Resorbable Bone Cement for Augmentation of Hip Fracture

PER MATTSSON
Dissertation presented at Uppsala University to be publicly examined in Grönlundsalen, Akademiska sjukhuset, ing. 70, Uppsala, Tuesday, May 31, 2005 at 09:15 for the degree of Doctor of Philosophy (Faculty of Medicine). The examination will be conducted in Swedish.

Abstract

Surgical treatment of hip fractures is frequently associated with secondary fracture displacement, in part due to weak osteoporotic bone. So far, improvements have focused on new metal implants although an alternative could be to augment the bone that surrounds the implant.

The aim of this thesis was to evaluate the use of calcium phosphate cement (Norian SRS) for augmentation of internally fixed hip fractures. Norian SRS is an injectable, biocompatible cement that hardens in situ without exothermic reaction. Over time it is remodeled and replaced by host bone.

In a biomechanical study the holding characteristics for different implants was measured when inserted with or without augmentation. The study showed that conventional bone cement (PMMA) improved maximum torque and pull-out for almost all modalities while Norian SRS increased the holding power mainly in low-density bone.

In a prospective and randomized study, patients with displaced femoral neck fractures were operated with internal fixation using screws alone or combined with Norian SRS for augmentation. The result showed improved stability when measured with radiostereometry (RSA) for the augmented fractures during the early rehabilitation period. The clinical evaluation of 118 patients included pain, walking aid, activities of daily living (ADLs), abductor muscle strength, mobility and range of motion. During the early course the augmented patients did better in some variables although over the total two-year study period there was no major difference between groups. Scintigraphic evaluation indicated that augmentation might compromise the circulation to the femoral head.

The final part included unstable trochanteric fractures fixed with a sliding screw device alone or the same device combined with Norian SRS for augmentation. Using RSA it was shown that augmentation significantly improved the fracture stability until healing. In a randomized multicenter study including 112 patients, augmentation with Norian SRS reduced pain during early rehabilitation and improved quality of life until healing.

In conclusion, augmentation with Norian SRS improved the early fracture stability in displaced femoral neck fractures while there was no major difference in clinical outcome. In unstable trochanteric fractures augmentation provided improved fracture stability and improved clinical course until healing.

Per Mattsson, Department of Surgical Sciences, Akademiska sjukhuset, Uppsala University, SE-75185 Uppsala, Sweden

© Per Mattsson 2005

ISSN 1651-6206
ISBN 91-554-6271-5
urn:nbn:se:uu:diva-5822 (http://urn.kb.se/resolve?urn=urn:nbn:se:uu:diva-5822)
List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals:


Contents

Introduction and background ................................................................. 9
Classification of fractures ................................................................. 12
   Femoral neck fractures ............................................................... 12
   Intertrochanteric hip fractures ..................................................... 12
Epidemiology .................................................................................... 14
Treatment alternatives ...................................................................... 15
   Femoral neck fractures ............................................................... 15
      Internal fixation ................................................................. 15
      Hemiarthroplasty ............................................................... 16
      Total hip arthroplasty ......................................................... 16
   Intertrochanteric fractures ......................................................... 17
Roentgen Stereophotogrammetric Analysis ....................................... 18
Scintigraphy .................................................................................... 19
Statistical methods .......................................................................... 21
Aims of the study ............................................................................ 22
Patients ......................................................................................... 23
Summary of papers .......................................................................... 24
   I. The effect of augmentation with resorbable or conventional bone cement on holding power for femoral neck fracture devices .................. 24
   II. Stability of internally fixed femoral neck fractures augmented with resorbable cement ............................................................... 25
   III. Calcium phosphate cement for augmentation did not improve results following internal fixation of displaced femoral neck fractures ............ 26
   IV. Augmentation of femoral neck fractures with calcium phosphate cement .................................................................................. 26
   V. Unstable trochanteric fractures augmented with calcium phosphate cement ............................................................................. 28
   VI. Resorbable cement for augmentation of internally fixed unstable trochanteric fractures. A prospective randomised multicenter study .... 28
Abbreviations and Definitions

Femoral neck fracture: Intracapsular fracture through the femoral neck or at the junction of the femoral head, not involving the articular surface of the femoral head.

Unstable intertrochanteric fracture: 3- or 4 fragment fracture without posterolateral-or medial support.

Norian SRS (Skeletal Repair System): Synthetic bone cement (calcium-phosphate) that over time will resorb and mediate new bone formation.

PMMA: Polymethyl-methacrylate (bone cement)

RSA (Radio Stereometric Analyses): A technique to obtain 3D measurement with high accuracy from radiographs.

Late segmental collapse: Late complication following avascular necrosis of the femoral head (AVN) after healing of an intracapsular fracture with localized or general deformity of weight bearing portion of femoral head at radiographic examination.

Non-union: Redisplacement or still visible fracture line at radiographic examination 6 months after the injury.
Introduction and background

Cooper was one of the first to divide hip fractures into intra- and extracapsular fracture types, based on the differences in prognosis (Cooper 1823). One of the first open reductions and internal fixations of a hip fracture was in 1878 by Langenbeck (Langenbeck 1878). Non-surgical treatment with body cast remained the treatment of choice the following 50 years because of high complication rate following open surgery, especially infections.

Smith-Peterson developed the three-flanged nail in 1931 and here the new modern era of femoral neck fracture treatment began. Numerous reports have described different methods of fixation. More than 60 different devices for fixation of femoral neck fractures had already been developed in 1974 (Tronzo 1974). In Sweden the von-Bahr, Hook-pin and Uppsala-screw fixation methods were introduced during the last decades, and the last two techniques are still the most widely used (Bahr. et al. 1974, Hansson 1982, Rehnberg et al. 1989).

Stromqvist reported that the choice of operative procedure may have an effect on the postoperative blood supply to the femoral head (Stromqvist 1983). Intracapsular tamponade may contribute to the development of segmental collapse in some patients with nondisplaced fracture (Holmberg and Dalen 1987, Stromqvist et al. 1988). Other factors that influence the circulation are hip position, hip traction and aspiration of hemarthrosis from the joint space (Maruenda et al. 1997). Although the intracapsular pressure does not change when blood is aspirated from the joint, the intraosseous pressure does and the pulse pressure increases within the femoral head (Harper et al. 1991). It is known that interruption of the arteriolar blood flow to the femoral head afflicted after displaced fracture disturbs healing (Mussbichler 1970, Calandruccio and Anderson 1980, Holmberg and Thorngren 1984).

Despite the development of all these fixation technique and knowledge of related complications in femoral neck fracture, the results reported today are almost the same as those reported 50 years ago, with a 20 – 40 % non-union rate and late segmental collapse. These depressing results, in the face of an increasing number of femoral neck fractures, have led to a revived interest.

Femoral neck fracture is a great orthopedic challenge and its treatment has long been under debate in the literature. Women begin to lose bone mass after menopause at a rate of 1-2 % per year, eventually leading to levels where minor trauma may cause a fracture. Even men develop osteoporosis but bone loss is less and men are older when they reach levels of osteoporo-
sis similar woman. Most hip fractures result from low energy trauma (Nyberg et al. 1996) less than 1 % being caused by high-energy trauma (Hedlund 1985).

Intertrochanteric fractures, especially those with several fragments, present a mechanical challenge while healing usually is no problem because the circulatory disturbance is minimal as the fracture is located outside the capsule. Several methods and techniques have been described to overcome the mechanical problems, such as rigid devices (Wilson et al. 1980) medial displacement reduction and valgus positioning (Aufranc 1967, Sarmiento and Williams 1970) and valgus osteotomy (Sarmiento 1973). By using dynamic devices that will allow secondary fracture impaction the reoperation rate in unstable trochanteric fractures has been reduced to 10% or less (Kyle et al. 1979, Larsson et al. 1990, Chinoy and Parker 1999). The advantage of intramedullary fixation is still a matter of debate. Nuber et al. show good results for short intramedullary nails when comparing DHS/PFN (Nuber et al. 2003) but Saudan et al. could not find any difference between the two devices (Saudan et al. 2002). A meta-analysis of 17 trials did not find any differences between dynamic screw-plate and dynamic screw-intramedullary nail (Audige et al. 2003).

A useful alternative to conventional plates is external fixation, especially in patients with aggravated general condition and a high ASA score (3-4). This type of device was associated with less blood loss, shorter operating time, shorter hospitalization and earlier mobilization (Kourtzis et al. 2001, Vossinakis and Badras 2002).

For both femoral neck fractures and unstable intertrochanteric fractures reduced bone strength due to osteoporosis strongly contributes to the mechanical problems associated with complications after internal fixation (Alho et al. 1988, Obrant et al. 1989, Sjostedt et al. 1994).

One of the main problems when stabilizing a fragile fracture is the weak osteoporotic bone itself, it seems attractive to reinforce the bone surrounding the hardware in order to increase the load capacity instead of developing new conventional metal implants. Previous attempts to use polymethylmethacrylate (PMMA) cement for structural augmentation of unstable intertrochanteric fractures have given rather good results although the technique has never gained wide acceptance (Harrington 1975, Schatzker et al. 1978, Muhr et al. 1979, Lau et al. 1983). This is probably due to drawbacks of PMMA including the risk for inducing thermal necrosis, healing disturbances due to interposition of cement at the fracture and difficulties in removing the cement if revision surgery becomes necessary (Apel et al. 1989) (Choueka et al. 1996). In recent years new cement types designated for fracture augmentation have been introduced that are susceptible to remodelling and replacement by host bone. The concept has been to use the cement for fixation of fractures to improve stability and to achieve a better clinical outcome (Witschger et al. 1991, Claes et al. 1995, Constantz et al. 1995, Bohner...
2000, Eshbach 2000, Dimaio 2002, Delloy et al. 2003). Out of the different degradable cement types available, Norian SRS (Skeletal Repair System), a calcium phosphate cement is the most widely documented (Constantz et al. 1995) (Clark and Ribbans 1990, Kopylov et al. 1996, Stankewich et al. 1996, Moore et al. 1997, Goodman et al. 1998, Yetkinler et al. 1999) (Kopylov P 2001a, Kopylov P 2001b). This cement is injectable, biocompatible, nonexothermic, hardens in situ and is replaced by host bone over time. Following injection an osteoconductive carbonated apatite is formed with chemical and physical characteristics similar to the mineral phase of bone. The cement has a compressive strength of 55 MPa, i.e. higher compressive strength than normal cancellous bone. During preclinical studies it has been shown that the calcium-phosphate cement is osteoconductive and undergoes gradual remodeling over time in a pattern similar to the remodeling of normal bone (Frankenburg et al. 1998). The experience with retrievals and biopsies from clinical cases is still very limited. From pilot studies (Goodman et al. 1998, Larsson et al. 1999, Schildhauer et al. 2000, Larsson and Bauer 2002) some of the patients treated for a displaced femoral neck fracture developed non-union or avascular necrosis and were therefore reoperated with a total hip arthroplasty. The patients’ femoral heads were retrieved and processed for histological analysis with special reference to the extent of remodeling and the resorption of calcium phosphate. The location of both fixation screws and the intervening hole through which resorbable cement was injected into the fracture void were easily visualized. Much of the resorbable cement showed extensive bone apposition, and areas of resorbable cement around one of the screws had clearly been resorbed and replaced by bone. Some of the resorbable cement from the injection hole also showed extensive bone apposition and evidence of vascular ingrowth and remodeling. In another case, a patient underwent total hip arthroplasty 20 months after fixation of a femoral neck fracture with internal fixation and cement augmentation. Although this specimen also showed a few areas of resorbable cement fragmentation, other areas showed extensive bone apposition with evidence of cell-mediated remodeling, including developing Haversian systems (Larsson et al. 1999).
Classification of fractures

Femoral neck fractures

The Garden classification system is one of the most widely used for femoral neck fractures (Garden 1961). Originally, the system was based only on anteroposterior radiographs while in a later version usage of the lateral view was added. This classification system has been criticized for large inter-observer variation, although less pronounced between stages I-II and III-IV (Frandsen et al. 1988). It has been shown that a simple differentiation into two groups has a better prognostic value than the original classification using four groups (Frandsen et al. 1988, Eliasson et al. 1989, Hernefalk and Messner 1996, Hernefalk et al. 1997). The AO/ASIF classification system has been criticized for being too complicated and of limited predictive value for treatment outcome (Blundell C M 1998). It was found that the most reliable subdivisions seem to be undisplaced, displaced and basal fractures. In the present thesis the Garden classification has been used.

Intertrochanteric hip fractures

Several topographic classification systems have appeared together with the anatomical classification of trochanteric fracture. Evans described a system where trochanteric fractures were divided into 5 subgroups that were summarized into two major groups, i.e. stable fractures (type 1a-b) and unstable fractures (type 1c-d and type 2) (Evans 1949). Other systems have classified fractures as either displaced or undisplaced or depending on whether medial comminution is present or not. After comparing five of the most commonly used classification systems, Jensen concluded that the modified Evans’ system was superior to the other systems in predicting the risk of fracture redislocation and subsequent technical complications (Jensen 1980).

Nowadays, the commonest classification is probably the system introduced by the AO/ASIF group (Müller 1990). This classification is organized into hierarchical triads. For every bone segment, three “types” of possible fractures exist (A,B,C) each of which can be divided into 3 “groups”. The 3 groups are each divided into “subgroups” according to increasing fracture
severity, indicating a greater difficulty in operative treatment, a higher like-
lihood of complications, and a poorer prognosis.

Both Jensen’s, modified Evans’ and AO/ASIF have been used for classi-
fication in this thesis.
Epidemiology

Fractures through the proximal femur are frequent and often a devastating event for the elderly. Today approximately 90% of hip fracture patients are 65 years or older. In Sweden more than 18,000 hip fractures occur annually (Thorngren 1994). In the United States this number is more than 300,000 (Hudson et al. 1998) and is expected to double by 2050 (Koval and Zucker-man 1994) (Montgomery and Lawson 1978). The dramatic ongoing demographic change, with an unprecedented increase in the number of old and very old people, may to a great extent explain the increasing number of hip fractures over the last decades. In a study from 1964 the patients’ mean age was 70 years (Alffram 1964). In the eighties it was almost 10 years higher (Hedlund 1985) (Bacon W E 1996).

When comparing the incidence of the two major types of hip fractures, i.e. intertrochanteric vs. femoral neck fractures, the former have increased more than the latter during the last 50 years and now represent about 50% of all hip fractures. We may now be seeing a break in this trend; a study from Malmo, Sweden showed that in 1992-95 the incidence was 297 per 10,000 inhabitants compared to 351 ten years earlier, although men aged 50 or more with intertrochanteric fracture are still an increasing group (Rogmark C 1999). The changes could be explained by successful osteoporosis prevention, an increasing proportion of non-Scandinavian immigrants with lower genetic risk of osteoporotic fractures, or a healthier elderly population. Another cause may be fewer prescriptions of sedatives.
Treatment alternatives

Femoral neck fractures

Internal fixation

In Sweden many patients with a displaced cervical hip fracture are treated with closed reduction and internal fixation with screws or pins. The advantages of internal fixation compared to total hip replacement include low implant cost, shorter hospital stay (in the absence of complications), shorter time in surgery and less blood loss. Disadvantages are the frequent local complications, mainly non-union and late segmental collapse with consequent osteonecrosis. Breakage of the osteosynthesis hardware is rare; migration of the fixation material during or after healing is more common. Infections or other general complications are not specific for femoral neck fracture.

Non-union is present when all reparative processes have ceased and bone quality has not been restored at the fracture site. Poor fracture stability, diastasis between the fragments and maladaptation may all contribute to the development of non-union. Radiographic examination often demonstrates sclerosis of the fracture ends and bone atrophy. On scintigraphy, reduced uptake at the fracture site, in contrary to a healing fracture where the radionuclide uptake is increased, characterizes a non-union. This complication is evident after about 6 months (Meyer 1985) and occurs in about 33% of the displaced fractures (Lu-Yao et al. 1994), while non-union is not as common in undisplaced fractures. Non-union accounts for two-thirds of all injury-site related complications following displaced femoral neck fractures. 70-85 % of these patients require reoperation due to persistent pain (Rodriguez et al. 1987) (Stromqvist et al. 1992). The incidence of non-union may be reduced by an optimal fixation technique (Stromqvist et al. 1992).

Late segmental collapse of the femoral head has been most commonly classified according to the system of Ficat (Ficat 1985). Many authors have recommended treatment on the basis of symptoms and the Ficat classification (Table 1) as determined by the use of plain radiographs (Aaron et al. 1989) (Scher and Jakim 1993) (Smith et al. 1995). Osteonecrosis is the result of ischemia due to injury of the major arteries supplying the femoral head during the initial trauma. Osteonecrosis is established when bone cell death has occurred, which happens within 24-48 hours after ischemia (Glimcher
and Kenzora 1979), and becomes evident several months after the fracture is healed. This condition occurs in about 16% of all displaced femoral neck fractures with relative consistency (Lu-Yao et al. 1994), but is uncommon after undisplaced fractures. Traumatic surgical technique may lead to damage of intraosseous vessels, but improper treatment with malreduction also increases the risk of osteonecrosis (Stromqvist et al. 1983b). It is noteworthy that the radiographic presence of late segmental collapse does not necessarily imply that patients suffer from pain. In contrast to non-union this condition requires reoperation with arthroplasty in about 30% of patients (Nilsson et al. 1989), (Stromqvist et al. 1992).

Although undisplaced fractures, where internal fixation is the recommended treatment, are less fraught with complications than displaced fractures, a recent study showed that the non union rate was 6.4% and the AVN rate was 4.0 % (Conn and Parker 2004).

**Hemiarthroplasty**

The original hemiarthroplasty consists of an uncemented stem with a unipolar head that fits into a preserved acetabulum. D’Arcy and Devas recommended the cemented Thompson prosthesis in 1976 (D´Arcy 1976). There is clear evidence that cemented hemi-arthroplasties give better results than uncemented ones (Khan 2002). Disadvantages include dislocation, deep infection, loosening and acetabular erosion, while the advantages encompass less need of secondary surgery and lower risk of dislocation when compared with total hip arthroplasty.

**Total hip arthroplasty**

There is a discussion in the literature as to the indication for osteosynthesis or primary arthroplasty among different patient populations, where selection criteria differ widely according to age, health, independence and life expectancy. Arthroplasty is recommended in patients with osteoarthritis, rheumatoid arthritis, pathological fractures, long treatment delay and cases with a very small head fragment. Arthroplasty is associated with complications such as dislocation, infection and implant migration. Higher costs are generated by longer procedure time and by the implant itself.

Many randomized studies have compared internal fixation and primary arthroplasty. The authors recommend arthroplasty for patients over 70 years of age with normal mental status and high functional demands (Skinner et al. 1989, Johansson 2000, Neander 2000, Rogmark et al. 2002, Bhandari et al. 2003, Tidermark et al. 2004)
Intertrochanteric fractures

Today there are four types of implant for the treatment of intertrochanteric fractures: sliding screws, intramedullary nails, sliding screws with a sliding plate and external fixator, although the latter is seldom used.

Sliding screws solved many mechanical problems when they were introduced as a treatment alternative. The implant allowed greater compression and relatively low implant cost. Disadvantages, such as cut out of the femoral head and slower post-operative restoration compared to intramedullary nails, have been reported (Pajarinen et al. 2005). The advantage of intramedullary fixation is still a matter of debate. Nuber et al. show good results for PFN when compared to DHS/PFN (Nuber et al. 2003), but Saudan et al. could not find any difference between the two devices (Saudan et al. 2002). Comparison of intramedullary nail to sliding screws with a sliding plate (Medoff) demonstrated no differences in ADL, hip function or health score except in subtrochanteric fracture were there were more failures in the group with sliding screws (Miedel et al. 2005) (Engstrom et al. 2003).

A meta-analysis of 17 trials did not find any differences between dynamic screw-plate and dynamic screw-intramedullary nail (Audige et al. 2003, Parker and Handoll 2004). An external fixator was useful in patients with aggravated general condition and a high ASA score (3-4). This type of device was associated with less blood loss, shorter time in surgery, shorter hospitalization and earlier mobilization. As for all external fixators, drawbacks include pin infections, loss of reduction, additional surgery for removal and device-related discomfort for the patient (Vossinakis and Badras 2002).

As mentioned previously, 2-part stable fractures seldom present any problems, while the 3- and 4- fragment fractures with posteromedial defect, which often include the minor trochanter fragment, show a significantly higher redisplacement rate of about 10% (Kyle et al. 1979). An increasing incidence of these fracture has been observed (Zetterberg and Andersson 1982) (Frandsen and Kruse 1983), which may be explained by an older population and a higher rate of osteoporosis.

Controlled, prospective and randomized studies established the benefits of antibiotic prophylaxis when fixation devices are inserted (Tengve and Kjellander 1978). Antibiotic prophylaxis in intertrochanteric fracture surgery is now routinely used in most hospitals and has contributed to reduction of postoperative infections to as little as 0-2%, compared with 16% in the 1970’s (Tengve and Kjellander 1978) (Hedstrom et al. 1987). A stable osteosynthesis is mostly obtained nowadays using implants, which allow early mobilization and promote healing of the fracture. Hardware breakage is an exceptional complication and when it appears it commonly depends on non-union (Alvarez et al. 2004).
Roentgen Stereophotogrammetric Analysis

Radiostereometric Analysis, RSA, is a highly accurate radiological technique that allows a precise description of linear as well as rotatory (i.e. three dimensional) fracture movements (Selvik 1989). High resolution methods are crucial for documenting the stability of new implants or techniques. RSA can achieve a resolution that is 5-50 times better than conventional radiography. More complex analyses of implant motion are also of interest to obtain a better understanding of any failure mechanisms. Today, RSA is the only method that can be used to evaluate these motions with sufficient accuracy in vivo. The method originates from Hallert and Hollender, who reported on a development in analytical photogrammetry (Hallert 1970). G. Selvik, a student of Hallert, developed a more sophisticated system that has been applied to many fields in orthopedics surgery (Karrholm 1989). During the last decade further development and improvements of the mathematics and applicability of the method have been made (Nyström 1990, Söderkvist 1993, Börlin 1997).

Two x-ray tubes placed perpendicular to each other were used to obtain simultaneous exposures. Film-to-focus was about 100-cm. Exact positioning of the x-ry tubes was not critical, since the three-dimensional coordinates of each x-ray tube were calculated at each examination. Radiographs were obtained with the patient supine and the hip of interest above a calibration cage of Plexiglas (uniplanar type), which was equipped with tantalum markers with known positions in all four walls. The two-dimensional position of the cage and the patient’s markers is recorded on a digitizing table and fed into a computer. The position of the cage image is used to reconstruct the laboratory co-ordinate system and the position of the two roentgen foci. This information is used to compute the three dimensional co-ordinates of the patient’s markers, based on their location on the radiographs. The computer chooses the most probable coupling between markers on the two radiographs. All markers in the same segment (caput femoris or femoral stem) are modeled as rigid bodies.

When two examinations have been computed, the true motions of these rigid bodies can be calculated. The motions of the chosen reference segment are used to mathematically "reposition" this segment to its original position at the postoperative examination. The other segments are subjected to the same motions, which enables calculations of the relative rotation and transla-
tions between the two examinations. These data are used to describe the migration of the fracture.

To ensure the femoral head translation was recorded at standardized positions, a central point in the femoral head was plotted on the radiographs of the first examination and was transformed to all subsequent examinations using the three-dimensional rigid body defined by the tantalum markers in the femoral head. This procedure allows for comparison between the patients. The tantalum balls in the trochanteric region were used as a fixed reference segment.

In most cases, double exposures in slightly different positions of the hip were done postoperatively.

The precision of the measurements was calculated in the separate studies as the mean difference between two double investigations ± 2.7 S.D. (99% confidence limits) based on a normal distribution (Mjoberg 1986).
Scintigraphy

Radiographic signs of healing complications are mainly secondary to vascular or metabolic disturbances, and therefore appear late in the course of healing. This has initiated the search for a method of determining femoral head vitality at an early stage. Scintimetric uptake as a measure of femoral head vitality after femoral neck fracture has become an accepted technique (Stromqvist 1983).

The investigation is performed by injecting $^{99m}$Tc-HDP (hydroxy-methylene-diphosphonate). After the injection, static (= planar) anterior and posterior registration was obtained with a gamma camera.

Tomographic registration is performed immediately after the static registration. Reconstruction and evaluation of tomographic and planar images is done on a Hermes workstation. The reconstructions are performed with an iterative technique followed by 3D filtering.

Tomographic investigations reveal any differences in blood flow to the femoral head that could not be detected on the ordinary plain image. Evaluation of planar images: Regions of interest (ROI) are selected over the head of femur and in the soft tissue lateral of femur head (background) bilaterally. Uptake ratios (fractured femur head/intact femur head) are calculated in 4 different ways: uptake in the anterior image or geometric mean uptake from anterior and posterior images, with and without background correction.

Evaluation of tomographic images: In a coronal view a volume of interest (VOI) 17*26*17 mm in the x, y and z planes, respectively, are visually selected over the center of the femoral heads. Uptake ratios are calculated as the mean counts in the VOI’s in the fractured femoral head/intact femoral head.
Statistical methods

Paper I: Analysis of variance (ANOVA) was used to determine if synthetic bone density, augmentation or implant type had an effect on the response. If a significant effect was noted, the differences were evaluated with the Fisher PLSD post-hoc test.

Paper II: The Mann-Whitney non-parametric test was used to compare the groups.

Paper III: Based on the assumption of a reoperation rate of 15% and 30% for the two treatment groups, respectively, a power analysis estimated a need for 56 subjects in each group to detect a significant difference with a power of 0.8. Unpaired Student’s t test was used to detect differences in means between groups while Chi square and Fischer’s exact test were used to study proportions.

Paper IV: The unpaired Student’s t test was used for comparison of means between the groups. Chi square test and Fischer’s exact test were used to study proportions.

Paper V: The Mann-Whitney non-parametric test was used to compare groups.

Paper VI: To test the null hypothesis of ‘no difference’ between the two groups for continuous outcomes, generalized linear models (GLM) analysis was employed. Chi square was used for cell frequencies greater than or equal to 5.0, and Fischer’s exact test for 2 x 2 and for non-ordered 2 x r when cell frequencies were less than 5. For ordered 2 x r contingency tables, asymptotic Mantel Haentzel Chi square was utilized for frequencies greater than or equal to 5.0 and the exact Mantel Haentzel Chi square test when frequencies were less than 5.
Aims of the study

The overall aim of the study was to evaluate the outcome when treating patients for hip fractures with calcium phosphate cement augmentation. The evaluation included biomechanical, clinical, radiological, circulatory and functional outcomes.

The specific aims of the study were:

- To compare maximal extraction torque and pull out load for femoral neck fracture implants inserted with standard technique or after augmentation with polymethylmetacrylate (PMMA) or calcium phosphate cement (Norian SRS).
- To measure the stability of femoral neck fractures with radiostereometric analysis during the early rehabilitation period when fixed with either cannulated screws alone or with screws and calcium phosphate (Norian SRS) for augmentation.
- To compare clinical and functional outcome following femoral neck fractures when using conventional cannulated screws with or without calcium phosphate cement (Norian SRS) for augmentation.
- To evaluate if injection of calcium phosphate (Norian SRS) in femoral neck fractures might compromise the vascularity to the femoral head.
- To measure by radiostereometric analysis the stability of unstable trochanteric fractures when fixed with a sliding screw plate system alone or with calcium phosphate cement (Norian SRS) for augmentation.
- To compare the clinical, functional and radiographic outcome of unstable intertrochanteric fractures when internally fixed with a sliding screw plate system alone or with calcium phosphate cement (Norian SRS) for augmentation.
Patients

### Femoral neck fracture

<table>
<thead>
<tr>
<th>Paper</th>
<th>Description</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>II</td>
<td>40 patients with femoral neck fracture 28 patients from paper IV and 12 from paper III Design: Prospective, randomised.</td>
<td>40</td>
</tr>
<tr>
<td>III</td>
<td>118 patients with femoral neck fracture Design: Prospective, randomised.</td>
<td>118</td>
</tr>
<tr>
<td>IV</td>
<td>94 patients with femoral neck fracture 28 patients from paper II and 90 from paper III Design: Prospective, randomised.</td>
<td>94</td>
</tr>
</tbody>
</table>

### Intertrochanteric fracture

<table>
<thead>
<tr>
<th>Paper</th>
<th>Description</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>V</td>
<td>26 patients with intertrochanteric fracture All patients also included in paper VI Design: Prospective, randomised.</td>
<td>26</td>
</tr>
<tr>
<td>VI</td>
<td>112 patients with intertrochanteric fracture Design: Prospective, multicenter, randomised.</td>
<td>112</td>
</tr>
</tbody>
</table>
Summary of papers

I. The effect of augmentation with resorbable or conventional bone cement on holding power for femoral neck fracture devices.

Background: This is a biomechanical study comparing maximum extraction torque and pull out load for femoral neck fracture implants inserted with standard technique or after augmentation with polymethylmetacrylate (PMMA)/(Palacos) or calcium phosphate cement (Norian SRS).

Method: Implants were inserted in foam blocks with three different densities for simulation of normal bone or slight or severe osteoporosis. Tested implants included three screws (AO, Olmed, Hansson), one screw with both threads and a barb (Hybrid), and one pin with a hook (LIH hook-pin). Implants were inserted by standard technique and after augmentation with PMMA or calcium phosphate cement. Testing was done using a servohydraulic testing machine (Mini-Bionix 858, MTS, MN, USA). The cubes with the implant inserted were placed in a specially designed fixture attached to the load cell. The fixture had the same inner size as the cubes with the center along the vertical axis of the testing machine while the free end of the implant was attached by a hydraulic grip to the testing machine. The same fixture was used for both torsion and pull-out. During torsion the cube could move along the vertical axis while, during pull-out, a strong metal lid with a hole in the center to allow passage of the implant was fixed by multiple screws to the top of the fixture.

Main Outcome Measurement: The effect of 1) Density of the synthetic bone (low, medium, high), 2) Augmentation (none, PMMA, SRS), and 3) Type of implant (AO, Olmed, Hansson, Hybrid, LIH) on the maximum extraction torque and pull out load was determined using a material testing machine. ANOVA with Fisher’s PLSD post-hoc test was used to determine statistical differences.

Results: PMMA significantly increased maximum torque and pull out load for all implants and block densities when compared without cement (p<0.0001) while enhancement with SRS was far less pronounced and most obvious in low density blocks. For screws normally inserted without predrilling (Olmed and Hansson) the use of SRS in high density blocks caused a significant reduction in maximum torque (p<0.0001) and pull out load.
SRS augmented specimens failed through the cement at the periphery of the threads while PMMA augmented specimens failed between the cement and the synthetic bone.

Conclusion: This study suggests that augmentation with PMMA around femoral neck fracture implants will increase the holding power significantly when compared to standard insertion technique as well as augmentation with calcium phosphate cement. Augmentation with calcium phosphate cement such SRS will increase the holding characteristics mainly in low density bone while in high density bone it might even reduce the maximum torque due to the need for predrilling when using the cement for augmentation.

II. Stability of internally fixed femoral neck fractures augmented with resorbable cement.

Background: Internal fixation of displaced femoral neck fractures is associated with a high risk of complications such as non-union or avascular necrosis. A stable fracture fixation can improve prognosis although stability is often counteracted by weak osteoporotic bone. The aim of this study was to evaluate whether augmentation with resorbable calcium phosphate cement could improve fracture stability during the early postoperative period as shown in biomechanical studies.

Patients and methods: 40 ambulatory patients with a displaced femoral neck fracture were randomised to treatment with cannulated screws alone (controls) or screws combined with calcium phosphate cement for augmentation (augmented). All patients were allowed unrestricted weight bearing after surgery. Fracture movement was measured with radiostereometry (RSA) at 1 and 6 weeks.

Results: At 1 week the augmented fractures had moved on average of 1.9±1.0 mm while movement in the controls was 5.5±3.4 mm (p<0.0001). The average total movement at 6 weeks was 6.9±2.9 mm and 10.9±5.1 mm, respectively (p<0.005). Varus angulation and distal migration of the femoral head were the most common movements for both groups although augmented fractures had moved significantly less at both 1 and 6 weeks. There were no significant differences in angulation between groups around the longitudinal and transversal axes or in migration along the transverse or sagittal axes.

Conclusion: Augmentation with calcium phosphate cement improved the stability of internally fixed femoral neck fractures during the first six weeks after surgery, with improvement being less pronounced at six weeks compared to one week.
III. Calcium phosphate cement for augmentation did not improve results following internal fixation of displaced femoral neck fractures.

A prospective randomized study in 118 patients.

Background: Does augmentation with calcium phosphate cement improve clinical and functional outcome following internal fixation of displaced femoral neck fractures?

Patients and Methods: 118 patients (95 women and 23 men, age 60-98 years) were included. All patients were physically active and ambulatory before the fracture. Patients were randomized to treatment with closed reduction and fixation with two cannulated screws alone (Controls) or screws combined with injection of calcium phosphate for augmentation around the screw threads and at the fracture site (Augmented). There were 58 patients in the augmented group and 60 controls. All patients were allowed free weight bearing. Clinical and radiographic examinations were done by a physiotherapist immediately after surgery, at 1 and 6 weeks and 6, 12 and 24 months.

Results: 24 patients, 14 augmented and 10 controls, died during the follow-up. There was 1 deep infection (Augmented). Another 34 patients were reoperated with a total arthroplasty (20 in the Augmented group and 14 Controls) due to loss of reduction, non-union or avascular necrosis (p<0.12). There was no difference in pain or muscle strength between groups. Some ADL parameters were slightly better in the augmented patients during the first weeks while no differences between groups were seen later on.

Conclusion: Due to a trend towards more reoperations in the augmented group, and only a temporary clinical improvement during early rehabilitation, augmentation as used in the present study cannot be recommended.

IV. Augmentation of femoral neck fractures with calcium phosphate cement.

Randomized scintimetric study of femoral head viability in 94 patients.

Background: Augmentation with cement of internally fixed femoral neck fractures might improve stability although there is a potential risk of impairment of the circulation to the femoral head. The purpose was to evaluate if filling of the fracture void with cement might compromise the blood circulation to the femoral head.

Patients and Methods: At a mean of 7 days (range 6-8 days) after surgery a 99mTc labeled hydroxy-methylene-diphosphonate scintigraphy scan was done to evaluate the blood flow in the femoral head. 600 MBA 99mTc-HDP
(hydroxy-methylene-diphosphonate) (Mallinckrodt Medical B.V., Petten, Holland) was injected intravenously. Static anterior and posterior gamma camera registrations were obtained 5 hours after the injection with a double head gamma camera (Maxxus, General Electric, Milwaukee, WI, USA) equipped with a low energy high resolution collimator. The acquisition was performed in a 256*256 matrix with an acquisition time of 10 minutes. In a subgroup that consisted of 18 patients a tomographic examination was performed to evaluate smaller parts of the femoral head and also for evaluation of any shadow effects from the cement. The tomographic registration (360°, 64 angles of 50 sec in 64*64 matrix) was performed immediately after the static registration. Reconstruction and evaluation of tomographic and planar images were done on a Hermes workstation (Nuclear Diagnostics AB, Stockholm, Sweden), applying an iterative technique (HOSEM, 8 subsets, 4 iterations) and subsequent 3D filtering (Butterworth, cut of 1.2 cycles/cm, order 10). For tomographic evaluation a volume of interest (VOI) of 2*3*2 pixels (17*26*17 mm in the x, y and z planes, respectively) was selected in the coronal view over the center of each of the femoral heads. Uptake ratios were calculated as the mean counts in the VOI’s on the fractured side/non-fractured side. The tomographic examinations of the cement-augmented fractures were focused in an area in the femoral head that was free from cement based on the conventional radiographs. For planar evaluation regions of interest (ROI) were selected over each of the two femoral heads and in the soft tissue lateral to the femoral head (background) bilaterally (Figure 1). Uptake ratios (fractured side/non-fractured side) were calculated in 2 different ways as uptake in the anterior image or as geometric mean uptake from anterior and posterior images (=√anterior · posterior). Plain radiographs were used to assess redisplacement, non-union or avascular necrosis of the femoral head over the first two years after surgery.

Results: The femoral head uptake was lower in the cement-augmented group compared with controls (p<0.007). Radiological non-union or AVN was more common in the augmented group compared with controls (p < 0.0007). The number of reoperations due to non-union and AVN was also more common in the augmented group (p = 0.034) while reoperations due to redislocation were less common in the augmented group compared with controls (p = 0.028). In the augmented group there was no significant difference in scintigraphic uptake between patients who were reoperated or not (p=0.74) while in the control group patients who were reoperated had a significantly lower femoral head uptake compared with those who were not reoperated (p<0.01).

Conclusion: We conclude that augmentation of femoral neck fractures with cement injection cannot be recommended as it may compromise the circulation to the femoral head and increase the risk of subsequent healing complications.
V. Unstable trochanteric fractures augmented with calcium phosphate cement.

A prospective randomized study using radiostereometry to measure fracture stability.

Background: Internally fixed unstable trochanteric fractures may be difficult to retain in position during healing. Secondary displacement can lead to malunion and poor functional result. The aim of this study was to measure whether augmentation with resorbable calcium phosphate cement improves fracture stability as has been shown in biomechanical studies.

Patients and Methods: 26 ambulatory patients with an unstable trochanteric fracture were randomized to treatment with a sliding screw device alone (Controls) or the same device combined with calcium phosphate cement for augmentation (Augmented). All patients were allowed unrestricted weight bearing after surgery. Fracture movement was measured with radiostereometry (RSA) at 1 and 6 weeks and at 6 months.

Results: Two patients died during the study period due to unrelated causes and another three were excluded due to technical problems with the RSA in two and concomitant illness in one. 21 patients (11 Augmented and 10 Controls) were followed according to the study protocol. At 1 week the augmented fractures had moved on average 1.9±1.7 mm while movement in the controls was 4.0±2.4 mm (p<0.05). The average total movement from the day after surgery until 6 months, when all fractures had healed, was 7.8±6.2 mm for the augmented fractures and 13.2±4.3 mm for the controls (p<0.05). Varus angulation was the most pronounced angulation for both groups although augmented fractures revealed less varus angulation compared with controls at all time points. Rotation around the longitudinal and transversal axes was small with no significant differences between treatment groups.

Conclusion: Augmentation with calcium phosphate cement improved the stability of unstable trochanteric fractures fixed with a sliding screw device. The improvement was most pronounced for varus angulation and lateral and distal migration of the head and neck fragment.

VI. Resorbable cement for augmentation of internally fixed unstable trochanteric fractures.

A prospective randomised multicenter study.

Background: The aim was to evaluate if internal fixation with a sliding screw device combined with augmentation using a resorbable cement (Norian SRS) improves the clinical, functional and radiological outcome when compared with fractures treated with a sliding screw device alone.
Patients and method: A series of 112 unstable trochanteric fractures were studied prospectively in a multicenter study. Three different pain modalities were evaluated. Activities of Daily Living (ADL), health status SF-36, hip abductor muscle strength and radiographic outcome were analysed.

Results: Six weeks after surgery, subjects in the cement-augmented group had significantly lower Global and Functional Pain Scores (p<0.003) and less pain after walking 50 feet (p<0.01). At six weeks, subjects in the cement group showed significant improvement, compared to the control group regarding ADL (p<0.05). At both six weeks’ and six months’ follow-up, patients in the cement group showed significant improvement, compared to the control group, when evaluated by SF-36. Regarding the other studied parameters, no significant differences were found between the groups.

Conclusion: We conclude that augmentation with calcium phosphate cement in unstable trochanteric fractures will reduce pain during early rehabilitation and improve quality of life during the course of healing when compared to conventional fixation with a sliding screw device alone.
General discussion

The ultimate aim when treating hip fractures in the elderly should be salvage of social independence. This also implies an effort to achieve a rapid and lasting return to prefracture function and uncomplicated fracture healing. Surgery is the treatment of choice for all hip fractures. The major complications of femoral neck fracture are nonunion, late segmental collapse and redisplacement, all of which are probably due to injured blood supply.

Unstable intertrochanteric fractures are more of a mechanical problem, due mainly to an inability to achieve fixation that can preserve good position at the fracture site throughout the course of healing. This is especially obvious in patients with comminuted, so-called unstable fractures. By using dynamic devices that allow secondary fracture impaction the reoperation rate in unstable trochanteric fractures has been reduced to about 10% or less.

Reduced bone strength due to osteoporosis strongly contributes to the mechanical problems associated with complications after internal fixation for both femoral neck fractures and unstable trochanteric fractures.

When using resorbable calcium phosphate cement (Norian SRS) to reinforce the weak bone that surrounds the metal implant, is it important to consider the potential advantages, as well as the disadvantages. The advantages include immediate mechanical strength, non exothermic hardening, biocompatibility, adaptiveness to different shapes of the fracture void, and replacement over time by host bone. The drawback is related to the mechanical characteristics. The material is strong enough in compression (55MPa) to withstand physiological loading although the material is weak in bending and shear (3-5MPa). It is important to understand these basic characteristics and use the cement only where it is subjected mainly to compressive loading. When loading conditions include shear and bending forces, the material should be combined with metal implants in such a way that the metal can neutralize the bending and shearing forces while the calcium phosphate cement counteracts the compressive loading. It seems reasonable to assume that in most instances resorbable bone cement will not replace metal implants but induce alterations in the design of the hardware and how it is used. The goal will be to find the most successful combinations of metal implants and resorbable bone cement.
The femoral head usually has cancellous bone of poor mechanical quality, which presents major problems for internal fixation of femoral neck fractures. It appears that it is the holding power in the cancellous femoral head that is the weakest point mechanically according to the “three point principle” to enhance mechanical stability (Bout et al. 1997), the other two being the lateral cortex and calcar femorale. Most patients who sustain a hip fracture already suffer from more or less severe osteoporosis, which further compromises the quality of the cancellous bone in the femoral head. Implant migration is therefore a fairly common problem in clinical practice. In order to prevent this complication several different implant designs have been developed.

Five different implants were used alone or augmented with conventional bone cement (PMMA) or resorbable cement (Norian SRS). All implants were tested in both maximal torque and maximal pull out in cubes made of polyurethane of three different densities.

Augmentation with PMMA caused a significant increase in both maximal torque and maximal pull out load for all implants tested and for all three different block densities when compared with the holding characteristics without cement.

The use of resorbable cement (Norian SRS) also improved holding characteristics although the gain was far less when compared with the increase when using PMMA. The most obvious increase was in blocks with the lowest density, i.e. blocks simulating severe osteoporosis.

Resorbable cement improved both the maximal pull out load and the maximal torque resistance significantly for all three block densities when used for augmentation of hook-pins, but did not improve the holding power of conventional screws at all.

The standard technique for two of the screws was insertion without predrilling. When using cement, predrilling was a prerequisite in order to create a canal for injection of the cement prior to insertion of the metal. It seems that the artificial bone material that was taken out during predrilling caused a reduction in holding power that was greater than the mechanical strength gained by injecting resorbable cement into the drilled hole. When using PMMA the improvement in mechanical strength of the cement added into the predrilled hole was far higher than the loss of strength caused by the predrilling procedure and the associated loss of material. Insertion of screws without predrilling probably causes more dense bone formation around the screw threads due to cancellous bone being squeezed by the advancing screw during insertion, an effect that seems more pronounced in low density specimens.

The difference in failure mechanism between calcium phosphate cement and PMMA augmented implants probably can be explained, at least in part, by differences in mechanical strength. Calcium phosphate cement is rela-
tively weak in shear, which explains the consistent failure at the outer end of the thread during pull out but also during torque when used for augmentation of screws. PMMA, with much higher shear strength compared to both calcium phosphate cement and the artificial bone, withstood both pull out loading and torque levels that were higher compared with what could be taken by the surrounding artificial bone. Consequently, the PMMA augmented blocks failed at the interface between the PMMA and the surrounding artificial bone by the bone giving way while the PMMA remained intact.

In clinical practice it is reasonable to believe that the cement mantel around each device will differ between individuals due to variations in the penetration depth into the surrounding bone caused by differences in the density of the cancellous bone.

Paper II

Redisplacement, non-union and late segmental collapse are common complications after internal fixation of femoral neck fractures. The basic pathogenesis in the majority of these complications is considered to be vascular damage to the femoral head (Stromqvist 1983, Nilsson et al. 1989). Inadequate reduction and osteosynthesis can increase the rate of early displacement (Rehnberg and Olerud 1989b, Rehnberg and Olerud 1989a). Intraoperative damage to the femoral head and neck caused by repeated attempts at reduction and repeated insertions of drills and screws may also be important for the outcome, as indicated by reports of improved results when treated by surgeons with a special interest in technique (Rehnberg and Olerud 1989c, Stromqvist et al. 1992). Poor fracture stability has been shown to correlate with early redisplacement and non-union (Rehnberg and Olerud 1989b).

Radiographic measurements of femoral neck fracture shortening have usually been based on measurement of extrusion of the osteosynthesis material in AP view (Fielding 1980).

Radiostereometry, RSA, is a radiological technique with an accuracy (Selvik 1989) that is 5-50 higher times compared to conventional radiography. More complex analysis of implant motion is also of interest to obtain a better understanding of any failure mechanism. RSA is today the only method that can be used to evaluate these motions with sufficient accuracy in vivo.

The aim of this paper was to measure early stability in femoral neck fractures augmented with resorbable cement (Norian SRS). The main finding was that augmentation with calcium phosphate cement provided better overall stability when compared to femoral neck fractures stabilized with screws alone.
The present in vivo findings are therefore in line with an earlier presented biomechanical study (Stankewich et al. 1996). Using a technique for augmentation similar to the calcium phosphate cementation in the present study they showed that cyclic loading of augmented specimens revealed higher stiffness and also higher maximum load to failure when compared to specimens fixed with conventional screw fixation without cement augmentation. Due to the radiostereometric analysis used in the present study it was possible to measure not only the overall fracture movement but also movement along and around three orthogonal axes with high precision. The major difference between the treatment groups was a reduced distal migration and varus angulation of the femoral head for the cement augmented fractures. The two treatment groups had similar patterns of movement although the magnitude was less for the augmented fractures. By using calcium phosphate cement for augmentation the distal migration was reduced to about half at both 1 and 6 weeks when compared to fractures fixed without augmentation. It has previously been reported in a clinical study that distal migration of the femoral head is the most pronounced displacement for fixed femoral neck fractures, in agreement with the findings in the present study (Ragnarsson and Karrholm 1991). When comparing the two time points in this study the enhanced stability achieved through augmentation was more pronounced at 1 week than at 6 weeks. This finding was interpreted to result from either a reduction in the mechanical strength of the SRS due to fatigue or due to resorption of the SRS, or an effect secondary to the biological events within the bone at the fracture site. Based on preclinical (Frankenburg et al. 1998) as well as clinical studies ((Larsson et al. 1999) the resorption phase of SRS seems to be rather long, making it unlikely that the reduced stability at 6
weeks was caused by resorption of the material. We are more prone to believe that fatigue was the factor behind the inferior performance of SRS at 6 weeks. In the proximal femur the loading pattern is complex and includes different directions of loading. This means that the SRS, when inserted in the proximal femora, was subjected to complex loading that might have fragmented the material, thereby reducing its mechanical strength.

The results are in accordance with previous clinical and biomechanical report of femoral neck fractures.

Paper III

We wanted to evaluate whether augmentation with calcium phosphate cement improves the clinical and functional outcome following internal fixation of displaced femoral neck fractures. The study focused on longer-term following up, i.e. 24 months.

The augmented group had only a modest positive effect during the early postoperative period, while later on there was no difference between treatment groups. This lack of differences in clinical outcome might be explained by the fact that calcium phosphate cement is unable to withstand repetitive loading over a long period of time. This also implies that the fatigue characteristics are not as good as the immediate mechanical properties observed during in vitro testing with a limited number of loading cycles. Another reason for the observed outcome may relate to the biological event that has taken place at the fracture site during the first phase of fracture healing.

The tendency towards more frequent late reoperations in the augmented group could not be fully answered by this study. A possible explanation might be that the cement provided improved fracture stability during the early rehabilitation period as shown in a previous study using radiostereometric analysis. Later in the healing process the cement at the fracture site may have interfered with the blood supply at the fracture area in such a way that the risk of non-union and avascular necrosis increased in the augmented group.

The clinical evaluation of ADLs indicated that augmentation by calcium phosphate had some impact during the early rehabilitation period. Patients in the augmented group were able to perform some of the activities of daily living more effectively and with less difficulty than the controls during the first six weeks. These observations can be explained by increased initial fracture stability. If so, the findings are in accordance with studies showing that increased initial fracture stability results in better clinical and functional outcome in the early postoperative period. It is proposed that stable fracture fixation will reduce pain during the early rehabilitation period. Based on the findings that the augmented fractures are more stable than the controls it was
somewhat surprising that there was no difference at all in pain or in the use of pain medication.

Subjects’ hip mobility was measured using the D’Aubigne mobility scale and range of motion. These tests showed slightly better mobility in the cement group during the first postoperative week, but later on there were no differences. This may indicate that mobility is not correlated to fracture stability.

Augmentation with calcium phosphate cement had only a modest positive effect during the early postoperative period while later on there was no difference between treatment groups. We therefore do not recommend augmentation with calcium phosphate cement for this indication, and with the technique utilized in the present study.

Paper IV

To evaluate whether filling of the fracture void with cement can compromise circulation to the femoral head, plain radiographs were used to assess redisplacement, non-union or avascular necrosis of the femoral head during the first two postoperative years. Almost every femoral neck fracture is associated with some degree of disturbance to the femoral head circulation. The extent of this initial vascular injury is of prognostic importance for development of late complications. Scintigraphic evaluation is a sensitive examination modality when looking at the vitality of the femoral head (Stromqvist et al. 1983a). Quantification is based on the relative increase of radionuclide uptake in the fractured femoral head compared to the normal side. The methodological error during calculation of the head to head ratio has been found to be 10% (Hansson 1982, Stromqvist et al. 1983b, Alberts et al. 1984). Postoperative scintigraphy had a high predictive value for late complications (Alberts et al. 1984, Stromqvist and Hansson 1984, Alberts and Jervaevus 1990).

The results from the scintimetric examination showed a significantly decreased ratio in the cement group compared to the control group. In order to explain whether the lower rate could be due to a false shadow effect related to the cement, both tomographic and conventional scintigraphic examinations were done in 19 patients. Evaluation of these examinations showed a good correlation in the uptake between the tomographic and conventional scintigraphic examinations. This shows that the reduced femoral head uptake was a true reduction and not an artifact caused by shadow effects of the cement.

The lower number of redisplacement in the cement augmented group indicates that the augmentation provided added stability while the lower scintigraphic uptake and more frequent non-union and AVN indicate that augmentation with a calcium phosphate cement injection interferes with the
already disturbed circulation to the femoral head. It might be that with longer follow up the number of reoperations would increase, i.e. the time for an apparent symptomatic complication has only been delayed. Radiological non-union or AVN was more common in the augmented group compared to controls (p < 0.0007). The number of reoperations due to non-union and AVN was also more common in the augmented group (p = 0.034) while reoperations due to redisplacement were less common in the augmented group compared to controls (p = 0.028). In the augmented group there was no significant difference in scintigraphic uptake between patients who were reoperated or not (p=0.74), while in the control group patients who were reoperated had a significantly lower femoral head uptake compared than those who were not reoperated (p<0.01). We conclude that augmentation of femoral neck fractures with cement injection can not be recommended as it might compromise the circulation to the femoral head and increase the risk of subsequent healing complications.

Paper V

Surgical treatment with a sliding screw device is the most common method for internal fixation of intertrochanteric fractures. These implants allow controlled telescoping and impaction of the fracture during weight bearing that will enhance fracture healing. Stable two-part intertrochanteric fractures (Evans 1949, Jensen 1980) seldom present any problem and have reported a failure rate of less than 5 percent (Laros 1990). Unstable intertrochanteric fractures are defined as three-part fractures with an additional postero-medial fragment including the lesser trochanter or four part fractures including the greater trochanter (31-A2.2 or 31-A2.3; Modified Evans type 4-5). These fractures are more frequently associated with complications, particularly in patients who are unable to restrain from full weight bearing during the early period. The aim of this study was to measure whether augmentation with resorbable calcium phosphate cement could improve fracture stability in this unstable fracture type as shown in biomechanical studies.
Intertrochanteric fracture before treatment

Treated with a sliding hip screw and Norian SRS in the fracture void

The main finding in the present study was that augmentation of unstable trochanteric fractures with calcium phosphate cement provided better stability, i.e. less fracture movement from the day after surgery until healing when compared to similar fractures fixed with a conventional sliding screw plate system alone. The present in vivo findings are in line with the biomechanical studies by Elder et al (Elder et al. 2000) and Yetkinler et al (Yetkinler et al. 2002). Using a technique for augmentation with calcium phosphate cement similar to that in the present study they showed that loading of augmented specimens revealed improved stability and higher stiffness when compared to specimens fixed with conventional sliding screw fixation without cement augmentation.

Little is known about the exact movement that occurs in a trochanteric fracture during the course of healing. The radiostereometric analysis made it possible not only to measure the overall fracture movement but also movement along and around three orthogonal axes. In unstable trochanteric fractures it is a common perioperative finding that the femoral head-neck fragment tends to rotate due to the torque applied during insertion of the lag screw. This perioperative finding has been taken as evidence of rotational fracture instability even after surgery. In order to prevent an expected postoperative fracture rotation and subsequent malunion, specific solutions and techniques have been proposed that often include the use of antirotational screws. In the present study it was shown that the rotation around the longitudinal and transversal axes in the augmented, as well as in the control group, was very limited. This finding is not in accordance with the common belief that antirotational screws are needed in trochanteric fractures. One reason for rotational stability being better than excepted was most likely interdigitation between fracture surfaces following early sliding and fracture impaction. Such interdigitation is perhaps a more reliable stabilizing factor.
than previously anticipated. Angulation around the sagittal axis, i.e. varus angulation, was significantly reduced when compared with fractures fixed with the sliding screw device alone. For linear movement the most typical finding was a lateral movement of the femoral head and neck fragment, i.e. medialization of the shaft fragment, combined with distal migration. Augmentation significantly reduced both the tendency toward lateral and distal migration of the femoral head and neck fragment.

We conclude that augmentation with calcium phosphate cement improved the stability of unstable trochanteric fractures fixed with a sliding screw device.

Paper VI

The consequences of hip fractures are not only a problem of the isolated individual but also of the community as a whole. The management and care of patients with hip fractures engages different sectors of society and there is a need of continuos surveillance. A majority of hip fracture subjects experience severe functional impairment following their injury, and many never recover their pre-fracture level of physical functioning (Jette et al. 1987, Marottoli et al. 1992). Physical impairments resulting from intertrochanteric fractures may adversely affect basic activities of daily living (ADLs). Early post-operative ambulation and the ability to undergo rehabilitation are critical to survival following a hip fracture. Subjects are less likely to initiate, control and sustain normal ambulation if it cannot be performed in a familiar and proprioceptive manner.

The aim of this paper was to evaluate if internal fixation with a sliding screw device combined with augmentation using a resorbable cement (Norian SRS) could improve the clinical, functional and radiological outcome when compared with fractures treated with a sliding screw device alone.

A reduction in post-operative pain might have important clinical significance, as less pain will permit earlier ambulation and return of activities of daily living. A stable fracture fixation that prevents motion between fracture fragments will reduce pain when compared with less rigid fracture fixation techniques. For sliding screw devices the concept includes fracture impaction to achieve better load sharing and fracture healing when compared with rigid implants. Unfortunately, the initial fracture impaction, and the dynamic fracture movement, seems to be associated with pain at weight bearing. In the present study, pain was significantly less at six weeks in the augmented group. This finding was interpreted as a result of augmentation providing a more stable fracture fixation when compared to metal fixation alone. At one week, as well as at six months, there was no significant difference in pain between groups. The lack of difference in pain at one week might be due, at least in part, to pain being caused not only by the bone injury but also by the
soft tissue injury due to both the trauma and the surgical procedure. At six months the fractures were healed and subsequently the pain, if present, was low in both groups.

For the different ADLs that were examined, the difference between the treatment groups was most pronounced at six weeks, while the difference at one week and six month was less obvious. As a result of the rather strict inclusion and exclusion criteria the included patients represented a fairly healthy subpopulation of patients suffering a trochanteric fracture. It has been shown that the patient’s general health (Ceder et al. 1980) and activity level before the fracture both will influence the outcome (Campion et al. 1987) (Broos et al. 1988) (Cheng et al. 1989). Carroll (1969) reported that the diagnosis, the level of ADL, and the degree of mental orientation of the patient prior to fracture all were of great importance for postoperative function (Carroll 1969).

SF-36 is a widely used and validated instrument for health-status measurement. On the different subscales the responses vary from Yes/No to a 6-point verbal rating scale. The SF-36 has been subjected to reliability testing in previous studies and it therefore seemed justified to use it in the present study (Gabriel et al. 1999, Randell et al. 2000) (Hall et al. 2000) (Jaglal et al. 2000) (McHorney et al. 1994). When looking to the different subscales at 6 weeks there was a quite strong significance in favour for the augmented group in health and vitality while less significant for pain and health transition, findings that might be explained by the augmented fracture being more stable and therefore less prone to cause pain during activities. At six months the differences in SF-36 were even more pronounced in favour of the augmented group when compared with six weeks. As previously mentioned the fractures were healed at six months and the more pronounced difference in SF-36 at six months is not obvious. Our interpretation was that the augmented group had a more rapid rehabilitation period, especially due to less pain. The less prolonged period of pain and severely impaired hip function in the augmented group might be the indirect cause of better SF-36 outcome at six months compared to the controls. For the different subscales a striking finding for both groups was the severe reduction in the patients’ assessment of physical health at six weeks. This reduction was far more pronounced at six weeks compared with one week after surgery. It seemed that the patients at one week after surgery still had not realized the effect the fracture would have on their physical health. At six weeks the patients were usually in the middle of their rehabilitation program, which might explain why the patients on average assessed their physical health so low. It was no surprise that the patients at six months claimed improvement in physical health compared to six weeks after surgery. Still, at six months physical health was significantly lower compared to the assessment at one week.

The hip abductor muscles and the anatomy of the proximal femur are important factors for normal gait and ambulation. Insufficient abductor muscle
strength resulting from neuromuscular dysfunction or trauma has been re-related to limp and impaired gait function (Delp et al. 1990). A reduced offset in the proximal femora due to shortening of the femoral neck might also reduce the abductive capacity of the hip. The inability of subjects to regain abductor muscle strength is associated with the likelihood of losing independent ambulation after a hip fracture (Barnes and Dunovan 1987). In the present study there was no significant difference between the treatment groups at any time point, although for both groups there was a substantial reduction in the abductor muscle force at six weeks, while at six months the difference was less for both groups when compared with the unaffected side.

Excessive limb shortening is a common problem in unstable three-part and all four-part trochanteric fractures due to pronounced fracture impaction. In the most severe cases the fracture might impact until the head neck fragment abuts the lateral cortex of the femoral shaft fragment. In the present study we measured the screw sliding until healing. Müller-Färber et al. (Muller et al. 1988) described a correlation between the amount of screw sliding and postoperative mobility. Screw sliding of less than 6.7 mm did not affect the level of mobility, whereas an average screw sliding of 13.4 mm resulted in reduced mobility and 18.7 mm or more resulted in the lowest mobility level. When using the different levels described by Müller-Färber et al. (Muller et al. 1988) the average sliding in the augmented as well as the control hips correlated to a medium reduction of the mobility level. By using conventional radiographs we were unable to detect any significant difference in permanent fracture displacement between the two groups.

An important radiographic measure of the success of fracture surgery is the adequacy of the fracture reduction. In the present study there was no difference between the augmented hips and the controls in terms of the adequacy of the fracture reduction observed in the immediate post-operative radiographs. This is an indication that any differences in outcomes were due to the presence or absence of the augmentation rather than to the surgical technique.

We conclude that augmentation with calcium phosphate cement in unstable trochanteric fractures will reduce pain during early rehabilitation and improve quality of life during the course of healing when compared with conventional fixation with a sliding screw device alone.
Conclusion

Augmentation with calcium phosphate cement increased the holding characteristics mainly in low density bone while in high density bone it even reduced the maximum torque due to the need for predrilling when using cement for augmentation. (Paper I).

Augmentation with calcium phosphate cement improved the stability of internally fixed femoral neck fractures during the first six weeks after surgery, with improvement being less pronounced at six weeks compared to one week. (Paper II)

Augmentation with calcium phosphate showed a trend toward a higher proportion of later reoperations in the augmented group and only a temporary clinical improvement during early rehabilitation. Augmentation as used in the present study cannot be recommended. (Paper III)

Augmentation with calcium phosphate cement of femoral neck fractures caused a lower scintigraphic uptake in the femoral head, resulting decreased blood circulation in the femoral head. The method cannot be recommended as it might compromise the circulation to the femoral head and increase the risk for subsequent healing complications. (Paper IV)

Augmentation of unstable intertrochanteric fractures with calcium phosphate cement significantly improves the stability of unstable trochanteric fractures fixed with a sliding device. The improvement was most pronounced for varus angulation and lateral and distal migration of the head and neck fragment. (Paper V)

Augmentation with calcium phosphate cement of unstable intertrochanteric fractures reduced pain during early rehabilitation and improved quality of life during the course of healing when compared with conventional fixation with a sliding screw device alone. (Paper VI)
Summary in English

Surgical treatment of hip fractures is frequently associated with secondary fracture displacement, in part due to weak osteoporotic bone. So far, improvements have focused on new metal implants although an alternative could be to augment the bone that surrounds the implant.

The aim of this thesis was to evaluate the use of calcium phosphate cement (Norian SRS) for augmentation of internally fixed hip fractures. Norian SRS is an injectable, biocompatible cement that hardens in situ without exothermic reaction. Over time it is remodeled and replaced by host bone.

In a biomechanical study the holding characteristics for different implants was measured when inserted with or without augmentation. The study showed that conventional bone cement (PMMA) improved maximum torque and pull-out for almost all modalities while Norian SRS increased the holding power mainly in low-density bone.

In a prospective and randomized study, patients with displaced femoral neck fractures were operated with internal fixation using screws alone or combined with Norian SRS for augmentation. The result showed improved stability when measured with radiostereometry (RSA) for the augmented fractures during the early rehabilitation period. The clinical evaluation of 118 patients included pain, walking aid, activities of daily living (ADLs), abductor muscle strength, mobility and range of motion. During the early course the augmented patients did better in some variables although over the total two-year study period there was no major difference between groups. Scintigraphic evaluation indicated that augmentation might compromise the circulation to the femoral head.

The final part included unstable trochanteric fractures fixed with a sliding screw device alone or the same device combined with Norian SRS for augmentation. Using RSA it was shown that augmentation significantly improved the fracture stability until healing. In a randomized multicenter study including 112 patients, augmentation with Norian SRS reduced pain during early rehabilitation and improved quality of life until healing.

In conclusion, augmentation with Norian SRS improved the early fracture stability in displaced femoral neck fractures while there was no major difference in clinical outcome. In unstable trochanteric fractures augmentation provided improved fracture stability and improved clinical course until healing.
Svensk sammanfattning


Det andra arbetet belyser hur stabiliteten påverkas i den tidiga läkningsfasen, 6 veckor, i ett kliniskt material. Detta mäts med hjälp av röntgenstereofotometri (RSA), vilket är en 3-dimensionell röntgentechnik som mäter rörelser med en precision på ungefär 0,3 mm. Måtpunkten har varit 1 vecka respektive 6 veckor. Resultatet visar att benbrottet är signifikant stabilare om man förstärker frakturområdet med Norian SRS men att signifikansen minskade vid 6 veckor jämfört med 1 vecka.


I delarbete fem studerades frakturstabiliteten med radiostereometri. Detta var på patienter med s k instabil typ B-fraktur (trokantär). Denna typ av fraktur är behäftad med den högsta risken för mekaniska komplikationer under läkningsförloppet. Resultatet i detta arbete visade signifikant bättre frakturstabilitet hos de patienter som fått sitt brott stabiliserat med både metallskruv och platta samt Norian SRS jämfört med fixering med enbart metall.

Det sista delarbetet utgjordes av en multicenterstudie, (3 ortopedkliniker i Sverige) där patienter med instabila trokantära höftfrakturer fixerades med enbart konventionell metall eller metall samt Norian SRS. Resultatet i denna studie visade att patienter med cementförstärkning hade mindre ont, uppvisade bättre ADL-funktioner samt dessutom bättre utfall i många livskvalitetsparametrar jämfört med patienter som opererades med enbart metallfixering.
Acknowledgements

I would like to express my sincere gratitude to everyone who helped my through this project.

Sune Larsson, Professor, my tutor, for introducing me into the world of science. A man with innumerable ideas and energy. Thanks for teaching me so much and pushing me all the way.

Olle Nilsson, Professor, for general support and for providing time for research.

Håkan Ström, M.D., my workroom mate and good friend, for generous contributions and constant support.


Michael Cornefjord, M.D., PhD. my good friend and next workroom mate, for generous contributions and support.

Leif Nyström, Umeå University, for excellent guidance and support when starting up the RSA laboratory.

Monica Gelotte, Department of radiology, for your skillful RSA examinations.

All my COLLEAGUES and STAFF at the Department of Orthopedic in the Akademiska Hospital.

This thesis was supported with grants from Norian SRS and Trygg Hansa.

Above all, my Anna-Stina and my family for endless support all these years.
References


Cooper A. A treatise on dislocations and fractures of the joints. Longman Hurst, London 1823.


Acta Universitatis Upsaliensis

Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine 46

Editor: The Dean of the Faculty of Medicine

A doctoral dissertation from the Faculty of Medicine, Uppsala University, is usually a summary of a number of papers. A few copies of the complete dissertation are kept at major Swedish research libraries, while the summary alone is distributed internationally through the series Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine. (Prior to January, 2005, the series was published under the title "Comprehensive Summaries of Uppsala Dissertations from the Faculty of Medicine").