Calcium phosphate cement for augmentation did not improve results after internal fixation of displaced femoral neck fractures

A randomized study of 118 patients

Per Mattsson and Sune Larsson

Department of Orthopedics, Uppsala University Hospital, SE-751 85 Uppsala, Sweden.
Correspondence PM: Per.Mattsson@surgsci.uu.se
Submitted 04-12-06. Accepted 05-06-13

Background **We wanted to evaluate whether augmentation with calcium phosphate cement can improve clinical and functional outcome following internal fixation of displaced femoral neck fractures.**

Patients **118 patients aged 60–98 years (95 women) 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: 60 patients) or screws combined with injection of calcium phosphate for augmentation around the screw threads and at the fracture site (augmented: 58 patients). All patients were allowed free weight bearing. Clinical and radiographic examinations were done by a physiotherapist directly after surgery, at 1 and 6 weeks, and at 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, nonunion or avascular necrosis (p = 0.1). There was no difference in pain or muscle strength between groups. Some activities of daily living (ADLs) were slightly better in the augmented patients during the first weeks, while there were no differences between groups later on.**

Interpretation **Due to a trend towards more reoperations in the augmented group, and only a temporary clinical improvement during the early rehabilitation, augmentation as we used it cannot be recommended.**

Internal fixation of displaced femoral neck fractures is associated with a high reoperation rate. A meta-analysis by Lu-Yao et al. (1994) revealed that about 30% of patients develop a nonunion and 80% of these will need a reoperation. In an additional 15% of cases the fracture will heal, but due to vascular damage induced by the trauma, avascular necrosis of the femoral head will develop. About 20% of those cases will need a hip replacement. In addition, about one-third will experience severe longstanding or even permanent functional disability following their injury (Zuckerman et al. 1993, Koval et al. 1995). Physical impairment resulting from femoral neck fractures may also adversely affect basic activities of daily living (Koval and Zuckerman 1995). The ability to undergo early rehabilitation seems critical for functional survival following a hip fracture.

The weak bone usually present in these patients often makes it difficult to achieve a stable fixation. In order to improve the mechanical strength of the bone-implant construct, augmentation of the weak bone surrounding the metal implant seems to be an attractive option. Over the last few years, synthetic bone substitutes have been introduced for use in fracture surgery with special emphasis on the enhancement of osteopenic bone. In a mechanical study by Stankewich et al. (1996), augmentation with calcium phosphate cement provided enhanced stiffness, stability and strength of fixed femoral neck fractures. When resorbable substances are used, the idea is that the initial reinforcement will

DOI 10.1080/17453670610045984

be followed by progressive resorption over time—associated with a simultaneous increase in structural support provided by the healing bone (Witschger et al. 1991, Constantz et al. 1995, Kopylov et al. 1996, Stankewich et al. 1996, Mainil et al. 1997, Moore et al. 1997, Frankenburg et al. 1998, Goodman et al. 1998, Knaack et al. 1998, Yetkinler et al. 1999, Larsson and Bauer 2002).

We designed a randomized study to evaluate whether augmentation of internally fixed femoral neck fractures with calcium phosphate cement could improve the clinical and functional outcome relative to conventional screw fixation alone.

Patients and methods

118 patients (aged 60–98 years, 95 women) with a displaced femoral neck fracture (Garden III–IV) were included. The authors operated on all patients at the Department of Orthopedics, Uppsala University Hospital. 58 patients were randomized to augmentation with Norian SRS ("augmented") (Norian Corp., Cupertino, CA) and 60 to fixation with screws alone (controls). Before the fracture, all patients had been physically active and ambulatory—either without any walking aid or with one cane as support. The study was approved by the ethics committee of Uppsala University.

Inclusion criteria were a femoral neck fracture in a patient over 60 years of age, surgical procedure within 72 h of admission, normal contralateral hip, and signed informed consent. Exclusion criteria were senility, earlier hip surgery, soft tissue infection at operative site, ongoing radiotherapy or chemotherapy due to malignancy, pathological fracture, clotting disorder, corticosteroid treatment exceeding 5 mg per day, concurrent fracture that would affect postoperative functional outcome, serious concomitant illness or mental instability, neurosensory-, neuromuscular or musculoskeletal deficiency that might have limited the patient's ability to perform objective functional tests.

The patients were randomized preoperatively using a closed-envelope system, in two groups: closed reduction and internal fixation with two cannulated screws alone (control group) or the same metal fixation combined with calcium phosphate cement augmentation (augmentation group).

All operations were performed under spinal anesthesia with sedation. Closed reduction was done on a traction table using an image intensifier. After reduction, two guide wires were inserted in parallel using a lateral approach with both wires placed centrally in the lateral view, while in the anteroposterior view the distal wire was inserted close to the inferior cortex and the proximal wire towards the superior cortex (Rehnberg et al. 1989). For patients randomized to fixation with screws alone, the lateral cortex was drilled and the two self-tapping cannulated screws (Olmed AB, Uppsala, Sweden) were inserted until the tip of the screw was within the subchondral plate. In patients randomized to augmentation with calcium phosphate cement, the cannulated drill was used to drill the entire length of the screw canal to the subchondral bone. A separate 4.5-mm drill hole was made in the lateral cortex between the guide wires to enable optimal access to the fracture site during injection of the cement. A mixer machine was used for preparation of the cement, after which it was injected in the two screw canals until they were completely filled. The screws were inserted while the cement was still soft. As the final step, a second cement injection was done through the third hole in the lateral cortex—with the purpose of filling the fracture void with cement (Figure).

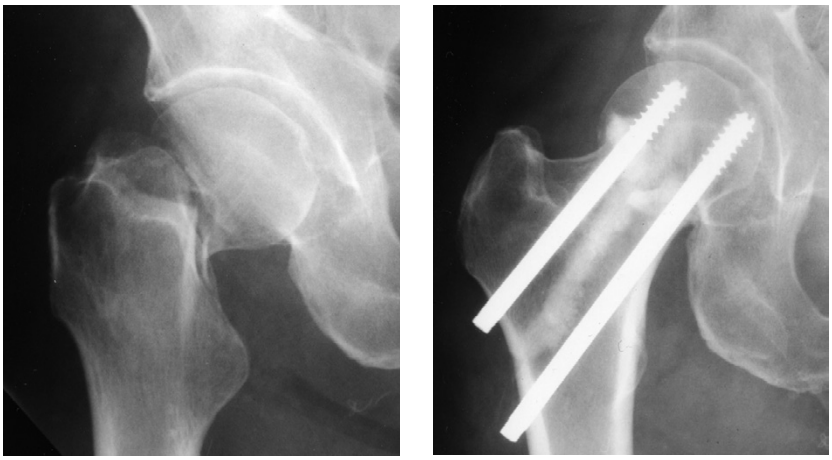
Typically, 10 cm^3 of SRS was used to fill the screw canals, while a similar package was used to fill the fracture void, i.e. 20 cm^3 of SRS in total was used. As the cement was radiopaque, the injection of cement could be followed and guided using the image intensifier.

The patients were followed with clinical examinations by a research physiotherapist at 1 and 6 weeks, and also at 6, 12 and 24 months.

Clinical and radiographic evaluation

The clinical evaluation included pain, walking aid, 6 activities of daily living, isometric abductor muscle strength, Merlé D'Aubigne mobility scale and range of motion. All patients were also examined radiographically with anterior/posterior, lateral and full pelvis views.

Subjects reported any pain at rest and during activity at each follow-up visit using a standard linear visual analog scale (VAS) (Carlsson 1983). Subjects were asked to describe the intensity of



Displaced femoral neck fracture before (left) and after (right) internal fixation with cannulated screws and calcium phosphate for augmentation.

their pain at each time point by marking a 100-mm horizontal visual analog scale to reflect their rating of their pain—ranging from "no pain" (0) to "pain as bad as it can be" (100). At each visit, the patients were asked about intake of pain medication.

6 parameters of activities of daily living (ADLs) were assessed: walking 3 m, getting in and out of a bath, getting on and off a toilet, getting in and out of bed, raising oneself from an armless chair, and putting on shoes.

Isometric testing of the hip abductor strength was performed at each visit using a hand-held dynamometer (Chatillon CSD 400; Ametec Inc., Paoli, PA) that was held at a point 10 cm proximal-lateral to the knee joint. The maximal muscle strength measurement was repeated 3 times on each visit with a few minutes of rest between testing. The average value of the three readings was used to describe abductor strength. The abductor strength in the contralateral (healthy) leg was measured in a similar way at the same time, and thus the patient served as his/her own control with respect to abductor muscle strength.

The passive hip mobility was measured using the Merlé D'Aubigne mobility scale, which measures 6 increments of hip mobility, ranging from a stiff hip to mobility over 90°. Hip flexion/extension was measured for each subject at each time point. Abduction/adduction and medial/lateral rotations were measured with a standard goniometer.

Plain radiographs with frontal, lateral and full pelvic views were performed preoperatively, postoperatively and at each follow-up to evaluate reduction, loss of reduction, hardware failure and possible healing complications. The preoperative radiographs were used to classify the fractures according to the Garden classification (Garden 1961) and OTA classification (Garden 1961).

Statistics

We performed a power analysis to estimate the sample size. Based on the assumption that the augmented group would exhibit a reoperation rate of 15% compared to a presumed reoperation rate of 30% in the control group, a sample size of 56 subjects for each study group would detect a significant difference between the two groups with an α of 0.05 and a β of 0.20 (i.e. a power of 0.8). Analyses were made with Student's t-test for unpaired comparison of means between the two groups. For categorical outcomes, we used the chi-square test when the expected cell frequencies were greater than or equal to 5.0 and Fisher's exact test when the cell frequencies were less than 5. A two-sided probability level of 0.05 or less was deemed to indicate statistical significance.

Results

24 patients, 14 in the augmented group and 10 controls, died during the follow-up period. The number of patients available at each follow-up for the augmented and control groups were 56 and 57

Table 1. Number of patients attending the follow-up. Individual patients were sometimes unable to attend at one time point due to, for instance, concurrent disease not related to the study, while they were able to attend at subsequent visits. This means that the numbers cannot be used for simple subtraction between the different time points

Follow-up	Augmented (n = 58)	Controls (n = 60)
1 week	58	60
reoperated	1	0
dead	1	1
not attending [a]	0	2
6 weeks	56	57
reoperated	3	6
dead	4	4
not attending [a]	3	2
6 months	46	45
reoperated	9	5
dead	5	3
not attending [a]	3	3
12 months	31	36
reoperated	8	3
dead	3	2
not attending [a]	5	7
24 months	17	26

[a] not attending for other reasons

Table 2. The number and reasons for reoperation of displaced femoral neck fractures treated with cannulated screws and calcium phosphate cement augmentation (augmented) or screws alone (controls) during the 2 years following surgery

Reason for reoperation	Augmented (n = 58)	Controls (n = 60)
Infection	1	0
Loss of reduction within 6 months of surgery	3	6
Nonunion	9	5
Avascular necrosis	8	3

at 6 weeks, 46 and 45 at 6 months, 31 and 36 at 1 year and 17 and 26 at 2 years, respectively (Table 1). The augmented group had a longer average operative time, including time for closed reduction, compared to the control group (26 min vs. 18 min) ($p < 0.001$). There was 1 deep infection in the augmented group and no infections in the controls. The infected patient was reoperated with a cemented total hip replacement using a two-stage procedure. There were 34 additional reoperations (20 in the augmented group and 14 in the control group) due to loss of reduction, nonunion or avascular necrosis ($p = 0.1$). All patients were reoperated with a total hip replacement (Table 2).

Pain during activity decreased in the augmented group from an average of 58 (SD 10) to 9.0 (SD 8) and in the control group from 54 (SD 9) to 7 (SD 9), from 1 week after surgery until 24 months. There was no significant difference in pain during activity between the two groups at any time point.

During the first 6 weeks, the augmented group had less difficulties in walking 3 m, and found it easier to get out of bed and to rise from sitting in an armless chair (data not shown). At later time points, there were no differences between the groups. For the other ADL variables there were no significant differences between the groups at any follow-up.

At 1 week, the D'Aubigne mobility scale was higher in the augmented group than in the controls ($p = 0.05$). Later on, there were no significant differences between the groups. At 1 week the isometric hip abductor strength, given as percentage of the unaffected side, was 51 (SD 14) for the augmented group and 52 (SD 14) for the controls. At 2 years, the corresponding values were 78 (SD 17) and 81 (SD 17), respectively, for the two treatment groups. When the subgroup consisting of patients who were followed through the whole study period was analyzed, there was still no difference between the treatment groups at any time point.

Discussion

We found a higher reoperation rate in the augmented group, although the difference between the treatment groups was not statistically significant. There was a non-significant shift in the cause for reoperation from loss of early reduction among controls to reoperations due to nonunion or avascular necrosis in the augmented group. When we designed the study, the sample size was derived from a power analysis with a clinical assumption with regard to the reoperation rate in the control group based on previous studies using a similar fixation technique. The reoperation rate in the control group was lower than expected, while it was higher than expected in the augmented group. We

used rather strict inclusion and exclusion criteria—in part to reduce the risk of patients being unable to attend follow-up examinations.

Still, the number of patients completing the study was lower than expected due to mortality, reoperation and inability to attend the follow-up due to concurrent diseases, reducing the power of the study. The tendency for a shift towards late reoperations being more frequent in the augmented group could not be fully addressed in 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 (Mattsson and Larsson 2003).

The specific ADLs chosen for this study represent activities that are likely to be associated with hip function, previously shown to be affected by the occurrence of a hip fracture (Lawton 1971, Magaziner et al. 1990, Marottoli et al. 1992). Several authors (Jette et al. 1987, Magaziner et al. 1990) have reported that a substantial proportion of elderly with a hip fracture do not regain the pre-injury levels of ability in daily living. Ceder et al. (1980) found that even as early as 4 months after fracture fixation, the main recovery of function in daily living had been achieved and then remained constant up to 1 year after surgery (Ceder et al. 1980). The clinical evaluation in our study indicated that augmentation by calcium phosphate had some effect on the ADLs studied 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 6 weeks. These observations may be explained by increased initial fracture stability.

In a previous study on unstable intertrochanteric fractures (Mattsson et al. 2005), patients treated with a sliding screw device combined with augmentation using calcium phosphate had significant less pain and improved ADL functions during the rehabilitation period compared with patients treated with a sliding screw alone. We interpreted this finding as caused by an improved fracture stability in the augmented group during the healing period as shown in an earlier study on unstable trochanteric fractures using RSA to assess stability (Mattsson and Larsson 2004).

In the present study we measured hip mobility using the D'Aubigne mobility scale and range of motion. These tests showed a slightly better mobility in the cement group in the first postoperative week, but later on there were no differences—which may indicate that there is no correlation between mobility and fracture stability.

Due to our strict inclusion and exclusion criteria, only rather healthy individuals were included. Our findings can therefore not be generalized to all patients with a femoral neck fracture.

The authors thank Stratec Medical AB, Stockholm, for providing implants for this study and Trygg-Hansa, Stockholm, for providing a research grant.

Carlsson A M. Assessment of chronic pain. I. Aspects of the reliability and validity of the visual analogue scale. Pain 1983; 16 (1): 87-101.

Ceder L, Thorngren K G, Wallden B. Prognostic indicators and early home rehabilitation in elderly patients with hip fractures. Clin Orthop 1980; (152): 173-84.

Constantz B R, Ison I C, Fulmer M T, Poser R D, Smith S T, VanWagoner M, Ross J, Goldstein S A, Jupiter J B, Rosenthal D I. Skeletal repair by in situ formation of the mineral phase of bone. Science 1995; 267 (5205): 1796-9.

Frankenburg E P, Goldstein S A, Bauer T W, Harris S A, Poser R D. Biomechanical and histological evaluation of a calcium phosphate cement. J Bone Joint Surg (Am) 1998; 80 (8): 1112-24.

Garden R S. Low-angel fixation in fracture of the femoral neck. J Bone Joint Surg (Br) 1961; 43 (4): 647-63.

Goodman S B, Bauer T W, Carter D, Casteleyn P P, Goldstein S A, Kyle R F, Larsson S, Stankewich C J, Swiontkowski M F, Tencer A F, Yetkinler D N, Poser R D. Norian SRS cement augmentation in hip fracture treatment. Laboratory and initial clinical results. Clin Orthop 1998; (348): 42-50.

Jette A M, Harris B A, Cleary P D, Campion E W. Functional recovery after hip fracture. Arch Phys Med Rehabil 1987; 68 (10): 735-40.

Knaack D, Goad M E, Aiolova M, Rey C, Tofighi A, Chakravarthy P, Lee D D. Resorbable calcium phosphate bone substitute. J Biomed Mater Res 1998; 43 (4): 399-409.

Kopylov P, Jonsson K, Thorngren K G, Aspenberg P. Injectable calcium phosphate in the treatment of distal radial fractures. J Hand Surg (Br) 1996; 21 (6): 768-71.

Koval K J, Zuckerman J D. Functional recovery after fracture of the hip. Clin Orthop 1995; (348): 751-8.

Koval K J, Skovron M L, Aharonoff G B, Meadows S E, Zuckerman J D. Ambulatory ability after hip fracture. A prospective study in geriatric patients. Clin Orthop 1995; (310): 150-9.

Larsson S, Bauer T. Use of injectable calcium phosphate cement for fracturefixation: a review. Clin Orthop 2002; (395): 23-32.

Lawton M P. The functional assessment of elderly people. J Am Geriatr Soc 1971; 19 (6): 465-81.

Lu-Yao G L, Keller R B, Littenberg B, Wennberg J E. Outcomes after displaced fractures of the femoral neck. A meta-analysis of one hundred and six published reports. J Bone Joint Surg (Am) 1994; 76 (1): 15-25.

Magaziner J, Simonsick E M, Kashner T M, Hebel J R, Kenzora J E. Predictors of functional recovery one year following hospital discharge for hip fracture: a prospective study. J Gerontol 1990; 45 (3): M101-7.

Mainil V P, Cordey J, Landolt M, Gogolewski S. The use of a resorbable augmentation device to secure plating of osteoporotic bones. An in vitro study. Int Orthop 1997; 21 (4): 217-22.

Marottoli R A, Berkman L F, Cooney L J. Decline in physical function following hip fracture. J Am Geriatr Soc 1992; 40 (9): 861-6.

Mattsson P, Larsson S. Stability of internally fixed femoral neck fractures augmented with resorbable cement. Scand J Surg 2003; 92: 215-9.

Mattsson P, Larsson S. Unstable trochanteric fractures augmented with calcium phosphate cement. Scand J Surg 2004; 93 (3): 223-8.

Mattsson P, Alberts A, Dahlberg G, Sohlman M, Hyldahl H C, Larsson S. Resorbable cement for augmentation of internally fixed unstable trochanteric fractures. J Bone Joint Surg (Br) 2005; 87 (9): 1203-9.

Moore D C, Frankenburg E P, Goulet J A, Goldstein S A. Hip screw augmentation with an in situ-setting calcium phosphate cement: an in vitro biomechanical analysis. J Orthop Trauma 1997; 11 (8): 577-83.

Rehnberg L, Olerud C, Sahlstedt B. Subchondral screw fixation of cervical hip fractures: joint congruence studied with combined arthrography and tomography. J Orthop Trauma 1989; 3 (3): 202-5.

Stankewich C J, Swiontkowski M F, Tencer A F, Yetkinler D N, Poser R D. Augmentation of femoral neck fracture fixation with an injectable calcium-phosphate bone mineral cement. J Orthop Res 1996; 14 (5): 786-93.

Witschger P M, Gerhart T N, Goldman J B, Edsberg L E, Hayes W C. Biomechanical evaluation of a biodegradable composite as an adjunct to internal fixation of proximal femur fractures. J Orthop Res 1991; 9 (1): 48-53.

Yetkinler D N, Ladd A L, Poser R D, Constantz B R, Carter D. Biomechanical evaluation of fixation of intra-articular fractures of the distal part of the radius in cadavera: Kirschner wires compared with calcium-phosphate bone cement. J Bone Joint Surg (Am) 1999; 81 (3): 391-9.

Zuckerman J D, Fabian D R, Aharanoff G, Koval K J, Frankel V H. Enhancing independence in the older hip fracture patient. Geriatrics 1993; 48 (5): 76-81.