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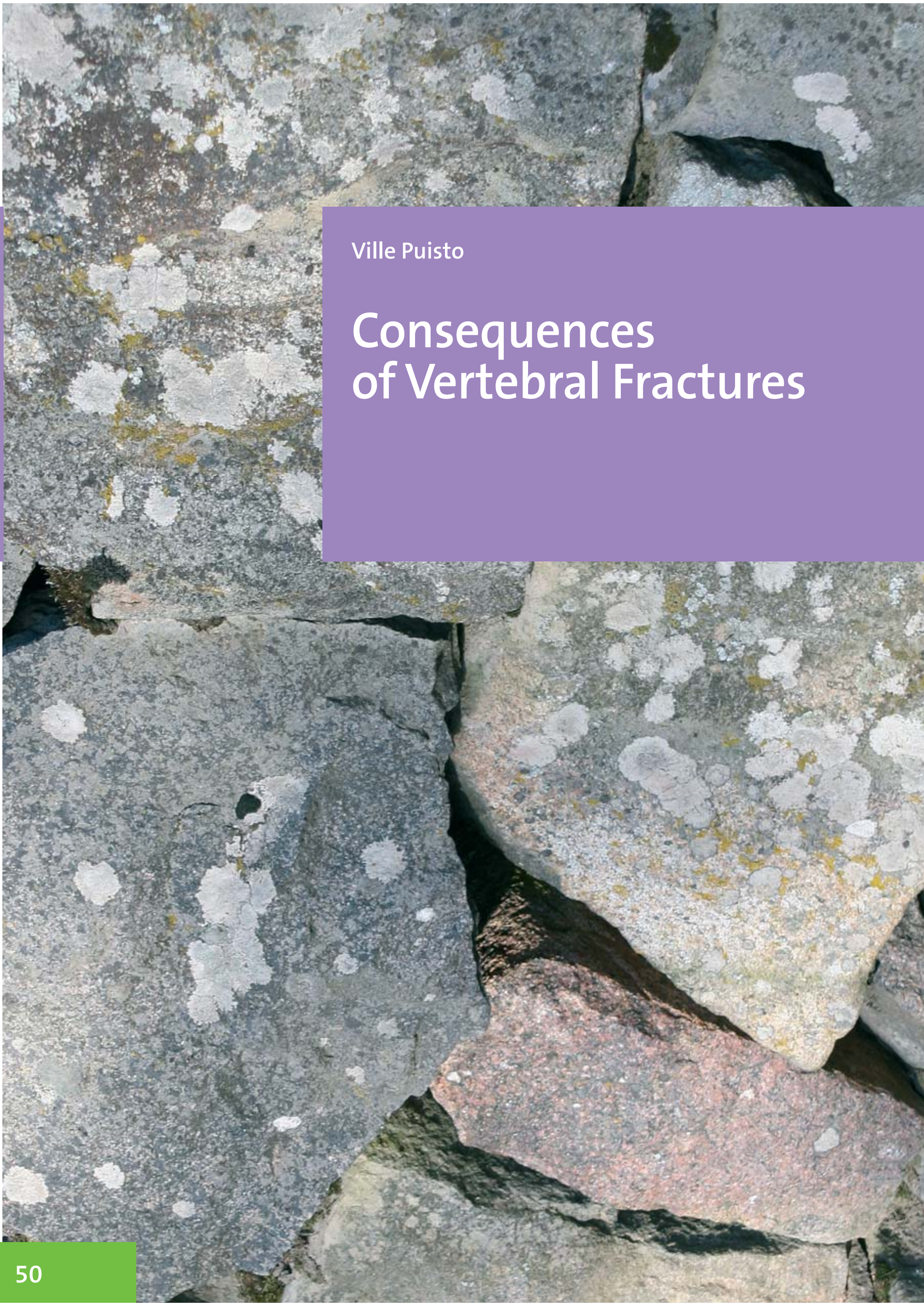

RESEARCH

Ville Puisto

Consequences of Vertebral Fractures

50

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Consequences of Vertebral Fractures

ACADEMIC DISSERTATION

To be publicly discussed with the permission of the Medical Faculty, University of Helsinki, in the lecture hall 1 of the Töölö Hospital. On 4th March 2011, at 12 noon.

University of Helsinki, Institute of Clinical Medicine, Department of Orthopaedics and Traumatology

National Institute for Health and Welfare, Helsinki

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To my family

ABSTRACT

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Vertebral fractures occur due to forces applied to spinal structures. When the bone tissue is weakened, vertebral fractures can result from a minor trauma. Adult vertebral fractures are commonly considered to be an indication for osteoporosis. In children osteoporosis is a rare condition, and pediatric vertebral fractures are usually clearly trauma-related.

The aims of this dissertation are to produce knowledge of the epidemiology of osteoporotic vertebral fractures and to analyse their association with total and cause-specific mortality, to find indicators with which to identify individuals who are at great risk of subsequent fractures, to study the incidence of pediatric vertebral fractures and need for their operative treatment and hospital care.

The Mobile-Clinic and Mini-Finland Health surveys of the adult population were used as materials in this research. Record linkages to the Finnish Hospital Discharge Register and the Official Cause of Death Register were used to study mortality and hospitalization in the same population group. These registers were also used to evaluate epidemiology, mortality, hospitalization and the need for operative management of pediatric vertebral fracture patients.

The main findings and conclusions of the present dissertation are: 1. The presence of a thoracic vertebral fracture in adults is a significant predictor of cancer and respiratory mortality. In women, but not in men, vertebral fractures strongly predict mortality due to injuries. Most of these deaths in the study group were hip fracture related. 2. Severe thoracic vertebral fracture in adults was a strong predictor of a subsequent hip fracture, whereas mild or moderate fractures and the number of compressed vertebrae were much weaker predictors. 3. Pediatric spinal fractures were rare: The incidence was 66 per one million children per year. In younger children cervical spine was most often affected, whereas in older children fractures of the thoracic and lumbar spine were more common. Maturation of spinal structures seems to play a major role in the typical injury patterns in children. Thirty per cent of pediatric spinal fractures required surgical treatment.

The current study focuses on consequences of vertebral fractures in general, without evaluating further the causation of the studied phenomena. Further studies are needed to clarify the mechanisms of association between vertebral fractures and specific causes of mortality. A severe vertebral fracture appears to indicate a substantial risk of a subsequent hip fracture. If such a fracture is identified from a chest radiograph, urgent clinical evaluation, treatment of osteoporosis and protective measures against falls are recommended.

Keywords: Epidemiological study, Vertebral Fracture, Mortality, Hip fracture, Osteoporosis, Fracture risk, Pediatric spine fracture, Incidence, Surgical treatment.

TIIVISTELMÄ

Ville Puisto. Consequences of vertebral fractures. [Nikamamurtumien seuraukset]. Terveyden ja hyvinvoinnin laitos (THL), Tutkimus 50, 96 sivua. Helsinki 2011.
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Nikamamurtumat syntyvät selkärankaan kohdistuvien voimien seurauksena. Terveen luukudoksen murtumiseen nikamassa tarvitaan kohtalaisen suuri vammaenergia, mutta heikentyneeseen luukudokseen voi syntyä kasaanpainumismurtuma jo hyvin pienen vamman seurauksena. Kirjallisuudessa nikaman kasaanpainumismurtumaa pidetäänkin yhtenä osteoporoosin ilmenemismuotona. Lapsilla osteoporoosi on harvinainen sairaus ja lasten nikamamurtumat johtuvatkin yleensä suuren vammaenergian aiheuttamasta luun murtumisesta.

Väitöskirjatutkimuksen tavoitteena oli selvittää osteoporoottisten nikamamurtumien esiintyvyyttä sekä niiden pitkäaikaisseurauksia, analysoida niihin liittyvä kuolleisuus, etsiä keinoja tunnistaa henkilöitä, joilla on suuri uuden murtuman riski, sekä selvittää lasten nikamamurtumien esiintyvyys ja leikkaus- ja sairaalahoidon tarve.

Materiaaleina tutkimuksessa käytettiin Kelan Autoklinikka ja Mini-Suomi -aineistoja. Tutkimushenkilöiden seurantatiedot saatiin sairaaloiden hoitoilmoitus- ja kuolinsyytilastoista.

Väitöskirjatutkimuksen tulokset osoittavat, että rintarangan nikamamurtumaan aikuisilla liittyy kohonnut syöpä- ja hengityselinkuolleisuus. Rintarangan nikamamurtuma ennakoi vahvasti tapaturmakuolemaa naisilla, mutta ei miehillä. Valtaosa näistä kuolemista liittyi lonkkamurtumaan. Aikuisten rintarangan voimakasasteinen nikaman kasaanpainumismurtuma ennusti voimakkaasti tulevaa lonkkamurtumaa, kun taas lievillä ja keskivaikeilla nikamamurtumilla ja nikamamurtumien lukumäärällä ei ollut ennustearvoa tulevaan lonkkamurtumaan.

Väestötyö osoitti, että lapsilla selkärankamurtumia on vuosittain 66 miljoonaa alle 18-vuotiasta lasta kohti. Nuorilla lapsilla kaularangan murtumat ovat yleisimpiä, kun taas vanhemmilla lapsilla rinta- ja lannerangan vammat ovat kaularangan vammoja yleisempiä. Selkärangan rakenteiden kypsymisellä näyttäisikin olevan keskeinen rooli eri-ikäisten lasten tyypillisissä selkärankamurtumissa. Kolmannes lasten selkävammoista vaatii leikkaushoitoa.

Lisää tutkimuksia tarvitaan selvittämään ilmiöiden syy-seuraussuhteita etenkin nikamamurtumien ja tautispesifisten kuolinsyiden yhteyttä. Henkilöille, joilla on todettu rintarangassa suuriasteinen nikaman painauma, tulisi tehdä systemaattinen kaatumisriskin ja luuston arviointi ja tarjota heille tarvittavat osteoporoosin ja kaatumisten ehkäisykeinot.

Avainsanat: Epidemiologinen tutkimus, Nikamamurtuma, Kuolleisuus, Lonkkamurtuma, Osteoporoosi, Murtumariski, Lasten selkärankamurtuma, Insidenssi, Leikkaushoito

CONTENTS

ABBREVIATIONS

MRI	Magnet resonance imaging
BMD	Bone mineral density
DEXA	Dual energy X-ray absorptiometry
T-score	A measure of bone mineral density used to evaluate the degree of bone fragility detected on DEXA scanning. An individual's T score is the number of standard deviations above or below the mean reference value for young healthy adults. Scores above –1 is considered normal and a score below –2.5 indicates osteoporosis.
ABQ	Algorithm-based qualitative method for diagnosing vertebral compression fractures
SQ	Semiquantitative method for diagnosing vertebral compression fractures
BMI	Body mass index (weight/height^2, kg/m^2)
RIA	Radioimmunoassay (DiaSorin, MI)
ICD	International Classification of Diseases
MCI	Metacarpal index
OR	Relative odds (odds ratios)
CI	Confidence interval
RR	Relative risk
SAS	Statistical Analysis System software (SAS Institute, Gary, North Carolina)
SD	Standard deviation

ORIGINAL PUBLICATIONS

I Puisto V, Rissanen H, Heliövaara M, Knekt P, Helenius I. Mortality in the Presence of a Vertebral Fracture, Scoliosis, or Scheuermann's Disease in the Thoracic Spine. Ann Epidemiol. 2008; 18(8): 595–601.

II Puisto V, Heliövaara M, Impivaara O, Jalanko T, Kröger H, Knekt P, Aromaa A, Rissanen H, Helenius I. Severity of vertebral fracture and risk of hip fracture: a nested case-control study. Osteoporos Int. 2011; 22(1): 63–8.

III Puisto V, Rissanen H, Heliövaara M, Impivaara O, Jalanko T, Kröger H, Knekt P, Aromaa A, Helenius I. Vertebral fracture and cause-specific mortality: A prospective population study of 3210 men and 3730 women with 30 years of follow-up. Eur Spine J. (submitted)

IV Puisto V, Kääriäinen S, Impinen A, Parkkila T, Vartiainen E, Jalanko T, Pakarinen M P, Helenius I. Incidence of Spinal and Spinal Cord Injuries and their Surgical Treatment in Children and Adolescents: A Population Based Study. Spine 2010; 35(1): 104–7.

1 INTRODUCTION

Vertebral fractures occur due to forces applied to spinal structures. It takes a relatively strong force to cause a vertebral fracture in healthy bone tissue, but when the bone tissue is weakened vertebral fractures can result from a minor trauma (Myers and Wilson 1997). Adult vertebral fractures are commonly considered an indicator of osteoporosis. In children osteoporosis is a rare condition, and pediatric vertebral fractures are usually clearly trauma-related. It has been estimated that 1–2% of fractures in children are located in the spine (Warner 2010).

Osteoporosis-related vertebral fractures are the most common osteoporotic fractures, but it has been estimated that only about one-third of them come to clinical attention (Cooper et al. 1993). They have important health consequences, including increased mortality (Kado et al. 1999 and 2003, Naves et al. 2003, Jalava et al. 2003, Pongchaiyakul et al. 2005, Hasserius et al. 2003 and 2005, Cooper et al. 1993, Center et al. 1999). While vertebral fractures show associations with increased mortality, there is no clear evidence that the excess deaths are due to any particular disease (Kado et al. 1999 and 2003, Naves et al. 2003, Jalava et al. 2003, Pongchaiyakul et al. 2005, Hasserius et al. 2003, Center et al. 1999). Cancer, pulmonary and cardiovascular deaths are suggested to explain the excess in mortality (Kado et al. 1999, Hasserius et al. 2003).

Vertebral fractures are known to predict further vertebral and hip fractures. Pool estimates of subsequent hip fracture risk in the presence of a vertebral fracture were approximately 2-fold in large meta-analyses (Klotzbuecher et al. 2000, Haentjens et al. 2003). There are only two studies, however, that have taken the morphology of vertebral fractures into account in the prediction of hip fracture. Hasserius (Hasserius et al. 2003) reported vertebral fracture prevalence and morphology in men and women admitted to hospital because of hip fracture. Schousboe (Schousboe et al. 2006) reported future hip fracture risk in women over 65 years of age with mild to severe vertebral deformity. In both of these studies, the association between hip fracture and vertebral deformity was of the same magnitude in patients with mildly to severely deformed vertebrae.

Further epidemiological research is needed to clarify the consequences of vertebral fractures and to identify subjects at a high risk of disabling fractures in order to allocate the healthcare resources rationally according to actual requirements (Cummings and Melton 2002). For resource allocation in health care systems, data from incidences of children's spinal injuries and the need for surgical interventions and hospital care are also needed. The current study focuses on consequences of vertebral fractures in general, without evaluating mechanisms of causation of the studied phenomena.

2 REVIEW OF THE LITERATURE

2.1 Introduction

Vertebral fractures occur due to forces applied to spinal structures. The ablility of the spine to carry load depends on the structural capacity of the vertebrae and the loading conditions that arise from activities of daily life or trauma (Myers et Wilson 1997). A bone is likely to break when loads imposed are greater than its strength. Activities that require forward bending of the upper body and lifting can cause 10-fold more compressive stress on the vertebra compared with standing upright (Myers and Wilson 1997, Duan et al 2001). This generated load can exceed the strength of a vertebra with very low bone mineral density (BMD) (Myers and Wilson 1997). Biomechanical literature suggests that majority of vertebral fractures are due to excessive loading to the spine, such as falling or bending forward to pick up an object from the floor (Myers and Wilson 1997, Duan et al. 2001).

In research, adult vertebral compression fractures are commonly considered an indicator of osteoporosis. The epidemiology and consequences of vertebral compression fractures have been of clinical and research interest for many years largely because osteoporosis is considered to be a condition that is often overlooked and undertreated. Osteoporosis is a clinically silent disease until it manifests in the form of a fracture. However, vertebral compression fractures present symptoms in only one-third of the cases (Cooper et al. 1993). In children osteoporosis is a rare condition, and paediatric vertebral fractures are usually clearly trauma-related.

2.2 Incidence and prevalence of vertebral fractures

Vertebral fractures are the most common osteoporotic fractures. Most of osteoporotic vertebral fractures are symptomless or present with minor symptoms, and therefore do not lead to radiological examinations and the diagnosis of vertebral fracture. It has been estimated that only about one-third of vertebral fractures come to clinical attention (Cooper et al. 1993), and that half of the symptomatic vertebral fractures are related to trauma (Myers and Wilson 1997).

The first population-based report of vertebral fracture incidences and prevalences was from the material provided by the Mobile Clinic in its population survey. The survey, which is also used in this dissertation (Härmä et al. 1986). The reported prevalences of thoracic spine fractures were 5.2 per 1,000 in the age group of 35–44, 5.1 per 1,000 in the age group of 55–64 and 29 per 1,000 in the age group of 75 and over. The incidence rate of vertebral compression fracture per 100,000 person-years was 32 in men and 37 in women (Härmä et al. 1986). In 1993 Cooper (Cooper et al.

1993) summarized the literature of vertebral fracture prevalence and found a wide variability between 2.9% and 25%. They also reported prevalence and incidences of vertebral fractures in Rochester post-menopausal women. The prevalence was 25.3 per cent with an estimated incidence of 17.8 per 1,000 person-years. The prevalence of vertebral fractures increased with age among French women from 19% in the 75–79 year-old group to 22% among those between 80 and 84 year-olds and to 41% among people of 85 years of age and over (Grados et al .2004). A significant correlation was also found between the number of vertebral fractures per woman and age (Grados et al. 2004). The prevalence of vertebral fractures in the Latin American Vertebral osteoporosis study was 12%, and an increase from 6.9% to 28% was reported from the age group of 50–59 to 80 and over (Clark et al. 2009).

Some of the studies that include both men and women have reported lower prevalence of vertebral fractures (Härmä et al. 1986, Kitazawa et al. 2001) than studies having postmenopausal women only. In Japan, the prevalence of vertebral fractures in population-based material were 4.7% overall, and 2.0% for 55–59 year-olds, 5.7% for 60–64 year-olds and 13% for 65–69 year-olds (Kitazawa et al. 2001). In some of the studies including men and women, vertebral fracture prevalence was of the same magnitude as in post-menopausal women alone. Samelson found the prevalence of vertebral fracture in 14% of men and women in the USA (Samelson et al. 2006). Vertebral fracture prevalence in Canada among people over 50 years of age was 20%, with a 5-year incidence in 24% (women) and 12% (men) (Chen et al. 2009)

In a Finnish study that evaluated thoracic magnet resonance imaging (MRI) findings from symptomless patients (aged 30–70) in Twin Cohorts, a 6.1% vertebral deformity prevalence was reported (Niemeläinen et al. 2008). When evaluating fractures of the lumbar spine, a fracture prevalence of 30% in healthy men aged 50–79 was observed (El Maghraoui et al. 2008). Gallacher et al. (2007) reported the distribution of moderate to severe vertebral fractures in patients with a prior non-vertebral fracture: 57% were thoracal and 22% lumbar and 21% had vertebral fracture in both regions. The total prevalence of vertebral fractures in these patients was 25%, and patients with osteoporotic lumbar spine T-scores in dual energy X-ray absorptiometry (DEXA), with a prior hip fracture were more likely to have a vertebral fracture compared to prior non-vertebral fracture patients with a normal lumbar t-score and without a hip fracture (Gallacher et al. 2007). Concentration of vertebral fractures in the mid-thoracic area and thoracolumbar junction was observed also in Japanese material (Kitazawa et al. 2001).

Different methods of diagnosing vertebral fractures give rise to a wide diversity in vertebral fracture prevalence and incidence statistics. The algorithm-based qualitative (ABQ) method and the semiquantitative method (SQ) are the primarily used medical research tools to diagnose and grade vertebral compression fractures.

In these methods, vertebral body height is measured in different parts of the body, and these measures are compared to diagnose and asses vertebral compressions. In clinical diagnosing, only visual evaluation of the vertebral body is usually used to diagnose vertebral compression fractures. The ABQ and SQ methods are more sensitive in identifying vertebral compressions. On the other hand, by these methods low-height vertebrae without endplate depression (degenerative changes or normal variations) may be more easily misdiagnosed as vertebral fractures (Härmä et al. 1986, Ferrar et al. 2007).

Thoracic spine and thoracolumbar junction presumably are the principal sites of osteoporotic vertebral fractures (Gallacher 2007), but the distributions of vertebral fractures differ between ABQ and SQ -methods, and fractures diagnosed clinically (Gehlbach et al. 2000). Also, when using the SQ method, fractures identified in radiographic follow-ups are likely to show a distribution different from that of prevalent fractures identified by the same method.

2.3 Pathophysiology and classification of thoracolumbar vertebral fractures

Over the time there have been many classifications of thoracolumbar vertebral fractures (Nicoll 1949, Holdswoth 1963, Denis 1983, Ferguson and Allen 1984, Magerl et al. 1994). In principle, fractures of the thoracolumbar spine can be classified into four groups based on the mechanism of injury (Kim et al. 2008).

2.3.1 Classification based on injury mechanism

Flexion-compression mechanism (wedge or compression fracture)

This mechanism usually results in an anterior column compression of vertebrae, with varying degrees of middle and posterior column compression.

Classification of Ferguson and Allen (Ferguson and Allen 1984) proposed three distinct patterns of injury. The first pattern involves anterior column failure while the middle and posterior columns remain intact. Imaging studies demonstrate wedging of the anterior component of the vertebral bodies. The loss of anterior vertebral body height is usually less than 50% (Ferguson and Allen 1984). This is a stable fracture (Figure 1). The second pattern involves both anterior column failure and posterior column ligamentous failure. Imaging studies demonstrate anterior wedging and may indicate increased interspinous distance. Anterior wedging can produce a loss of vertebral body height greater than 50%. This has an increased possibility of being an unstable injury. The third pattern involves failure of all 3 columns. Imaging studies demonstrate not only anterior wedging, but also varying degrees of posterior vertebral body disruption. This is an unstable fracture. Additionally, the possibility exists for spinal cord, nerve root, or vascular injury from free-floating fracture fragments dislodged in the spinal canal.

Figure 1. Stable vertebral compression fracture.

Axial-compression mechanism

This mechanism results in an injury called a burst fracture (Figure 2), and the pattern involves failure of both the anterior and middle columns (Denis 1983). Both columns are compressed, and the result is loss of height of the vertebral body. Five subtypes are described, and each is dependent on some concomitant forces, namely rotation, extension, and flexion. The 5 subtypes are (1) fracture of both endplates, (2) fracture of the superior endplate (most common), (3) fracture of the inferior endplate, (4) burst rotation fracture, and (5) burst lateral flexion fracture (Ghanayem et al. 1997). McAfee classified burst fractures based on the constitution of the posterior column (McAfee et al. 1983). In stable burst fractures, the posterior column is intact; in unstable burst fractures, the posterior column has sustained a significant insult. Imaging studies of both stable and unstable burst fractures demonstrate loss of vertebral body height. Additionally, unstable fractures may have posterior element displacement and/or vertebral body or facet dislocation or subluxation. As with a severe wedge fracture, the possibility exists for spinal cord, nerve root, or vascular injury from posterior displacement of fracture fragments into the spinal canal. Denis showed that the frequency rate of neurologic sequelae could be as high as 50% (Denis 1983).

Figure 2. Burst fracture of L1 vertebrae.

Flexion-distraction mechanism

This mechanism results in an injury called a Chance fracture (Figure 3). The pattern involves failure of the posterior column with injury to ligamentous components, bony components, or both (Wood 2008). The pathophysiology of this injury pattern is dependent on the axis of flexion. Several subtypes exist, and each is dependent on the axis of flexion and on the number and degree of column failure. The classic Chance fracture has its axis of flexion anterior to the anterior longitudinal ligament; this results in a horizontal fracture through the posterior and middle column bony elements along with disruption of the supraspinous ligament (Wood 2008). Imaging studies show an increase in the interspinous distance and possible horizontal fracture lines through the pedicles, transverse processes, and pars interarticularis. The flexion-distraction subtype has its axis of flexion posterior to the anterior longitudinal ligament. In addition to the previously mentioned radiographic findings, this type of injury also has an anterior wedge fracture. Because all 3 columns are involved, this is considered an unstable injury. If the pars interarticularis is disrupted in either type of fracture, then the instability of the injury is increased, which may be radiographically demonstrated by significant subluxation. Neurologic sequelae, if they occur, appear to be related to the degree of subluxation (Wood 2008).

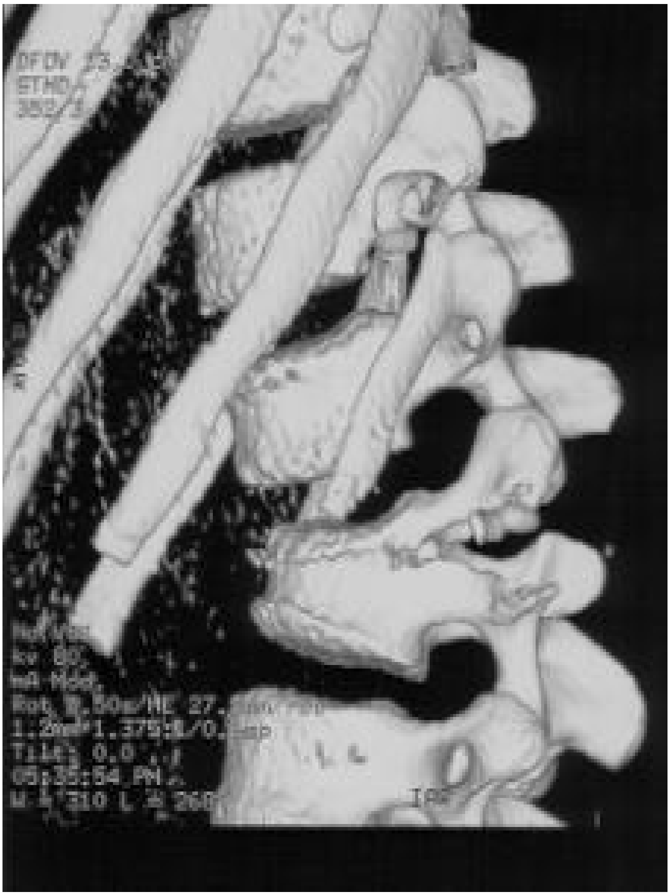

Figure 3. L1 Chance fracture.

In children, a Chance injury may affect only disc space and/or ligamentous structures making thus radiographic evaluation challenging. This kind of injury is highly unstable (Warner 2010).

Rotational fracture-dislocation mechanism

The precise mechanism of this fracture is a combination of lateral flexion and rotation with or without a component of posterior-anteriorly directed force (Wood 2008). The resultant injury pattern is failure of both the posterior and middle columns with varying degrees of anterior column insult. The rotational force is responsible for the disruption of the posterior ligaments and articular facet (Wood 2008). With sufficient rotational force, the upper vertebral body rotates and carries the superior portion of the lower vertebral body along with it. Denis subtyped fracture-dislocations into flexion-rotation, flexion-distraction, and shear injuries (Denis 1983). The flexion-rotation injury pattern results in failure of both the middle and posterior columns along with compression of the anterior column. Imaging studies may demonstrate vertebral body subluxation or dislocation, increased interspinous distance, and an anterior wedge fracture. The flexion-distraction injury pattern represents failure of both the posterior and middle columns. The pars interarticularis is also disrupted (Denis 1983). Imaging studies demonstrate an increased interspinous distance and fracture line(s) through the pedicles and transverse processes, with extension into the pars interarticularis and subsequent subluxation. The combined rotational and posterior-to-anterior force vectors result in vertebral body rotation and annexation of the superior portion of the adjacent and more caudal vertebral body. Imaging studies demonstrate both the nature of the fracture and dislocation. Each of these fractures is considered unstable. Neurologic sequelae are common (Wood 2008).

Minor Fractures

Minor fractures include fractures of the transverse processes of the vertebrae, spinous processes, and pars interarticularis. Minor fractures do not usually result in associated neurologic impairment and are considered mechanically stable (Whang and Vaccaro 2010).

2.3.2 AO Classification of thoracic and lumbar injuries

The AO Classification of thoracic and lumbar fractures is primarily based on pathomorphological criteria (Magerl et al. 1994). The injuries are divided into three groups (A–C), and each group contains three subgroups and a further specification. The severity of the fractures progresses from type A to type C.

Type A injuries are caused by axial compression, with or without flexion, and they affect almost exclusively the vertebral body. The height of the vertebral body is reduced, and the posterior ligamentous complex is intact. Translation in the sagittal and horizontal plane does not occur. The subgroups of type A injuries are; A1) impaction fractures, A2) split fractures, and A3) burst fractures (Magerl et al. 1994).

Type B injuries are fractures where transverse disruption of one or both spinal columns has occurred. Flexion-distraction initiates posterior disruption and elongation (B1 and B2) and hyperextension with or without anteroposterior shear causes anterior disruption and elongation (B3). The subgroups of type B injuries are; B1) posterior disruption predominantly ligamentous, B2) posterior disruption predominantly osseous, B3) anterior disruption through the disc (Magerl et al. 1994).

Type C injuries are anterior and posterior element injuries with rotation. Their common characteristics include two-column injury with rotational or horizontal displacement plane in all directions. The subgroups of type C injuries are; C1) type A injury with rotation, C2) type B injury with rotation, C3) rotational shear injuries (Magerl et al. 1994).

2.3.3 Genant's classification of vertebral compression fractures

Genant's classification of vertebral compression fractures is widely used in research of osteoporotic vertebral fractures (Genant et al. 1993). It grades severity of vertebral compression as normal (grade 0), mildly deformed (grade 1, 20–25% reduction of anterior, middle, and/or posterior vertebral body height), moderately deformed (grade 2, 26–40% reduction in any height), and severely deformed (grade 3, over 40% reduction in any height) (Figure 4).

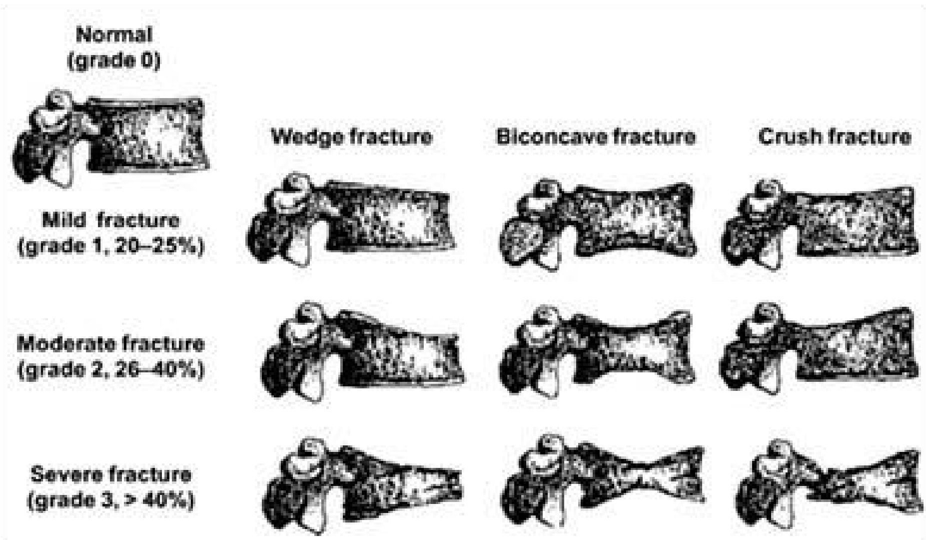

Figure 4. Genant's classification of vertebral compression fractures (Genant et al. 1993).

2.4 Pathophysiology and classification of cervical fractures

The normal anatomy of the cervical spine consists of 7 cervical vertebrae separated by intervertebral disks and joined by a complex network of ligaments. These ligaments keep individual bony elements behaving as a single unit. Most cervical spine fractures occur predominantly at 2 levels. In adults one-third of the injuries occur at the level of C2, and one-half of the injuries occur at the level of C6 or C7 (Bono and Carreras 2010). Most fatal cervical spine injuries occur in upper cervical levels, either at craniocervical junction C1 or C2. Cervical spinal injuries are best classified according to mechanisms of injury (Wood 2008).

Flexion injury

Most common flexion injuries of the cervical spine include simple wedge compression fracture without posterior disruption, flexion teardrop fracture, anterior subluxation, bilateral facet dislocation, clay shoveler fracture, and anterior atlantoaxial dislocation (Wood 2008).

Simple wedge fractures occur usually with a flexion injury. Longitudinal pull is exerted on the nuchal ligament complex that, because of its strength, usually remains intact. The anterior vertebral body bears most of the force, sustaining simple wedge compression anteriorly without any posterior disruption. The posterior column remains intact, making this a stable fracture (Wood 2008).

A flexion teardrop fracture occurs when flexion of the spine, along with vertical axial compression, causes a fracture of the anteroinferior aspect of the vertebral body (Wood 2008). This fragment is displaced anteriorly and resembles a teardrop. For this fragment to be produced, significant posterior ligamentous disruption must occur. Since the fragment displaces anteriorly, a significant degree of anterior ligamentous disruption exists. This injury involves disruption of all 3 columns, making this an extremely unstable fracture that frequently is associated with spinal cord injury (Wood 2008).

Anterior subluxation in the cervical spine occurs when posterior ligamentous complexes rupture. The anterior longitudinal ligament remains intact. No associated bony injury is seen. Since the anterior columns remain intact, this fracture is considered mechanically stable by definition. Anterior subluxation is rarely associated with neurologic sequelae. However, in clinical practise this injury is often considered to be potentially unstable because of the significant displacement that can occur with flexion (Wood 2008).

Bilateral facet dislocation is an extreme form of anterior subluxation that occurs when a significant degree of flexion and anterior subluxation causes ligamentous disruption to extend anteriorly, which causes significant anterior displacement of the spine at the level of injury. At the level of injury inferior articulating facets of the upper vertebrae pass superior and anterior to the superior articulating facets of the lower involved vertebrae because of extreme flexion of the spine. This is an extremely unstable condition and is associated with a high prevalence of spinal cord injuries. A significant number of bilateral facet dislocations are accompanied by disk herniation. In patients with these injuries further neurologic damage may occur if the injured disk retropulses into the canal during the application of cervical traction (Wood 2008).

Clay shoveler fracture occurs in the case of abrupt flexion of the neck, combined with a heavy upper body and lower neck muscular contraction. This results in an oblique fracture of the base of the spinous process, which is avulsed by the intact and powerful supraspinous ligament. Fracture also occurs with direct blows to the spinous process or with trauma to the occiput that causes forced flexion of the neck. This fracture is considered stable, and it is not associated with neurologic impairment (Wood 2008).

Flexion-rotation injury

Common injuries associated with a flexion-rotation mechanism include unilateral facet dislocation and rotary atlantoaxial dislocation (Figure 5) (Wood 2008).

Figure 5. Rotational fracture-dislocation of C6/C7.

Unilateral facet dislocation occurs when flexion, along with rotation, forces one inferior articular facet of an upper vertebra to pass superior and anterior to the superior articular facet of a lower vertebra, coming to rest in the intervertebral foramen. Although the posterior ligament is disrupted, vertebrae are locked in place, making this injury stable. The injury seldom is associated with neurologic deficits. Closed reduction with cervical traction may be attempted as a treatment (Bono and Carreras 2010).

Rotary atlantoaxial dislocation injury is a specific type of unilateral facet dislocation. This injury is considered unstable because of its location (Bono and Carreras 2010).

Extension injury

Common injuries associated with an extension mechanism include hangman fracture, extension teardrop fracture, fracture of the posterior arch of C1 (posterior neural arch fracture of C1) and posterior atlantoaxial dislocation.

Hangman fracture is a traumatic spondylolisthesis of C2 It is commonly caused by motor vehicle collisions and entails bilateral fractures through the pedicles of C2 due to hyperextension (Bono and Carreras 2010). This type of fracture is considered an unstable fracture, although it seldom is associated with spinal injury, since the anteroposterior diameter of the spinal canal is greatest at this level, and the fractured pedicles allow decompression. When associated with unilateral or bilateral facet dislocation at the level of C2, this particular type of hangman fracture is unstable and has a high rate of neurologic complications.

Extension teardrop fracture manifests with a displaced anteroinferior bony fragment. This fracture occurs when the anterior longitudinal ligament pulls the fragment away from the inferior aspect of the vertebra because of sudden hyperextension (Bono and Carreras 2010). The fracture is common after diving accidents and tends to occur at lower cervical levels. It also may be associated with the central cord syndrome due to buckling of the ligamenta flava into spinal canal during the hyperextension phase of injury. This injury is stable in flexion but highly unstable in extension.

Fracture of the posterior arch of C1 occurs when the head is hyperextended and the posterior neural arch of C1 is compressed between the occiput and the strong, prominent spinous process of C2, causing the weak posterior arch of C1 to fracture. The transverse ligament and the anterior arch of C1 are not involved, making this fracture stable (Bono and Carreras 2010).

Vertical compression injury

Common injuries associated with a vertical compression mechanism include Jefferson fracture (burst fracture of the ring of C1), burst fracture (dispersion, axial loading), atlas fracture, and isolated fracture of the lateral mass of C1 (pillar fracture).

Jefferson fracture is caused by a compressive downward force that is transmitted evenly through the occipital condyles to the superior articular surfaces of the lateral masses of C1. The process displaces the masses laterally and causes fractures of the anterior and posterior arches, along with possible disruption of the transverse ligament. A quadruple fracture of all 4 aspects of the C1 ring occurs. The disruption of the transverse ligament allows displacement of the lateral masses. If total disruption of the transverse ligament has occurred, the fracture is highly unstable.

Burst fracture of the vertebral body occurs when downward compressive force is transmitted to lower levels in the cervical spine: the body of the cervical vertebra can shatter outward, causing a burst fracture (Wood 2008). This fracture involves disruption of the anterior and middle columns, with a variable degree of posterior protrusion of the latter. If the loss in vertebral height is more than 25%, there is posterior protrusion, or neurologic deficit, and the fracture is considered unstable.

Multiple or complex injuries

Common injuries associated with multiple or complex mechanisms include odontoid fracture, fracture of the transverse process of C2 (lateral flexion), atlanto-occipital dislocation (flexion or extension with a shearing component), and occipital condyle fracture (vertical compression with lateral bending).

2.4.1 Upper cervical fractures

Upper cervical spine (occiput to C2) injuries are considered unstable because of their location. Nevertheless, since the diameter of the spinal canal is greatest at the level of C2, spinal cord injury from compression is the exception rather than the rule (Wood 2008). Common injuries include fracture of the atlas, atlantoaxial subluxation, odontoid fracture, and hangman fracture. Less common injuries include occipital condyle fracture, atlanto-occipital dislocation, atlantoaxial rotary subluxation, and C2 lateral mass fracture.

Atlas fractures

Four types of atlas fractures (I, II, III, IV) result from impaction of the occipital condyles on the atlas, causing single or multiple fractures around the ring. The first two types of atlas fracture are stable and include isolated fractures of the anterior and posterior arch of C1. The third type of atlas fracture is a fracture through the lateral mass of C1. The fourth type of atlas fracture is the burst fracture of the ring of C1. It is also is known as the Jefferson fracture. This is the most significant type of atlas fracture from a clinical standpoint because it is associated with neurologic impairment (Bono and Carreras 2010, Wood 2008).

Atlantoaxial subluxation

When flexion occurs without a lateral or rotatory component at the upper cervical level, it can cause an anterior dislocation at the atlantoaxial joint if the transverse ligament is disrupted. Because this joint is near the skull, shearing forces also play a part in the mechanism causing this injury, as the skull grinds the C1–C2 complex in flexion. Since the transverse ligament is the main stabilizing force of the atlantoaxial joint, this injury is unstable. Neurologic injury may occur from cord compression between the odontoid and posterior arch of C1 (Bono and Carreras 2010, Wood 2008).

Atlanto-occipital dislocation

When severe flexion or extension exists at the upper cervical level, atlanto-occipital dislocation may occur. Atlanto-occipital dislocation involves complete disruption of all ligamentous relationships between the occiput and the atlas. Death usually occurs immediately from stretching of the brainstem, which causes respiratory arrest (Bono and Carreras 2010, Wood 2008).

Odontoid process fractures

There are three types of odontoid process fractures that are classified based on the anatomic level at which the fracture occurs. Type I odontoid fracture is an avulsion of the tip of the dens at the insertion site of the alar ligament. Although a type I fracture is mechanically stable, it often is seen in association with atlanto-occipital dislocation and must be ruled out because of this potentially life-threatening complication. Type II fractures occur at the base of the dens and are the most common odontoid fractures. This type is associated with a high prevalence of nonunion due to the limited vascular supply and small area of cancellous bone. Type III fracture occurs when the fracture line extends into the body of the axis. Nonunion is not a major problem with these injuries because of a good blood supply and the greater amount of cancellous bone. With types II and III fractures, the fractured segment may be displaced anteriorly, laterally, or posteriorly. Since posterior displacement of segment is more common, the prevalence of spinal cord injury is as high as 10% with these fractures (Bono and Carreras 2010, Wood 2008).

Occipital condyle fracture

Occipital condyle fractures are caused by a combination of vertical compression and lateral bending. Avulsion of the condylar process or a comminuted compression fracture may occur secondary to this mechanism. These fractures are associated with significant head trauma and usually are accompanied by cranial nerve deficits (Bono and Carreras 2010, Wood 2008).

2.5 Causes of vertebral fracture

2.5.1 Basic causes of vertebral fracture

Vertebral fractures occur due to forces applied to spinal structures. The trauma necessary to break the bone of the spine is quite large in healthy bone tissue. Activities that require forward bending of the upper body and lifting can cause 10-fold more compressive stress on the vertebra compared with standing upright (Myers and Wilson 1997, Duan et al 2001). This generated load can exceed the strength of a vertebra with very low BMD (Myers and Wilson 1997). Biomechanical literature suggests that most of vertebral fractures are due to excessive loading on the spine, such as falling or bending forward to pick up an object from the floor (Myers and Wilson 1997, Duan et al. 2001).

A large part of vertebral fractures in adults occur in every day activities and relate to poor bone quality (Cooper et al. 1993, Myers and Wilson 1997). Weakening of the bone strength can be caused by osteoporosis or some other disease of the bone, such as infection or metastasis. However, when all fractures are considered, weakening of the bone strength is a moderate risk factor, and falling is the strongest single risk factor, for fractures (Järvinen et al. 2008, Kannus et al. 2002 and 2005). Pediatric vertebral fractures are usually clearly trauma related.

Prevention of vertebral fractures includes prevention of accidents and falls as well as limiting activities that require lifting and forward bending in people with low BMD. Prevention of osteoporosis is discussed in the osteoporosis chapter.

2.5.2 Low bone strength (osteoporosis)

Osteoporosis is a disease of the bone, in which bone mass is weakened due to microarchitectural deterioration of bone tissue (Anon 1993). Bone homeostasis is maintained by the osteoclast, which is responsible for bone resorption, and the osteoblast, which is responsible for bone formation. The bone peak mass is reached at the age of 20–30, deterioration of bone mass starts approximately at the age of 40 and accelerates in women after menopause (Väänänen 1996). Osteoporosis can be caused both by a failure to build bone and reach peak bone mass as a young adult and by bone loss later in life.

Osteoporosis is classified into primary and secondary osteoporosis. The secondary form is associated with several medical conditions and drug states. Primary osteoporosis is diagnosed when no secondary cause for osteoporosis is detected. Risk factors for osteoporosis include history of fracture in a first-degree relative, white race, advanced age, female sex, poor health or fragility, cigarette smoking, low body weight, estrogen deficiency such as that caused by early menopause (age <45 y) or prolonged premenopausal amenorrhea (>1 y), low lifelong calcium or vitamin-D intake, alcoholism, and inadequate physical activity (Sirola 2003, Walker-Bone et al. 2001)

The clinical importance of osteoporosis and its significance for public health lies in fractures, which increase mortality, extensive disability and suffering, and high economic costs (Kanis 2002, Cummings and Melton 2002). A measure of bone mineral density, T-score, is used to evaluate the degree of bone fragility detected on DEXA. An individual's T-score is the number of standard deviations above or below the mean reference value for young healthy adults. Osteoporosis is defined by the World Health Organization as a T-score of –2.5 or less (WHO 1994). T-score is the value compared to control subjects who are at their peak bone mineral density, while Z-score reflects a value compared to patients matched for age and sex. Markers of bone turnover may be used to evaluate bone homeostasis. Current data also indicates that they serve as independent predictor of fracture risk (Aro 2006).

Epidemiology

There are very few population-based epidemiological studies on osteoporosis, and the estimates of the incidence and prevalence of osteoporosis are very inexact, largely because the means to diagnose osteoporosis are not well suited for epidemiological research. It has been estimated that there are 400 000 osteoporosis patients in Finland (Osteoporoosin käypä hoito 2006). The number of osteoporotic patients have been estimated to be 26 million in the United States (Melton LJ 1995).

Osteoporotic patients have increased risk for hip fracture. Between 1998 and 2002 there occurred approximately 7 000 hip fractures in Finland annually, whereas the annual rate of hip fracture was 1 500 in 1960 (Sund 2006). Reports indicate that In Malmö area in Sweden the increase in hip fractures in recent years (Rogmark et al. 1999) has discontinued. A similar trend has been observed in New South Wales in Australia (Boufous et al. 2004), Ontario in Canada (Jaglal et al. 2005) and in Finland (Kannus et al. 2006).

Prevention of osteoporosis

Primary prevention of osteoporosis includes a risk factor assessment and educational resources to eliminate risk factors for bone loss. The main components of primary prevention are factors related to nutritional factors and exercise, but also avoidance of deleterious substances and habits, such as smoking (Law and Hackshaw 1997). High alcohol intake may not reduce bone mass, but increases the risk of falls (Laitinen and Välimäki 1993). Accordingly, an adequate intake of calcium and vitamin D (Lips 1996), regular exercise (Kiratli 1996, Järvinen and Kannus 1997), moderate intake of alcohol together with cessation of smoking should be encouraged. Fall prevention may also be considered as primary prevention of fractures in elderly people (Kannus et al. 2005).

Secondary prevention of osteoporosis concentrates on prevention of fractures after an initial fracture or on the detection of low BMD. Compared to primary prevention, further protection by osteoporosis medication and hormonal products may be necessary.

Associated Mortality and Morbidity

Patients who have sustained one osteoporotic fracture are at increased risk for developing additional osteoporotic fractures (Haentjens et al. 2003, Lindsay et al. 2001, Klotzbuecher et al. 2000). Osteoporosis-related hyper-kyphosis due to vertebral fractures is related with reductions in lung vital capacity. The impairments in vital capacity are most notable at kyphotic angles over 55 degrees (Harrison et al. 2007) (Figure 6).

Figure 6. Osteoporotic vertebral fracture and related hyper-kyphosis in the thoracic spine.

Osteoporosis-related vertebral and hip fractures are both associated with increased mortality (Kado et al. 1999 and 2003, Naves et al. 2003, Jalava et al. 2003, Pongchaiyakul et al. 2005, Hasserius et al. 2003 and 2005, Cooper et al. 1993, Center et al. 1999, Abrahamsen et al. 2009, Bliuc et al. 2009). Low bone mineral density without fractures has also been associated with increased risk of non-trauma mortality (Browner et al. 1991).

Osteoarthritis has been linked with osteoporotic and osteopenic BMD and the patients suffering from osteoarthritis have been shown to have signs of increased bone turnover (Mäkinen et al. 2007). Furthermore, osteoporotic patient may be prone to bone loss in the operated area after arthroplasty (Alm et al. 2009).

2.5.3 Other causes of vertebral fractures

A minority of all adult vertebral fractures are purely traumatic or caused by a pre-existing disease such as cancer or osteomyelitis at fracture site. (Wood 2008, Camillo 2008, Curlee 2008)

Traumatic vertebral fractures occur when relatively strong forces are applied to spinal structures. Traumatic vertebral fractures can be wedge or compression fractures, burst fractures, Chance fractures, subluxation or dislocation fractures or minor fractures of the spinal structures (Wood 2008). In contrast to osteoporotic vertebral compressions, these fractures are often unstable and require stabilisation procedures. They may also include an additional spinal cord, nerve root, or vascular injury of the spinal structures (Wood 2008).

Pathological vertebral fractures are most commonly caused by cancer in the bone. Primary bone cancers that can cause pathologic fractures include myeloma and osteosarcoma. More often the cancer in the bone is due to metastatic disease, such as prostate-, breast-, and lung cancer, for example (Curlee 2008). Osteomyelitis results either from hematogenous spread of bacteria or direct bacterial migration to the bone (Camillo 2008).

2.6 Prevention strategies of vertebral fracture

Most of adult vertebral fractures are osteoporosis and trauma (excess load) related. Prevention of these fractures should be focused on prevention of osteoporosis as discussed in the previous chapter. Also prevention of falls and prevention of excess loadings on the spine are important (Meyrs 1997, Kannus et al. 2005)

In contrast to adult vertebral fractures, most of the pediatric spinal fractures are caused by traffic accidents and falls. Preventive measures against these injuries, as well as improvements of traffic safety regulations, could be the most effective way to reduce spinal fracture rates in children.

2.7 Symptoms and diagnosis of vertebral fractures

Most of osteoporotic vertebral fractures are symptomless or present only minor symptoms and therefore, do not lead to radiological examinations and the diagnosis. It has been estimated that only about one-third of vertebral fractures come to clinical attention (Cooper et al. 1993) Traumatic and pathologic vertebral fractures usually present with symptoms.

Pain in the fractured region of the spine is the most common symptom of vertebral fracture. Some patients may also have hip, abdominal, or thigh pain. Numbness, tingling, and muscle weakness could mean compression of the nerves at the fracture site. Losing control of urine or stool or inability to urinate may be present if the fracture is pushing on the spinal cord itself. Increased kyphotic posture may also occur in the presence of vertebral compression fractures (Bono and Carreras 2010, Wood 2008).

Vertebral fractures are usually diagnosed with x-ray examination. Native x-rays (posteroanterior and lateral) of the spine usually give a adequate picture of the fracture. CT scan of the spine may be necessary if instability of the spinal bone structures is suspected. MRI of the spine may be needed to identify compression of nerves or spinal canal if incontinence or urine retention, muscle weakness, or numbness is present (Bono and Carreras 2010, Wood 2008).

2.8 Treatment of vertebral fractures

Treatment goals in vertebral fractures include protecting nerve function and restoring alignment and stability of the spine. Pain relief as well as prevention of subsequent fracture risk are also objectives of the treatment (Bono and Carreras 2010, Wood 2008).

Vertebral compression fractures, stable burst fractures and minor fractures of the spine are usually treated with pain medication. A hyperextension brace may be required for sitting and standing activities for 6 to 12 weeks to restore alignment and stability of the spine. Vertebroplasty or kyphoplasty may be performed if pain persists after an osteoporotic vertebral compression fracture (Bono and Carreras 2010, Wood 2008). However, recent randomized controlled trials have questioned their efficacy (Buchbinder et al. 2009, Kallmes et al 2009).

Unstable spine fractures require surgical treatment. The goals of operative treatment are to decompress the spinal cord canal and to stabilize the disrupted vertebral column. The most common approaches for management of the thoracolumbar fractures are the posterior approach, the posterolateral approach, and the anterior approach. The posterior approach with a midline incision and a laminectomy allows for access to the posterior elements. It does not however, permit access to the vertebral bodies, which limits the use of the posterior approach in fracture management. The posterior approach is useful for stabilization procedures that involve fixation of the posterior bony elements and pedicle screw application. The posterolateral technique improves access to the vertebral bodies. It is useful when only a limited exposure of the ventral elements is required. It may be combined with a posterior stabilization procedure when limited ventral exposure is needed. The anterior approach allows access to the vertebral bodies at multiple levels. Transthoracic exposure is required in order to access the vertebral bodies down to L1. Lower fractures require a transabdominal-retroperitoneal exposure (L1–L2) or the retroperitoneal approach alone (L2–L5). It is most useful for decompression of injuries and spinal canal compromise caused by vertebral body fractures (Bono and Carreras 2010, Wood 2008).

2.9 Vertebral fracture, mortality and morbidity

Vertebral compression fractures in older adults are commonly induced by excess loads and related to osteoporosis. They can cause pain at the fracture region in the spine, but usually present with minor symptoms. Impairments in nerve function due to spinal nerve compressions is a rarity in osteoporotic vertebral compressions, but alteration in spinal alignment, usually hyperkyphosis in the thoracic region, may occur, due to multiple compression fractures.

Osteoporosis-related vertebral fractures increase morbidity and mortality (Klotzbuecher et al. 2000, Haentjens et al. 2003, Kado et al. 1999 and 2003, Naves et al. 2003, Jalava et al. 2003, Pongchaiyakul et al. 2005, Hasserius et al. 2003 and 2005, Cooper et al. 1993, Center et al. 1999, Bliuc et al. 2009). Traumatic vertebral fractures can cause impairments in nerve function due to spinal cord or spinal nerve damages and cervical fractures are associated with increased mortality (Augutis and Levi 2003, Cirak et al. 2004, Martins 1998, Surkin. 2000, Yang et al. 2004).

2.9.1 Mortality

As told above, osteoporosis-related vertebral fractures are linked with increased mortality (Kado et al. 1999 and 2003, Naves et al. 2003, Jalava et al. 2003, Pongchaiyakul et al. 2005, Hasserius et al. 2003 and 2005, Cooper et al. 1993, Center et al. 1999, Bliuc 2009). This increase in mortality has been shown in asymptomatic (Kado et al. 1999, Naves et al. 2003, Jalava et al. 2003, Hasserius et al. 2003, Pongchaiyakul et al. 2005) as well as clinically diagnosed vertebral fractures (Lau et al. 2008, Pongchaiyakul et al. 2005, Cauley et al. 2000, Hasserius et al. 2005, Center et al. 1999, Johnell et al. 2004). The risk of death in the presence of a asymptomatic vertebral fracture has ranged from 1.2– to 4.4-fold. (Kado et al. 1999, Naves et al.

2003, Pongchaiyakul et al. 2005, Hasserius et al. 2003, Jalava et al. 2003) and from 1.6– to 9.0-fold with symptomatic vertebral fractures (Lau et al. 2008, Pongchaiyakul et al. 2005, Cauley et al. 2000, Hasserius et al. 2005, Center et al. 1999, Johnell et al. 2004). The highest mortality rate is within the first year after fracture. After that the risk declines, but remains elevated compared to general population (Kanis et al. 2004, Center et al. 1999, Johnell et al. 2004, Bliuc et al. 2009).

While osteoporotic vertebral fractures show associations with increased mortality, there is no evidence that excess deaths are due to any particular disease (Kado et al. 1999 and 2003, Naves et al. 2003, Jalava et al. 2003, Pongchaiyakul et al. 2005, Hasserius et al. 2005, Center et al. 1999). Severe vertebral deformities and kyphosis are known to predict mortality in women (Kado et al. 1999). The follow-up periods have been relatively short. In a 10-year population-based follow-up study, vertebral deformities were associated with cancer deaths in women and with pulmonary and cardiovascular deaths in men (Hasserius et al. 2003, Kado et al. 1999). Low bone mineral density has also been associated with increased risk of non-trauma mortality (Browner et al. 1991).

The association between vertebral fractures and increased mortality has not been causal; a fracture is likely to be a marker or indicator of general fragility of the victim only.

2.9.2 Morbidity

Osteoporotic vertebral fractures predict further fractures, but it is not known whether this is due to increased risk of falling, osteoporosis, or both. In a large meta-analysis, vertebral fractures were associated with an increased risk for future wrist, vertebral, hip and all non-spine fractures (Klotzbuecher et al. 2000). The strongest association was between prior and subsequent vertebral fractures: postmenopausal women with a pre-existing vertebral fracture had approximately 4 times greater risk of a subsequent vertebral fracture than those without prior fractures. This risk increased with the number of prior vertebral fractures. The subsequent hip fracture risk with a prior vertebral fracture was approximately 2-fold. The risk was 1.4-fold for wrist fracture, 2.3-fold for all non spine fractures and pooled overall fracture risk with prior vertebral fracture was approximately 2-fold. Haentjens observed a 2.2-fold risk for hip fracture in subjects with a vertebral fracture in their meta-analysis (Haentjens et al. 2003).

There are only two studies that have taken the severity of vertebral fractures into account in the prediction of future hip fracture. Hasserius (Hasserius et al. 2003) reported vertebral fracture prevalence and morphology in men and women who were admitted to hospital because of a hip fracture. Schousboe (Schousboe et al. 2006) reported future hip fracture risk in women over 65 years of age with mild to severe vertebral deformity. In both of these studies, the association between hip fracture and vertebral deformity was of the same magnitude in patients with mildly to severely deformed vertebrae.

Osteoporosis-related kyphosis due to vertebral fractures is related to reductions in lung vital capacity, as concluded in a systemic review (Harrison et al. 2007). The impairments in vital capacity were most notable at kyphotic angles over 55 degrees.

2.10 Vertebral fractures in children

In pediatric patients, vertebral fractures are usually caused by accidents. Incidence estimates of these injuries are often uncertain because of differing reporting methods, data collection systems and classification patterns (Cirak et al. 2004). In addition, most incidence data are based on clinical case series in a single or multiple institution(s), and these estimates include only patients referred to hospital and exclude premorbid mortality (McGrory et al. 1993, Platzer et al. 2007, Kim et al. 2008).

Osteoporotic vertebral fractures are rare in children. They typically occur in the thoracic spine in children with other significant medical comorbidities, such as solid organ transplantation (Helenius et al. 2006) or inflammatory joint disease (Mäyränpää et al. 2007, Valta et al. 2007).

It has been estimated that in developed countries every fourth child sustains annually an injury necessitating medical care or hospitalization (Roberts et al. 1996, Danseco et al. 2000, Parkkari et al. 2000 and 2003) and that 1–2% of fractures in children are located in the spine (Warner 2010). Recently, Polk-Williams (Polk-Williams et al. 2008) raported reported blunt cervical spine injury in 1.6% of all pediatric trauma patients under 3 years of age. Of the pediatric spine injuries, 40 to 80 per cent has been reported to have occurred at the cervical spine (McGrory et al. 1993, Kokoska et al. 2001), whereas most of the spinal fractures in adults occur in thoracolumbar junction (Magerl et al. 1994). The annual incidence for cervical spine fractures has been estimated to be 74 per 10^6 in US children (McGrory et al. 1993).

Cervical fractures in children are associated with increased mortality (Augutis and Levi 2003, Cirak et al. 2004, Martins 1998, Surkin 2000, Yang et al. 2004). The most important type of fatal injury is high spinal cord injury, which leads to respiratory paralysis. Typical injuries in these cases are occipitoatlantial and C1–C2 dislocations. Severe abdominal injury, such as liver, spleen or bowel injury may coexist in patients with a lumbar Chance fracture, and these typically carry increased risk of mortality (Reid et al. 1990).

Pathophysiology of cervical fractures in children resembles that in adults.

Cervical spinal injuries in children are traditionally categorized into infantile, young juvenile and old juvenile injuries (Kim et al. 2008). Infantile injury is defined as an injury that occurs prior to the adequate development of head control by the infant. Young juvenile injury refers to an injury that occurs after the development of adequate head control, but below the age of eight years. These injuries are primary above C4, with C2 and C3 being the most commonly affected level. In children younger than eight years, the fulcrum of flexion and extension is centred in the upper cervical spine, mainly at the C2 and C3 disc spaces. Old juvenile injury includes children older than eight years. The fulcrum of cervical motion is mid-cervical during this age, and most primary ossification centres (except the tip of the dens) have completed fusion by the age of eight to ten years.

There are no studies to asses morbidity with prior pediatric spine fracture. Pye studied the subsequent fracture risk based on fractures self-reported at the age of 8–18 (Pye et al. 2009). These self-reported pediatric fractures were not associated with future hip or vertebral fractures or low bone mass (measured in DEXA), suggesting that pediatric fractures are not caused by osteoporosis and they don't predict osteoporosis later in life.

2.11 Scoliosis

Idiopathic scoliosis is a structural lateral curvature of the spine arising in otherwise healthy children usually during puberty, and it represents the most common form of spinal deformity in childhood (Weinstein 2001, Nissinen et al. 1989). The diagnosis is made once other causes of scoliosis, such as vertebral anomalies, have been ruled out. The male-female ratio for small curvatures in the range of 10 degrees is 1:1. In curvatures of larger magnitude, however, female dominance may grow as high as 1:10 (Weinstein 2001, Helenius et al. 2005). Epidemiological studies of Finnish pubertal and prepubertal schoolchildren indicate that the prevalence of scoliosis is 4–9% (Nissinen et al. 1989 and 1993). Scoliosis with a curvature of over 60 degrees is commonly associated with a restrictive lung disease (Newton et al. 2005). Increased mortality has been reported in subjects with untreated scoliosis (Nilsonne et al. 1968) and in subjects with untreated infantile, juvenile or severe (over 70 degrees) scoliosis (Pehrsson et al. 1992). In a natural history study of adults with adolescent idiopathic scoliosis, subjects were productive and functional at a high level at 50-year follow-up (Weinstein et al. 2003). Cardiorespiratory mortality was increased only in patients with thoracic scoliosis of 100 degrees or more.

2.12 Scheuermann's disease

Scheuermann's disease is characterized by a fixed thoracic kyphosis with wedged thoracic vertebrae and endplate changes (Weinstein 2001). It affects 0.5–8% of healthy subjects, with a prevalence in the male population (Ascani et al. 1977, Murray et al. 2003). The cause of this condition remains unclear. Scheuermann's disease is not known to increase mortality; nevertheless, long-term prognostic studies are few. Murray et al. (Murray et al. 2003) followed 67 patients with Scheuermann's disease for 32 years. Mortality was not increased, although patients with kyphosis of over 100 degrees had a restrictive lung disease.

2.13 Concluding remarks

The incidence and prevalence estimates of vertebral fractures vary a lot in previous studies. Osteoporotic vertebral fractures are associated with increased mortality and further osteoporotic fractures. There is, however, no strong evidence that mortality associated with these fractures is due to any particular disease. The mechanisms of this association are unclear. The association does not have to be causal because a fracture in an older age can well be a sign of the individual's general fragility only.

Few studies have taken into account the severity of vertebral fracture in prediction for further fractures. In these studies, the severity of vertebral compression has shown little effect on future fracture risk.

In pediatric patients, vertebral fractures are usually caused by accidents. Osteoporotic vertebral fractures in children are very rare. Incidence estimates of the injuries in children are often uncertain because of differing reporting methods, data collection systems and classification patterns. Most of the incidence data are based on clinical case series in a single or multiple institution(s).

3 AIMS OF THE STUDY

The general aim

The general aim of the study was to produce new information on epidemiology and on consequences of vertebral fractures.

The specific aims

1. To analyse total and cause-specific mortality and morbidity after osteoporotic vertebral fractures.
2. To find indicators to identify individuals who are at high risk of subsequent hip fracture after vertebral fracture.
3. To define incidences of children's spinal fractures on a population based study, and to evaluate the need for surgical interventions and hospital care.

4 STUDY POPULATIONS AND METHODS

For this dissertation, multiple databases to study vertebral fractures in children and adults were used. To assess the consequences of osteoporotic vertebral fractures in adults, Mobile-Clinic and Mini-Finland Health survey populations were used. Follow-up data was received from the Finnish Hospital Discharge Register and Official Cause of Death Register. To assess vertebral fracture incidences and the need for operative treatment in children, the Finnish Hospital Discharge Register and the Official Cause of Death Register were used.

4.1 The Mobile-Clinic Health Examination

Study population and baseline examination

The Mobile-Clinic of the Finnish Social Insurance Institution carried out a multiphase screening examination in between 1973 and 1976. Altogether, 19,000 men and women aged from 15 to 92 years (83% of those invited) from 12 populations in four regions of Finland were examined. From the original study population, 16,010 subjects were re-examined 4–7 years (mean 5 years) later. The groups examined comprised either whole population of a community or a random sample of it. The mean age of subjects was 45.0 years. The baseline examinations included a medical examination and chest radiographs (posteroanterior and lateral in 10x10 photofluorograms). Background information was collected with a premailed questionnaire, which included questions about medical history. The answers were checked and, when necessary, completed by a nurse at the examinations.

Definition of determinants

Information on leisure time physical activity obtained by means of the questionnaire was categorised into three classes: low, moderate and high activity. Self-rated general health was classified according to a three-point scale: good, moderate, and poor. Self-rated health measured in this manner has proved reliable in test-retest analysis (Martikainen et al. 1999). Standing height and weight were measured, and BMI was used as a measure of relative weight. Smoking history was obtained in a standard interview and categorised as follows: never smoked; ex-smoker; current smoker of cigars, pipe or of fewer than 20 cigarettes a day, and current smoker of 20 cigarettes or more a day. The basic questionnaire also inquired about average weekly consumption of beer, wine and strong beverages during the preceding month. The overall alcohol consumption was then calculated and expressed in grams of ethanol per week. The level of education was classified into three categories based on the years of education: lower education (i.e. completion of an 8-year period of comprehensive schooling, or less); intermediate education (i.e. lower or upper secondary schooling of 9–13 years); and higher education, including studies or degrees taken at universities or other higher education establishments (over 13 years).

Follow-up of mortality

The mortality of the study population has been monitored continuously. The information, including the cause of death, using the International Classification of Diseases (ICD) codes for causes of death, was obtained from Statistics Finland.

4.2 The Mini-Finland Health Examination

Study population and baseline examination

The Mini-Finland Health Survey between 1978 and 1980 was based on a stratified two-stage cluster sample (N=8,000) drawn from the population register to represent Finnish adults aged 30 years or over. In the first stage, 40 representative areas were selected. In the second stage, a systematic sample of inhabitants was drawn from each area. The subjects were interviewed at home, asked to fill in a questionnaire, and invited to attend a screening examination. Information was elicited on risk factors (e.g. smoking, BMI, alcohol consumption, diet), disease histories, symptoms and signs, and findings suggestive of cardiovascular, respiratory, musculoskeletal and other common diseases. A total of 6,925 subjects attended the baseline examination, and full-size chest radiographs (posteroanterior and lateral) were obtained of 3,215 men and 3,737 women (90% of the sample).

Definition of determinants

The definition of the used determinants (leisure time physical activity, self-rated general health, height, BMI, smoking history, alcohol consumption, education) was done in the same way as it was done in the Mobile-Clinic material. Venous blood samples were taken, and the sera were kept frozen at –20°C until 2003 when the serum 25-hydroxyvitamin-D concentrations were determined using the radioimmunoassay (RIA) (Knekt et al. 2008).

Nested case-control setting

To evaluate the effect of the severity of vertebral fractures in future hip fracture risk, a case-control setting was adopted. Record linkage to the National Hospital Discharge Register identified 182 subjects from the Mini-Finland survey who had been hospitalized for primary treatment of hip fracture by the end of 1994. All hip fractures as primary or secondary diagnoses were defined according to the eighth edition of the ICD, with a three-digit code – 820. Two to three controls of the same sex per each hip fracture case were drawn from the Mini-Finland cohort by individual matching for municipality and age. A follow-up started from the baseline examination, and the end points of the follow-up were the occurrence of hip fracture, death of a subject, or the end of 1994. However, only subjects who had survived until the end of the follow-up (occurrence of hip fracture in a matched case, or end of the follow-up period) were considered potential candidates for the control group. Their age was not allowed to diverge more than nine years from that of the case in question. No acceptable control was found for 13 cases, and these were consequently excluded from the study population. There were nine cases with only one matched control and eight cases with two matched controls.

Follow-up

Morbidity and mortality in the cohort have been continuously followed up since the baseline examination. Information on mortality and causes of death, according to the ICD-codes, was obtained from Statistics Finland.

4.3 Follow-up of mortality

The Official Cause of Death Register is coordinated by Statistic Finland. The data on fatal pediatric spinal injuries and mortality data of the subjects in Mobile-Clinic and Mini-Finland Health Surveys was obtained from this register. The causes for all injury-related and sudden deaths are confirmed at autopsy according to Finnish legislation. Each death is given an ICD-10 code for the main cause of death.

4.4 The follow-up of incident hip fractures

Data on hip fractures of the Mini-Finland Health Survey subjects was received from the Hospital Discharge Register. The National Hospital Discharge Register is a nationwide register that includes all in-patient treatment episodes in Finland. The Register is coordinated by the Finnish National Research and Development Centre for Welfare and Health. It is the oldest nationwide discharge register in the world, and it has been shown to cover acute hospital-admitted injuries of the population adequately (annual coverage of injuries nearly 100%) and record them accurately (annual accuracy >95%) (Keskimäki and Aro 1991, Parkkari et al. 2000 and 2003). Registered data include age, gender, place of residence, the name of the hospital, duration of the stay, and the ICD codes for the mechanism of injury, medical diagnoses and operation(s) performed.

4.5 Incidence of pediatric spinal injuries and their surgical treatment

The National Hospital Discharge Register was used to study pediatric spine fracture incidences and the need for their operative treatment. All spinal injuries between 1997 and 2006 in children aged from 0 to 17 years were included. The study population was divided into two subgroups according to age: young children (below eight years of age), and older children and adolescents (eight years or older). For incidence calculations we obtained the official year-end and gender specific population data for each year. The mean of two consecutive yearly values represented the population of that year.

4.6 Radiological evaluation

In the baseline readings of Mobile-Clinics and Mini-Finland Health Examination surveys, chest radiographs were assessed by two radiologists, who viewed every picture independently. Vertebral fractures were diagnosed from the Th1 to Th12 level clinically. Severity of vertebral deformity was not graded.

In the nested case-control study, the baseline chest radiographs were read without any information about the vertebral fracture diagnosis of the surveys' readings, or subsequent hip fracture status of the subjects. Vertebral fractures were identified at levels Th3–12. The severity of each vertebral compression was measured and graded as normal (grade 0), mildly deformed (grade 1, 20–25% reduction of anterior, middle, and/or posterior vertebral body height), moderately deformed (grade 2, 26–40% reduction in any height), and severely deformed (grade 3, over 40% reduction in any height) according to Genant´s classification (Genant et al. 1993). Scoliosis was diagnosed in patients with the Cobb angle of at least 10 degrees (Cobb 1948) in the thoracic spine. The diagnosis of Scheuermann's disease was based on Sørensen's radiographic criteria (Sørensen 1964) of three adjacent wedged vertebrae, angled at least five degrees.

The results of the current SQ evaluation were compared with the clinical diagnoses of vertebral fractures made by two radiologists at the time of the baseline examination. The agreement between the clinical diagnoses at the baseline and the present SQ readings showed a kappa value of 0.40 for mild to moderate vertebral compression, and of 0.45 for severe compression. The agreement of vertebral fracture diagnosis between the baseline radiologists at Mobile-Clinic survey was 0.46. A similar reference reading had been obtained earlier from the Mobile-Clinic material, in which the kappa values showed 0.52–0.28 agreement between the two radiologists and the reference reader (Härmä et al. 1986).

In the Mini-Finland Health Survey, hand radiographs were taken mainly to diagnose osteoarthritis (Kärkkäinen 1985). The readings of hand radiographs were carried out by a radiologist without any information on the clinical findings or on metacarpal measurements assessed by another radiologist (Kärkkäinen 1985). The measurements for metacarpal index (MCI) were made at the midpoint of the second metacarpal bone of the right hand (n = 3,561) with a digital caliper to the nearest 0.1 mm (Kärkkäinen 1985). The coefficients of intraobserver reliability were 0.91 for both the inner and outer cortical diameter (Kärkkäinen 1985). The relation between osteoporotic findings in hand radiographs with vertebral fractures was evaluated in this dissertation.

4.7 Statistical methods

The logistic regression model (Cox 1970) was used to estimate the cross-sectional associations between known risk factors for osteoporosis and the prevalence of vertebral fractures. Adjusted relative odds (OR) and their 95% confidence intervals (CI) were estimated on the basis of this model.

Cox's proportional hazards regression model (Cox 1972) was used to estimate the strength of the association between vertebral fractures, and total and cause-specific mortality in longitudinal analysis. The factors, which showed cross-sectional associations with vertebral fractures and predicted mortality, were entered in the models as confounding or effect-modifying factors. Adjusted relative risks (RR) and 95% CIs were estimated based on these models. Significance of interaction was tested by entering the interaction terms into the models. Statistical significance of interaction terms was tested with the likelihood ratio test.

In the nested case control setting, two to three controls of the same sex for each hip fracture case were drawn from the study cohort by individual matching for municipality and age. Their age was not allowed to diverge more than nine years from that of the case subjects in question. The conditional logistic model was used to estimate the strength of associations between vertebral deformities and the risk of hip fracture. Relative odds with 95% CI were computed for subgroups of vertebral compressions (Breslow and Day 1980). Potential confounding and effect-modifying factors were also entered into the models.

The Cochran-Armitage trend test and the χ^2-test were used to perform incidence calculations in pediatric patients (Armitage 1971). P values of 0.05 or below were considered statistically significant. Descriptive statistics were applied (counts (n), means and the standard deviation of the means [SD]).

Kappa-coefficients were calculated to estimate the agreement between data obtained using various methods or from separate sources (Fleiss 1981). Systematic differences were tested by the McNemar's test (Fleiss 1981). Validity of the methods proper in relation to references was expressed in terms of sensitivity (true positives correctly identified / all true positives) and specificity (true negatives correctly identified / all true negatives).

The Statistical Analysis System (SAS) software (SAS Institute, Gary, North Carolina) was used for statistical analysis.

4.8 Ethical aspects

The Mobile-Clinic and Mini-Finland health examinations preceded current legislation on medical research. Thus, participants were fully informed about the study, they attended it on a voluntary basis, and the use of the collected information for medical research was explained to them.

To obtain data from the Hospital Discharge Register and the Official Cause of Death Register for pediatric spine study, no formal Ethics Committee evaluation was required nor performed.

5 RESULTS

Vertebral fractures in adults were associated with increased cancer, respiratory and injury mortality. The risk for subsequent hip fracture was significantly increased in subjects with a severe vertebral fracture. Adult vertebral fractures associated with known risk factors for osteoporosis. Pediatric vertebral fractures were clearly trauma-related and cervical fractures in children were associated with increased mortality. One-third of the pediatric vertebral fractures required operative treatment.

5.1 Vertebral fractures and mortality (I and II)

The Mobile-Clinic Health Survey (I)

The prevalence of vertebral fractures in the Mobile-Clinic Health Survey population was 0.6% (90/16,010). In the Mobile-Clinic study population, adults with a vertebral fracture had an increase risk of death during the 25-years of follow-up compared with those without a vertebral fracture in the same study population (Table 1). The increase of total mortality in the presence of a vertebral fracture was explained by an excess of cancer and respiratory deaths. The increased risk of cancer death persisted, even when subjects with a history of cancer and the first five years of follow-up were excluded to avoid the effect of metastatic fractures, and when age, sex, education, smoking, BMI and self-rated general health were entered in Cox's model to control confounding. In this analysis, the adjusted RR for cancer death in subjects with a baseline vertebral fracture was 2.02 (95% CI 1.23–3.31, p=0.01), compared with those without a vertebral fracture in the same study population (Table 2). After excluding the first 10, 15 and 20 years of the follow-up, the corresponding rates were 2.24 (1.27–3.97, p=0.01), 2.15 (1.02–4.53, p=0.07) and 1.10 (0.27–4.43, p=0.89).

Table 1. Total mortality in the absence and presence of a vertebral fracture. The Mobile-Clinic Health Survey.

	Number of subjects followed-up	Deaths	Adjusted relative risk	95% CI
Vertebral fracture in the thoracic spine				
No	15,920	7,362	1.00	
Yes	90	72	1.39	1.10–1.75

Adjusted for age and sex.

Table 2. Relative risk of cancer death in absence and presence of a vertebral fracture. Subjects with a history of cancer at baseline and the first five years of the follow-up excluded. The Mobile-Clinic Health Survey.

	Number of subjects followed-up	Cancer deaths	Adjusted relative risk	95% CI
Vertebral fracture in the thoracic spine				
No	14,835	1,432	1.00	
Yes	71	16	2.02	1.23–3.31

Adjusted for age, sex, general health, smoking, BMI and education.

Of the 16 fatal cancers among those with a vertebral fracture, three occurred in the lung, two in the prostate, two in the stomach, one in the breast, one in the ovaries, one in the colorectal region, one in the pancreas, and one was categorised as a non-specific cancer of the gastrointestinal tract. The remaining four cases comprised one lymphosarcoma, one reticulosarcoma, one non-Hodgkin lymphoma and one multiple myeloma.

The presence of a vertebral fracture also predicted mortality from respiratory causes in Mobile Clinic material. In the whole of cohort, adjusted for age, sex, general health, smoking, BMI and education, the association remained statistically significant (Table 3).

Table 3. Relative risk of respiratory death in the absence and presence of a vertebral fracture. The Mobile-Clinic Health Survey.

	Number of subjects followed-up	Respiratory deaths	Adjusted relative risk	95% CI
Vertebral fracture in the thoracic spine				
No	16,010	616	1.00	
Yes	90	11	2.04	1.12–3.73

Adjusted for age, sex, general health, smoking, BMI and education.

The Mini-Finland Health Survey (III)

The prevalence of a vertebral fracture in the Mini-Finland Health Survey population was 0.8% (56/6,952). Total mortality in the absence and presence of a vertebral fracture in the Mini-Finland Health Survey is presented in Table 4. In Mini-Finland Health Survey significant differences emerged between men and women in the associations of vertebral fractures and cause-specific mortality. The presence of a vertebral fracture in the thoracic spine predicted slightly mortality from natural causes in men RR 1.49 (95% CI 0.89–2.48) (Table 5), respiratory diseases in particular RR 3.50 (95% CI 1.24–9.86) (Table 6). P-values for the interaction terms of gender and vertebral fracture were 0.03 and 0.004, respectively.

Table 4. Total mortality in the absence and presence of a vertebral fracture. The Mini-Finland Health Survey.

	Number of subjects followed-up	Deaths	Adjusted relative risk	95% CI
Vertebral fracture in the thoracic spine				
No	6,884	3,356	1.00	
Yes	56	47	1.49	0.92–2.29

Adjusted for age and sex.

Table 5. Relative risk of non-injury deaths in men in the absence and presence of a vertebral fracture. The Mini-Finland Health Survey.

	Number of subjects followed-up	Non-injury deaths	Adjusted relative risk	95% CI
Vertebral fracture in the thoracic spine				
No	3,191	1,561	1.00	
Yes	19	15	1.49	0.89–2.48

Adjusted for age, body mass index, education level, smoking, alcohol consumption, physical activity, serum vitamin-D, and self-rated general health.

Table 6. Relative risk of respiratory deaths in men in the absence and presence of a vertebral fracture. The Mini-Finland Health Survey.

	Number of subjects followed-up	Respiratory deaths	Adjusted relative risk	95% CI
Vertebral fracture in the thoracic spine				
No	3,191	132	1.00	
Yes	19	4	3.50	1.24–9.86

Adjusted for age, body mass index, education level, smoking, alcohol consumption, physical activity, serum vitamin-D, and self-rated general health.

In contrast, a strong association was observed between vertebral fracture and mortality from injuries among women RR 8.51 (95% CI 3.48–20.77) (Table 7), whereas none of the men with a vertebral fracture died due to an injury. P-value for the interaction term of gender and vertebral fracture was 0.01.

Table 7. Relative risk of injury deaths in women in the absence and presence of a vertebral fracture. The Mini-Finland Health Survey.

	Number of subjects followed-up	Injury deaths	Adjusted relative risk	95% CI
Vertebral fracture in the thoracic spine				
No	3,693	61	1.00	
Yes	37	6	8.51	3.48–20.77

Adjusted for age, body mass index, education level, smoking, alcohol consumption, physical activity, serum vitamin-D, and self-rated general health..

In five of the six fatal injuries among women with a vertebral fracture, a subsequent fracture was stated as the main cause of death. Four of these fatal fractures were hip fractures and the fifth was a pelvic fracture. The sixth injury death had resulted from a non-specific contusion of the lower limb.

5.2 Vertebral fractures and hip fracture risk (II)

Future hip fracture risk after a vertebral fracture was studied in the Mini-Finland material. Thoracic vertebral fractures predicted a subsequent hip fracture. In the presence of severe vertebral compression (>40% reduction in vertebral body height) the adjusted relative odds for a subsequent hip fracture was RR 12.06 (95% CI 3.80–38.3) after controlling for education, physical activity, smoking, alcohol consumption and self-rated general health. Mild to moderate vertebral fracture grades showed no prediction for hip fracture (Figure 7). After excluding the first 5 and 10 years of the follow-up, the corresponding relative odds was RR 10.56 (95% CI 2.79–39.9) and RR 6.77 (95% CI 1.62–28.2). Of the incident cases with a hip fracture, 43, 27, 9 and 2 had compressions in one, two, three and four vertebral bodies, respectively. After controlling for Genant's severity grade, the adjusted relative odds for a hip fracture per increment of one compressed vertebra was RR 1.22 (95% CI 0.79–1.88, p-value for trend 0.37).

Low MCI index has also shown to predict hip fracture in this study population (Haara et al. 2006). In the current study, the interaction term between vertebral fractures and low MCI was measured to evaluate the association of thoracal and hand osteoporosis in prediction for hip fracture. High age, low BMI , tall stature, and smoking were associated with low MCI. The interaction term between vertebral fractures and low MCI was not statistically significant in prediction of hip fracture (P=0.42). This was interpreted so that both act mainly as independent risk factors. Age, sex and MCI adjusted relative risk of hip fracture in the presence of a vertebral fracture was 2.31 (95% CI 1.20–4.43) (unpublished data).

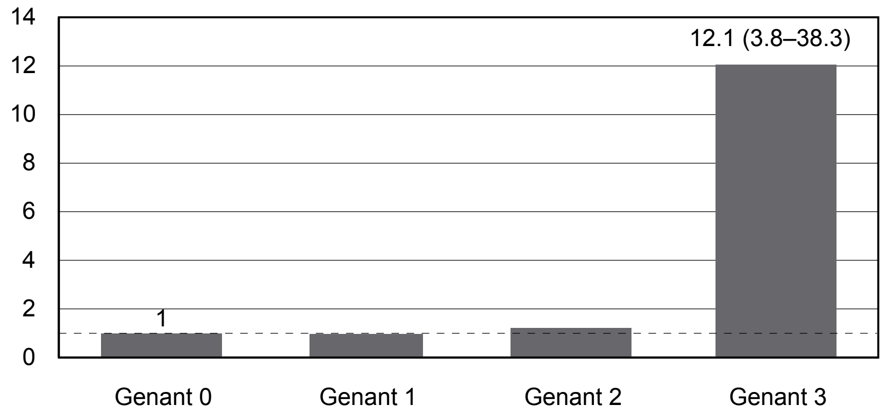

Figure 7. Adjusted risk of a subsequent hip fracture in 15 years follow-up according to Genant's severity grade of vertebral fractures.

5.3 Pediatric vertebral fractures (IV)

In the pediatric study population, the incidence of spine fractures remained stable during the ten-year observation period with a mean annual incidence of 66 per 10^6 of the reference population aged below 18 years. This represented 2.3% of all hospital-admitted fractures in children. The proportions of cervical, thoracic, and lumbar spine fractures were 29%, 31%, and 40%, respectively. The most common causes of spinal injuries were traffic accident (35%), falling to the ground (28%) and falling at the same level (14%). In patients below eight years of age, cervical spinal fractures were more common than fractures of the thoracic and lumbar spine, while in the older age group (≥eight years) lumbar and thoracic spine fractures were more common than cervical spine fractures.

Pediatric cervical vertebral fractures were associated with mortality. The mean annual incidence of fatal spinal injury was 2.4 per 10^6 persons (0.60% of all traumatic deaths) with 27 reported cases during the follow-up period in Finland. Cervical spinal cord injury, with or without cervical spine fractures, accounted for 80% of the fatalities. Cervical spinal cord injuries are not classified into upper or lower in the autopsy recordings. The reported fatal cervical fractures or dislocations consisted of fractures of C1 (4.0% of all), C2 (20%), and C3–7 (12%) as well as of cervical spine dislocations (8%).

Thirty per cent of the children with spinal fractures underwent surgery, giving an average annual incidence of 20 procedures per 10^6 persons. The most common procedures were posterior lumbar spine stabilization, anterior cervical spine decompression and stabilization, and posterior thoracic spine stabilization (Table 8). The mean hospital stay was 7.2 days for all spine fractures.

Table 8. Most common surgical procedures for paediatric spinal injuries over the ten year observation period (1997–2006) in Finland.

Procedure	Percentage
Halovest application	5.0%
Anterior cervical spine procedure	9.5%
Anterior thoracic spine	1.4%
Posterior thoracic spine	10%
Anterior lumbar spine	1.4%
Posterior lumbar spine	20%

6 DISCUSSION

The main findings of the present dissertation are as follows: 1.The presence of a vertebral fracture significantly predicts mortality and the increase can be explained as due to excess deaths by cancer and respiratory diseases. Furthermore, a thoracic vertebral fracture significantly predicts injury death in women. Most of these deaths are hip fracture related 2. A severe thoracic vertebral fracture is a strong predictor of a subsequent hip fracture, whereas mild or moderate fractures and the number of compressed vertebrae have no prediction value for a subsequent hip fracture. 3. The incidence of pediatric spinal fractures is low. In younger children, cervical spine is most often affected, whereas in older children thoracic and lumbar spine fractures are more common. Thirty per cent of pediatric spinal fractures require surgical treatment.

6.1 Validity of the data

A major strength of the current dissertation is the study materials used. The Official Cause of Death Register and the Hospital Discharge Register are nationwide registers with excellent coverage of the whole Finnish population. Mobile-Clinic and Mini-Finland health examinations provide a large amount of unique study materials the value of which is enhanced by a high participation rate in those examinations.

The estimates of pediatric spine fractures were based on the Hospital Discharge Register, which covers, with nearly 100% accuracy, the whole population. Since all pediatric spine fracture patients are most likely to be admitted to hospital, presumably the presented numbers of fracture incidences are accurate. Compared to previous studies, the follow-up periods of the current studies were longer.

In the estimates of vertebral compression fractures in adult population, purely traumatic vertebral fractures could not be excluded from the study population. However, vertebral compression fractures were strongly associated with known risk factors for osteoporosis, suggesting that majority of these fractures were osteoporosis-related. High-energy and pathologic hip fractures could not be excluded from the study. However, these fractures form the minority of all hip fractures, and exclusion of these would probably not have significantly changed the results.

Another weakness of the current study is that in adults only fractures of the thoracic spine were evaluated, excluding lumbar and cervical fractures. Nevertheless, the thoracic spine and the thoracolumbar junction presumably are the principal sites of osteoporotic vertebral fractures (Gallacher et al. 2007, El Maghraoui et al. 2008). One should also note that distributions of vertebral fractures differ between diagnostic methods. The SQ shows a large peak of vertebral fractures at the middle thoracic spine, which differs from the distributions found by means of both ABQ and the clinical diagnosis. Also, when using the SQ method, fractures identified in radiographic follow-ups are likely to show a different distribution than prevalent fractures identified by the same method. Concerning the identification of vertebral fractures, the SQ method is more sensitive than the clinical diagnosis, but obviously less specific than the ABQ method (Jiang et al. 2004). The SQ method is based on apparent vertebral height reduction, whereas the ABQ method diagnoses vertebral fractures on the basis of endplate depression, regardless of the reduction in vertebral height. The SQ method may therefore more easily misdiagnose low-height vertebrae without endplate depression (degenerative changes or normal variations) as vertebral fractures (Jiang et al. 2004, Ferrar et al. 2007)

As discussed above, the method used in the diagnosis of vertebral fractures can have a major effect on the results. We compared the results of the SQ evaluation of vertebral fractures that were used to evaluate subsequent hip fracture risk in the Mini-Finland Health Survey with the clinical diagnoses of vertebral fractures made by two radiologists at the time of the baseline examination in the same material. The agreement between the clinical diagnoses at the baseline and the present SQ readings showed a kappa value of 0.40 for mild to moderate vertebral compression, and of 0.45 for severe compression. These modest kappa values presumably resulted from rather poor sensitivity of the clinical readings; the radiologists failed to identify almost half of the fractures identified by the SQ readings. This finding agrees with the results presented by Gehlbach (Gehlbach et al. 2000) indicating that clinical radiologists may miss half of the moderate and severe fractures identified by the SQ method from chest radiographs.

A limitation in this dissertation is that the individual studies in adults could not analyze the injury mechanisms of vertebral fractures. Biomechanical literature suggests that most of these fractures are due to excessive loading on the spine, such as falling or bending forward to pick up an object from the floor (Myers et Wilson 1997, Duan et al. 2001). Future research should focus on these issues to find effective ways for fracture prevention.

6.2 Comparison with previous literature

Mortality associated with adult vertebral fractures

Vertebral fractures in the current studies predicted total mortality. This finding agrees with previous studies (Kado et al. 1999 and 2003, Naves et al. 2003, Jalava et al. 2003, Pongchaiyakul et al. 2005, Hasserius et al. 2003 and 2005, Cooper et al. 1993, Center et al. 1999, Bliuc et al. 2009). The risk of death in the presence of a asymptomatic vertebral fracture has ranged from 1.2– to 4.4-fold. (Kado et al. 1999, Naves et al. 2003, Pongchaiyakul et al. 2005, Hasserius et al. 2003, Jalava et al. 2003, Pongchaiyakul et al. 2005). Our results of 1.4 and 1.5-fold risk of death are within this range.

The increase in mortality in the presence of a vertebral fracture was associated with excess of cancer and respiratory deaths in the Mobile-Clinic material, while in the Mini-Finland material vertebral fractures predicted injury deaths in women and respiratory deaths in men. The increased risk of respiratory death in patients with a vertebral fracture and related thoracic hyperkyphosis is a possible explanation for our finding of elevated risk of respiratory deaths. However, the severity of vertebral fracture related kyphosis was not measured in the current study.

The association between cancer deaths and vertebral fracture was strong in the Mobile-Clinic material. This relation has been described before in two publications (Kado et al. 1999, Hasserius et al. 2003). In both of these studies, however, the association was found only in women. Since all the prevalent cancers at baseline and the first five years of follow-up were excluded, it seems unlikely that metastatic disease of the spine is the explanation for our findings. In general, the expected survival time in metastatic disease of the spine is over 5 years in highly specialized thyroid carcinoma, 3 years in myeloma, 2 years in mammary cancer, 1 year in prostate and kidney cancers, and under 1 year in lung cancer and melanoma. Anyway, the relationship between vertebral fracture and cancer is most likely complex and it is not known which of them comes first.

There are several potential explanations for the association between vertebral fractures and cancer deaths. Dietary factors, such as vitamin D intake, play a major role in osteoporosis, and they may also have a role in cancer biology. Biological modulators, such as cytokines, nitric oxide, and parathyroid hormone -related protein are produced by malignant neoplasms and may affect skeletal metabolism (Raisz 1988, Evans 1996, Moncada and Higgs 1993, Ralston et al. 1995, Collin-Osdoby et al. 1995). The Wnt/beta-catenin signaling pathway regulates cell fate and behaviour during embryogenesis, adult tissue homeostasis and regeneration (Zhang et al. 2007, Polakis 2000). When inappropriately activated, the pathway has been linked to colorectal carcinoma and melanoma, and when attenuated it may contribute to Alzheimer's disease and osteoporosis.

The associations between vertebral fractures and cause-specific mortalities partly differ between the Mobile-Clinic and Mini-Finland Health Surveys. Vertebral fracture in thoracic spine predicted mortality from respiratory diseases in both materials, but the association between vertebral fracture and cancer deaths was not observed in the Mini-Finland material. This may be due to a smaller study sample in the Mini- Finland survey. Some of the associations seen in the large study sample may not be evident in smaller materials. Furthermore, the relatively small number of cases increases the risk of chance in our results. The association between vertebral fractures and injury mortality was not evaluated in the Mobile-Clinic Health Surveys, since this association has not, to this author's knowledge, been presented in previous literature, and was found in the Mini-Finland material only after the analysis of the Mobile-Clinic Health Surveys.

Finally, as noted previously, the observed associations between vertebral fractures and increased mortality do not have to be causal: a fracture can be a marker of a general fragility of the victims only – a phenomenon not totally covered by adjustment procedures in epidemiologic research.

Subsequent hip fracture risk associated with adult vertebral fractures

The subsequent hip fracture risk with prior vertebral fracture was approximately 2-fold in two large meta-analyses (Klotzbuecher et al. 2000, Haentjens et al. 2003). This association was also evident in the present study. Hasserius reported the prevalence and severity of vertebral deformities in male and female hip fracture patients (Hasserius et al. 2003) in a study in which two population-based materials served as controls. The association between vertebral deformity and subsequent hip fracture was stronger in severe vertebral deformities, although the OR`s were far less than 2-fold compared with mild vertebral deformities. Schousboe (Schousboe et al. 2006) reported on associations of at least 10-year-old vertebral deformities with the risk of incident hip fracture in women over 65 years of age. The mean follow-up period in their study was 13 years. In that study, the RR for hip fracture was less than 2-fold in subjects with mild to severe vertebral deformity compared with those showing no deformity in the same study population. To our knowledge, associations between vertebral fracture severity and subsequent fracture risk as strong as those found in the present study have so far not been published.

The difference in the results between previous studies and our study may have several explanations. The study populations differ from each other. Hasserius (Hasserius et al. 2003) recruited selectively, from one Swedish region, only mentally capacitated subjects who were admitted to hospital during the daytime, whereas Schousboe (Schousboe et al. 2006) assessed the association only among women over 65 years of age. The nationally representative sample of men and women with a wider age range in our study may offer a more solid basis for evaluating the association and generalizing about the results. The long follow-up of our cohort may have revealed hip fractures more sensitively, whereas selective mortality may lead to weaker associations in cross-sectional studies. We evaluated only thoracic spine from chest radiographs, whereas both of the prior studies identified vertebral deformities of the whole spine. The definitions of vertebral fracture morphology were similar in all of these studies. The findings of Ferrar (Ferrar et al. 2007) that non-osteoporotic short vertebral height may be misdiagnosed as vertebral fractures are supported by this study. As this may be the case in mild to moderate fracture grades, which had no prediction values in the present study, severe vertebral compressions are more likely to be true osteoporotic fractures. In the current study, the number of affected vertebrae carried no predictive significance, but one needs to keep in mind that there were only few persons with multiple fractures.

Pediatric vertebral fractures

Few population-based data exist on the incidence of spinal fractures in children and adolescents. In a study of patients seen at the Mayo Clinic over a forty-year time period, the age-adjusted incidence of cervical spine injury was 7.41 per a population 10^5 per year (McGrory et al. 1993). This incidence is four times higher than in our study. There are several reasons which might explain this difference. The Mayo Clinic study represent time period from 1950 to 1991. As most of the spinal injuries are motor-vehicle related, improvements in the safety regulations of motor-vehicles might well explain some of the difference (Parkkari et al. 2003). It is also possible that the incidence of cervical spine injuries in children is still higher in the U.S. than in Finland.

Our study supports previous findings, according to which upper cervical spine fractures are more common in children under eight years of age than in older children (McGrory et al. 1993, Plazer et al. 2007, Dietrich et al. 1991). Previous studies have reported somewhat contradictory results about the proportion of cervical spine injuries of all spine injuries in children. Traditionally, 60–80% of children's spine injuries are reported to be in the cervical spine area (Kokoska et al. 2001, Reilly 2007). Recently, Platzer (Platzer et al. 2007) reported the results of the Vienna General Hospital trauma registry. In their material, 37% of spine injuries in children were located in the cervical spine. Based on the current population based study, the proportion of cervical spine injuries appears to decline with age: in the younger children (<eight years of age), 64% of all spinal fractures and dislocations are in the cervical spine, whereas in the older age group this proportion is much lower (25%) and similar to adults (Magerl et al. 1994) Polk-Williams (Polk-Williams et al. 2008) reported blunt cervical spine injury in 1.59% of all paediatric trauma patients under three years of age, and even distribution of injuries between upper and lower cervical spine. Our findings that 2.3 % of the pediatric fractures occurred in the spine, and upper cervical spine injuries represented 32% of all cervical spine injuries in younger children are of the same magnitude.

Since most of the pediatric spinal injuries are caused by traffic accidents and falls, preventive measures against these injuries, as well as improvements of traffic safety regulations seem to be the most effective way to reduce spinal injury rates in children.

7 CONCLUSIONS

1. The concluding remarks of the studies evaluating mortality in adults with vertebral fracture

- Vertebral fracture in the thoracic spine predicts increased mortality from respiratory diseases.
- Thoracic vertebral fracture predicts injury death in women. Most of these deaths are hip fracture related.
- Thoracic vertebral fracture predicts mortality from natural causes in men.
- Further research should focus on the mechanism between vertebral fractures and cause-specific mortalities, e.g. deaths from cancer.

2. The concluding remarks of the study evaluating subsequent hip fracture risk in adults with vertebral fracture

- Severe vertebral compression strongly predicts subsequent hip fracture.
- Chest radiography should not be performed in order to diagnose osteoporosis. However, if a severe vertebral fracture is identified in a chest radiograph, urgent clinical evaluation can be recommended in order to offer treatment, care and follow-up as indicated.

3. The concluding remarks of the study evaluating children's spinal fracture incidences and the need for surgical interventions

- Pediatric spinal fractures are rare. Location of these injuries change with age, and maturation of the spinal structures seem to play a major role in typical injury patterns.
- Traffic accidents and falls are the most common causes of vertebral fractures in children.
- One-third of the pediatric spinal fractures require surgical intervention.

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Ville Puisto

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