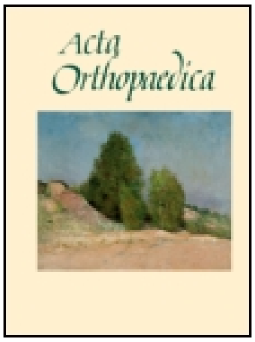

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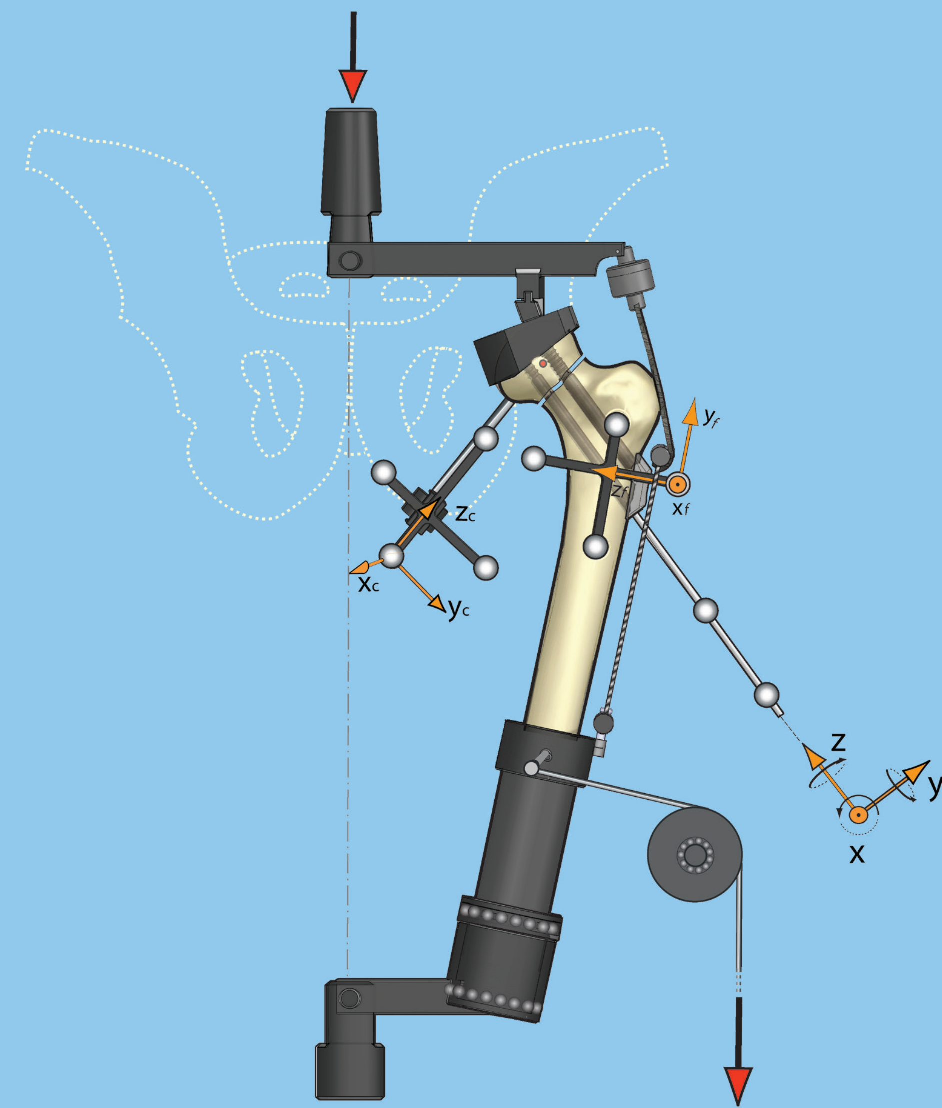

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Trude Basso

Doctoral Thesis

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Contents

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List of papers

1 Basso T, Klaksvik J, Foss O A. The effect of interlocking parallel screws in subcapital femoral-neck fracture fixation: a cadaver study. Clin Biomech (Bristol, Avon) 2014; 29(2): 213-7.

2. Basso T, Klaksvik J, Foss O A. Locking plates and their effects on healing conditions and stress distribution: A femoral neck fracture study in cadavers. Clin Biomech (Bristol, Avon) 2014; 29(5): 595-8.

3. Basso T, Klaksvik J, Syversen U, Foss O A. A biomechanical comparison of composite femurs and cadaver femurs used in experiments on operated hip fractures. J Biomech 2014; 47(16): 3898-902.

4. Basso T, Klaksvik J, Syversen U, Foss O A. Biomechanical femoral neck fracture experiments: A narrative review. Injury 2012; 43(10): 1633-9.

Abbreviations

BMD	–bone mineral density
BW	–bodyweight
BWm	–bodyweight meter
BMU	–basic multicellular unit
CHS	–compression hip screw
CT	–computer tomography
DXA	–dual energy X–ray absorptiometry
4GCF	–fourth generation composite femur
FNP	–femoral neck plate
JRF	–joint resultant force
µ	–micro
mm	–millimeter
N	–Newton
Pa	–pascal
RSA	–radiostereometric analyses

Introduction to femoral neck fractures

Bone, a brief overview

Bone contains bone cells and bone matrix that together enclose the bone marrow (Clarke 2008). Osteoblasts are differentiated from mesenchymal stem cells. They produce organic matrix (osteoid) in which the main constituent is type 1 collagen. Osteoblasts further regulate deposition of bone minerals that form the inorganic matrix (hydroxyapatite). A fraction of the osteoblasts differentiate into osteocytes when trapped in the bone matrix. Osteocytes never proliferate and are believed to regulate bone remodeling which is the combination of bone resorption and bone formation (Noble 2008). Osteocytes change their gene expression when subject to mechanical loading and unloading and are therefore proposed to be the mechanosensory cell in bone, maybe together with bone lining cells (Bonewald 2011). Bone lining cells are also derived from osteoblasts and cover all surfaces of adult bone where they form the blood-bone barrier (Parfitt 1989). Osteoclasts on the other hand are differentiated from hematopoietic stem cells. They resorb bone by secretion of hydrochloric acid and catalytic enzymes that release calcium from the bone during bone remodeling (Clarke 2008).

Osteoblasts, osteocytes and osteoclasts together form a basic multicellular unit (BMU) in which bone remodeling occur (Figure 1). This process is affected by a number of regulatory actions. Endocrine, paracrine and autocrine signals (Zaidi 2007) and mechanosensing (Bonewald 2011) are all necessary to maintain bone homeostasis and microarchitecture. The process of bone remodeling is highly complex and a more detailed description is beyond the scope of this thesis.

Basic biomechanics

Like in most human bones, the functional units of the compact outer shell of the femur, the cortex, are well organized osteons running approximately parallel to its length axis. The porous core, the spongiosa, has a large surface area due to its interconnected trabeculae and is also referred to as cancellous bone or trabecular bone. The characteristic trabeculae found in the proximal femur are maybe the most striking example of bone-modelling due to forces found in the human body (Figure 2). The trabeculae indicate the direction of the joint resultant force (JRF), the tensile stress and the effect muscular forces have on the local bone strength. After complete removal of trabecular bone in the femoral neck and head, the magnitude of load needed to cause a femoral neck fracture was reduced less than 10% ex vivo (Holzer et al. 2009). This demonstrates the importance of an adequate cortex as the vast majority of the JRF is directed through the relatively thin cortical shell surrounding the femoral neck.

Mechanically human bone is an anisotropic material, meaning that the intrinsic stiffness (Young's modulus) varies with direction (Turner and Burr 1993). Osteons of cortical bone constitute equal intrinsic stiffness in the two transverse directions but differs in the longitudinal direction and is therefore defined transversely isotropic. Cancellous bone is often considered orthotropic where the intrinsic stiffness is different in all three perpendicular directions. Human bone is a viscoelastic material in which fluid, mainly water, flows through the ultrastructure of the bone during loading and function as a shock absorber (Turner and Burr 1993).

Humans show great variation in body composition and body size which naturally affect the femoral anthropometry. The femoral variety has been long recognized, and in 2009 Toogood and colleagues (2009) presented results from an anatomic examination of 375 cadaver femurs assumed to be normal. They found that both the femoral neck version and the neck-shaft angle ranged more than 40° between femurs with a mean neck-version of 10° and a neck-shaft angle of 129°. There are gender specific differences in femoral head position relative to the neck, but no differences in neck-shaft parameters such as the femoral neck version and neck-shaft angle.

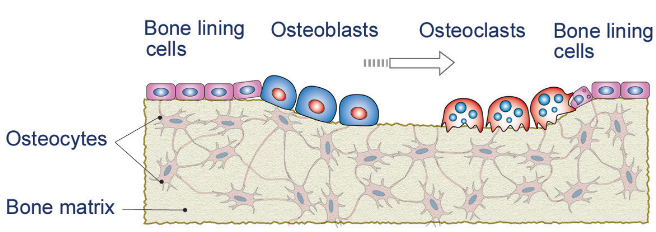


Figure 1. Bone remodeling in a basic multicellular unit.

Figure 2. CT image demonstrating the trabeculae in the proximal femur.

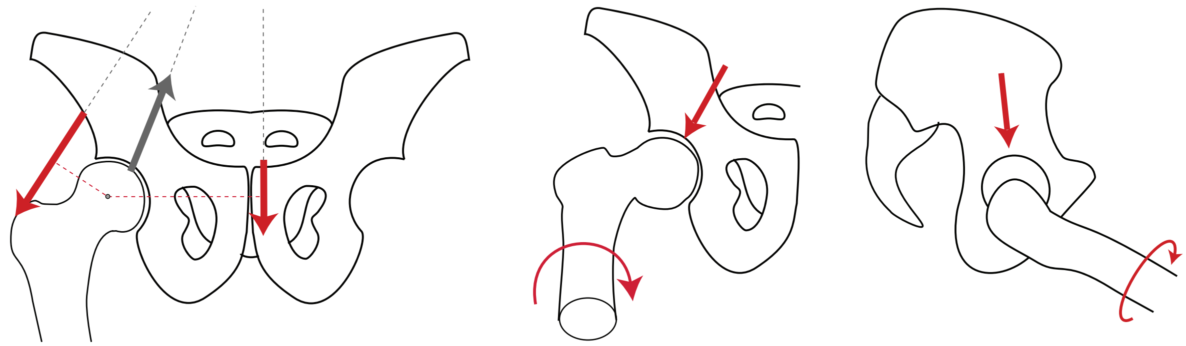


Figure 3. a. Single leg stance. The grey arrow represents the joint reaction force and the red arrows represent the abductor resultant and bodyweight.

b. Anterior loading of the femoral head lead to an internally directed torque.

The loaded human femur is subject to combined compressive and tensile forces and torque. During weight-bearing the femur is compressed and the spatial position of the femoral head medial to the anatomical axis of the diaphysis further results in femoral bending with tension on the lateral cortices. The femoral bending is restricted by the thick cortical buttress of the inferior femoral neck and soft tissues surrounding the bone. These adaptations result in bone strains within the physiologic range (Duda et al. 1998, Sverdlova and Witzel 2010). The internally directed torque occurs due to the anteversion of the femoral neck and head when the distal condyles are constrained from rotation during weight-bearing. The femoral head articulates with the acetabulum and is covered with cartilage. The cartilage together with the synovial fluid result in a very low friction coefficient in the natural human hip (Poitout 2004).

The hip joint resultant force (JRF) depends on the amount of weight-bearing and is mainly determined by bodyweight (BW) and muscular forces. For simplicity, the weight of the human leg is estimated to 1/6 of the total BW. During symmetrical standing, only minor muscular forces about the hip are necessary to keep the body in balance. Therefore the theoretical JRF acting on each femur during balanced standing equals the BW minus the weight of the two legs divided by two, i.e. one-third of the total BW. However, measured forces in vivo have been somewhat higher (Davy et al. 1988, Rydell 1966).

During single-leg stance the supporting leg must carry the full BW minus the weight of the supporting leg (Figure 3a). The center of gravity has now shifted away from the supporting leg increasing the lever arm to the weigh-bearing hip. Consequently an increased amount of muscular forces are necessary on the lateral aspect of the proximal femur to balance the pelvic. During walking, JRF has been measured in vivo in the range of 2–3 times BW (Davy et al. 1988, Bergmann et al. 2001). The forces generated by the abducting muscles of the hip have been calculated to 1–2 times the BW (McLeish and Charnley 1970, Heller et al. 2005). During stair-climbing or walking up-hill the femoral head is loaded anteriorly and the internally directed torque increases more than 20% (Bergmann et al. 2001) (Figure 3b).

Hip fractures

Fractures from the subtrochanteric region up to the femoral head are defined as hip fractures (Parker and Johansen 2006). At the millennium the annual world-wide hip fracture incidence was estimated to 1.6 million (Johnell and Kanis 2006). This accounted for a calculated loss in disability adjusted life years (DALYs) of 2.35 million. Due to the population growth, this number is expected to rise dramatically in the decades to come. By 2050 the incidence of hip fractures is predicted to be in the range of seven to 21 million (Gullberg et al. 1997). Hip fracture incidence varies geographically, and the highest rates are found in Scandinavia (Holroyd et al. 2008). Although the hip fracture incidence in Oslo has decreased from a peak during the 1990’s to a level below reported rates in the late 1970’s, it still remains the highest in the world (Stoen et al. 2012).

The incidence of hip fractures increases exponentially with age (Lofthus et al. 2001, Cummings and Melton 2002, Stoen et al. 2012) and mean age at fracture is approximately 80 years (Gjertsen 2011). The majority of patients report falling from standing height or less, whereas five to ten per cent of the patients do not report a causative fall (Dargent-Molina et al. 1996, Abolhassani et al. 2006, Parker and Johansen 2006). Approximately 50% of hip fracture patients have bone mineral density (BMD) 2.5 standard deviations (SD) below normal density in healthy, young adults (Oden et al. 2013). Seventy to eighty per cent of all hip fractures occur in women (Cummings and Melton 2002, Parker and Johansen 2006, Gjertsen 2011).

Femoral neck fractures

In Norway 55–60% of the 9–10,000 annual hip fractures occur in the femoral neck (Lofthus et al. 2001, Gjertsen 2011). It is common practice to classify these fractures according to degree of fragment displacement and morphology. Regarding degree of displacement, and for clinical purposes, simply distinguishing between displaced (Figure 4a) and undisplaced

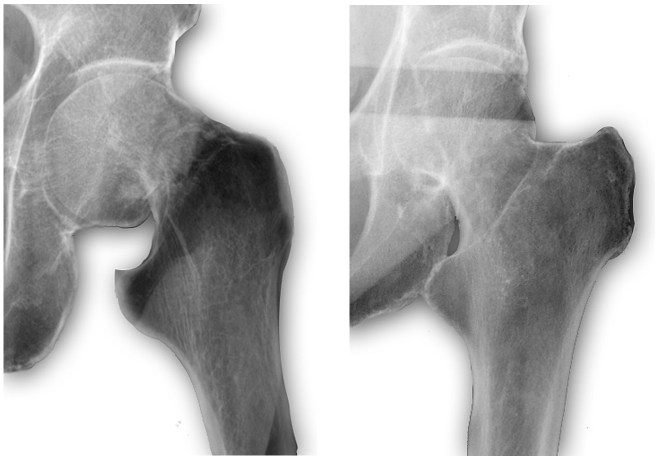


Figure 4. a. Displaced femoral neck fracture. b. Undisplaced femoral neck fracture.

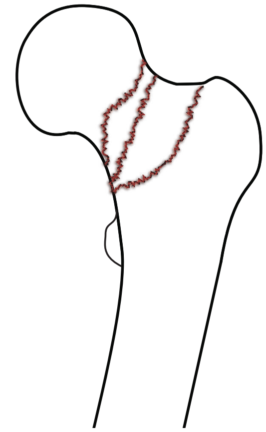


Figure 5. Subcapital, transcervical and lateral fractures

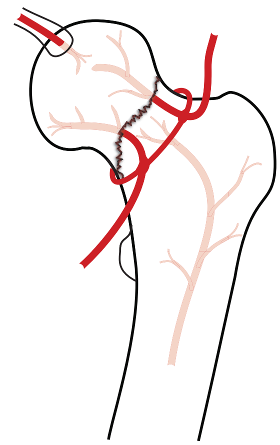


Figure 6. Schematic illustration of the blood supply to the femoral head

(Figure 4b) fractures seems most reasonable (Keating 2010). Approximately one-third of all femoral neck fractures show little or no fracture displacement (Gjertsen 2011). Multifragmentation of the posterior femoral neck wall can be found in 14–50% of the displaced fractures (Klenerman and Marcuson 1970, Khan et al. 2009).

Morphologically, femoral neck fractures can be subdivided in subcapital, transcervical and lateral fractures according to location (Figure 5). Following minor trauma in old patients, subcapital fractures are most frequent (Klenerman and Marcuson 1970). These fractures initiate at the superior head-neck junction where the cortical shell is at its thinnest (Mayhew et al. 2005). From there the fracture line moves in inferior direction following the old epiphyseal scar (Klenerman and Marcuson 1970). An inferior tongue of the strong inferior buttress is often attached to the proximal fragment (Garden 1961, Klenerman and Marcuson,1970). In young patients femoral neck fractures are most often a result of high energy trauma. The fracture then tends to appear more vertical and might also run more lateral on the femoral neck compared to fractures in old people (Ly and Swiontkowski 2008). These fractures are often referred to as transcervical fractures (Damany et al. 2005). However, it appears that the incidence of true transcervical fractures is very low and that most of these fractures are actually subcapital fractures (Klenerman and Marcuson 1970, Keating 2010). Fractures close to the trochanteric region are referred to as lateral-, basicervical- or extracapsular femoral neck fractures and are rare fractures found in only two per cent of hip fracture cases (Saarenpaa et al. 2002).

The femoral neck and head receive their blood supply from three main sources (Trueta and Harrison 1953): 1. The intraosseous vessels. 2. The retinacular vessels (of the anastomosing lateral and medial femoral circumflex arteries normally originating from the deep femoral artery). 3. The arteries in the ligamentum teres (of the obturator artery) (Figure 6). Naturally, the intraosseous circulation is abrupted following complete fracturing. The vascular supply to the femoral head is further compromised as the retinacular vessels enter the femoral head at the area of fracture, namely the old epiphyseal scar. The affection of the vascular supply following a femoral neck fracture causes avascular necrosis of the femoral head in approximately 6–10% (Loizou and Parker 2009, Keating 2010).

Why are old people at risk?

It is well known that the human skeleton reduces its strength with ageing. The peak bone mass normally appears in the second or third decades of life (Heaney et al. 2000, Zebaze et al. 2010). It is influenced by genetic factors, exercise (loading) and intake of vitamin D and calcium (Heaney et al. 2000). With decreasing levels of sex hormones, such as during menopause, the balance of bone resorption and bone formation turns negative within a BMU. In addition, the remodeling rate increases and the result is a significant loss of bone strength with age (Seeman and Delmas 2006). Men (without hypogonadism) do not experience a rapid change in sex hormone levels during midlife, and the loss of bone is mainly due to decreased bone formation and not the increased remodeling rate adding to the effect in postmenopausal women (Zebaze et al. 2010). The result of these changes is osteoporosis with a gradual thinning of an increasingly more porous cortex and thinning and loss of trabeculae along with other microstructural changes in mineralization and collagen orientation. These factors reduce the ability of bone in old subjects to resist fracture (Zebaze et al. 2010).

Humans tend to reduce their modes of activity with age. This affects bone-strength due to local stress adaptation in bone (Frost 2003). In the proximal femur, the superolateral cortex is less loaded when bipedalism is the major form of load-bearing activity when compared to individuals performing more diverse activities such as climbing stairs and squatting. Mayhew and colleagues found evidence for age-related thinning in the superolateral area of the femoral neck when examining 77 female cadaver femurs and postulated a buckling theory for fractures of the femoral neck (Mayhew et al. 2005). They suggested that this area, most susceptible to compressive loads during a sideways fall, would buckle under stress and create a fracture. Zebaze and colleagues (2010) also examined post-mortem proximal femurs and found a striking effect of age on porosity and cortical thickness. They further pointed out that there was a weak or non-existing correlation between the observed change in microstructure and dual-energy x-ray absorptiometry (DXA) obtained values for BMD in several of the femurs. This might in part explain why only 50% of patients with a fractured femoral neck have osteoporosis according to a T-score below 2.5 SD from a healthy young population (Oden et al. 2013).

Besides the compromised bone strength, the most obvious factor contributing to a femoral neck fracture is a fall. More than 90% of the patients report a pre-fracture trauma such as falling from standing position (Dargent-Molina et al. 1996, Keating 2010). The large EPIDOS study included 7,575 women aged ≥ 75 years in a prospective cohort to identify risk factors leading to a fall-related hip fracture (Dargent-Molina et al. 1996). After controlling for age and BMD, reduced gait speed and ability of tandem walk as measures of impaired neuromuscular function, and poor vision significantly increased the risk of later hip fracture.

Fracture healing

Most femoral neck fractures run along or within the epiphyseal plate separating the epiphysis (femoral head) from the proximal femoral metaphysis (Klenerman and Marcuson 1970). The epiphyseal plate itself is considered part of the metaphysis which follows the same principles of fracture healing as diaphyseal bone (Claes et al. 2011). Fracture healing is a complex process dependent on numerous local and systemic factors and only a brief description will be given in this thesis.

Absolute stability over the fracture leads to direct fracture healing with osteonal bridging. Under less stable fracture healing situations, intermediate stages of various connective and cartilaginous tissues appear. Type of fracture site tissue is determined by the fracture gap and geometry and of the magnitude of the interfragmentary motions (Augat et al. 2005). With increasing fracture site stability, the subsequent intermediate tissues show decreasing tolerance to interfragmentary strain (Perren 2002). The process finally leads to endochondral woven bone formation preceding organized, remodeled bone. The periosteal layer of the femoral neck is thin, incomplete, more mineralized and less cellular than in extracapsular parts of the femur (Allen and Burr 2005). Consequently, a fractured neck of femur must heal endosteally without the support of an external callus, which put great demand on the osteosynthesis to provide lasting stability.

Figure 7. Hemiarthroplasty.

Children and adolescents have a thick, cell-rich periosteum, and evidence of faster fracture healing compared to adult bone is well documented (Augat et al. 2005). However, it has not yet been established whether old age with an accompanying reduced bone strength has a direct influence on the process of fracture healing (Augat et al. 2005, Giannoudis et al. 2007, Goldhahn et al. 2012).

Surgical treatment

"Many surgeons are now convinced that the "unsolved" fracture should be renamed the "unsolvable" fracture, and the defeatist attitude of Sir Astley Cooper (1822) still lingers in present-day practice. This is reflected by the increasing tendency to abandon treatment by reduction and fixation, and to replace the femoral head with a prosthesis."

– (Garden, 1964)

As the quotation describes, treatment of femoral neck fractures has long been subject to controversy. Surgical options for treatment of femoral neck fractures include prosthetic replacement of the femoral neck and head and fixation of the proximal fragment. Femoral head ostectomy is occasionally performed, but will not be further discussed in this thesis.

Prosthetic replacement

Dr. Austin T. Moore is regarded a pioneer in hemiarthroplasty (Figure 7). His first patients received prosthetic replacements during the 1940s, and this treatment has been an option for patients with femoral neck fractures ever since. In the late 1950s John Charnley proposed total hip replacement where the acetabulum was lined with a cup in addition to the femoral neck and head replacement. Until recently this treatment option was mainly offered to patients suffering from osteoarthritis of the hip and not patients with hip fracture, but this is now changing (Hopley et al. 2010).

Due to considerable evidence of superiority over internal fixation, the majority of old patients sustaining a displaced femoral neck fracture today have their femoral neck and head replaced by hemiarthroplasty (Bhandari et al. 2005, Frihagen et al. 2007, Gjertsen 2011). A Cochrane review from 2010 concluded that cemented hemiarthroplasties performed better than uncemented prostheses and there was no significant difference regarding unipolar or bipolar hemiarthroplasty. They also found indications of better functional outcome following total hip replacement compared to hemiarthroplasty (Parker et al. 2010). The latter has been supported by two recent meta-analyses (Hopley et al. 2010, Yu et al. 2012). However, a recently published long-term follow up of a randomized controlled trial found that patients with mental impairment who received total hip replacement had a complication rate of 16% similar to the patients treated by internal fixation for a displaced femoral neck fracture (Johansson 2014). This study was rather small, but demonstrates that total hip replacement might not be the best treatment option for all patients with femoral neck fractures.

Internal fixation

Before the introduction of internal fixation, traction was the common treatment of patients with femoral neck fractures. Dr. Marius Nygaard Smith-Petersen was not the first to present a femoral neck fracture implant, but his three-flanged steal nail, which was introduced in 1930–1931 was considered an important improvement at that point (Smith-Petersen et al. 1931, W.A.L. 1953). Since then, numerous implants and methods have been presented by enthusiastic surgeons and researchers (Garden,1961). Up to the 1970s, at least 77 different implants for use in hip fractures had been designed (Tronzo 1974). Internal fixation of femoral neck fractures is today performed in most patients with undisplaced fractures regardless of age (Gjertsen et al. 2011, Parker and Johansen 2006). In addition, young patients with displaced fractures often receive internal fixation to make restoration of pretrauma function possible and also to postpone arthroplasty (Ly and Swiontkowski 2008).

All implants used to stabilize a femoral neck fracture must resist the bending forces in the proximal femur to avoid varus displacement of the femoral head and potential screw loosening and displacement of the fracture. Likewise, screw loosening and fracture displacement might happen if the implant cannot resist the posteriorly directed torque about the femoral diaphysis resulting in retroversion of the femoral head fragment. Although some impaction at the fracture site seems necessary to achieve adequate stability for fracture healing and also to enable early mobilization of the patients, implants should also be able to restrict the actions of the compressive forces on the femoral neck to maintain the femoral offset important for muscular function.

There are sporadic reports of intramedullary nailing of displaced femoral neck fractures (Mir et al. 2011), but this treatment option is not an established procedure and today nailing is mainly performed in the presence of ipsilateral femoral neck and shaft fractures (Ostrum et al. 2013). Today most suppliers of orthopedic implants offer at least two alternatives for fixation of femoral neck fractures, namely a multiple pin / screw system and a gliding hip screw system. Multiple pin / screw systems and gliding hip screw systems come in different sizes and shapes, but are all based on the same two principles. At the moment there is no evidence for the superiority of either multiple pin or screw systems nor gliding implants (Parker and Gurusamy 2011). The ongoing FAITH study plans to enroll 1,500 patients with femoral neck fractures to compare the outcomes from patients randomized to multiple screws to those treated by a gliding implants (Swiontkowski 2008). A new member in the femoral neck fixation family is the locking plate. In the following, a short review of these three principles is given.

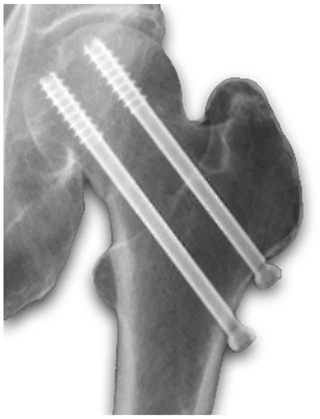


Figure 8. Multiple screws.

1. Multiple pins and screws

Fixation of the proximal fragment by multiple pins or screws (Figure 8) has been performed since the 1930s (Moore 1937). Two, three or four pins or screws are inserted from the proximal lateral diaphysis. Local preferences exist regarding the use of pins with some kind of bone anchor or threaded or partially threaded screws. Geographical variations in the number of pins and screws used to fixate femoral neck fractures also exist. In Scandinavia, two screws or pins have long been the method of choice, whereas three screws or pins are considered gold standard in North America (Ly and Swiontkowski 2008, Gjertsen et al. 2010). There is little evidence for the superiority of any fixation method and also for the optimum number of screws or pins (Parker and Gurusamy 2011).

In the porous bone of the proximal femur. it is a generally accepted goal to achieve three point fixation of the pins or screws. The first point being a safe anchorage in the dense subchondral bone of the femoral head, the second a position close to the internal cortices of the femoral neck, and the third the lateral cortex of the femoral diaphysis. Lindequist and col-

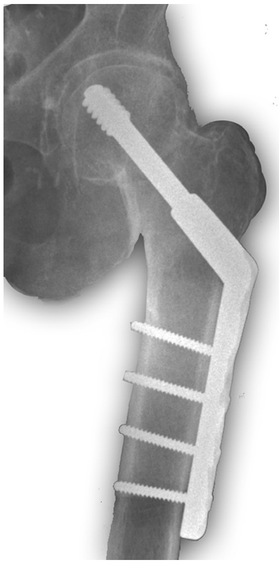


Figure 9. Gliding hip screw.

leagues (1993) examined screw positions in 87 femoral neck fractures and verified the importance of cortical support of the implants through the femoral neck.

When stabilizing bone fragments with one or more individual pins or screws, the fracture stability is determined by the additive holding power of each unit. Failure of one unit leads to increased stress on the remaining units with risk of cascade failure. This puts great demand to both the design of the implant's anchor and to the local bone quality. Regarding fixation with three screws, experimental studies have shown increased mechanical stability using a triangular pattern compared to a vertical screw orientation and that the apex down configuration reduces the risk of a later subtrochanteric fracture compared to apex up configuration (Selvan et al. 2004, Oakey et al. 2006, Lichtblau et al. 2008). A recent clinical report including 202 patients treated for a femoral neck fracture with either a triangle screw configuration or an inverted triangle configuration, found a significant difference in union rate in favor of the inverted triangle configuration (Yang et al. 2013). They also discussed an apparent increased risk of subtrochanteric fractures when two distal screws are placed horizontally.

2. Gliding hip implants

Gliding implants (Figure 9) were introduced in the 1940s and became increasingly popular after the introduction of the self-adjusting nail-plate (Pugh 1955). Neck shortening and varus collapse are common following fixation of femoral neck fractures (Zlowodzki et al. 2008). Rigid fixations will theoretically increase the risk of implant cut-throughs and cut-outs from the femoral head under repetitive loading. Gliding implants provide angular stability and allow for femoral neck shortening as the gliding screw anchored in the femoral head backs into a proximal barrel on the lateral supporting plate.

A new implant combines multiple screw fixation and the gliding hip screw principle (Brandt and Verdonschot 2011). Up to four telescoping screws are locked in a lateral supporting plate and the implant thereby provides flexible angular stability. Biomechanical studies and early clinical reports have been promising (Brandt and Verdonschot 2011, Parker and Stedtfeld 2010), however, recently published clinical series report a considerable number of medial screw penetration and cut-outs following fixation with this implant (Korver et al. 2013, Biber et al. 2014, Eschler et al. 2014).

3. Locking plate systems

Over the last ten years, locking plates for use in femoral neck fractures have been introduced (Aminian et al. 2007, Berkes et al. 2012, Lin et al. 2012, Nowotarski et al. 2012,). Locking plate technology was first introduced to bridge and stabilize long bone fractures as an alternative to compression plate fixation (Egol et al. 2004). In femoral neck fractures, bridging the fracture is impossible due to the anatomy. Locking plates used for these fractures function to provide angular stability and load sharing between the individual screws. Theoretically this would improve stability of femoral neck fractures in porous bone. Unfortunately, in the heavily loaded hip, increased rigidity resulting from locked fixation seems to increase the risk of mechanical failure of both bone and implants (Glassner and Tejwani 2011, Berkes et al. 2012, Hunt et al. 2012). More research is necessary to evaluate the use of locking plate technology in the proximal femur.

Fixation in porous bone

In the elderly, the cortical shell surrounding the femoral neck and the spongy bone of the femoral head must be assumed to be considerably porous (Mayhew et al. 2005, Thomas et al. 2009). If the implants' anchors cannot find safe support in the subchondral bone, one of the three points of safe fixation in the proximal femur has failed. It is also tempting to speculate whether a thin porous cortex predisposes to excessive femoral neck shortening due to compressive forces. This predisposes to unstable healing conditions with a theoretical increased risk of delayed union or nonunion due to unphysiological fracture site motions. Using radiostereometric analyses (RSA), Ragnarsson and colleagues (1991) examined both pin- and screw fixated femoral neck fractures and showed that the greatest movements occurred during the first postoperative month and that the time to stability of the bone-implant construct reached twelve months in some fractures.

In biomechanical experiments it has been shown that the holding-power of screws correlates with bone quality and there are indications, yet no final scientific evidence, for this correlation in vivo (Goldhahn et al. 2008). In fact, a recent cohort study including 140 patients with femoral neck fractures did not find an association between BMD and failure rate following internal fixation (Viberg et al. 2014).

Numerous attempts have been made to improve the stability of an implant operated into porous bone (Curtis et al. 2005). Several options exist to anchor the implant within the femoral head: screws with varying tread designs, screws with additional talons, pins with hooks and helical blades (Olsson et al. 2002, Bramlet and Wheeler 2003, Roerdink et al. 2009, O'Neill et al. 2011). A screw's holding power is determined by its inner and outer diameter, the pitch (distance between threads), depth and length of the screw threads (Chapman et al. 1996, Ramaswamy et al. 2010). The helical blade theoretically reduces the removal of bone during implant-insertion and increases the load-bearing surface with respect to conventional screw threads (Windolf et al. 2009). Rigid angular-stable locking of screws within a plate results in no movement between the different components of the implant. In engineering terms it creates a single beam construct four times stronger than implants with loosely attached components (Gautier et al. 2000). As the total load is now shared between the individual angular-stable screws in an all for one fashion, safe anchorage in porous bone is theoretically made easier (Kubiak et al. 2006).

Complications

Patients with femoral neck fractures treated with either internal fixation or hemiarthroplasty have a one-year mortality of more than 25% (Gjertsen et al. 2010). A randomized controlled trial including 222 patients with displaced femoral neck fractures found that reoperations within 24 months were performed in 42% of patients treated with internal fixation versus 11% in patients treated with hemiarthroplasty (Frihagen et al. 2007). A consecutive study including 224 patients with undisplaced fractures treated with internal fixation reported reoperations in 15% of the cohort at a mean follow-up of 32 months (Rogmark et al. 2009).

The Norwegian Hip Fracture Register has registered complications leading to subsequent surgery since 2008. Failure of the osteosynthesis is the most frequent reason for re-operations followed by deep wound infections, nonunions, necrosis of the femoral head, local pain due to the implant, dislocations of hemiarthroplasties, new fractures around the implant, hematoma, cut-outs of the implant through the femoral head, superficial wound infections and malunions (Engesæter et al. 2013). In addition to complications requiring new surgery, patients with femoral neck fractures often suffer from lasting reduced physical function and pain (Gjertsen et al. 2010 . Engesæter et al. 2013), some of which may be due to altered hip biomechanics such as femoral neck shortening (Zlowodzki et al. 2008).

In a retrospective study including 8,930 patients operated for a hip fracture, medical complications occurred in 19% (Lawrence et al. 2002). Cardiac and pulmonary complications were most frequent. Patients with serious cardiac and pulmonary complications had a 30 day mortality rate of 22% and 17%, respectively. After one year the mortality was 36% and 44% in these two groups. They found gastrointestinal bleeding in 2%, and venous thromboembolism and transient ischemic attacks / stroke in 1%. In a prospective cohort of patients without dementia at time of admission for a hip fracture, 39% developed delirium pre- or postoperatively (Lundstrom et al. 2003). These patients had increased risk of developing dementia within five years and also a higher mortality rate. Pressure sores is another well-known complication in patients with hip fractures (Haleem et al. 2008).

Testing

Objectives of ex vivo hip fracture experiments

Clinical outcome following femoral neck fractures in patients selected for internal fixation (IF) can be improved by better preoperative selection, optimizing surgical procedures of existing devices and by introducing improved implants and techniques. Ex vivo biomechanical experiments are performed to evaluate aspects of surgical treatments that are difficult to explore clinically. Such studies can thereby provide complementary information to clinical research. Ideally, preclinical testing, such as ex vivo biomechanical experiments, should be the first step on the way to introducing new technologies in orthopaedic surgery (Malchau et al. 2011). In fact, new fracture fixation designs are often based on implants already established, and biomechanical laboratory experiments can according to current regulations provide sufficient evidence for releasing a novel design (Schemitsch et al. 2010).

Specimen

Using human cadaver femurs are still regarded the gold standard by most researchers when conducting laboratory experiments on hip fracture fixation (Linden et al. 2006, Windolf et al. 2009, von der Roderer et al. 2010). Cadaver femurs reflect the great variation in strength and anthropometry found in vivo. Human bones also enable the creation of rough fracture surfaces. Unfortunately, limited access to donors, strict ethical regulations and rapid material breakdown make their use somewhat troublesome (Cartner et al. 2011). This has made the use of synthetic composite femurs increasingly popular. The most widely used composite femur is one made from fiberglass reinforced epoxy and polyurethane foam to resemble cortical and cancellous tissue. This particular composite femur replicates healthy bone found in male subjects <80 years (Gardner et al. 2010). The mechanical properties of whole bone composite femurs have previously been found comparable to human femurs (Cristofolini et al. 1996, Heiner 2008, Gardner et al. 2010). Composite femurs were also found to be good analogs to human bones regarding pull-out force of screws (Zdero et al. 2007 and 2008). On the contrary, a later study found that the pull-out force was significantly higher in composite femurs than in cadaver femurs (Topp et al. 2012).

Test setups

Ex vivo hip fracture experiments most often employ a materials testing machine with some kind of hip-jig fitted. The distal and proximal fixations determine the degree of freedom of the mounted femur. If the femur is restricted from moving under load–application, the stress distribution in the bone, including bending and torque, is decided by the spatial femur–orientation relative to the load direction. The load must then be transmitted directly from the actuator in the materials testing machine onto the femoral head through an acetabular substitute. Some research groups prefer to keep the diaphysis in a neutral position without adduction, abduction, flexion or extension (Brandt et al. 2010). Others again use a calculated mechanical axis for each single femur (Oakey et al. 2006). A distal anchorage that allows angulations and rotations of the femurs opens the possibility of simulating abductor muscles and the iliotibial tract. Under these circumstances, the load must be applied over lever arms. Abductor forces can be simulated by attaching a device to the greater trochanter and then fasten it to a horizontally aligned lever arm (Wik et al. 2011). Another solution is to let a distally fastened strap override a trochanteric device before attaching it to the jig at the superior aspect. In this way, both the abductors and the iliotibial tract are simulated (Krischak et al. 2007, Windolf et al. 2009, Roderer et al. 2010). The posteriorly directed torque is considered important in enhancing micromotions potentially leading to loosening of the implant, particularly concerning femoral stems. Although it is possible to apply torque in constrained femurs (Brandt et al. 2006), more degrees of freedom in the hip–jig make a separate application of torque possible. The torque can then be applied to the femoral head (Deneka et al. 1997) or the distal diaphysis (Aamodt et al. 2001).

Loading regimes can be divided into static and dynamic loading. The latter is often referred to as cyclic loading where one particular cycle might consist of a single (Kauffman et al. 1999) or combined force delivered e.g. in a sinusoidal manner (Benterud et al. 1994, Brandt et al. 2010) or as a loading trajectory with alternating forces simulating a walking or stair-climbing situation as described from in vivo measurements (Bergmann et al. 2001). The load force might be increased in a stepwise manner (von der Linden et al. 2006, Brandt et al. 2010), incremented linearly (Haynes et al. 1997, Lichtblau et al. 2008) or held stable during the test period. Some researchers prefer to combine two or more methods to optimize the test setup. A commonly used combination involves a static, non–destructive load to evaluate stiffness, followed by cyclic loading for a given number of cycles (Swiontkowski et al. 1987,

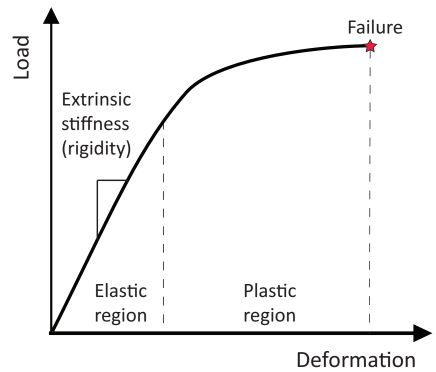


Figure 10. Load–deformation curve.

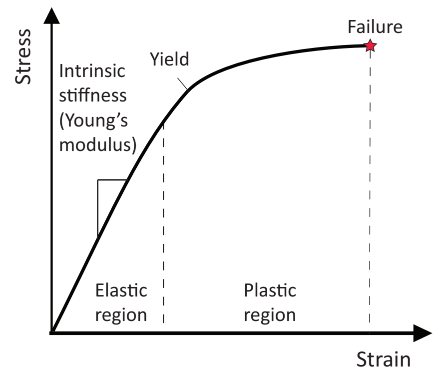


Figure 11. Stress–strain curve.

Jazrawi et al. 2001). The experiment can then be finished with a destructive setup to determine load to failure (Kauffman et al. 1999, Aminian et al. 2007, Zdero et al. 2010, Rupprecht et al. 2011b). It is important to bear in mind that application of a singe force might result in complex stressing of the femur due to the femoral anatomy. E.g. axial loading of a proximal femur tilted posteriorly results in combined compressive, tensile and shear stresses if the distal femur is constricted in the hip-jig. The magnitude of force applied to each specimen can be standardized so that all femurs are subject to the same forces, or scaled according to BW of the donor.

Outcomes

Rigidity

Axial compression of the proximal femur will cause deformation, or deflection, of the femoral head. Graphically the head–deformation, or deflection, can be plotted against load to provide a load–deformation curve (Turner and Burr 1993) (Figure 10). This curve can be divided in an elastic region where no plastic deformation occurs and a plastic region where deformations are permanent. The slope of the elastic region of this curve expresses the extrinsic stiffness of the bone or bone–implant construct also referred to as rigidity. Rigidity defines the property of a solid body to resist deformation. The rigidity of a bone–implant construct can be compared to that of intact bone or to a comparable construct. Further compression will reveal yield load with damage accumulation such as micro–fracturing and cause plastic deformation and eventually failure in fracture. Stiffness and load–to–failure are widely used endpoints (Roderer et al. 2010).

Strain

Strain in this context can be defined as local stretching or compression of the examined cortex due to applied stress. The load–deformation curve can be transformed to a stress–strain curve (Turner and Burr 1993) (Figure 11). Stress is defined as applied force per unit area and reported in Pascal (Pa = 1 N per m^2) (Turner and Burr 1993). The slope in the elastic region of the curve now represents the intrinsic stiffness, also referred to as Young's modulus. In bone the Young's modulus varies in different directions and the bones e.g. the femur, is said to be anisotropic. The ability of the bone to accumulate microstructural damage before complete failure describes the ductility, or inversely the brittleness, of the bone. Bone in general is not very ductile and the ductile qualities do not appear to change in untreated osteoporosis (Turner and Burr 1993).

The most applied method to investigate local strain is to attach strain gauges to an object that will later be subject to loading. Other methods to measure strain in bone include extensometers, fiber optic sensors and non-contact strain measurements such as 3D image correlation photogrammetry (Turner and Burr 1993, Tyson et al. 2002, Fresvig et al. 2008). Measures of strain on the femoral cortex or the implant itself are not common in the literature dealing with fixation of hip fractures, but examples do exist (Mizrahi et al. 1980, Eberle et al. 2010).

Stability

During the course of repetitive loading, elastic deformations will occur every load cycle in a stable situation. Pure elastic deformations describe the stiffness of a construct. Fracture fixation in human bone is unlikely to provide absolute stability and combined elastic and plastic deformations occur. Using the initial measurements as reference, the total plastic deformations occurring after a set number of cycles can be evaluated. Pretest–posttest analyses best describe plastic deformations important for the hip biomechanics, whereas stability during cyclic loading gives an idea of the fracture healing conditions.

A fracture fixating system must provide sufficient stability to allow for successful fracture union. Whereas static compression tests can provide information on maximum tolerated load before construct failure, cyclic loading is necessary to evaluate instability due to repeated stress as occurs in a clinical setting. Implant loosening and femur deformation are important outcomes from a clinical point of view. Implant loosening can lead to fracture redisplacements, unphysiological interfragmentary strains with resulting delayed unions, malunions, nonunions (Ragnarsson et al. 1993), and fractures around the implant. Femur deformations alter the hip biomechanics which may lead to impaired function, particularly if femoral neck shortening is prominent (Zlowodzki et al. 2008).

Measures of stability can be captured directly from the testing machine (Benterud et al. 1994, Deneka et al. 1997). Extensometers over the fracture have also been used (Baitner et al. 1999). Today many biomechanical laboratories use a three dimensional (3D) motion tracker system to measure the relative movements of the fragments. To do this, markers must be placed on each of the fragments being examined. The relative marker positions are then captured by e.g. optical, ultrasound or alternating or changing magnetic field techniques (Windolf et al. 2009, Roderer et al. 2010, Nowotarski et al. 2012). The use of full 3D technology enables high-resolution measurements of fragment motion.

Aims of the study

There were two main objectives for this PhD thesis. The first was to evaluate a new implant for femoral neck fracture fixation. The second was to evaluate clinical relevance of biomechanical femoral neck fracture experiments.

Study I: The primary aim of this study was to explore whether the new locking plate affected the postoperative migration of the femoral head fragment when compared to conventional fixation by three parallel screws. The secondary aim was to explore possible adverse effects, such as new fractures, following fixation with the new implant. *(Paper 1)*

Study II: The primary aim of this study was to investigate how adding a locking plate to fracture–fixating screws affected micromotion of the femoral head fragment. The secondary aims were to see whether BMD affected the micromotion magnitudes and to explore how the load distribution and stiffness of the proximal femur were affected by screw fixation and locking plate fixation. *(Paper 2 and unpublished material)*

Study III: The aim of this study was to compare 4th generation composite femurs (4GCFs) with human cadaver femurs with respect to anthropometry, cortical bone deformation (strain), stability of operated femoral neck fractures and failure modes to evaluate whether 4GCFs can be an adequate substitute for cadaver femurs in hip fracture experiments. *(Paper 3)*

Study IV: The aim of this literature study was to provide background information necessary to comprehend biomechanical femoral neck fracture models and to evaluate their results. Based on this study we wanted to propose experimental setups for optimum clinical relevancy. *(Paper 4)*

Materials and methods

Test specimen

Human cadaver femurs

After receiving approval from the Regional committee for Medical and Health Research Ethics (REK), 24 fresh frozen human cadaver femurs were obtained from LifeLegacy Foundation (Tucson, AZ, USA). We included femurs from donors of both sexes with a minimum age at death of 60 years. We specified an interest in femurs from donors assumed to have impaired bone strength without localized bone pathology, such as a diagnosis of osteoporosis. The femurs were stored at –20° C in saline-soaked cloth prior to use.

All femurs were examined by high resolution computed tomography (CT) and femurs with signs of pathology other than osteoporosis were to be excluded (Somatom Definition Flash, Siemens, Erlangen, Germany). None of the femurs had signs of localized bone pathology. CT-scanning was preferred over conventional radiographs to enable later computer modelling and evaluation of cortical thickness in the femoral neck.

DXA with an advanced hip assessment software module was performed for all femurs to measure BMD and calculate T-scores and to obtain accurate anthropometric measures of the included femurs (Lunar iDXA, GE Healthcare, WI, USA). According to the minimum total hip T-score in all pairs, five pairs were osteoporotic (< –2.5), four were osteopenic (–2.5 to –1) and three were normal (> –1). Table 1 gives an overview of the included cadaver femurs.

Composite femurs

Four left large and six left medium fourth generation composite femurs (4GCF) were included (product numbers 3406 and 3403). These artificial femurs were purchased from Sawbones, a division of the Pacific Research Laboratories, Vashon, Washington, USA. Both the large- and medium-sized composite femurs (Figure 12) are modeled to simulate healthy men with good bone quality aged less than 80 years (Gardner et al. 2010). The large-sized 4GCF was modeled after a 183 cm / 91 kg Caucasian male and the medium-sized 4GCF was modeled after a 175 cm / 84 kg Caucasian male according to the manufacturer. These composite femurs were chosen for their popularity in recent laboratory research (Brandt et al. 2006, Roerdink et al. 2009, Nowotarski et al. 2012).

Table 1. Demographics

ID	Gender	Age	T–score (left)	T–score (right)
1	F	83	–4.5	–4.5
2	F	60	–2.9	–2.5
3	M	67	0.0	–0.3
4	M	67	–3.7	–4.0
5	F	75	–2.3	–2.5
6	M	61	–1.3	–1.3
7	F	80	–1.5	–1.2
8	M	71	–0.5	–0.0
9	F	82	–0.5	–1.0
10	M	68	–0.7	–0.1
11	F	98	–4.3	–4.5
12	F	65	–1.3	–1.5

Figure 12. Medium (left) and large (right) 4GCFs.

Preparation of femurs before testing

With the exception of soft-tissue removal on the cadaver femurs, all femurs underwent the same preparation before testing. Neck-shaft angles were measured using a goniometer. The neck version was measured with the femur resting on the posterior, distal condyles and the posterior trochanter. A digital

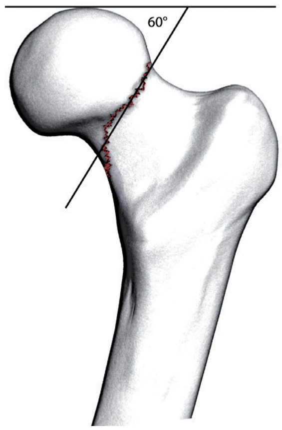


Figure 13. Fracture line.

Figure 14. Three cannulated screws (a) and three cannulated screws and a locking plate (b).

spirit level was used to decide the femoral neck versions. Still with the distal condyles intact, the fracture line was marked 60° to the horizontal from the superior head-neck border down using a digital spirit level (Figure 13). This fracture simulates a non-impacted, subcapital femoral neck fracture allowing for stable fixation with cortical support around the entire femoral neck. As these fractures were created ex vivo a distinction of displaced and undisplaced fractures was not applicable.

The diaphysis was marked 25 cm distal to the uppermost tip of the greater trochanter and the condyles were removed. The bone was cemented (Meliodent, Heraeus, Hanau, Germany) into a cylinder from the 25 cm mark down using a custom-made jig to determine the center-axis of the femur. Subject-specific trochanteric strap-guides for the lateral tension band were made of bone cement. As standardized torque was to be applied, attempt was made to minimize additional subject-specific torque by neutralizing the proximal anteversion and letting the tension band run parallel to the length axis of the femur in the sagittal plane.

Fracture and fracture fixation

A cortical saw cut was made along the marked fracture line. In the medial collum the cut continued into the cancellous bone to avoid femoral head attachment of the inferior buttress. Finally, a mallet blow to the head completed the fracture.

An aiming guide was used under fluoroscopic control for correct placement of the guide pins. The aiming guide allowed three sizes of an inverted triangle configuration so the implant could be adapted to the size of the femur. The pins were positioned at 130° with respect to the length axis of the diaphysis and placed approximately 5 mm from subchondral bone. The inferior pin was riding the inferior buttress with the posterior pin inserted along the posterior cortex. After pin-placements, the first femur of each pair was randomly allocated to one of the two fixation methods by coin toss.

The two modes of fixation were:

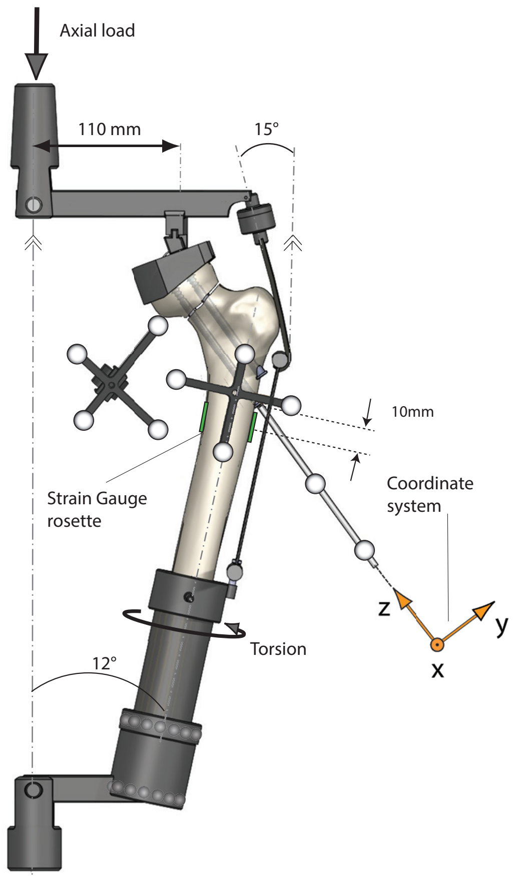
- Three cannulated, partially threaded cancellous screws in an inverted triangle configuration (Dynaloc Bone Screws; Swemac Innovations, Linköping, Sweden). All screws were 6.7 mm in diameter and made of titanium-alloy (Figure 14a).
- Three cannulated, partially threaded cancellous screws in an inverted triangle configuration locked in a lateral plate that was not attached to the lateral cortex (Figure 14b). The screws were locked to the plate by set-screws (Dynaloc System; Swemac Innovations, Linköping, Sweden). All screws were 6.7 mm in diameter and made of titanium-alloy.

All screws were threaded at the head end to assure secure fixation of the marker tool used for motion capturing.

The Trondheim hip fracture simulator

The femurs were mounted 12° in adduction in a jig built with reference to data presented by McLeish and Charnley (1970) (Figure 15). This jig was fitted in a materials-testing machine where a central actuator applied axial loads to the hip jig (MTS 858 MiniBionix II, MTS Systems Corporation, Eden Prairie, Minnesota, USA). In addition, torque was induced by a wire-pulling construct with a separate actuator acting on the cylinder-bed. The hip jig, the testing machine and the distally applied torque constitute the Trondheim hip simulator.

To mimic physiologic hip loading during normal walking with this particular hip BW must be applied from the simulated center-axis onto a horizontal lever arm. This lever arm has an interchangeable acetabular cup mounted 11 cm from the actuator at the distant end resembling the average hemipelvic width. In addition, a lateral tension band is attached distally in the jig and passes the trochanter major before it is attached in medial direction with an angle of 15° to the lever arm.



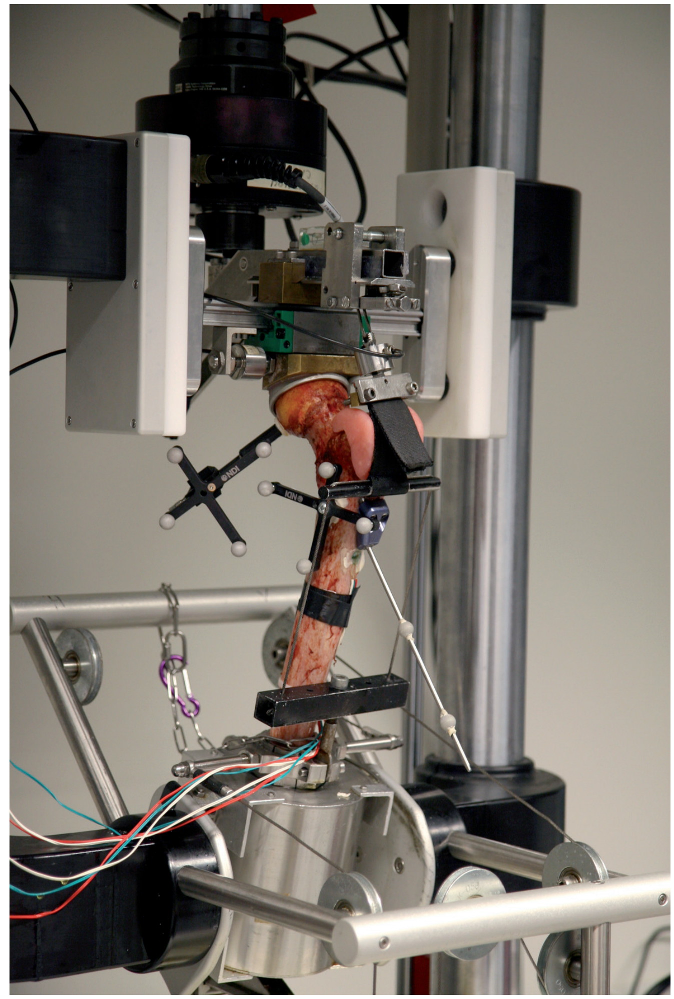


Figure 15. Schematic illustration of the hip jig (left) and picture of the hip simulator (right).

BW of the donors and reported weight of the human models for the composite femurs were used to calculate the forces to be applied. For these experiments two cyclic load regimes (Figure 16) were applied at 0.5 Hz:

- Cycles 1–10,000: Partial weight-bearing (80% of axial loading at normal weight-bearing) and 1.8% BW-meter torque simulated hip loading during walking in the fracture healing period (Koval et al. 1998, Bergmann et al. 2001).
- Cycles 10,001–20,000: Full weight-bearing was simulated and the torque was increased to 2.2% BW-meter as measured in vivo during stair climbing (Bergmann et al. 2001).

Minimum axial load and torque during one cycle were 15% of full weight-bearing in accordance with in vivo data (Bergmann et al. 2001).

Two active load-cells assured load-control for compression and torque. In addition, passive load-cells were placed in the acetabular cup and at the proximal attachment of the tension band to enable calculation of the hip joint resultant force (JRF). Outputs from the passive load cells were recorded by

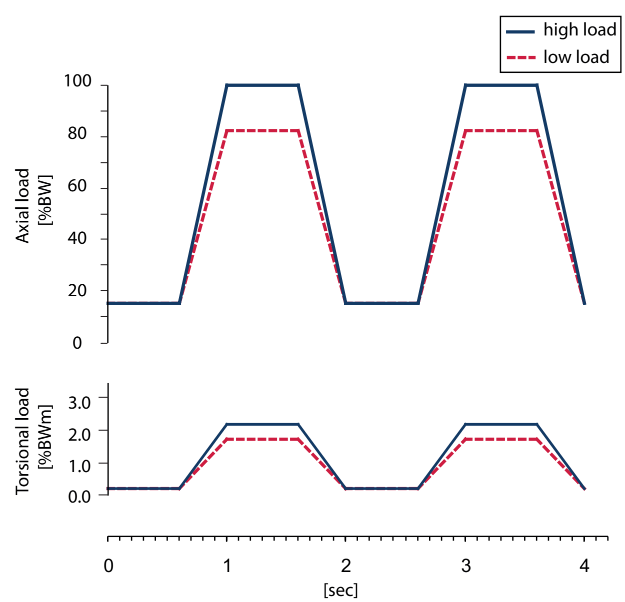


Figure 16. Cyclic load regimes.

Figure 17. Polaris Spectra.

a measurement amplifier (UPM 100; HBM, Darmstadt, Germany). The mean JRF at onset of the first load regime for all tested femurs was 2.4 × BW (SD 0.2) of which the tension band force contributed 1.5 × BW (SD 0.2) or 62% of the total load. The mean JRF at onset of the last load regime was 3.0 × BW (SD 0.2), and 61% was attributed to the tension band. These values correspond well with published data from telemetric in vivo studies (Davy et al. 1988, Bergmann et al. 2001) and from calculations done to define the abductor resultant force (McLeish and Charnley 1970 , Heller et al. 2005).

Motion capturing

To measure relative movements in the femur an optical three-dimensional (3D) measurement system (Polaris Spectra, NDI, ON, Canada) was employed (Figure 17). Rigid body marker tools (Polaris Passive 4-Marker Rigid Body, NDI, ON, Canada), each consisting of four retro-reflective passive markers with a minimum reciprocal distance of 50 mm, were attached to the femoral head and the proximal anterior diaphysis. The markers were fixed to the bone by screws and glue (X60, HBM, Darmstadt, Germany). Sustained fixation of the markers was controlled when the femurs were stripped down. A custom-made two-marker tool was fixed to the distal screw, which was threaded at the head end. The center of the femoral head was calculated using a sphere-fitting method on multiple digitized surface points of the surface of the femoral head (Labview 8.6, National Instruments, Austin, TX, USA).

A marker tool aligned along the length axis of the diaphysis defined the initial coordinate system (Figure 18). The final coordinate system was defined by relating the z-axis to the length axis of the distal screw (with the attached two-marker tool) and the x-axis running perpendicular to the length axis of the diaphysis. A positive rotation about the x-axis represents rotation to varus. Negative rotations about the y-axis show retro-rotation and negative rotation about the z-axis describes

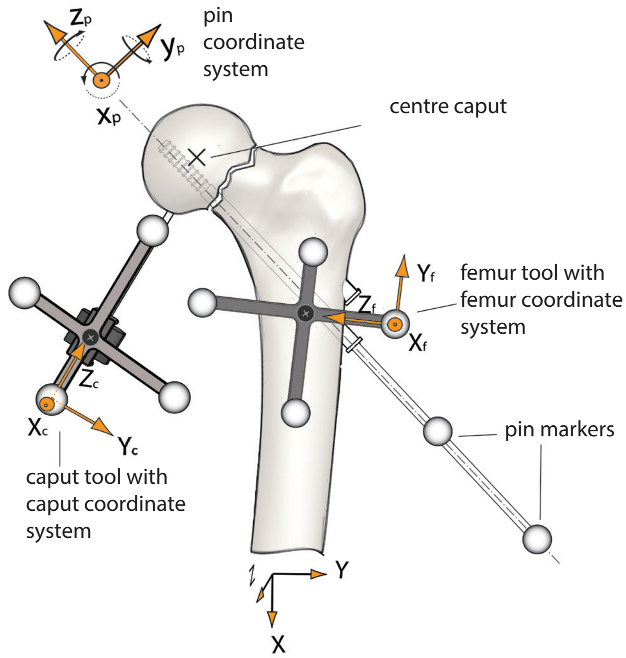


Figure 18. Coordinate systems

internal rotation of the head fragment. The final coordinate system was used to define rotation and migration of the femoral head center with respect to the x-, y- and z-axes.

Initial positioning of the center of the femoral head was recorded at the onset of both loading regimes. Plastic deformation was defined as the difference between the initial positioning and measurements captured when the femurs were unloaded at the start and end of the cyclic loading. Micromotions (three translations and three rotations) were defined as the differences in marker positions from maximum to minimum load and were recorded every 100 cycles.

Measurement error for the motion capturing was calculated using two subsequent measures on intact proximal femurs. The following formula was used:

$$s_w = \sqrt{\frac{1}{2} \cdot \frac{\sum_{i=1}^{n} d_i^2}{n}}$$

where d_i was the difference of the two measures for the i^{th} femur (Bland and Altman 1996). Measurement error was 0.068° for total rotations and 0.083 mm for absolute translations.

Cut-off values and failures

Clinically, 5 mm shortening of the femoral neck resulted in impaired function and quality of life (Zlowodzki et al. 2008). Considering that only the first postoperative period was simulated in this experiment, 2 mm migration of the femoral head center was considered to be large enough to be of potential clinical relevance due to altered hip biomechanics. When the two modes of fixations were to be compared, we also considered a difference of 2 mm to be of potential clinical relevance.

Failures were defined as new visible fractures in the femurs occurring during loading or as piston displacement exceeding 25 mm. For the paired comparisons both femurs of a pair were excluded from statistical calculations if one had failed. All failure modes were documented.

Strain measurements

Multi-axial pre-wired strain-gauge rosettes, composed of three strain-gauges angulating 45° with respect to one another were used to measure principal strain (Tokyo Sokki Kenkyujo Co. Ltd, Tokyo, Japan). One strain-gauge rosette was placed 10 mm distal to the inferior pin-hole on the lateral cortex and another was placed on the exact same level on the medial cortex.

All soft tissue was removed from the cortex of the cadaver femurs. For all femurs the surface was carefully smoothened with sandpaper. Acetone and etchant (Scotchbond Etchant, 3M ESPE, St Paul, Minnesota, USA) was used for degreasing and N_2-gas dried the surface. Priming the surface (Scotchbond Multipurpose Primer, 3M ESPE, St Paul, Minnesota, USA) was followed by gluing the rosettes to the cortical surface (X60, HBM, Darmstadt, Germany) so that strain-gauge #3 always followed the length axis of the femoral diaphysis.

The accuracy of the strain measurements was 1%. Outputs from the strain gauges were recorded by a measurement amplifier (UPM 100; HBM, Darmstadt, Germany). The principal strains on the medial and lateral proximal diaphysis were calculated during data acquisition. Strain measurements were presented as the average value of three cycles recorded at maximum load. To compare strain on intact proximal femurs with that of operated specimens, the percentage difference was calculated.

Review of biomechanical femoral neck fracture experiments

Relevant publications were identified using non-systematic searches in PubMed, Scopus and Cochrane. The lists of references from the reviewed articles were also investigated.

Statistics

Sample size considerations

The sample size for study I was calculated (IBM SPSS Sample Power 3; IBM Corp., Armonk, NY, USA) based on the following assumptions: A paired difference of 2 mm when comparing the two methods was considered the smallest effect important to detect. A SD_{diff} of 1.5 mm was assumed (Windolf et al. 2009). To test the null hypothesis that the locking plate had no additional effect compared to fixation by individual screws, eight pairs of cadaver femurs were needed to achieve power > 90%, level of significance set at 0.05. Powering the study for failure rate would require a large number of femurs, which was not feasible.

It was not possible to make sensible sample size estimations for study II due to the lack of background information in previously published materials. Critical magnitudes of micromotions for successful fracture healing in the femoral neck are not known. The results were therefore presented with theoretical effect sizes and conclusions strictly theoretical.

When testing the material properties of 4GCFs, Heiner and colleagues included six femurs. They reported that inter-specimen variability amongst composite femurs was considerably less than amongst cadaver femurs (Heiner 2008). Gardner and colleagues reported inter-specimen variability of less than 10% for 4GCF (Gardner et al. 2010). Based on this, the number of included composite femurs for the comparative study (study III) was set to 10.

Statistical calculations

All statistical calculations were performed using IBM SPSS Statistics (version 20 and 21, Chicago, Ill, USA) and IBM SPSS Sample Power (version 3; IBM Corp., Armonk, NY, USA). Level of significance was set to 0.05 for all statistical calculations. Visual inspection of QQ plots and the Shapiro-Wilk test were used to explore whether the outcome variables were normally distributed and parametric or non-parametric tests were chosen accordingly. The following statistical methods were chosen:

Study I: The difference of pretest and posttest data recorded when the femurs were unloaded defined plastic deformations. Migrations and rotations of the femoral head fragments relative to the proximal diaphyses were tested using a related samples t-test. Nine pairs survived the first load regime and statistics were based on these data. Only seven pairs completed 20,000 cycles, and data from the last load sequence along with description of failures were solely descriptively presented according to the power-analysis.

Study II: Visual inspection of micromotion-data showed that repeated cycles had no substantial effect on the micromotion of the head fragment. The average of 100 measurements from each femur was therefore used for descriptive statistics and paired comparisons. Linear mixed models analysis was used to analyze the micromotion data. The six motion outcome variables (dependent variables) were continuous. Each of the six movements was analyzed separately, holding the type of osteosynthesis as a factor. Initially, the other five movements were included as covariates, with sequential removal of non-significant movement covariates to define the most parsimonious models by Akaike's information criterion (Cheng et al. 2010). Variance components covariance structure was used for the random effects. The residuals were found to be normally distributed. Cohen's d was calculated for effect size. Related-samples Wilcoxon signed rank test was used to evaluate strain and to compare elastic deformations in intact and operated femurs. The Hodges–Lehman procedure provided an estimate the median differences (95% CI) between the two groups. Fisher's exact test was used to test the relationship between T-score (normal/osteopenia and osteoporosis) and the magnitude of total microrotations (data split at median).

Study III: To adjust for intra-pair (two femurs from one donor) related factors and two modes of fixation, the average outcome value for each cadaver pair was used. Composite femurs were regarded independent. Stability of the femoral head fragment and principal strain on the lateral and medial aspects of the proximal femur in cadaver femurs and 4GCFs were compared using independent samples Mann–Whitney U tests. Femoral anthropometry and modes of failure were presented descriptively.

Summary of results

Study I

Does the new locking plate affect postoperative migration of the femoral head when compared to conventional fixation with three parallel screws?

In six out of nine femoral pairs that survived 10,000 cycles, the migration of the femoral head center was reduced when the locking plate was used. There was a highly significant correlation of migration between the two femurs of a pair (r = 0.953). The mean paired difference in head center migration was statistically significant at 1.6 mm (95% CI 0.1–3.1), but this was below the predefined cut-off for the onset of a postulated clinically relevant difference of 2 mm. Ninety percent of the femoral head center migrations occurred with shortening of the femoral neck and varus rotation (Figure 19).

Femoral head fragment rotations were minor, and we could not detect a significant effect of adding the locking plate. Seven femoral pairs survived 20,000 cycles and the 2 mm threshold had then been reached in six out of seven femurs in both treatment groups (Figure 20).

Does the new locking plate increase the risk of new fractures?

The total number of individual femurs that failed in fracture or excess piston displacement during 20,000 cycles was seven out of 24. Five femurs failed with fracture of which three femurs were operated with the locking plate. In addition two femurs from the same donor had a total collapse of the femoral neck. Five failed femurs were osteoporotic (T-score < –2.5) and the remaining two were osteopenic (–2.5 to –1). All failures occurred in femurs from female donors operated using the aiming guide for the smallest-sized inverted-triangle configuration due to small femur size. All femoral head fragments in failed femurs had rotated internally and in varus. Three femurs had fractures down the medial neck (Figure 21a) with additional involvement of the lesser trochanter of which one passed through a lateral screw-hole. Two femurs had fractures originating in the screw-holes on the lateral cortex that spread to the intertrochanteric region (Figure 21b). The three fractures that involved the lateral screw-holes were all fixed with the interlocking plate.

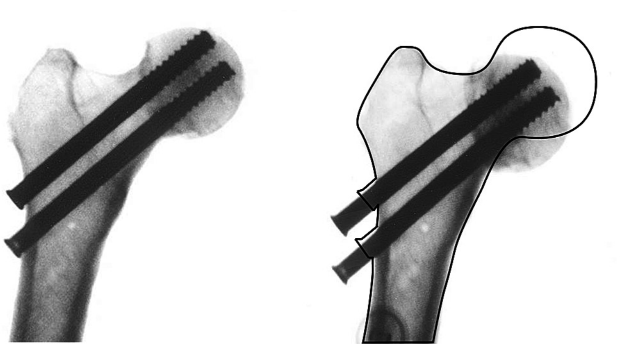


Figure 19. A typical example of plastic deformation of the proximal femur following cyclic loading.

Study II

How does adding a locking plate to fracture–fixating screws affect micromotions of the femoral head fragment?

In accordance with the direction of the hip joint resultant force, the major micromotions were found to be valgus-varus rotation (x-axis, 0.44°) and translation along the y-axis (0.25

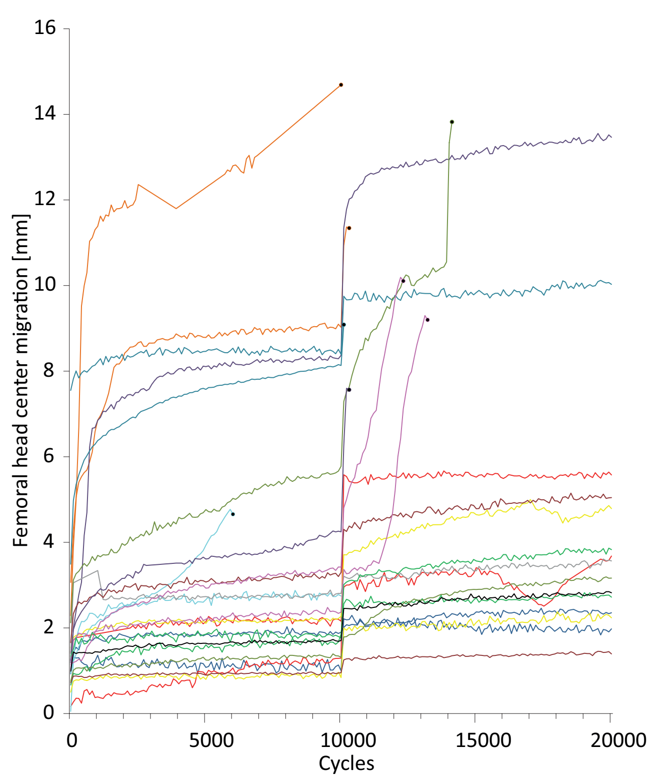


Figure 20. Plastic deformation of each single, unloaded femur during 20.000 cycles, note new loading regime at 10.000 cycles. Measurements every 100 cycles. Interpolation line when missing data points. Femoral pairs in same color. Black dots at point of failure.

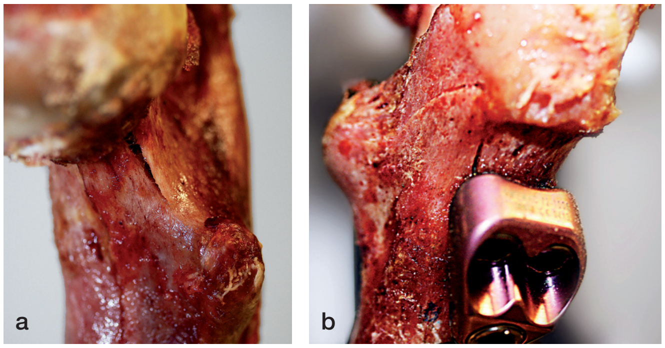


Figure 21. a. Fracture down the medial neck. b. Fracture with screw-hole involvement.

mm) (Figure 22). The locking plate reduced the rotation about the femoral neck (z-axis) by 27%. This difference between the two groups was significant (p = 0.035) with a medium effect size (d = 0.62). This study could not detect any difference in micromotions in valgus–varus or antegrade–retrograde rotations, or in the three translations.

Does BMD affect the micromotion magnitudes in fractured femurs operated with individual screws or interlocked screws?

A total of nine femurs were osteoporotic according to T-score ≤ -2.5. We could not detect any association between T-score and the magnitude of micromotions of the femoral head fragment. This accounted for both femurs operated with individual screws (p = 0.242) and femurs fixed with a locking plate (p = 0.545).

How does internal fixation of a femoral neck fracture affect the stiffness and load distribution of the proximal femur and does adding this locking plate change these parameters when compared to individual screw fixation?

For intact proximal femurs, the median (95% CI) lateral strain was 824 µm/m (730 to 1,054) and the medial strain was −1,399 µm/m (−1,745 to −1,043). Fracture fixation of the femurs changed the load distribution compared with the intact state. The lateral strain decreased significantly by 21.5% with an estimated reduction of 188 µm/m (147 to 248). The

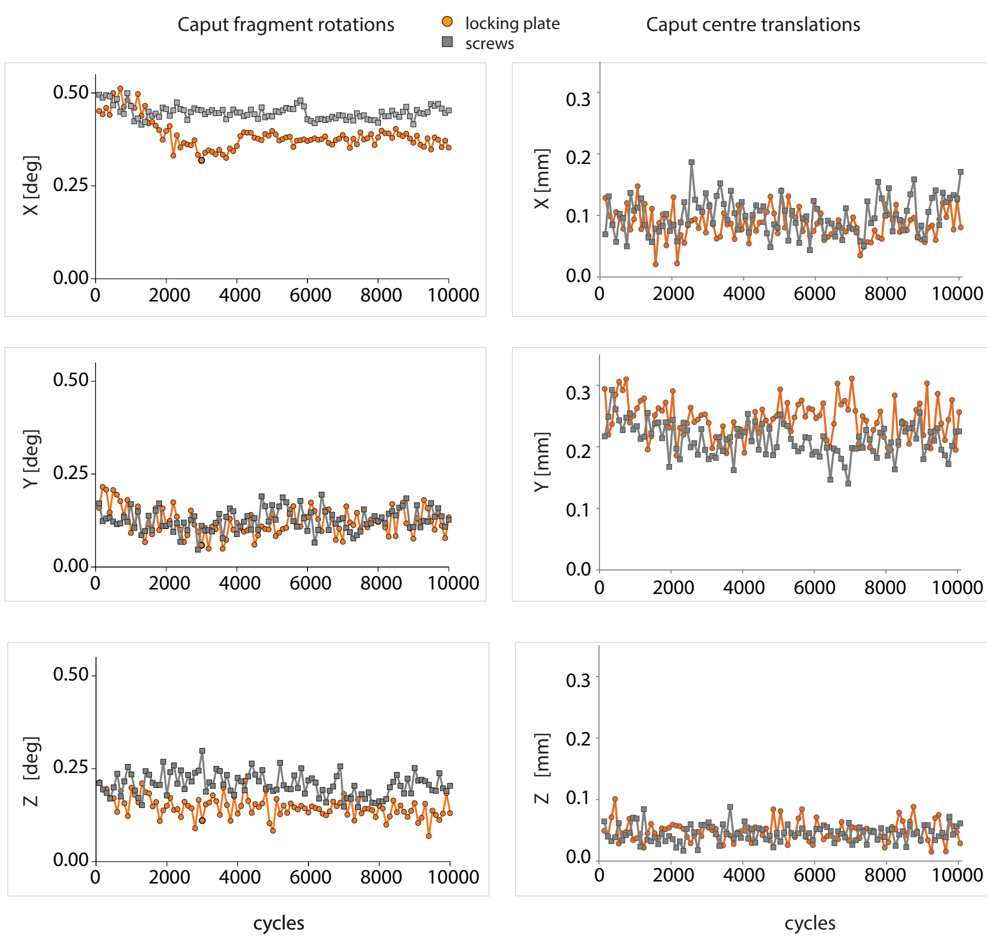


Figure 22. Average micromotion in the locking plate group and in the screws group decomposed into three translations and three rotations.

observed increase in medial strain was statistically significant, but minor at only 55.5 µm/m (15 to 85), or 4.5%. Compared to intact femurs, elastic translational deformations of the femoral head were reduced by 31% following internal fixation of fractured femoral necks. The elastic rotational deformations increased by 48%. Both the change in elastic rotations and elastic translations were significant. The experiment could not detect a significant difference in load distribution between the two implant groups in either the medial or the lateral aspects of the proximal femoral diaphysis or in the resistance to elastic deformation of the femoral head fragment.

Study III

Can fourth generation composite femurs serve as substitutes for cadaver femurs in hip fracture experiments?

Regarding femoral anthropometry, the median (95% CI) femoral head anteversion and neck–shaft angle for large–sized 4GCFs were 5° (3 to 5) and 115° (113 to 115) respectively. For medium-sized 4GCFs they were 10° (7 to 12) and 127° (127 to 128) and for cadaver femurs 11.5° (6.5 to 14) and 123.5° (123 to 126). The principal strains one both the medial and lateral aspects of the proximal femoral diaphysis were significantly higher in 4GCFs than in cadaver femurs. The stability of the femoral head fragment in operated femurs was significantly better in 4GCFs than in cadaver femurs (Figure 23). Median (95% CI) head fragment migration was 0.8 mm (0.4 to 1.1) in the 4GCF group and 2.2 mm (1.5 to 4.6) in the cadaver group. The intra-group variance in femoral head migration was lower in the 4GCF group with an interquartile range of 1 mm compared to 3.8 mm in the cadaver group. Following cyclic loading, two medium-sized 4GCFs failed with a transverse fracture through the inferior screw-hole. This pattern of fracture was not observed in any of the five fractured cadaver femurs that all fractured down the medial neck or in the intertrochanteric region. In addition, cadaver femurs showed plastic deformations prior to failure, whereas the 4GCFs behaved stable until sudden fracture.

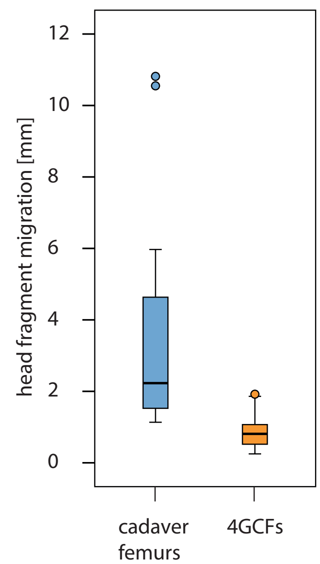


Figure 23. Head fragment migration

Study IV

Review of biomechanical femoral neck fracture studies and proposed experimental designs for optimum clinical relevance

The study revealed a wide variety of biomechanical setups used when investigating femoral neck fractures. This variety is necessary to cover as many aspects of femoral neck fractures as possible, but also makes direct comparison of study results and assessment of clinical relevancy difficult. Following this extensive review of available literature, we believe that biomechanical femoral neck fracture experiments would improve and increase their impact if the recreation of the in vivo situation was optimized. Our suggestions on how to optimize femoral neck fracture experiments in terms of clinical relevancy is summarized in the Discussion of results section.

Discussion

General discussion

The basis of this thesis is ex vivo biomechanical experiments concerning surgical treatment of femoral neck fractures. Such studies make direct high resolution measurements of stability, rigidity and strain of the bone and bone-implant constructs possible. Laboratory studies enable standardized fractures, implantations and loading regimes. In addition the possibility of comparing two treatments in pairs of femurs is a great advantage compared to clinical studies. Fracture stability, implant loosening, implant cut-outs, implant breakage and new fractures are known complications to femoral neck fractures that can be explored ex vivo. Of more theoretical observations are construct rigidity and cortical bone deformation. The most obvious shortcoming of biomechanical laboratory studies is their limitation in describing in vivo bone response to mechanical and biological stimuli. Investigation of avascular necrosis, infections, fracture healing, stress shielding and late implant loosening due to local bone necrosis requires response from live bone. Evaluation of pain and functional impairment not only requires vital bone, but also vital patients. From this we can conclude that this experimental method is best suited for evaluation of short-term complications following surgical treatment of femoral neck fractures.

Current regulations in North America allow new orthopedic implants to be approved for clinical use if the implant is based on already established principles and has been made by already well-known materials (Schemitsch et al. 2010, Zywiel et al. 2012). In the European market, medical devices are categorized from class I to III according to intended use and indications for use. Class I medical devices are considered low risk and class III high risk. Although orthopedic implants are classified in class III, no evidence of the safety and efficiency of the new product is required as long as the manufacturer can document such evidence for the use of other similar implants already in use (Rolton et al. 2013). A European Conformity (CE) can be awarded by a number of notified bodies in different countries. As a consequence of these regulations, a biomechanical experiment (level 1 evidence) can be the only study preceding clinical introduction of a new implant. This is in great contrast to introduction of new pharmaceuticals that requires level 4 evidence (randomized controlled trials) that might take years to accomplish (Schemitsch et al. 2010, Zywiel et al. 2012). The lack of strict public regulations of clinical introduction of orthopedic devices should put great demands on the design on biomechanical studies set up to evaluate new implants. As of today there is no consensus on how to set up an ideal experiment, and each laboratory has its own preferred method. A natural consequence is that comparisons of published results and evaluation and interpretation of such studies are made difficult.

Due to the lack of proper validation for the use of composite femurs in femoral neck fracture experiments, human cadaver femurs were chosen for the evaluation of the new fixation device. Our laboratory has traditionally used fresh frozen femurs for biomechanical experiments (Aamodt et al. 2001, Ostbyhaug et al. 2010, Wik et al. 2010) and fresh frozen femurs were chosen accordingly. During the course of our study embalmed femurs were shown to provide similar mechanical properties to fresh frozen ones and could have been an alternative (Topp et al. 2012). Our aim was to evaluate the implants for use in old patients with femoral neck fractures that constitute the major bulk of the patients. Femurs from donors over 60 years were included and we specified a particular interest in donors with assumed or known osteoporosis. Sex, height and BW were obtained during autopsy. In addition, measurements of the pelvic width were requested to enable subject-specific adjustments in the hip jig, but this could only be obtained from a few subjects, and the data could not be implemented. For later studies, inclusion of subject specific lever arms should be considered to further optimize the test setups. For the comparative study of composite femurs and cadaver femurs, 4th generation composite femurs from Sawbones were chosen (Sawbones, Pacific Research Laboratories, Inc. Vashon, Wa, USA). This was due to the extensive use of these replicas in biomechanical experiments (Brandt et al. 2006, Roerdink et al. 2009, Alves et al. 2010, Zdero et al. 2010, Eberle et al. 2012, Nowotarski et al. 2012).

Due to current indications for internal fixation of femoral neck fractures, a simple subcapital fracture was created. This fracture simulated the most frequent undisplaced femoral neck fracture found in the elderly population (Klenerman and Marcuson 1970). As a result of this, our results cannot be used to describe the effect of locking plates on displaced femoral neck fractures with varying degree of posterior fracture comminution. In Norway it is common practice to stabilize undisplaced femoral neck fractures with two parallel screws. The locking plate evaluated in our study is designed for fixation with three screws and the plate-screw construct was accordingly tested against three screws. All screws were inserted with the same aiming guide to form an inverted triangle configuration so that the only difference between the two groups was whether the locking plate had been employed or not.

Paired designs are commonly chosen in comparative experiments in order to minimize the effects of femur variation and thereby create comparable test groups. The sample variance is crucial in comparative statistics as increased variance decreases the statistical power. Consequently, a high degree of dependence between subjects used in comparative studies reduces the required sample size. The femoral size, neck-shaft angle, neck-and head version and other geometrical factors show great variation between subjects (Toogood et al. 2009). In addition, the relative distribution of cortical and trabecular bone and bone porosity change with ageing (Mayhew et al. 2005, Zebaze et al. 2010). All these factors influence the biomechanical properties of human femurs and have the potential to affect the outcomes in experimental hip fracture studies. Using a paired study design, left and right femurs from the same donor can be randomly assigned to one of two modes of treatment (Brandt et al. 2006, von der Linden et al. 2006, Krischak et al. 2007, Windolf et al. 2009, Roderer et al. 2010). If paired femurs from the same donor cannot be obtained, or when more than two groups are to be compared, pairing the groups according to BMD seems to be the method of choice (Aminian et al. 2007, Rupprecht et al. 2011a and b). The problem with this method of grouping is that the above mentioned factors, such as anthropometric properties, are not being controlled for. To adjust for this, sample size could be increased, but this does not appear to be done in reality. In our setup we only included pairs of femurs and left and right femur from the same donor were randomly allocated to one of two fixation methods. In study 1 we found an intra-pair correlation of femoral head migration of 0.953, and this demonstrates the importance of comparing two femurs from the same donor.

Both static- and cyclic compressive tests or combined compressive, bending and torsion tests are frequently used methods in biomechanical implant testing of hip fractures. Static compression test has been argued a better option for biomechanical testing of hip fractures due to an expected increased intersubjective variability that might occur during cyclical loading (Selvan et al. 2004). The authors argued that during the simulated time span e.g. 20,000 cycles, fracture healing would have started in vivo. Implanting a telemetrized intramedullary nail after a comminuted femoral diaphyseal fracture in man showed a 50% decline in implant load-bearing after seven weeks. Despite the somewhat non-comparable fracture-situations, it still shows that strengthening of internally fixated bone happens slowly during fracture healing (Schneider et al. 2001). 20,000 cycles simulate the average number of steps during one week in patients who have undergone total hip arthroplasty (Morlock et al. 2001). During the fourth postoperative day, hip fracture patients stand up or walk for approximately 50 minutes (Taraldsen et al. 2014). Even though it must be assumed that that patients with a femoral neck fracture walk considerably less than patients with total hip replacements, we believe that fracture healing, in the sense of considerable bone strengthening, is not likely to have occurred during the first 20,000 steps in mobilized hip fracture patients. In addition, there has been shown great discrepancies on outcome after static and cyclic loading conditions on the same experimental population, and the authors suggest cyclical loading to be the superior method of the two (Benterud et al. 1994).

To simulate the clinical situation with repetitive hip loading, a cyclic loading regimen with a combined axial load and torque was chosen for our study. The femurs were tested under two consecutive loading regimes. First, for 10,000 cycles we used data obtained by Koval and co-workers to calculate a simulated postoperative weight-bearing. They compared loading of the injured leg to the uninjured leg and found an increase from 51% after one week to 87% after 12 weeks (Koval et al. 1998). For the first load-sequence, 80% of full weight-bearing was used to calculate the forces to be applied. For the next 10,000 cycles full weight-bearing was simulated. This strategy of gentle physiologic loading was chosen to avoid provoked differences between the implants that could not be expected to occur in a clinical setting. Unfortunately, due to occurring failures of the operated femurs, results from the last load-regime could only be used for descriptive statistics, and the study could have provided more information if the loading had been kept at a constant.

In our setup the abductor resultant force was simulated by letting a distally attached trochanteric strap be guided over the greater trochanter before proximal attachment to a horizontal lever arm. With shortening of the femoral neck, a patient must try to compensate for the reduced lever arm by increasing the work load of the abducting muscles. Increased muscular work load results in increased hip joint resultant force. If the patient is not able to perform this compensation, a Trendelenburg gait pattern results where the patient is not able to keep the pelvic in horizontal position. In biomechanical femoral neck fracture experiments, an expected gradual shortening of the femoral neck complicates the setup, as the abductor-strap / device must be tightened to keep the horizontal lever arm leveled. To our knowledge, no researchers, including ourselves, have described correcting this error during the course of the test. The result is a “Trendelenburg situation” in the hip-jig for the femurs that experienced major femoral neck shortening.

Up till recently, forces applied to the specimen have been standardized so that all specimens are subject to the same magnitude of force regardless of the weight of the donor, sex etc. The result is that femurs harvested from a 55 kg female donor and femurs harvested from an 85 kg male donor are stressed with the same load during testing. It is likely that this kind of standardization has been a major source of error in preclinical testing. We defined the applied force according to individual BW instead of using standardized Newtonian force as suggested and implemented by Cristofolini’s group (Cristofolini et al. 2009).

Discussion of results

Study I

Here we evaluated the effect of the new locking plate on plastic deformation of the femoral head following cyclic loading and further whether this locking plate appeared to affect the risk of fixation failure. Femoral neck shortening and varus displacement of the femoral head following internal fixation of femoral neck fractures are commonly found in a clinical setting. Neck shortening has been shown to negatively affect the clinical outcome in healed fractures (Zlowodzki et al. 2008, Zielinski et al. 2013). Although our study revealed that interlocking of the three screws significantly reduced the deformation of the proximal femur, the new implant was not able to resist the unwanted femoral neck shortening and varus displacement of the femoral head. The difference between the two implant groups was minor and therefore of questionable clinical relevance. The two femurs of each pair had a correlation of femoral head migration of 0.953 which demonstrates that other factors than choice of implant seem to be more important for this outcome parameter. Although our material was not large enough to make sub-analyses of predisposing factors for plastic deformation, bone composition and bone anthropometry must be assumed to be important. Despite the application of a physiologic posteriorly directed torque the experiment could not reveal a difference in rotational deformation of the head fragment between the two groups.

Seven out of 24 femurs had failed by 20,000 cycles. There were five fractures of which three had involvement of the lateral screw-holes. Lateral screw hole involvement was only observed in femurs fixed with the locking plate indicating increased stress on the lateral cortex compared to individual screw fixation. The last two femurs failed with collapse of the femoral neck and were both from the same donor. All failed femurs were osteoporotic or osteopenic and had been fixed with the smallest sized inverted triangle configuration due to small size of the bone.

Aminian and colleagues compared fixation of vertically oriented femoral neck fractures in cadaver femurs with cannulated screws, a gliding hip screw, a condylar hip screw and a proximal femoral locking plate (n = 8 in all groups) (Aminian et al. 2007). They found that all femurs operated with three cannulated screws failed during incremental loading to 1,400 N. These constructs were considered failures due to a lateral protrusion of the screws of 5 mm and varus displacement of the femoral head. The femurs operated with the proximal femoral locking plate survived both incremental loading and 10,000 cycles of 1,400 N and were found to provide the highest stiffness and failure strength of the tested implants. During load-to-failure testing, these constructs failed with cutting out of the implant through the femoral head. Nowotarski and colleagues also compared four fixation techniques in composite femurs with vertically oriented femoral neck fractures (Nowotarski et al. 2012). They reported that a femoral neck locking plate provided increased rotational rigidity, increased failure load and reduced displacement of the proximal fragment when compared to three screws in an inverted triangle configuration. The authors did not report modes of failure. A clinical series of patients with femoral neck fractures operated with a locking plate resulted in serious failures in nine out of 18 patients (mean age 72 years) (Berkes et al. 2012). The constructs failed with screw breakage in five, penetration of the femoral head in one and pull out of the bicortical diaphysis-screw in one as the proximal fragment displaced in varus. This implant appears to provide rigidity not compatible with the bone strength of the heavily loaded fractured femurs. Another clinical report of a younger patient population (mean age 47 years) did not experience mechanical failures following locking plate fixation (Lin et al. 2012). Although our experiment also revealed an increased resistance to deformation when a locking plate was added, the effect was considerably less in our study compared to the two biomechanical studies by Aminian and Nowotarski. This may be attributable to different fracture morphologies and that the locking plate used in our experiment did not have an attachment to the lateral cortex resulting in a less rigid construct. Our experimental setup also differed from the other two studies as neither of the two studies had simulated the lever arms of the hip, but applied load directly onto the femoral head. The femurs in our experiment failed with fractures down the medial neck and through the lateral screw holes. We did not experience any cases of implant breakage and cut-out of the screws through the femoral head as was reported by Berkes. There are two main reasons that seem most likely to explain this discrepancy. Firstly, our experiment only simulated the first 20,000 steps following surgery and this might be too early to experience mechanical complications like implant breakage and cut-outs. Secondly, the locking plate used in our experiment results in a less rigid fixation allowing for femoral neck shortening and varus collapse as the implant is allowed to back out from the lateral cortex.

Study II

In this study we explored how this new locking plate affected the repetitive micromotions between the fracture fragments during cyclic loading. Subcapital femoral neck fractures are intra-capsular and the fractures must heal without a stabilizing external callus. Nonunions remain a considerable complication following femoral neck fracture treatment (Parker et al. 2007). From animal experiments we know that magnitude of interfragmentary motion is important for the course of fracture healing (Perren 2002, Augat et al. 2005, Claes et al. 2011). Our experiment revealed that micromotions about the femoral neck (z-axis) were significantly reduced in the locking plate group, representing an improved resistance to shear forces. Theoretically these reduced micromotions might improve endosteal healing and sprouting angiogenesis, and also resist femoral neck shortening in vital bone. If this applies to clinical reality must of course be explored in vital bone. We are not aware of other studies that have measured micromotions over a hip fracture and it is therefore not possible to compare our result to published materials. The gentle loading regimen chosen for this experiment resulted in overall small magnitudes of micromotion. However, early mobilization of patients with hip fracture results in impaction at the fracture site, and we believe that the magnitudes observed in our experiment might well reflect the actual micromotions occurring in clinical reality.

Fractured and implanted femurs showed a minimal increase in medial compression of 4.5% and a larger decrease of 21.5% in lateral tension compared to intact proximal femurs. Whether the femur had been operated with individual or interlocked screws did not affect the load distribution in our study. From our results we can conclude that there is a shift in load distribution in the proximal femoral diaphysis following internal fixation with less lateral tension, but since the change on the medial side was only minor, we cannot make a conclusion on the total shift in stress distribution. Unfortunately it was not possible to glue strain gauges on the femoral neck due to the fracture. To compensate for this, the elastic translational and rotational deformations of intact proximal femurs were compared to operated femurs. The results show that the proximal femur increases its resistance to translational deformation whereas resistance to elastic rotational deformations is reduced. In other words, three screws through the femoral neck stiffens the proximal femur on which a fractured, yet fixed femoral head fragment, shows increased elastic rotations when compared to the intact state. There are few publications presenting cortical strain data from femoral neck fracture experiments and such studies have often been performed in order to validate computer models (Eberle et al. 2010, Peleg et al. 2010). Eberle and colleagues measured cortical strain on the proximal femur in intact cadaver specimens and after implantation of a compression hip screw (CHS) with an antirotation screw (n = 6) or a femoral neck plate (FNP) with three partially threaded screws (n = 6) in unfractured femurs (Eberle et al. 2011). They found a shift from tensile strain to a minimal compressive strain pattern on the superior neck in both groups and concluded that these implants now acted as load-bearing devices. The elimination of tensile strains on the superior femoral neck corresponds well with our finding of increased stiffness of the proximal femur. The CHS group showed a 50% reduction in compressive strains at the lesser trochanter. On the contrary, the FNP increased the compressive strains at the same location by 60% and further increased compression on the inferior femoral neck by almost 60%. The authors did not draw any conclusions regarding the reason for the observed differences between the two implant groups. In our experiment the cortical compression on the medial proximal diaphysis was almost unaffected by the implants, but as our strain gauges were positioned distally for the minor trochanter direct comparisons and conclusions could not be made. For later studies more strain gauges must be included for better understanding of the total load distribution and this particularly refers to the anterior and posterior aspects of the proximal diaphysis.

The lack of correlation between the stability of the head fragment and BMD contradicts findings in other reported biomechanical studies (Goldhahn et al. 2008). A possible explanation for this is our application of donor-specific loads exclusively in the physiological range. At present, there seems to be little scientific evidence of a clinical association between BMD and the outcome in operated hip fractures (Goldhahn et al. 2008, Viberg et al. 2014). Either there is no association between bone quality and surgical outcome, or maybe BMD is not a good measure to predict the bone's ability to make a stable osteosynthesis possible. Indeed, a weak or non-existing correlation between observed variation in microstructure and DXA obtained BMD values has been presented (Zebaze et al. 2010). Moreover, it is unlikely that a simple fall would result in a hip fracture in a subject with normal bone quality. Nevertheless, only 50% of hip fracture patients are estimated to have a diagnosis of osteoporosis according to T-score ≤ –2.5 (Oden et al. 2013). The lack of correlation between deteriorated bone and outcomes following femoral neck fractures might be attributable to incomplete methods for describing bone quality.

Study III

The neck-shaft angles and anteversion angles of medium-sized 4GCFs and the cadaver femurs in our study were both in accordance with a large reference material (Toogood et al. 2009). The large-sized 4GCFs fall outside two SDs from the reference population regarding neck-shaft angle, whereas the measured anteversion falls within one SD.

4GCFs showed larger elastic deformations in the upper femur than cadaver femurs despite subject-specific loading in both groups of femurs. Gardner and colleagues (2010) found that 4GCF had 33% lower axial stiffness than reported values for cadaver femurs and our results support this finding.

An unambiguous difference in the stability of operated femurs with femoral neck fractures was found between 4GCFs and cadaver femurs, and this experiment clearly demonstrates the problems arising when using composite femurs in hip fracture experiments. Particularly the cortical replica seems to provide unrealistically high stability to the bone-implant construct under cyclic loading compared to cadaver bone. Whereas the cadaver femurs showed gradual plastic deformations prior to failure, no such sign was observed in the two fractured 4GCFs. These two bones appeared stable until sudden fracture. Also, the transverse fractures in the proximal diaphysis seen in the 4GCFs did not occur in any of the failed cadaver femurs. This finding reflects different material properties of human and synthetic bone, which has also been claimed by other researchers (Gardner et al. 2010). The problem has been previously addressed and attempts have been made to solve the problem (Wahnert et al. 2011). Unfortunately, the complex structure of human bone seems to be difficult to mimic when creating artificial bone models.

This study has obvious limitations. One mode of fixation should ideally been used in all fractured femurs. Inclusion of thirty-four femurs makes this a rather large biomechanical study, however the number of femurs within each group limited the possibility of statistical analyses, and therefore anthropometric measures and failures could only be presented descriptively.

Study IV

High quality preclinical investigation is essential to secure the patient's welfare, and the ability of critical awareness of such studies is essential, also to the orthopedic surgeon. Clinically, failure of internal fixation in femoral neck fractures rarely occur due to excessive axial loading as observed during load-to-failure axial compression tests. Biomechanical experiments should aim at creating physiological setups to reveal possible advantages or disadvantages for the patient and not primarily test the extremes. Loading of 80% BW or less seems to be the most realistic scenario to simulate the fracture healing period (Koval et al. 1998). As previously suggested by others, we agree that dynamic tests are more prone than static tests to recreate failure starting at the implant-bone interface as seen in patients (Benterud et al. 1994).

Increased distance from applied joint force to the fracture surface inversely correlates with failure-load in biomechanical tests for hip fracture implants, and vertical fracture-lines cause unstable fracture situations under axial loading (Stankewich et al. 1996). Stiffer implants, like a sliding hip screw or intramedullary nail, will therefore show superior fixation strength in test setups with lateral fractures, particularly when high fracture angles are created. The choice of experimental fracture may explain why stiffer implants often performs superior in biomechanical femoral neck fracture studies, a finding that has proven difficult to verify clinically (Parker and Stockton 2001, assessed as up-to-date 2010). The experimental fracture should aim at mimic the clinical situation and the vast majority of femoral neck fractures in the elderly are subcapital fractures (Klenerman and Marcuson 1970).

Summary

Today most patients with undisplaced femoral neck fractures are surgically treated with internal fixation. We performed a biomechanical evaluation in human cadaver femurs to evaluate a new locking plate. The new implant was tested against three screws, a conventional treatment method. Our results show that when the locking plate was used, postoperative deformation of the proximal femur was slightly reduced. In addition, the locking plate reduced micromotion about the femoral neck by 25%. The overall risk of failure was the same in both groups, but as opposed to the screw group, the locking plate group had fracture involvement of the lateral screw holes. All failed femurs occurred in osteoporotic or osteopenic subjects (T-score < –1), but we did not find an association of bone mineral density and magnitude of micromotion.

The use of composite femurs in hip fracture experiments increases. In a comparative study between medium and large sized fourth generation composite femurs (4GCFs) and cadaver femurs we found that internal fixation of femoral neck fractures in 4GCFs resulted in significantly more stable osteosynthesis than in cadaver femurs. In addition, cortical tensile and compressive strains were higher in 4GCFs and the anteversion angle and neck–shaft angle of large sized 4GCFs differed from the average human femurs.

A literature study revealed a wide variety of biomechanical setups used when investigating femoral neck fractures. To cover the different aspects related to fixation of femoral neck fractures, some variety is necessary. Unfortunately, the different setups make direct comparison of results and assessment of clinical relevancy difficult. We believe that biomechanical femoral neck fracture experiments would improve and increase their impact if the recreation of the in vivo situation was optimized. Our suggestions on how to optimize femoral neck fracture experiments in terms of clinical relevancy are summarized in this thesis.

Conclusions

Evaluation of a new locking plate

Adding the new locking plate to three screws slightly, but significantly improved the resistance to postoperative deformation of the proximal femur. Qualities of the femur itself were more important for the extent of postoperative deformation than type of implant. The locking plate increased the resistance to shear forces about the femoral neck and there was no association between BMD and the magnitude of micromotions.

All failures occurred in femurs with deteriorated bone that was operated with the smallest sized inverted triangle configuration regardless of choice of implant. The overall risk of failure was not increased, but the locking plate seemed to increase risk of lateral screw hole involvement.

Evaluation of Fourth Generation Composite femurs for use in femoral neck fractures

4GCFs with internally fixed femoral neck fractures provide unrealistically stable bone–implant constructs and further seem to fail with fractures not observed in cadaver femurs. In addition, large–sized 4GCFs have femoral neck versions and neck–shaft angles that considerably deviate from human femurs. We conclude that 4GCFs should not be used for evaluation of hip fracture implants intended for use in old patients.

Suggestions for optimizing biomechanical femoral neck fracture experiments

Cadaver femurs from donors with representative age, gender and bone quality should be included. Dynamic loading should be performed with forces within the physiological range. Experimental fractures should be carefully selected to avoid bias. Preclinical discovery of potential harmful implants should impede clinical use and positive experimental findings should lead to further clinical testing.

Further perspectives

For future ex vivo experiments our test setup can be improved by adjusting the lever–arm from the central actuator to the acetabular cup according to post–mortem measurements of the donor. It can further be optimized by estimating the actual torque based on anteversion angle for each femur. In addition I suggest that the magnitude of load should be kept at a constant for statistical reasons.

Regarding the new locking plate, I suggest a prospective clinical study with high resolution outcome parameters such as migration measured with RSA to be performed. Particularly the reduced micromotion about the femoral neck is interesting from a clinical point of view. Our results indicate increased failure rate when the smallest sized aiming guide had been used, and we do not recommend this particular configuration to be tested in patients.

The effect of deteriorated bone, and microstructural changes in particular, on outcomes after fragility fractures is not well described. To me it seems unlikely that deteriorated bone should have no impact on the stability of various osteosynthesis. This should be explored in future studies.

Maintaining the hip biomechanics, like the femoral offset, is considered important in patients treated with total hip arthroplasty. Little is known about loss of offset in patients with hip fracture and its impact on functional outcome in patients treated with arthroplasty or internal fixation. This would be an interesting subject for new studies.

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