Department of Clinical Science and Education
Södersjukhuset, Section of Orthopedics,
Karolinska Institutet
Stockholm
Sweden

TREATMENT OF DISPLACED PROXIMAL HUMERAL FRACTURES IN ELDERLY PATIENTS

PER OLERUD

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To Ulrika,
Fredrik and Charlotta

CONTENTS

ABSTRACT

The optimal treatment for patients with displaced fractures of the proximal humerus, especially elderly patients with osteoporosis, is still controversial. For the 2- and 3-part fractures according to the Neer classification, there is a trend towards more frequent surgical interventions with modern locking plates. For the more comminuted 4-part fracture with a higher risk for avascular necrosis, a primary hemiarthroplasty (HA) has been the accepted treatment. The alternative treatment for these fractures is non-operative with a short immobilization period and early physiotherapy.

The latest Cochrane review regarding this topic concludes that there is insufficient evidence from randomized controlled trials (RCTs) to determine which interventions are the most appropriate for the management of different types of fractures. It is also stated that future trials should use validated outcome measures, including patient-assessed functional outcomes such as health-related quality of life (HRQoL). However, due to their design, quality-of-life instruments may be less sensitive for detecting small but yet important changes, i.e. they may have a limited responsiveness.

In a prospective cohort study with a 2-year follow-up, 50 elderly patients with a displaced 2-part fracture of the proximal humerus were treated with open reduction and internal fixation with a locking plate. The result showed that locking plates appear to be a good treatment alternative with an acceptable complication rate and an acceptable functional outcome.

In an RCT with a 2-year follow-up, 60 elderly patients with a displaced 3-part fracture of the proximal humerus were allocated to treatment with open reduction and internal fixation with a locking plate or non-operative treatment. The results of the study indicated an advantage in functional outcome and HRQoL in favor of the locking plate as compared to non-operative treatment, but at a cost of additional surgery in 30% of the patients. The main advantage of the locking plate appeared to be an improved range of motion (ROM).

In an RCT with a 2-year follow-up, 55 patients with a displaced 4-part fracture of the proximal humerus were allocated to treatment with a primary HA or non-operative treatment. The results of the study demonstrated a significant advantage in quality of life in favor of HA as compared to non-operative treatment. The main advantage of HA appeared to be less pain, while there were no differences in ROM.

145 patients with a displaced proximal humeral fracture were included in a study with the aim to evaluate the responsiveness of the EQ-5D instrument. The EQ-5D displayed good internal and external responsiveness and can be recommended for use as a quality-of-life measure in patients with this particular injury.

An additional conclusion of the studies was that, regardless of primary treatment, a displaced fracture of the proximal humerus results in a substantial negative effect upon the patients' HRQoL.

LIST OF PUBLICATIONS

This thesis is based on the following papers, which are referred to in the text by their Roman numerals (*Studies I–IV*)

I. QUALITY OF LIFE AND FUNCTIONAL OUTCOME AFTER A 2-PART PROXIMAL HUMERAL FRACTURE: A PROSPECTIVE COHORT STUDY ON 50 PATIENTS TREATED WITH A LOCKING PLATE.
Olerud P, Ahrengart L, Söderqvist A, Saving J, Tidermark J.
Journal of Shoulder and Elbow Surgery 2010; 19: 814-822.

II. INTERNAL FIXATION VERSUS NONOPERATIVE TREATMENT OF DISPLACED 3-PART PROXIMAL HUMERAL FRACTURES IN ELDERLY PATIENTS: A RANDOMIZED CONTROLLED TRIAL.
Olerud P, Ahrengart L, Ponzer S, Saving J, Tidermark J.
Journal of Shoulder and Elbow Surgery 2011, E-pub March 23.

III. HEMIARTHROPLASTY VERSUS NONOPERATIVE TREATMENT OF DISPLACED 4-PART PROXIMAL HUMERAL FRACTURES IN ELDERLY PATIENTS: A RANDOMIZED CONTROLLED TRIAL.
Olerud P, Ahrengart L, Ponzer S, Saving J, Tidermark J.
Accepted for publication in the Journal of Shoulder and Elbow Surgery.

IV. RESPONSIVENESS OF THE EQ-5D IN PATIENTS WITH PROXIMAL HUMERAL FRACTURES.
Olerud P, Tidermark J, Ponzer S, Ahrengart L, Bergström G.
Submitted.

LIST OF ABBREVIATIONS

ADL	Activities of daily living
AUC	Area under the curve
AVN	Avascular necrosis
BC	Before Christ
BMD	Bone mineral density
BMI	Body mass index
CT	Computerized tomography
DASH	Disabilities of the arm, shoulder and hand score
DXA	Dual X-ray absorptiometry
EC	External criterion
EQ-5D	The five-dimensional scale of the EuroQol
Fx	Fracture
GT	Greater tubercle
HA	Hemiarthroplasty
HRQoL	Health-related quality of life
LP	Locking plate
LT	Lesser tubercle
NO	Non-operative
OA	Osteoarthritis
OTA	Orthopaedic Trauma Association
QoL	Quality of life
ORIF	Open reduction and internal fixation
RCT	Randomized controlled trial
ROC	Receiver operating characteristic
ROM	Range of motion
SPMSQ	Short portable mental status questionnaire
SRM	Standardized response mean
VAS	Visual analogue scale
QUALYs	Quality-adjusted life years
95% CI	95% confidence interval

INTRODUCTION

HISTORICAL BACKGROUND

The first documentation of treatment of a proximal humeral fracture was "published" in 460 BC[11] by Hippocrates, who described a method of weight traction to aid bone healing. The final result is unknown.

Little was written about this subject until the latter part of the 19th century when some papers discussed closed reduction followed by a period of immobilization and later, range of motion exercises. This seemed to be an adequate treatment for non-displaced fractures, but the outcome was bad for displaced fractures.

The first surgical treatment of a fracture dislocation of the proximal humerus reported in the literature was performed in 1884.[22] The humeral head was removed and the patient was ready for dismissal 13 days later when he had an attack of diarrhoea from which he died 1 week later.

The first osteosynthesis was performed in 1890. The surgeon "replaced" the head in the glenoid cavity and "pegged" the fracture. The patient survived and primary fracture healing was achieved with a fair clinical result.[22]

During the first decades of the 20th century the surgical technique was further developed. Several different implants were used such as wires, screws and suture materials. The treatment was accompanied by a high rate of infections, mal-unions, avascualar necrosis (AVN) and osteoarthritis (OA), which reduced the general enthusiasm.

In the early 1950s, when antibiotics had become available, methods of intramedullary nailing were developed.[91,100,109] The next step was taken at the end of 1960s when the AO Group in Switzerland developed devices including plates for internal fixation. They advocated open reduction and stable internal fixation to allow early mobilization. Initially, good results were presented, but the results were difficult to reproduce, especially in elderly patients. One reason for this was the tendency for loosening of the hardware in osteoporotic bone. As a reaction to this, earlier techniques, such as minimal osteosynthesis and non-operative treatment, regained their popularity.

During the past decade, plates with angular stable screws or pegs, with the potential to better preserve the reduction, especially in osteoporotic bone, have been developed. Their popularity has been tremendous and they have almost become the golden standard when orthopedic surgeons choose an implant for internal fixation.

In his classic work from 1970, Charles Neer[87] reported promising results after hemiarthroplasty (HA) in patients with fractures of the proximal humerus. However, the good results were difficult to reproduce. During the last two decades several improvements in the prosthetic design have been made, but the results regarding functional outcome is still rather disappointing.[89] More recently, some surgeons have started to use the reversed prosthesis in the most difficult cases, but there are, so far, very few papers reporting the outcome, especially in the longer time perspective.

EPIDEMIOLOGY

Fractures of the proximal humerus account for approximately 6% of all fractures.[35,62] The fracture is the third most common fracture in elderly patients after fractures of the hip and distal radius.[4] The overall incidence increased rapidly until the end of the 1990s,[9,69] whereupon it seems to have stabilized and is now reported to be approximately 250/100 000 persons per year.[8]

Osteoporosis is a significant factor for these fractures.[62,99] The incidence in younger people is quite low, but it rapidly increases with age.[37] Early in life the incidence is higher for men compared to women, probably as a result of the higher rate of high-energy trauma in younger men. Later in life, the incidence is higher in women as a result of their more fragile skeleton. In the age group 80 years and older the female: male ratio is approximately 4:1.[37,99] The calculated risk for having a proximal humeral fracture is 1.6% for a 75-year-old woman and 5.0% for a 90-year-old woman.[4]

CLASSIFICATION

In managing fractures in general it is important to have a reliable classification system. The system should be sensitive enough to identify the different fracture patterns and specific enough to support an accurate diagnosis. Moreover, the classification system should preferably be comprehensive enough to be used in clinical outcome studies, but also simple enough to be used as a tool for clinical decision-making.

Historically, there have been a lot of attempts to classify the fractures of the proximal humerus. The first known attempt was made in 1896 by Kocher,[73] who based his classification on the level of the fracture. Other authors used the mechanism of injury,[38] the amount of contact between the fragments,[43] the degree of displacements[72] and the vascular status of the articular fragments.[65]

The two most widely used classifications today are the AO/OTA classsification[81,85] and the Neer classification.[86-88]

The AO/OTA classification[81,85] is based on the complexity of the fracture and, for the proximal humerus, it is also based on the vascular anatomy. The fractures are divided into 3 different categories: *Group A*, extra-articular, unifocal fracture, with an intact vascular supply; *Group B*, partially extra-articular, bifocal, with possible vascular compromise; and *Group C*, articular, with a high likelihood of vascular compromise.[97] Each group is subdivided into 3 categories, from less to more serious lesions, and each of the subgroups is further subdivided into 3 sub-subgroups, giving the classification system 27 different subgroups.

The Neer classification[86-88] is a development of Codman's classification from 1934[29] based on the 4 different anatomical fragments of the proximal humerus, i.e. the anatomical head, the greater tuberosity, the lesser tuberosity and the shaft.

Charles Neer stressed the importance of the biomechanical forces and the degree of displacement for more complex fractures. He suggested, based on his studies, that when any one of the 4 fragments was displaced more than 10 mm and/or angulated more than 45 degrees, the fracture should be regarded as displaced. Consequently, if any of the fragments were displaced less than this, the fragment should not be regarded as a separate fracture fragment. The system was further developed by Neer himself in 1975

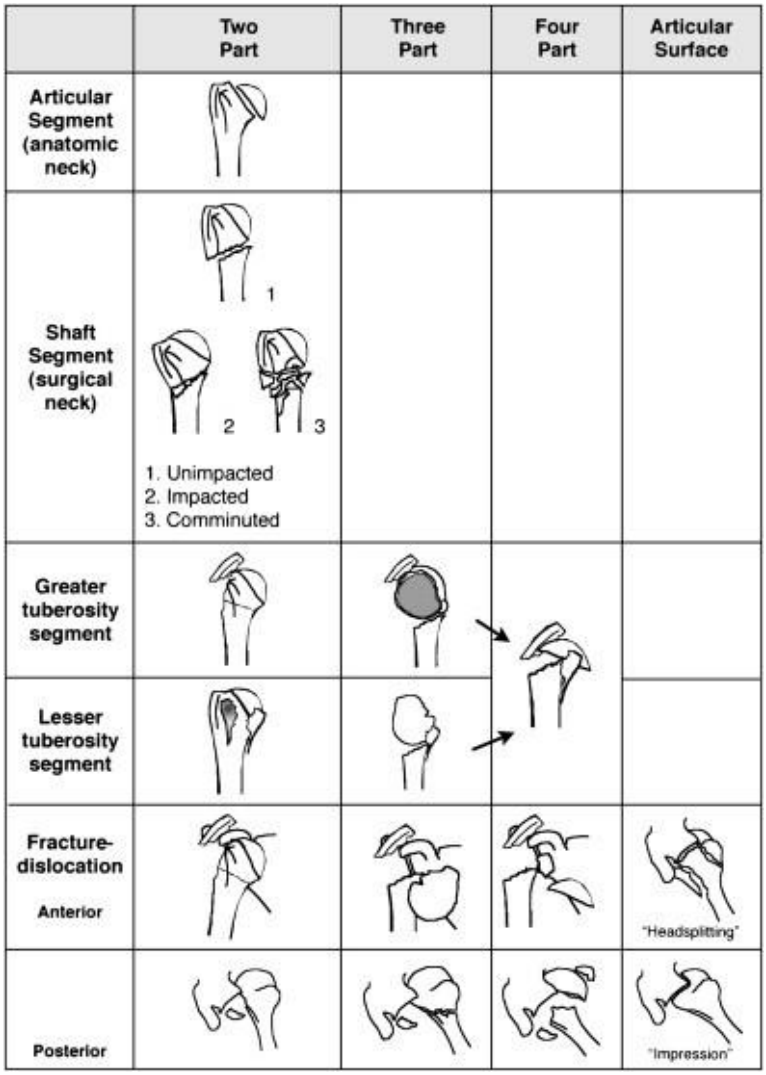
and in 2002.[88] The classification is easy to learn and has been widely used in both clinical practice and in outcome studies.

The following fracture types can be identified (**Figure 1**):

- The 1-part fracture or undisplaced fracture.
- The anatomical neck fracture.
- The 2-part fracture; a displaced surgical neck fracture or a displaced fracture of the greater or lesser tuberosity.
- The 3-part fracture; a displaced surgical neck fracture with a displaced fracture of the greater or lesser tuberosity.
- The 4-part fracture; a displaced surgical neck fracture with a displaced fracture of the greater and lesser tuberosity.
- The fracture-dislocation and head-splitting fractures.

Figure 1. The Neer Classification system.

From *Robinsson et al: Classification and Imaging of Proximal Humerus Fractures. Orthop Clin North Am;2008; 39:393-403.*



Both the Neer and AO/OTA classification have been criticized for poor intra- and inter-observer reliability.[102-103] Attempts to improve the reliability of the classifications by using computerized tomography (CT) have given mixed results.[10,25,84 ,103] The most recent study by Brunner et al.[20] reported moderate intra- and interobserver reliability for both classifications with conventional radiographs and 2-dimensional CT scans. The study also showed that 3-dimensional volume-rendered CT scans can improve the accuracy of both classification systems. This technique improved the interobserver reliability of both systems to good and the intraobserver reliability to good for the AO/OTA method and to excellent for the Neer classification.

Most studies in the modern literature are based on the Neer classification and this classification has been used in the studies in this thesis. The following fracture types have been studied: the 2-part fracture, a displaced surgical neck fracture (*Studies I* and *IV);* the 3-part fracture, a displaced surgical neck fracture with a displaced fracture of the greater or lesser tuberosity (*Studies II* and *IV)*; the 4-part fracture, a displaced surgical neck fracture with a displaced fracture of the greater and lesser tuberosity (*Studies III* and *IV*).

TREATMENT

50 – 80% of the proximal humeral fractures are undisplaced[9,37,86] and can be treated non-operatively.[48,75,107] There is also general agreement that the indication for surgery is almost absolute in fractures where there is no bony contact between the head and shaft fragments, in fracture dislocations and in head-splitting fractures. The valgus-impact fracture[36,94] is a special type of a 4-part fracture where the medial line between the head and the shaft is not broken and, consequently, the medial vascular integrity is preserved and the risk of AVN is lower than in the normal 4-part fracture, and the general opinion is that this fracture should preferably be treated with internal fixation and not HA.[67,94]

Operative treatment of displaced fractures in young patients is not controversial due to their better bone quality, higher functional demands and lower surgical risk.

The main controversy regarding the treatment of proximal humeral fractures pertains to elderly patients with varying degrees of osteoporosis in displaced fractures sustained after low-energy trauma.

The 2-part fracture

The 2-part surgical neck fracture accounts for approximately 10–15% of all proximal humeral fractures.[37] N on-operative treatment may suffice for fractures with moderate displacement,[107] but it is uncertain whether this is good enough in patients with higher functional demands and in those with more displaced fractures. Various techniques for internal fixation have been used in the past, e.g. conventional plating or nailing,[98] but the complication and reoperation rates have been unsatisfactory. Locking plates, i.e. plates with angular stable screws or pegs, are theoretically promising for overcoming the problem of fixation in osteoporotic bone and recent studies have shown better results, although there are still considerable problems.[12,21,57,61]

The 3-part fracture

The 3-part proximal humeral fracture accounts for approximately 10% of all proximal humeral fractures.[37] The availability of modern orthopedic implants such as locking plates with improved purchase in osteoporotic bone has contributed to a trend towards more frequent surgical interventions. Open reduction and internal fixation with locking plates have the potential to restore the anatomy in an excellent manner, but there is a risk of complications related to both the implant[21,45,57,61] and the surgery itself.[28] Conservative treatment with short immobilization and early physiotherapy is a non-invasive, simple and safe option and acceptable results after non-operative treatment have been reported.[37,58,111]

There are only two previous randomized controlled trials (RCTs) comparing internal fixation with non-operative treatment in patients with proximal humeral fractures. First, the study by Zyto et al.,[112] who in 1997 reported the outcome of non-operative treatment compared with tension band wiring in 40 patients with displaced 3- and 4-part fractures. Second, the study by Fjalestad and co-workers[47] including 50 patients with displaced 3- and 4-part fractures, comparing non-operative treatment with a locking plate with a 12-month follow-up. However, the single paper from this trial published so far is focused on quality-adjusted life years (QALYs) and societal costs. No differences regarding these aspects were reported.

The 4-part fracture

The 4-part fracture accounts for approximately 3% of all proximal humeral fractures[37] and is considered to be one of the most difficult to treat. Charles Neer stated as early as in 1970s that 4-part fractures should be treated with a fracture arthroplasty and reported overall good results.[87] More recent authors have found it difficult to reproduce these results and the functional outcome reported after a primary fracture arthroplasty has varied.[1,5,52,76,92] In spite of this, a primary HA has been the accepted treatment for 4-part fractures in elderly osteoporotic patients who are fit for surgery and can be expected to be able to participate in a postoperative rehabilitation programme.[110] An alternative treatment is a non-operative approach with a short immobilization period and early physiotherapy. This is a simple and safe option and acceptable results have been reported.[77,111]

There is only one previous randomized controlled trial (RCT) comparing primary HA with non-invasive treatment in patients with proximal humeral fractures.[105] In that study, published in 1984, Stableforth compared an uncemented Neer prosthesis with closed manipulation in 32 patients with a displaced 4-part fracture. The reported outcome regarding pain and function favored HA. However, the validity of these results has later been questioned, mainly due to the considerable variation in follow-up time and the lack of validated outcome measures, as well as questions regarding the method of randomization.[56]

QUALITY OF LIFE

In studies on the treatment of injuries and diseases of the shoulder, the outcome is frequently reported using such basic measures as range of motion, fracture healing and the need for revision surgery. Additionally, the functional outcome is often reported

using region-specific outcome instruments such as the Constant[33-34] and DASH (Disabilities of the arm, shoulder and hand)[63] scores. A major disadvantage of these specific instruments is that they do not allow a comparison of the outcomes in patients with different or multiple injuries/diseases, which, for instance, is necessary in cost-effectiveness analyses in healthcare evaluations.[14] To partly overcome this disadvantage, instruments for assessing the health-related quality of life (HRQoL) have been developed. Reporting the patients' own assessment of their HRQoL will contribute to a more complete picture of how the injury/disease influences all areas of life and thereby enhance our ability to improve future healthcare programmes.

Quality of Life (QoL) is a term used to refer to an individual's total well-being. QoL in relation to HRQoL is a broader concept than personal health and also takes social well-being into account. The concept of QoL includes functional ability, the degree and quality of social and community interaction, psychological well-being, somatic sensation and life satisfaction.[16] The definition of health also clearly states that health is more than just the absence of disease, illness and sickness. It also includes dimensions of physical health, psychological well-being and life satisfaction. HRQoL focuses more on the impact of a perceived health state as a result of an injury or illness. However, the terms QoL and HRQoL are often used interchangeably.

Responsiveness

Due to their design, the quality-of-life instruments may be less sensitive for detecting small, but yet important, changes, i.e. they may have a limited responsiveness.[18,40] Responsiveness is considered to be an important characteristic of patient-based outcome measures[46] and two major aspects of responsiveness can be described, namely internal and external responsiveness.[64] Internal responsiveness refers to situations in which the respondents are measured at at least two points in time, between which it can be expected that a change has taken place in the studied variable or variables. External responsiveness employs an external criterion (EC) representing a standard with which the instrument whose responsiveness is to be evaluated is compared, e.g., by using correlation analyses or ROC curves.[40] The determining factor here is the association between the EC and the other measure, which implies that the EC must represent the qualities the researcher wishes to capture with the new measure. Use of both forms of responsiveness has been recommended to obtain a comprehensive and accurate picture of the responsiveness of a measure.[64]

The EQ-5D

The EQ-5D[19] is a non-disease-specific instrument for describing and evaluating the HRQoL. The instrument comprises several dimensions and can be used across different patient populations. Moreover, the EQ-5D incorporates preferences for evaluating the health states and produces a single index (EQ-5D $_{\text{index}}$ score) that can also be used to construct quality-adjusted life years (QUALYs). The reliability and validity of the EQ-5D have been evaluated in different patient populations and, in a recent review of the assessment of quality of life among older people in which a number of instruments were evaluated, it was concluded that there was 'good evidence' for the validity, reliability and responsiveness of the EQ-5D.[60] The responsiveness of the EQ-5D has not been evaluated previously for patients with a proximal humeral fracture.

CURRENT EVIDENCE

The latest Cochrane review regarding the treatment of proximal humeral fractures[56] concludes that there is insufficient evidence from RCTs to determine which interventions are the most appropriate for the management of different types of proximal humeral fractures. The limited evidence available does not confirm that surgery is preferable to conservative treatment, and complications associated with surgery need to be considered. It is also stated that future RCTs should use validated outcome measures, including patient-assessed functional outcomes.

AIMS OF THE STUDIES

STUDY I

The aim of the study was to report the outcome after a displaced 2-part fracture of the proximal humerus in elderly patients treated with a locking plate in a prospective cohort study with a 2-year follow-up. The primary aim was to report the HRQoL and our secondary aims were to report the functional outcome according to the Constant and DASH scores.

STUDY II

The aim of the study was to report the outcome after a displaced 3-part fracture of the proximal humerus in elderly patients allocated to treatment with a locking plate or non-operative treatment in an RCT with a 2-year follow-up. The primary aim was to report the HRQoL according to the EQ-5D and the secondary aims were to report the functional outcome according to the Constant and DASH scores.

STUDY III

The aim of the study was to report the outcome after a displaced 4-part fracture of the proximal humerus in elderly patients allocated to treatment with a hemiarthroplasty or non-operative treatment in an RCT with a 2-year follow-up. The primary aim was to report the HRQoL according to the EQ-5D and our secondary aims were to report the functional outcome according to the Constant and DASH scores.

STUDY IV

The aim of this study was to evaluate the internal and external responsiveness of the EQ-5D, i.e. the instrument's ability to capture clinically important changes in patients with a proximal humeral fracture within the context of a prospective study.

PATIENTS

ETHICS

All studies were conducted according to the Helsinki Declaration and each protocol was approved by the local ethics committee. All patients gave their informed consent to participate.

INCLUSION CRITERIA AND FOLLOW-UP

STUDY I

50 patients with an acute displaced 2-part fracture of the surgical neck of the humerus according to the classification of Neer[86-87] treated with open reduction and internal fixation with a locking plate were included (**Table 1**). The fracture inclusion criteria, based on conventional radiographs and CT, were a displacement of the shaft of > 50% of its width and/or > 45º of angulation in relation to the head fragment. A minimally displaced/undisplaced fracture of the greater and/or lesser tubercles, i.e. not fulfilling the criteria to be considered a separate fracture segment according to Neer[86-87] was not considered to be an exclusion criterion. The patient inclusion criteria were age 55 years or older, a fracture sustained after a low-energy trauma, no previous shoulder problems, independent living conditions and no severe cognitive dysfunction. The patients were summoned at 4 (mean 4.2), 12 (mean 12.6) and 24 (mean 25.8) months. At the final follow-up, 7 patients (14%) were deceased and none was lost to follow-up.

STUDY II

60 patients with an acute displaced 3-part fracture of the surgical neck of the humerus according to the classification of Neer[86-87] were allocated to treatment with open reduction and internal fixation (ORIF) with a locking plate or non-operative treatment (**Table 1**). The fracture inclusion criteria, based on conventional radiographs and CT, were a displacement of the shaft of more than 10 mm and/or > 45º of angulation in relation to the head fragment, combined with a displacement of the greater or lesser tubercle of more than 10 mm in relation to the head fragment. A minimally displaced/undisplaced fracture of the other tubercle, i.e. not fulfilling the criteria to be considered a separate fracture segment according to Neer, was not considered to be an exclusion criterion. The patient inclusion criteria were age 55 years or older, a fracture sustained after a low-energy trauma, no previous shoulder problems, independent living conditions and no severe cognitive dysfunction. One patient (3%) in the non-operative group opted to be excluded from the study after randomization and 1 (3%) patient in the locking plate group was treated with a primary HA. According to the radiological examinations, this patient had a 3-part fracture with a displaced greater tubercle and a minimally displaced lesser tubercle (2 mm), but at surgery a displacement of both tubercles exceeding 10 mm was diagnosed, i.e. it was a true 4-part fracture according to the Neer classification. The patients were summoned at 4 (mean 4.2), 12 (mean 12.3) and 24 (mean 25.3) months. At the final follow-up 2 patients (7%) in each group were deceased and 1 patient (3%) in each group was lost to follow-up.

STUDY III

55 patients with an acute displaced 4-part fracture of the surgical neck of the humerus according to the classification of Neer[86-87] were allocated to treatment with a primary HA or non-operative treatment (**Table 1**). The fracture inclusion criteria, based on conventional radiographs and CT, were a displacement of the shaft of more than 10 mm and/or > 45º of angulation in relation to the head fragment, combined with a displacement of the greater and lesser tubercle of more than 10 mm in relation to the head fragment. The patient inclusion criteria were age 55 years or older, a fracture sustained after a low-energy trauma, no previous shoulder problems, independent living conditions and no severe cognitive dysfunction. The patients were summoned at 4 (mean 4.3), 12 (mean 12.7) and 24 (mean 26.6) months. At the final follow-up 3 patients (11%) in the HA group and 2 patients (7%) in the non-operative group were deceased. 1 patient (4%) in the non-operative group was lost to follow-up.

STUDY IV

The 165 patients from *Studies I–III* with an acute proximal humeral fracture were included in a prospective study; 50 patients with a 2-part fracture[86-87] treated with a locking plate (*Study I)*, 60 patients with a 3-part fracture[86-87] randomized to non-operative treatment or treatment with a locking plate (*Study II*) and 55 patients with a 4-part fracture[86-87] randomized to non-operative treatment or treatment with a primary HA (*Study III*) (**Table 1**). Additional inclusion criteria were age 55 years or older, a fracture sustained after a low-energy trauma, no previous shoulder problems, independent living conditions and no severe cognitive dysfunction. One patient opted to be excluded from the study after randomization. At the 4-month follow-up 5 patients were deceased, 5 were lost to follow-up and 3 had missing values for the EQ-5D and DASH. At the 12-month follow-up 8 patients were deceased, 6 were lost to follow-up and 1 had a missing value for the EQ-5D. In summary, the 145 patients that attended both follow-ups and had answered the EQ-5D and DASH questionnaires on both follow-up occasions constituted the study group.

Table 1. Patient inclusion algorithm for all studies.

Study 1	**Study II**		**Study III**		**Study IV**
n = 50	**n = 60**		**n = 55**		**n = 145**
2-part fracture	3-part fracture		4-part fracture		The 145 patients who attended both follow-ups and had answered the EQ-5D and DASH questionnaires on both follow-up occasions
Locking plate	Non-operative treatment	Locking plate	Non-operative treatment	Hemi-arthroplasty	
n = 50	n = 30	n = 30	n = 27	n = 28	n = 145

METHODS

AGE AND GENDER

All patients were 55 years old or older and had a displaced fracture of the proximal humerus. The mean age in *Study I* was 75 years with 80% of the patients being women; in *Study II* the mean age was 74 years with 81% being women and in *Study III* the mean age was 77 years with 86% being women. In *Study IV*, including patients from *Studies I–III*, the mean age was 75 years with 84% being women

RANDOMIZATION

The randomization procedures in *Studies II* and *III* were performed with independently prepared, numbered, opaque and sealed envelopes.

FRACTURE CLASSIFICATION

All patients included had a displaced fracture of the proximal humerus. The fractures were classified according to the Neer's classification system **(Figure 1)**.[86-88]

Originally this classification is based solely on conventional radiographs. In order to improve the precision, we performed a CT-scan in all patients.[25] For further presentation and discussion of the classification, please see the heading Introduction, subheading Classification.

ANAESTHESIOLOGICAL ASSESSMENT

All patients were examined and cleared by an anaesthetist before inclusion. The assessment included a decision as to whether the patient was fit enough for the planned treatment modalities. Consequently, in the randomized *Studies II* and *III* the assessment included a decision as to whether the patient was fit enough for both randomization procedures.

COGNITIVE FUNCTION

Cognitive function was assessed with the Short Portable Mental Status Questionnaire (SPMSQ).[93] This 10-item mental test (**Table 2**) classifies cognitive function into 4 categories: 8–10 correct answers = cognitive function intact; 6–7 correct answers = cognitive function mildly impaired; 3–5 correct answers = cognitive function moderately impaired and 0–2 correct answers = cognitive function severely impaired. Only patients without severe cognitive function (SPMSQ $\geq$ 3) were included.

Table 2. SPMSQ.

1.	What is the date today?	Right / Wrong
2.	What day of the week is it?	Right / Wrong
3.	What is the name of this place?	Right / Wrong
4.	What is your telephone number or alt. street address?	Right / Wrong
5.	How old are you?	Right / Wrong
6.	When were you born?	Right / Wrong
7.	Who is the prime minister now?	Right / Wrong
8.	Who was the prime minister before him?	Right / Wrong
9.	What was your mother's maiden name?	Right / Wrong
10.	Subtract 3 from 20 and keep subtracting 3 from each new number all the way down.	Right / Wrong

ADL

The activities of daily living (ADL) status was assessed using the Katz index.[70] This index is based on an evaluation of the functional independence or dependence of patients in bathing, dressing, going to the toilet, transferring, continence and feeding. ADL index A indicates independence in all 6 functions and index B independence in all but 1 of the 6 functions. Indexes C-G indicate dependence in bathing and additionally 1 to 5 more functions.

LIVING CONDITIONS

Only patients from independent living conditions, i.e. own home, old people's home or block of service flats were included.

DUAL X-RAY ABSORPTIOMETRY

Dual-emission X-ray absorptiometry (DXA) with a Lunar$^{(R)}$ densitometer was used to calculate bone mineral density (BMD). Osteoporosis was defined as a T-score of more than 2.5 SD below the mean value for young adults, according to the WHO definition.[68]

RANGE OF MOTION

Range of motion (ROM) was measured with a goniometer. The patients were sitting with their arms free. Flexion was estimated in the sagittal plane and abduction in the frontal plane.

PAIN

Pain was assessed on a visual analogue scale (VAS, 0–100; 0 = no pain; 100 = worst possible pain).[82]

CONSTANT SCORE

The Constant score[33-34] is a scoring system for measuring shoulder function regardless of the diagnosis. The normal population values depend on age, gender and the activity level of the patient.[32] The best possible score is 100 and includes an assessment of shoulder function in 4 dimensions: pain (15), activities of daily living (20), range of motion (40) and strength (25) (**Table 3**). Isometric muscle strength was assessed by means of a Nottingham Mecmesin Myometer (Mecmesin, Nottingham, United Kingdom). With regard to the strength assessment, we followed the recommendations of Constant and Gerber,[33] i.e. patients who were unable to achieve the test position of 90° were assigned a strength score of 0.

Table 3. The Constant score.

	Dimension	Min	Max
I	Pain	0	15
II	Activties of daily living	0	20
III	Range of motion	0	40
IV	Strength	0	25
	Total score	0	100

DASH SCORE

The DASH[63] questionnaire is a region-specific outcome instrument developed as a measure of upper extremity disability and symptoms. The main part, the 30-item disability/symptom scale, was used in this study. The questionnaire includes questions regarding the degree of difficulty experienced to perform different physical activities due to arm/shoulder/hand problems (21 items), the severity of each of the symptoms pain, activity-related pain, tingling, weakness and stiffness (5 items) and the impact upon social activities, work, sleep and self-image (4 items). The scores from each of the items are used to calculate a scale score (DASH score) ranging from 0 (no disability) to 100 (most severe disability). The score is well validated [7] and the Swedish version of DASH has been shown to have good reliability, validity and responsiveness.[3,54]

QUALITY OF LIFE

Quality of life was assessed with the EuroQol.[19] The EuroQol consists of 4 components, the health status part (EQ-5D), a visual analogue scale (EQ-VAS), the valuation part and background data. The first part, the 5-dimensional scale (EQ-5D), was used in the studies. The EQ-5D is a standardized non-disease-specific instrument that measures the quality of life in 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension is divided into 3 degrees of severity: no problem, some problem and major problems.

We used the preference scores (EQ-5D $_{index}$ scores) generated from a large UK population (UK EQ-5D Index Tariff)[42] when calculating the scores for our study populations. A value of 0 indicated the worst possible health state and a value of 1 indicated the best possible health state. This is a divergence from the UK EQ-5D Index

Tariff where some health states were given negative scores. However, the appropriate scaling of negative scores is controversial[79] and the same approach was used when generating the values for an age-matched Swedish population.[24]

All studies included an assessment of the patients' HRQoL the week before the fracture. To validate the method of rating the prefracture HRQoL and to analyze recall bias, the EQ-5D $_{index}$ scores prior the fracture were compared with those of the age-matched Swedish reference population[24] (**Table 4**).

In *Study I* (mean age 75 years, 80% being female) the prefracture EQ-5D $_{index}$ score was 0.86.

In *Study II* (mean age 74 years, 81% being female) the prefracture EQ-5D $_{index}$ score was 0.85.

In *Study III* (mean age 77 years, 86% being female) the prefracture EQ-5D $_{index}$ score was 0.87.

In *Study IV* with patients recruited from *Studies I–III* (mean age 75 years, 84% being female) the prefracture EQ-5D $_{index}$ score was 0.86.

Table 4. The EQ-5D$_{index}$scores for an age matched Swedish reference population.

	EQ-5D$_{index}$scores		
Age (years)	**60–69**	**70–79**	**80–88**
Total	0.80	0.79	0.74
Male	0.83	0.81	0.74
Female	0.78	0.78	0.74

ASSESSMENT OF OUTCOME

In *Studies I–III* the final 24-month follow-up was performed by an independent orthopedic surgeon not previously involved in the treatment. In the outcome analyses in *Studies II* and *III* all patients remained in their randomization group regardless of secondary procedures according to the intention-to-treat principle.

RESPONSIVENESS

The responsiveness of the EQ-5D was evaluated in *Study IV*. Internal responsiveness was expressed using the observed change and the standardized response mean (SRM) in relation to the change in the EQ-5D $_{index}$ score between prefracture value (baseline) and the 4-month follow-up. External responsiveness was expressed by employing the DASH-score as an external criterion (EC). According to recommendations from earlier research, a minimally important difference (MID) of the DASH score was considered to be ≥ 10 points.[54,101] By using the DASH change scores between the 4- and 12 months follow-up, 4 groups of patients were constructed, which were: Clearly improved patients reported an improvement in the DASH score of ≥ 10 points, marginally improved patients had positive (improvement) change scores of less than 10 points, marginally deteriorated patients had negative change scores of less than 10 points and clearly deteriorated patients reported negative change scores of ≥ 10 points

on the DASH. Two methods were used to evaluate the external responsiveness. Firstly, by employing receiver operating characteristic (ROC) curves[40] to calculate the sensitivity and the "false positive rate" (1 – specificity) based on the change scores (4-month follow-up – 12-month follow-up) from the EQ-5D $_{index}$ score. The above-presented EC was used in the ROC analyses. The ROC curves demonstrate the ability of the change scores to discriminate between patients with different dichotomized outcomes. The proposed hypothesis was that the EQ-5D $_{index}$ score should be able to significantly discriminate between the outcomes according to the EC. Comparisons of groups with differences of at least ≥ 10 points on the EC were made.

Secondly, logistic regression was employed to produce a relative estimate of how much variance in the EC could be explained by the change scores (4-month follow-up – 12 month follow-up) from the EQ-5D, i.e., how much a one-point alteration in the EQ-5D change scores influenced the risk of belonging to a defined outcome (the term "risk" is applied here in a statistical sense and no casual relationship between the change scores and the EC is intended).

Finally, a correlation analysis of the change scores from the EQ-5D and the DASH (4-month follow-up – 12-month follow-up) was performed using Spearman's rho test. The direction of the correlation should be positive and the strength of the coefficient was predicted to be at least ≥ 0.30. (Please, also see Statistical Methods.)

TREATMENT MODALITIES

Non-operative (conservative) treatment

Patients randomized to non-operative treatment (*Studies II* and *III*) had their arm immobilized in a sling for 2 weeks and after that they were allowed to use it at their own convenience as long as they adhered to the rehabilitation regimen. After 2 weeks the patients were referred to a physiotherapist and pendulum exercises and passive elevation/abduction up to 90 degrees was started, and after 4 weeks the patients were allowed a free active ROM.

Locking plate

All patients were given 2 g cloxacillin (Ekvacillin®, AstraZeneca, Södertälje, Sweden) preoperatively, followed by 2 additional doses during the first 24 hours

Internal fixation with a locking plate (*Studies I* and *II*) was performed in a modified beach-chair position utilizing a deltopectoral approach and with the aid of an X-ray image intensifier. The Philos® plate (Synthes, Stockholm, Sweden) was used in all patients (**Figure 2).** This plate is anatomically shaped and is recommended to be placed at least 8 mm distal to the upper end of the greater tubercle (rotator cuff insertion) and slightly dorsal to the long head of the biceps. It allows 9 locking screws in the proximal fragment and is available in different lengths allowing either locked or non-locked screws in the shaft. Fractures of the lesser and/or greater tubercle with displacement and/or instability were fixed with non-absorbable sutures.

After surgery the arm was placed in a sling and all patients were referred to a physiotherapist. The sling was used for 4 weeks and after that the patients were allowed to use it at their own convenience. Pendulum exercise and passive elevation/abduction

up to 90 degrees were started from the first postoperative day and after 4 weeks the patients were allowed a free active range of motion (ROM). Strengthening exercises were begun after 3 months

Figure 2. A displaced 3-part proximal humeral fracture treated with a locking plate (Philos®).

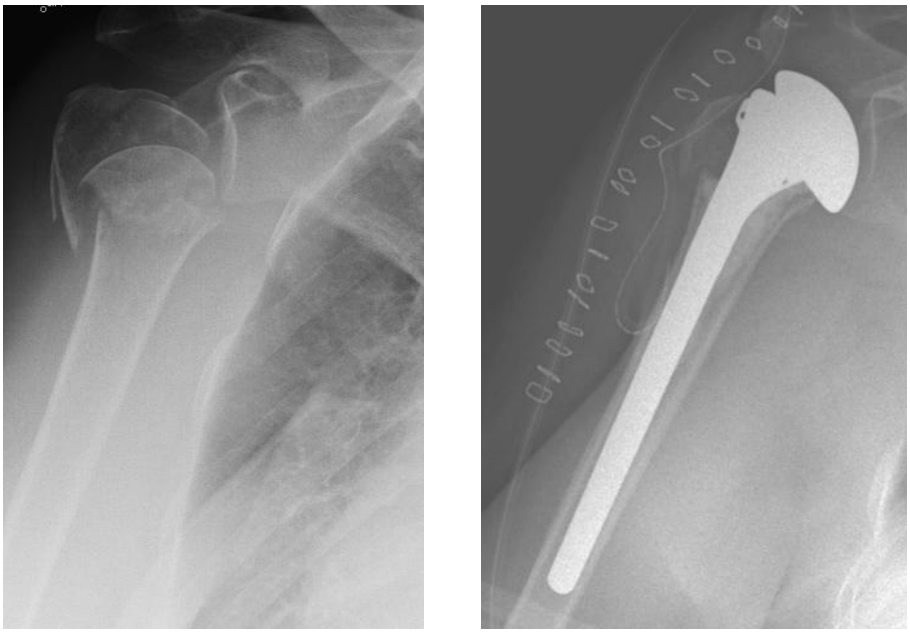
Hemiarthroplasty

All patients were given 2 g cloxacillin (Ekvacillin®, AstraZeneca, Södertälje, Sweden) preoperatively, followed by 2 additional doses during the first 24 hours. Hemiarthroplasty (*Study III*) was performed in a modified beach-chair position utilizing a deltopectoral approach. The Global Fx® prosthesis (DePuy, Sollentuna, Sweden) was used in all patients (**Figure 3).** This is a modular prosthesis with a fixed angle and a conventional head. It has 3 fins, 1 directly opposite the head and 1 on each side, allowing fixation of the tubercles to the stem. Heavy non-absorbable sutures were tagged on the bone tendon interface of both tubercles. The fracture interval was carefully opened, the head fragment removed and the shaft was reamed. Drill holes were made in the shaft for later fixation of the tubercles. The height and retroversion of the prosthesis were defined using an extramedullary device, whereupon the stem was cemented in place. Cancellous bone graft from the head fragment was placed between the shaft and the tubercles in order to facilitate union. The tubercles were then reduced as anatomically as possible and fixed with non-absorbable sutures horizontal to the prosthesis and the other tubercle and vertical to the shaft. One extra suture was placed medially to the prosthesis and embracing both tubercles.

After surgery the arm was placed in a sling and all patients were referred to a physiotherapist. The sling was used for 6 weeks and after that the patients were allowed to use it at their own convenience. Pendulum exercise and passive elevation/abduction up to 90 degrees were started from the first postoperative day and after 6 weeks the

patients were allowed a free active range of motion (ROM). Strengthening exercises were begun after 3 months

Figure 3. Displaced 4-part proximal humeral fracture treated with a hemiarthroplasty (Global Fx ®).



RADIOLOGICAL ASSESSMENT

Postoperatively and at each follow-up a conventional X-ray with standardized frontal and lateral projections was performed.

In *Studies I* and *II* (LP groups), the fracture reduction and implant position were assessed on the postoperative radiographs. We measured the head/shaft angle, dorsal/ventral angle and the distance between the superior border of the greater tubercle and the vertex of the head.[61] A good reduction was defined as a head/shaft angle of 135º ± 20º and a dorsal/ventral angle of 0º ± 25º.[61] The position and utilization of the plate was recorded, i.e. the distance from the top of the greater tubercle, the length of the plate (3 or 5 holes), the number of screws in the head fragment and the number and type (angular stable or conventional) screws in the shaft and, finally, if there was any screw penetrating the humeral head. At each follow-up we assessed any redisplacement with changes in the head/shaft angle and dorsal/ventral angle. Furthermore, any additional screws penetrating the head or loosening of the plate were recorded.

In *Studies II* and *III* (non-operative groups) we assessed the position in which the fracture finally healed, i.e. head/shaft angle, dorsal/ventral angle and the distance between the superior border of the greater tubercle and the vertex of the head.[61] The fracture was defined as healed if it was stable between 2 radiographic controls and there was visible evidence of callus formation. Non-unions was defined as progressive redisplacement of the fracture or visible fracture lines. We also recorded any signs of AVN and OA. AVN was defined as presence of a subchondral fracture (crescent line),

loss of sphericity of the humeral head or segmental collapse. OA was defined as narrowing of the joint line.

In *Study III* (HA group) we assessed the position of the greater tuberosity in both planes[13,39] and whether any redisplacement or resorption of the greater tuberosity had occurred.

STATISTICAL METHODS

The statistical software used in *Study I* was PASW/SPSS 17.0 for Windows. The Wilcoxon signed-ranks test was used to compare the Constant score, DASH and EQ-5D between follow-ups. The Mann-Whitney U test was used to compare patients aged under or over 70. The tests were 2-sided. The results were considered significant at $p < 0.05$.

The statistical software used in *Studies II* and *III* was PASW/SPSS 18.0 for Windows. Scale and ordinal variables were tested using the Mann-Whitney U test. The Wilcoxon signed-ranks test was used to compare the EQ-5D between before fracture and at follow-ups. Nominal variables were tested using the Chi-square test or Fisher's exact test. All tests were 2-sided. The results were considered significant at $p < 0.05$. In order to maximize the power of the statistical tests, we did not apply any correction factor to the p values, e.g. the Bonferroni correction, which may increase the possibility of a Type I error.

The statistical software used in *Study IV* was PASW/SPSS 18.0.1 for Windows. A paired samples t-test (2-sided) was used to compare changes between scores from the prefracture state (pre) and 4 months later (post). The results were considered significant at $p < 0.05$. However, statistical significance is partially dependent on sample size, which is not relevant in analyses of responsiveness[64,90] and therefore statistical significance should not be regarded as the central result.

Change score: Change scores were calculated both for baseline to the 4-month follow-up (EQ-5D) and for the 4-month follow-up to the 12-month follow-up (EQ-5D and DASH).

Standardized Response Mean (SRM): the observed change divided by the standard deviation of the observed change. The SRM provides a measure for comparing instruments and the construct makes it less sensitive to sampling sizes than the often used standardized effect size (SES)[6]. The SRM is regarded as large (> 0.8), moderate (0.5–0.8) or small (< 0.5).[6,31,66] Confidence intervals (95%) for the SRM were calculated according to Beaton et al.[6]

ROC curves were used to depict the sensitivity and specificity of different change scores. This analysis gives information about the size of the area under the curve (AUC), which is the probability of correctly identifying patients with a specified outcome according to the EC. This area ranges from 0.5, meaning no discriminatory accuracy, to 1.0, which approached perfect accuracy in distinguishing patients by this criterion. The calculation of ROC curves depends on the existence of a dichotomized EC. The odds ratio (OR) from logistic regression was calculated with the EC as the dependent variable and the change scores as independent variables.

RESULTS

STUDY I

Baseline data

Baseline data for all patients included (n = 50) are displayed in **Table 5**. The mean age in women was 74.5 years and 76.5 years in men. The mean DXA total body T score was -1.7 and 18 out of 49 (37%) patients had a T-score of more than 2.5 SD below the mean value for young adults and, consequently, satisfied the criteria for osteoporosis according to the WHO definition. The vast majority of the fractures (80%) were plain 2-part fractures or 2-part fractures with an undisplaced or minimally displaced greater tubercle. The dislocation of the greater (n = 26) and lesser tubercle (n = 10) amounted to a mean of 1 mm (0–5).

Table 5. Baseline data for all patients included.

Mean (SD) age in years		74.7 (10.9), range 55 to 93
Gender, female, n (%)		40 (80)
Mean (SD) cognitive function		8.7 (1.4), range 4 to 10
Mean (SD) EQ-5D $_{index}$ score prefracture		0.86 (1.6), range 0.22 to 1.00
ADL A and B, n (%)		49 (98)
ASA , n (%)	1	6 (12)
	2	27 (54)
	3	15 (30)
	4	2 (4)
Mean (SD) DXA total body T score*		-1.7 (1.5), range -4.7 to 1.9
Fracture type	Plain 2-part	21 (42)
	2-part with undisplaced GT	19 (38)
	2-part with undisplaced MT	3 (6)
	2-part with undisplaced GT & MT	7 (14)

* 1 missing value

Clinical and radiological outcome

The assessment of the postoperative fracture reduction showed a mean head/shaft angle (frontal projection) of 135º (range 114º to 150º), a mean dorsal/ventral angle (lateral projection) of 9º (-10º to 43º) and a mean distance between the greater tubercle and the vertex of the head of 8 mm (0 to 19 mm). A good reduction, i.e. a head/shaft angle of 135º ± 20º and a dorsal/ventral angle of 0º ± 25º [61] was achieved in 45 patients (90%). The Philos plate was positioned at a mean of 6 mm (-2 mm to 15 mm) below the top of the greater tubercle. The mean number of screws in the head fragment was 7 (5 to 8). A screw penetration of the head on the postoperative radiograph was found in 6 patients (12%), being minor and single in all but 2 cases.

In 23 of the 46 patients (50%) available at 4 months, the fracture position was unchanged and in 21 (46%) the head/shaft angle had decreased by a mean of 22º (5 to 82º) and in 6 of these patients, there was also a mean increase in dorsal angulation of 17º (7 to 28º). Additional screw penetration of the head had occurred at 4 months in 6 of the 44 patients (14%) at risk. All secondary screw penetrations occurred in patients with a changed fracture position. There was a dislocation of the greater tubercle before the 4-month follow-up in 5 of the 26 patients (19%) with an initially undisplaced or minimally displaced fracture of the greater tubercle. There were no additional changes in fracture position and no additional screw penetrations in any of the patients after the 4-month follow-up.

In total, 8 patients (16%) were reoperated upon during the 2-year follow-up period (**Table 6**), 3 patients due to a suboptimal position of the implant, 3 patients due to secondary displacement, 1 patient due to non-union and 1 patient due to a deep infection.

Table 6. Data on the 8 patients undergoing reoperations.

Fracture type	T-score	Reduction	No. of head screws	Indication	Reoperation/reoperations	Time (months)
2-part + GT	-3.5	145°/15°	8	Primary screw penetration	Screw extraction	0.2
2-part + LT	+1.2	147°/15°	8	Deep infection	Wound revision and lavage	0.8
					Extraction of plate + spacer	0.9
					Wound revision and lavage	1.7
					Global Fx hemiarthroplasty	2.9
					Extraction of prosthesis	25.4
2-part+GT+LT	-2.2	146°/43°	8	Major redislocation	Global Fx hemiarthroplasty	1.5
2-part	-2.9	138°/2°	8	Minor redislocation, Secondary screw penetration	Screw exchange	1.6
2-part + GT	-0.1	135°/11°	5	Minor redislocation, Secondary screw penetration	Screw extraction	2.8
				Non-union	Global Fx hemiarthroplasty	10.9
2-part	-1.1	132°/8°	8	Primary screw penetration, Stiffness	Extraction of plate	6.1
2-part	+0.6	138°/10°	8	Non-union	Reosteosynthesis, PHILOS + autologus bone transplant	17.4
2-part	-1.1	138°/-9°	7	Impingement	Extraction of plate	18.3

Functional outcome and HRQoL

The functional outcomes according to the Constant and DASH scores at the different follow-ups are displayed in **Table 7**. There was a significant improvement in the Constant score between 4 and 12 months ($p < 0.001$) while the marginal improvement between 12 and 24 months was not significant. The same pattern was seen for the DASH score, although it was not statistically significant in any of the comparisons.

The HRQoL ($EQ\text{-}5D_{index}$ score) decreased from 0.86 before the fracture to 0.62 at 4 months. At 12 months the score was 0.65 and at 24 months 0.68 (**Figure 4**). The values at all follow-ups were significantly lower than before the fracture ($p < 0.001$ in all 3 comparisons).

A comparison of the outcome for patients aged under 70 with those over 70 showed better values for the younger age group in the Constant, DASH and EQ-5D $_{index}$ scores, although they were statistically significant only at the 12-month follow-up.

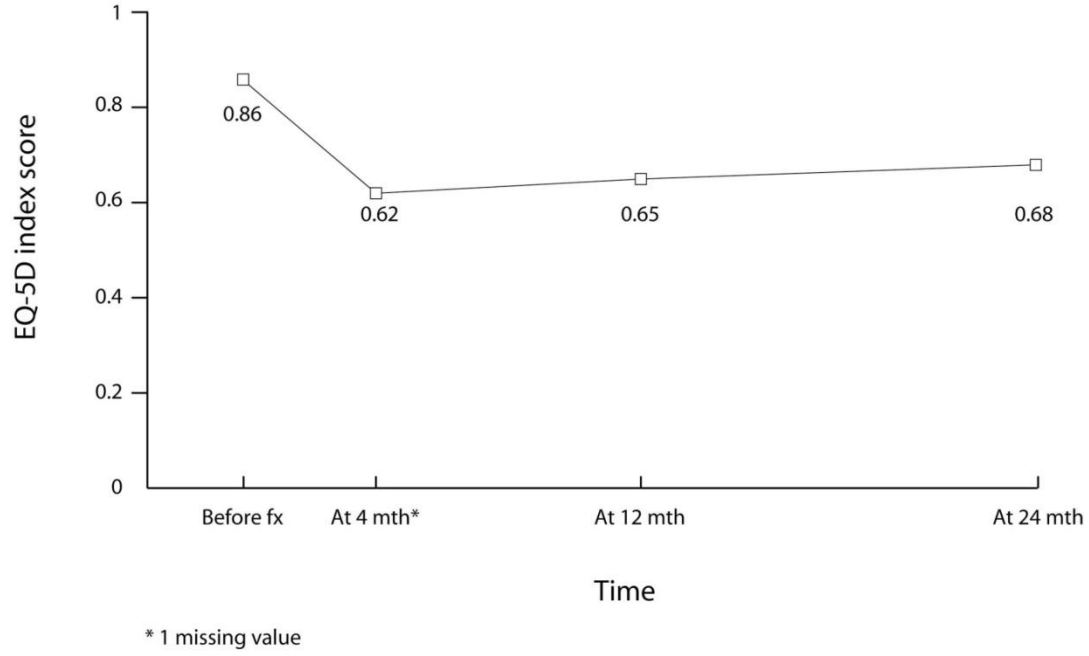
A comparison of the outcome for patients with a secondary displacement of the greater tubercle with those without showed worse values for those with a secondary displacement at all follow-ups, although they did not reach statistical significance.

Table 7. The mean Constant and DASH scores. all patients available at each follow-up.

	4 months*	**12 months**	**24 months**
Constant score (0–100)	**50.1**	**59.4**	**61.1**
I. Pain (0–15)	10.1	11.2	12.8
II. ADL (0–20)	12.4	14.9	14.1
III. ROM (0–40)	21.4	26.4	26.9
IV. Strength (0–25)	6.3	6.9	7.2
DASH (100–0)	**36.8**	**33.8**	**32.4**

* 2 missing values

Figure 4. The mean EQ-5D $_{index}$ score for all patients available at each follow-up.



* 1 missing value

STUDY II

Baseline data

Baseline data for all patients included in relation to randomization group (n = 59) are displayed in **Table 8**. The mean age was 75.1 years for women and 68.7 years for men. The mean DXA total body T-score was -1.4 and 15 out of 59 patients (25%) had a T-score of more than 2.5 SD below the mean for young adults and, consequently, satisfied the criteria for osteoporosis according to the WHO definition.[68] The vast majority of the fractures, 58 out of 59 (98%), were 3-part fractures with a displaced greater tubercle. 25 (43%) of these fractures had an associated undisplaced or minimally displaced lesser tubercle. The lesser tubercle was undisplaced in 9 patients and displaced 1 mm in 5, 2 mm in 4, 3 mm in 4 and 5 mm in 3 patients. The single 3-part fracture with a displaced lesser tubercle had no fracture of the greater tubercle.

Table 8. Baseline data for all patients included in relation to randomization group.

	Locking plate n = 30	**Non-operative n = 29**
Mean (range) age in years	72.9 (56 to 92)	74.9 (58 to 88)
Gender, female, n (%)	24 (80)	24 (83)
Mean (range) cognitive function	9.4 (5 to10)	9.2 (6 to10)
Mean (range) EQ-5D $_{index}$ score prefracture	0.85 (0.19 to 1.0)	0.85 (0.41 to 1.0)
ADL A and B, n (%)	29 (97)	29 (100)
Non-dominant arm, n (%)	19 (63)	16 (55)
Mean BMI (kg/m^2)	26.6 (19 to 37)	25.9 (14 to 39)
Mean (SD) DXA total body T score	-1.3 (-4.1 to 1.3)	-1.4 (-4.3 to 1.6)
Fx type 3-part with displaced GT	29 (97)	29 (100)
3-part with displaced LT	1 (3)	0 (0)

Clinical and radiological outcome

The assessment of the postoperative fracture reduction showed a mean head/shaft angle (frontal projection) of 129º (range 106º to 150º), a mean dorsal/ventral angle (lateral projection) of 9º (-10º to 30º) and a mean distance between the greater tubercle and the vertex of the head of 3 mm (-5 mm to 15 mm). A good reduction,[61] i.e. a head/shaft angle of 135º ± 20º and a dorsal/ventral angle of 0º ± 25º was achieved in 25 patients (86%). The plate was positioned at a mean of 7 mm (-4 mm to 22 mm) below the top of the greater tubercle and a 3-hole plate was utilized in 26 patients and a 5-hole plate in the remaining 3. The mean number of screws in the head fragment was 7 (4 to 8). A screw penetration of the head was found on the postoperative radiograph in 5 patients (17%). The penetration was 1 mm in 3 patients, 2 mm in 1 and 3 mm in 1. The fracture position was unchanged in 20 of the 26 patients (77%) available at 4 months and not reoperated. In 6 patients (23%) the head/shaft angle had decreased by a mean of 10º (3º to 23º) and, additionally, in 4 of these 6 patients, there was also a mean increase in dorsal angulation of 13º (2º to 28º).

Additional screw penetration of the head had occurred at 4 months in 3 of the 26 patients (12%) at risk. All secondary screw penetrations occurred in patients with a changed fracture position. There was a secondary displacement of the greater tubercle before the 4-month follow-up in 4 of the 25 patients (16%) at risk with a mean of 18 (2 to 30) mm. The single 3-part fracture with a displaced lesser tubercle showed no detectable secondary displacement. There were no additional changes in fracture position and no additional screw penetrations in any of the patients after the 4-month follow-up.

Three patients (10%) in the locking plate group displayed signs of AVN, 2 minor and 1 severe, 2 of whom were reoperated.

In the locking plate group, 9 patients (30%) had additional surgery during the 2-year follow-up period (**Table 9**). 4 patients (13%) required major additional surgery: 1 due to a primary infection, 1 due to a haematogenous infection, 1 due to non-union and 1 due to severe AVN. 5 patients (17%) had minor additional surgery, all during the second year, with removal of the plate and release of adhesions. The indication for surgery was secondary screw penetration in 1 patient, postoperative stiffness in 2 and impingement in 2. All but 1 of these patients had improved function according to DASH between the 12 and 24-month follow-ups with a mean of 6.2 points (range 0–15.8).

Table 9. Data on the 10 patients undergoing additional surgery after primary treatment.

Group	Gender/ age	Fx type	T-score	Reduction	No. of screws	Indication	Reoperation/reoperations	Time	DASH 24 mths
LP	M / 58	3-GT	-1.5	140°/12°	8	Deep infection	Wound revision, repeated lavage, extraction of plate and spacer	3.7	47.5
LP	F / 74	3-GT	-4.1	115°/12°	5	Non-union	Reosteosynthesis, LP + autologous bone transplant	10.0	80.8
LP	F / 67	3-GT	0	111°/3°	8	Deep infection	Wound revision + extraction of plate, healed fx	12.9	64.2
NO	M / 73	3-GT	-0.6	NA	NA	Impingement	Arthroscopic acromioplasty	13.4	39.2
LP	M / 66	3-GT	2.3	150°/6°	6	Impingement	Extraction of plate, release	14.7	5.0
LP	F / 59	3-GT	1.2	123°/1°	8	Stiffness, screw penetration	Extraction of plate, release	18.1	0.0
LP	F / 56	3-GT	-2.4	129°/3°	7	Stiffness	Extraction of plate, release	20.0	0.0
LP	F / 66	3-GT	-0.3	131°/-10°	8	Stiffness	Extraction of plate, release	23.1	25.0
LP	F / 82	3-GT	-0.7	130°/30°	8	AVN, minor	Extraction of plate, release	23.4	24.2
LP	F / 77	3-GT	-2.6	140°/10°	7	AVN, severe	Extraction of plate and hemiarthroplasty	24.8	Missing

M = male; F = female; Reduction = valgus angle/dorsal angle; No. of screws = no. of head screws; Time = time elapsed from the primary operation in months; NA = not applicable; mths = months.

One patient in the non-operative group had a non-union. The other 28 fractures healed with a mean head/shaft angle (frontal projection) of 121º (range 87º to 193º), a mean dorsal/ventral angle (lateral projection) of 48º (-6º to 117º) and a mean distance between the greater tubercle and the vertex of the head of 0 mm (-8 to 20 mm). Only 4 of the fractures (14%) healed in a position that satisfied the criteria for a good

reduction.[61] The patient with a non-union opted to abstain from surgical intervention. A contributing factor to this decision was a late diagnosis of axillary nerve palsy. One patient (3%) had additional minor surgery during the 2-year follow-up, an arthroscopic acromioplasty due to impingement resulting from a malunited greater tubercle (**Table 9**). Moreover, 2 patients (7%) displayed signs of minor AVN and 1 patient (3%) had posttraumatic osteoarthritis.

Functional outcome and HRQoL

The functional outcomes according to the Constant and DASH scores are displayed in **Table 10** and the HRQoL (EQ-5D $_{index}$ score) in **Figure 5**. The figures for the Constant and DASH scores, as well as the EQ-5D $_{index}$ score, were all in favor of the locking plate group on all follow-up occasions, although not reaching statistical significance.

The mean pain score according to VAS was 17 in the locking plate group compared to 20 in the non-operative group (p = 0.94). The mean range of flexion at the final follow-up was 120° in the locking plate group compared to 111° in the non-operative group (p = 0.36) and the mean range of abduction was 114° vs 106° (p = 0.28).

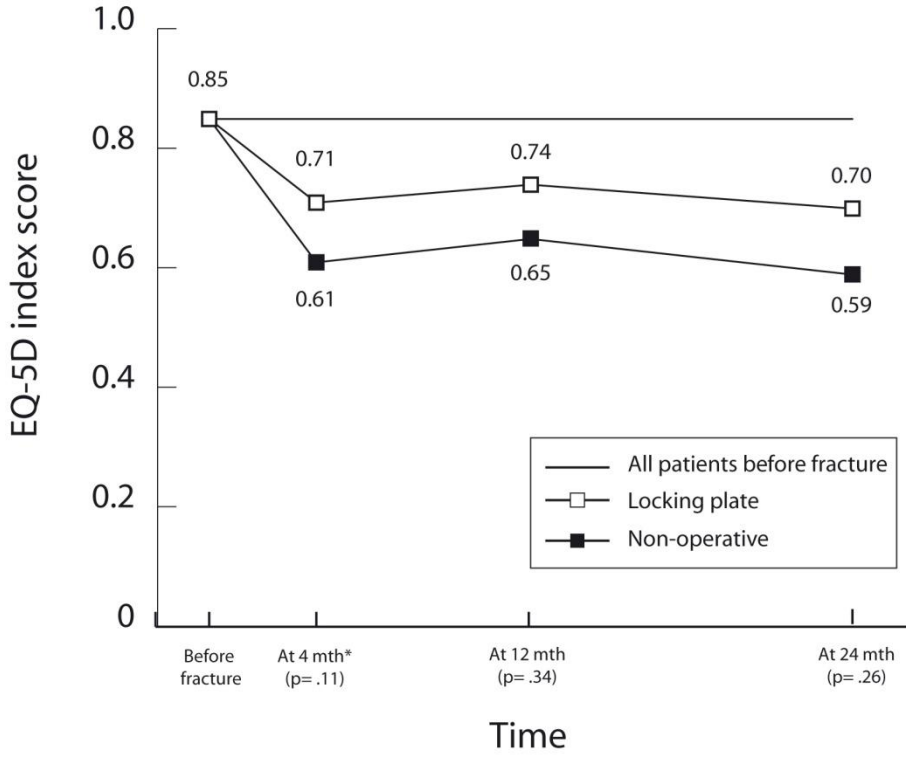
The EQ-5D $_{index}$ score in the locking plate group decreased from 0.85 before the fracture to 0.71 at 4 months. At 12 months the score was 0.74 and at 24 months 0.70 (**Figure 5**). The values at all follow-ups were significantly lower than before the fracture (p = 0.002, 0.003 and 0.006, respectively).
In the non-operative group the HRQoL (EQ-5D $_{index}$ score) decreased from 0.85 before the fracture to 0.61 at 4 months. At 12 months the score was 0.65 and at 24 months 0.59 (**Figure 5**). The values at all follow-ups were significantly lower than before the fracture (p < 0.001, < 0.001 and = 0.001, respectively).

Table 10. The mean Constant and DASH scores for all patients available at each follow-up.

	4 months			**12 months**			**24 months**		
	LP	**NO**	**p**	**LP**	**NO**	**p**	**LP**	**NO**	**p**
Constant score (0–100)	**52.3***	**48.8**	**0.48**	**61.5 ***	**56.8**	**0.18**	**61.0**	**58.4**	**0.64**
I. Pain (0–15)	10.0*	9.5	0.48	11.9*	10.6	0.15	12.4	11.2	0.12
II. ADL (0–20)	13.8*	12.8	0.42	14.9*	14.2	0.52	14.1	14.6	0.75
III. ROM (0–40)	22.2*	20.6	0.61	27.0 *	24.1	0.11	27.3	24.7	0.41
IV. Strength (0–25)	6.3*	6.0	0.64	7.6*	8.0	0.97	7.3	7.9	0.88
DASH (100–0)	**36.2***	**35.7***	**0.85**	**29.1**	**35.1**	**0.32**	**26.4***	**35.0***	**0.19**

* 1 missing value

Figure 5. The mean EQ-5D $_{index}$ score for all patients available at each follow-up.



* 1 missing value in each group.

STUDY III

Baseline data

Baseline data for all patients included in relation to randomization group (n = 55) are displayed in **Table 11**. The mean age was 77.8 years for women and 69.8 years for men. The mean DXA total body T score was -1.5 and 15 out of 55 patients (27%) had a T-score of more than 2.5 SD below the mean value for young adults and, consequently, satisfied the criteria for osteoporosis according to the WHO definition.[68]

Table 11. Baseline data for all patients included in relation to randomization group.

	Hemiarthroplasty n = 27	**Non-operative n = 28**	**p**
Mean (range) age in years	75.8 (58 to 90)	77.5 (60 to 92)	0.49
Gender, female, n (%)	23 (85)	24 (86)	1.0
Mean (range) cognitive function	9.5 (5 to 10)	8.9 (6 to 10)	0.02
Mean (range) EQ-5D $_{index}$ score prefracture	0.88 (0.31 to 1.00)	0.87 (0.49 to 1.00)	0.56
ADL A and B, n (%)	27 (100)	28 (100)	1.0
Non-dominant arm, n (%)	12 (44)	13 (46)	0.88
Mean BMI (SD) (kg/m^2)	27.7 (4.8)	25.8 (3.8)	0.18
Mean (SD) DXA total body T score	-1.7 (1.5)	-1.3 (1.6)	0.46

Clinical and radiological outcome

The mean humeral head height was 10 (SD 7) mm. 14 patients had a maximum humeral head height of 10 mm, 6 patients of 11 to 15 mm and 6 patients of more than 16 mm. 20 of the 26 patients (77%) operated upon with a primary HA had a maximum humeral head height of 14 mm, which has previously been reported to be the upper cut-off value for achieving a good outcome.[39] A mean secondary dislocation of the greater tubercle of 20 (SD 10) mm was observed in 5 patients (19%). Additionally, 1 patient had a complete resorption of the greater tubercle and 2 patients had partial resorptions.

In the HA group, 3 patients (11%) had additional surgery during the 2-year follow-up period (**Table 12**). The patient operated upon using a locking plate had the implant removed after 6.3 months due to secondary screw penetration, 1 patient underwent an acromioplasty and release of adhesions after 8.6 months due to impingement and stiffness and 1 patient with a redisplacement of the greater tubercle was reoperated upon with rereduction and refixation after 17.7 months. There were no infections or nerve injuries.

One patient (4%) in the non-operative group had additional surgery (**Table 12**). In this patient a complete displacement of the shaft without bony contact was detected after 1 month and the patient was operated upon with a hemiarthroplasty. 1 of the remaining 27 patients (4%), a male with severe alcohol abuse, had a non-union but opted not to be reoperated upon. In the remaining 26 patients the fracture healed, but 2 of them opted to abstain from the final radiograph. In the 24 patients with available final radiographs, the fractures healed with a mean head/shaft angle (frontal projection) of 122º (range 81

to 236º), a mean dorsal/ventral angle (lateral projection) of 53º (0 to 120º) and a mean distance between the greater tubercle and the vertex of the head of -3 mm (-12 mm to 17 mm). Only 1 fracture (4%) healed in a position that satisfied the criteria for a good reduction,[61] i.e. a head/shaft angle of 135º ± 20º and a dorsal/ventral angle of 0º ± 25º. Moreover, 3 patients (11%) displayed signs of AVN and 5 patients (19%) had posttraumatic osteoarthritis.

Table 12. Data on the 4 patients undergoing additional surgery after primary treatment.

Group	Gender/ age	Indication	Surgical intervention	Time	DASH 24 mths
NO	F/80	Complete displacement of the shaft without bony contact	Hemiarthroplasty	1.1	76.7
HA	F/74	Secondary screw penetration after locking plate; see text	Extraction of plate, healed fracture	6.3	37.5
HA	F/63	Impingement, stiffness	Acromioplasty, release of adhesions	8.6	7.5
HA	M/58	Displaced greater tubercle	Refixation of greater tubercle	17.7	61.7

HA = hemiarthroplasty; NO = non-operative; M = male; F = female; Time = time elapsed from the primary operation or the start of the non-operative treatment in months; mths = months.

Functional outcome and HRQoL

The functional outcome according to the Constant and DASH scores are displayed in **Table 13** and the HRQoL (EQ-5D $_{index}$ score) in **Figure 6.** At the 24-month follow-up the EQ-5D $_{index}$ score was significantly better in the HA group ($p = 0.02$).

The mean pain score according to VAS at the final follow-up was 15 in the HA group, compared to 25 in the non-operative group ($p = 0.17$).

The mean range of flexion at the final follow-up was 93° in the HA group, compared to 95° in the non-operative group ($p = 0.85$) and the mean range of abduction was 86° vs 87° ($p = 0.89$).

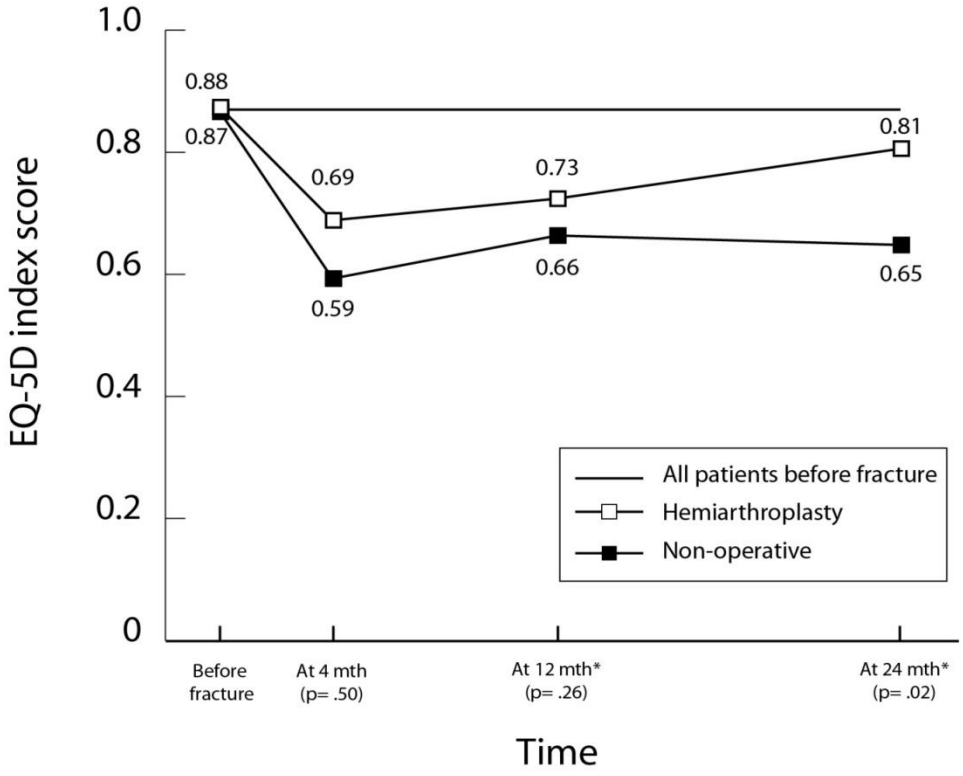
In the HA group the EQ-5D $_{index}$ score decreased from 0.88 before the fracture to 0.69 at 4 months. At 12 months the score was 0.73 and at 24 months 0.81 (**Figure 6**). The values at all follow-ups were significantly lower than before the fracture ($p < 0.001$, < 0.001 and $= 0.06$, respectively).

In the non-operative group the HRQoL (EQ-5D $_{index}$ score) decreased from 0.87 before the fracture to 0.59 at 4 months. At 12 months the score was 0.66 and at 24 months 0.65 (**Figure 6**). The values at all follow-ups were significantly lower than before the fracture ($p < 0.001$ in all 3 comparisons).

Table 13. The mean Constant and DASH scores for all patients available at each follow-up.

	4 months			12 months			24 months		
	HA	**NO**	**p**	**HA**	**NO**	**p**	**HA**	**NO**	**p**
Constant score (0–100)	**36.0**	**41.4**	**0.21**	**48.9**	**47.7**	**0.76**	**48.3**	**49.6**	**0.81**
I. Pain (0–15)	9.4	9.8	0.70	11.2	10.6	0.65	12.1	11.0	0.36
II. ADL (0–20)	10.4	11.8	0.40	13.7	13.1	0.53	12.9	13.8	0.57
III. ROM (0–40)	15.4	16.9)	0.48	21.2	19.2	0.46	20.2	20.1	0.89
IV. Strength (0–25)	0.7	3.0	0.008	2.8	4.8	0.18	3.1	4.7	0.45
DASH (100–0)	**42.8**	**41.5**	**0.92**	**32.0**	**35.0**	**0.71**	**30.2**	**36.9**	**0.25**

Figure 6. The mean EQ-5D $_{index}$ score for all patients available at each follow-up.



STUDY IV

Baseline data and measurement characteristics for the study population (n = 145) are given in **Table 14**.

Table 14. Baseline data on all patients.

Mean age, years (range; SD)	74.7 (55 to 93; 9.6)
Cognitive function, SPMSQ (range; SD)	9.2 (5 to 10; 1.1)
Gender, female (%)	122 (84)
ADL A or B (%)	145 (100)
EQ-5D $_{index}$ score	
Mean (SD)	0.86 (0.18)
Median	0.85
Range	0.21 to 1.0
Floor effect (%)	0 (0)
Ceiling effect (%)	70 (48)

Internal responsiveness: The mean change score from pre-fracture status to the 4-month follow-up for the EQ-5D was -20.9 (SD = 23.3; $p < 0.001$). The corresponding SRM was 0.90 (95% confidence interval 0.74; 1.06) and therefore considered to be large. This was in accordance with our hypotheses.

External responsiveness: Change scores from the EQ-5D, results from independent t-tests and SRMs are given for the 4 defined groups of patients based on the EC in **Table 15**. The clearly improved or clearly deteriorated groups according to the EC (DASH score) report change scores of around 12 points on the EQ-5D, which corresponded to moderately strong SRMs and statistically significant changes between the 4 and 12-month follow-ups. The marginally improved or marginally deteriorated patients had change scores of around zero in the EQ-5D.

The ROC analyses showed that it was possible to discriminate between patients with different degrees of improvement or deterioration. The AUCs were from 0.71 to 0.81 and all were statistically significant (**Table 15**).

In the logistic regression the patient group with the comparatively favorable outcome was used as the reference group. Subsequently, ORs above unity indicate that the odds for belonging to the group with the less favorably outcome increased among patients with a (comparatively) less advantageous development on the EQ-5D. All ORs were statistically significant and above unity (**Table 16**). Furthermore, when change scores from the EQ-5D were used to classify patients into the defined groups according to the EC the proportion of correctly classified patients spanned from 57% up to 86%. Subsequently, more patients than what can be expected by chance (50%) were correctly classified.

Finally, change scores from the EQ-5D and DASH were correlated and the Spearmans rho was 0.47 ($p < .01$), which was regarded as moderately strong and in accordance with the hypothesis.

Table 15. External responsiveness statistics for the EQ-5D $_{index}$ score. Change scores from the DASH between the 4-month and 12-month follow-ups were used as an external criterion (EC); see Methods for details.

Variable	Observed change Mean (SD)	p value[1]	SRM (95% CI)
EQ-5D $_{index}$ score 4 months–12 months (n = 145)			
Clearly improved[2] (n = 57)	12.3 (18.4)	< 0.001	0.67 (0.41; 0.93)
Marginally improved[3] (n = 45)	0.4 (12.4)	n.s.	0.03 (-0.26; 0.32)
Marginally deteriorated[4] (n = 27)	0.8 (21.3)	n.s.	0.04 (-0.34; 0.41)
Clearly deteriorated[5] (n = 16)	-12.4 (17.2)	< 0.05	-0.72 (-1.21; -0.23)

[1] Paired samples t -test.

[2] Improvement in DASH score ≥ 10 points

[3] Improvement in DASH score < 10 points

[4] Deterioration in DASH score < 10 points

[5] Deterioration in DASH score ≥ 10 points

Table 16. External responsiveness for change scores from the EQ-5D $_{index}$ score. Change scores from the DASH between the 4-month and 12-month follow-ups were used as an external criterion (EC); see Methods for details on how the groups were defined.

	Receiver operating characteristics (ROC)	Logistic regression	
	Area under the curve (95% CI)	Odds ratio (95% CI)	Proportion correctly classified
EQ-5D $_{index}$ score			
Clearly improved vs marginally/clearly deteriorated	0.77*** (0.67; 0.86)	1.06** (1.02; 1.09)	57%
Marginally improved vs clearly deteriorated	0.75** (0.60; 0.89)	1.06** (1.02; 1.11)	74%
Marginally deteriorated vs clearly improved	0.71** (0.59; 0.84)	1.04* (1.01; 1.07)	68%
Clearly deteriorated vs marginally/clearly improved	0.81*** (0.79; 0.92)	1.08*** (1.04; 1.13)	86%

*** = p < 0.001; ** p < 0.01; * = p < 0.05

GENERAL DISCUSSION

The overall aim of this thesis was to evaluate the outcome after treatment of 2-, 3- and 4-part fractures of the proximal humerus in lucid, relatively healthy elderly patients (*Studies I–III*) and to evaluate the responsiveness of the EQ-5D in patients with proximal humeral fractures (*Study IV*).

THE LOCKING PLATE IN 2-PART FRACTURES

Despite a modern fixation technique and good primary reduction, there are still some problems connected with maintaining a satisfactory reduction with a locking plate in the treatment of elderly patients with a displaced 2-part fracture. Screw penetration of the humeral head, both primary and secondary, appears to be a particular problem. Moreover, this fracture results in a functional impairment which in turn leads to a substantial negative effect upon the patients' HRQoL.

Our results pertaining to functional outcome and the need for revision surgery are difficult to compare with those of previous studies since most previous studies include multiple fracture types, i.e. 2-, 3-, and 4-part fractures, and also younger patients. We opted to include a strictly defined population of only elderly patients (mean age 75 years, range 55 to 93) with displaced 2-part fractures as we believe that, in conformity with the situation in patients with displaced femoral neck fractures, we have to try to identify treatment regimens that are based not only on the particular fracture type but also on the individual patient's age, functional demands and co-morbidities.

The functional outcome according to the Constant score in our patients, 61 at the final follow-up, was clearly lower than the values for healthy individuals in the same age group (60 to 90 years).[32] However, the results are comparable to those of 2 previous retrospective studies using the Philos plate. In a study by Handschin et al.[57] including 8 patients with a 2-part fracture, the Constant score was 64. Björkenheim et al.[12] reported a Constant score of 84 in a subgroup of 22 patients who had 2-part fractures; however, this study also included younger age groups and patients with less displaced 2-part fractures. The Constant score including all fracture types for patients aged 61–70, 71–80 and > 80 years was 72, 66 and 59, respectively. This finding of a worse outcome with increasing age was also confirmed in our study.

In a prospective study on 119 patients with proximal humeral fractures treated with a Philos plate, 31of whom had a 2-part fracture, Hirschmann and co-workers[61] reported a Constant score of 65 after 1 year and a DASH score of 21, the latter evidently being better than our DASH scores of 34 and 32 after 1 and 2 years, respectively. However, this comparison is also difficult to interpret as the results for the displaced 2-part fractures were not reported separately and 50% of the patients were under 70 years old.

There has been considerable confusion concerning the strength assessment of the Constant score, giving a maximum score of 25 points, because the assessment is performed with the shoulder in 90° of abduction. The main controversy has concerned how to assess patients who are unable to reach this position. We opted to follow the recommendations of Constant et al.,[33] i.e. patients who were unable to achieve the test position of 90° were assigned a strength score of 0. This may end in an underestimation of our results for the Constant score compared to previous studies.

We had an overall reoperation rate of 16%, which is comparable to recent studies utilizing locking plates, where the reoperation rate ranges from 9% to 25%.[21,57,61] In principle, we had 4 different causes for reoperation: (1) suboptimal position of the implant; (2) secondary displacement; (3) non-union; and (4) infection, with the two first-mentioned being the most common.

THE LOCKING PLATE VS NON-OPERATIVE TREATMENT IN 3-PART FRACTURES

There seems to be an advantage in functional outcome and quality of life in favor of the locking plate as compared to non-operative treatment in elderly patients with a displaced 3-part fracture of the proximal humerus. However, despite a modern fixation technique and overall good primary reductions in the locking plate group, 13% of the patients had a severe complication requiring a major reoperation and 17% had a minor secondary surgical intervention. Regardless of the primary treatment, operative or non-operative, this fracture results in a functional impairment which in turn leads to a substantial negative effect upon the patients' HRQoL.

The results for ROM, function and HRQoL were all in favor of the locking plate group and the differences of almost 9 points in the DASH score and 0.11 points in the EQ-5D $_{index}$ score are both considered to be clinically relevant. However, the study failed to confirm the statistical significance of these differences.

The negative effect on the HRQoL was considerable regardless of the primary treatment. The deterioration in the EQ-5D $_{index}$ score at 2 years in the locking plate fracture group was 0.15, which is of the same magnitude as in 2-part fractures treated with a locking plate (*Study I*). In comparison, the deterioration in the EQ-5D $_{index}$ score in the non-operative group was 0.26.

Our rate of 30% additional surgery in the locking plate group after 2 years, 13% major reoperations and 17% minor, is difficult to interpret as there are few comparable prospective studies with a 2-year follow-up. When comparing with previous studies with a 1-year follow-up it is important to remember that after 1 year only 7% of our patients had undergone reoperation. The 7% 1-year reoperation rate compares favorably with the 19%–28% previously reported rate in prospective studies with a 1-year follow-up including a mixed population of 2–3 and 4-part fractures.[21,61,106] The fact that the majority of the reoperations were performed during the second year supports the recommendation that a 2-year follow-up should always be performed in studies on this type of fracture.

Our results pertaining to functional outcome after 2 years in the locking plate group, DASH score 26 and Constant score 61, are comparable to those in previous prospective studies with an at least 1-year follow-up. In these studies the average DASH score varies from 15 to 21 points and the Constant score from 62 to 74.[21,61,106] However, the comparison is difficult to interpret because all of these studies included a mixed population of 2, 3 and 4-part fractures and also younger patients. The comparison with the Constant score is even more difficult as this score is highly age-dependent and there has also been a controversy concerning how to assess strength in patients who are unable to achieve 90° of abduction. We opted also in this study to follow the recommendations of Constant,[33] i.e. patients who were unable to achieve the test

position of 90° were assigned a strength score of 0. This may lead to in an underestimation of our results for the Constant score compared to previous studies.

All but 1 of the fractures in the non-operative group healed, but the majority of them were malunited. Only 14% of the fractures healed in a position that satisfied the criteria for a good reduction.[61] Nevertheless, the ROM was surprisingly good with a mean forward flexion of 111° and a mean abduction of 106°. A limited number of papers have reported 2-year outcomes after non-operative treatment. Zyto et al.[111] reported a mean Constant score of 59, mean forward flexion of 120° and a mean abduction of 100° after 10 years in 9 patients with 3-part fractures treated non-operatively.

Three patients (10%) in the locking plate group displayed signs of AVN, 2 minor and 1 severe, compared to 2 patients (7%) in the non-operative group, both minor. These figures are similar to those previously reported in the literature.[58,87] Two of our patients with AVN required additional surgery, both in the locking plate group. One patient with major AVN was reoperated upon with a hemiarthroplasty and 1 patient with minor AVN underwent extraction of the plate and release of adhesions.

THE LOCKING PLATE TECHNIQUE

Despite the angular stability of the screws and our effort to maximize the number and length of the screws in the head fragment, there were signs of initial instability after locking plate fixation of both the 2- and 3-part fractures *(Studies I* and *II)*. This was reflected by a redisplacement into varus in 23–46% of the patients, 6–29% of whom also had an increased dorsal angulation, all occurring during the first 4 months. The redisplacement was of a minor magnitude in the majority of the patients and, in those not suffering a major redisplacement or a secondary screw penetration, reoperation was never indicated, although even a minor or moderate redisplacement would most probably have an impact on the functional outcome. In some of our patients with redisplacements resulting in reoperation, we could identify possible contributing factors, e.g. malreduction, an insufficient number of screws in the head fragment and severe osteoporosis.

A relatively high incidence of primary screw penetrations has been reported after fixation with locking plates. Our finding of 12% (*Study I)* and 17% (*Study II*) were comparable to the 12–14% reported in previous studies.[21,27] However, the screw penetrations were minor and eccentric in the majority of the patients and did not constitute an indication for secondary surgical intervention. When we started to use the locking plate we intended to maximize purchase in the osteoporotic bone by using as long screws as possible. Despite checking with an X-ray image intensifier, avoiding minor screw penetration seems to be a difficult part of the surgical procedure. We are now more aware of this problem and therefore try to be even more observant and aim at placing the screws 2–3 mm from the subcondral bone. However, it always comes down to finding a balance between a maximum possible fixation and the risk of secondary screw penetration due to secondary displacement.

The fixation of the tubercle, especially the greater tubercle, remains a substantial problem. In our patients with a 3-part fracture (all but 1 with a displaced greater tubercle; *Study II*), there was a secondary displacement of the greater tubercle in 16%. An interesting finding in our patients with a 2-part fracture (*Study I*) was that there was a dislocation of the greater tubercle in almost 20% of those with an initially undisplaced

or minimally displaced fracture of the greater tubercle. Moreover, the majority of the fractures of the greater or lesser tubercle in that study, 72%, were undisplaced and not visible on conventional radiographs and, for surgeons not routinely using preoperative CT, these fractures would at best have been detected during surgery. Additionally, the patients with a secondary displacement of the greater tubercle in *Study I* showed worse values in all outcome assessments, although not being statistically significant, probably due to a lack of study power for this particular issue. These results underline the importance of using preoperative CT and also imply that undisplaced tubercle fragments require additional fixation. An additional finding of *Studies I* and *II* is that the preoperative classification of fracture type was in conformity with the intraoperative classification in all but 1 patient. According to the radiological examinations, that patient had a 3-part fracture with a displaced greater tubercle and a minimally displaced lesser tubercle (2 mm), but at surgery a displacement of both tubercles exceeding 10 mm was diagnosed, i.e. it was a true 4-part fracture according to the Neer classification and the patient was treated with an HA. This finding of agreement between the preoperative classification based on conventional radiographs and CT and the intraoperative findings indicates that the Neer classification[86-88] is usable both as a tool for clinical decision-making and in clinical outcome studies.

Are there any methods available that can provide a lower risk of redisplacement? Conventional non-locking plates have been shown to have a very high complication rate in elderly patients.[98] Intramedullary devices may be an option in the subgroup of 2-part fractures that do not include a fracture of the greater and/or lesser tubercle,[104] but for the remaining patients with 2- and 3-part fractures the preferred surgical method today is probably a locking plate. However, the challenge in elderly patients is considerable owing to poor bone quality. Our patients in *Studies I* and *II* had a mean T-score of -1.7 and 1.4, respectively, and 37% and 25%, respectively, met the criteria for manifest osteoporosis.

We now almost always use the maximum number of screws in the head fragment in elderly patients in order to increase stability and we are aiming at achieving a better medial support.[50] Furthermore, there are also some new plate designs utilizing smooth angular-stable pegs with a steeper angle in order to improve fixation, thus theoretically reducing the risk of penetration of the head and preventing subacromial impingement.[51] However, the possible advantage of this implant remains to be tested in prospective comparative studies.

HEMIARTHROPLASTY VS NON-OPERATIVE TREATMENT IN 4-PART FRACTURES

There seems to be an advantage in quality of life in favor of HA compared to non-operative treatment in elderly patients with a displaced 4-part fracture of the proximal humerus. Furthermore, primary HA appears to be a safe surgical procedure with relatively low complication and reoperation rates. Regardless of the primary treatment, operative or non-operative, the 4-part fracture resulted in a functional impairment of the shoulder and arm resulting in a substantial negative effect upon the patients' HRQoL.

The HRQoL according to the EQ-5D improved in the HA group after the 4-month follow-up, in contrast to the situation in the non-operative group in which there was a deterioration after 4 months. The different developments in the HRQoL over time

resulted in a significantly better EQ-5D $_{index}$ score in the HA group at the 2-year follow-up. The same pattern was seen in the DASH and pain scores, while the ROM was similar in both groups. Our interpretation of the results is that the main advantage of a primary HA, compared to non-operative treatment, was reduced pain, a difference that seemed to increase during the first 2 years. This finding of good relief of pain after a primary HA is in conformity with previous studies.[1,74,92]

The study was able to statistically confirm the difference in the EQ-5D $_{index}$ score, but it failed to confirm the differences in the DASH and pain scores, most probably due to insufficient power. The results for the Constant score did not follow the same pattern as that of the other outcome measures, except for ROM, and showed similar results in both groups at 2 years. The reason for this discrepancy between the Constant score versus the EQ-5D, DASH and pain scores is unclear. A possible explanation may be that the Constant score is not self-reported and is therefore less sensitive to subjectively experienced, yet important, differences in outcome.[59]

The negative effect upon the HRQoL was considerable and significant regardless of the primary treatment. The negative effect was moderate in the HA group and resulted in a reduction in the EQ-5D $_{index}$ score of 0.07 after 2 years. By comparison, the deterioration after 2 years in the 3-part fracture in a comparable group of patients with a 3-part proximal humeral fracture treated with a locking plate was 0.15 (*Study II*). The negative effect upon the quality of life was more pronounced in the non-operative group. The deterioration in the EQ-5D $_{index}$ score after 2 years in this group was 0.22, which is of the same magnitude, 0.26, as for patients with displaced 3-part fractures treated non-operatively (*Study II*).

Although the outcome regarding pain was acceptable in the HA group, the outcomes regarding ROM and strength are still disheartening. Our result with a Constant score of 48 is comparable to that of previous studies with at least a 1-year follow-up, with Constant scores ranging from 41 to 54.[15,53,78,89,95] However, the comparison is difficult to interpret since the study populations differ a lot regarding age and the type of fracture. Our strict approach to the assessment of the Constant score also in this study may have ended in an underestimation of the results.

Our finding of a DASH score of 30 after 2 years is even more difficult to interpret as studies on 4-part fractures reporting DASH 2 years after HA are lacking. By comparison, the DASH score after 2 years in a comparable group of patients with a 3-part proximal humeral fracture treated with a locking plate was 26 (*Study II*). Further comparisons with that particular study are interesting. For example, the pain according to VAS at 2 years after a 3-part proximal humeral fracture treated with a locking plate was 17, compared to 15 in the present study. The mean flexion and abduction after a 3-part fracture treated with a locking plate was 120° and 117°, respectively, compared to 93°and 86° in the present study. So, one of the main differences between a 3-part fracture treated with a locking plate and a 4-part fracture treated with an HA seems to be the ability to restore ROM.

The difficulties in restoring the ROM after an HA are well known. A primary HA for a true 4-part fracture is a real challenge for the surgeon. Excessive lengthening may result in pain and excessive shortening will affect ROM and strength.[30,41] The positioning and healing of the tubercles, especially the greater tubercle, is another important factor to be considered. The recommended optimal distance between the vertex of the prosthetic head and the top of the greater tubercle, i.e. the humeral head height, differs in the

literature. Demirhan and co-workers[39] stated that the humeral head height should be a maximum of 14 mm in order to achieve a good functional outcome. We were able to achieve a good position of the greater tubercle according to this criterion in almost 80% of our patients, indicating that the quality of surgery was acceptable. Obviously, there are other challenges besides obtaining a good primary positioning of the prosthesis and the tubercles, e.g. maintaining the position of the tubercles in the osteoporotic bone and still allowing mobilization as early as possible. Nearly 20% of our patients had a secondary displacement of the greater tubercle. However, only 2 of the patients treated with a primary HA were reoperated upon. One patient underwent an arthroscopic acromioplasty and release of adhesions due to extreme stiffness and one patient was reoperated upon due to a secondary displacement of the greater tubercle.

One patient in the non-operative group was operated upon using an HA due to a complete displacement of the shaft in relation to the head, which resulted in a loss of bony contact. All but one of the remaining 27 fractures healed, but nearly all of them were malunited. In addition, 3 patients developed an AVN. Despite this fact, the ROM was surprisingly good with a mean flexion and abduction of 95° and 87°, respectively. Our results regarding the Constant score, 50 points at 2 years, are difficult to compare since there are no previous studies reporting the 2-year outcome after non-operative treatment solely for patients with 4-part fractures. In a comparable group of patients with a 3-part proximal humeral fracture treated non-operatively (*Study II*), we found a mean forward flexion of 111° and a mean abduction of 106° after 2 years. The DASH score in the same study was 35, compared to 37 in the present study.

THE HEMIARTHROPLASTY TECHNIQUE

There is a general consensus that one of the most important factors for a good outcome is the healing of the greater tubercle in a good position.[13,76,78,95] We used the Global Fx® fracture prosthesis in all patients in our study. This is a fracture prosthesis of the 2nd generation, which is modular with different sizes of the stem and head. It has a relatively large metaphyseal part which, theoretically, may interfere with osseous healing of the tubercles. More modern fracture prostheses have a narrower neck, which, at least theoretically, may improve osseous healing of the tubercles. However, it remains to be proved that these potential improvements in design will result in better functional outcomes. For example, Loew et al.[78] reported no significant difference in the Constant score after a mean follow-up of 30 months on comparing an anatomical prosthesis and a fracture prosthesis.

Since a lack of healing of the tubercles has been identified as one of the main factors leading to a poor functional outcome after shoulder arthroplasty in fracture patients, some surgeons have recently started to use the reversed shoulder arthroplasty, which is less dependent on the function of the rotator cuff. In a retrospective study with a 1-year follow-up comparing 17 patients operated upon between 1996 and 2001 using a conventional prosthesis with 16 patients operated upon between 2002 and 2004 using a reversed prosthesis, Gallinet et al.[49] report a significantly better flexion (97° versus 54°), Constant score (53 versus 39) for the reversed prosthesis, but no differences in the DASH score (37 versus 41). The results for the reversed prosthesis in that study are comparable to our results after a conventional HA regarding flexion (93°) and Constant score (48), while the DASH score for the reversed prosthesis was slightly worse

compared to our results (30). Other authors report similar results. In a retrospective study of 43 fractures treated with a reversed prosthesis, Bufquine et al.[23] report a mean forward elevation of 97^{o} and a Constant score of 44, which is virtually similar to our results after HA. Klein et al.[71], also in a retrospective study, report a mean flexion of 112°, a Constant score of 68 and a DASH score of 47. Finally, Cazeneuve et al.[26] reported a Constant score of 53 after a mean follow-up of 6.6 years in 36 fractures. The authors emphasized that the Constant score was reduced compared to a previous follow-up and that 63% of the patients displayed radiological loosening of the glenoid component. In summary, the reported outcome for the reversed prosthesis seems promising in single series but is not generally better overall than those reported for a primary HA. Results from prospective, preferably randomized, trials with a longer follow-up period are necessary before any further conclusions can be drawn.

QUALITY OF LIFE

The negative effect on the HRQoL was considerable regardless of the type of fracture and of primary treatment. The deterioration in the EQ-5D $_{index}$ score for 2-part fractures treated with a locking plate was 0.18, for 3-part fractures treated with a locking plate 0.15 and for 3-part fractures treated non-operatively 0.26. The corresponding figures for the 4-part fractures treated with HA was 0.07 and for 4-part fractures treated non-operatively 0.22. The reduction was generally substantial and of the same magnitude as that reported for patients with different types of hip fractures.[44,83] This finding contrasts with the general notion that injuries of the upper extremity generally have a minor influence on the quality of life compared to those of the lower extremity and further underlines the need for future studies in this particular field in order to improve the treatment.

An additional advantage of EQ-5D data now being available also for patients with proximal humeral fractures is that our data allow a comparison of the outcome in patients with different or multiple injuries/diseases and can be used to construct QALYs, which, for instance, is necessary in cost-effectiveness analyses in healthcare evaluations.[14]

Our results are, however, in contrast to those recently reported by Hallberg et al.,[55] who reported that all domains of the SF-36 were normalized 2 years after injury in 37 patients with a proximal humeral fracture. These results are difficult to interpret since the fracture type and treatment are not reported for any of the patients and the study population may not be comparable to ours, which only includes patients with displaced fractures. Furthermore, the conclusion that the quality of life according to SF-36 was normalized is based on a comparison with a reference population instead of a preinjury recall for each individual patient.

RESPONSIVENESS OF THE EQ-5D

The responsiveness of the EQ-5D in patients with proximal humeral fractures was good. The internal responsiveness of the EQ-5D was deemed to be good based on the large SRM and the statistically significant change score for the period between baseline and the 4-month follow-up. The external responsiveness of the EQ-5D was also acceptable as indicated by the ROC curve and logistic regression analysis showing that

the instrument was able to discriminate between patients with different degrees of improvement or deterioration between the 4- and 12-month follow-ups based on the EC (DASH).

The internal responsiveness can be quantified by the standard effect size (SES) and/or the SRM. As previously stated,[108] the SRM is probably the preferred statistical measure as it employs the standard deviations of the change scores as the denominator, which may be advantageous in comparison with the often used SES, where the standard deviation of the baseline scores is used and thus does not reflect change over time. We interpret the large change score and SRM for the EQ-5D $_{\text{index}}$ score as an indication of good internal responsiveness.

The results from the ROC analysis and the logistic regression supported the external responsiveness of the EQ-5D. To ensure a clinically relevant difference between the reference group and the comparison group, we entered groups that differed by at least 10 points according to the EC (DASH) between the 4- and 12-month follow-ups in the ROC analyses and the logistic regressions. As can be seen, the mean values on the EQ-5D in the clearly improved or clearly deteriorated groups were of exactly the same magnitude but, as expected, in opposite directions. It should also be noted that the marginally improved and marginally deteriorated groups, i.e. patients with differences in the DASH score below the limit considered to be clinically important (< 10 points), did not differ at all on considering the mean values of the EQ-5D. This seems reasonable and was expected since both of these instruments, even though they are correlated, do not, and should not, measure the same thing.

The definition of an MID to be used as an EC can constitute a challenge and, according to a recent review, an MID should preferably be based on several sources of information.[96] In this study the DASH was used as the EC and the chosen MID was based on results from two separate studies, using different methodologies, both of which found a cut-off of 10 points in the DASH to reflect a clinically meaningful difference.[54,101] The convergence of these results appears to support the meaningfulness of this MID.

The correlation between change scores from the DASH and the EQ-5D was moderately strong and in the predicted direction, thus supporting the external responsiveness of the EQ-5D. This further supports the responsiveness of the EQ-5D in this patient group.

The ceiling effect shown in previous studies[17] suggests that the EQ-5D might be less responsive to changes in conditions with low morbidity. In elderly patients with a proximal humeral fracture, a condition with major morbidity, this should not be a significant problem. 48% of our patients reported the best possible score, 1.00, before the fracture while only 9% did so at the 4-month follow-up.

Responsiveness is one important attribute of HRQoL measures.[2] In a review of patient-based outcome measures, Fitzpatrick et al.[46] state that there are 8 important criteria for the selection of an instrument in a clinical trial: appropriateness, reliability, validity, responsiveness, precision, interpretability, acceptability and feasibility. In our opinion, the results of the present study confirm that the EQ-5D has good responsiveness, acceptability and feasibility, i.e. that the instrument is sensitive to important changes in the population, is highly acceptable for completion by the respondents with a response rate of above 98% at all assessments and, finally, it is easy to use by the researcher.

Responsive outcome measures are necessary to evaluate the efficacy and effectiveness of patient care. For instance, an outcome instrument with unknown or unsatisfactory responsiveness for a specific condition may not be able to detect a favorable outcome for a certain treatment and lead the researchers to draw the erroneous conclusion that the treatment was ineffective. Therefore, evaluating the responsiveness of different outcome instruments in defined patient populations, preferably within the context of a prospective trial, is an important task for research.[46] Moreover, several methods are available to evaluate responsiveness[46,64] and, accordingly, in this study we have employed a number of these methods in order to assess responsiveness in a comprehensive manner.

SAMPLE SIZES

At the time when the studies were planned (2002) there was only 1 published RCT comparing non-operative treatment with internal fixation[112] and 1 published RCT comparing non-operative treatment with HA[105]. Moreover, there were not yet any data available regarding the outcome after treatment with locking plates. Finally, there were no available data for the primary outcome measure used in these studies, i.e. the EQ-5D, in patients with proximal humeral fractures. Therefore, we did not have any reliable data to perform formal power analyses, but we made a crude estimation of power based on assumptions. The estimation indicated that a sample size of 50–60 patients would be sufficient in both RCTs (*Studies II* and *III*).

A power analysis based on our present data from *Study II* indicates that a sample size of 160–180 patients would have been required to provide a power of 80% to identify a difference in the EQ-5D $_{index}$ score of 0.10 after 2 years with a significance level of 0.05.

While *Study III* was able to statistically confirm the difference in the EQ-5D $_{index}$ score, it failed to confirm the differences in the DASH and pain scores, most probably due to insufficient power.

Although this lack of power in the comparison between the randomization groups is obviously a limitation of *Studies II* and *III*, in our opinion, the studies still provide valuable prospective data regarding the 3 treatment modalities, e.g. data on HRQoL.

STRENGTHS AND LIMITATIONS

A strength of the thesis is that all included studies are prospective and 2 of them are also randomized controlled ones (*Studies II* and *III*) including well-defined study populations with defined types of fractures that are easy to diagnose on conventional radiographs in combination with CT. The surgical treatment was performed with modern implants: in *Studies I* and *II* a locking plate and in *Study III* a fracture HA which was considered to be one of the best at the time when the study was started (2003). Furthermore, the quality of the surgery was what can be expected from orthopedic surgeons experienced in shoulder surgery.

The outcome was assessed with well-validated outcome instruments, including a self-reported quality of life instrument, and the follow-up rate was good. Moreover, the final outcome was assessed by an unbiased observer, i.e. an orthopedic surgeon not

previously involved in the treatment. However, it would have been even better if this observer would have been blinded to the treatment modality.

The fact that our interpretation of the quality of life data is based on our patients' ability to correctly recall their health status prior to the shoulder fracture may be considered a weakness. However, since a prospective collection of preinjury HRQoL data is not possible in trauma studies, we have to rely on preinjury recall or a comparison with population figures. Our patients' assessments of their prefracture EQ-5D $_{index}$ score were slightly higher than in comparable age groups of the Swedish reference population,[24] which may be explained by our inclusion criteria, which selected healthier elderly individuals. For example, we opted not to include patients with severe cognitive dysfunction and/or dementia because they would have difficulties assimilating the rehabilitation conditions and would not benefit from the surgical intervention. Furthermore, a recent study reports that older patients can accurately recall their previous health status up to 6 weeks back.[80] Therefore, we believe that the effect of recall bias can be considered to be limited.

Finally, it would have been useful to include a CT at the final follow-up in the HA group in order to more accurately assess the position and healing of the tubercles.

CONCLUSIONS

STUDY I

The results of the study showed an acceptable complication rate and an acceptable functional outcome after treatment with a locking plate in elderly patients with a displaced 2-part fracture of the surgical neck of the proximal humerus.

STUDY II

The results of the study indicated an advantage in functional outcome and HRQoL in favor of the locking plate as compared to non-operative treatment in elderly patients with a displaced 3-part fracture of the proximal humerus, but at a cost of additional surgery in 30% of the patients.

STUDY III

The results of the study demonstrated a significant advantage in quality of life in favor of HA as compared to non-operative treatment in elderly patients with a displaced 4-part fracture of the proximal humerus. The main advantage of HA appeared to be less pain, while there were no differences in ROM.

STUDY IV

The EQ-5D displayed good internal and external responsiveness in patients with proximal humeral fractures and can be recommended for use as a quality-of-life measure in patients with this particular injury.

ADDITIONAL CONCLUSION

Regardless of the primary treatment, a displaced fracture of the proximal humerus results in a substantial negative effect upon the patients' HRQoL of the same magnitude as that reported by patients with hip fractures.

CLINICAL IMPLICATIONS

The locking plates appear to be a good treatment alternative in elderly patients with a displaced 2-part fracture of the surgical neck of the proximal humerus with an acceptable complication rate and an acceptable functional outcome. However, rigorous attention has to be paid to the surgical technique, especially so as to avoid screw penetration and to achieve good reduction and maximum initial stability.

There seems to be an advantage in functional outcome and quality of life in favor of the locking plate as compared to non-operative treatment in elderly patients with a displaced 3-part fracture of the proximal humerus. The main advantage appeared to be an improved ROM. However, despite a modern fixation technique and overall good primary reductions in the locking plate group, 13% of the patients had a severe complication requiring a major reoperation and 17% had a minor secondary surgical intervention.

There appears to be an advantage in the quality of life in favor of HA as compared to non-operative treatment in elderly patients with a displaced 4-part fracture of the proximal humerus. The main advantage appeared to be less pain. However, despite use of a modern fracture prosthesis and an appropriate surgical technique with a low reoperation rate, there were no differences in ROM.

The possible gain in function and HRQoL after treatment with a locking plate in 2- and 3-part fractures and HA in 4-part fractures, balanced against the risk and inconvenience of surgery, is probably justified in the healthy elderly patient with high functional demands and when surgery is performed by an experienced surgeon. On the other hand, the overall acceptable outcome and limited need for secondary surgical interventions in the non-operative group indicate that conservative treatment is probably sufficient for the most elderly patients with lower functional demands or when a surgeon with adequate experience is not available.

ABSTRACT IN SWEDISH

Den optimala behandlingen av axelfrakturer (proximala humerus) är fortfarande kontroversiell, speciellt hos äldre patienter med osteoporos. För 2- och 3- fragments frakturer enligt Neers klassifikation är det en trend att allt oftare behandla kirurgiskt med moderna vinkelstabila plattor. För de mer splittrade 4- fragmentsfrakturerna, med större risk för avaskulär nekros, har halvplastik blivit en accepterad behandlingsmetod. Den alternativa behandlingen för dessa frakturer är icke-kirurgisk med en kort period med immobilisering följd av aktiv sjukgymnastik.

I den senaste systematiska översikten från Cochrane avseende proximala humerusfrakturer är slutsatsen att det inte finns tillräcklig evidens från randomiserade kontrollerade studier för att kunna avgöra vilken behandling som är mest optimal för respektive frakturtyp. Det rekommenderas också att behandlingsresultaten i framtida studier utvärderas med instrument som är validerade och som dessutom beskriver resultaten ur patientens perspektiv, t.ex. instrument som mäter hälsorelaterade livskvalitet. Det finns dock en risk för att dessa instrument, pga. av sin design, kan ha en begränsad känslighet för små men betydelsefulla förändringar i patienternas hälsotillstånd, dvs. de kan ha en begränsad responsiveness.

I en prospektiv kohort studie med 2 års uppföljning, behandlades 50 patienter med en felställd 2-fragmentsfraktur i proximala humerus med en vinkelstabil platta. Resultaten visade att vinkelstabil platta förefaller vara ett bra behandlingsalternativ med acceptabel komplikationsfrekvens och ett acceptabelt funktionellt resultat.

I en randomiserad kontrollerad studie med 2 års uppföljning, behandlades 60 patienter med en felställd 3- fragments fraktur i proximala humerus antingen med en vinkelstabil platta eller icke-kirurgiskt. Resultaten indikerade bättre funktion och livskvalitet hos patienter behandlade med vinkelstabil platta, men till priset av reoperation hos 30% av patienterna. Den största fördelen med vinkelstabil platta tycktes vara att behandlingen gav ett bättre rörelseomfång i axeln.

I en randomiserad kontrollerad studie med 2 års uppföljning behandlades 55 patienter med en felställd 4-fragments fraktur i proximala humerus antingen med en primär halvplastik eller icke-kirurgiskt. Resultaten visade en signifikant bättre hälsorelaterad livskvalitet hos patienter behandlade med halvplastik. Den största fördelen med halvplastik tycktes vara mindre smärta medan det inte fanns några skillnader i rörelseomfång.

145 patienter med en felställd fraktur i proximala humerus inkluderades i en studie med syfte att utvärdera responsiveness för EQ-5D. EQ-5D visade god responsiveness och kan rekommenderas som instrument för utvärdering av hälsorelaterad livskvalitet hos patienter med denna frakturtyp.

En övergripande slutsats av samtliga studier var att, oavsett primär behandling, resulterade en felställd proximala humerusfraktur i en påtaglig försämring av patienternas hälsorelaterade livskvalitet.

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ORIGINAL PAPERS I–IV