WHAT IS ALREADY KNOWN ON THIS TOPIC

Antithrombin III is a costly intervention that is widely used for critically ill patients

Four minor meta-analyses of randomised and non-randomised trials in selected populations have previously shown inconclusive evidence on mortality

WHAT THIS STUDY ADDS

Trial sequential analysis showed that there is evidence of absence of beneficial effects (10% mortality reduction or more) of antithrombin III in critically ill patients

Antithrombin III increases the risk of bleeding

significant. This might or might not support the previously generated hypothesis that antithrombin III is beneficial in patients who do not receive adjuvant heparin.[w1] In this subgroup analysis, however, we split one trial[w1] into two "separate trials" with and without concomitant use of heparin. If this trial was not split, the subgroup without adjuvant heparin becomes insignificant. These results could suggest that antithrombin III cannot be recommended for patients without adjuvant heparin, but it might be relevant to explore this further in future trials. The negative interaction between antithrombin III and heparin has been recognised on a molecular level.[3]

Nevertheless, if antithrombin III is used in clinical practice adjuvant heparin should be avoided as the potentially harmful interactions are unclear.[7 8]

Conclusion

We have shown that antithrombin III seems ineffective in any population of critically ill patients regarding mortality and it even increases the risk of bleeding events. Its use in critically ill patients cannot be recommended based on the available evidence, but it may be relevant to explore this further in future trials.

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Hemiarthroplasty or internal fixation for intracapsular displaced femoral neck fractures: randomised controlled trial

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ABSTRACT

Objective To compare the functional results after displaced fractures of the femoral neck treated with internal fixation or hemiarthroplasty.

Design Randomised trial with blinding of assessments of functional results.

Setting University hospital.

Participants 222 patients; 165 (74%) women, mean age 83 years. Inclusion criteria were age above 60, ability to walk before the fracture, and no major hip pathology, regardless of cognitive function.

Interventions Closed reduction and two parallel screws (112 patients) and bipolar cemented hemiarthroplasty (110 patients). Follow-up at 4, 12, and 24 months.

Main outcome measures Hip function (Harris hip score), health related quality of life (Eq-5d), activities of daily living (Barthel index). In all cases high scores indicate better function.

Results Mean Harris hip score in the hemiarthroplasty group was 8.2 points higher (95% confidence interval 2.8 to 13.5 points, P=0.003) at four months and 6.7 points (1.5 to 11.9 points, P=0.01) higher at 12 months. Mean Eq-5d index score at 24 months was 0.13 higher in the hemiarthroplasty group (0.01 to 0.25, P=0.03). The Eq-5d visual analogue scale was 8.7 points higher in the hemiarthroplasty group after 4 months (1.9 to 15.6, P=0.01). After 12 and 24 months the percentage scoring 95 or 100 on the Barthel index was higher in the hemiarthroplasty group (relative risk 0.67, 0.47 to 0.95,

P=0.02. and 0.63, 0.42 to 0.94, P=0.02, respectively). Complications occurred in 56 (50%) patients in the internal fixation group and 16 (15%) in the hemiarthroplasty group (3.44, 2.11 to 5.60, P<0.001). In each group 39 patients (35%) died within 24 months (0.98, 0.69 to 1.40, P=0.92)

Conclusions Hemiarthroplasty is associated with better functional outcome than internal fixation in treatment of displaced fractures of the femoral neck in elderly patients.

Trial registration NCT00464230.

INTRODUCTION

The surgical treatment for displaced intracapsular femoral neck fractures has been controversial for at least 50 years. More surgical complications and reoperations occur after internal fixation than after arthroplasty, but there is no consensus as to which treatment gives the best functional results. Three meta-analyses, including mainly the same randomised controlled studies of the treatment of displaced femoral neck fractures, found reoperation rates after arthroplasty of 7%,[1] 11%,[2] and 11%[3] compared with 40%, 35%, and 33% for internal fixation. Two of the meta-analyses contained analyses of postoperative pain, function, and quality of life, without showing any difference between the treatment groups.[2 3]

We examined treatment with two parallel screws compared with a bipolar cemented hemiarthroplasty with regard to functional outcome and quality of life in the treatment of displaced intracapsular fractures of the femoral neck.

METHODS

Patients—Patients aged 60 years or older who presented with an intracapsular femoral neck fracture with angular displacement in either radiographic plane and who were previously ambulant were eligible for inclusion. Exclusion criteria were being unfit for arthroplasty according to anaesthesiologist, previous symptomatic hip pathology (such as arthritis), pathological fracture, delay of more than 96 hours from injury to treatment, or living outside the hospital's designated area. The follow-up period was 24 months, with scheduled follow-up visits at 4, 12, and 24 months. The surgeon on call performed the randomisation. Recruitment was from September 2002 to March 2004.

Intervention—Patients underwent a Charnley-Hastings bipolar cemented hemiarthroplasty or closed reduction and internal fixation with two parallel cannulated screws (Olmed). The surgeons on call carried out all the operations, with no changes in departmental routines for the study. Spinal anaesthesia was used for both procedures. The hemiarthroplasty patients were given intravenous cefalotin, and patients in both groups were given heparin subcutaneously daily until they could move relatively well. Early mobilisation was encouraged, with weight bearing as tolerated. Both interventions were standard operations in the department before the study.

Objectives and outcomes—Hip function was rated with Harris hip score.[4-6] Primary outcome was the score after 12 months. Health related quality of life was rated by Eq-5d (Euroqol).[7 8] The Barthel index was used to rate ability to perform activities of daily living.[9 10] Complications and reoperations were noted. The surgeon recruiting the patient noted the Harris hip score before the fracture. At follow-up a physiotherapist noted the Harris hip score and a research assistant registered the Eq-5d, Barthel index, and a 12 item abbreviated mini-mental state examination[11]; both were blinded to the intervention. When necessary we used information from nursing home staff and family members for the Harris hip score and the Barthel index.

Statistical methods—Power calculation showed we needed 220 patients, allowing for some mortality and loss to follow-up. We used Pearson's χ^2 for dichotomous variables and *t* tests for Harris hip score, Eq-5d index score, and analyses of continuous variables. See bmj.com for further details.

RESULTS

Follow-up—Of the 445 patients presenting with fracture, 260 were eligible for inclusion and we recruited 222. Details of recruitment and flow of patients during the study can be found on bmj.com.

Demographics and perioperative results—At baseline the groups were similar. Twenty eight surgeons performed a median of five operations each (range 1-26). Nine patients (8%) in the internal fixation group were changed to hemiarthroplasty because of irreducible fractures (eight) or poor screw purchase (one). Duration of surgery, amount of blood loss, and need for blood transfusion were higher in the hemiarthroplasty group. There was no association between time from admission to surgery or surgeon's experience and complications.

Functional outcomes—The functional results for all three scales—Harris hip score, Eq-5d, and Barthel index—favoured the hemiarthroplasty group, although this was not significant at all time points for all scales (table). A subgroup analysis of the patients in the internal fixation group whose fracture healed without complications (n=53) compared with the patients randomised to hemiarthroplasty showed scores in favour of the hemiarthroplasty group at 12 and 24 months. The parallel subgroup comparison of patients from the internal fixation group who underwent reoperation with hemiarthroplasty (n=39) and the entire hemiarthroplasty group showed scores favouring hemiarthroplasty at 4 months. See bmj.com.

Complications, reoperations, and mortality—In the internal fixation group the relative risk of a complication was 3.44 ((5% confidence interval 2.11 to 5.60, P=0.42) and the relative risk of reoperation was 4.20 (2.30 to 7.65, P=0.92). Median time to complication was 137.5 days in the internal fixation group (range 8-730) and 18 days (range 6-730) in the hemiarthroplasty group (P=0.01). Sixteen patients had to have more than one further operation (two to six); 14 of them were in

the internal fixation group (relative risk 6.88, 95% confidence interval 1.60 to 29.55, P=0.002). The 30 day mortality was 7 (6%) in the internal fixation group and 10 (9%) in the hemiarthroplasty group (0.68, 0.27 to 1.73, P=0.42). After 24 months, 39 patients (35%) in each group had died (0.98, 0.6927 to 1.40, P=0.92).

DISCUSSION

In patients with displaced intracapsular femoral neck fractures, hemiarthroplasty results in better hip function, higher health related quality of life, and more independence than internal fixation. The primary outcome measure, the Harris hip score at 12 months, was a mean of 6.7 (95% confidence interval 1.5 to 11.9) points higher in the hemiarthroplasty group.

Strengths and weaknesses

In interpreting the secondary outcomes we made multiple comparisons, increasing the risk of false positive results. Secondly, in some cases where we found significant differences, the confidence intervals are wide and nearly include zero. The trend in favour of hemiarthroplasty as treatment for displaced femoral neck fractures, however, is clear in all the outcome measures, and the Eq-5d visual analogue scale at 24 months was the only score with a non-significant difference in favour of the internal fixation group.

Both interventions were familiar to the surgeons before the study, and both methods are modern and well defined. We achieved a high follow-up rate, and evaluation was performed blinded with recognised assessment scales. It may be perceived as a weakness in our study that a large number of surgeons with varying experience participated. Our rates of complications and reoperations are high but comparable with those seen in previous studies.[1-3 12-14]

Previous studies have not had as unequivocal results. Some studies may have used types of hemiarthroplasty that work less well in more active patients.[1 13 15 16] Several studies show better results for arthroplasty at the early follow-ups but with less or no difference at later time points.[12 14 17-19] This might be because rehabilitation after arthroplasty is faster, but eventually internal fixation patients get to the same level of function. Another explanation might be that the effect of femoral neck fracture is diluted by other diseases and conditions over time. A crossover-like effect, caused by the large number of revisions from internal fixation to arthroplasty combined with loss of statistical power because of mortality, might also weaken the treatment effects at later follow-ups.

Even though the outcome of our study seems convincing, in light of the results of the meta-analyses,[2 3] it is still possible that hemiarthroplasty and internal fixation produce the same functional results. It seems at least highly unlikely, however, that the results are better after internal fixation.

Mortality

One argument in favour of internal fixation may be mortality. A common clinical concern is that a hemiarthroplasty is too extensive an operation for these patients, especially in the acute setting. The available meta-analyses[1-3 20] and our results show a non-significant tendency towards lower mortality in the internal fixation group, but only one previous randomised study found significantly higher mortality in the hemiarthroplasty group.[21] A study powered to detect a difference in mortality would have to be large,

Functional outcomes in patients* after hip fracture according to allocated treatment

	Internal fixation	Hemiarthroplasty	Mean difference or relative risk (95% CI)	P value
Mean (SD) Harris hip score				
At 4 months	59.6 (19.5) (n=89)	67.7 (15.8) (n=84)	8.2 (2.8 to 13.5)	0.003
At 12 months	65.8 (15.9) (n=87)	72.6 (17.5) (n=74)	6.7 (1.5 to 11.9)	0.01
At 24 months	67.3 (15.5) (n=71)	70.6 (19.1) (n=68)	3.3 (−2.5 to 9.2)	0.26
Mean (SD) Eq-5d index score and visual analogue scale				
Index score:				
At 4 months	0.53 (0.29) (n=79)	0.61 (0.30) (n=70)	0.10 (−0.003 to 0.20)	0.06
At 12 months	0.56 (0.33) (n=70)	0.65 (0.30) (n=62)	0.10 (−0.008 to 0.22)	0.07
At 24 months	0.61 (0.31) (n=52)	0.72 (0.23) (n=52)	0.13 (0.01 to 0.25)	0.03
Visual analogue scale:				
At 4 months	53 (18.5) (n=69)	62 (21.0) (n=60)	8.7 (1.9 to 15.6)	0.01
At 12 months	57 (21.6) (n=59)	63 (24.3) (n=54)	6.2 (−2.4 to 14.7)	0.16
At 24 months	60 (18.0) (n=45)	60.0 (21.0) (n=43)	−0.8 (−9.1 to 7.5)	0.84
No (%) of patients with Barthel index score of 95 or 100				
At 4 months	41 (47) (n=88)	40 (50) (n=80)	0.93† (0.68 to 1.27)	0.66
At 12 months	31 (36) (n=87)	39 (53) (n=73)	0.67† (0.47 to 0.95)	0.02
At 24 months	24 (35) (n=69)	36 (53) (n=68)	0.63† (0.42 to 0.94)	0.02

*Number varies because not all information could be obtained for all patients.
†Relative risk.

WHAT IS ALREADY KNOWN ON THIS TOPIC

In patients with displaced femoral neck fractures 30-40% of those treated with internal fixation need a further operation, whereas hemiarthroplasty has a reoperation rate of 5-10%

Meta-analyses have failed to show a difference in functional results

WHAT THIS STUDY ADDS

Hemiarthroplasty gave better functional results, higher health related quality of life, and more independence than internal fixation

Better results were found for hemiarthroplasty even when compared with patients with internal fixation that healed without complications

requiring several thousand patients,[1 2] but if the tendency of an increased early mortality of 3-4% of patients after arthroplasty is a true incidence, it would be of considerable importance

We have shown that a bipolar hemiarthroplasty with a well documented cemented femoral stem gives superior results compared with fixation with two parallel screws.

Kenneth Nilsen, Wender Figved, Evind Kaare Osnes, Bjørn Robstad, Marte T Magnusson, Willimijn Vervaat, Åsa Axelsson, Vibeke Lambert-Grave, and Helene Søberg participated in the collection of data.
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