The acute osteoporotic vertebral compression fracture

Its natural course and characteristics

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"Three months after the fracture, I no longer needed to visit the hospital because the doctor said that the X-ray showed healing of the fracture. But I continued to have problems two years after the fracture. I went to acupuncture, to the chiropractor, and so on. Since I believed that the X-ray showed healing of the fracture, I thought that the pain would soon leave. But too much time passed without the pain subsiding. During two years of my life, I missed out on so many things. If there was a good treatment, I would have taken."

From my relative with an osteoporotic vertebral compression fracture

CONTENTS

LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. **The course of the acute vertebral body fragility fracture: its effect on pain, disability and quality of life during 12 months.**
Suzuki N, Ogikubo O, Hansson T. (2008) Eur Spine J 17(10): 1380-90

II. **The prognosis for pain, disability, activities of daily living and quality of life after an acute osteoporotic vertebral body fracture: its relation to fracture level, type of fracture and grade of fracture deformation.**
Suzuki N, Ogikubo O, Hansson T. (2009) Eur Spine J 18(1): 77-88

III. **Previous vertebral compression fractures add to the deterioration of disability and quality of life after an acute compression fracture.**
Suzuki N, Ogikubo O, Hansson T. Eur Spine J (submitted)

IV. **Characteristics of the acute and prevalent osteoporotic vertebral compression fractures.**
Suzuki N, Hansson T. Eur Spine J (submitted)

DEFINITIONS AND ABBREVIATIONS

vertebral fracture	a break in the continuity of the vertebral bone
vertebral deformity	changes in the shape of the vertebral body visible on a lateral spinal radiograph, especially when using quantitative morphometric methods in epidemiological studies including vertebral fracture and degenerative or congenital change
incident fracture	vertebral fracture assessed by a series of radiographs taken over time [6], usually using a morphometric method comparing a baseline X-ray with a following examination
prevalent fracture	vertebral fracture assessed by an evaluation of spinal radiographs taken at a single time point [6], usually using a morphometric method, and not differentiating between an acute and a previous fracture
acute fracture	a fracture not older than approximately one month
previous fracture	a fracture which happened before the acute fracture
subclinical fracture	a vertebral fracture not clinically diagnosed, i.e. a vertebral fracture detected in a population-based radiographic survey
adjacent fracture	a fracture which exists on an adjacent vertebra
osteoporosis	a skeletal disorder characterized by compromised bone strength predisposing a person to an increased risk of fracture [80]
bone fragility	fracture or the risk of a fracture, even with minor trauma
ADL	activities of daily living
ANOVA	analysis of variance
EQ-5D	five-dimensional scale of the EuroQol instrument
MD	median
MRI	Magnetic Resonance Image
ns	not significant
QoL	quality of life
SD	standard deviation

ABSTRACT

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Its natural course and characteristics

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Aim

The vertebral body fracture is the most frequent type of all osteoporotic fractures. In spite of this, there is considerable uncertainty regarding its frequency, the severity and duration of the pain, and the magnitude of impairment in terms of disability and disturbed activities of daily life during the post-fracture period. The overall aim of this thesis was to investigate the natural course and the characteristics of the acute osteoporotic vertebral compression fracture in order to better understand and improve treatment for this type of fracture.

Patients and methods

Eligible patients were all patients over 40 years of age who sought medical care at the emergency unit at Sahlgrenska University Hospital (studies I-III) or referred to the X-ray Department at Capio Diagnostic Center (study IV) because of back pain with a radiographically-confirmed acute vertebral body fracture which resulted from a low energy trauma. In studies I-III, a total of 107 patients were followed over one year using postal questionnaires. In study IV, a total of 448 patients were included.

The pain, disability, ADL, and QoL were measured after 3 weeks, and 3, 6 and 12 months (studies I-III). The patient and fracture characteristics on the first X-ray visit were evaluated in all the studies.

Results

Studies I-III. For all the outcome measures, the largest improvements, 10-15%, occurred between 3 weeks and 3 months. Thereafter, all the outcome measures levelled off or even worsened. One year after the fracture event, the patients' conditions were poor: 60.5 for the pain intensity score, 53.9 for the disability score, 47.6 for the ADL score, and 0.52 for EQ-5D. These average values are similar to values seen preoperatively in patients with a herniated lumbar disc disease or in patients who are 100% disabled from work due to back or neck problems. The most influential factors were the initial fracture

deformation severity and the number of previous fractures, whereas fracture level, fracture type, and gender influenced to a lesser extent.

Study IV. The acute fracture characteristics were similar to those found in previous population-based studies of incident and prevalent fractures and in studies I-III. In the prevalent fracture analysis, concave fractures were frequent below L2 whereas wedge fractures were more frequent above L2. Mildly deformed fractures increased in the caudal direction and moderately deformed fractures increased in the cranial direction. Severely deformed fractures were frequent in the mid-thoracic spine and at the thoracolumbar junction.

Conclusions

One year after the acute fracture, it was striking to find that 76% of the patients still had a high pain intensity and the mean QoL score was 35% lower than the population value for the same age group. This finding is quite different from the generally believed good prognosis for such a fracture. There is potential for better treatment. The relationship between the poor outcomes and the initial facture deformation severity specifically suggests the indication for invasive treatment, such as vertebroplasty or kyphoplasty.

Keywords: Vertebral body fracture, Osteoporosis, Pain, Quality of life, Disability, Compression fracture, Prognosis, Treatment, Prevalent fracture, Epidemiology

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SUMMARY IN JAPANESE
要約

骨粗鬆症性脊椎圧迫骨折；
その自然経過と特徴について

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目的
脊椎圧迫骨折は骨粗鬆性骨折の中でもっとも頻度の高い骨折である。それにも関わらず、時間経過におけるその痛みの頻度や程度、さらには日常生活の障害程度などについて、はっきりした研究はなされていない。この一連の論文の目的は骨粗鬆症性脊椎圧迫骨折の自然経過とレントゲン的、疫学的特徴を明らかにし、今後の治療に役立てることである。

対象および方法
Studies I-III：サルグレンスカ大学病院の救急外来に腰痛のため受診し、微小外力による新規圧迫骨折をレントゲン上認めた 40 歳以上の患者が対象である。この研究への参加の同意が得られ、1 年間にわたる郵送による質問表への返答が得られたのは 107 名であった。痛み、痛みによる生活障害程度、ADL、QOL について骨折後 3 週、3 ヶ月、6 ヶ月、12 ヶ月に評価した。同時に骨折のレントゲン的特徴なども評価した。
Study IV：サルグレンスカ大学病院の救急外来に腰痛のため受診した患者およびヨーテボリの主要なレントゲンセンターである Capio Diagnositc Center にレントゲン撮影を腰痛のため依頼された患者で微小外力による新規圧迫骨折をレントゲン上認められた 40 歳以上の患者についてその骨折のレントゲン的特徴などについて評価した。

結果
Studies I-III：すべての質問表評価において 3 週後と 3 ヶ月後の間にて最も顕著な状態の改善が見られた。それでも 3 週後の値と比較すると平均約 10-15%の改善しか見られなかった。しかし、その後はすべての評価は変わらないか、逆に悪化する傾向さえ見られた。1 年後の状態は決して良いものではなく、pain intensity score は 60.5、disability score は 53.9、ADL score は 47.6、EQ-5D は 0.52 であった。これらの状態は手術前の椎間板ヘルニアの患者や、腰痛や頚部痛のため 1 ヶ月以上完全に仕事を休んでいる患者の状態に匹敵するものであった。この障害状態に最も関連している因子として初期の骨折程度と既存骨折の数があげられたが、骨折高位や骨折型、性別などの影響は少なかった。
Study IV：臨床的に診断された新規圧迫骨折および患者の特徴はこれまでの population based study における incident fracture や prevalent fracture の特徴と類似していた。さらに Studies I-III では多くの患者が研究に参加しなかったため患者選択

のバイアスが起きた可能性があったにも関わらず、その患者の特徴はこの Study IV と類似していた。既存骨折の解析では中央陥凹型は L2 より遠位に多く、楔状型は L2 より近位に多かった。軽度変形骨折は尾側方向に向かって増加し、中度変形骨折は頭側方向に向かって増加した。重度変形骨折は胸椎中央部と胸腰椎移行部に集中する傾向があった。

考察

骨折後 1 年にても 76%の患者がひどい痛みを感じており、QOL も同年代の平均値と比べると 35%も低い値であり、この骨折は予後良好と以前より信じられていたが、それと反するものであった。一因としてこの強固な外固定なしの早期 mobilization が有効でない可能性も否定できない。また、3 ヶ月以降状態が改善しないこと、重度変形骨折および既存骨折の数が主要な予後不良因子であることを考えると、3 ヶ月しても症状が改善しないような既存骨折を伴う重度変形骨折は、最近開発された比較的侵襲が少なく有効性の高い vertebro-または kypho-plasty を考慮してもいいのではないかと思われる。

INTRODUCTION

The natural course of an acute vertebral compression fracture

In a clinical situation, the type and severity of symptoms can vary from patient to patient and also over time. A patient may sometimes experience pain that is very severe despite a minor injury. Another patient may experience little or no pain despite a major injury. Some patients experience severe initial pain that improves rapidly over time, while others experience mild initial pain that worsens over time. The studies of this thesis were motivated by the fact that the natural course of this very common fracture was largely unknown. Knowledge of the prognosis of the pain, ADL and QoL after an acute fracture would aid in the improvement in treatment and advice for these disabled patients.

BACKGROUND

1. Epidemiology of vertebral body fractures

1.1. Prevalence and incidence

The vertebral body fracture is the most frequent type of osteoporotic fracture [13]. Approximately 30-50% of women and 20-30% of men develop vertebral fractures and half of them develop multiple fractures during their lifetime, compared with a 15.6% lifetime risk of a hip fracture [92]. In Sweden and Japan, the prevalence and incidence rates of vertebral fractures are among the highest in the world [29, 33, 95]. The age-adjusted incidence rate of a vertebral body fracture in Swedish women has been found to be 17.7 in 1000 person-years [29]. The prevalence rate in Japanese women 70 years of age is 30-40% [33]. Since the incidence rate of this fracture increases with age, it is also likely that the fracture prevalence rate will increase in the near future due to the increasing proportion of elderly in most populations [62]. In addition, remarkable increases in incidence and prevalence rates among similar age groups, especially among those of older age, were noted between the 1950s and 1980s in Sweden [5]. A rising incidence of elderly with osteoporosis, a higher frequency of falls, and a higher incidence of deleterious falls have been suggested as reasons for this increase [63, 82].

Once a vertebral compression fracture occurs, it can be a risk factor for future fractures, including non-spinal fragility fractures [40, 59, 77]. The occurrence of a vertebral fracture has also been found to be associated with an increased mortality [14, 15, 58].

1.2. Economic impact

In Sweden, the average medical cost for the first year after a vertebral fracture has been estimated as 12544 €, as compared to 14221 € for a hip fracture [8]. This demonstrates that the vertebral compression fracture is significant not only in terms of high prevalence, but also in terms of medical expenditure.

2. Study design

For studying vertebral body fractures, two different types of study designs may be used: population-based or clinical case. Most studies are population-based, and report the number and effect of prevalent fractures.

2.1. Population-based study

A population-based study evaluates the average effects among all people with vertebral fractures, including symptomatic and asymptomatic patients who do not seek medical care, and tries to detect subtle changes that may not be

reported as symptoms. Changes in vertebral body shape, visible on a lateral spinal radiograph, do not always represent a fracture. Congenital abnormalities, Scheurmann's disease, malignancies and degenerative conditions may resemble fracture changes. Since a population-based study usually uses morphometric approaches for defining and quantifying vertebral fractures, there is the risk that other deformities may be included. For this reason, changes in vertebral body shape, visible on a lateral spinal radiograph, especially when using quantitative morphometric methods in epidemiological studies, are also referred to as ***vertebral deformities*** rather than ***vertebral fractures*** [65, 66]. Two different types of fractures or deformities can be studied, prevalent or incident.

2.1.1. Prevalent deformity (fracture) study

In this situation, the X-ray is taken only at one certain point in time. It is not known when the deformity (fracture) actually occurred. For this reason, acute and previous fractures, as well as non-fracture-related deformities, can also be included.

2.1.2. Incident fracture (deformity) study

The incidence fracture refers to a fracture occurring between two different X-ray examinations. Among other measures, changes in vertebral height can be quantified using these two X-rays. In the literature, the reported duration between the two examinations has usually been between 1-3 years, depending on the study design, however some studies have been more than 20 years [5, 65, 93, 94, 96, 100, 109]. An incident fracture study includes recent and old fractures and sometimes also deformities, especially when the time interval between the examinations is long.

2.2. Clinical case study

Most clinically-diagnosed fractures are detected during an investigation of back pain. However, some patients with fractures experience little to no symptoms, and therefore do not seek medical attention. For this reason, patients with clinically-diagnosed vertebral fractures usually have worse symptoms than patients with vertebral fractures detected in population-based studies [92]. Despite such selection bias, this type of study is the only way to assess the time course of this fracture.

Table 1. Characteristics of clinical and population-based studies of patients with vertebral fractures.

Population-based studies:
- Include asymptomatic patients
- Include patients with mild to severe fracture
- Results generally represent long-term effects; most fractures probably occurred years ago
- For cross-sectional studies, the true age of the fracture is unknown

Clinical case studies:
- Patients usually are symptomatic
- Representativeness of controls and cases is difficult to ascertain
- Many studies lack control patients

3. Radiographic diagnosis of vertebral body fractures

Radiographs of the thoracic and/or lumbar spines still remain the standard method to diagnose a vertebral fracture. However, determining the presence of an acute fracture from a single X-ray is, in many cases, far from easy.

3.1. Visual analog vs. morphometric methods

The visual analog method is the standard method used in the clinical situation. An experienced clinician or radiologist can visually detect changes in vertebral shape on an X-ray, and thus diagnose the acute vertebral fracture [54]. To reduce inter-observer variability, morphometric methods have been developed in order to provide more objective and reproducible criteria to assess a vertebral fracture. Morphometry alone cannot establish the diagnosis of the vertebral fracture at sufficient levels of sensitivity and specificity. Morphometric methods can only detect deformity aberrations which include both fractures and degenerative or congenital changes. Radiological criteria other than the height measurement need to be implemented in order to differentiate between ***fractures*** and ***deformities*** of different origins [117]. Moreover, fracture acuteness is difficult to diagnose at the time of injury in elderly patients with osteoporosis and it is even more difficult when the patient has an old fracture(s). For these reasons, the presence of multiple fractures is determined using serial X-rays, comparing the vertebral shape change, or by using MRI. In studies I-III, the standard clinical procedures to diagnose a vertebral fracture were implemented, i.e. subsequent X-rays or MRI examinations were scrutinized when performed.

3.2. Radiographic criteria to detect vertebral body fractures

There are many methods available to detect fractures from X-rays. Morphometric or semiquantitative methods are usually used in population-based studies. The visual analog method is the standard method used in clinical practice.

- *visual analog method*

  This method is used to visually detect changes in vertebral shape and thus diagnose a fracture. Its acuteness is mainly determined by the presence of evident sharp edges and no callus formation [5, 55].

- *semiquantitative method*

  This method defines a vertebral body deformity as having a 20-25% or more reduction in height and 10-20% or more reduction of the vertebral body area, without measuring [34-36].

- *morphometric method*

  Morphometric methods use the following criteria for determining a vertebral body deformity:

  - vertebral height ratio: when the anterior or middle height is 0.85 or less than the intact posterior height, and when not intact, compared with the posterior height of an intact adjacent vertebra [78]

  - vertebral height ratio: 3-4 SD or more below the population value [25, 76]

If serial radiographs are available, an incident fracture is defined as the following:

- *semiquantitative method*

  - higher deformity grade than at the baseline evaluation [34-36]

- *morphometric method*

  - 15-20% or more reduction in any of the height measures of a specific vertebra [6, 85]

  - absolute reduction in height of 4 mm or more [29]

4. Evaluation of clinical symptoms

4.1. Pain

A multitude of pain symptoms has been attributed to vertebral fractures.

4.1.1. Prevalence

Among the patients with and without incident vertebral fractures (fracture was defined as 15% or more reduction of the vertebral height on serial X-rays with an one year interval), 53% and 21%, respectively, reported some frequency of back pain [93]. This means that approximately half of the patients with radiographic evidence of a vertebral fracture(s) reported having no back pain.

4.1.2. Duration

It is generally believed that pain after a compression fracture persists only for weeks or a few months at the most [101]. Some studies, however, have reported patients with pain lasting for several years, e.g. even up to 12 years, after this type of fracture [4, 47, 48, 87].

4.1.3. Intensity

It was reported that spontaneous pain intensity, as measured using a visual analogue scale, did not significantly decrease until 15 days after the fracture, and decreased by approximately 40% when measured at 30 days [37]. Others reported that acute fracture pain decreased by 22% at day 7, and by 33% at day 14 [73]. However, there are no studies which have evaluated the pain intensity for an extended period of time. Thus, there is considerable uncertainty about the frequency, extent and severity of the acute pain, and even more about the duration of pain.

4.2. ADL and QoL

It is well reported that a vertebral body fracture has a negative impact on the patient's activities of daily living (ADL) and health-related quality of life (QoL) [1, 8-10, 17, 21, 28, 30, 42, 47, 70, 72, 84, 99, 102]. Both pro- and retrospective data show that the deterioration of health after a vertebral fracture can last for many years and with sequel that usually are worse than for other bone fragility fractures [41, 42, 47, 81]. In two Swedish studies, the effects of a vertebral fracture on QoL were prospectively studied. It was found that the compression fracture had a more negative and long-lasting impact on the patient's QoL than any other type of osteoporotic fracture, including the hip fracture [8, 42]. However, these studies did not analyze the relationship between QoL and the characteristics of the fracture, i.e. type of fracture, and grade of fracture deformation, and fracture location.

5. Treatment

The main goals of treating an acute vertebral compression fracture are to achieve pain relief and mobilization, in order to prevent further bone loss and/or fracture(s). Pain relief can usually be achieved using oral analgesics, however for severe pain, a rigid or semirigid thoracolumbar hyperextension orthosis may be useful. Mobilization should begin as soon as the acute pain begins to subside, i.e. 1-2 weeks following fracture. Patients should be encouraged to sit or stand for short periods, several times each day, and then slowly begin ambulation. Once the acute pain has subsided, the patient should begin a program of spinal extension exercises to strengthen the paraspinal musculature [101]. In Japan, there has been more focus on preventing further

vertebral collapse. A corrective extension cast is often applied since it is believed that early rigid outer fixation can prevent further collapse and pseudarthrosis [107, 114-116]. A survey among 429 hospitals in Japan showed that, for the treatment of fragility vertebral fractures, 4% of the hospitals usually did not use any orthosis or cast, whereas as many as 92% did. Broken down, the survey also showed that 43% of the orthosis were semirigid, 40% were rigid, 32% were casts, and 28% were soft corsets (multiple answers allowed) [68]. There are no convincing results that any of these treatment strategies for the acute vertebral fracture are more successful than the other.

Open surgery is sometimes considered necessary in patients in whom a progressive neurologic deficit or intractable pain develops. These operations are usually extensive and technically advanced due to the fragile bone. Over the past decade, new minimally-invasive techniques, vertebroplasty and kyphoplasty have been developed. There are many reports of their efficacy [20, 38, 50, 52, 64, 74, 87-89, 108], but still it is difficult to decide when and what type of patients should be treated using this technique.

6. Predictors of fracture prognosis

In the literature, there are only two studies that have investigated the prognosis of clinical symptoms after a compression fracture [73, 105]. In one of the studies, it was shown that patients with an obvious wedge fracture had severe, sharp pain which gradually decreased within four to eight weeks. Fractures with minimal superior endplate discontinuity tended to progress gradually to complete collapse of the vertebral body, causing a dull, less severe, although recurring pain [73]. The other study reported the development of a new X-ray classification system (swelled-front-type, bow-shaped-type, projecting-type, concave-type, and dented-type). In this study, it was concluded that swelled-front-type, bow-shaped-type, and projecting-type fractures had a poor prognosis, with late collapse and often showing a vacuum cleft. On the other hand, a good prognosis was found for concave-type and dented-type fractures [105].

In other studies, the influence of a ***prevalent*** fracture on pain, ADL and QoL has been examined. Type of fracture has been shown to have no influence on pain, ADL and disability [28]. A fracture(s) in the lumbar spine has been shown to worsen pain [16] and lower QoL [83, 102]. The number of fractures also influences the pain [97] and QoL [102]. The severity of the fracture has an effect on pain [28, 48] and QoL [75].

Using dynamic MRI, one study showed that the subsequent progression of a vertebral collapse tended to increase, as shown by a greater non-contrast area

in the injured vertebrae [60], but there was no evaluation of the relationship between symptoms and this MRI change.

AIMS OF THE THESIS

The overall aim of this thesis was to investigate the natural course and the characteristics of the acute osteoporotic vertebral compression fracture in order to better understand the prognosis of this fracture for improving treatment.

The specific aims of the studies were the following:

- to evaluate the natural course of pain, disability, ADL and QoL during one year in patients who suffered an acute osteoporotic vertebral compression fracture (study I),

- to analyze how fracture characteristics of the acute osteoporotic vertebral compression fracture, such as fracture type and fracture deformation, influence pain, disability, ADL and QoL during one year (study II),

- to analyze the influence of a previous vertebral compression fracture (number, level and closeness to the acute fracture) on pain, disability, ADL and QoL in patients with an acute osteoporotic vertebral compression fracture (study III),

- to investigate the characteristics of acute and prevalent osteoporotic vertebral compression fractures in a representative cohort of fractured patients (study IV).

PATIENTS AND METHODS

7. Study design

In studies I-III, an observational longitudinal prospective design was used for analyzing radiographic data, registry data and data obtained through postal questionnaires on four different occasions during the year following an acute vertebral compression fracture. In study IV, a retrospective cross-sectional study design was used for analyzing registry and radiographic data.

8. Inclusion criteria

8.1. Studies I-III

Eligible patients were all patients over 40 years of age who sought medical care at the emergency units at Sahlgrenska University Hospital (SU/S and SU/M), Gothenburg, Sweden, because of back pain and had a radiographically-confirmed acute vertebral compression fracture which resulted from a low energy trauma. The study was conducted from December 2003 to November 2006. The presence of an acute fracture was primarily decided by the attending radiologist. For study purposes, two experienced spine surgeons separately re-evaluated the radiographs.

8.2. Study IV

Patients eligible for study IV included all patients over 40 years of age who were X-rayed at the emergency units at Sahlgrenska University Hospital (SU/S and SU/M), as well as patients referred to the X-ray department at Capio Diagnostic Center, Gothenburg, Sweden, between December 2005 and November 2006, and had a radiographically-confirmed acute vertebral compression fracture.

The selection of the fractured patients differed somewhat between the units. At the Sahlgrenska units, the suspicion of an acute fracture was determined from the radiologist's written statement and the X-ray was re-evaluated by two spine surgeons. At the Capio Diagnostic Center, the presence of an acute fracture was assessed retrospectively, first searching the electronic files with a large number of search terms that could suggest the presence of an acute fracture. All the examinations localized through this search were then scrutinized by a spine surgeon.

9. Exclusion criteria

9.1. Studies I-III

Patients that were excluded from studies I-III were those with any other type of acute fracture (forearm, hip, etc.), fracture(s) related to malignancy,

infection, or any other bone disease, except osteoporosis, that could affect the mechanical integrity of the vertebrae in the lumbar or thoracic spines. Patients having or suspected as having more than one acute fracture were also excluded from studies I-III.

9.2. Study IV

The same exclusion criteria as in studies I-III were applied to study IV, with the exception of patients with any other type of acute fracture, which were not excluded.

10. Patient participation

10.1. Studies I-III

A total of 341 patients were invited to participate in the studies. The details of the included patients can be seen in Figure 1. Due to internal missing data in the response to von Korff's disability score, six patients had to be excluded from the analysis of this particular instrument.

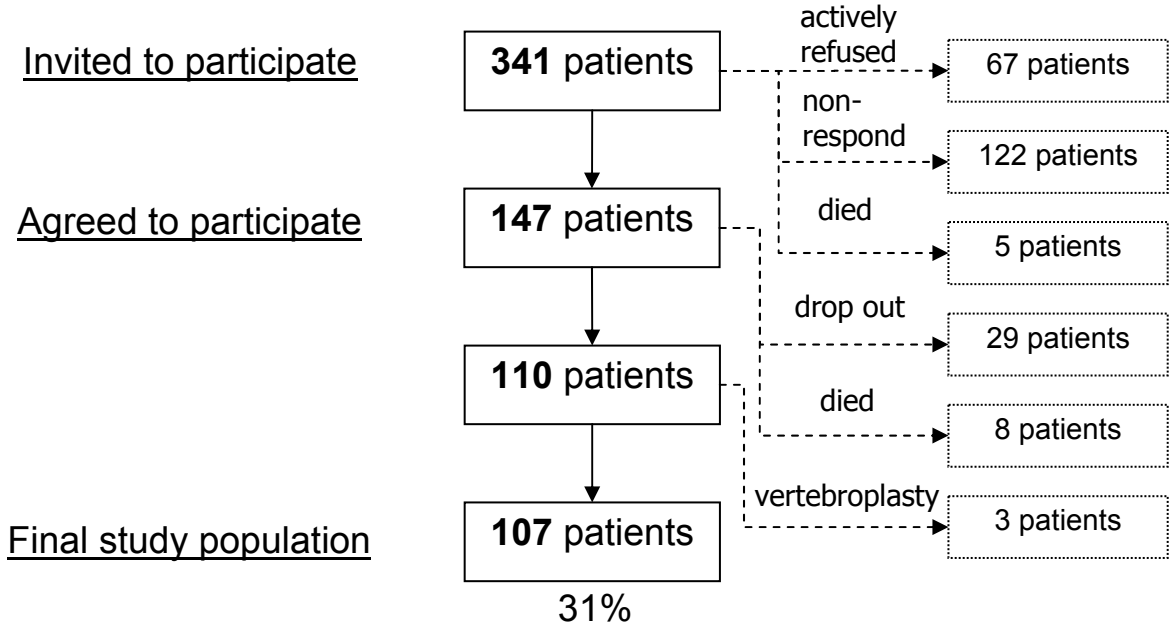

Figure 1. Patient participation in studies I-III.

10.2. Study IV

A total of 844 patients, 304 and 540 patients from the two respective centers, fulfilled the first inclusion criteria, i.e. the suspicion of at least one acute compression fracture irrespective of fracture age, cause or pathology (Figure 2). Out of the 844 patients, 448 were diagnosed as having an acute fracture.

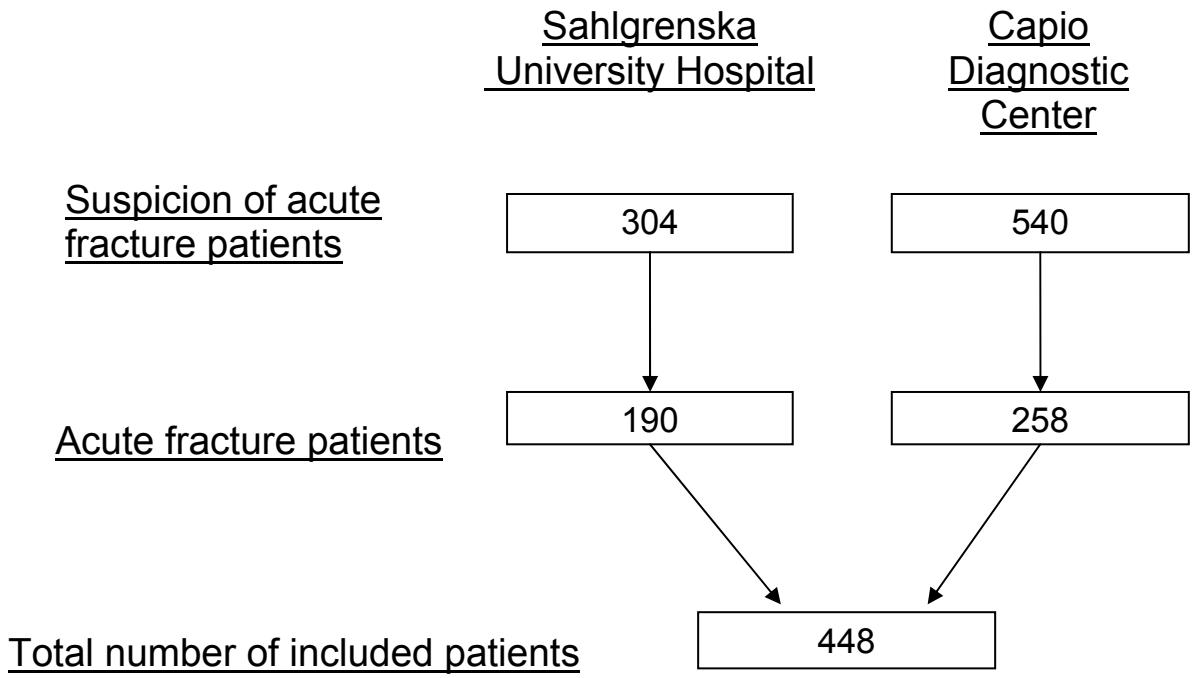

Figure 2. Patient participation in study IV.

11. Non-responders (Studies I-III)

A total of 234 patients refrained from participation. The average age for these patients, irrespective of reason, was 81.1 years (SD 13.2), which was higher than the average age for those included in the studies. The percentages of women and men were 64% and 36%, respectively.

12. Treatment (Studies I-III)

All the patients were mobilized as soon as possible, usually more or less immediately and without casts or braces. If pain prevented such an early mobilization, a soft brace was used. Twelve of the patients used a soft brace for different lengths of time. Analgesics were usually prescribed and the advice to the patient was to try to resume normal physical activity as soon as possible. The prognosis told to the patient was that the pain would disappear within weeks to some months. If problems continued, the patient was instructed to contact his/her general practitioner.

13. Preventive treatment (Studies I-III)

Out of 107 patients, 14 reported that they had taken medication during the year prior to the actual fracture in order to increase their bone mineral.

14. Radiographic examination

14.1. Studies I-III

Lateral and frontal view radiographs of the spine were taken at the first visit to the hospital's emergency unit. The X-ray examination was used for the determination of the following: presence of an acute fracture, previous fracture, fracture level, fracture type and grade of deformation, adjacent fracture, thoracic kyphosis, and lumbar lordosis. The acute vertebral body fracture was determined based on the following: 1. the existence of the fracture deformation compared with the normal neighboring vertebrae, 2. the presence of pain at or near the fracture deformation, 3. an evident sharp edge in the deformed region, and 4. no callus formation at the fractured vertebra [5]. In questionable cases, the previous or subsequent examinations were used to confirm the acuteness, if available. Information from MR images, when available, was also used for determining the fracture acuteness. In cases of divergent opinions, the cases were discussed until a consensus was reached.

Three osteoporotic fracture types, i.e. wedge, crush, and concave, have been described (Figure 3) [91]. With a wedge fracture, the anterior border is collapsed while the posterior border remains intact or nearly intact. The crush fracture refers to a collapse of the entire vertebral body. With a concave fracture, the central portion of the vertebral body is collapsed [91].

The grade of fracture deformation was evaluated by the semiquantitative method presented by Genant [34-36]. The extent of deformation was graded on visual inspection and without direct vertebral measurement according to the following: normal (grade 0), mildly deformed (grade 1, approximately 20-25% reduction in anterior, middle, and/or posterior height and a reduction in the area of 10-20%), moderately deformed (grade 2, approximately 25-40% reduction in any height and a reduction in the area of 20-40%), and severely deformed (grade 3, approximately 40% reduction in any height and area) (Figure 3).

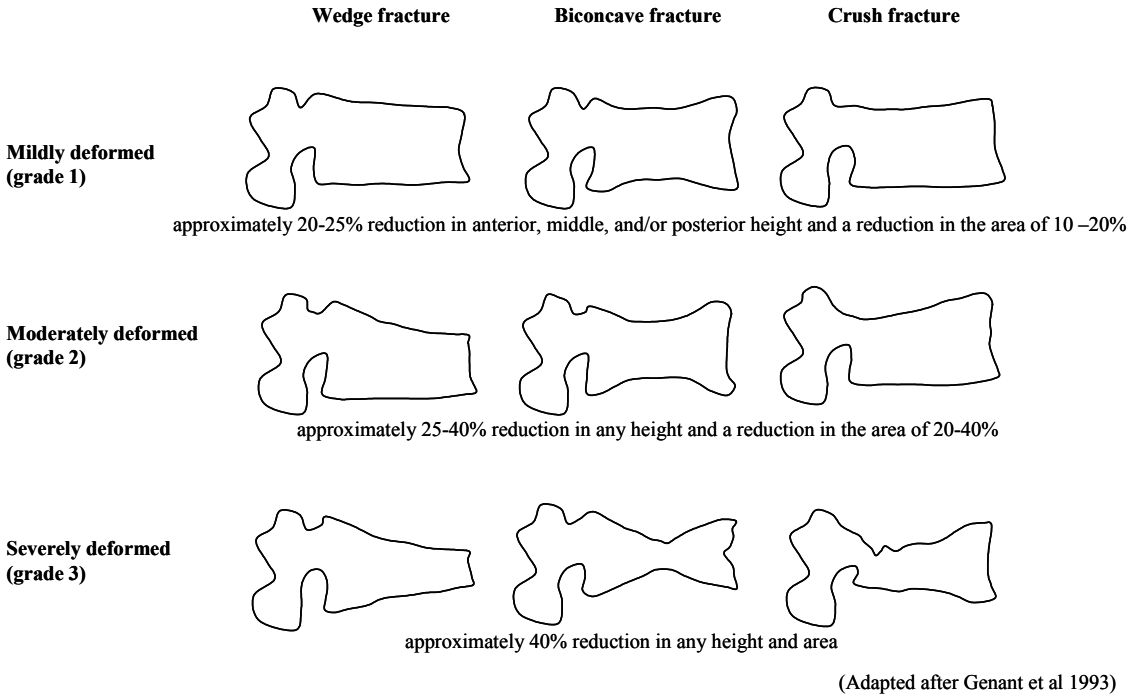

Figure 3. The visual semiquantitative grading system used to determine the grade of fracture deformity for the three fracture types (adapted from Genant et al [36]).

Thoracic kyphosis was measured as the angle between the cranial endplates of T3 or T4 and the distal endplate of the T12 vertebra. Lumbar lordosis was measured as the angle between the cranial endplate of L1 and the distal endplate of L5. A complete depiction of the entire thoracic and lumbar spines was not available in all the fractured patients. For this reason, the thoracic kyphosis could be determined in only 47 patients, while the lumbar lordosis could be determined in 94 patients. This meant that some of the previous fractures located in the upper part of the thoracic spine and in the lower part of the lumbar spine might have been missed. The vertebral levels included in the diagnostic X-ray examination of the spine can be seen in Table 2.
An adjacent fracture was defined as an acute fracture that occurred on the vertebral level just above or below a previous fracture.

Table 2. X-rayed vertebral levels.

X-rayed level	Number of patients	Percent (%)
L5-T1	37	34.6
L5-T4	2	1.9
L5-T5	2	1.9
L5-T6	3	2.8
L5-T7	15	14.0
L5-T8	16	15.0
L5-T9	19	17.8
L5-T10	4	3.7
L4-T1	4	3.7
L3-T1	2	1.9
L1-T1	2	1.9
T12-T1	1	0.9
Total	107	100.0

14.2. Study IV

Lateral and frontal view radiographs of the spine taken at the first visit to the emergency unit and at the Capio Diagnostic Center were used for the evaluation. The same X-ray evaluation method was used as in studies I-III. The number of adjacent fracture(s) was two if there were three consecutive fractures, or three if there were four consecutive fractures, etc. (Figure 4).

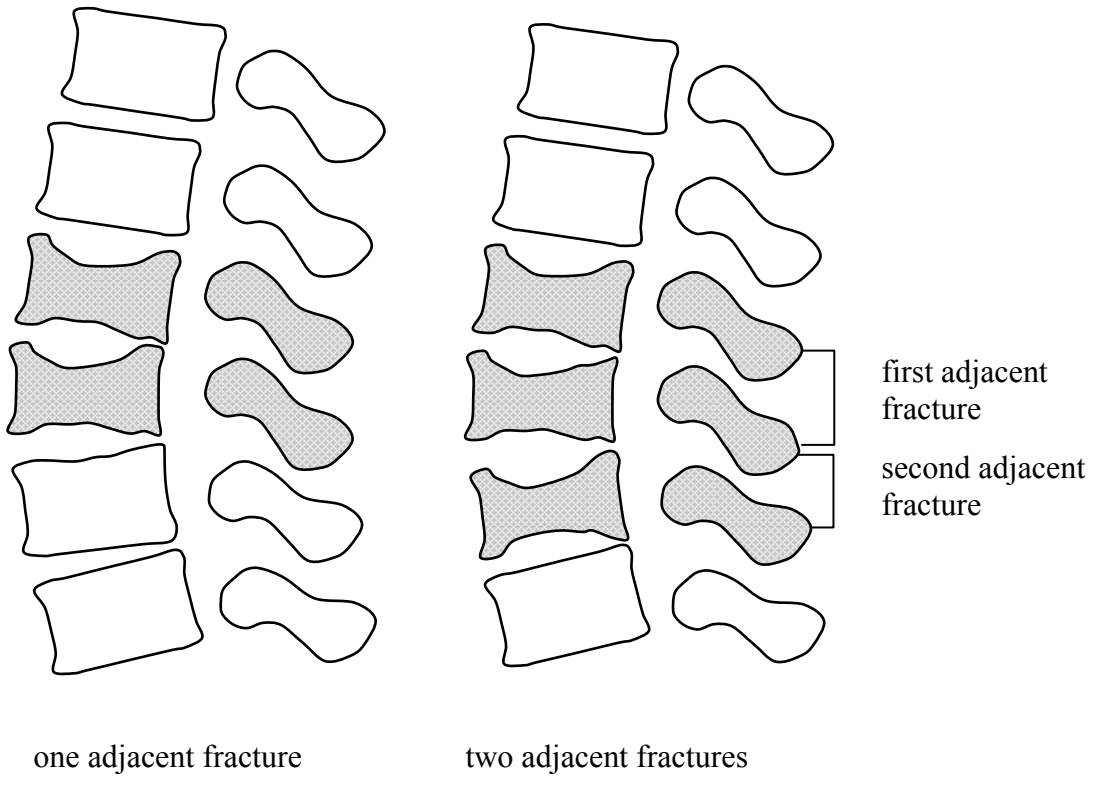

Figure 4. Adjacent fracture.

As in studies I-III, a complete depiction of the entire thoracic and lumbar spines was not available in all the fractured patients. For this reason, the thoracic kyphosis could be determined in only 196 patients while the lumbar lordosis could be determined in 396 patients. The levels included in the diagnostic X-ray examination can be seen Table 3.

Table 3. X-rayed vertebral levels.

X-rayed level	Number of patients	Percent (%)
L5-T1	155	34.6
L5-T4	2	0.4
L5-T5	1	0.2
L5-T6	7	1.6
L5-T7	26	5.8
L5-T8	63	14.1
L5-T9	71	15.8
L5-T10	56	12.5
L5-T11	23	5.1
L4-T1	2	0.4
L3-T1	12	2.7
L2-T1	20	4.5
L1-T1	7	1.6
T12-T1	3	0.7
Total	448	100.0

15. Fracture level diagnosis by subsequent examination

15.1. Studies I-III

A total of 27 patients had a subsequent X-ray examination and 11 patients had a subsequent MRI examination. In three patients (2.8%), the fracture level was changed after these examinations.

15.2. Study IV

A total of 44 patients had a subsequent X-ray examination and 27 patients had a subsequent MRI examination. In 26 patients (5.8%), the fracture level was changed after these examinations.

16. Questionnaires (Studies I-III)

In studies I-III, four different questionnaires were used: von Korff pain intensity and disability questionnaire, Hannover ADL questionnaire and EQ-5D. Within 10 days after the first visit to the hospital's emergency unit, all eligible patients received written information about the study and an invitation to participate. The patients who agreed to participate received the first packet of questionnaires, at the latest, 3 weeks after the fracture had been diagnosed

and thereafter at 3, 6, and 12 months. The patients returned the filled-in questionnaires, which made later comparisons unlikely. All four questionnaires were used at every follow-up.

16.1. von Korff pain intensity and disability score

This instrument is self-administered and was designed and validated for use outside the hospital setting among patients with chronic back pain, among other problems [112, 113]. It includes three pain intensity and four disability items (Appendix 1). The three pain items ask the patient to rate their current back pain intensity, their worst pain, and their average pain since the start of the pain problem, where 0 refers to "no pain" and 10 refers to "pain as bad as could be". The *pain intensity score* is calculated as the average of the three 0-10 ratings, multiplied by 10, to yield a score from 0-100; low values on the score mean less pain. Three of the disability items also have a 10-graded response possibility. One item asks about the interference of back pain on daily activities, ranging between 0 "no interference" to 10 "unable to carry on any activities". Two items ask about how the back pain has changed the ability to take part in family, social or recreational activities, or the ability to work (including household); both items range between 0 "no change" and 10 "extreme change". The fourth disability question asks about the number of days the patient, due to the pain, has been kept from performing usual activities during the last 6 months. This fourth question was not used in the studies of this thesis. The *disability score* is calculated as the average of the three 0-10 interference ratings in daily, social and work activities, multiplied by 10, to yield a score from 0-100; low values on the score mean less disability. The scores have been used in several Swedish and international studies of long-term back pain [44, 46].

16.2. Hannover ADL score

This questionnaire is self-administered and consists of 12 items (Appendix 2). It assesses functional limitations in activities of daily living (ADL) among patients with musculoskeletal disorders. The patient is asked to circle one of three possible responses, which include the following: 1. Either unable to do or able only with help (score=0), 2. Yes, but with some difficulties (score=1), or 3. Yes, without difficulties (score=2). The 12 items are scored, summed and transformed on to a scale from 0 (worst back function) to 100 (best back function) [67]. The questionnaire has been used in Swedish and international studies of long-term back pain [43, 44, 46].

16.3. EQ-5D

EQ-5D is a generic health-related quality of life measure. It provides a single index. The individuals classify their own health status into 5 dimensions:

mobility, self-care, usual activity, pain/discomfort, and anxiety/depression, within three levels (i.e. no problems, moderate problems or severe problems) (Appendix 3). The instrument yields a total of 243 possible health states, and the Time Trade Off method is used to rate the different states of health. The value 0 indicates "dead" and 1 indicates "full health" [23, 24]. Negative values are possible and represent conditions worse than dead. In Sweden, the instrument has been validated on extensive cohorts of back pain patients and in patients with ages similar to those in the studies of this thesis (Table 4) [11].

Table 4. EQ-5D index score and percentage of patients reporting moderate or severe problems in the five dimensions from a Swedish reference population with relevant age groups.

Age	40-49 N =547 %	50-59 N=617 %	60-69 N=387 %	70-79 N=338 %	80-88 N=122 %
Mobility					
Total	6.0	10.5	18.6	26.9	44.3
Male	6.0	11.0	18.4	23.0	48.8
Female	6.0	10.2	18.8	30.0	42.0
Self-care					
Total	1.5	1.9	1.3	3.6	12.3
Male	2.0	1.7	1.1	6.1	19.5
Female	1.0	2.2	1.5	1.6	8.6
Usual activities					
Total	8.2	11.0	8.5	9.8	21.3
Male	6.8	8.9	6.8	8.1	19.5
Female	9.4	12.9	10.2	11.1	22.2
Pain/discomfort					
Total	38.9	47.5	62.8	58.0	69.7
Male	36.1	46.9	58.4	56.8	65.9
Female	41.3	48.0	67.0	58.9	71.6
Anxiety/depression					
Total	26.1	28.2	31.3	26.9	36.9
Male	22.1	24.0	25.3	23.0	36.6
Female	29.5	32.0	37.1	30.0	37.0
EQ-5D index value					
Total	0.86	0.83	0.80	0.79	0.74
Male	0.86	0.84	0.83	0.81	0.74
Female	0.85	0.82	0.78	0.78	0.74

17. Statistical analyses

The following summary of statistical methods is largely based upon the comprehensive descriptions provided by Altman and Stevens [2, 103].

17.1. Data level

Statistical methods are specific to a certain type of data. Data can either be categorical or numerical (otherwise known as qualitative and quantitative) [2]. The data level is a prerequisite to the choice of the statistical method. The nature of the attribute being measured will determine the rules that can be applied to the measurement. Traditionally, a mathematical structure defined by Stevens [103] defined four levels of assigning numbers in measurement, called scales of measurement. The four levels of measurements are called nominal, ordinal, interval and ratio.

17.2. Choice of statistical methods

The choice of statistical method to be use is based on the data level as well as on how the variables are measured. The statistical tests are based on assumptions about the parameters of the population from which the samples were drawn. Parametric tests require that the assumptions of normality and homogeneity of variance are met to a reasonable extent. Non-parametric tests do not specify the normality of variance assumption. In studies I-III, the scores derived from the questionnaires were treated as data on the interval level and analyzed in a parametrical way. Considering the risk of normality not being met, in this thesis the scores were treated as being on an ordinal level and also analyzed in a non-parametric fashion. An overview of the statistical methods used in this thesis is presented in Table 5.

Table 5. Overview of the statistical methods used in the thesis.

	Questionnaire analysis					Gender, age, type and grade of fx, previous fx, kyphosis, lordosis, adjacent fx analysis		
	two groups *	three groups **	differ-ence by time	prognosis factor analysis	previous fx number influence	pre-domi-nance	factor relation #	group comp-arison ##
Descriptive statistics								
Mean (SD)	●	●	●					
Median	●	●	●					
Difference between groups								
parametric method								
Independent t-test	●							●
ANOVA		●						●
Repeated measure ANOVA			●					
non-parametric method								
Mann Whitney U test	●							
Kruskal-Wallis test		●						
Friedman test			●					
chi-square test							●	
chi-square for goodness of fit						●		
Post-hoc analysis								
parametric method								
Bonferroni/Dunn procedure		●	●					●
non-parametric method								
Wilcoxon t-test with Bonferroni correction			●					
Mann Whitney U test with Bonferroni correction		●						
Correlation								
parametric method								
Peason's correlation coefficient							●	
non-parametric method								
Spearman's correlation coefficient					●		●	
Regression								
multiple linear regression analysis				●				

*: gender, age (over 70 and below 70), cause of trauma (with and without trauma), time since fx (within one week and more than one week), post fx status (return home and hospitalized), acute fx location (thoracic and lumbar), previous fx (exist and not exist), previous fx location (thoracic and lumbar)
**: type of fx, grade of fx
#: nominal data; chi-square test, ordinal data; Spearman, continuous scale data; Pearson
##: age, kyphosis, lordosis difference in each group (e.g. gender, type of fracture, etc.)
fx: fracture

17.2.1. Data analysis

The SPSS (Statistical Package for the Social Sciences, v.14, Windows, Chicago, USA) statistical software was used for analyzing the data. All tests were two-sided. The results were considered to be significant at $p<0.05$.

17.2.2. Descriptive statistics

Questionnaire scores were presented as mean and standard deviation or median.

17.2.3. Differences between groups and hypothesised values

The proportions of cases that fell into the various categories of a single variable were tested with the chi-square test for goodness of fit comparing with hypothesised values.

Differences between two groups were tested using an independent t-test for variables on the interval level, the Mann Whitney U test for variables on the ordinal level, and the chi-square test for variables on the nominal level. Differences between more than two groups were tested using ANOVA for variables on the interval level and with Kruskal-Wallis test for variables on the ordinal level. If the ANOVA test was significant, the Bonferroni/Dunn procedure was used as a post-hoc test. If the Kruskal-Wallis test was significant, Mann Whitney U test with Bonferroni correction was used as a post-hoc test.

For comparison of repeated measurements on interval or ordinal level variables, repeated ANOVA or the Friedman test were used, respectively. If they were significant, the Bonferroni/Dunn procedure or Wilcoxon t-test with Bonferroni correction were used as a post-hoc test, respectively.

17.2.4. Association, correlation and regression

Pair-wise associations were tested using Pearson's correlation coefficient test for the variables on the interval level and using Spearman's correlation coefficient test for the variables on the ordinal level.

Multiple linear regression analysis (stepwise method) was used for the analysis of the combined influence factors for each questionnaire score at each follow-up.

17.3. Internal missing value

Partial non-responses on any of the questionnaires at each dimension were coded as an estimated value from the other dimensions in the same questionnaire or as a value in the same questionnaire dimension but from a subsequent occasion. This was done when only one value was missing in one dimension of each questionnaire. In cases where it was difficult to estimate the value, it was excluded, even if only one dimension value was missing.

18. Ethical approval

The studies were ethically approved by the Research Ethical Committee of the Medical Faculty, University of Gothenburg, 17th June 2003 (S 270-03).

RESULTS

19. The course of the acute vertebral body fragility fracture: its effect on pain, disability, and quality of life during 12 months (Study I)

19.1. Basic characteristics of the patients and fractures

Table 6 summarizes basic characteristics of the patients and fractures.

Table 6. Basic characteristics of the patients and fractures.

Patient characteristics	Number of patients, Age or Day
Total population	107
Age, mean±SD (range)	75.5±11.9 (42-96)
Gender	
Male, age mean±SD (range)	35 (32.7%), 76.1±11.2 (43-92)
Female, age mean±SD (range)	72 (67.3%), 75.3±12.3 (42-96)
Fracture location	
Thoracic fracture	58 (54.2%)
Lumbar fracture	49 (45.8%)
Type of fracture	
Wedge	74 (69.2%)
Concave	20 (18.7%)
Crush	13 (12.1%)
Grade of fracture deformation	
Mild	22 (20.6%)
Moderate	50 (46.7%)
Severe	35 (32.7%)
Number of previous fracture(s)	
0	56 (52.3%)
1	27 (25.2%)
2	9 (8.4%)
3	3 (2.8%)
4	6 (5.6%)
5>	6 (5.6%)
Kyphosis mean±SD (n=47) (degrees)	43.6±15.8
Lordosis mean±SD (n=94) (degrees)	30.5±16.5
Adjacent fracture	23 (45.1%)
(% among the patients with previous fracture)	
Cause of trauma	
A level fall	62 (57.9%)
Lift of a heavy object	2 (1.9%)
Some unidentified trauma	2 (1.9%)
Traffic accident	4 (3.7%)
No recollection of trauma	37 (34.6%)
Time elapsed before visiting the emergency unit	
Within the first week	72 (67.3%)
Within one month	16 (14.9%)
Unidentified	19 (17.8%)
Hospitalization or not	
Immediate return home	82 (76.6%)
Hospitalized	23 (21.5%)
Nursing home	2 (1.9%)
Hospital stay, days, mean±SD (range)	16.7±8.1 (3-35)
Brace	12 (11.2%)

19.2. Location of the acute fracture

The acute fractures diagnosed in study I were located between T6 and L4, and were most frequent at T12 and L1. 54.2% were thoracic fractures and 45.8% were lumbar fractures (Figure 5).

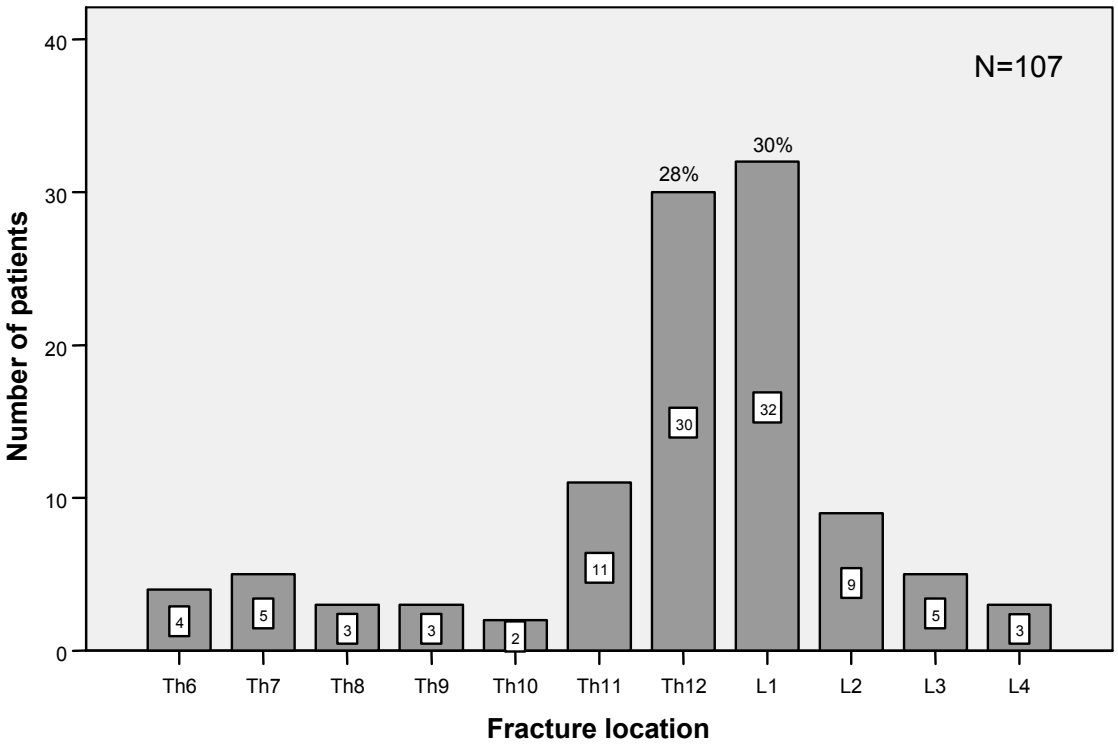

Figure 5. Locations of the acute fractures in 107 patients.

19.3. Pain, disability, ADL and QoL

All the questionnaire scores improved during the first three months ($p<0.05$), but thereafter the scores remained at levels far from normal, at least during the remainder of the follow-up year (Table 7, Figure 6).

Table 7. Outcomes of the four questionnaires at the follow-ups.

	3 weeks		3 months		6 months		12 months	
	mean	median	mean	median	mean	median	mean	median
			p	p	p	p	p	p
von Korff pain intensity score	70.9	73.0	61.5	67.0	60.7	63.3	60.5	63.3
			0.000	0.000	0.000	0.000	0.000	0.000
von Korff disability score	68.9	73.3	56.4	63.0	51	56.7	53.9	60.0
			0.000	0.000	0.000	0.000	0.000	0.000
Hannover ADL score	37.7	33.3	48.0	50.0	45.8	42.0	47.6	42.0
			0.000	0.000	0.000	0.000	0.000	0.000
EQ-5D	0.37	0.52	0.52	0.69	0.54	0.69	0.52	0.69
			0.000	0.000	0.000	0.000	0.000	0.000

p values are given for differences between 3, 6, and 12 months and baseline (3 weeks)

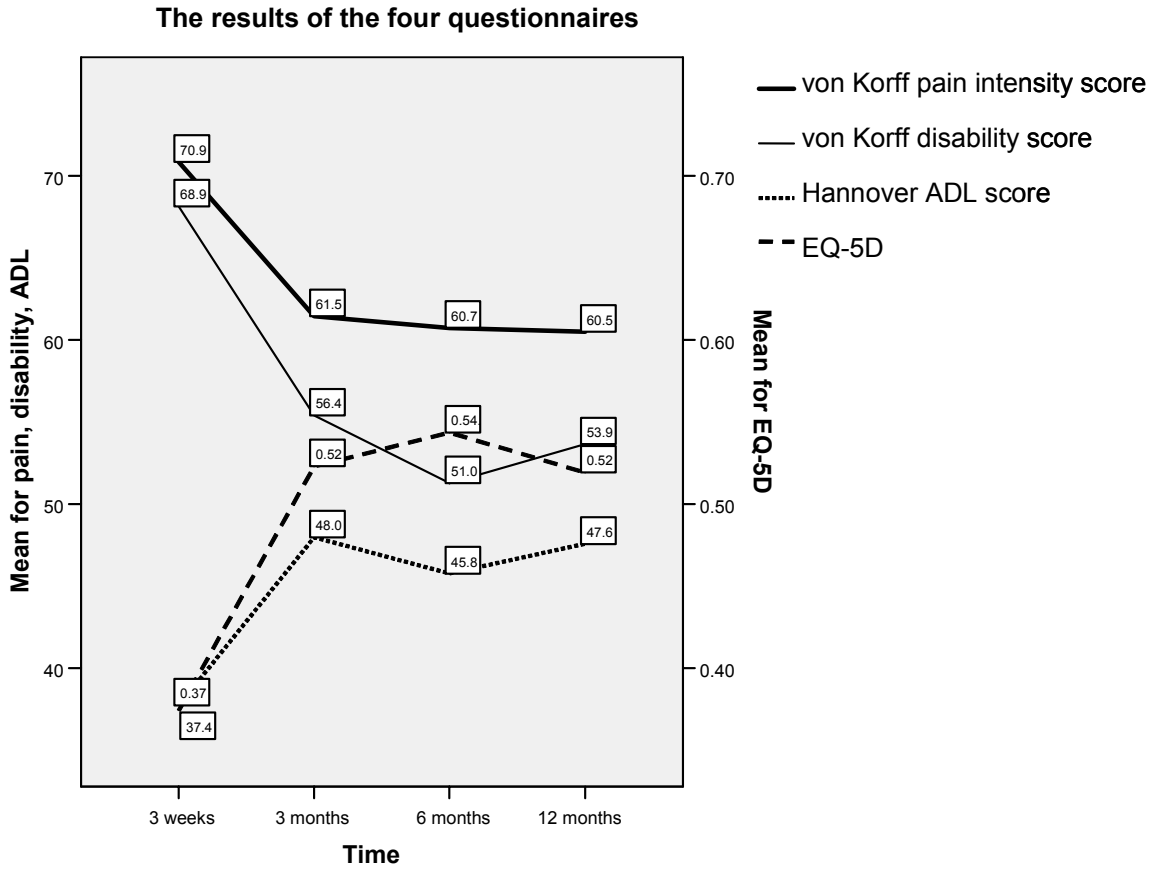

Figure 6. Average pain intensity, disability, ADL, and QoL acutely (3 weeks) and after 3, 6 and 12 months.

19.4. Pain analysis

When the initial pain intensity for each individual was grouped into quartiles, 50 patients (46.7%) belonged to the fourth quartile with a pain intensity between 75 and 100, 54 patients (50.5%) belonged to the second and third quartiles, and only 3 patients (2.8%) belonged to the lowest quartile with a pain intensity less than 25. After 12 months, less than 10% of the patients had a pain intensity below 25, while 81 patients (75.7%) still experienced a pain intensity over 50 (Figure 7).

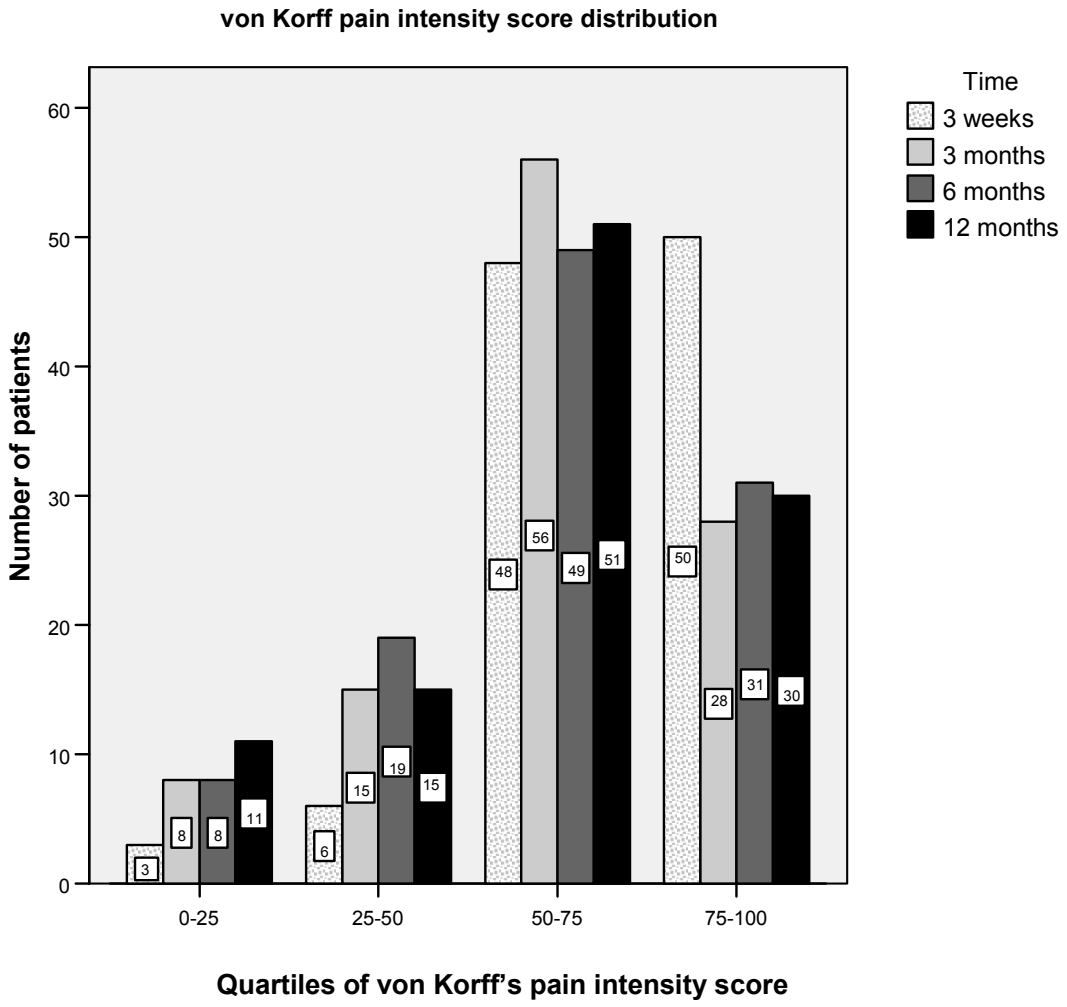

Figure 7. Pain intensity distributed into quartiles at the four follow-ups.

19.5. QoL analysis

When EQ-5D was divided into its 5 dimensions (mobility, self-care, usual activity, pain/discomfort, and anxiety/depression), and analyzed according to the percentage of the patients who had moderate or severe problems, the pain/discomfort dimension was the most seriously affected (Figure 8).

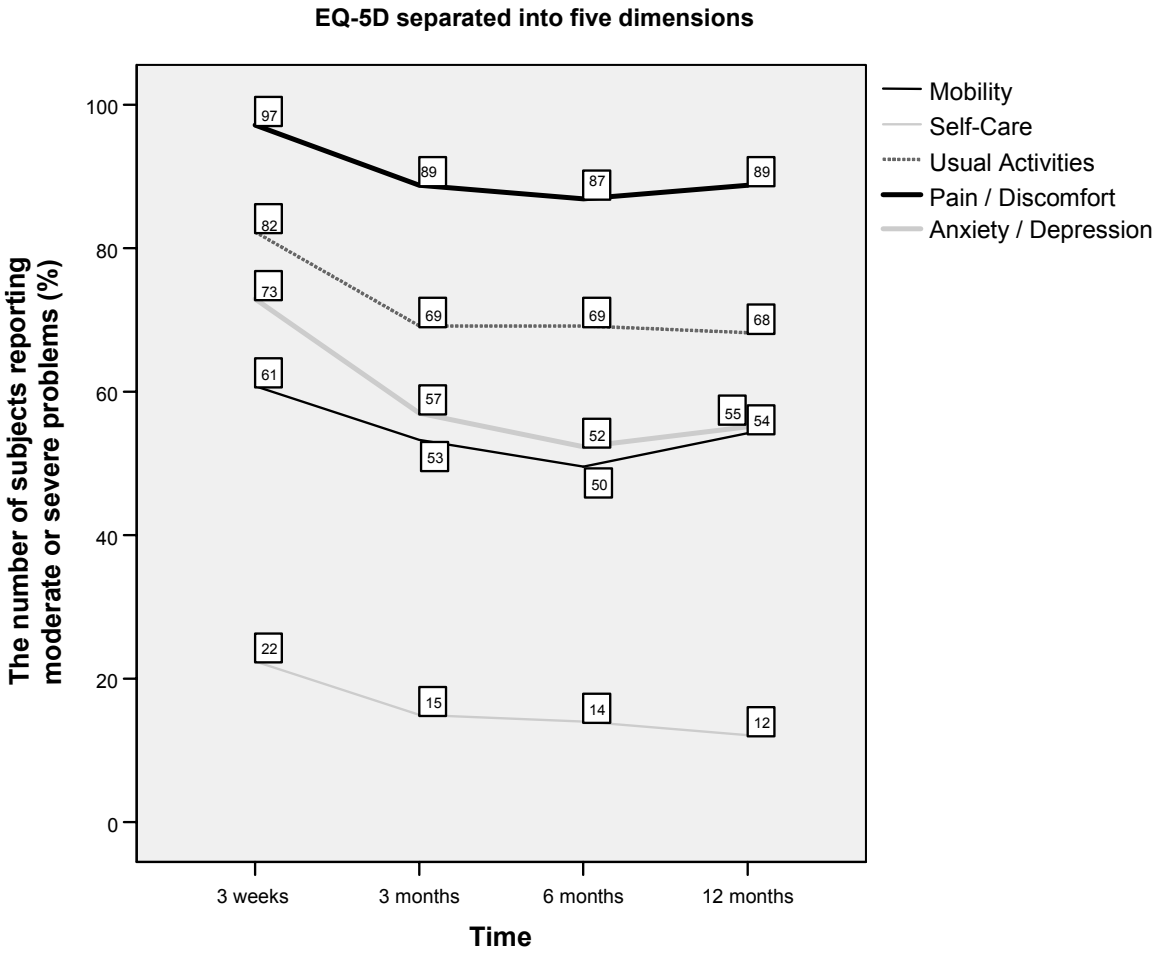

Figure 8. The frequency of patients reporting moderate or severe problems for the five dimensions of EQ-5D at the four follow-ups.

19.6. Gender differences on questionnaire outcomes

With the exception of the 6 month Hannover ADL score and the 3 month von Korff pain intensity, all other outcome scores were worse for women than for men. The mean values were always worse for women all the follow-ups.

19.7. Age differences on questionnaire outcomes

When the patients were grouped into 70 and over 70 years of age (72 patients) or under 70 (35 patients), no score differences for any of the outcome measures could be detected at any follow-up time. No correlations between age and any of the outcome measures were found.

19.8. Time since fracture diagnosis and outcomes

When the patients were grouped according to those who sought medical care within one week and those who sought care after one week, there was no difference between the groups for any of the outcome measures at any time during the follow-up period.

19.9. Cause of trauma and outcomes

Comparison of the patients who reported a known fracture trauma (fall, lift, unidentified trauma, or traffic accident) with the patients with no recollection of a trauma revealed no differences for any of the outcome measures at any time during the follow-up.

20. The prognosis of pain, disability, ADL and QoL after an acute osteoporotic vertebral body fracture: its relation to fracture level, type, grade and previous fracture (Studies II & III)

20.1. Fracture level and outcomes

When the fractures were grouped according to level, i.e. thoracic vs. lumbar spine, the lumbar spine fractures continued to improve slightly, even after the substantial initial improvements. In the thoracic spine, on the other hand, all the outcomes continued to deteriorate after the early improvement. However, there was no statistically significant difference between the thoracic or lumbar spine fractures at any time during the one-year follow-up (Figure 9). When all the different fracture levels were tested, none of the levels significantly differed from the other.

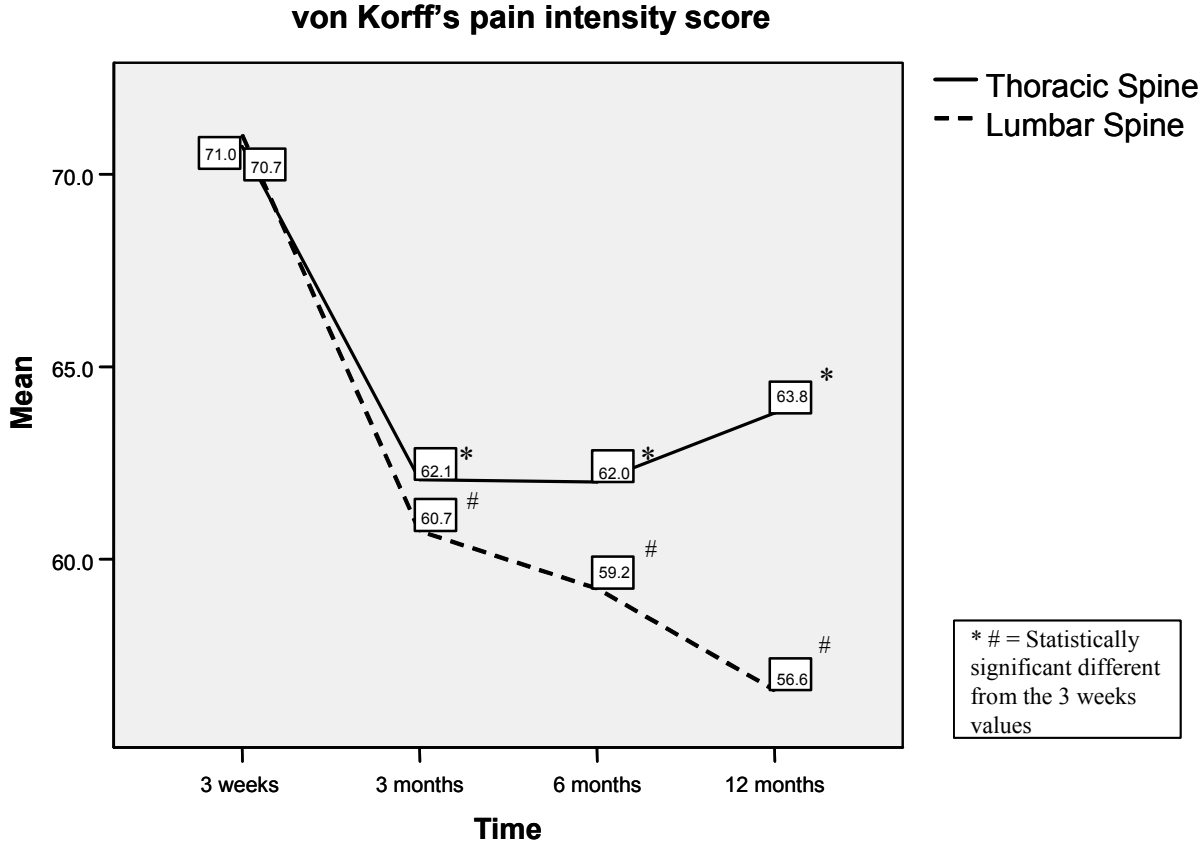

Figure 9. von Korff pain intensity score at 3 weeks, and 3, 6 and 12 months after the acute vertebral fracture.

20.2. Fracture type and outcomes

For the wedge type fracture, all scores significantly improved between the initial measurement and the three month follow-up (Table 10). After three

months, the scores for the wedge fractures remained at this improved level, although, far from normal.
After the improvement during the three first post-fracture months, patients with a concave fracture continued to improve steadily throughout the follow-up year, but still without normalizing by the end of the study.
The crush fracture type clearly showed the worst prognosis for all the outcome measures. The initial improvement was of a lower magnitude and none of the one year scores were significantly different from the initial situation (p>0.05) (Table 8, Figure 10).

Table 8. Outcome scores for the 3 different fracture types at 3 weeks, and 3, 6 and 12 months.

		Wedge (n=74) (n=69) [§]		Concave (n=20) (n=19) [§]		Crush (n=13) (n=13) [§]		Difference between type	
		Mean	MD	Mean	MD	Mean	MD	p (para)	p (non-para)
von Korff's	3 weeks	70.1	73.0	72.5	73.3	72.3	70.0	ns	ns
pain intensity	3 months	60.6*	67.0*	58.8*	70.0*	70.2	63.3	ns	ns
score	6 months	59.8*	63.2*	60.7*	61.7*	66.2	63.3	ns	ns
	12 months	60.0*	63.2*	56.7*	67.0*	69.3	70.0	ns	ns
von Korff's	3 weeks	67.4	73.3	72.6	80.0	71.8	70.0	ns	ns
disability	3 months	56.0*	60.0*	57.7	67.0*	56.5	63.0	ns	ns
score	6 months	49.4*	56.7*	53.0*	56.7*	56.9	66.7	ns	ns
	12 months	53.9*	60.0*	50.5*	60.0*	59.0	60.0	ns	ns
EQ-5D	3 weeks	0.39	0.52	0.33	0.28	0.37	0.62	ns	ns
	3 months	0.56*	0.69*	0.53*	0.62*	0.29	0.62	0.042[#]	ns
	6 months	0.57*	0.69*	0.55*	0.65*	0.40	0.69	ns	ns
	12 months	0.51*	0.66*	0.63*	0.71*	0.39	0.69	ns	ns
Hannover	3 weeks	37.4	33.0	37.7	39.6	39.4	41.7	ns	ns
ADL score	3 months	50.8*	50.0*	40.7	41.8	43.3	50.0	ns	ns
	6 months	47.5*	40.0*	41.5	37.5	42.7	50.0	ns	ns
	12 months	48.1*	41.7*	46.9	48.0	45.8	54.0	ns	ns

[#] between wedge and crush fracture difference
* compared with the 3 week result, p<0.05
[§] number of patients for the von Korff disability score analysis=total 101 patients
MD: median
$p_{(para)}$ indicates p value by parametric test (ANOVA)
$p_{(non\text{-}para)}$ indicates p value by non-parametric test (Kruskal-Wallis test)

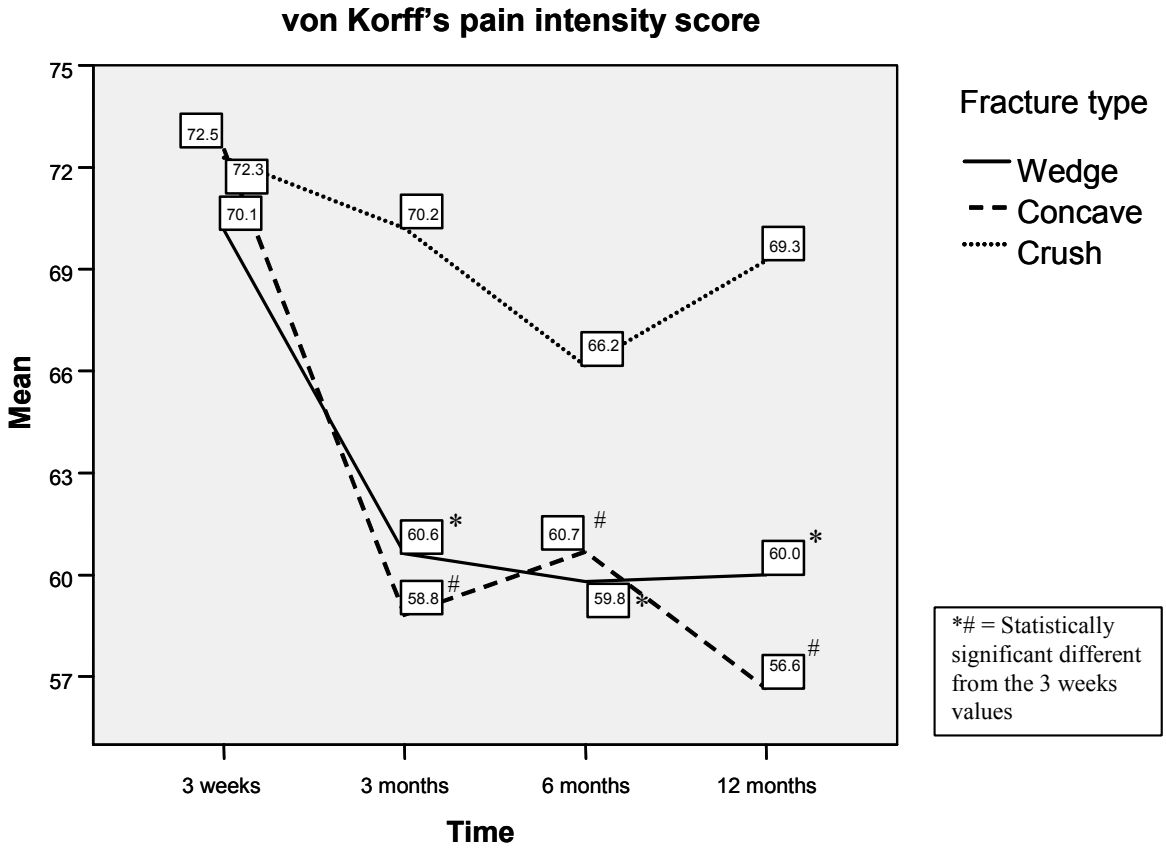

Figure 10. von Korff pain intensity scores for the 3 different fracture types during the 1-year follow-up period.

20.3. Grade of fracture and outcomes

The general trend for greatest improvement during the first three months also held true for the three grades of fracture deformation. It was striking to find, with the exception of the Hannover ADL score, that the three deformation grades represented three distinct severity entities of pain intensity, disability and quality of life (Table 9, Figure 11).

Table 9. Grade of fracture deformation and its relation to pain intensity, disability, ADL and QoL during the 1-year follow-up period.

		Mild (n=22) (n=20) [§]		Moderate (n=50) (n=48) [§]		Severe (n=35) (n=33) [§]		Difference between grade	
		Mean	MD	Mean	MD	Mean	MD	p (para)	p (non-para)
von Korff's	3 weeks	62.4	66.8	70.0	73.0	77.4	76.7	0.014[#]	0.048[#]
pain intensity	3 months	54.4	61.7*	59.3*	67.0*	69.0*	70.0*	0.024[#]	ns
score	6 months	53.2	55.0*	59.5*	60.0*	67.3*	70.0*	0.045[#]	ns
	12 months	49.1	58.3*	59.5*	63.2*	69.1*	67.0*	0.005[#]	0.021[#]
von Korff's	3 weeks	61.8	68.2	67.6	75.0	75.2	80.0	ns	0.037[#]
disability	3 months	48.0*	51.5*	55.9*	58.5*	62.1*	67.0*	ns	ns
score	6 months	44.6*	55.0*	50.2*	55.0*	56.2*	60.0*	ns	ns
	12 months	45.7	53.3	51.9*	58.5*	61.8*	66.7*	ns	ns
EQ-5D	3 weeks	0.49	0.62	0.38	0.40	0.30	0.26	ns	ns
	3 months	0.63	0.69*	0.53*	0.69*	0.45	0.62	ns	ns
	6 months	0.62	0.69*	0.58*	0.69*	0.44	0.62	ns	ns
	12 months	0.60	0.71	0.54*	0.67*	0.44	0.62	ns	ns
Hannover	3 weeks	42.3	37.5	40.6	37.5	30.8	29.0	ns	0.046[#]
ADL score	3 months	52.5	47.9*	48.5*	50.0*	44.3*	45.8*	ns	ns
	6 months	47.0	43.8	48.7*	47.9*	40.8*	37.5*	ns	ns
	12 months	59.5*	58.2*	46.1	38.0	42.2*	37.5*	0.047[#]	ns

[#] between mild and severe fracture difference
* compared with 3 week results, $p<0.05$
[§] number of patient for the von Korff disability score analysis=total 101 patients
MD: median
$p_{(para)}$ indicates p value by parametric test (ANOVA)
$p_{(non\text{-}para)}$ indicates p value by non-parametric test (Kruskal-Wallis test)

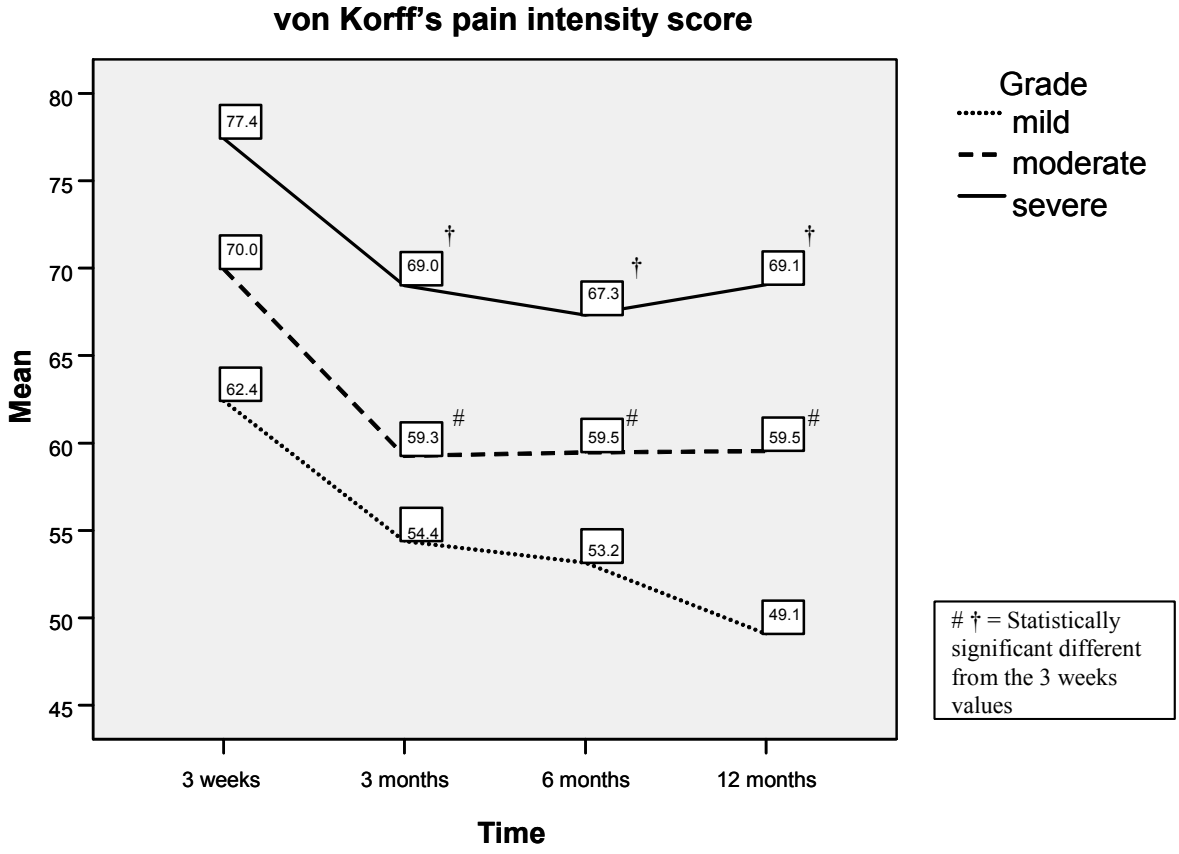

Figure 11. Average pain intensity in mildly, moderately and severely deformed acute fractures after 3 weeks, and 3, 6 and 12 months.

20.4. Previous fracture and outcomes

All the scores at all the follow-ups were worse in patients with a previous fracture(s). The differences between those patients with and without a previous fracture(s) were statistically significant for all the scores, except the pain intensity score (Table 10, Figure 12).

Table 10. Scores from the 4 questionnaires in acute fracture patients with or without a previous fracture(s)

		Without previous fracture (n=56) (n=54)§		*With previous fracture (n=51) (n=47)§*		*Difference between with and without previous fracture*	
		Mean	*Median*	*Mean*	*Median*	*p (para)*	*p (non-para)*
von Korff pain intensity score	3 weeks	68.9	68.5	73.0	76.7	ns	ns
	3 months	59.3	63.3	63.8	70.0	ns	ns
	6 months	57.0	57.0	64.8	70.0	ns	ns
	12 months	56.5	60.0	64.9	70.0	ns	0.020
von Korff disability score	3 weeks	64.5	63.3	74.0	80.0	0.045	0.023
	3 months	53.5	51.5	59.7	63.0	ns	ns
	6 months	45.0	48.5	58.0	66.7	0.017	0.008
	12 months	48.4	48.5	60.3	67.0	0.030	0.009
EQ-5D	3 weeks	0.47	0.64	0.26	0.09	0.003	0.002
	3 months	0.57	0.69	0.47	0.62	ns	0.020
	6 months	0.63	0.69	0.45	0.62	0.006	0.003
	12 months	0.57	0.71	0.46	0.62	ns	0.008
Hannover ADL score	3 weeks	41.0	37.5	34.1	25.0	ns	ns
	3 months	53.9	52.0	41.5	41.7	0.009	0.013
	6 months	51.9	52.0	39.0	33.0	0.010	0.014
	12 months	53.9	54.0	40.6	33.3	0.008	0.019

§ the number of patients in the von Korff disability score analysis
$p_{(para)}$ indicates p value by parametric test (independent t-test)
$p_{(non\text{-}para)}$ indicates p value by non-parametric test (Mann-Whitney test)

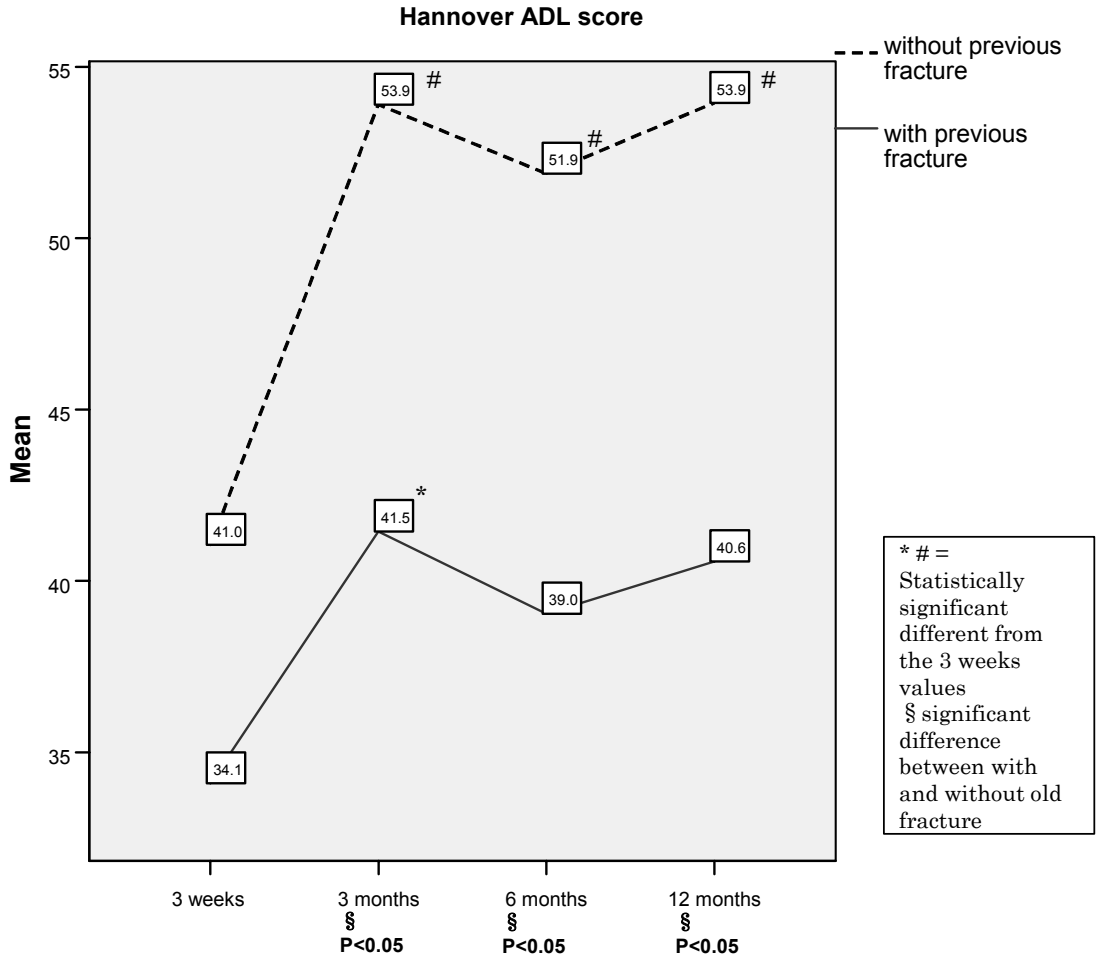

Figure 12. Hannover ADL scores at 3 weeks, and 3, 6 and 12 months after the acute vertebral fracture.

21. Analysis of the factors that influenced the prognosis of pain, disability ADL and QoL after an acute osteoporotic vertebral body fracture (Studies II-III)

The factors that showed a statistically significant influence on the questionnaire outcomes in the multiple linear regression analysis (stepwise method) are shown in Table 11. The questionnaire scores at every follow-up were independent variables. Dependent variables were fracture type, grade of fracture deformation, fracture location, number of previous fracture, gender and age. For the analysis, dummy variables were used for fracture location, grade of fracture deformation, fracture location and gender. Fracture type dummy variable was 1. concave (coded 1), not concave (coded 0) and 2. crush (coded 1), not crush (coded 0). For the grade of fracture deformity, the dummy variable was 1. mild (coded 1), not mild (coded 0) and 2. severe (coded 1), not severe (coded 0). For fracture location, the dummy variable was 1. thoracic fracture (coded 1), lumbar fracture (coded 0) and 2. thoracolumbar joint (T12-L1) fracture (coded 1), not thoracolumbar joint fracture (coded 0). Gender coding was female (coded 1) and male (coded 0).
Pain was mainly related to the fracture severity. Disability and EQ-5D were mainly related to the number of previous fractures. Hannover ADL score was related to gender and the number of previous fractures.

Table 11. Statistically significant relation factors from the multiple liner regression analysis.

			fracture type		grade of fracture		acute fx location		previous	gender		
Questionnare	occasion		concave	crush	mild	severe	Th	TL	fx number	female	age	R-square
von Korff pain intensity score	3 weeks	β				0.239						0.057
		p				0.013						
	3 months	β				0.244				0.221		0.110
		p				0.010				0.019		
	6 months	β				0.214						0.046
		p				0.027						
	12 months	β				0.261						0.068
		p				0.007						
von Korff disability score	3 weeks	β			-0.224							0.050
		p			0.021							
	3 months	β							0.194			0.038
		p							0.046			
	6 months	β							0.256			0.066
		p							0.009			
	12 months	β							0.231			0.053
		p							0.017			
EQ-5D	3 weeks	β							-0.204			0.042
		p							0.035			
	3 months	β		-0.206				0.197	-0.257			0.114
		p		0.027				0.033	0.006			
	6 months	β							-0.215			0.037
		p							0.026			
	12 months	β										
		p										
Hannover ADL score	3 weeks	β		0.220		-0.318				-0.297		0.133
		p		0.036		0.003				0.002		
	3 months	β							-0.214	-0.285		0.136
		p							0.021	0.002		
	6 months	β							-0.209			0.035
		p							0.031			
	12 months	β			0.204					-0.194		0.072
		p			0.033					0.043		

β: standarized partial regression coefficient
p: two sided t-test
fx: fracture
Th: thoracic spine fracture
TL: thoracolumbar junction (T12-L1) fracture

22. Characteristics of the acute and prevalent osteoporotic vertebral compression fractures (Study IV)

22.1. Basic characteristics of the patients having an acute vertebral compression fracture

The basic characteristics of the patients and acute fractures in study IV are summarized in Table 12.

Table 12. Basic patient and acute fracture characteristics in study IV.

Patient and fracture characteristics	Number of patients or Age
Total population	448
Age, mean±SD (range)	76.8±10.9 (40-98)
Gender	
Male, age mean±SD	131 (29.2%), 74.1±12.0
Female, age mean±SD	317 (70.8%), 77.9±10.2
Fracture location	
Thoracic fracture	210 (46.9%)
Lumbar fracture	238 (53.1%)
Type of fracture	
Wedge	325 (72.5%)
Concave	84 (18.8%)
Crush	39 (8.7%)
Grade of fracture deformation	
Mild	117 (26.1%)
Moderate	214 (47.8%)
Severe	117 (26.1%)
Number of previous fracture(s)	
0	246 (54.9%)
1	102 (22.7%)
2	42 (9.4%)
3	33 (7.4%)
4	20 (4.5%)
5>	5 (1.1%)
Kyphosis mean±SD (n=196) (degrees)	46.7±16.7
Lordosis mean±SD (n=396) (degrees)	35.6±15.5
Adjacent fracture (n=202)	118 (58.4%)
Cause of trauma (n=438)	
A level fall	199 (45.4%)
Lift of a heavy object	12 (2.7%)
Other trauma causes	26 (5.9%)
No recollection of trauma	201 (45.9%)
Time elapsed before visiting the emergency unit (n=438)	
Within the first week	146 (33.3%)
Between one to three week	75 (17.1%)
Within one month	39 (8.9%)
More than one month	60 (13.7%)
Unidentified	118 (26.9%)

22.2. Location of the acute fracture

The distribution of the acute fracture levels is shown in Figure 13. There were 210 thoracic (46.9%) and 238 lumbar (53.1%) fractures. The most frequent fracture levels were T12 and L1.

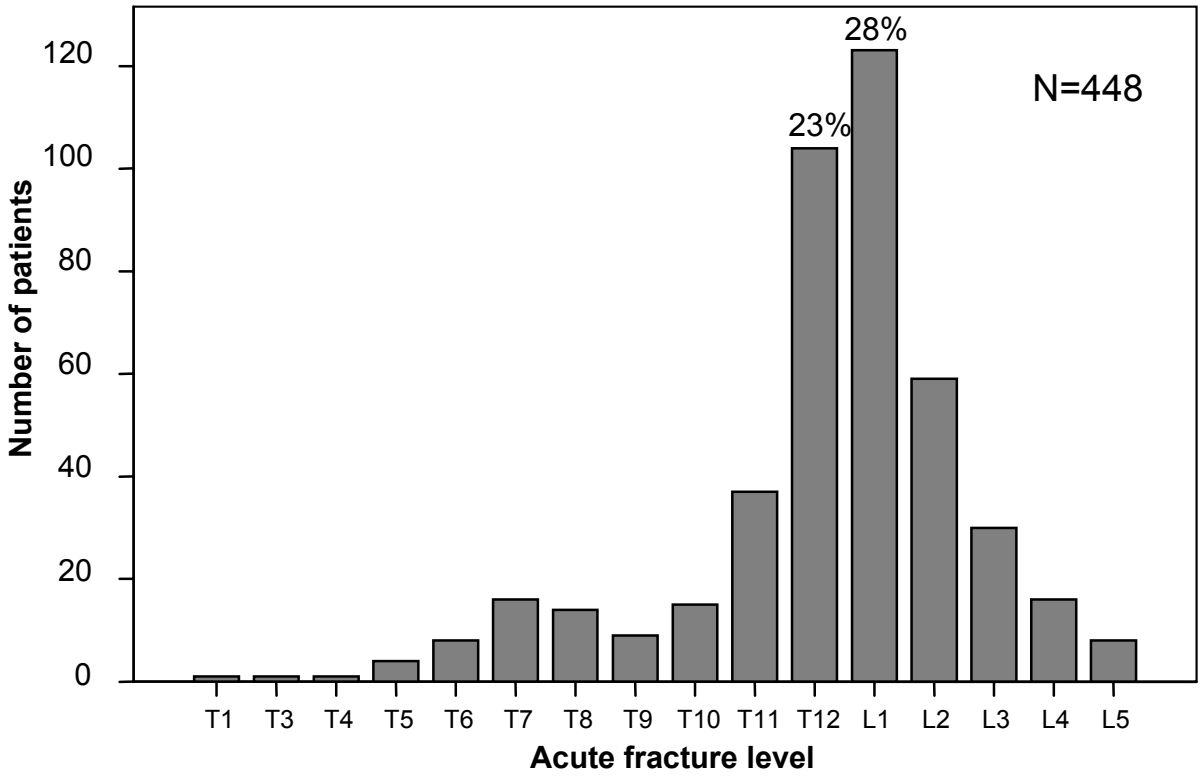

Figure 13. Distribution of the acute fracture location according to level.

22.3. Kyphosis and lordosis

Out of 448 patients, it was only possible to satisfactorily determine the kyphosis in 196 patients. The average kyphosis of the thoracic spine was 46.7 (SD 16.7) degrees. The lordosis could be determined in 396 of the 448 patients and had an average of 35.6 (SD 15.5) degrees. Both the thoracic kyphosis and lumbar lordosis were correlated to the number of thoracic fractures (r_s=0.39, p<0.00, r_s=0.25, p<0.00 respectively). The lumbar lordosis, on the other hand, was negatively correlated to the number of lumbar fractures (r_s=-0.23, p<0.00) and the thoracic kyphosis was not correlated to the number of lumbar fractures.

22.4. Analysis of all detected fractures

The 448 individuals diagnosed with an acute vertebral fracture had a total number of 1318 fractures. The location and frequency of the fractures can be seen in Figure 14.

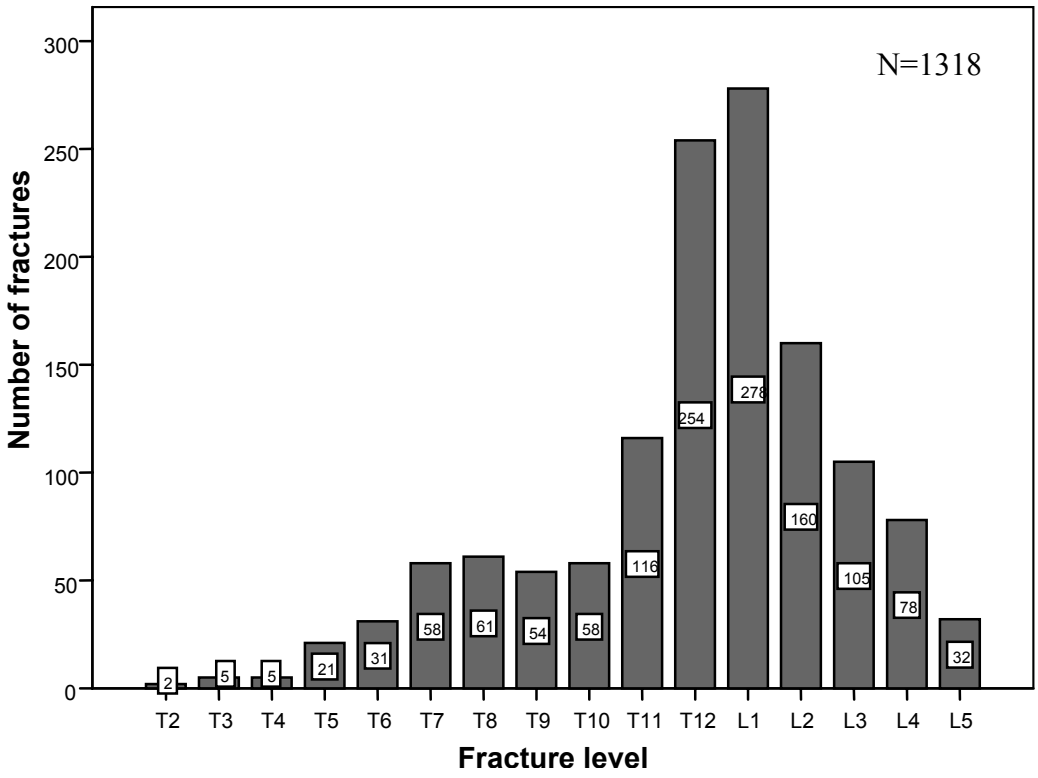

Figure 14. Distribution of the locations of all detected fractures (1318) in 448 patients with an acute fracture.

22.4.1. Adjacent fracture

Among the 202 patients who had multiple fractures, 118 patients (58.4%) had adjacent fracture(s). The distribution of the adjacent fracture locations can be seen in Figure 15. The adjacent fractures were mostly clustered at T11-T12, T12-L1 and L1-L2.

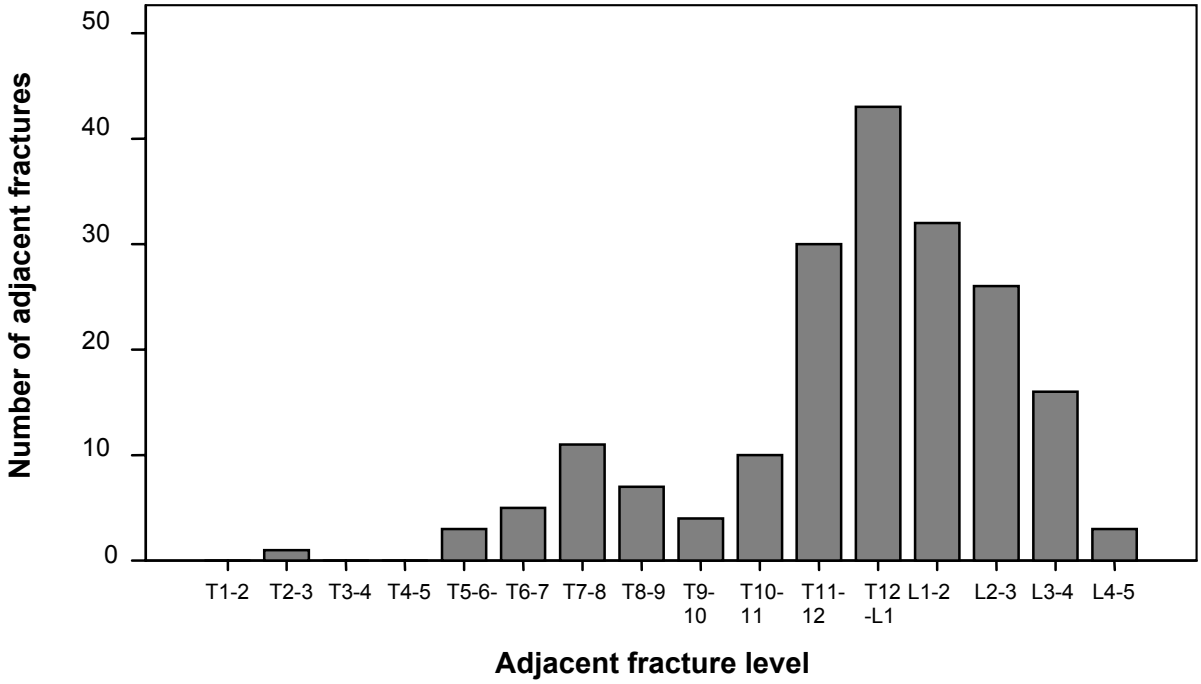

Figure 15. Distribution of the adjacent fracture locations.

22.4.2. Fracture type among all detected fractures

Analysis of the fracture type for all the 1318 fractures showed that the frequency of the concave fracture type increased in the lumbar spine, especially from L2 in the distal direction. The wedge fracture type, on the other hand, increased in the thoracic spine and at the L1 level (Figure 16).

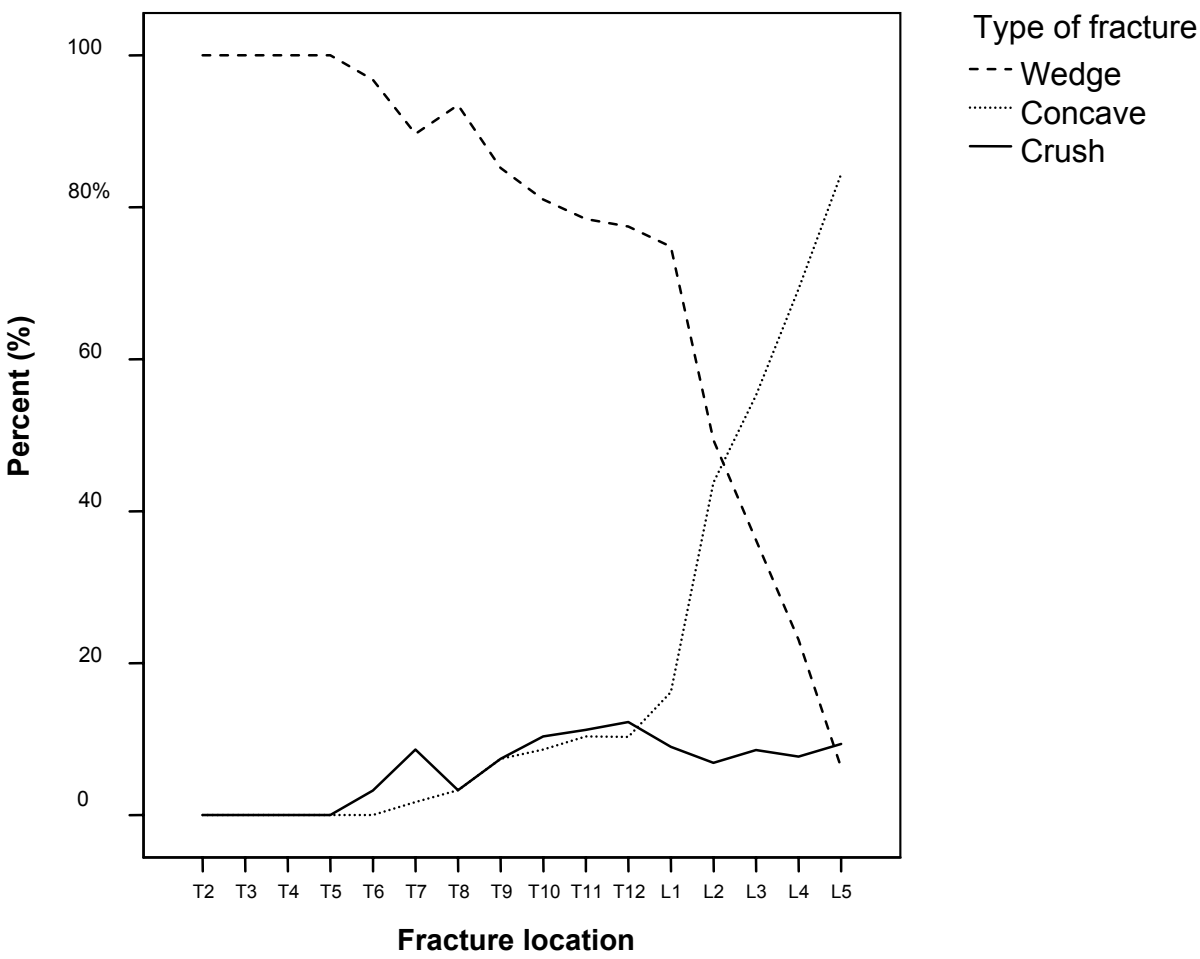

Figure 16. Relative distribution of the three different types of fractures according to their location in the spine for the total number of diagnosed fractures.

22.4.3. Grade of fracture deformity among all detected fractures

There was a trend showing that the percent of mildly deformed vertebrae increased in the caudal direction, whereas the moderately deformed vertebrae increased in the cranial direction. For the severe fractures, a bimodal distribution was observed, with peaks at the T7 and T12 levels (Figure 17).

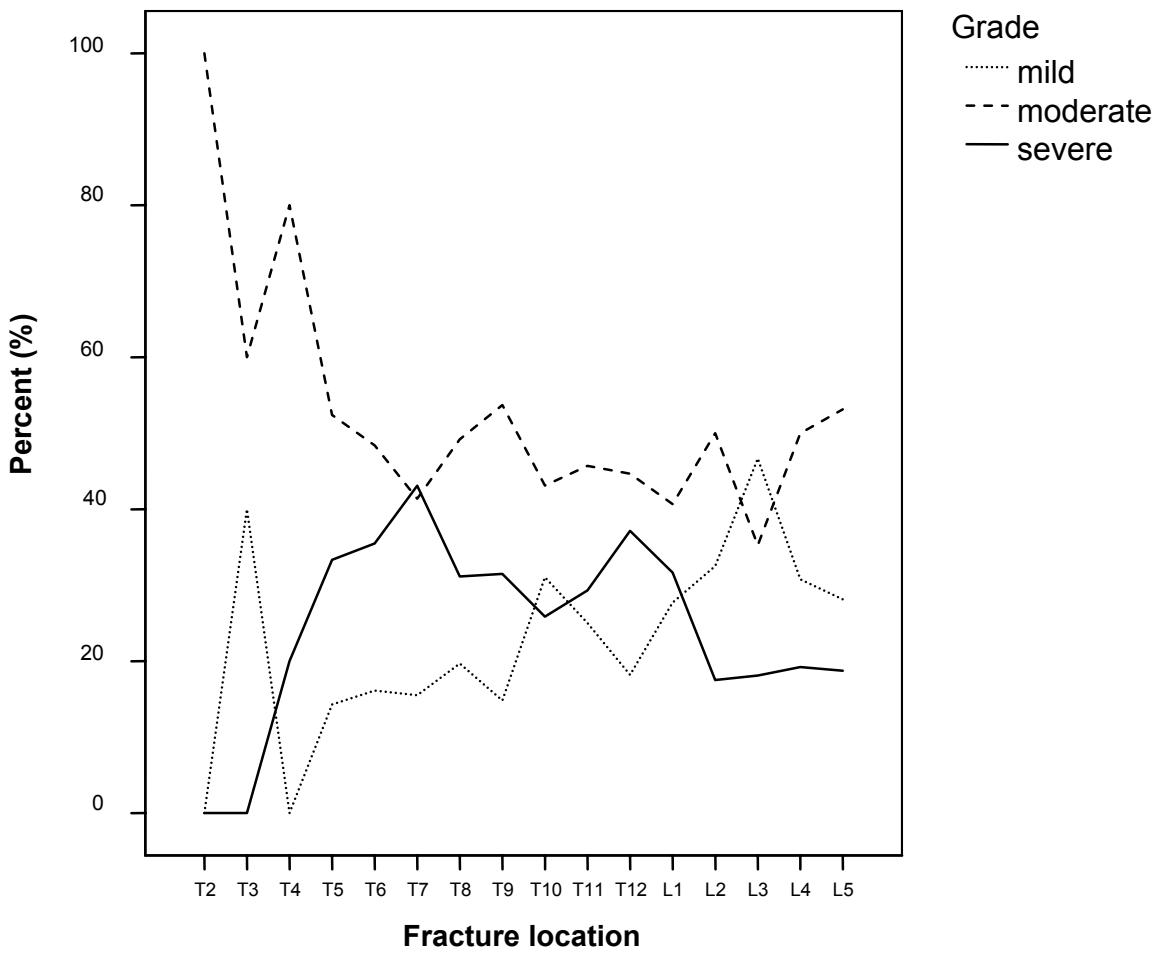

Figure 17. Relative frequency of the grade of fracture deformation among all the diagnosed fractures.

GENERAL DISCUSSION

23. Pain, disability, ADL, and QoL evaluations after an acute osteoporotic vertebral compression fracture (Study I)

The natural course of the osteoporotic vertebral compression fracture has not been studied thoroughly. This study was the first to analyze the course of this type of fracture over a longer period of time. The problems accompanying an acute vertebral compression fracture has been regarded as self-limiting, within weeks or a few months, and as having a good prognosis, at least for the majority patients [101]. The results of study I showed on the contrary that this fracture type was the starting point of a long-lasting painful and disabling health condition that drastically reduced the patient's health-related quality of life.

23.1. Pain

The initial pain intensity, in the study, recorded three weeks after the occurrence of the fracture was lowered during the first three months, but remained on a high level for the remainder of the one year follow-up. The initial pain intensity, as measured with von Korff's pain intensity score, was quite high (mean 70.9, SD 19.3; more than 97% reported > 25 on the pain intensity score which is regarded as clinically significant). The pain intensity after six months and one year remained high (mean score 61). It was of the same magnitude as the average pain intensity in a Swedish cohort of men and women who were fully work disabled for more than four weeks for back or neck pain [46]. Although not directly transferable, the pain intensity in the fractured patients after a whole year was just as severe as the preoperative pain in patients included in the Swedish National Spine Register, subsequently undergoing surgery for lumbar disc herniation (VAS: back 45, leg 64) or central spinal stenosis (VAS: back 55, leg 61) [104]. In the USA, one third of all the annually estimated 700,000 osteoporotic vertebral body compression fractures are believed to cause chronic pain [87]. The findings in the present study suggest that more than ¾ of the patients develop severe pain, lasting at least one year after this type of fracture. This finding is corroborated by another Swedish study, where it was noted that in more than 70% of the women, the occurrence of a vertebral body fracture was the beginning of a painful condition that could last at least up to 22 years [47].

23.2. Disability and ADL

The patient's disability rating pattern was quite similar to that for pain. In comparison to age-matched patients with non-osteoporotic chronic low back

pain, it was found that the disability was greater among those with a vertebral fracture [69]. In the present study, considerably lower values (worse) for ADL and back function were noted at all follow-up occasions in comparison to large cohorts of patients from six different countries with disabling low back pain [46]. When the impairment after a vertebral fracture was analyzed in 1010 women 6 years after the fracture, it was found that those with a previous fracture had up to seven times greater odds of reporting difficulties with a variety of activities than those without [39]. Similarly, it was noted that the odds of impaired function (defined as problems with ≥ 3 physical or instrumental ADLs) were 2.3 times higher among those with an earlier clinically-diagnosed vertebral fracture [27]. It has also been found that impairment of ADL does not have to be related to the presence of pain, particularly not in patients with two or more prevalent fractures [56].

23.3. Quality of life

The initial QoL, measured with EQ-5D, was quite low and similar or worse than what has been noted for long-lasting disabling low back and neck pain and comparable to the preoperative levels for a lumbar herniated disc or central spinal stenosis [46, 53, 104]. In a wider context than problems of the spine, the 3, 6 and 12 month EQ-5D values among the fractured patients found in the present study were similar or lower than the values found preoperatively in patients with hip or knee osteoarthritis, undergoing subsequent total joint replacement [45]. In comparison to the average EQ-5D value of 0.52 reported 1 year after the fracture in the present cohort, the corresponding values in hip fracture patients 1 year after total hip replacement surgery was 0.73 and after internal fixation surgery was 0.63 [7]. The EQ-5D values in the population of the city of Stockholm for the age groups represented in this study have been found to be just above 0.80 [12].

The worsening trend between 6 and 12 months was noticeable not only in the QoL recordings, but also for pain and disability as well, and seemed to emphasize the profound negative and lasting effect of this fracture [84]. In another Swedish cohort study, it was noted that all of the SF-36 (short form 36) dimensions were significantly lowered, even 2 years after a vertebral body fracture, which was worse than after a hip fracture [42].

24. Influential factors on pain, disability, ADL, and QoL (Studies II & III)

Studies II and III revealed the factors that were most significantly related to the severe condition of the patients after one year. These factors included the existence of a previous fracture(s) and the severity of the acute fracture

deformation. The fracture level, type of fracture and gender influenced to a lesser extent the pain, disability and QoL one year after the fracture.

24.1. Age

No correlations could be found between age and the questionnaire outcome scores at any follow-up ($p>0.05$). When the age was divided into two groups, below 70 years (35 patients) and, 70 and over 70 years (71 patients), no differences could be found between the age groups ($p>0.05$). Furthermore, multiple linear regression analysis confirmed that age was not a significant factor in this respect. Also, a Swedish population study using EQ-5D found that the scores for individuals between 60-79 years of age were very similar, i.e. not so much change by age group, which can partly explain the findings of the present study [11, 12].

24.2. Gender

Differences between genders were noted on von Korff's pain intensity score at 3 and 12 months, EQ-5D at 3 weeks and 3 months, and Hannover ADL score at 3 weeks, and 3 and 12 months. The multiple linear regression analysis also showed that gender differences significantly influenced the outcome measures. Several studies of different back problems have found that women consistently report more functional limitations, physical disability and slower recovery from disability than men [3, 46, 79, 86]. The common finding has been that women are more likely to report or over-report ill health and disability while men tend to underreport their infirmities [49, 61, 111]. The higher prevalence of not only osteoporotic vertebral fractures but also other disabling conditions like osteoarthritis, chronic joint pain, spinal stenosis and other degenerative spinal disorders among women are factors that contribute to the higher reporting [32, 104, 111].

24.3. Cause of trauma

When patients with a known trauma that caused the fracture were compared with those without a known trauma, it was found that the cause of trauma had no impact on the outcomes. Also, the grade and type of fracture were not related to the cause of trauma. It could be speculated that the patients without a known trauma had more severe osteoporosis, which could cause more pain and limited ADL, however, such differences could not be found.

24.4. Time elapsed to the visit hospital

No relations were found between the questionnaire outcomes and the time the patients waited before they sought medical attention and were diagnosed having a fracture. This is not surprising since most of the patients in this study did not get any treatment, other than possibly analgesics.

24.5. Hospitalization

Hospitalized patients had significantly worse EQ-5D and Hannover ADL at 12 months. Selection bias could possibly explain these findings since the patients who were hospitalized were older and perhaps had more comorbidities.

24.6. Fracture location

Few investigations about the relationship between fracture location and pain, disability, ADL or QoL have been reported. Two studies have shown that prevalent *lumbar* vertebral compression fractures lead to lower QoL and more severe pain than the prevalent *thoracic* vertebral fracture [16, 83, 102]. A stabilizing effect of the thoracic cage has been suggested as a reason for fewer problems after thoracic fractures [83]. The findings of studies II and III suggest a different development, at least during the first post-fracture year, between fractures in the thoracic and lumbar spines. While the lumbar fractures tended to improve steadily over the study year, the thoracic fractures tended to deteriorate after the initial three month improvement, which was noted in both the lumbar and thoracic spines. The occurrence of thoracic fractures has been reported to be related to an increase of the thoracic kyphosis [19, 22, 26], and this increase is associated with pain and disability [31, 70] possibly due to an increased spinal intramuscular pressure and accompanying ischemia causing muscle fatigue [106]. This could be a more reasonable explanation to the findings in the thoracic spine noted in studies II and III.

24.7. Fracture type

There are few studies that have evaluated the long-term effects of vertebral fracture type. No differences in pain or disability were found when wedge, concave or crush fracture types were compared in a cross-sectional study [28]. When random samples of men and women over 50 years of age were recruited from 30 European centers, all three fracture types were linked to an adverse outcome in a similar way [51].

In studies II and III, the acute wedge and concave fracture types resulted in less pain and better QoL than the crush fracture type. It is reasonable to assume that the somewhat milder symptoms after wedge or concave fractures could be explained by the fact that these fracture types included a much higher portion of mildly or moderately graded fracture deformations.

24.8. Grade of fracture deformation

The multiple linear regression analysis showed that the severe grade of fracture deformation significantly influenced the outcomes, especially pain intensity. Other studies have shown that severe vertebral fracture deformities

are associated with chronic and severe back pain and greater limitation of physical activities which involve the back [28, 70]. Although it seems reasonable that the greatest deformations create the worst problems, the exact mechanisms for this are still largely unknown. However, one mechanism was revealed when dynamic contrast-enhanced MRI was performed [60]. In this study, it was shown that the crush fracture caused more subsequent collapse than the other fracture types. The crush type fracture was likely to injure the perfusion to the vertebral body. In studies II and III, the crush fracture type had, by far, the highest inclusion of severely deformed vertebrae. It is possible that especially the severely deformed crush fracture may undergo a continuous collapse, similar to the collapse often seen in the head of femur after dislocated cervical neck fractures. However, without repeat X-ray examinations after the index X-ray, the possibilities of a continuous collapse occurring predominantly in the crush or severely deformed fractures could not be confirmed.

24.9. Number of previous fractures

The presence of one or more previous vertebral compression fractures added to the negative effect a subsequent acute fracture on disability, ADL, and QoL, but not on pain. This negative effect of a previous fracture(s) increased with number of fractures. As reported earlier, part of this finding can be explained by the fact that prevalent vertebral compression fractures worsen back pain [28, 31, 72, 93, 94, 97, 98] and QoL [41, 83, 99, 102, 110]. In the present studies, the most likely explanation for the negative effect that a previous fracture exerts is that the patients who had a previous fracture(s) already were more disabled and had a lower QoL when the subsequent acute fracture occurred. Less likely, although not impossible, would be that the previous fracture itself worsened the course of the acute fracture without lowering scores before the time of acute fracture event. The fact that the previous fracture's effect on pain was less pronounced could be explained by the findings that the influence of an incident fracture on QoL and disability can last at least 5 years [39, 41, 56], while pain lasts somewhat shorter, 2-4 years [4, 48]. It is likely that at least some of the previous fractures in this study were so old, such that the pain was already on a decline. Cockerill and co-workers reported that an incident fracture occurring as a subsequent one (during a mean follow-up period of 3.8 years and with a QoL evaluation 1.9 years (median) after the repeat X-ray examination) lowered QoL more than that of controls, irrespective of the presence or not of a prevalent fracture [17]. If, however, the incident fracture occurred as a first fracture episode, no differences were noted between the cases and controls, the latter group

including both subjects with and without prevalent fracture [17]. This suggested that it was the second fracture which resulted in the long lasting (> 3 years) deterioration of QoL. Furthermore, several earlier studies have shown that the number of prevalent fractures, especially moderately and severely deformed prevalent fractures, is related to impaired QoL [83, 90], as well as pain and disability [28, 48, 92]. Such results are consistent with the findings of the present studies, where relations between the number of previous fractures and impaired QoL, disability and ADL were also demonstrated.

24.10. Adjacent fracture

As for the previous fracture, the influence of an adjacent fracture on pain, disability and QoL has not been settled. A negative influence of an adjacent fracture was reported in one study [16], but not corroborated by others [83, 102]. The present studies could not detect any negative effects of an adjacent fracture.

25. Characteristics of the acute osteoporotic compression fracture (Study IV)

The characteristics of the acute osteoporotic compression fracture found in study IV were in accordance with earlier reports of prevalent and incident vertebral fractures, including gender [18], age, fracture location [18, 51, 57, 71, 100] and fracture type [22, 51] distribution.

In studies I-III, there was a high refusal rate of participation (69%), mainly due to old age. To generalize the results of these studies, the characteristics of representative patients who suffer an acute vertebral compression fracture need to be known. Therefore, the patient characteristics in study IV were compared with those in studies I-III. Similar characteristics were found between the studies (Table 13).

Table 13. Comparison of patient characteristics between studies I-III and IV.

Patient characteristics	Studies I-III	Study IV
Total population	107	448
Age, mean±SD	75.5±11.9	76.8±10.9
Gender		
Male, age mean±SD	32.7%, 76.1±11.2	29.2%, 74.1±12.0
Female, age mean±SD	67.3%, 75.3±12.3	70.8%, 77.9±10.2
Fracture location		
Thoracic fracture	54.2%	46.9%
Lumbar fracture	45.8%	53.1%
Type of fracture		
Wedge	69.2%	72.5%
Concave	18.7%	18.8%
Crush	12.1%	8.7%
Grade of fracture deformity		
Mild	20.6%	26.1%
Moderate	46.7%	47.8%
Severe	32.7%	26.1%
Number of previous fracture(s)		
0	52.3%	54.9%
1	25.2%	22.7%
2	8.4%	9.4%
3	2.8%	7.4%
4	5.6%	4.5%
5>	5.6%	1.1%
Kyphosis mean±SD (degrees)	43.6±15.8	46.7±16.7
Lordosis mean±SD (degrees)	30.5±16.5	35.6±15.5
Cause of trauma		
A level fall	45.4%	45.4%
Lift of a heavy object	1.9%	2.7%
Other trauma causes	5.6%	5.9%
No recollection of trauma	34.6%	45.9%
Time elapsed before visiting the emergency unit		
Within the first week	67.3%	33.3%
Within one month	14.9%	26.0%
More than one month	0%	13.7%
Unidentified	34.6%	26.9%

26. Clinical implications

Clinical important consequences of these studies will be:

- The patients get a more accurate individualized short and long term prognosis.
- Plan for a long-lasting pain treatment in the majority of the patients is needed.
- Early suggestion for more radical treatments, e.g. vertebroplasty or kyphoplasty, to the patients with the worst prognosis is possible.

LIMITATIONS

- It is difficult to distinguish whether a fracture is acute or not, especially for patients with severe osteoporosis and multiple compression fractures. Some patients who present with sudden back pain are erroneously diagnosed as having an acute vertebral fracture(s), when in fact the deformity has been present on earlier films [92]. Since an acute fracture, in all the studies in this thesis, was determined through clinical signs and plain X-rays, there is the possibility that some of the fractures interpreted as acute might rather have been relatively old.
- Since, in most cases, only one X-ray examination was evaluated, it is possible that subsequent fractures during the study year could have contributed to the problems during the follow-up period (studies I-III).
- Little was known about the patients prior to the acute fracture. For this reason, it is possible that some of the patients, due to comorbidity, for example, already had a deteriorated health-related quality of life which was subsequently worsened by the new fracture (studies I-III). This was, to some extent, compensated for by the fact that the scores used, e.g. EQ-5D, had age-stratified population data.
- The number of the patients was too low to allow for a proper analysis of the effect of fracture level, for example. (studies II and III).
- Since a large number of patients refused to participate in studies I-III, there is the risk of selection bias.
- Some of the patients had X-ray examinations of their spines that did not include the entire thoracic or lumbar spines. For this reason, an old fracture(s), e.g. in the proximal thoracic spine, could have been missed and in such a way have skewed the previous fracture analyses in studies III and IV.

CONCLUSIONS

- The acute osteoporotic vertebral compression fracture generally has been regarded as a condition with self-limiting problems and as having a relatively positive prognosis. From the results of this thesis, it can be concluded that this type of fracture has a more severe impact on pain, disability, ADL, and QoL than generally believed.
- The results of the present care and treatment for the majority of the patients with an acute vertebral compression fracture are quite unsatisfying.
- The initial severe fracture deformation was the worst prognostic factor for severely lasting pain and disability, and the deterioration of ADL and QoL.
- Factors such as fracture level (lumbar fractures tended to improve steadily while thoracic deteriorated), type of fracture (wedge and concave fractures resulted in less pain and better QoL than the crush fractures), and gender influenced to a lesser extent the outcomes during the year after the acute fracture.
- The deterioration of QoL, disability and ADL but not pain after an acute vertebral fracture was worsened in patients who had a previous vertebral compression fracture(s).

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APPENDIX

Appendix 1

von Korff pain intensity and disability scores

Pain intensity items

(1) How would you rate your pain right now? [Current pain]

No pain										Pain as bad could be
0	1	2	3	4	5	6	7	8	9	10

(2) After the fracture, how intense was your worst pain? [Worst Pain]

No pain										Pain as bad could be
0	1	2	3	4	5	6	7	8	9	10

(3) After the fracture, how intense was your pain? (That is, your usual pain at times you were experiencing pain.) [Average Pain]

No pain										Pain as bad could be
0	1	2	3	4	5	6	7	8	9	10

Disability items

(4) After the fracture, how much has the pain interfered with your daily activities? [Daily Activities]

No interference										Unable to carry on any activities
0	1	2	3	4	5	6	7	8	9	10

(5) After the fracture, how much has the pain changed your ability to take part in recreational, social and family activities? [Social Activities]

No change										Extreme change
0	1	2	3	4	5	6	7	8	9	10

(6) After the fracture, how much has the pain changed your ability to work (including housework)? [Work Activities]

No change										Extreme change
0	1	2	3	4	5	6	7	8	9	10

von Korff pain intensity score
= (((response question 1) + (response question 2) + (response question 3)) / 3) * 10

von Korff disability score
= (((response question 4) + (response question 5) + (response question 6)) / 3) * 10

Appendix 2

Hannover ADL score

1 Can you reach up and get, for example, a book from a high shelf or cupboard?
0. Either unable to do or able only with help
1. Yes, but with some difficulties
2. Yes, without difficulties

2 Can you lift a full suitcase and carry it for 10 meters?
0. Either unable to do or able only with help
1. Yes, but with some difficulties
2. Yes, without difficulties

3 Can you wash and dry yourself from head to toe?
0. Either unable to do or able only with help
1. Yes, but with some difficulties
2. Yes, without difficulties

4 Can you bend forward to pick up a small lightweight object from the floor?
0. Either unable to do or able only with help
1. Yes, but with some difficulties
2. Yes, without difficulties

5 Can you wash your hair over a washbasin?
0. Either unable to do or able only with help
1. Yes, but with some difficulties
2. Yes, without difficulties

6 Can you sit for one hour on a hard chair?
0. Either unable to do or able only with help
1. Yes, but with some difficulties
2. Yes, without difficulties

7 Can you stand continuously for 30 minutes (for example in a queue)?
0. Either unable to do or able only with help
1. Yes, but with some difficulties
2. Yes, without difficulties

8 Can you raise yourself in bed from a lying position?
0. Either unable to do or able only with help
1. Yes, but with some difficulties
2. Yes, without difficulties

9 Can you put on and take off socks or similar garments?
0. Either unable to do or able only with help
1. Yes, but with some difficulties
2. Yes, without difficulties

10 Can you bend sideways from a seated position to pick up a small object on the floor just beside your chair?
0. Either unable to do or able only with help
1. Yes, but with some difficulties
2. Yes, without difficulties

11 Can you lift a box (about 8kg) onto a table?
0. Either unable to do or able only with help
1. Yes, but with some difficulties
2. Yes, without difficulties

12 Can you run 100 meters fast without stopping in order to catch a bus?
0. Either unable to do or able only with help
1. Yes, but with some difficulties
2. Yes, without difficulties

Hannover ADL score = (total score) / (2*(number of valid answers))*100

Appendix 3

EQ-5D

Mobility
1. I have no problems in walking about.
2. I have some problems in walking about
3. I am confined to bed.

Self-Care
1. I have no problems with self care.
2. I have some problems washing or dressing myself.
3. I am unable to wash or dress myself.

Usual Activities (e.g. work, study, housework, family or leisure activities)
1. I have no problems with performing my usual activities.
2. I have some problems with performing my usual activities.
3. I am unable to perform my usual activities.

Pain/Discomfort
1. I have no pain or discomfort.
2. I have moderate pain or discomfort.
3. I have extreme pain or discomfort.

Anxiety/Depression
1. I am not anxious or depressed.
2. I am moderately anxious or depressed.
3. I am extremely anxious or depressed.

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