis, the morphology of the distal femur alters with advancing age, affecting the fracture demographics. The prosed new classification adapted to the characteristics of distal femur fractures in elderly patients is promising and could improve classification compared with today's used classification systems.

Restricted weight-bearing for eight weeks after surgery had a negative effect on fracture fixation and a persistent negative impact on gait recovery, indicating worse function and increased mortality.

Restricted weight-bearing should therefore be avoided in elderly patients with distal femur fractures.

2. Sammanfattning på svenska

Epidemiologiska studier där distala femur frakturer undersökts visar på en drastisk ökning av frakturer associerade till lågenergitrauma i äldre åldrar. Åldersrelaterade förändringar i ben leder till förlust av benmassa och ökad porositet, vilket innebär en ökad risk för frakturer men ger också upphov till ett annat frakturmönster än hos yngre individer. Motsvarande åldersrelaterade förändringar sker även i muskler, vilket resulterar i minskad muskelmassa och styrka, vilket försämrar förmågan att rehabilitera sig efter en fraktur.

Med intensionen att minska kirurgiska komplikationer är det vanlig att begränsa belastningen vid gång efter kirurgisk fixering av distala femurfrakturer. Det innebär att belastningen på det brutna benet endast får vara ca 30 % av kroppsvikten. Det saknas emellertid kunskap om hur en period av begränsad belastning vid gång långsiktigt påverkar resultatet hos äldre patienter med distala femurfrakturer.

Avhandlingens syfte var att utvärdera hur patientens vardagsfunktion, kirurgiska fixering och förmåga att återhämta sig påverkades av åtta veckors begränsad belastning vid gång. Avhandlingen syftade också till att bedöma frakturdemografi hos äldre personer och skapa en ny frakturklassificering, anpassad till egenskaperna hos distala femurfrakturer hos äldre.

I en randomiserad studie jämfördes begränsad belastning vid gång under åtta veckor med full belastning direkt efter operation. Det primära utfallsmåttet var patientrapporterad vardagsfunktion. Sekundära utfallsmått var postoperativ frakturreposition, sekundär dislokation av frakturerna under läkning, patienternas verkliga kroppsviktbärande förmåga och återhämtning av gångförmågan bedömd under en ettårsuppföljning. Det fanns ingen noterbar skillnad i patientrapporterad vardagsfunktion.

Genom operation på ett sträckbord med femurstöd skapades förutsättningar för en anatomisk reposition. Alla frakturer fixerades med en lång platta som applicerades med minimal-invasiv teknik. Det förekom inga oläkta frakturer eller plattbrott under den ettåriga uppföljningen, men en signifikant sekundär frakturkompression, i medeltal 4,9 ± 4,2 mm. För gruppen med begränsad belastning vid gång sågs en liten men signifikant ökning av sekundär frakturkompression. Fem av sex större sekundära frakturkompressioner och mekaniska komplikationer inträffade också i denna grupp.

Endast en tredjedel av patienterna i gruppen med begränsad belastning vid gång klarade av den rekommenderade belastningen på 30 % av kroppsvikten. Gruppen uppvisade även en betydligt lägre gånghastighet efter 16 veckor och ett år postoperativt.

En undersökning av demografin hos 342 patienter, 65 år eller äldre, med distala femurfrakturer visade en dominans av spiralfrakturer i det nedre delen av skaftet, en dominans som dessutom ökade med stigande ålder. Två tredjedelar av patienterna hade peri-implantatfrakturer associerade med knä- och höftproteser eller tidigare frakturfixation. En ny frakturklassifikation för distala femurfrakturer för äldre patienter utvecklades. Reliabilitetstester av den nya klassificeringen visade på betydande överensstämmelse mellan olika bedömare.

Sammanfattningsvis visar avhandlingens resultat att den förändrade morfologin i nedre delen av lårbenet med stigande ålder påverkar frakturdemografin. Den nya frakturklassifikationen som är anpassad för de karakteristiska egenskaperna hos distala femurfrakturer hos äldre patienter visar lovande resultat och förmodas kunna förbättra klassificeringen jämfört med det klassificeringssystem som används idag.

En begränsad belastning vid gång under de första åtta veckorna postoperativt hade en negativ effekt på frakturfixering och en bestående negativ påverkan på återhämtning av gångfunktionen, vilket indikerar sämre funktion och ökad dödlighet. Begränsning av belastning vid gång efter operation bör därför undvikas hos äldre patienter med distala femurfrakturer.

3. List of Papers

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

I. Paulsson M, Ekholm C, Jonsson E, Geijer M and Rolfson O.
Immediate Full Weight-Bearing Versus Partial Weight-Bearing After Plate Fixation of Distal Femur Fractures in Elderly Patients. A Randomized Controlled Trial
Published in the Journal "Geriatric Orthopaedic Surgery & Rehabilitation" Volume 12: 1–14: 2021

II. Paulsson M, Ekholm C, Rolfson O, Tranberg R and Geijer M.
Using a traction table for fracture reduction during minimally invasive plate osteosynthesis (MIPO) of distal femoral fractures provides anatomical alignment
Manuscript submitted

III. Paulsson M, Ekholm C, Rolfson O, Tranberg R and Geijer M
Secondary displacement was common in healing distal femur fractures in a cohort of elderly patients
Manuscript submitted

IV. Paulsson M, Ekholm C, Rolfson O, Geijer M and Tranberg R
Temporary partial weight-bearing restriction in elderly patients treated with a plate fixation after a distal femur fracture had a negative long-term impact on gait recovery
Manuscript submitted

V. Paulsson M, Geijer M, Rolfson O, Pekkari T, Tranberg R and Ekholm C
New classification of geriatric distal femur fractures. A proposal
In manuscript

4. Abbreviations

ACL	Anterior cruciate ligament
ADL	Activity of daily life
AO/OTA	Arbeitsgemeinschaft für osteosynthesefragen/ Orthopeadic Trauma Association
AP	Anterior/posterior view
ASA	American Society of Anesthesiologists Classification
BC	Before christ
BMI	Body mass index
CI	Confidence interval
CT	Computed tomography
DAIR	Debridement antibiotics implant retainment
DCS	Dynamic compression screw
DFF	Distal femur fracture
DFR	Distal femoral replacement
DP	Dual plating
DS	Distal shaft
EQ-5D	EuroQol-5 Dimensions
FJS-12	Forgotten Joint Score
FoF	Fear of falling
FRS	Functional recovery score
FWB	Full weight-bearing
GRF	Ground reaction force
HS	Hip screws
ICC	Intra-class correlation
ICD	International Statistical Classification of Diseases and Related Health Problems
IMN	Intramedullary nail (Antegrade)

IQR	Interquartile range
K-wire	Kirschner- wire. Thin metal rod with a sharp tip and is used for temporary fixation.
LISS	Less invasive stabilisation system
MDC	Minimal detectable change
MID	Minimal important difference
MIPO	Minimally-invasive plate osteosynthesis
MPR	Multiplanar reformations
MP	Metaphyseal
NPPIF	Non-periprosthetic peri-implant fracture
NWB	Non-weight-bearing
OKS	Oxford Knee Score
ORIF	Open reduction internal fixation
PL	Plate and screws
P.O.R.D.	Posterior reduction device
QoL	Quality of life
PROM	Patient-reported outcome measures
PWB	Partial weight-bearing
RCT	Randomised controlled study
RIMN	Retrograde Intramedullary nail
ROM	Range of motion
RSA	Radiostereometric analysis
SD	Standard deviation
SE	Standard error
SMFA	Short musculoskeletal functional assessment
SPMSQ	Short Portable Mental Status Questionnaire
THR	Total Hip Replacement
TKR	Total Knee Replacement
TUG	Timed-up-and-go
UPCS	Unified periprosthetic classifications system
VAS	Visual Analogue scale

5. Brief definitions

Bias

Bias is a systematic error which tends to statistically overestimate or underestimate the population parameter you are trying to measure. A common type of bias is selection bias which occurs when there are systematic differences in groups. Bias can lead to incorrect conclusions.

Bone mineral density

Bone mineral density (BMD) refers to the quantity of mineral matter found within a specific volume of bone.

Classification systems

Classification systems are systematic arrangements in groups or categories according to established criteria.

Confidence interval

A confidence interval is a range of values that is likely to contain a population value with a certain degree of confidence. Typically, a 95% confidence interval is used to estimate the range of values that is 95% likely to contain the true mean of the population.

Incidence

Incidence is the number of new injury or disease cases within a specified population during a particular timeframe.

Minimal detectable change

Is the smallest amount of difference in a patient's score that can be detected while also ensuring that a measurement error does not cause it.

Minimal important difference

Is the smallest change in an outcome that patients or clinicians might consider significant.

Mortality

A mortality rate refers to the number of deaths that occur within a population during a set timeframe.

Osteopenia

According to the World Health Organisation (WHO), a T-score between -1.0 and -2.5 standard deviation is defined as osteopenia.

Osteoporosis

According to the WHO, a T-score below -2.5 standard deviation is defined as osteoporosis.

***P*-value**

The *P*-value, or probability value, is a numerical representation of how probable it is for your data to have occurred by chance.

Randomised controlled trial

In a randomized controlled trial, participants are randomly placed into either an experimental group that receives the intervention being tested or a comparison group that receives an alternative or conventional treatment.

Standard deviation

Standard deviation measures the extent of variation or dispersion of the mean.

Power

Statistical power is the likelihood of a significance test detecting a significant effect in a sample when one truly exists.

T-score

A T-score is a numerical comparison that determines the difference between your bone mass and that of a healthy young person with average bone density.

Reliability

Reliability in statistics refers to the stability or consistency in measurement: the capacity to reproduce the results repeatedly

Table of contents

6

Introduction

6.1 History of treatment of femoral fractures

Fractures of the long bones have occurred throughout the history of humankind. The documentation of fractures and fracture treatment is sparse before the era of the ancient Egyptians. In 1862, Edwin Smith made an archaeological find in Luxor, a papyrus roll, which is thought to be one of the oldest texts (16th century BC) on the descriptions of fractures. It contains instructions on how to examine fractures; however, treatment suggestions are lacking. A study on long bones from Egypt investigating 204 adult skeletons from 2700-2180 BC found a healed femoral shaft fracture with mild malalignment. This suggests that femoral fractures have been treated successfully for over 4000 years [1].

6.2 Anatomy of the distal femur

6.2.1 BONY ANATOMY

The femur is the longest of the long bones, connecting the hip joint with the knee joint and transmitting the force applied when standing from the knee to the pelvis. The distal femur accommodates the proximal part of the knee joint (Figure 1). With its characteristic bicondylar construction, the knee joint has proven advantageous. The knee has only undergone minor changes throughout 300 million years of evolution, and bicondylar knees with menisci and ligaments have been found in ancestors of reptiles and mammals [2]. The distal femoral metaphysis with epicondyles has insertions for muscular origins and ligaments.

The femoral condyles and epicondyles have intricate shapes, and there is a high degree of variation between individuals in form and size [3]. There are also differences between sexes [4, 5].

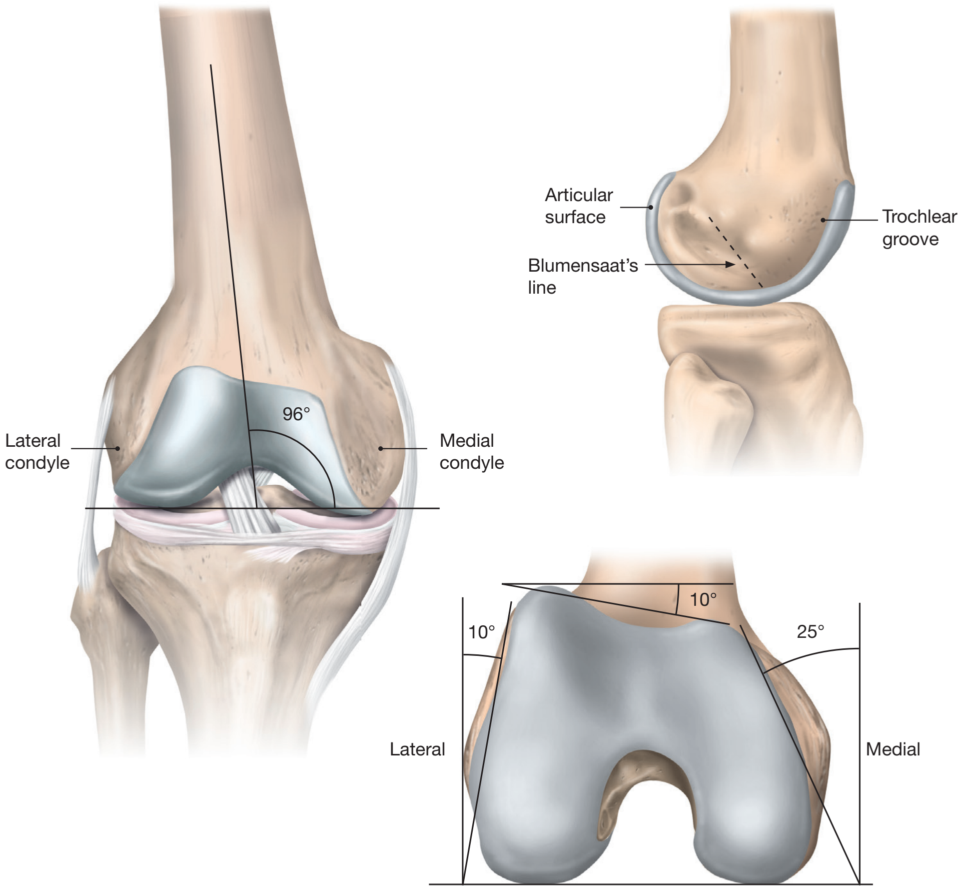

Figure 1. The distal part of the right femur (frontal view to the left). The collateral ligaments are attached to the femoral epicondyles. The menisci and the anterior cruciate ligaments are also illustrated. On the upper right, the knee is seen from the lateral view, showing the characteristic shape of the condylar surface. The Blumensaat line marks the cortex of the intercondylar notch. Furthest down on the right is an axial view of the distal femur. The condyles are asymmetrical.

The femur shaft has a cortical bone structure and connects the proximal and distal metaphyseal areas. The cortical bone is dense and thick at the midshaft, leaving only a narrow medullary canal in younger persons.

The isthmus defines a segment midshaft where the medullary canal has the narrowest diameter [6]; distal of the isthmus, the shaft widens into a flared part that transitions into the metaphysis.

6.2.2 MUSCLE ANATOMY

The adductor muscles insert on the medial epicondyle. On the dorsal aspect of the femur, the linea aspera offers the origin for muscles accomplishing knee flexion. The gastrocnemius muscles originate on the dorsal aspects of the condyles. Several muscles and tendons pass past the knee and attach to the tibia, the quadriceps muscle joins into the patella, and the patellae ligament is attached to the tuberosity of the tibia and contraction of the quadriceps extends the knee. The fascia lata and hamstring flexor also pass from the origin of the thigh to the proximal part of the tibia. The muscle tonus of these muscles affects the displacement of a distal femur fracture (DFF). A typical fracture displacement pattern of the DFF is a hyperextension of the distal fragment caused by the pull of gastrocnemius muscles in combination with the pulling power of the quadriceps.

6.2.3 GEOMETRY OF THE FEMUR

The long axis of the femur is defined as a line from the centre of the femoral head to the anterolateral insertion of the posterior cruciate ligament. A second line connects the joint surfaces of the condyles. The angle is highly variable but usually around 4° valgus [3]. Individual side-to-side differences exist in femoral anteversion [3, 7-10] but also in anterior bow angle, femoral head size, and offset [11].

6.3 Classification systems of DFFs

Since Neer classified supracondylar femur fractures in 1967 [12], many classification systems for DFFs have been suggested. Some proposed systems focus on native fractures [12-15], and there have been multiple suggestions for classification systems for periprosthetic fractures adjacent to a total knee replacement (TKR) [16-19]. Some of these periprosthetic classification systems describe the stability of the prosthesis fixation [20-22], and some classification systems also suggest surgical treatment for periprosthetic fractures [21-24].

Recently, classification systems for fractures adjacent to a previous implant (non-periprosthetic peri-implant fractures, NPPIFs) have been suggested [25, 26]. However, no validated or well-established system exists for NPPIFs at this point. The well-established universal classification system by Arbeitsgemeinschaft für osteosynthesefragen/ Orthopeadic trauma association (AO/OTA) has, in its latest update in 2018, a qualification for NPPIFs. Still, it does not specify the proximity of the implant to the fracture or the type of osteosynthesis implant [15].

There is no consensus on when a fracture of the distal end of the femur should be called a DFF, and as a result, different definitions are being used [27, 28]. The inherent difficulty in defining a fracture as a DFF lies in determining a border between the diaphysis with cortical bone and the metaphysis with cancellus bone. Offering a solution to this problem, in 1988, Urs Heim introduced the "square box", defined by drawing a square box where the epicondyles' width equals the metaphysis's height" (Figure 2). The cranial side of the square determines the border between the diaphysis and metaphysis [14]. The square roughly corresponds with the transition of the metaphysis into the flared distal shaft in younger adults; however, the anatomical variation is vast in this area, and there are no clear radiological borders to define where the shaft ends and the metaphysis starts.

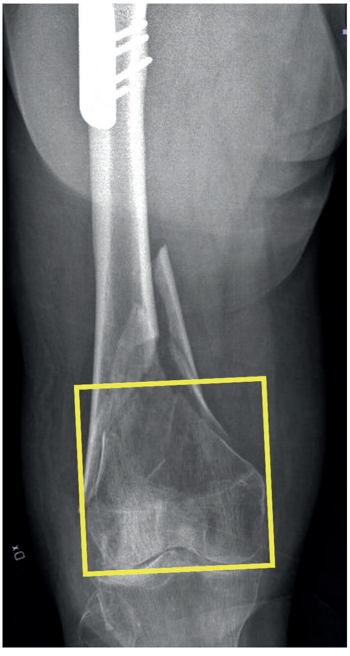

Figure 2. A distal femur fracture. The yellow square indicates Urs Heim's "square box", an arbitrary method of defining the border between the shaft and metaphysis where the width of the epicondyles is equal to the height of the metaphysis. Often, however, distal femur fractures of the elderly patient are found in the borderline area, which makes classification with AO/OTA challenging.

Complicating the inherent difficulty in defining a border is the alteration of morphology and anatomy with rising age [29, 30]. These age-related changes may also affect the mechanical properties and, thereby, fracture patterns of DFFs in older people. No fracture classifications are adopted for osteoporotic fractures in the distal femur. In other locations, such as the pelvic region, classification systems for osteoporotic fractures have been suggested [31, 32] and also in osteoporotic thoracolumbar spine fractures [33].

6.4 Epidemiology of DFFs

Results of epidemiologic studies on DFFs vary depending on the population assessed and the time point of investigation. A bimodal incidence of DFF has commonly been presented. One peak affects young males aged 20 inflicted by high-energy trauma, and the other peak consists of older women aged 70 caused by low-energy trauma [34-38]. However, recent studies have detected a rise in osteoporotic fractures in elderly patients following low-energy trauma, with a female predominance, and a decline of high-energy-induced fractures in younger males [39-44]. In a study of the total Finnish population, Kannus *et al.* [45] compared the incidence of osteoporotic knee fractures, which comprised distal femur, patellae, and proximal tibiae, between 1970 and 1999. The relative increase in incidence in women was 214% during this period, and estimations suggested a rise of another 140% in incidence through 2030. However, epidemiological patterns can also differ between different geographical regions; in a survey on the incidence of femoral fractures in Taiwan, proximal fractures increased with advancing age. In contrast, the shaft and distal fractures declined with advancing age [46].

The incidence of periprosthetic fractures is also rising due to the increasingly aged population and more patients having prosthetic implants [47]. The incidence of fractures related to non-periprosthetic implants is also probably increasing, although data on fracture epidemiology is lacking [25, 26, 48, 49].

6.5 Fracture healing in aged and osteoporotic bone

The highest capacity to heal fractures is found in growing individuals with an immature skeleton [50]. The healing conditions are similar to those needed for bone growth, with a good blood supply and thick periosteum [51]. In older patients, age-related diseases such as osteopenia or osteoporosis will affect the mechanical properties of bone and alter responsiveness to mechanical stimuli [52]. Increased age also leads to decreased bone formation and altered biomechanical properties [51].

Furthermore, ageing has a negative effect on the fracture-healing process itself in multiple ways. Both chronically ill and healthy older persons have been found to have increased levels of inflammation, which can negatively affect angiogenesis and cellular differentiation, essential in fracture healing, resulting in delayed callus maturation and consequently decelerated fracture healing [53, 54]. The haemostatic cascade, growth factor expression, and endothelial cells are also involved in bone healing and are also affected by age, resulting in delayed and impaired neovascularisation and consequently negatively impacting wound and fracture healing in elderly patients [51, 55].

6.6 Osteoporosis

Osteoporosis is common; about 50% of all females in Sweden will have osteoporosis when aged 80-84 [56]. Although the total European population is projected to be constant over the next 25 years, the proportion of older individuals (65 years or older) will increase by 56% in men and 41% in women, and very old individuals, aged 85 years or more, will increase by 129 % in men and by 73 % in women. Hip fractures are estimated to double in the next 50 years [56]. Coughlan *et al.* [57] estimated that 50% of women and 20% of men over 50 years of age will experience an osteoporosis-related fracture. Despite the increasing incidence of osteoporosis and its tremendous economic burden on society [58, 59], only a minority of older individuals are treated for osteoporosis [60].

The continuous loss of bone mass, weakened muscle strength with advancing age, and decreased postural balance increase the risk of low-energy fractures such as falls from a standing height or less [61-63]. These fragility fractures are associated with increased mortality in elderly patients with DFFs [64, 65].

Taken together, the prevention of fragility fractures and optimising treatment of elderly patients with fragility fractures are both becoming increasingly important [66].

6.7 How the process of ageing affects bone morphology

Already in 1832, Astley Cooper observed weakening of the thighbone and increased risk for fractures with increased age [67]. Today we know that age affects the human skeleton throughout life. Once the bones mature after adolescence, they remain morphologically unchanged during midlife (age 20-50). The constant remodelling process of resorption and deposition is balanced, and the net bone mass is maintained. From late midlife and onwards, the remodelling is slower, affecting deposition more than resorption and reducing the mineralised bone matrix. The remodelling process mainly occurs at the surface of the bone in the medulla. The trabecular bone has a larger surface than the cortical bone. The initial loss of bone matrix occurs primarily in the trabecular bone. The trabeculae are thinning due to this process (Figure 3). In women, after menopause, the loss of bone matrix and deterioration of trabeculae is even further enhanced, causing perforations of the trabeculae [68, 69]. These perforations of the trabeculae are thought to be one of the reasons for an increased incidence of fractures in postmenopausal women [70]. With time the surface area of the trabecular bone is decreased, and when age advances over 60, cortical bone loss instead dominates [71].

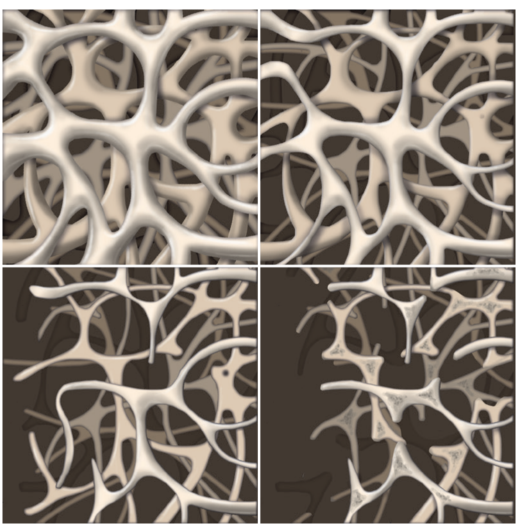

Figure 3. Age-related bone loss of the trabecular bone. At the far upper left is the trabecular bone, unaffected by age-related bone loss. Over time, the trabeculae are thinning, eventually perforating, and lastly, diminishing.

The unbalanced remodelling eventually causes resorption in the medullary canal. There is an increase in the femur's outer and inner diameter, which is more profound in women after 50 years of age [72]. The resorption also engages the Haversian and the Volkmann canals, which grow in size and converge into giant pores, making the cortical bone porous and brittle [29, 68]. With advancing age, the cortical bone becomes even more porous and thin and transforms into a trabecular type of bone [73] (Figure 4).

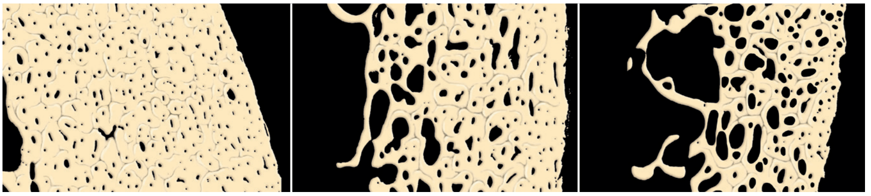

Figure 4. Age-related bone loss in the cortical bone. To the left is the cortical bone, only mildly affected by bone loss. With advancing age, the medullary canal enlarges, thinning the cortex. The Haversian and Volkmann canals widen and converge, creating porosity and weakening the cortical bone's mechanical properties.

At this stage, the trabecular bone has lost most of its trabeculae and has transformed into what appears to be thin cortical bone [29]. The enlargement of the transitional zone, where the cortical and trabecular bone joins, advances with age and can extend into previously cortical sites like the midshaft of a long bone [71, 73] (Figure 5). It is suggested that with age, relatively lower torsional and bending loads of the metaphyseal regions of the femur may contribute to less favourable remodelling, thus increasing the risk of fracture in older age [74, 75]. There are also morphological changes that occur in the shaft that could increase the risk for fractures [69, 76-78]. Studies have shown a decrease in density and an increase in porosity, especially in older females, which affects both stiffness and strength [79-81]. Theories state that due to these age-related changes, the bowing deformation of the femur occurs in older women [72, 82, 83] (Figure 5). The corresponding bowing is not seen in men. The shape of the condyles and epicondyles in the distal metaphyseal area are also subject to age-related changes [84, 85]. However, the relationship between age-related changes in the metaphysis and increased fracture risk has not yet been thoroughly studied.

In patients surgically treated with total hip replacement (THR), the remodelling over five years causes the bone density to decrease locally in the proximal part of the femur but also in the shaft and distally. It also affects the contralateral femur, probably by an altered gait pattern [86].

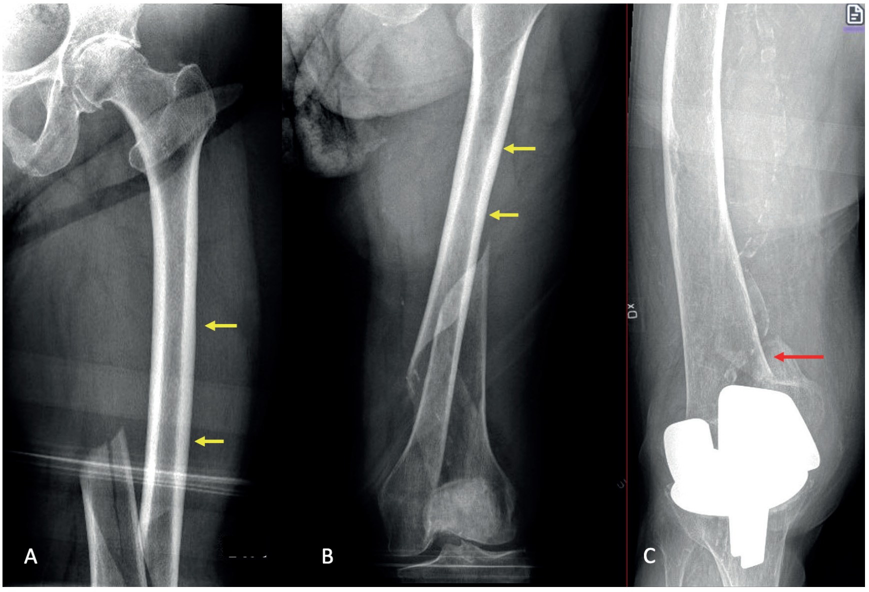

Figure 5. Age-related changes to the femoral shaft. The yellow arrows in A and B represent the outlines of the femoral isthmus. In femur A, the isthmus is longer and located in the midpart of the femur, representing the conditions of adult bone without severe age-related changes. Femur B has the isthmus migrated proximally due to age-related changes to the shaft. Femur C has characteristics of advanced bone loss, with a thin cortex (red arrow), enlarged diameter and shaft bowing.

6.8 Age-related loss of muscles

The loss of muscle mass and strength is part of ageing and is caused by a gradual decline in muscle protein synthesis, which is not related to a disorder in the renewal of protein, but to a decreased anabolic response to food intake [87, 88]. With ageing, the protein metabolism becomes more resistant to the effects of insulin, similar to insulin resistance in obesity [89, 90]. The decrease in sex hormones further aggravates the loss of muscle mass [87]. Increased levels of inflammation, commonly seen in ageing persons, are also associated with muscle loss [91]. The process of muscle loss is not linear; some factors, like physical inactivity, can accelerate and perpetuate the loss of muscle mass and strength. Sarcopenia is a significant loss of muscle mass and strength that negatively affects walking ability and can be measured by walking speed [92]. It is common in older individuals, and as many as 71% of patients with hip fractures have sarcopenia [93].

The age-related processes of bone loss and sarcopenia occur parallel, resulting in so-called "osteosarcopenia" [94]. It has been suggested that muscle loss causes decreased bone loading, further contributing to age-related bone loss [95].

6.9 Surgical fixation of DFFs

Historically, treating lower limb fractures has been under the motto "rest until healed". However, this led to a problem with stiff joints and contractures, and in 400 BC, Hippocrates recommended cautious exercise of the injured limb as soon as the inflammation had settled [96]. A thighbone fracture could be immobilised with splints for 50 days. These recommendations from Hippocrates were forgotten, and the interest in the "early movement" of joints did not re-emerge until the 18th and 19th centuries. Traction as treatment was also introduced, allowing some early joint movement. Surgical fixation of fractures, in general, was not popularised until the introduction of antibiotics [96]. However, surgical fixation of DFFs was not the treatment of choice until the late 1960s, mainly because of the high rate of complications [12, 97]. One frequently occurring complication was the loss of fixation and varus collapse. The blade plate was introduced in the late 1950s, and derivates were successfully used in osteoporotic bone in the early 1970s [98]. In parallel, antegrade intramedullary nails in extra-articular DDF gained popularity [99]. Retrograde intramedullary nails (RIMN) were introduced in 1990 [100]. In 1996, Butt *et al.* [101] conducted a randomised controlled trial (RCT) comparing non-operative treatment (traction) with dynamic compression screw (DCS) plates. The surgical treatment was advocated as it showed fewer complications than the non-operative treatment. The less invasive stabilisation system (LISS) was introduced in the same period [102]. However, recent evaluations of different fixation constructs have shown comparable rates of non-union in plates with locking screws and nails [103-108].

6.9.1 THE IMPORTANCE OF ANATOMICAL ALIGNMENT IN THE FIXATION OF DFFS

Despite the fixation options available today, surgical fixation of DFF is still demanding [109]. The reports of non-anatomical postoperative reduction rates show relatively high numbers, indicating the difficulty of the procedure [106, 110-112]. The operative alignment of DFF could be divided into four significant dimensions: restoration of femoral length, coronal, sagittal angulation [113], and rotational angulation[10].

In a recent RCT by Dunbar *et al.* [106], the overall postoperative malalignment after plate fixation in DFF over 5° was 32%. Valgus deformity was the most common, at 27.4%, and varus deformity occurred in 4.8 % of the cases, but no sagittal malalignment was found. Sagittal malalignment was, however, reported to be common in comminute periprosthetic DFFs [114]. Postoperative malalignment may increase the risk of non-union [115, 116]. The rotational alignment of the femur has been suggested to be particularly challenging to control during fracture fixation [117-119] and even more so in minimally-invasive plate osteosynthesis (MIPO) [120-122]. Compared to the unfractured leg, a consensus on the degree of rotational malalignment that should be defined as clinically relevant has not yet been reached. However, 15° has been suggested as reasonable [10, 118, 123, 124]. Postoperative malalignment has been highly correlated to the degree of malalignment in healed fractures [115]. Malunions of femoral fractures have been shown to negatively affect knee function, and gait, resulting in articular cartilage shearing, which can, in turn, develop into painful osteoarthritis [125-127].

6.9.2 FIXATION IN OSTEOPOROTIC BONE

Age-related bone density and bone quality deterioration affect the stability of osteosynthesis in elderly patients [29, 51, 128, 129]. A growing proportion of these patients have also had previous surgery on their femurs, making surgery even more difficult [26, 35, 47]. With the development of hardware and surgical techniques during the last decades, anatomical distal femoral locking plates have become a standard treatment (alongside RIMN), as they are versatile in allowing peri-implant fixation [129-139]. Using a long bridging plate with locking screws has also been shown to have biomechanical advantages [140-143], such as the lowest incidence of loss of fixation, more flexibility, and better capability to withstand permanent deformation in osteoporotic bone compared to other fixation options [144-149]. The bridging plate has also been reported to decrease the risk of non-union [150-153]. The MIPO technique is advantageous in the fixation of DFF, with less violation of blood supply and a decrease of non-union [154-162]. Plates with a large contact area between bone and plate effectively reduce the stress at the bone-implant interface and reduce the risk of failure [128, 163]. The concept of dual plating (DP) of DFF has been popularised in the last decade. In a recent review of the literature, DeKeyser *et al.* [164] concluded that biomechanical studies had shown increased stability of the fixation construct and no increased risk for neurovascular injuries using a medial MIPO plate, and non-union rates were not higher for DP than lateral plating. In another review of DP, Lodde *et al.* [165] reviewed the union rates after DP and found promising results favouring its use. However, clinical studies comparing union rates in older patients with fragility fractures are lacking.

In other locations, postoperative fracture subsidence of the metaphyseal fragment or even cut-out of the osteosynthesis are not uncommon reasons for mal- or non-union in osteoporotic bone [128, 166-168]. In DFFs, metaphyseal and distal shaft migration and cut-outs have been studied mainly in experimental models [145, 169-172]. Galea *et al.* [173] assessed the migration of locking screws in the distal fragment throughout the healing in patients with DFFs aged 22-89 years and found a mean of 5 mm migration throughout a one-year follow-up.

An alternative surgical treatment of DFFs in elderly patients with comminuted fractures is the distal femoral replacement (DFR), which could also be an option for a loose TKR combined with a fracture. The entire distal femur fragment is excised and replaced by a stemmed hinged TKR. Mortality and complications are not higher with DFR than with ORIF and could be a future treatment option in selected frail elderly patients [134, 174, 175]. There is, however, a need for future prospective trials as current reports on the DFR are, at this stage, primarily observational [176].

6.10 The concept of restricted weight-bearing

The battle between immobilisation to achieve bone healing and moving joints to preserve joint function was already addressed by Hippocrates (400 BC) [96]. Some 2500 years later, this conflict remains; although we now fixate fractures internally, the thought of protecting the osteosynthesis by off-loading the fracture still prevails [177].

Almost a century ago (1935), Kleinberg reported on rapid union following early weight-bearing in a femoral neck fracture [178]. Similar reports with successful treatment of DFFs with early weight-bearing were published half a century ago (1975) [179].

Although the evidence is lacking that weight-bearing restriction has any beneficial effects on healing and a decrease in rates of complications after surgical treatment [177, 180], it is still widely used in fractures distal to the hip [181]. In a Canadian interview study from 2016 [182], 20 orthopaedic surgeons were interviewed on why they prescribed restricted weight-bearing in patients with hip fractures, despite the strong evidence in favour of early full weight-bearing. Factors include the choice of construct, type of fracture, previous experience of construct failure, and lack of local audit.

Despite good intentions of restricting weight-bearing to reduce fixation failures, studies have shown that the quality of reduction and the implant position are the two most important factors determining the risk for fixation failure, not the weight-bearing regimen [183, 184]. Recent reports have shown that restrictive weight-bearing in elderly patients with DFFs did not, in fact, decrease the rate of complications [177, 185-189]. On the contrary, reports have reported increased complication rates in DFFs [130] and hip fractures [190, 191] with a restricted weight-bearing protocol. The restriction of postoperative weight-bearing in elderly patients with hip fractures also negatively influences function [192, 193] and increases mortality rates [190, 194]. Besides lacking evidence of decreased rates of surgical fixation failure and non-unions by using restricted weight-bearing, the ability to comply with weight-bearing restrictions after surgery has been demonstrated to be low [195-198]. In elderly patients with hip fractures, compliance is even lower [192, 199]. Equivalent studies have not, however, been conducted in patients with DFFs.

6.11 Gaps of knowledge in the treatment of DFF

Although weight-bearing restrictions are commonly used following surgical fixation of the DFF regardless of the patient's age [181], there is a lack of knowledge on the effects of a period of restricted weight-bearing on elderly patients in regards to post-rehabilitation function and recovery [180, 200]. There is also a lack of knowledge on the compliance of weight-bearing strategies and how they affect gait recovery.

Using a traction table for closed reduction and fixation might be helpful in the challenging task of surgically fixating DFFs; there are, however, no reports on postoperative alignment using this surgical setup.

Using a lateral bridge-plating MIPO is thought to be one state-of-the-art fixation method for DFFs in elderly patients; however, more knowledge is needed on the secondary displacement of healing DFFs in old and osteoporotic bone [108, 131, 134].

There needs to be more knowledge on how morphological age-related changes in bone affect the spectrum of fracture patterns and fracture patterns associated with previous implants. A new classification is needed to better identify the age-related morphological changes of DFFs and can classify all fractures regardless of the presence of implants.

7

Aims

Study I: The primary aim of this study was to compare the function index of short musculoskeletal function assessment (SMFA) between partial weight-bearing (PWB) (first eight weeks postoperatively) and immediate full weight-bearing (FWB) in elderly patients treated for DFFs. The secondary aim was to compare the other indexes of SMFA and EuroQol-5 Dimensions (EQ-5D), pain measured by visual analogue scale (VAS) and range of motion (ROM).

Study II: This study aimed to evaluate (with computer tomography (CT) scans) to which degree anatomic alignment could be achieved with closed reduction of DFFs on a traction table with a dedicated femoral support when performing a MIPO. The results were compared with previously published findings using a conventional setup (supine operating table).

Study III: The primary aim of this study was to evaluate secondary fracture displacement during healing (one-year follow-up) in a cohort of elderly patients treated with a bridging distal femur locking plate. The secondary aim was to evaluate whether bone mineral density, body mass index (BMI), or restricted weight-bearing postoperatively (eight weeks) affected secondary displacement.

Study VI: The primary aim of this study was to investigate whether a period of restricted postoperative weight-bearing for eight weeks had a long-term effect on gait recovery (actual weight-bearing and cadence) for elderly patients with DFFs during a one-year follow-up period. The secondary aim was to differentiate between actual weight-bearing and the effects of the imposed weight-bearing restrictions by assessing the ability of these patients to adhere to the restricted weight-bearing protocol.

Study V: The first aim of this study was to design and propose a new clinically relevant classification system for DFFs in elderly patients based on observations and the fracture distribution from a cohort of 342 patients ≥ 65 years old. The second aim was to test the reliability of the proposed classification with inter-rater agreement tests.

8

Patients

8.1 Patient cohort (Studies I-IV)

Studies I-IV shared the patient cohort of the RCT from 2012 (first of January) to 2016 (30th June) conducted at the Department of Orthopedics, Sahlgrenska University Hospital, Gothenburg, Sweden.

Eligible patients were aged 65 years or older with a traumatic fracture of the distal part of the femur of AO/OTA types 33 (A2-3, B1-2, C1-2) and 32(c) (A1-3, B2-3, C2-3) and UPCS; IV (3B1, 3C-3D) and V (3B1, 3C-3D) [15]. Peri-osteosynthesis implants fracture were also eligible [25].

8.1.1 EXCLUSION CRITERIA

Exclusion criteria were prior physical impairment or concomitant injuries that could significantly affect the postoperative rehabilitation, ongoing systemic infections, pathological fractures, alcohol or drug abuse, and preinjury inability to ambulate independently. Using walking aids, such as crutches or walkers, did not warrant exclusion. Other exclusion criteria included open fractures of types II and III according to the Gustilo-Andersson classification [201], cognitive impairment (6 points or fewer) according to the Short Portable Mental Status Questionnaire (SPMSQ) [202] and the inability to communicate in the Swedish language.

8.1.2 PREINJURY DEMOGRAPHIC AND PATIENT-RELATED DATA

Data were collected at the time of study inclusion. Function Recovery Score (FRS) [203] was used for assessing preinjury function. Length, weight and walking aids, as well as living conditions before the injury, were documented.

After surgery, the length of hospital stay and whether there was a need for a temporary stay at a nursery facility. At follow-up, living conditions and walking aids were documented. The need to permanently move to a nursing home was evaluated at the 52-week follow-up.

8.2 Patient cohort (Study V)

For the patient cohort of Study V, all consecutive patients treated for femoral fractures, 65 years or older, at the Department of Orthopedics, Sahlgrenska University Hospital, Gothenburg, Sweden, from 2006 (first of January) to 2016 (31 of December) and diagnosed with the ICD-10 codes S72.4 (distal femur fracture), S72.3 (diaphyseal femur fracture) and M96.6F (periprosthetic femur fracture) were identified through a review of patient medical records. Individuals with a femoral fracture distal to the isthmus were eligible for inclusion.

8.2.1 EXCLUSION CRITERIA

Exclusion criteria included polytrauma with high-energy injuries resulting in multiple fractures on the ipsilateral femur, pathological fractures (both cancer and atypical), and fractures associated with numerous revisions or prior surgeries resulting in distorted femur anatomy. In addition, patients with incomplete radiographs, poor quality radiographs making classification impossible, or patients with only CT imaging of the fracture were excluded. Bony avulsion of the collateral ligamentous insertion on the femoral condyle (AO/OTA 33A1.1 and 33A1.2) was also an exclusion criterion.

The RCT patient cohort from Studies I-IV was also included in Study V (Figure 6).

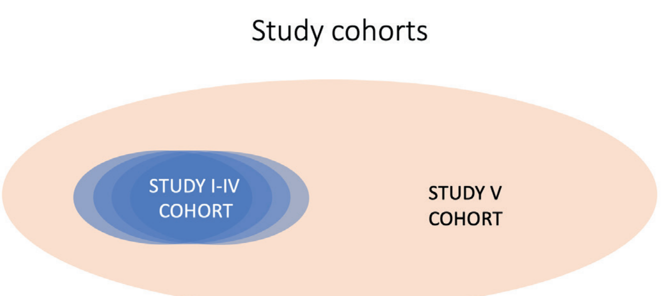

Figure 6. The study cohorts. Studies I-IV shared the same cohort and was a part of Study V's cohort.

9

Methods

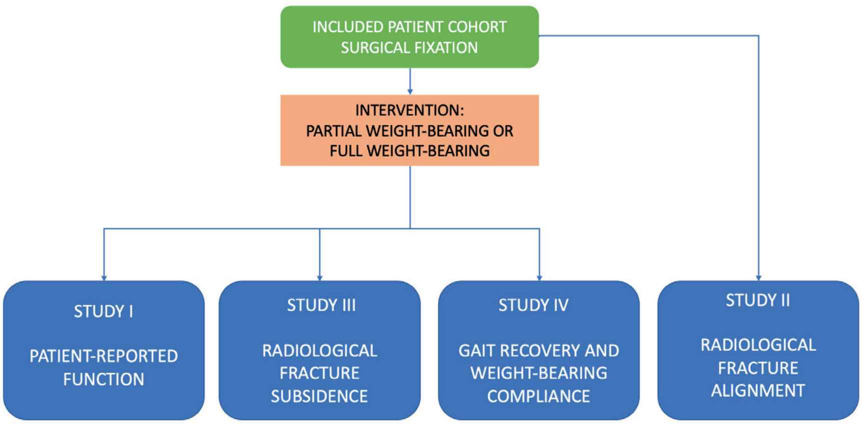

Figure 7. Flowchart of the patient cohort from the randomised controlled trial and their distribution to Studies I-IV. Studies I, III, and IV compared outcomes after randomisation, while Study II evaluated radiological outcomes independently of randomisation.

9.1 Surgical fixation

All included patients in Studies I-IV (Figure 7) underwent standardised surgery according to a detailed protocol by one of seven consultant orthopaedic trauma surgeons as soon as possible after admission. The surgical setup for all patients was with the fractured leg in traction and the patient supine on an operating table. For dorsal support of the fracture, an adjustable femoral supporting device (POsterior Reduction Device P.O.R.D. Orthofix™ SRL, Verona, Italy) was used [204]. The commonly-occurring apex posterior angulation of the DFF was reduced by flexing the knee about 20° by lowering the foot stand. The femoral support could be adjusted in height to improve the reduction further and keep the femur horizontal. Only gentle traction was allowed. The foot rotation in the traction device was set with the foot pointing upwards (Figures 8, 9). The rotation of the foot was to be slightly adjusted to allow the dorsal contours of the femoral condyles to align horizontally for a true lateral view with the image intensifier. The main objective for a true lateral of the knee was to determine the correct plate position since the plate was applied minimally invasively, and no arthrotomy was done. No further actions were undertaken to improve the rotational alignment, as specified by the protocol. Bi-planar fluoroscopy was used. When closed reduction was obtained, the leg was washed and draped (Figure 10).

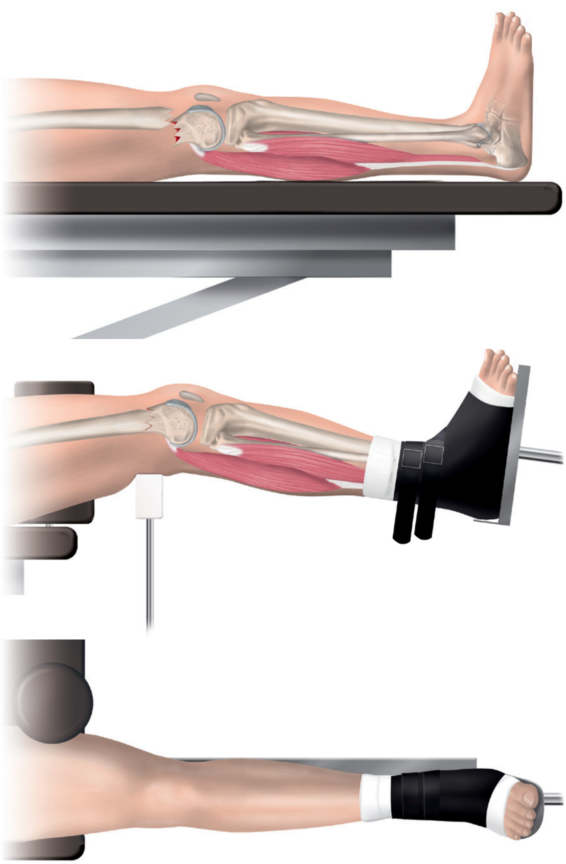

Figure 8. Top illustration, the commonly occurring apex posterior angulation of the distal femoral fracture. Middle illustration, closed reduction of the displaced fracture by a femoral support, supporting the fracture from dorsal, gentle traction and lowering the foot stand. Bottom illustration, the leg is in traction with the foot pointing upwards (seen from above), which reduces preoperative coronal or rotational malalignments.

A small longitudinal skin incision was made longitudinally over the lateral epicondyle (Figure 10,11). After a longitudinal incision of the fascia lata, the lateral epicondyle was cleared from the periosteal tissue. An LCP® Distal Femoral Plate (Synthes™, Oberdorf, Switzerland) was introduced to fit the lateral femoral epicondyle and the femoral diaphysis with a percutaneous technique. A large clamp pressed the plate onto the lateral condyle and shaft. When the plate was correctly seated, it was temporarily fixed with K-wires distally and proximally, verified by the image intensifier (Figure 12, 13). A plate with 13 holes was used for patients of short stature, while fixation for all the other fractures was obtained with a plate with 15 holes. The proximal fixation comprised three bi-cortical locking screws in the plate through stab incisions. Anatomical reduction of the fracture was prioritised over the approximation of the plate to the femoral shaft. The proximal screws were to be spread over the proximal portion of the plate to distribute the load. Distally, five bi-cortical locking screws fixated the metaphyseal fragment (Figure 14,15). The fixation construct was MIPO bridge-plating, allowing no periosteal stripping or additional hardware across the fracture.

Figure 9. The patient set up on the operating table with the fractured leg in mild traction and fracture supported by an adjustable femoral supporting device (POsterior Reduction Device P.O.R.D. Orthofix™ SRL, Verona, Italy) [204].

Figure 10. The patient on the operating table with the fractured leg in traction. After the closed reduction, the patient was washed and draped.

Figure 11. An incision was made distally over the lateral femur epicondyle. The fascia lata was longitudinally incised, and the lateral epicondyle was freed from the periosteum and soft tissue.

Figure 12. The plate was slid under the fascia lata and temporarily fixated with K-wires. A large clamp firmly pressed the plate onto the lateral condyle and diaphysis.

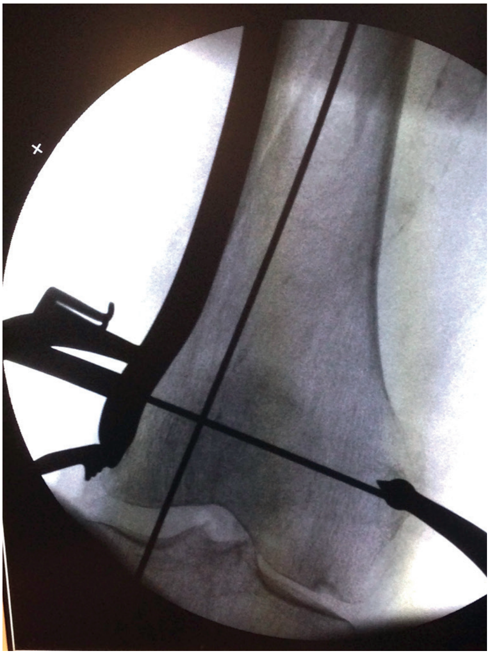

Figure 13. Image from the image intensifier. A large clamp firmly pressed the plate onto the lateral condyle and diaphysis. The plate was temporarily fixated with K-wires.

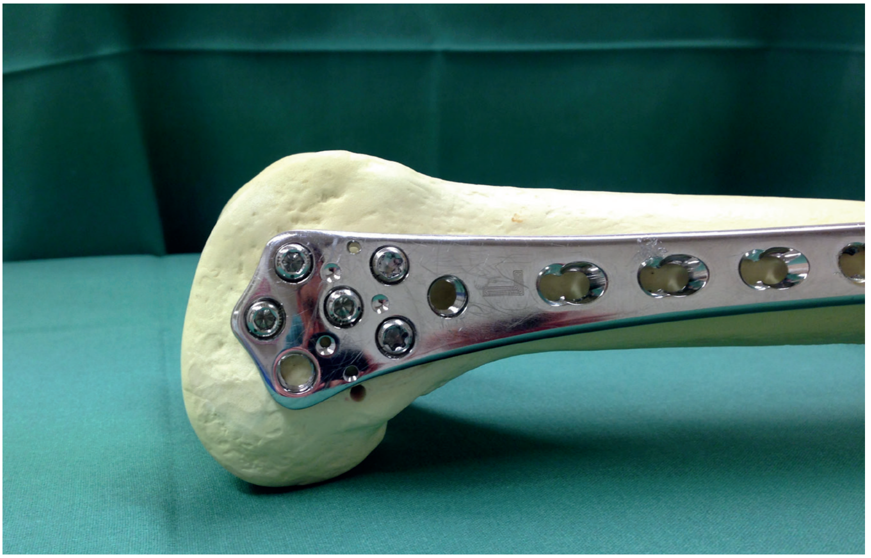

Figure 14. The distal femur (sawbone, lateral view) with an anatomical locking plate, with the distal screw pattern. Five screws were used, and the most dorsal distal holes were left empty.

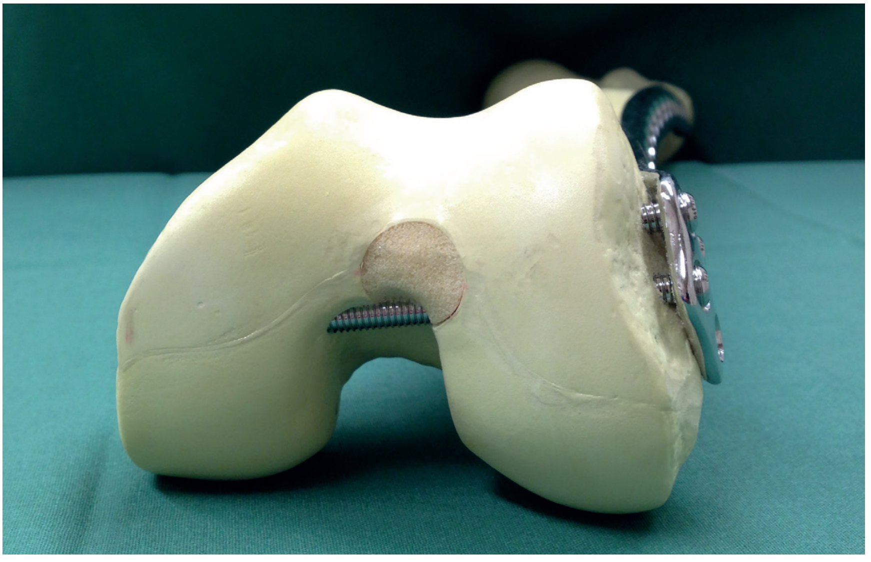

Figure 15. The distal femur (sawbone, distal view) with an anatomical locking plate. The plate is seated flush on the lateral epicondyle. The locking screw direction is towards the medial epicondyle.

9.2 Intervention

After surgical fixation, the patients were randomised to either immediate FWB or PWB for the first eight weeks postoperatively. The first author conducted the randomisation process using an in-house web-based simple randomisation program. In the PWB group, weight-bearing was set to 30% of body weight, and after eight weeks of restricted weight-bearing, the patients in the PWB were allowed to bear weight in full. In the FWB group, patients could immediately bear weight as tolerated. Patients in both groups were allowed to use whatever walking aids they needed postoperatively.

Patients in both intervention groups received physiotherapy according to hospital routine, including exercises that could be carried out in bed or while standing. Patients in both treatment groups received thorough instructions from a physiotherapist on how to follow the allocated intervention.

9.3 Outcome measures

Patients were followed up at eight-, 16-, and 52 weeks postoperatively.

9.3.1 PATIENT-REPORTED OUTCOME MEASURES (PROMS, STUDY I)

9.3.1.1 SMFA (Short Musculoskeletal Functional Assessment)

The primary outcome measure in Study I was function assessed by PROMs. The SMFA questionnaire was used, which is a shortened version of the 101-item questionnaire Musculoskeletal Function Assessment (MFA), which has been extensively validated and tested for reliability and responsiveness [205]. The shorter 46-item derivation (SMFA questionnaire) is also designed to assess patients with common musculoskeletal disorders of the extremities and their implication on everyday life [206, 207].

The SMFA questionnaire is comprised of two sections. The patient's dysfunction index is assessed by 34 questions covering four categories: daily activities, emotional status, arm and hand function, and mobility. The remaining twelve questions cover the bothersome index. The score ranges from 0 to 100, and higher scores indicate more significant dysfunction or bother. The SMFA is validated and translated into Swedish [208].

The primary outcome of study I was the mobility index. The other categories of the SMFA were secondary outcome measures.

9.3.1.2 EQ-5D and EQ-5D (Visual Analogue Scale, VAS)

The self-reported outcome questionnaire, EQ-5D, developed by the EuroQol group, has been used in a large number of studies and is validated in different countries [209, 210]. The EQ-5D has two different versions, of which the three-level EuroQol five-dimension instrument was used in Study I [211]. Calculation of the EQ-5D index was performed according to Dolan *et al.* [212]. The EQ-5D has high responsiveness for patients with hip fractures [213-215]. EQ-5D and EQ-5D (VAS) were used for the secondary outcome. The PROM was compared between groups using means. For the index PROM, a preinjury PROM was obtained using the recall method. Patients were asked to report their functional status during the last week before the injury, which is within the recommended time frame of two weeks [216-218].

9.3.1.3 Pain measured using VAS

VAS is a well-established PROM for pain, including for older patients [219, 220]. The level of pain was assessed in mm on a 100 mm scale. Postoperative pain measured with the simple VAS for pain has shown high responsiveness in measuring patient-reported outcomes and performed equally well as EQ-5D in a study on revision hip arthroplasty [221].

9.3.1.4 Walking aids

The use of walking aids to mobilise was documented. The use of walking aids was documented at study inclusion and each follow-up. There were no study restrictions on the use of walking aids. Walking aids were categorised as (1) cane/stick, (2) crutch, (3) walker, (4) walking frame, (5) standing walker and (6) wheelchair.

9.3.2 ASSESSOR-REPORTED OUTCOMES (STUDY I)

9.3.2.1 Range of motion (ROM) was measured in degrees with a goniometer at follow-up.

9.3.2.2 Timed-up-and-go (TUG) and walking speed test were performed at 16 weeks postoperatively. All patients were appointed to a physiotherapist who was assigned to administer the tests, without knowledge of their assigned weight-bearing allocation. The TUG test measures the time it takes (in seconds) for a patient to rise from a chair and walk a distance of three meters, then turn and walk back to the chair and sit down [222]. The TUG test is a valuable tool for evaluating functional mobility [223-225]. In the walking speed test (m/s), the patient was asked to walk as fast as possible for 30 meters [226]. Walking speed tests have high validity, regardless of pace and distance. However, maximal speed tests over longer distances have higher reliability in older individuals and are suggested for evaluating health and skeletal muscle mass [227]. In studies assessing recovery of fast speed gait at one year after hip fracture, speeds of 0.71 to 0.99 m/s are common, compared to age-adjusted gait speeds of 1.0 to 1.2 m/s for older adults [228]. A gait speed of at least 1.2 m/s is reported to be necessary to cross the street before the light changes in urban settings [228].

9.3.3 RADIOLOGICAL OUTCOME MEASURES (STUDIES II AND III)

Computed tomography scans were made for both complete femurs within one week after surgery and at the follow-ups at eight-, 16- and 52 weeks post-operation. The scans used a metal artefact reduction algorithm and were archived as 3 mm contiguous slices.

In Study II, the postoperative reduction was assessed by comparing the fractured femur to the unfractured femur. Study III evaluated the migration and fracture subsidence by comparing the subsequent CT scans of the fractured femur at the follow-ups. The doctoral student made all measurements twice six months apart and was measured on an axial multiplanar reformations (MPR) tool of the web-based software Xero Viewer (AGFA, Mortsel, Belgium). Increasing the CT slice thickness to 50 mm facilitated the determination of the femoral outlines.

9.3.3.1 Rotation (Study II)

The rotational angle for each femur was obtained by calculating the difference between a distal and proximal angle on axial planes perpendicular to the long axis of the femur. The proximal angle was measured by a line from the femoral medullary canal's centre and through the lesser trochanter's apex. The distal angle was achieved by connecting the dorsal condyles with a line (Figure 16). If the patient had a TKR, the corresponding parts of the prosthesis were used for the distal measurement. The vertical side of the image was used for reference.

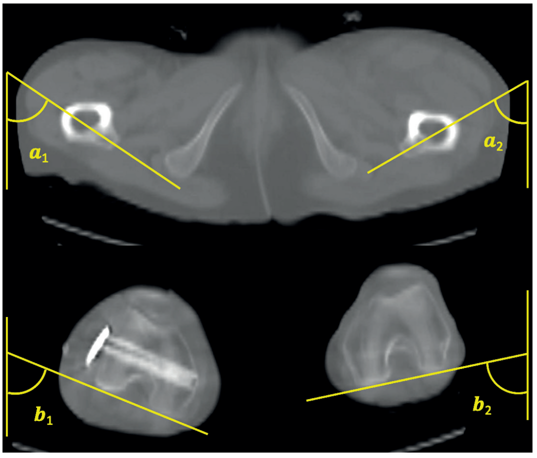

Figure 16. The rotational angles were measured on axial planes. **a_x**; Proximal rotation by a line passing through the femoral medullary canal's centre and the lesser trochanter's apex. **b_x**; Distal rotation by connecting the dorsal condyles with a line. The vertical side of the image was used for reference.

9.3.3.2 Coronal angle (Studies II and III)

The coronal angle was measured between the mechanical axis of the femur (the centre of the femoral head through the centre of the knee) and the distal joint line (Figure 17). In patients who had had previous surgery on the proximal femur (THR or osteosynthesis implant), the centre of the femoral head was used, although the offset of the femoral head in relation the proximal shaft was not always anatomical.

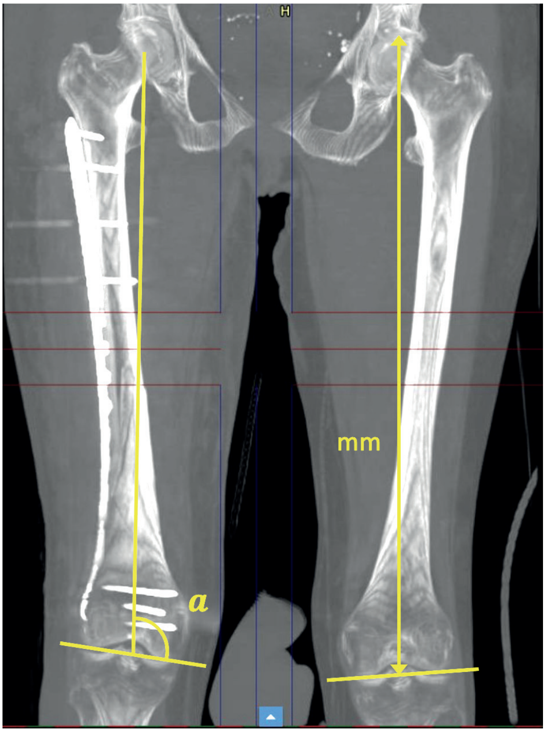

Figure 17. The coronal angle (varus-valgus) ***a;*** between the mechanical axis of the femur (the centre of the femoral head through the centre of the knee) and the distal joint line was measured (left side of the image). The length (right side of the image) of the femur was measured from the centre of the line that connected the most distal contour of the condyles and the most cranial part of the femoral head.

9.3.3.3 Femoral Length (Studies II and III)

The length of the femur was measured from the centre of a line that connected the most distal contour of the condyles and the most cranial part of the femoral head (Figure 17). In patients who had had previous surgery on the proximal femur, the apex of the lesser trochanter was used as a reference measurement.

9.3.3.4 Sagittal angle (Study II)

The sagittal angle (genu antecurvatum/recurvatum) could not be assessed by using Blumensaats' line [229] because of metal artefacts from osteosynthesis or TKR in combination with osteoporotic bone. The sagittal angle was assessed on a sagittal MPR plane perpendicular to the dorsal femoral condyles. The sagittal angle was measured between two lines; one line followed the longitudinal axis of the distal shaft, while the other line cut the centre of the funnel-shaped transition from the flared portion of the distal shaft into the condylar area (Figure 18).

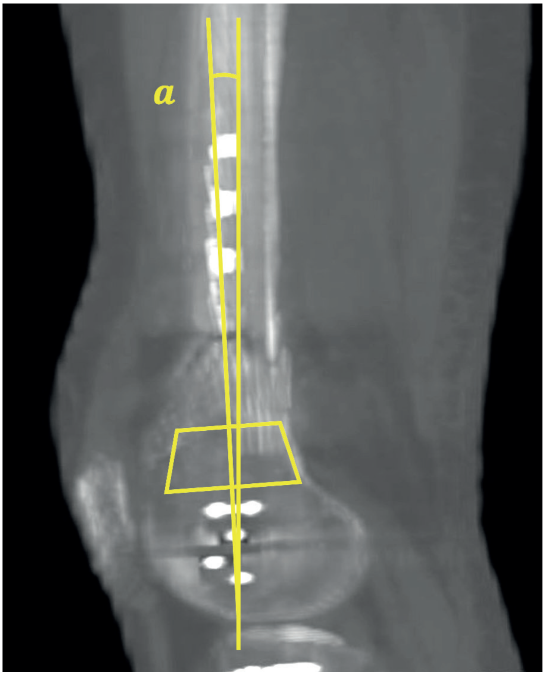

Figure 18. The sagittal angle ***a;*** was measured between two lines; one line followed the longitudinal axis of the distal shaft, while the other line cut the centre of the funnel-shaped transition from the flared portion of the distal shaft into the condylar area.

9.3.3.5 Secondary displacement (Study III)

Secondary displacement of the distal metaphyseal fragment was measured between the centre of the core of one specified locking screw (the most proximal and dorsal of the five distal locking screw clusters) and the most distal point of the joint surface. Measurements were done on both the medial and lateral condyles (Figure 19).

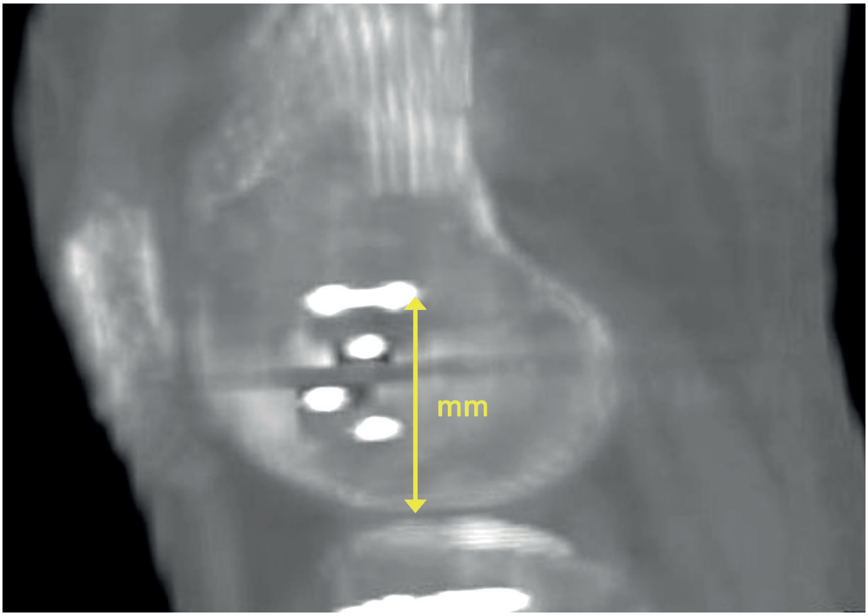

Figure 19. Secondary displacement of the distal metaphyseal fragment was measured between the centre of the core of one specified locking screw (the most proximal and dorsal of the five distal locking screw clusters) and the most distal point of the joint surface. Measurements were done on both the medial and lateral condyles.

9.3.4 GAIT ANALYSIS (STUDY IV)

Gait analyses were made postoperatively before hospital discharge and at eight-, 16- and 52-week follow-ups.

9.3.4.1 Gait measurements

F-scan™ (Tekscan, Boston, Massachusetts), a mobile, wireless, in-shoe pressure-sensing system, was used with a laptop, equipped with F-scan™ software, Clinical 6.7™. The sensors (Figures 20 and 21) were connected to a belt worn by the patient, and the wireless connection to the laptop enabled the patient to walk unrestricted within a 5-meter radius (Figure 22). The F-scan™ system uses pressure-sensitive ink contained in small cells (3.9 pressure-sensing cells per cm^2). The resistance of the pressure-sensitive ink changes with pressure and, thereby, the force it is exposed to. By converting the changes in resistance into digital signals, the measurements are wirelessly transmitted to a computer for real-time analysis.

Figure 20. F-scan™ (Tekscan Boston, Massachusetts) sensor insole.

Figure 21. Shoes fitted with F-scan™ (Tekscan Boston, Massachusetts) sensor insole.

Figure 22. F-scan^{TM} (Tekscan Boston, Massachusetts) wireless equipment. The sensors connected to a belt with a transmitter allowed the patient unrestricted walking within a certain radius.

Ten pairs of unused new walking shoes (Polecat™) in different sizes were used to avoid the bias of different shoes. The patients wore the same pair of shoes for all measurements, only used for this study (Figure 22).

The sensors are thin and sensitive to mechanical wear and were sandwiched between the shoe and the inner sole to protect them from damage. If damages to the sensors occurred, they would present as missing pressure areas on the screen of the F-scan™ software. Sensors were replaced when damaged sensors were noticed.

The accuracy and reliability of the F-scan™ system have been evaluated during the development and evolution of the system over the past decades [230]. Reliability tests have shown excellent agreement in measuring plantar foot pressures [231]. Chen *et al.* [232] showed great accuracy of ground reaction force (GRF) when comparing the F-scan™ with floor-mounted force plates (gold standard), except for the first 21% and the last 10% of the support phase, which was less reliable than the force plates. The "step" calibration method used in that study required the patient to be able to stand on one foot at a time, which was not possible in the current study. A calibration bladder can be an acceptable alternative for calibration [233]. Hsiao *et al.* [234] showed that a calibration using the Tekscan™ Equilibration device would be most accurate if the calibration bladder's pressure equals the body weight's pressure. GRF (Newton) can be calculated to pressure if the weight or force and the area (in cm^2) are known:

$$GRF = kPa \times 0.1 \times Area(cm^2)$$

9.3.4.2 Procedure of measurements

The sensors are temperature sensitive [235], and therefore the shoes (with sensors) were worn by patients for about five minutes to warm them up before performing the walking series. Once the patient started walking and the assessor initiated the recording sequence, the software system recorded for eight seconds. The patient had to complete at least four stance phases of each foot to get a valid series. The software, F-scan research™ was used to analyse the acquired data. The software provides peak GRF, which is the force of the actual weight-bearing. The default setting of the software is to discard the first and last phases. Figure 23 shows the mean pressure distribution of one walking series.

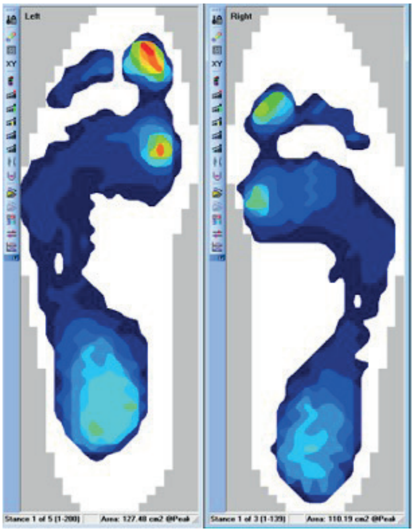

Figure 23. The software F-scan research™ presents the vertical force as footprints with different colours, from dark blue for light pressure to red for high pressure.

Cadence (steps per minute) was calculated from the data of the walking series by measuring the mean time of three consecutive steps (complete walking cycles, stance and swing phases).

9.4 Assessment of fracture demographics (Study V)

Radiographs of the fractures for all eligible patients identified from the medical records review were retrieved. Only femur fractures distal to the isthmus were included. The fractures were classified based on radiographs with an anterior/posterior (AP) and a lateral view projection. Since peri-implant fractures include implants distant from the fracture, at least one hip projection was included

The demographic distribution was assessed by classification (doctoral student) using the 2018 AO/OTA classification. The unified classification of periprosthetic fractures (UCPF) also included [15]. However, the 2018 AO/OTA classification does not specify NPPIFs. A modification to an NPPIF classification presented by Egol *et al.* [25] was used, and osteosynthesis implants were categorised into three types: Antegrade intramedullary nail (IMN), plate and screws (PL) and hip screws (HS). The proximity of the fracture to the implant was defined as near (less than one cm) and far (more than one cm).

9.5 Classification design and development

An expert panel comprised of two experienced consultant orthopaedic trauma surgeons and an experienced consultant radiologist developed the proposed classification for DFF in elderly patients. The original observations were that 1) the fracture patterns in elderly patients differed from that of the younger patients, 2) the comminution did not follow the fracture patterns provided by AO/OTA, 3) and peri-implant fractures did not have a different fracture pattern than native fractures. These observations were the starting point for initiating the work of designing a new classification system and these observations were confirmed after reviewing the fracture pattern distribution in the dataset. The expert panel agreed on the following essential requirements for the new classification system: 1) the classification should describe the frequently occurring and typical spiral-shaped fracture patterns in the distal shaft and transient area connecting the metaphysis and distal shaft, 2) the classification should adequately describe comminution in osteoporotic bone, and 3) the classification should include peri-implant fractures (both replacements and osteosyntheses).

9.5.1 RELIABILITY TEST I (STUDY V)

The first reliability and agreement test was conducted according to guidelines [236]. The proposed new classification system was compared to the 2018 AO/OTA [15] by classifying the complete data. Both classifications comprise multiple categories, and each class was tested separately. To avoid bias, the assessors were blinded to the demographic data of the cases [237]. The three assessors included a registrar with moderate clinical experience, a medical student with limited clinical experience, and an experienced orthopaedic consultant. The registrar and medical student were introduced to the classification systems during a 30-minute-long instructional session using a set of training cases. The classification assessments were done independently at their own pace, also documenting the time spent per assessment.

9.5.2 RELIABILITY TEST II (STUDY V)

A second inter-rater reliability test of the new classification was conducted [236]. A set of 70 cases was obtained by extraction of the original dataset, preserving the proportional distribution of peri-implant fractures and fracture classes. Each patient was randomly selected from the class quota. The assessors were one experienced musculoskeletal radiologist and four experienced orthopaedic traumatologists, and the classification assessments were done independently at their own pace.

9.6 Statistical methods

Statistical analyses were performed in SPSS Statistics versions 26 to 29 (IBM, New York, USA). The normality of continuous data was analysed with Q-Q plots. Normally distributed continuous data were presented as mean and standard deviation (SD), while median and interquartile range (IQR) or standard error (SE) were presented if the distribution was not normal.

9.6.1 STUDY I

An independent samples t-test was used for continuous variables and Fisher's exact test for categorical variables for comparisons between groups. For comparisons between different time points, a paired samples t-test was used. Statistical significance was set at $P > 0.05$. A power analysis requires a minimal important difference (MID); however, a MID for the SMFA function index was unavailable when initiating the study [238]. SD can also be used for power analysis, and an SD of 15 was considered reasonable [239]. A 10-point difference with 80% power and alpha set at 0.05 would be detected with a group size of 35 patients in each group. For Mann-Whitney U was used to compare smaller groups (TUG and walking speed) with normally distributed data.

9.6.2 STUDY II

The intra-rater agreement of the CT measurements was used to calculate intra-class correlation (ICC), with two-way mixed effects and an absolute agreement of 95% [240].

9.6.3 STUDY III

The student's t-test was used for assessing paired comparisons in a normal distribution. Wilcoxon's signed-rank test was used for non-normal distribution, and the Mann-Whitney U test was used for independent group comparisons. The Chi-square test was used for categorical data comparison. Statistical significance was set at $P < 0.05$. For correlation analysis, Spearman rank correlation was used. The intra-rater agreement of the CT measurements was used to calculate intra-class correlation (ICC), with two-way mixed effects and an absolute agreement of 95% [240].

9.6.4 STUDY IV

The Mann-Whitney U Test was used to calculate statistically significant differences between groups, although normally distributed, due to the small sample sizes in this study.

9.6.5 STUDY V

Fleiss' kappa was used to calculate the interrater-observer agreement [241]. The calculated kappa coefficient κ was set to a 95% confidence interval (CI). Evaluation of the strength of agreement of the κ statistic was done according to Landis and Koch [242] (< 0.00 Poor, 0.00-0.20 Slight, 0.21-0.40 Fair, 0.41-0.60 Moderate, 0.61-0.80 Substantial, 0.81-1.00 Almost Perfect). The percentage of the absolute agreement was also calculated.

10

Results

10.1 Results (Studies I-IV)

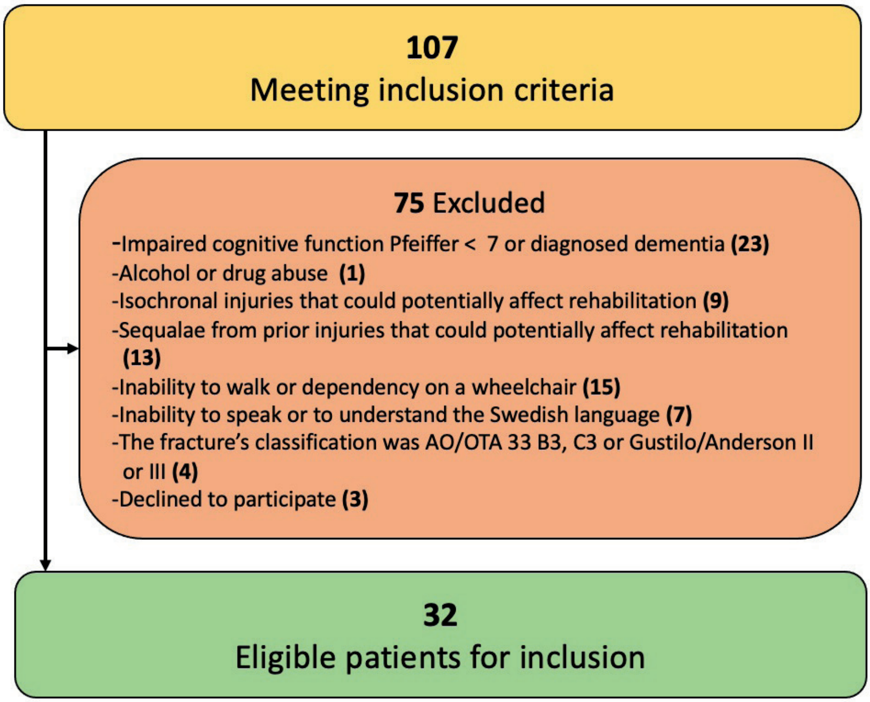

Figure 24. Flowchart of inclusion and exclusion process of patients in the randomised controlled trial (Studies I-IV).

Between January 2013 and June 2016, 32 patients were enrolled in the study cohort. Eligible and excluded patients are shown in Figure 24.

Twenty-one patients were randomised to PWB and 11 to immediate FWB (Figure 25).

10.1.1 ASSESSMENT OF FUNCTION USING PROM (STUDY I)

In the PWB group, two patients who died before the eight-week follow-up and one lost to follow-up were excluded. Thus, 11 patients in the FWB group and 18 patients in the PWB group were available for inclusion in the analysis (Figure 25).

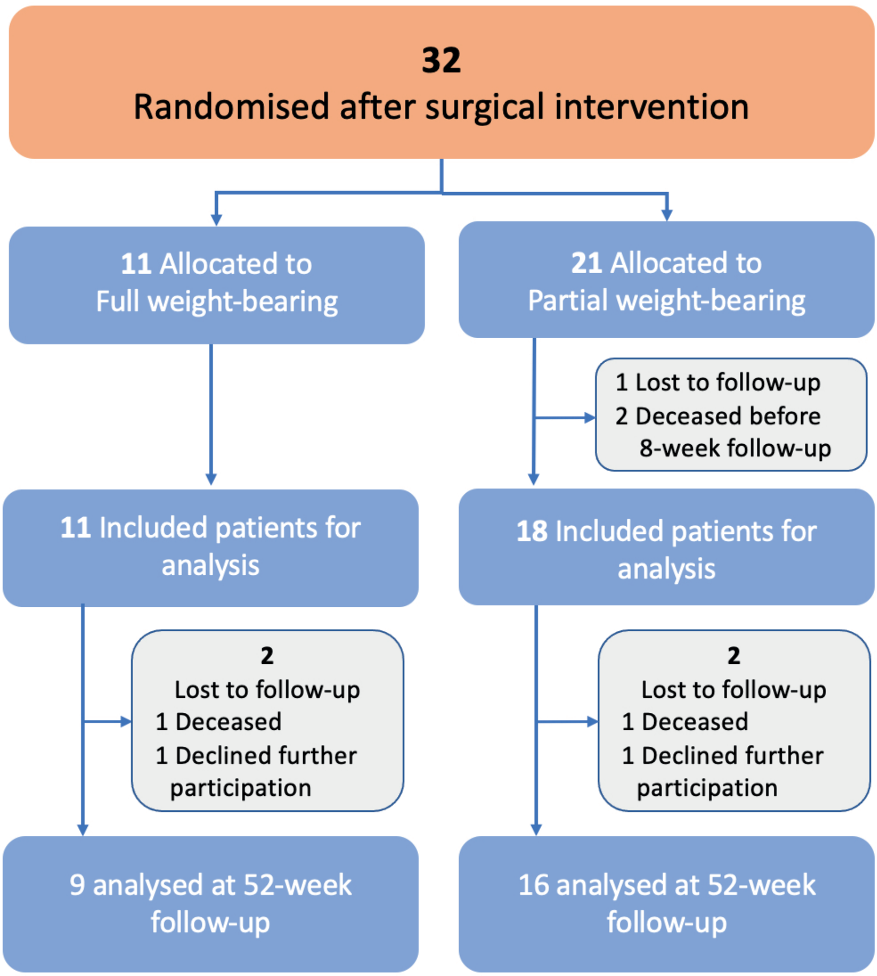

Figure 25. Flow chart of patients included in the randomised controlled trial and randomised after surgical fixation. Patients included for analyse in this figure represents Study I.

There were no statistically significant differences between the treatment group regarding demographic or clinical characteristics, except a significant difference in surgery duration between FWB and PWB groups without any apparent explanation. At admission, the mean American Society of Anesthesiologists Classification (ASA) score was 2.48 in the PWB group and 2.18 in the PWB group. The FRS score was 95.3% in the PWB and 97.1% in the FWB groups, respectively (Table 1).

Table 1. Demographic and patient-related data

		Partial weight-bearing (n=21)	Full weight-bearing (n=11)
Age, mean (SD)		81.5 (8.0)	79.2 (9.0)
Sex, n women (%)		18 (86%)	10 (91%)
BMI, mean (SD)		25.3 (3.8)	27.6 (4.7)
ASA class, n			
ASA I		1	2
ASA II		9	5
ASA III		11	4
FRS (%)		**Missing n=2**	
	100%	52.4%	63.6%
	96%	19%	18.2%
	92%	4.8%	0
	88%	4.8%	18.2%
	77%	4.8%	0
	70%	4.8%	0
Length of hospital stay, mean days (SD)		14.3 (5.7)	14.6 (6.6)
Temporary stay in nursery home n		4	3
Length of nursery home stay, mean days (SD)		9.7 (17)	17.1 (36)
Permanent stay in nursery home n		3	0

BMI; Body mass index, ASA; American Society of Anesthesiologists Classification, FRS; Function recovery scale, SD; Standard deviation

The distribution of fracture types according to AO/OTA fracture classification was similar in both groups, although the rate of peri-implant fractures was higher in the PWB group (Table 2).

Table 2. AO/OTA fracture classification of the randomised controlled trial cohort

	Partial weight-bearing (n=21)	Full weight-bearing (n=11)	TOTAL
32(c)	61.9%	63.6%	62.3%
33A	23.8%	18.2%	21.9%
33B		9%	3.1%
33C	14.3%	9%	12.5%
PP	57.1%	36.4%	50%
NPPIF	19%	27.3%	21.9%
COMB		9%	3.1%
PERI-IMPLANT	68.7%	54.5%	68.8%

AO/OTA; Arbeitsgemeinschaft für Osteosyntesefragen / Orthopaedic Trauma Association, PP; Periprosthetic, NPPIF; Non-periprosthetic peri-implant fracture, COMB; Combination of PP and NPPIF

Comparing means of the PROMs (SMFA, EQ5D, pain VAS) and assessor-reported ROM between the treatment groups showed no statistically significant difference at any time point. When analysing SMFA function- and bothersome indices from both treatment groups, the scores were higher at the one-year follow-up than before the injury (mean function index: 44 vs 30, $P = 0.001$, and mean bothersome index: 37 vs 21, $P = 0.011$).

Preinjury walking aids and walking aids needed at follow-ups are presented in Table 3. There was no statistically significant difference in the need for walking aids between the groups at preinjury or follow-ups.

Table 3. Need for walking aids pre-and postinjury

	Pre-injury		8-weeks		16-weeks		52-weeks	
Walking aids, n	**PWB**	**FWB**	**PWB**	**FWB**	**PWB**	**FWB**	**PWB**	**FWB**
n	17	10	17	11	17	10	14	9
No	5	3	1		1	1	2	1
Cane		1			1		1	2
Crutch	3	1	1	3	3	3	3	2
Rollator walker	9	5	4	6	9	6	7	4
Walker without wheels			7	1	1			
Walker with arm rest			3	1				
Wheelchair			1		2		1	

PWB; Partial weight-bearing, FWB; Full weight-bearing

Postoperative pain and pain during follow-up are presented in Table 4. In the FWB group, there was more pain postoperatively and at the eight-week than in the PWB group, but less than the PWB group at 16-week follow-ups and the 52-week follow-up. The differences between the groups were not statistically significant.

Table 4. Pain measured by visual analogue scale, 0-100 mm

	Postop		8-weeks		16-weeks		52-weeks	
	PWB	**FWB**	**PWB**	**FWB**	**PWB**	**FWB**	**PWB**	**FWB**
Pain walking, mean	48	55	27	34	21	20	21	16
Pain resting, mean	18	23	3	4	2	6	0	0

PWB; Partial weight-bearing, FWB; Full weight-bearing

The results of the TUG and walking speed test at 16 weeks (Table 5)

Table 5. Timed-up-and-go (TUG) and walking speed test at 16-weeks

	Partial weight-bearing (n=8)		Full weight-bearing (n=7)		*P-value*
	Mean	**SD**	**Mean**	**SD**	
TUG	25.4	12.2	20.2	10.3	0.34
Walking speed	0.69	0.057	1.00	0.40	0.002

SD; Standard deviation

10.1.2 POSTOPERATIVE ALIGNMENT (STUDY II)

Of the 32 included patients in the RCT, four were excluded due to distorted femoral anatomy from previous surgery, making measurements unreliable, and three were excluded due to incomplete CT scans.

The mean rotational difference was 5.8° (SD 4.3°, range 18.2° internal rotation to 10.6° external rotation). One patient had more than 15° of malrotation (18.2°). The distribution was normal and presented in Figure 26.

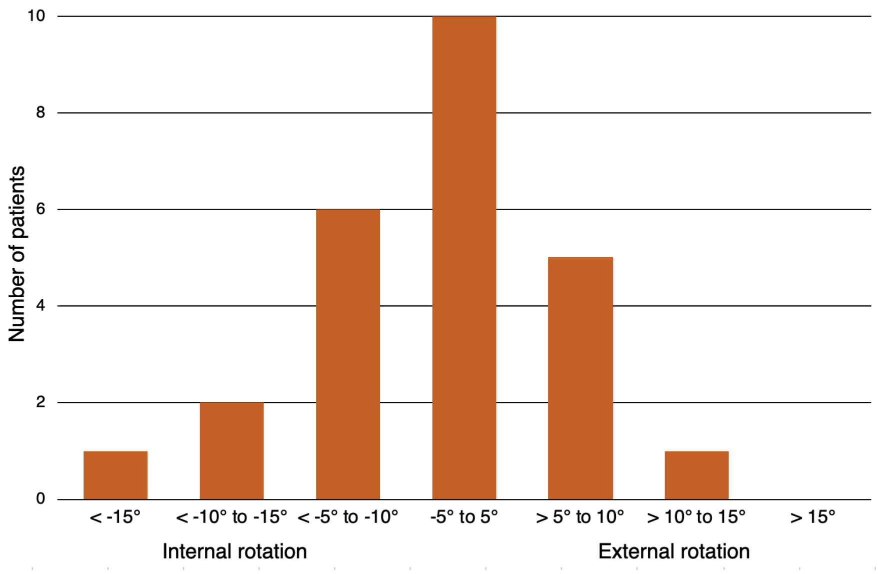

Figure 26. The distribution of rotational side-to-side differences (comparison between fractured and unfractured femur). Internal rotation of the fractured femur is represented by negative values, and external rotation by positive values.

The femoral length difference was 5.0 mm in median, IQR 3.0 - 6.8 mm. The coronal angulation difference (varus/valgus) was 1.2° in median, IQR 0.4 - 2.0°, and the median difference in sagittal angulation (genu antecurvatum/recurvatum) was 0.8°, IQR 0.4 -1.2°. All patients were categorised as "excellent", according to threshold values for malalignment suggested by Handolin *et al.* [113].

The intra-observer agreement test results of repeated measurements assessed by ICC were

> 0.9 for rotational angles, coronal (varus/valgus) and length, which is categorised as excellent reliability [240]. The ICC of sagittal angles (ante/recurvatum) were > 0.5 and categorised as moderate reliability [240].

10.1.3 SECONDARY DISPLACEMENT DURING FOLLOW-UP (STUDY III)

Continuous secondary displacement led to statistically significant femoral shortening. At the 52-week follow-up, fracture subsidence in mean was 4.9 mm (SD 4.1, 95% CI 3.0; 6.8, $P < 0.001$). The mean fracture subsidence of the distal fragment at 52 weeks, locking screw vs distal joint surface at the medial and lateral condyles, was less than the overall shortening. The median subsidence at the medial condyle was 1.5 mm (SE 30.8, 95% CI 1.0; 2.7, $P < 0.001$) and at the lateral condyle, 2.2 mm (SE 28.2, 95% CI 1.5; 3.1, $P < 0.001$).

Alterations of the coronal angles had predominantly occurred by the eight-week follow-up, but there were also notable changes between the eight- and 16-week follow-ups. In four of 25 patients, the coronal angle had increased over 3° (varus or valgus) at the 16-week follow-up.

There was a small but significant difference comparing the PWB group with the FWB group in femoral shortening at the 52-week follow-up, 1.8 mm (SE 14.0, 95% CI -4.5; -0.5, $P = 0.023$). Major displacements and adverse events were more frequent in the PWB group, although the difference was not significant, $P = 0.363$. There was no correlation between BMI, bone mineral density and secondary displacement, but the patients with major secondary displacements and adverse events had a significantly higher degree of osteoporosis, $P = 0.039$.

The intra-observer agreement test results of repeated measurements assessed by ICC for the total femur were all > 0.9, categorised as excellent reliability [240].

10.1.4 GAIT RECOVERY AND WEIGHT-BEARING (STUDY IV)

Twenty-six patients were included for analysis in this study. Three patients declined participation, one died postoperatively, one sustained a secondary coronal condyle fracture and could not be mobilised, and one was lost to follow-up. Nine of the 26 patients were randomised to the FWB group and 17 to the PWB group.

Two patients did not manage to comply with the PWB postoperatively and declined postoperative measurements. Nine measurements recorded with minor sensor defects were not detected at the time of measurement (included in technical issues, Table 6). They could not be used for weight-bearing analysis but were possible to use for cadence analysis. In Table 6, the missing measurements are compiled.

Table 6. Missing measurements at postoperative follow-ups

	Postop	8 weeks	16 weeks	52 weeks
Partial weight-bearing (n=17)				
Technical issues	1	6	4	1
Patient declined	2	1	4	3
Missed inadvertently	2	1	1	0
Death	0	1	1	2
Full weight-bearing (n=9)				
Technical issues	0	1	0	1
Patient declined	0	0	1	0

The patients in the PWB group bore significantly less than those in the FWB group, in mean 32% less postoperatively (95% CI -50; -13, $P < 0.001$) and 36% less (95% CI -61; -18, $P = 0.01$) at the eight-week measurement. However, there was no statistically significant difference at the subsequent follow-up. Postoperatively, four out of 12 patients restricted their weight-bearing to 30% or less in the PWB group, and three out of nine in the FWB group bore more than 70%. The distribution of weight-bearing during follow-up is shown in Figure 27.

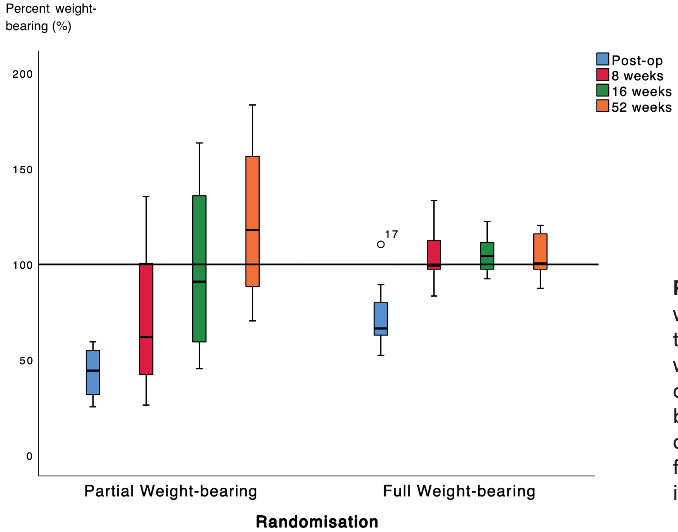

Figure 27. Boxplot with whiskers showing the distribution of weight-bearing depending on weight-bearing allocation during the one-year follow-up. Number 17 is an outlier.

The cadence (steps/minute) was lower in the PWB than the FWB group during the entire follow-up. The difference was, however, statistically significant at the 16- and 52-week follow-ups (Figure 28).

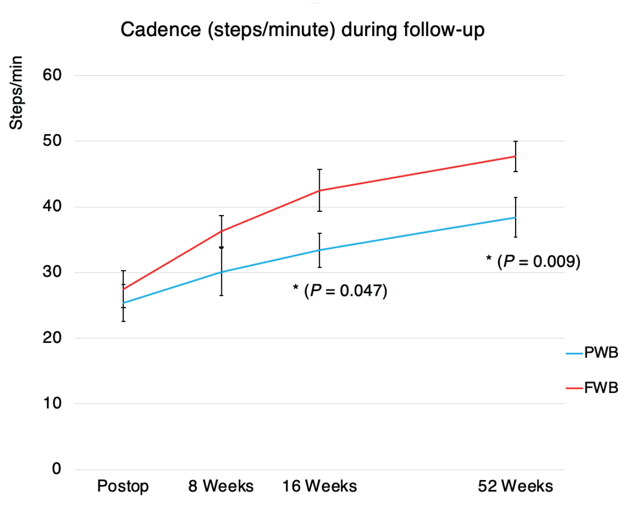

Figure 28. The mean cadence (steps per minute) per group, with standard error bars during the one-year follow-up. A consistent difference throughout the follow-up period is seen between the partial weight-bearing (blue) and full weight-bearing (red) groups, which was statistically significant at the 16-week and 52-week follow-ups (*).

10.2 Results, Study V

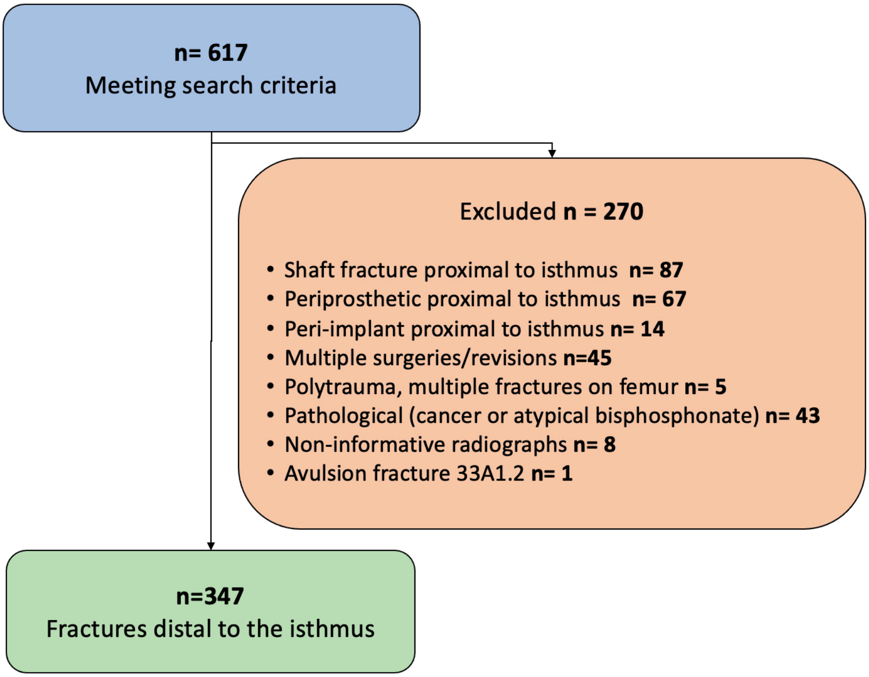

Figure 29. Flowchart showing the patients meeting search and exclusion criteria.

10.2.1 FRACTURE DEMOGRAPHICS

Of 617 fractures identified, 270 were excluded. A total of 347 fractures remained for analysis (Figure 29).

Included in this study were 342 patients with a mean age of 84.2 years (SD 8.4, range 65-103 years).

The percentage of male patients was 11% (38 patients) with a mean age of 79 years (range 68-96 years). Of the five patients with bilateral fractures, all were female. The percentage of peri-implant fractures (both periprosthetic and NPPIF) was 68%, and of those, 87 fractures were directly involved or adjacent (< 1 cm) to an implant, whereas 178 fractures were not directly associated with an implant. One patient had signs of a loose TKR (0.3%).

The distribution of fractures according to the 2018 AO/OTA fracture classification is presented in Table 7, and for NPPIF in Table 8

Table 7. Distribution of fractures according to 2018 AO/OTA classification

AO/OTA	n	UCPF	n
32A1	119	IV.3B1	3
32A2	4	IV3.C	56
32B2	72	IV.3D	3
32B3	24	V.3B1	50
33A2.1	10	V.3B2	1
33A2.2	13	V.3C	31
33A2.3	17	V.3D	16
33A3.1	4	**SUM**	**160**
33A3.2	47		
33A3.3	2		
33B1.1	9		
33B2.1	6		
33B3	1		
33C1.1	4		
33C2.1	1		
33C2.2	10		
33C2.3	2		
33C3.2	1		
33C3.3	1		
SUM	**347**		

AO/OTA; Arbeitsgemeinschaft für osteosynthesefragen/ Orthopaedic trauma association, UCPF; Unified classification for periprosthetic fractures

Table 8. Distribution of non-periprosthetic peri-implant fractures

	n	Near <1 cm	Far >1 cm
IMN	32	17	15
PL	39	4	35
HIP SCREWS	2	-	2
IMN + TKR	3	2	1
PL + TKR	10	-	10
SUM	**86**	**23**	**63**

IMN; Intra medullary nail, PL; Plate and screws, TKR; Total knee replacement

The distributions of the fracture classes depending on the presence of implants are presented in the pie charts in Figure 30. There were similar proportions of distal shaft fractures (AO/OTA 32(c)) in charts; no implants, TRK and THR. A larger proportion of distal shaft fractures is seen in the chart with osteosynthesis (30 C) and the chart with combinations (30 E). The mean age was higher in these two groups.

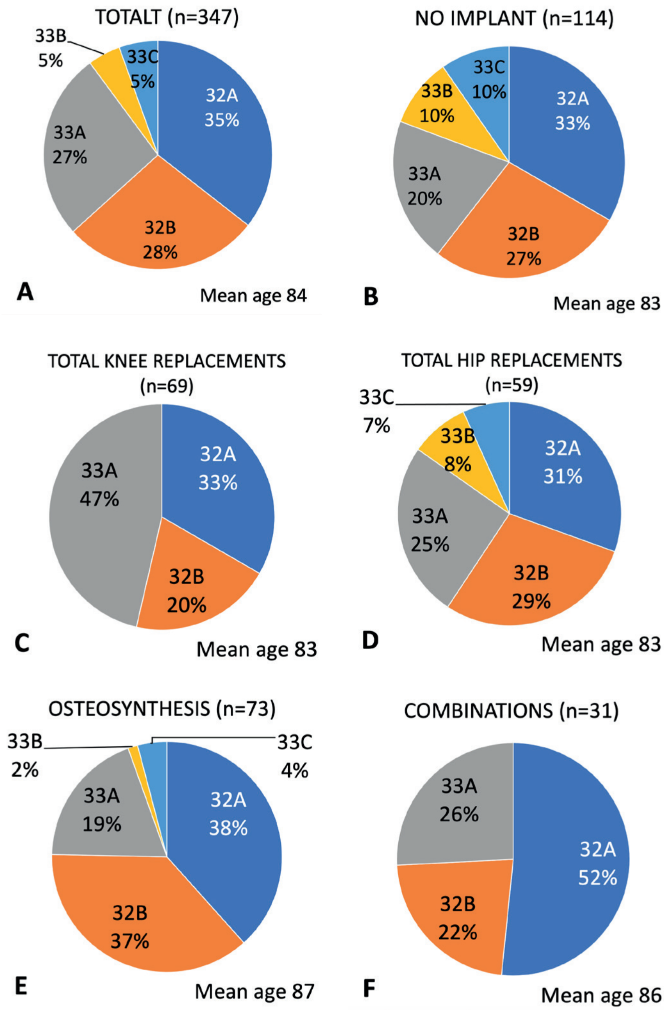

Figure 30. Pie charts showing the distribution of fracture classes. A; Total cohort. B; Fractures without implants, C; Total knee replacements, D; Total hip replacement; E; Osteosynthesis and F; Combinations of both prostheses and osteosyntheses.

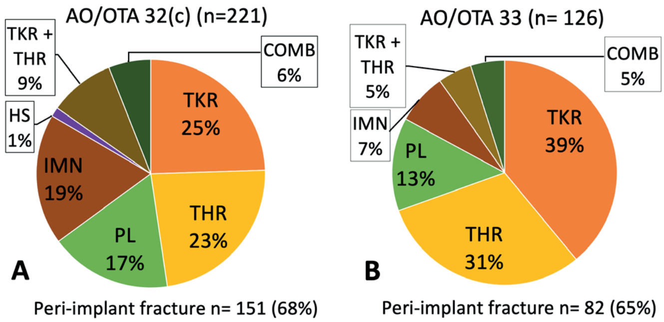

Figure 31. A; Distribution of peri-implant fractures in distal shaft fractures (AO/OTA 32(c)). B; Metaphyseal fractures (AO/OTA 33). TKR; total knee replacement, THR; total hip replacement, PL; plate, IMR; intramedullary nail; COMB; Fractures with a combination of periprosthetic and non-periprosthetic peri-implant fractures

Figure 31A shows the proportions of peri-implant fractures in the distal shaft (AO/OTA 32(c)) and in Figure 31B, the proportions of peri-implant fractures in the metaphysis (AO/OTA 33) are presented. Both fracture locations showed similar percentage of peri-implant fractures (68% vs 65% for the distal shaft and metaphysis, respectively), but there were more NPPIFs in the distal shaft and a predominance of periprosthetic fractures in the metaphysis.

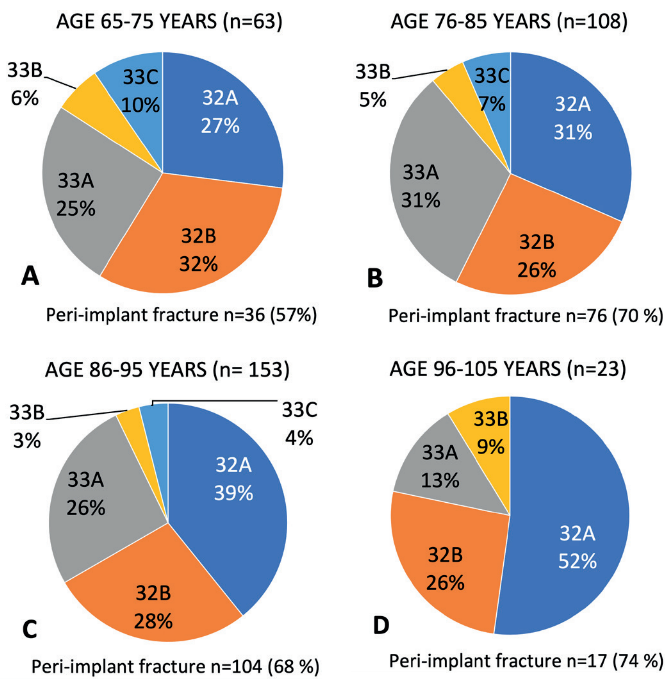

Figure 32.A-D, Pie charts showing the distribution of AO/OTA fracture classes by age groups.

The fracture distribution in ten-year age spans is presented in Figure 32. Fractures in the distal shaft proportionally increased with higher age, from 59% (65-75 years) to 78% (96-105 years). The intra-articular metaphyseal fracture (AO/OTA 33C) was more frequent in the youngest age group and non-existent amongst the oldest patients.

Two characteristic fracture patterns emerged in the survey of the 347 cases. The first pattern, which also was the most common (88% of all fractures), was a spiral type distal shaft fracture and they were common both with or without comminution (Figure 33). The second pattern was a transverse fracture at the transient junction of the diaphysis to the metaphysis, often with comminution and displacement. The fracture type appeared to be of the compression type (Figure 34).

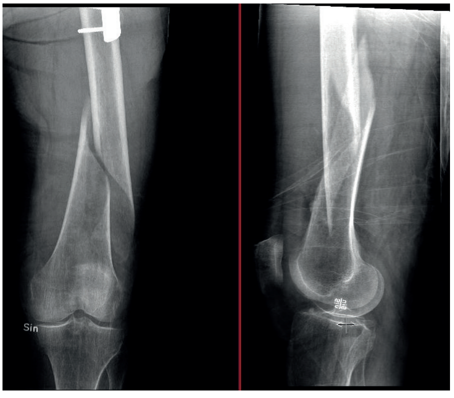

Figure 33. A typical spiral-type fracture pattern in the distal shaft (anterior-posterior and lateral views).

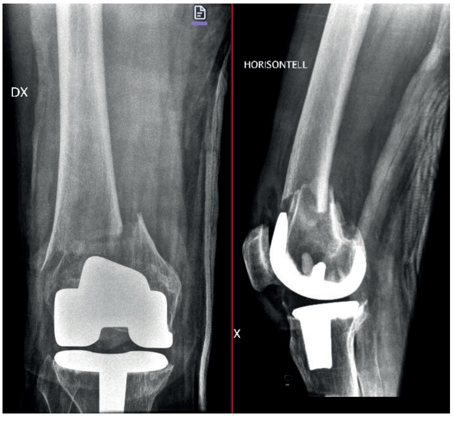

Figure 34. A typical fracture pattern at the diaphyseal-metaphyseal junction appeared to be of compression type and transverse (anterior-posterior and lateral views).

10.2.2 NEW CLASSIFICATION SYSTEM DEVELOPMENT

The characteristic spiral type fracture in the flared, distal part of the femoral shaft was named distal shaft (DS) and commonly extended proximally as far as the isthmus [6]. The transient junction connecting the shaft with the metaphysis and the end segment was named metaphysis (MP). Based on the fracture pattern observations, we chose to use the fracture characteristics pattern to distinguish between DS and MP and not the Heim's square as used in the AO/OTA [14]. For describing the metaphyseal segment's extra, partial and intra-articular fractures, the well-established AO classes, A, B and C classes, were used.

Comminution in the metaphyseal area was common, although there did not appear to be any specific patterns of comminution and was described herein by adding a (+).

For describing the three types of partial intra-articular fractures (B), the following AO/OTA qualifications were used: l for lateral, m for medial. The third type, a coronal fracture (Hoffa-type), was denoted by the lower-case c.

Ten percent of all fractures were nondisplaced fractures and they were given a modifier (0).

A recurrent fracture pattern started from the metaphyseal area and extended substantially into the shaft and was given a modifier (7).

This modifier (7) was also given to spiral fractures in the distal shaft that had a fracture line extending into the metaphysis and mouthed out in a nondisplaced intra-articular fracture. Peri-implant fractures were given lower-case letters in square brackets: [h] for total hip replacement, [k] for total knee replacement, [p] for plate and screws, [n] for intramedullary nail and [hs] for hip screws. The implant's involvement in the fracture was defined as near (1) when implant and fracture were 1 cm or closer (Figure 35).

The new classification for DFFs does not aim to classify fractures proximal to the isthmus, fractures in polytrauma patients nor fractures associated with signs of unstable and loose prosthetic components.

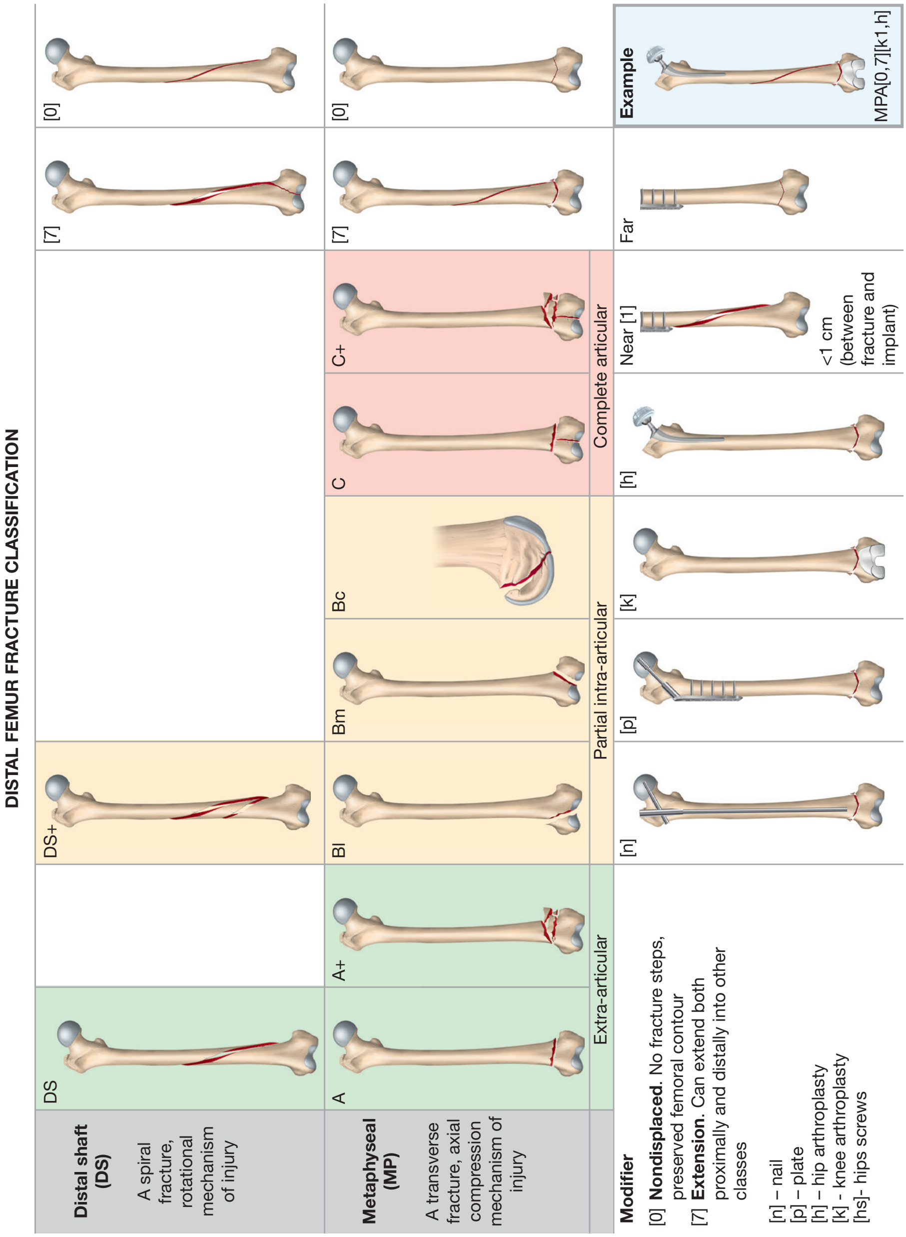

Figure 35. Chart of the new classification for distal femur fractures.

10.2.3 RELIABILITY TEST 1

In the first reliability test the data set was classified with the new classification and the 2018 AO/OTA and the Kappa (κ) was compared (Table 9). The mean agreement in the new classification was κ = 0.72, corresponding to a substantial agreement [242]. The mean absolute agreement was high, 91.6. The 2018 AO/OTA classification had a mean agreement of κ= 0.576 (moderate agreement) and the mean absolute agreement was 82.7. The total time spent for classifying all cases was only provided by one assessor (medical student). Nine hours for the AO/OTA, while the new classification took 4 hours and 17 minutes.

Table 9. Inter-rater reliability for 347 cases, the new distal femur fracture (DFF) classification vs 2018 AO/OTA, 3 assessors

	n= categories	Kappa	95% CI	*P-value*	Absolute Agreement %
New DFF classification					
DS/MP	2	0.880	0.818-0.942	<0.001	94.2
MP A/B/C	3	0.642	0.524-0.758	<0.001	86.8
BL/BM/BC	3	1.000	1.000-1.000	<0.001	100.0
Comminution (+)	2	0.569	0.508-0.631	<0.001	78.5
Extension (7)	2	0.216	0.155-0.278	<0.001	86.2
Non-displaced (0)	2	0.640	0.578-0.702	<0.001	95.1
Implant 1	5	0.919	0.872-0.966	<0.001	93.7
Implant 2	5	0.893	0.846-0.940	<0.001	97.6
		0.72			**91.6**
AO/OTA					
Type 32/33	2	0.802	0.740-0.864	<0.001	90.2
A/B/C	3	0.602	0.548-0.656	<0.001	81.3
First nr	3	0.592	0.548-0.636	<0.001	73.2
Second nr	3	0.160	0.085-0.236	<0.001	45.2
UM 1	4	0.597	0.534-0.659	<0.001	94
UM 2	4	0.725	0.650-0.800	<0.001	83.1
UM 3	4	0.519	0.205-0.832	0.001	78.3
UM 4	4	0.241	0.134-0.348	<0.001	98.2
(c)	2	0.729	0.667-0.790	<0.001	86.6
UCPF 1	2	0.940	0.846-1.000	<0.001	97.3
UCPF 2*					
UCPF 3	3	0.744	0.669-0.818	<0.001	87.7
UCPF 4	2	0.255	0.163-0.348	<0.001	77.2
		0.576			**82.7**

AO/OTA; Arbeitsgemeinschaft für Osteosyntesefragen/Orthopedic Trauma Association, CI; confidence interval, UM; Universal Modifications, Q; Qualifications, UCPF; Unified classification peri-prosthetic fractures, UCPF 2 *; was removed as it only contains number 3 for femur

10.2.4 RELIABILITY TEST 2

In the second reliability test of the new classification system, the mean agreement was κ = 0.65, which corresponds to a substantial agreement [242]. The mean absolute agreement was 86.7.

10.3 Mortality and adverse events in Studies I-IV

In the RCT cohort, one-year mortality was 12.5%. One patient died of a pulmonary embolism while still admitted to the hospital. The other deaths occurred at 21, 182 and 364 days after surgery. There was no statistically significant difference in mortality between the groups.

There were also some mechanical complications observed (Table 10). Two patients suffered secondary lateral condyle coronal fractures (Hoffa-type fractures) of Letenneur type 1 [243] without new trauma before the eight-week follow-up. These coronal fractures could not be detected on imaging studies retrospectively. One patient had a deep infection and a DAIR (Debridement antibiotics implant retainment) and healed with no complication. One patient with a BMI of 33 with a long comminuted spiral fracture of the distal shaft experienced a minor permanent plate deformation with varus angulation of the healed fracture at 52 weeks despite a restricted weight-bearing regimen for eight weeks. There was also a screw breakage of the most proximal screw fixating the femoral shaft with a THR stem and a gap between the proximal tip of the plate and the femoral shaft (Table 10, Figure 35).

Table 10. Mechanical adverse events and major secondary displacements

2018 AO/OTA	Secondary displacement	Adverse event	Weight-bearing
32A2.1(c) [2] V.3D	Screw-breakage proximally at 3 months	Loss of fixation proximally	PWB
32B3(c) [2,13] IV.3C	Increased varus	Permanent deformation of plate	PWB
33A3.2 [2,7,9] IV.3D	Subsidence of lateral and medial condyle	Hoffa fractures and cut-out	PWB
33A2.3 [2,7,9] V.3B1	Subsidence of lateral condyle, TKR	Valgus angulation of TKR	FWB
33A2.3 [2,7,9] IV.3C	Subsidence of lateral condyle	Hoffa fracture lateral condyle	PWB
33C2.1 [2] IV.3C	Subsidence of medial condyle	Medial cut-out	PWB

AO/OTA; Arbeitsgemeinschaft für Osteosynthesefragen/Othopeadic Trauma Association

No fracture needed revision for non-union or plate breakage. All fractures healed during the one-year follow-up, except one patient with delayed healing who was diagnosed with an atypical non-bisphosphonate fracture. After additional compression screws (compressing the fracture) were added to the fixation at 14 months, the fracture healed.

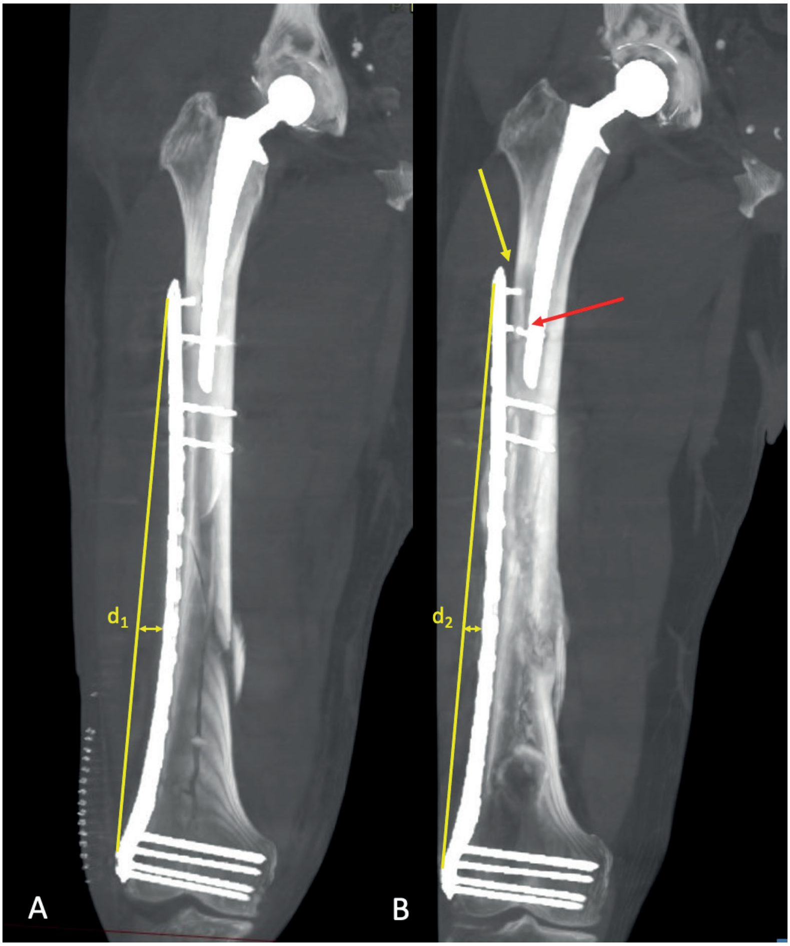

Figure 36. A; Patient with a 32(c) IV.3C fracture with normal bone density and a BMI of 33. The fracture subsidence was discreet at the medial and lateral condyle, 2.2 mm and 2.6 mm, respectively. **B;** At 52 weeks the total femoral shortening was 10 mm and the varus angulation had increased by 4.3°. By increasing the thickness of the CT slices to 50 mm, the contours of the plate could be made visible. The distance (**dx**) between a line drawn from both tips of the plate and a determined reference on the plate shows that the plate has been permanently deformed at the 52-week follow-up. The red arrow is pointing at broken screw and the yellow arrow in pointing at an increased gap between the proximal tip of the plate and the femoral shaft.

11

Discussion

11.1 Age and definitions of age

The title of this thesis is "Distal femur fracture in the elderly patient". The meaning of "elderly patient" indicates aged, older individuals, and the patients included in the studies in this thesis are 65 years or older. However, the definition of being an "old person" is relative. The United Nations has defined an older adult as 60 years or older. There is also a sociological stereotype of being "old", and such stereotypes are common in Western societies. They can positively and negatively affect perceptions of how "old people" see themselves and how the community sees them [244]. These stereotypes also affect the perception of an older adult's ability to recover after an illness [245]. The purpose of selecting "older" individuals in this research was to make the study population more homogeneous in a morphological aspect. Since younger and older adults have different physiological starting points, [246], the ability to rehabilitate and heal after fractures are assumed to be affected by age and, thereby, a confounder when evaluating rehabilitation and healing. However, age and ageing are complex, tolerated better in some individuals than others, and dependent on multiple parallel degenerative processes [247]. Age can be divided into several categories. Chronological age, which was chosen as a cut-off in the current studies, is simple and known, but chronological age does not represent the actual health status of the individual. Biological age better reflects the presence of pathological processes and is a more potent indicator of health status than chronological age [247]. However, determining the biological age is much more complex than determining the chronological age. It requires multiple investigations [246] and is impractical in a clinical study setting.

Age-dependent biological changes, such as decreased bone and muscle mass, impose particular surgical treatment and rehabilitation challenges. Significant research has been done on fragility fracture in hip fractures over the past decades. Patients with hip fractures share demographic characteristics like age, comorbidity, and mortality rates with patients with DFFs [248, 249]. Although the research results on hip fractures might apply to elderly patients with DFF, it is essential to obtain knowledge on elderly patients with DFFs, as this would provide the evidence needed to optimise the care of these frail patients.

11.2 Morphology of distal femur fragility fractures

Aged and osteoporotic bone has other mechanical properties than the bone of younger adults [29, 51]. This manifests in several ways; the fracture patterns change with progressing age, as shown in Paper V. To my knowledge, the increase in spiral-shaped distal shaft femur fractures with higher age has not been previously reported in the literature. The altered fracture patterns with increasing age also contribute to uncertainty about defining a DFF [103, 154, 158]. Most often, the definition from AO/OTA [15] fracture classification is used (AO/OTA 33); however, it is not always clear if the "square box" definition has been applied. This uncertainty on the definition of DFF has potential implications since the commonly seen long spiral-shaped fracture of the distal shaft would, according to the "square box", be classified as AO/OTA 32. A well-cited report by Elsoe *et at.* [41] assessed the incidence of DFF defined as AO/OTA 33 in all ages. However, it was unclear if the "square box" definition of DFF was used. AO/OTA 33 A was the most commonly occurring fracture (36%); however, periprosthetic fractures (27.9%) were not classified according to the AO/OTA classification. From the result of Paper V, two-thirds of all distal end femoral fractures were distal shaft fractures in elderly patients. The predominance of distal shaft fractures boarding the proximity of the distal metaphysis in elderly patients might influence the reported incidence of DFF, depending on the definition of DFF, which rarely is reported.

This uncertainty in the definition of DFF in elderly patients would be diminished by the new proposed classification that includes distal shaft fractures in the classification of the DFF. One of the disadvantages of the 2007 AO/OTA classification system [19] is the inability to distinguish between fractures located at different parts of the shaft, resulting in the risk of missing a distal end femur fracture if it is located in the flared distal shaft just proximal to the "square box". This weakness was overcome in the 2018 AO/OTA update with qualifications for distal, middle or proximal shaft fractures. Even so, age-related morphological changes, including the proximal expansion of the transitional zone connecting the flared distal shaft with the metaphysis, result in fractures that do not fit into the updated AO/OTA classification either.

In the proposed new DFF classification, the fracture morphology, either oblique/transverse metaphyseal fracture (MP) or spiral fractures of the distal shaft (DS), is used to distinguish shaft fractures from metaphyseal fractures, rather than the "square box". In the first reliability test (Paper V), the kappa value for differentiating MP vs DS with the new classification was 0.88 compared to 0.82 using the 2018 AO/OTA system (differentiating 33 vs 32). Both kappa values were interpreted as almost perfect, according to Landis and Koch [242]. The slightly higher kappa in the new classification might indicate a simplified process of classifying DS vs MP compared with the AO/OTA "square box" method for 32 vs 33. However, future reliability studies are needed to confirm this.

Another advantage of the new classification is its comprehensive ability to classify peri-implant fractures within the same classification system. The 2018 AO/OTA system uses a separate classification for periprosthetic fractures, UPCS, but lacks classifications for NPPIFs. The downside of having multiple classification systems for the same fracture is that it is time-consuming; it took twice the time to classify the dataset with the 2018 AO/OTA system compared to the new classification. Although the use of the AO/OTA is taking much longer than the new classification, peri-implant fractures could not be classified within the AO/OTA classification. Having multiple classification systems might also affect reported fracture incidence. In Paper V, two-thirds of all fractures in individuals aged 65 years or older were peri-implant fractures. The rate is similar in metaphyseal (AO/OTA 33) and distal shaft (AO/OTA 32c) fractures. The presence of previous implants appeared to have no bearing on the fracture pattern, a finding not previously reported. Another finding not previously reported is the decreased incidence of intra-articular fracture with advancing age.

11.3 Surgical fixation

The ultimate surgical procedure for DFF has yet to be presented, and surgical hardware and techniques are still being improved [134]. In the RCT study, the surgical fixation used with a long bridge plate applied with the MIPO technique is one of the state-of-the-art fixation techniques for DFF [131, 134]. However, there has not yet been sufficient high-quality research to provide evidence of the superiority of one fixation method over any other [104]. In a recent multicentre RCT study with 126 patients comparing fixation with RIMN and plates for DFF, using SMFA as the primary outcome, no difference was found [106]. However, six different nail brands were used and seven different plate systems; these systems probably have slightly different characteristics. The plate configuration was highly variable, with between three and 20 screw holes above the fracture. Most, but not all, plates were applied with the MIPO technique and patients of all ages (16-90 years) were included. A restricted weight-bearing regimen was used in all patients, with six weeks of postoperative PWB (ten-to-twelve weeks in the case of intra-articular fractures). By three months after their operation, 66% of the patients were reported as fully weight-bearing, although it is unclear how this was assessed. The restricted weight-bearing regimen will most likely affect the functional outcome differently in the younger and the older patients and thus is also a potential bias which should, together with the above-listed variations in surgical treatments, be considered when interpreting the surgical results from the study by Dunbar *et al*. These factors probably reflect the variation in clinical treatments in the 20 trauma centres (including patients). It also reflects the challenges of conducting large multi-centre RCTs.

Although the cohort was small in the present RCT study, and there were missing data at 52 weeks, it is one of the first prospective studies on an exclusively older cohort that showed no non-unions or plate breakages, despite a high percentage peri-implant fractures (both periprosthetic and NPPIF). These results can be compared with those reported in a systematic review by Koso *et al.* [103] on healing and non-unions in DFF and shaft fractures. 4.8% of all primary fixated DFF were reoperated due to non-union and 3.6% due to loss of fixation. It was concluded that the quality of fixation was critical to achieving uneventful healing in both distal and shaft fractures of the femur. The quality of fixation was paramount during surgery in the present RCT study. During the plate application, special attention was paid to firmly press the plate onto the lateral epicondyle and shaft to maximise the contact area between the plate and the femur [250]. The aim was to enhance the mechanical fixation in osteoporotic bone by using a combined technique of conventional plating, which relies on the contact between plate and bone, and the locking plates, which have a higher pull-out strength than the traditional screws [128, 163].

The surgical setup on the traction table facilitated the reduction and MIPO bridge-plate fixation. It resulted in good anatomical alignment, which might be attributed to the fixation quality and the absence of non-unions [115]. Dunbar *et al.* [106] found a coronal malalignment (both varus or valgus) of > 5° in 32.2% of their plate-fixated patients, compared to none of the patients in Paper II. Furthermore, the rotational fracture reduction (not measured by Dunbar *et al.*) showed less malalignment in Paper II than in other reports [120, 122].

Despite having adequate fixation and good postoperative alignment, several patients suffered substantial secondary displacements and two secondary coronal condyle fractures (Hoffa) were observed. Almost all migration and secondary displacement occurred in the distal metaphyseal fragment, indicating that the metaphyseal bone could not withstand the axial forces from ambulation. Major secondary displacements and secondary coronal fractures occurred in both native and peri-prosthetic fractures, similar to previous studies [251]. The fracture subsidence in the metaphyseal fragment found at 52 weeks in Paper III was comparable with the previous study on the topic, in which radiostereometric analysis (RSA) was used instead of CT scans [173]. However, the included age span was wider (22-89 years) in the RSA study compared to 65 years or older in Paper III.

In Paper III, the restricted weight-bearing did not decrease secondary displacement or adverse events; on the contrary, secondary displacement was significantly larger in the PWB group. Although the difference (2 mm) may have no clinical implications, it still shows that restricting weight-bearing does not prevent secondary displacement. Furthermore, five of six major secondary displacement events and secondary fractures occurred in the PWB group.

A suggested method to prevent migration and cut-outs in osteoporotic metaphyseal bone is cement augmentation [129], and experimental studies have shown promising biomechanical results in osteoporotic bone [252-254]. Still, concerns have been made about removing screws in case of a revision [255].

The optimal mechanical healing conditions for each fracture and patient most likely depend on factors such as fracture type, length of the femur and body weight. Although it is possible to alter the stiffness of the fixation construct with the length of the plate and screw placement, it is impossible to define a general fixation construct that can provide all fractures and patients with optimal healing conditions [256-259]. Since the plate construct flexes while loaded, the healing conditions differ at the medial and lateral cortex, inducing asymmetrical callus [260]. Interestingly, similar healing rates have been found in axially flexible lateral bridge-plate and axially rigid nail fixation.

The healing conditions provided by the fixation construct in the present RCT study (bridging plate) resulted in fracture healing without plate failure. In previous reports, obesity (BMI > 30 kg/m^2) was a risk factor for healing complications [261], but there was no correlation between high BMI and secondary displacement in Paper III. However, one patient with a high BMI with an extended comminuted spiral fracture of the distal shaft experienced a permanent plate deformation, resulting in varus angulation of the healed fracture at 52 weeks, despite a restricted weight-bearing regimen for eight weeks.

Different alterations to lateral plates have been suggested to improve mechano-biology and fracture healing. A semi-rigid plate would theoretically create better healing conditions if the patient can toe-touch weight-bear [262]. Another proposed design is the biphasic plate which has higher flexibility at lower loads and is stiffer with less flexibility at higher loads [263]. In an animal study (sheep), the biphasic plate showed promising healing results while fully weight-bearing [264]. Clinical trials on patients have not yet been published. Summarising the current evidence of surgical treatment of DFF, there is no evidence to claim that lateral plate or RIMN is superior to the other. However, they both have high union rates. Considerable postoperative malalignment is still reported; surgical setup on a traction table facilitated closed reduction and MIPO fixation. There is commonly migration and secondary displacement in the distal fixation of osteoporotic DFF, which could affect function and pain after healing of the DFF. Further improvement of plates and RIMN and their fixation in osteoporotic bone is warranted.

11.4 Functional outcome (PROM)

The radiological outcome can be used to evaluate the success of the surgical treatment. However, the radiological outcome and rates of complications can only indirectly indicate the functional outcome. An assessor-measured effect like ROM can also be used for evaluating the outcome after surgical fixation in DFF [265]. When combined with other outcomes, it can provide helpful information on the presumed function of the knee. However, there was no difference in ROM between the weight-bearing groups in Paper I.

The use of PROMs has gained popularity in recent decades, mainly when the research question involves the assessment of function and the satisfaction or disability of the patients. PROMs can be generic or specified for an anatomical region. SMFA [266] is a general PROM used to compare different orthopaedic treatments and age groups [106, 267]. The function index of SMFA was used in Study I as the primary outcome, which showed no statistical difference comparing PWB and FWB. Furthermore, there was no difference in the other indices of SMFA or EQ-5D at any of the follow-ups.

Previous studies on the functional outcomes (PROMs) in DFF depending on weight-bearing are non-RCT studies. Lieder *et al.* [187] retrospectively evaluated 125 patients with DFFs who were allocated to either FWB or restricted weight-bearing toe touch, dependent on the preference of the surgeon. PROM (Patient-Reported Outcomes Measurement Information System, PROMIS) was used as a secondary outcome; no difference between weight-bearing allocations could be detected. In a prospective non-randomised study on weight-bearing after plate fixation, Bruggers *et al.* [188] found no difference in Oxford knee score between the allocated weight-bearing groups, non-weight-bearing (NWB) and FWB. Studies on other fracture locations may serve as a comparison with the lack of studies in DFF. Gross *et al.* [268] included 90 surgically treated (IMN) tibia shaft fractures and allocated them to either full or non-weight-bearing for six weeks. No difference in any outcome, including SMFA, could be detected at any time. In a prospective study, Ariza-Vega *et al.* [193] evaluated functional outcomes with a PROM (Functional Independence Measure, FIM) after surgical fixation of 194 hip fractures. The orthopaedic surgeon decided allocation to FWB or non-weight-bearing for two-to-four weeks. Restricted weight-bearing was a strong determinant for worse functional scoring three months and one year after the operation. However, since the patients were not randomised into weight-bearing allocations, the surgeon's discretion regarding which patients should restrict weight-bearing might impart bias. According to the clinical trial registry, there is one ongoing RCT on the results after FWB vs PWB after DFF (ClinicalTrials.gov Identifier: NCT03167099). Fifty-three patients have been included; the primary outcome is radiological healing; the secondary outcome is differences in Knee Society Score. Hopefully, the results of that study will contribute to more knowledge on this topic.

Generic and knee-specific PROMs have been analysed in a large national cross-sectional study by Vestergaard *et al.* [269]. A total of 7133 patients with knee fractures (distal femur, patella and proximal tibia) were evaluated with one, three and five-year follow-ups. The aim was to report median scores of knee-specific and generic knee PROMs after knee fractures and identify risk factors for poor outcomes.

Knee-specific scores, OKS (Oxford Knee Score) and FJS-12 (Forgotten Joint Score), and generic scores, EQ-5D-5L index and EQ-5D 5L VAS, were used. DFFs were found to have a worse outcome than the tibia and patella fractures, and fractures had a worse outcome in FJS than ACL reconstructions. No preinjury score was available, and no comparisons between surgical fixation methods or weight-bearing strategies were made. No major differences were not observed in PROM outcomes between the three- and five-year follow-ups. However, some risk factors for worse results were identified, including female sex, age > 40 years, and non-operative treatment. However, non-operative treatment is used in 21% of patients older than 65 years and treated for a DFF, according to the Swedish Fracture Registry (3830 registered DFF) [270]. By today's standards, non-surgical treatment is mainly used in non-ambulant patients [271]. Non-ambulant patients will most likely have worse PROM scores than ambulant patients, which could be a selection bias and should be considered when interpreting the results of Vestergaard *et al.'s* study. A Cochrane systematic review in 2022 by Claireaux *et al.* [104] compared surgical interventions for

DFF by outcomes of validated PROMs, adverse events, patient-reported quality of life (QoL) and pain. However, the results from the studies were insufficient to provide evidence to inform clinical practice.

So far, proving the superiority in function outcome of different weight-bearing strategies or surgical treatment in lower extremity fractures with PROMs as the outcome has been challenging. The question is whether the conducted studies are too small, if the PROMs are too blunt instruments to measure the difference, or if there is a difference to find.

In a review of generic and specific PROMs for assessing outcomes in patients with hip fractures, Haywood *et al.* (2017) [272] concluded that no clear recommendation on any PROM was possible due to limited evidence on data quality, responsiveness, interpretation, test-retest reliability, acceptability and feasibility. It was concluded that future PROMs must be more robust, have higher methodological quality and be validated.

An inherent problem with using PROMs for measuring treatment effects is low responsiveness and fluctuation of scores independently of a detectable change in outcome for the patient [273]. Complicating the interpretation of the SMFA results is the general worsening of function in all patients as an effect of the fracture, together with normal age-related deterioration of health status, which has been observed in previous studies in an older cohort with DFFs [267, 274] and hip fractures [275-278]. The results from Paper I also showed a worse function at 52 weeks follow-up compared to preinjury scores, emphasising the long-lasting impact DFFs have on the function of elderly patients.

Designing new and validating existing PROMs is crucial to provide researchers with enhanced, robust PROMs that can predictably detect differences between surgical treatments or rehabilitation strategies.

11.5 Restricted weight-bearing

When the RCT study was designed in 2011, restricting weight-bearing for eight weeks was used as a standard postoperative protocol in the study hospital. A period of restricted weight-bearing to decrease surgical failures is still frequently used [106, 181], despite lacking evidence that restricted weight-bearing has any beneficial outcome for DFF or any other fracture in the lower extremity [177, 180]. Recent studies have not found an increased rate of fracture-associated complications after immediate FWB in DFF [130, 185, 186, 188]. In a retrospective analysis of 51 patients aged 64.3±20.7 years, Consigliere *et al.* [130] found secondary displacement and hardware complications more commonly (non-significant) in the non-weight-bearing group than in the FWB group. Those findings correspond with the result in Paper III, where 5/6 major secondary displacements and adverse events occurred in the PWB group. Large studies on complications and mortality associated with restricted weight-bearing in patients with DFFs are not currently available. However, the effects of restricted weight-bearing in elderly patients have been evaluated in larger studies of hip fractures. Warren *et al.* [191] assessed mortality and complications related to treatment (deep vein thrombosis, pressure wounds, etc.) in 7947 patients with hip fractures and found that both complications and mortality rates were significantly lower if FWB from the first postoperative day was allowed. Other studies have found similar results [190]. These results are interesting, considering the low compliance of weight-bearing in elderly patients with hip fractures [192, 199, 279]. However, the ability to comply with weight-bearing restrictions is not just low in patients with hip fractures but in the majority of injured and uninjured evaluated individuals, regardless of age [195-198]. The RCT study is the first to assess weight-bearing compliance with two weight-bearing regimens, PWB and FWB, in elderly patients with DFF. The results show that a low percentage of the patients managed to partially weight-bear postoperatively. Still, there was a significant difference in actual weight-bearing between the FWB and PWB groups, implying the intention and effort of the patients to comply with the restricted weight-bearing protocol. Trying to understand the reasons for the low ability of elderly individuals with fractures to perform PWB, a study on young, healthy individuals without injuries showed that four times more energy was needed for PWB compared to FWB [280]; an equivalent survey of elderly patients has, to my knowledge, not been published. In elderly patients with fractures, however, loss of muscle strength is common [93] and probably contributes to low compliance.

The intention to comply with weight-bearing instruction must, however, be significant, as there is growing evidence of increased mortality and worse functional outcome with a negative impact on recovery when restricted weight-bearing is applied [190, 191, 193, 281], even though compliance to restricted weight-bearing is rare [192, 199, 279].

11.6 Psychological factors of restricted weight-bearing

Reports on the psychological impact of restricting weight-bearing are limited. It is, however, not unlikely that patients who are told that there is a risk of fixation failure if they overload the fractured leg will become more anxious about mobilising than patients who are told that the fixation will endure full body weight and that early mobilisation is paramount.

The psychological mechanisms after a lower limb fracture in elderly patients are complex and individual. Eckert *et al.* [282] found that post-traumatic psychological symptoms were common after falls in patients with hip or pelvic fractures and associated with a fear of falling (FoF). Interestingly, individual characteristics, such as psychological inflexibility, were highly correlated with anxiety and a predictor for fall-related post-traumatic symptoms and FoF. As many as 50-65% of patients suffering from a hip fracture have FoF, which has a negative impact on recovery [283, 284]. Low physical activity and sedentary behaviour are strongly associated with a higher degree of FoF [285]. Voshaar *et al.* [286] found that FoF might be more important than pain and depression in predicting functional recovery after a hip fracture. Reports have also stated that psychological consequences from falls and fractures may limit function beyond what might be expected because of the effects of physical disabilities alone [287]. Restricted weight-bearing and its psychological impact could negatively affect FoF or fall efficacy, but this correlation has yet to be established.

Although not evaluated in scientific studies, another possible mechanism for delayed recovery after restricted weight-bearing is induced postural instability and sway. As the patients are not allowed to support their body weight on the fractured leg, they try to off-load, which gives a weight-bearing asymmetry, which has been shown to decrease postural stability in younger, healthy individuals [288]. Equivalent tests have not been conducted on older individuals, to my knowledge. Still, it is not unlikely that postural stability will naturally decrease with increased age and that the PWB will amplify postural instability.

11.7 Recovery of gait

One of the main findings of the studies in this thesis was the delay in gait recovery after eight weeks of restricted weight-bearing. At 16 weeks and 52 weeks after the operation, the difference in cadence (steps per minute) was significantly lower in the PWB group than in the FWB group. Cadence and walking speed are closely correlated in older females [289]. There was also a statistically significant difference in maximal walking speed at 16 weeks 0.31 m/s $P = 0.002$, measured by an independent assessor. The minimal detectable change (MDC) in maximal walking speed is 0.10 m/s for elderly patients with hip fractures [228]. These findings confirm the results from the cadence analysis that there is likely a significant and clinically relevant decrease in gait speed in those patients who were randomised to PWB for eight weeks. No previous study, to my knowledge, has evaluated how a period of restricted weight-bearing affects gait recovery during a one-year follow-up. These findings are important as gait speed in elderly with lower extremity fractures strongly predicts future adverse health outcomes and death compared to healthy older people [192, 290-294].

There was a non-significant difference in TUG 5.2 seconds $p = 0.34$. Although a difference greater than 1.6 seconds is claimed to be clinically relevant in the rehabilitation process after hip surgery [295], conclusions on these results have to be made with caution, as the numbers are small and the difference is non-significant.

The mechanisms of the delayed recovery and associated risk factors for frail elderly patients after restricted weight-bearing have not been thoroughly studied [200]. Besides the psychological aspects discussed above, one possible reason for the delayed recovery is the decrease in physical activity during the restricted weight-bearing period and following muscle decline, which might contribute to the long-lasting decline in physical performance long after the restricted weight-bearing period has ended.

Physical activity has many health-related advantages. In contrast, physical inactivity or sedentary behaviour has been associated with muscle weakness and less ability to cope with activities in daily life [296, 297]. Furthermore, the oldest patients have the slowest recovery and the most significant risk for activity of daily life (ADL) function decline [298]. Sarcopenia, a significant loss of muscle mass and strength that negatively affects walking ability, is common in older individuals. As much as 71% of patients with hip fractures have sarcopenia [93]. High age, in combination with metabolic conditions such as type 2 diabetes and physical inactivity, increases the risk of sarcopenia [299, 300].

The effect of a period of inactivity and disuse aggravates sarcopenia [301, 302]. It has also been shown to decrease the ability of injured muscles to heal and induce muscle atrophy through multiple cellular pathways [303]. Indeed, studies have shown that after ten days of bed rest in older adults, one kilogram of muscle mass is lost [304]. Loss of muscle strength occurs at two- to five-fold faster rates than the loss of muscle mass and constitutes a higher risk for disability and death than the loss of muscle mass [305]. In elderly patients who might already be compromised and have small margins, a period of disuse can profoundly affect metabolic health and muscle atrophy, influencing muscle strength and function [306], and may lead to a tipping point inducing a negative spiral of events, dramatically increasing the risk of irreversible metabolic changes and new falls, complications and death [301, 307, 308].

Different percentages of one-year mortality in geriatric patients with DFF have been reported, from 13.4% one-year mortality in 283 elderly patients surgically treated for DFF [309] to 30% in a recent review [132]. In the present RCT study, the one-year mortality was 12.5%.

According to Siebens *et al.* [310], who conducted a prospective study of 224 hip fracture patients treated with arthroplasty, the likelihood of being discharged to previous living conditions is higher if immediate full weight-bearing was allowed. In the present RCT study, three patients (all in the PWB group), aged 87, 94 and 95, had to move from independent living to a nursing home. The patient, aged 87, suffered a secondary Hoffa fracture and could not be mobilised to independent walking. Still, due to the high age of the other two patients, it is difficult to determine if the restriction in weight-bearing is the leading cause of the change in living conditions.

11.8 Disuse osteoporosis

The finding that the distal fixation in DFF in the PWB group experienced a small but still significantly larger fracture subsidence than the FWB group, together with five of six major secondary displacements and adverse events that occurred in the PWB group, is interesting; similar finding has been reported in other studies on DFF [130].

A possible explanation for these findings could be disuse osteoporosis [311]. The mechanism behind disuse-induced bone loss in weight-bearing bones (femur, tibia) is a lack of mechanical stimulation on muscular insertions in combination with reduced weight-bearing [312]. A period of six weeks of non-weight-bearing following lower limb surgery resulted in microstructural and biomechanical degradation and a dramatic increase of porosity in the cortical bone, which did not return to the preinjury state 13 weeks after permission of FWB [313]. The disuse osteoporosis occurs mainly in cortical bone, thinning the inner transient layer and transforming it into trabecular bone, increasing the risk of fractures in areas with a thin cortex [314]. Animal studies on mice have shown that PWB (30% of body weight) does not prevent musculoskeletal disuse.

Loading the disused leg as the only measure of restoring bone mass will not be enough to regain preinjury levels of bone mass and strength. However, highly intense training programs combined with bone-specific agents could achieve this [312]. Still, such measures are not routinely used in the clinical setting[75].

In elderly patients, it could be suggested that disuse osteoporosis and loss of muscle strength, which occur relatively quickly, have a greater negative effect on fixation stability and gait recovery than the eventual benefits of off-loading the fracture. The restricted weight-bearing has thereby an opposite effect to its intention. However, this correlation has yet to be proven.

The long-term effects of less physical activity on bone density and microstructure have been indirectly assessed. Most females who sustained a hip fracture in their 60s to 70s were less physically active during their fertile period than paired controls [315].

In Paper III, there was no correlation between the level of osteoporosis and secondary displacement. However, the patients who suffered major secondary displacements and adverse events had a significantly higher degree of osteoporosis ($p = 0.039$) than those who did not.

12

Limitations

The primary outcome of the RCT was the function index of the SMFA. When planning the RCT, there was insufficient published research on SMFA to obtain both an anchor-based and a distribution-based minimal clinically important difference, which also was adjusted to the particular population [238, 316], resulting in an unrealistic power analysis.

The premature discontinuation of a surgical RCT is, unfortunately, in general, high [317] and is often, like in this research, caused by slow recruitment, which in this RCT occurred because of inadequate funding, organisational failure, and unrealistic projections regarding the number of eligible participants [318]. Despite the premature discontinuation, valuable data was obtained, which could be analysed.

Although randomisation should diminish or even rule out confounding factors such as age [319], differences were observed between the groups [320]. At admission, the median age in the PWB group was 81.5 years versus 79.2 years in the FWB group. The ASA score was in mean of 2.48 in the PWB group and 2.18 in the PWB group, and the FRS score was 95.3% in the PWB group and 97.1% in the FWB group. None of these differences was statistically significant but could impact the results. The randomisation process was simple (in-house web-based simple randomisation program), without randomisation blocks, which led to unevenly sized groups and reduced the precision of the study [320].

Measurements of the sagittal alignment were challenging in Study II, which the relatively low ICC also reflects. The combination of metal artefacts of TKR, osteosynthesis and osteoporotic bone and 3-mm thick CT slices did not allow angle measurements with the Blumensaats line for reference [229]. The method used for measuring sagittal angulation in Study II has not been validated, and the results should be interpreted with that in mind. Measurements of the proximal angles of the rotational alignment were made using the lesser trochanter because of frequently occurring hip implants, in contrast to previous studies using the centre of the femoral head, collum femoris, and greater trochanter often in multiple slices [120-122]. To my knowledge, using the lesser trochanter as a reference has not been validated

Missing measurements occurred in Studies I-IV. Most of the included patients were elderly (mean age 81 years), and they had difficulties with participation, with several missing measurements as a consequence (primarily in the PWB group). A systematic review by Somerson *et al.* [321] found that loss to follow-up was common (10.3%) in orthopaedic RCT studies and could be a source of potential bias. However, we found no significant difference in age or ASA between those patients participating and lost to follow-up. Thingstad *et al.* [322] conducted an RCT on two rehabilitation strategies (comprehensive geriatric care versus orthopaedic care) after hip fractures. They found that participants with a low preinjury function level were more likely to be lost to follow-up than those without. In the present RCT study, FRS [203] was used for assessing preinjury function, and of the ten patients lost to follow-up at 52 weeks, four were deceased (one in the FWB group), and six declined further participation (one in the FWB group). The FRS in the lost-to-follow-up group was in mean 95% (one missing score) and did not indicate a low preinjury function as a likely reason in the present study.

13

Conclusions

In the RCT (Studies I-IV), patients 65 years or older, were randomised to eight weeks of PWB (30% of the body weight) vs immediate FWB. Fixation was achieved on a traction table by a MIPO with a lateral bridge plate applied, and the last follow-up was performed at 52 weeks.

No differences were detected in the functional outcomes, PROM (SMFA, EQ-5D), Pain VAS, or ROM between the FWB and PWB groups. However, SMFA function for both groups was worse at 52 weeks than pre-injury, emphasising the lasting impact of DFFs on the life of elderly patients.

The fixation construct could not prevent significant subsidence of the metaphyseal fragment. Furthermore, restricted weight-bearing did not prevent secondary displacements and complications. There was a small (2 mm) but significantly larger secondary displacement in the PWB than in the FWB group. Five of six major secondary displacements and adverse events occurred in the PWB group. However, no fracture needed revision for plate breakage or non-union during the one-year follow-up.

Although patients in the PWB group had difficulties complying with the restricted weight-bearing, it still resulted in significantly delayed recovery of weight-bearing ability and gait (cadence). At the 16-week and the one-year follow-up, the cadence was significantly lower in the PWB group than in the FWB group, as was the walking speed (maximal walking speed for 30 meters).

Using the surgical setup technique for DFF with MIPO on a traction table with a dedicated femoral support led to "excellent" results in all evaluated patients, according to the malalignment score from Handolin *et al.* [113]. Only one of 25 patients showed malrotation, using the threshold for malrotation suggested by Croom *et al.* of a 15° side-to-side difference [10], which is a lower rate of malrotation than previously published reports on MIPO for DFFs.

The epidemiological survey of fracture classes in 347 consecutive fractures of the distal femur in elderly patients showed a predominance of distal shaft fractures and that fracture patterns were similar also in the presence of previous surgical implants. The observed difficulty of classifying the age and osteoporotic fractures with modern fracture classification systems motivated a new classification system proposal for DFF in elderly patients. The proposed new classification was substantially faster and showed promising substantial inter-rater agreement compared with a moderate agreement for the AO/OTA.

The results from the present thesis harmonise with similar studies conducted on elderly patients with hip fractures and observational studies on patients with DFF. Restricted weight-bearing has a negative impact on fixation in osteoporotic bone and recovery of function and gait, which could strengthen the external validity of the results of the thesis.

Summarising the findings of this thesis, there was no difference in function but an increased rate of adverse events and impaired distal fixation in osteoporotic bone with negative long-term effects on gait recovery in the PWB group compared with the FWB group. The results demonstrated an underestimated risk when postoperative weight-bearing restrictions after osteosynthesis of DFFs are used and should therefore be avoided in this group of patients.

14

Future perspectives

It has been suggested that the ability to perform PWB can be learned [323, 324]. The question is, perhaps, why should we even try to force frail elderly patients to endure an overwhelmingly challenging rehabilitation and expose them to higher risks of persistent lower functional outcomes and higher mortality when there is a lack of evidence to support its use [180, 200]?

Already half a century ago, in 1971, it was known and desirable to achieve a good fixation of DFF and to allow immediate full weight-bearing [98]; the question is, why is it that some 50 years later, that quest is still not achieved and still causing debate?

14.1 Future research

Patients self-limit their load on a fractured limb [325]. Thus, teaching the patients to interpret their pain and letting their own biofeedback system determine their mobilisation would provide an easy-to-implement method of early and safe mobilisation.

Future studies should focus on improving fixation for elderly patients with DFFs, allowing full weight-bearing and minimizing surgical complications in osteoporotic bones. Clinical studies with the biphasic plate could contribute to that.

Additionally, to improve walking speed and mobility in patients with hip fractures, postoperative training on gait, balance, and functional exercise is necessary [292, 293, 322]. There are strong indications that elderly patients with DFFs should be given the same opportunities to fully weight-bear and rehabilitate as hip fracture patients [326]. Furthermore, research on the psychological aspects of DFF and their impact on recovery is crucial. Postoperative rehabilitation programs should aim to improve physical skills and confidence simultaneously [287].

As for the next step related to the research conducted in this thesis, it is recommended to carry out a future study that involves multicentre validation of the new classification. Furthermore, investigating callus formation through 3D CT scans during the one-year follow-up period could provide valuable insights into the mechanism of callus formation using a bridge-plate fixation construct.

15

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16

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