Fragility fractures in fragile people –

Epidemiology of the age quake

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Maurice Chevalier
Old age isn't so bad when you consider the alternative.

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Abbreviations

25OHD	25-hydroxy Vitamin D
BMD	Bone Mineral Density
BMP	Bone Morphogenetic Protein
DXA	Dual Energy X-ray Absorptiometry
EHLASS	European Home and Leisure Accident Surveillance System
HA	Hydroxyapatite
IDB	Injury Data Base
NSHDS	Northern Sweden Health and Disease Study
PTH	Parathyroid hormone
UFO	Umeå Fracture and Osteoporosis study
WHO	World Health Organization

List of papers

Study I U Bergström, U Björnstig, H Stenlund, H Jonsson, O Svensson. Fracture mechanisms and fracture pattern in men and women aged 50 years and older: a study of a 12-year population-based injury register, Umeå, Sweden. Osteoporos Int 2008 Sep;19 (9):1267-73.

Study II U Bergström, H. Jonsson, Y Gustafson, U Pettersson, Hans Stenlund, O. Svensson. Hip fracture incidence curve is right-shifting – drastic increase in hip fractures among the oldest old. A forecast of the age quake. Accepted for publication Acta Orthopaedica 2009. E-pub ahead.

Study III U. Bergström, H. Jonsson, Y Gustafson, B Olofsson, U Pettersson, O. Svensson. Serial fractures – age and fracture site important predictors for a second fracture. Results from 13-years population based data In manuscript.

Study IV U. Pettersson, P. Nordström, J. Nilsson, U. Bergström, I.Bergdahl, U. Lerner, G. Hallmans, O. Svensson. Vitamin –D levels and risk for hip fractures in northern Sweden- The UFO Study. In manuscript.

Sammanfattning

Frakturer hos gamla är ett stort folkhälsoproblem och benskörhet (osteoporos) är en stark bidragande faktor till den ökande frakturbenägenheten. Hos de absolut äldsta är det dock inte bara skelettets beskaffenhet som bidrar till att antalet frakturer ökar. Andra faktorer som hjärt-/kärlsjukdomar, demens, försämrad balans och minskad muskelkraft bidrar också till en ökad falltendens och frakturrisk. Det finns nu en hel del som tyder på att en ny, skör population håller på att bildas bland de äldsta– de som överlevt och lever med svåra sjukdomar. De närmast decennierna kommer vi dessutom att få se effekten av att de stora barnkullarna från andra världskriget blir gamla. Befolkningen över 80 år kommer i vissa delar av världen att tredubblas. Detta kommer att medföra både ekonomiska och sociala konsekvenser för hela samhället. Mer än 70 000 svenskar drabbas årligen av fragilitetsfraktur och siffran förutspås att fördubblas fram till år 2030. De frakturer som främst associeras till benskörhet är höft-, kot- och handledsfrakturer. I norra Skandinavien, med Sverige och Norge i topp, finns den högsta förekomsten av höftfrakturer i världen. De senaste åren har dock visat en sjunkande trend bland befolkningen 50+. Detta kan bero på en reell minskning på grund av förebyggande arbete med fallprofylax, benskörhetsmedicinering och på en allmänt bättre hälsa hos de äldre.

I Umeå genomförs sedan mitten av 80-talet en registrering av samtliga traumafall vid Norrlands Universitetssjukhus. Från 1993 har dessa registrerats i en databas där ett 50-tal parametrar kring patienten och olyckan dokumenterats. Denna databas uppdateras kontinuerligt och omfattar till idag information om traumafall 16 år tillbaka. Avhandlingen belyser frakturpanoramat och frakturutvecklingen över tid hos män och kvinnor 50 år och äldre. Genom en samkörning av lokala databaser i Västerbottens Biobank och traumadatabasen har även D-vitaminets betydelse för ökad frakturrisk kartlagts.

För att beskriva de skillnader som föreligger i frakturmönstret i olika åldrar och hos män och kvinnor har jag beskrivit hur bakomliggande skademekanism påverkar frakturförekomsten. Vid ökad ålder krävs lägre energi vid traumat för att orsaka en fraktur, dessutom drabbas olika delar av skelettet beroende på ålder– höft, bäcken och axel vid äldre äldre, medan handled och fotled dominerar hos de yngre äldre. Vid en analys av dem med högsta risk för att få flera frakturer är också stigande ålder en starkt bidragande faktor. Kvinnor har efter 50 års ålder större risk för att drabbas av en fraktur men män har högsta risken för att få flera frakturer.

Höftfrakturernas stora betydelse accentueras ytterligare, främst i risken för att få en ny fraktur men även den markant stigande förekomsten av denna fraktur bland de äldsta kvinnorna. Detta är också den fraktur som har mest förödande effekt på människors liv och är mest resurskrävande överhuvudtaget. En analys av höftfrakturfrekvensen nu och för 15 år sedan visar att det finns en sjunkande trend för den totala förekomsten i population över 50 år men också en ökning av höftfrakturerna hos de absolut äldsta.

Inte bara yttre faktorer påverkar risken för fraktur. D-vitamin är nödvändigt för skelettets hållfasthet, bland annat genom att stimulera kalcium-upptaget från tarmen. En stor del av D-vitaminet syntetiseras via huden och är beroende av solljus och en del kan vi ta upp via kosten. I vår nordliga del av världen når solljuset endast under kortare perioder av året upp till den kritiska nivå då UV-B strålarna förmår stimulera D-vitaminsyntesen i huden. Genom att korsköra frakturdatabasen med Västerbottens biobank har vi analyserat D-vitaminets betydelse för höftfrakturer. Vår studie visar att patienter med höftfrakturer har en signifikant lägre nivå av D-vitamin i jämförelse med kontrollpersoner flera år innan de drabbas av sin fraktur.

För den som drabbas av en fraktur kan det förefalla vara en helt slumpartad händelse men granskar man en hel population framträder ett mönster beroende på ålder, kön och bakomliggande skade-mekanismer. Även ”olycksfåglar” med flera frakturtillfällen uppvisar mönster som vi inom sjukvården bör kunna identifiera tidigare och på olika sätt hjälpa till för att förehindra ytterligare frakturer. Stora samhällsåtgärder för att förebygga olyckor har redan genomförts inom trafiken, på arbetsplatser och i offentliga miljöer. Mycket av frakturprofylaxen bygger dock på förändringar på individbasis och i hemmet. Genom strukturerad analys av skademönster, individens skelettmetabolism, falltendens och andra bidragande faktorer bör vi kunna förebygga många frakturer med betydande vinster för individen och samhället.

Abstract

Osteoporosis-related fracture is already today a major public health problem and the number of hip fractures is expected to double to 2030. Sweden has one of the highest hip fracture incidences worldwide. This may be explained by several factors: e.g. age, genetic, climatologic, geographic and a relative vitamin D deficiency, secondary to the limited sunlight exposure especially during winter months. Intrinsic and extrinsic factors contribute to a fracture, although a prior low energy fracture is one of the strongest predictors for a subsequent one and this should be a target for secondary fracture prevention in an orthopaedic setting.

Since 1993 all injured patients admitted to the emergency floor and all in-hospital fractures at Umeå University Hospital, Sweden, were registered according to the Injury Data Base, former EHLASS. There were 31,173 fracture events (one or more fractures at the same time), of which 13,931 were in patients' ≥ 50 years old. The fracture database was co analyzed with the Northern Sweden Health and Disease Study cohort in a nested case-control study for investigations of associations between osteoporotic fracture and serum markers, lifestyle data, nutrition etc.

We found that there were differences in fracture pattern depending on age and sex. Both injury mechanism and fracture site were strongly dependent of age. The most severe fragility fracture, hip fracture, had a decreasing incidence. However, the incidence curve was right-shifting leading to an increase, both in numbers and in incidence of hip fractures among the oldest women. To identify people at high risk for fractures, re-fracture patients are useful. No less than 21% of the fracture patients had suffered more than one fracture event, accounting for 38% of all fracture events. The total risk ratio for a subsequent fracture was 2.2 (2.1-2.3 95% CI). In males the highest risk for re fracture was in the age cohort 70-79 years (RR 2.7, 2.3-3.2 95%

CI), in females > 90 years (RR 3.9, 3.2-4.8 95% CI).

Another possible risk factor in this subarctic population is the lack of sunlight, leading to a Vitamin D deficit. The overall adjusted risk of sustaining a hip fracture in this population was 2.7 (1.3-5.4 95%CI) in subjects with a plasma 25 hydroxyvitamin D below 50 nmol/l. The association was, however, different according to age at baseline. Thus in subjects aged 60 years and above at baseline, the adjusted odds ratio of sustaining a hip fracture was 6.2 (1.2-32.5 95%CI) for the group of individuals with a plasma 25OHD below 50 nmol/l, whereas no significant association was found in the youngest age group.

In the next 30 years the ongoing demographic changes will accelerate. The World War II baby boomers will cause an age quake. We can already see signs heralding a new fracture pattern: an increasing cohort of mobile but fragile elderly, with considerable co-morbidity is now at risk for fragility fractures. In fracture patients, clinical information is sufficient to pinpoint patients with a high risk for re-fractures. It is therefore clinically important to use the information provided by the fracture event. We suggest that trauma units and primary care units should screen for risk factors and inform patients about the treatment options, and to organize fracture liaison services. This seems to be especially cost-efficient for our oldest and frailest patients. Secondary prophylaxis and follow-up treatment after cardiovascular disorders are now a matter of course worldwide, but the screening for risk factors, in order to prevent a second fracture, is often neglected. This is one of the most important issues of health care.

Introduction

The Scandinavian countries have a time-honored tradition with nationwide registrations. In Iceland the population has been registered since 1000 AD according to birth, work, health conditions and causes of death. One particular note was made when an Icelander had to give up horse riding. This was a traumatic moment with major consequences in daily life. In a clever study on hip osteoarthritis genetics this outcome parameter was used. National registers on different issues are becoming increasingly common in Sweden. In orthopaedics there are several national registers. The combined contribution from all over the country makes good overview and allows for early detection of any failures or successes.

Beginning in the middle of the 1980s Umeå University hospital has continuously registered trauma patients admitted to the emergency ward. Since 1993 registrations were fed into a database and in 2005 the database was completely synchronized according to coding, making it possible to perform larger epidemiological studies on trauma patients in the Umeå area.

My point of interest is fracture pattern in the population aged 50 years or older. Firstly, this is a fast growing age cohort in society and together with adolescent children the one at highest risk for a fracture. Secondly, in most studies on fractures in the elderly osteoporosis is a big issue. Females are often clustered into “postmenopausal”, generalizing a very heterogeneous group. Males are also clustered into the large age cohort- “elderly”, i.e. - age >65. I wanted to focus on this issue. In the oldest old the general “porosity” of muscles, brain, bone and internal organs can not be treated with inhibitors of bone resorption only. A broader view is mandatory when dealing with this enormous present and future health problem.

Background

In contrast to what might be suggested from dusty skeletons in museums, the skeleton is a metabolically active organ that continuously remodels throughout life. There is a constant removal of bone by osteoclasts followed by the formation of bone matrix by the osteoblasts that subsequently becomes mineralized. The regulation of bone remodeling is both systemic and local. The major systemic regulators include vitamin D, parathyroid hormone (PTH) and other hormones such as growth hormone, glucocorticoids, thyroid hormones, and sex hormones. Local regulators of bone remodeling like cytokines and growth factors that affect bone cell functions have been identified. In fact, recent studies show that bone is an endocrine organ: osteoblasts synthesize osteocalcin that has a profound effect on general metabolism.

Osteoporosis

Osteoporosis is defined by Bone Mineral Density (BMD) at a level 2.5 SD below the average in young healthy women (WHO 1994). The most validated technique for measuring BMD is the dual energy x-ray absorptiometry (DXA). However, BMD alone is not optimal in detecting subjects at high risk of fracture; it has a high specificity but low sensitivity. Actually, many "osteoporotic" fractures occur in patients whose BMD exceeds -2.5, i.e. per definition not osteoporotic.

Epidemiology

Sweden has one of the highest risks of osteoporotic fragility fractures, more than 70,000 fractures per year. This will rise due to the increase in the elderly population and cohort effects described later. Fracture sites most associated with osteoporosis are hip, vertebra and distal forearm.

A hip fracture—a fracture on the proximal part of the femur, including cervical and trochanteric area— is the most serious among osteoporotic fractures. It is mostly due to fall from standing height or less. Hip fracture is a major and increasing global public health problem and in many countries hospital costs associated with hip fracture already exceed that of all other fractures combined. In recent years an encouraging decline in hip fracture incidence has been noticed (Jaglal et al 2005, Kannus P et al 2006, Nymark T et al 2006), perhaps because of improved general health among the elderly. However, in epidemiological work, hip fracture patients are implicitly regarded as a homogeneous group, but clinically, this population is indeed heterogeneous—perhaps more so than in any other trauma diagnosis. In terms of treatment, nursing and rehabilitation, these patients represent a challenge, by far bigger than any other orthopaedic problem in most developed countries. About one third of elderly population sustains a fall annually, 5% will suffer a fracture and 1% a hip fracture—the nastiest one (Gibsin et al 1987). About 20% of hip fracture patients die within the first year (Poor et al 1995) and less than 50% regain the pre-trauma level of function (Melton et al 2003). Worldwide, the incidence varies, but in general, incidence rates increase exponentially with age in both genders. Females dominate (~80%) and 90% of the fractures occur in people over 50 years (Melton et al 1995). Age- and sex adjusted hip fracture incidence rates are generally higher in white than in black or Asian populations (Maggi et al 1991). Highest rates are observed in northern Europe, and Sweden has twice the hip fracture incidence of e.g. France. However, the differences in BMD worldwide are too small to account for the variations in fracture occurrence, indicating that BMD is only one of several risk factors. Environmental and genetic factors may imply an important role of these variations (Elfors et al 1994).

Vertebral fracture is the most difficult one to define morpho-metrically and clinically. The epidemiology is also vague because many vertebral fractures cause initially no or minor clinical signs and radiographic examinations are often not performed in elderly people with unspecific back pain. Only about ¼ of the fractures are estimated to come to clinical attention (Johnell et al 2004, Kanis et al 2004, van Staa et al 2001). This is a pity since vertebral fractures are the most important ones when working with hip fracture prevention.

Distal forearm fracture is the most common fracture, often caused by falls on outstretched hand. Compared with hip and vertebral fractures these yields a mild to moderate disability, approximately 1% of the patients become dependent as a result of the fracture (Chrischilles et al 1991).

Fracture recidivism

Studies on fracture recidivism show a large variability in the association of a prior fracture. A fairly recent review article showed that a history of prior fracture at any site carries an increased risk factor for future fractures (Klotzbuecher et al 2000). In the prospective cohort study in Dubbo, Australia, most fractures occurred within the first 5 years after the first one (Center et al 2007). After 10 years the fracture rate did not differ from the population's initial fracture rate.

In Edinburgh 13.2 % of the fracture patients aged 45 years and older subsequently sustained a new fracture within a 12-year period. The overall relative risk of a new fracture was 3.89 (Robinson et al 2002). When retrospectively studying previous fractures in hip fracture patients, no less than 45% had sustained a prior low-trauma fracture, 17% hip fractures (Edwards et al 2007). The combination hip-hip fracture is the one most thoroughly investigated, no doubt because hip fractures give the statistically most reliable figures. Investigating cumulative incidence for a new hip fracture Lönnroos et al found that it was 5.08% year one and 8.11% year two (Lönnroos et al 2007). Also, wrist fractures strongly predict a new fracture, the risk of a new wrist fracture is tripled and the risk for any other fracture is doubled (Barret-Conner et al 2008).

Fracture healing

Osteoporosis and advanced age may contribute to delayed or impaired fracture union. In animal models, fracture union takes longer in older and/or oophorectomized animals (Lill et al 2003, Meyer et al 2001, Kubo et al 1999) and biomechanical testing has not unexpectedly shown that implant attachment is poorer in osteoporotic cadaveric bones. Similar problems have been reported in clinical studies showing increased complication rates in patients treated for proximal femur fractures with a pattern of increased cut-out, re-fracture, or fixation failure in patients with osteoporosis (Goldhahn et al 2008). Healing of nailed femoral diaphyseal fractures is also significantly delayed in older osteoporotic patients (Nikolaou et al 2009). Why fracture healing is impaired in the elderly is still unknown: perhaps an altered temporal expression of genes, changes in progenitor cell populations or numbers (Akune et al 2004), reduced ability to support osteoclastogenesis (Cao et al 2005, Reinhard et al 2006) and angiogenesis may all be of importance.

Fracture surgery

Despite improvements in both implants and surgical technique the operative treatment of osteoporotic fractures remains as a challenge (Giannoudis et al 2006). Bone mineral density correlates linearly to the holding power of screws (Perren 2003, Chapman et at 1996). Therefore in osteoporotic bone, implant failure or non-union occur in 2-10% of the fractures, malunion in 4-40% and re-operation is necessary in 3-23% (Stover 2001, Bohlofner et al 1996, Syed et al 2004), but implant breakage is a rare event.

The general principle of fracture management in fragile bone includes relatively stable techniques such as intramedullary nails, bone impaction, buttress fixation, fixed angle devices, and joint replacement. Fracture healing may also be stimulated pharmaco-logically by bone morphogenetic proteins (BMP), parathyroid hormone (PTH) and bone resorptive inhibitors. Studies have shown better pin fixation and less pin infection when using hydroxyapatite (HA)-coated versus uncoated external fixation pins (Moroni et al 2001). Similar results have been reported for trochanteric fractures (Moroni et al 2004).

For vertebral compression fractures there has been an advance in the fracture treatment when vertebraplasty and kyphoplasty were introduced. Vertebroplasty is an injection of bone cement directly into the vertebra and kyphoplasty means inserting a balloon into the verterbra to restore height, subsequent injection of cement into the cavity. Both techniques lead to relief of pain but their value has to be further investigated in randomized trials.

The fragile population

During the last century or so an ever increasing proportion of people have got the opportunity to become very old because of improved hygiene, vaccination, nutrition and also improved treatment of e.g. cardiovascular disease and cancer (Piccirillo et al 2008). Instead of dying from infectious diseases, myocardial infarction or cancer, more people survive to suffer from stroke and/or dementia. Simultaneously, better treatment and care of these patients have improved survival (Hallström et al 2008, Terent 2003) and thus life is prolonged even among the frailest patients. Increasingly, the musculoskeletal system has become the weakest link. This is an entirely unprecedented situation in the history of humankind.

The age quake

Worldwide, there are reports of an approaching age quake in the ages 65 years and older. In the United States the group increased by 14% 1992-2005, and it is predicted to be 44% during 2006-2019 (Melton et al 2005). Forecasts 2005-2020 in Canada describe a 62% increase in males and 51% in females (Jagal et al 2005). The most dramatic eruption of the age quake, though, will burst in Asia 1990-2025 where no less than a two-fold increase will expand the 65+ population from 921 million to 2.2 billion. In Sweden we can detect the same pattern where the number of people aged 80+ is estimated to double by the year 2050 (Fig 1). This increase can be related to the post-World War II baby boom, but also to the remarkable improvement of modern medicine and public health. Major consequences are inevitable in almost all aspects of society. Unfortunately, health care planners do not seem to have recognized what has already happened and what is in the offing. Emergency care is roughly organized the same way as previously.

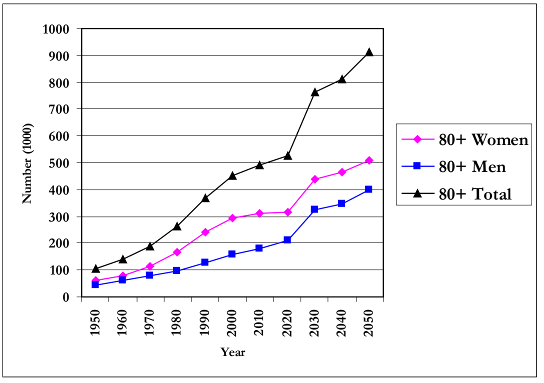


Figure 1 Expected population growth of octogenarians+ in Sweden (SCB)

In Umeå, 30% of people 90+ have suffered from stroke and about 50% have been diagnosed with a dementia disorder (von Heideken et al 2006). There has been a 50% increase of demented subjects among patients with hip-fractures during the last decades (Gustafson et al 1991, Lundström et al 2007, Stenvall et al 2007). In addition, very old people are prescribed an ever increasing number of drugs that enhance the risk of falling, such as antidepressants and benzo-diazepines (Lövheim et al 2007, von Heideken et al 2005). Consequently, we thus now are faced with an increasing and entirely different population of old people than a few generations ago, and this trend will continue, changing the panorama of disease and injury.

Co-morbidity

Cardiovascular disease

Cardiovascular disease, the most common cause of death, is over all more frequent in men than in women. Women are on average 10-15 years older than men when they suffer from heart diseases (Health statistics 2006). In the Nordic countries morbidity and mortality from cardiovascular diseases has decreased both in men and women. The reduced mortality can be explained both by decreased incidence due to improved lifestyle, a result of devoted and successful public health programs but also by enhanced survival among those with the disease, a consequence of improved methods of treatment.

Stroke and dementia increase the risk of hip fractures 2 – 4-fold each (Ramnemark et al 1998, Sato et al 2004) and among hip fracture patients there has been a more than doubled proportion of stroke-afflicted (Ramnemark et al 2000). Patients suffering from stroke and/or dementia also have a dramatically increased risk of postoperative complications that will strain our healthcare resources even more in the future.

Polypharmacy

Polypharmacy in the oldest old is, as previously mentioned, very common and without any evidence base. In Sweden the prescription of drugs such as antihypertensives, anti-arrhythmics and benzodiazepines has increased by 50% in the population 70 years or older between 1993 and 2005. Increasing use of antidepressants is another risk factor for hip fractures— in fact almost 30% of all geriatric patients are admitted to a hospital due to side effects from drug treatment (Odar-Cederlöf et al 2008). Drug interactions and changes in metabolism of xenobiotics may also contribute to falls leading to fractures. Ridiculously scarce basic research on metabolism and physiology in the elderly has been done and pharmacological studies on subjects aged 85+ are not performed, allegedly for “ethical reasons”.

Mental disorders

Depression is the most common mental disorder in old people. They also suffer more than younger people from anxiety and psychotic disorders. Prescriptions of psychoactive drugs provide an indicator of mental illness. Analysis of prescription statistics shows that use of both sedatives and antidepressants are highest in subjects aged 85 years or older.

Contributing factors

Factors contributing in causing fracture may not only reside in external factors such as slippery roads, cords or carpets. By crosslinking the fracture database with Västerbotten Biobank, Northern Sweden Health and Disease Study (NSHDS) creating the UFO— Umeå Fracture and Osteoporosis study, we are now able to analyze biochemical parameters, intake of vitamin A and D, physical activity etc that may have an associated impact when estimating fracture risk.

Falls

Falls is the main injury mechanism for fractures in general and particularly in elderly people. About 5% of falls result in fractures and other serious injuries occur in 5-10 % (Tinetti et al 1989, Rubenstein et al 1994, van Weel et al 1995, Oakley et al 1996, Rivara et al 1997). A Finnish study found that age-adjusted incidence of fall injuries increased by 127% in females and 124% in males from 1970 to 1995 (Kannus et al 1999) Therefore, an analysis of underlying injury mechanisms is required for more efficient fracture prevention. A clinical history, inability to stand on one leg and a subjective estimation of biological age may be sufficient in fall risk assessment (Gerdhem et al 2005). There are few previous epidemiologic studies on fracture mechanisms (Kannus et al 2001, Gomberg et al 1999), and evidently, more solid knowledge is needed regarding fall and fracture prevention.

Vitamin D

Vitamin D deficiency causes rickets in children, i.e. bone deformities due to impaired ossification (Pettifor 2003). Adults develop osteomalacia, a defective mineralization of the osteoid on all surfaces of bone. Vitamin D depletion has also been linked with an increased risk for a variety of other ailments such as cardiovascular disease, diabetes, some cancers and infectious diseases (Lui et al 2006, Lips et al 2001, Bischoff-Ferrari et al 2006, Scientific Advisory 2007). Calcium and vitamin D are important participants in bone metabolism: calcium for mineralization; D-vitamin modulates the uptake of calcium in the intestines but also has many other effects, e.g. in neuromuscular function. Vitamin D is synthesized in the skin after sun exposure by UV-B (280–315 nm), and also derives from the diet, such as fatty fish and dairy products. In younger persons, vitamin D is mostly endogenous but with increasing age dietary intake becomes more important. This is probable due to less sun exposure and decreased cutaneous synthesis.

Serum levels of vitamin D vary over the year with lower level in the winter, due to less hours of adequate sunlight. In Sweden, bone mineral density correlates vitamin D levels over the year with a few percent higher levels in the summer (Nyman et al 2002), a variation indicating a deficiency that may be related to lower production of vitamin D. Supplementation during winter improves the bone health in postmenopausal women (Dawson-Hughes et al 1991). Adequate sunlight exposure, the time when the sun raises more than 30° over the horizon, is just a couple of hours during summer time and nothing during the winter in northern Sweden. It has been suggested that the higher incidence of hip fractures found in northern Sweden compared to the southern part is partly explained by a relative vitamin D deficiency, secondary to the limited sunlight exposure during winter months.

Complications

Infection

11% of all nosocomial infections in the elderly are surgical site infections (Crossley et al 1998). This complication increases the mortality more than fivefold and the duration of hospitalization twofold (McGarry et al 2004). It is reported (Lee et al, 2006) that in orthopaedic patients ≥65 years a surgical site infection increased the mortality risk fourfold in comparison with uninfected controls.

Cognitive disorders

Another issue of major concern is cognitive disorders. Anyone can react to a disease, injury or intoxication, e.g. with morphine, sedatives or painkillers. About one third of the elderly hip fracture patients already suffer from a substantial cognitive reduction, and a third sustain delirious episodes during the hospital stay. Even for a fracture surgeon with a limited interest in extraskeletal issues, impaired cognitive function does matter, since these patients cannot follow ordinations, which may ruin even the most elegant osteosynthesis. Delirium thus increases the complication rate enormously. Therefore the patient's mental state is important information to the surgeon: clearly there is such a thing as a head larger than the femoral head. Delirium is often avoidable, since it is by definition due to another cause, e.g. urinary infection, pain, over-medication. A common error is to treat delirium with more sedatives and painkillers – that only serves to make the situation go from bad to worse.

Mortality

Short-time mortality is increased after a fracture. Hip and vertebral fractures are mostly associated with premature mortality up to 5-10 years after the fracture (Center et al 1999, Vestergaard et al 2007, Cualey et al 2000). In Dubbo, Australia, hip fractures conveyed the highest risk in the first year when 30% of the deaths occurred. But all fractures, minor and major, were associated with increased mortality risk. Non-hip and vertebral fractures were responsible for 29% of the increased mortality. The occurrence of a subsequent fracture was associated with a three- to fourfold increased mortality risk within the next 5 years (Bliuc et al 2009).

Aim of the study

Society is faced with an unparalleled demographic development characterized by an ever-increasing number of old and very old people who actually seem to constitute a different population than old people just a few generations ago. We are therefore facing enormous medical and social challenges because of the increased group of frail patients. The aim of the study is, by use of the Injury Data Base (IDB), to make an epidemiological survey of patterns and changes in fractures according to intrinsic and extrinsic factors in the population aged 50 years or older in the Umeå area, Sweden, 1993-2005 with the aim to:

- Describe the different fracture patterns in terms of fracture site, mechanism and incidence in different age cohorts in males and females aged 50 years and older

- Investigate if there have been any secular trends in hip fractures as a sign of ongoing changes in the elderly population

- Identify fracture patients at high risk for a second fracture in order to be able to pinpoint those that should be a target for preventive actions such as fall prevention, bone resorption inhibitors etc

- By cross-linking information from different databases, investigate the prevalence of low vitamin D levels and whether low plasma 25(OH)D levels are associated with the risk of incident hip fractures in middle-aged men and women, participating in the Umeå Fracture and Osteoporosis study (UFO).

The ultimate goal is to identify future public health measures to counter the effects of the age quakes on number and severity on fragility fractures.

Material and methods

Injury Database

Umeå, Sweden, at the Gulf of Bothnia (64°N), is a university town with a population around 100,000. The mean number of inhabitants age 50 years and older in the hospital catchment area over the study period (1993-2005) was 43,223 (SCB). The area was served by only one emergency unit and one radiology unit. Therefore, all treatment-requiring fractures were included. All injuries were registered in the emergency department and fed into the Injury Database, former EHLASS, a European project designed for identification of dangerous products. During 1993-2005, 126,599 injury events, causing 31,173 fractures, were registered, using 58 parameters describing the injury circumstances. Unique personal identification numbers were used. At the emergency unit the patient answered a questionnaire about the circumstances of the injury. Data were also collected from ambulance personnel, bystanders and/or relatives. In some cases supplementary details were obtained by interview during the recovery phase. Information from all available medical records, and sometimes from police reports, was included in the data set. By checking against the hospital's compulsory registration for external reason for in-patient treatment, a putative loss of in-patients in the data set was eliminated. At the emergency department both in- and out-patients from the area are treated. The general practitioner on call for the area was also stationed at the hospital outside ordinary working hours. The database is built on a patient questionnaire and records from the doctor at the emergency ward. The staff responsible for the registration comprised about 15 people over the study period. Up to 3 diagnoses were registered per patient. Injury mechanisms were grouped into low-energy falls (fall <1 m), high-energy falls (fall >1m, fall in stairs), slipping (83% on ice), miscellaneous (torsion, hit by an object, crushing etc.) and vehicle-related incidents. The location of fracture was recorded according to the Nordic Medico Statistical

Committee, and has been grouped according to anatomic sites.

Validation

Validation of the injury database was performed by comparing to the hospital's computerized radiology archive and to the operation register. When data from 1,307 (10%) of the fractures randomly selected over 8 years were compared to the radiologists' reports, the accuracy was 90%. During registration the database was also constantly controlled by logic validation tests, standardized according to EHLASS.

VästerbottenMedical Biobank

The Västerbottten Medical Biobank contains samples from more than 50 different studies. The largest of them, the Northern Sweden Health and Disease Study Cohort, contains three subcohorts (fig 1):

- MONICA cohort—Monitoring Trends and Determinants in Cardiovascular Disease project
- Mammary Screening Cohort—local mammary screening program. From 1997 repeated screening is established within the mammary screening program with sampling every second year, in the age group 50-69 years within the county
- VIP– Västerbotten intervention program cohort

Since 1985 all inhabitants in the Västerbotten county have been invited to a health check up to the year of their 40, 50 and 60th year of age. They were asked to donate a blood sample for future research and to fill in a voluminous questionnaire about physical activity habits, food intake etc. The dietary survey in this health check-up consists of questions about the subject's average intake of 65 different foodstuffs during the last year. Consumption was measured in a nine-graded scale from "never" to "4 times per day or more". The normal meal portions were also estimated containing the different components e g fish, potatoes, vegetables etc. The questionnaire has been validated and shown to have a good reproducibility (beta 0.53 – 0.99) and validity (beta 0.28 – 0.61) compared with measurements from a 24-hours diet recall (Johansson et al 2002).

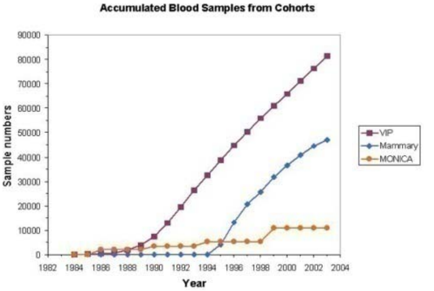
UFO- Umeå Fracture and Osteoporosis Study

At the time of merging between the EHLASS injury data base and the NSHDS, creating the UFO study, there were 130,000 questionnaires and 90,000 blood samples collected from around 90.000 unique subjects in the NSHDS. Around 17% of the patients in the injury data base were represented in the biobank and 85% of them had donated a blood sample and answered the questionnaire prior to the fracture.

The Umeå Fracture and Osteoporosis study (UFO) is a prospective case-control study where individuals from the NSHDS cohort was co-analyzed with IDB the Injury database, capturing all osteoporotic fractures occurring in the city of Umeå from 1993 and onwards. Patients with a fragility fracture (wrist or hip) were compared with non-fractured individuals regarding bone mass, genetic factors, use of tobacco, physical activity, hormonal data and intake of different nutrients such as retinol, β-carotenes, calcium and vitamin D as well as intake of coffee and alcohol. Markers of bone metabolism (osteocalcin and C-telopeptide of collagen cross-links, (CTx)), hormones (PTH and cortisol), calcium, retinol, retinylesters, fatty acids and 25-hydroxy vitamin D_2 and D_3 are analyzed from the donated blood samples.

As of 31st of December 2003, 106 subjects were identified as having left a blood sample before they sustained a low trauma hip fracture. Each facture case was compared with two controls, selected from the same NSHDS cohort and matched for sex, age at recruitment (within one month), and date of blood sampling (within one week). For 4 of the cases, only one control was identified, yielding a total cohort of 314 subjects (79% women).

Figure 1 Number of blood samples in the NSHDS cohort.



Statistics

Study I

The age and gender specific incidence of fractures in this material were a mean value over the 12-year period. The absolute fracture numbers were the total numbers 1993-2004.

Study II

The incidence in different age groups was calculated as number of hip fractures divided by mean population. The age-adjusted incidence was calculated with the Swedish population of 2000 as standard population i.e. when calculating incidence rate for the total population each year, the age distribution of 2000 has been used for all other years. The incidence rate ratio (IRR) and mean incidence were calculated with a 95% CI. The Poisson regression was calculated with overdispersion.

Study III

The relative risk (RR) was calculated as $RR=P_{(exposed)}/P_{(nonexposed)}$. Follow up-time was defined as time from index fracture to end point (i.e. new fracture, death or Dec 31 2005).

Study IV

Odds ratios (OR), as an estimate of the relative risk for fracture, were calculated for matched sets (case-control) and for different cut points of plasma 25(OH)D using conditionally logistic regression models. Both unadjusted and multivariate-adjusted associations were calculated with adjustments made for height, BMI and smoking. A population attributable risk (PAR) of hip fracture for low plasma 25(OH)D levels was calculated as: PAR = pd [(OR-1)/OR], with pd = proportion of cases exposed to the risk factor and OR is the corresponding odds ratio adjusted for confounding factors.

Results

Incidence and prevalence In this population-based material 1993 – 2004, fracture incidence had a bipolar distribution in both sexes. In males the absolute numbers of fractures were decreasing after puberty whereas in females the numbers of fractures increased after age 40, continuing until age 80. At age 50 – 54 the females bypassed the men in incidence as well as in absolute number of fractures. (Fig 3)

Mechanism Regarding injury mechanism in the population 50 years and older, 13,279 fracture events, 53% of the fractures were due to a low energy fall, ie, less than 1 m. The injury mechanisms were fairly equally distributed in 50 – 59 years. In the oldest, low energy falls dominated (Fig 4). 46 % of all fractures occurred indoors and 44% outdoors, 10% unknown.

Location Anatomic site of the fracture differs according to injury mechanism as well as to age. Low-energy falls were associated with a more proximal fracture location in both upper and lower extremities. Slipping tended to cause more distal extremity fractures (Fig 5).

Figure 2 Fracture Incidence and prevalence

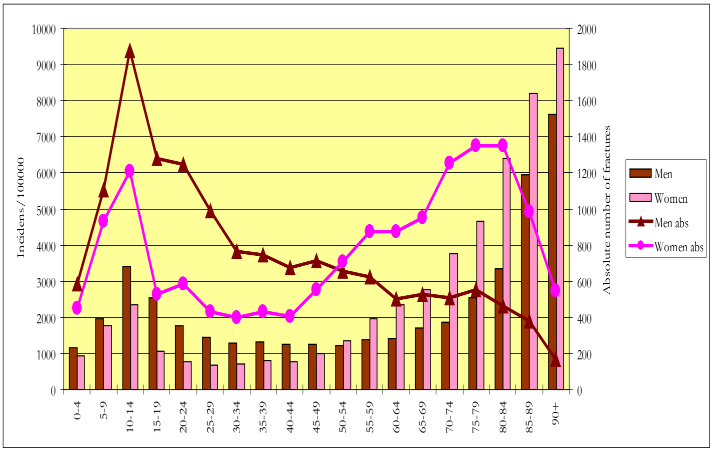


Figure 3 Injury Mechanism in different age cohorts.

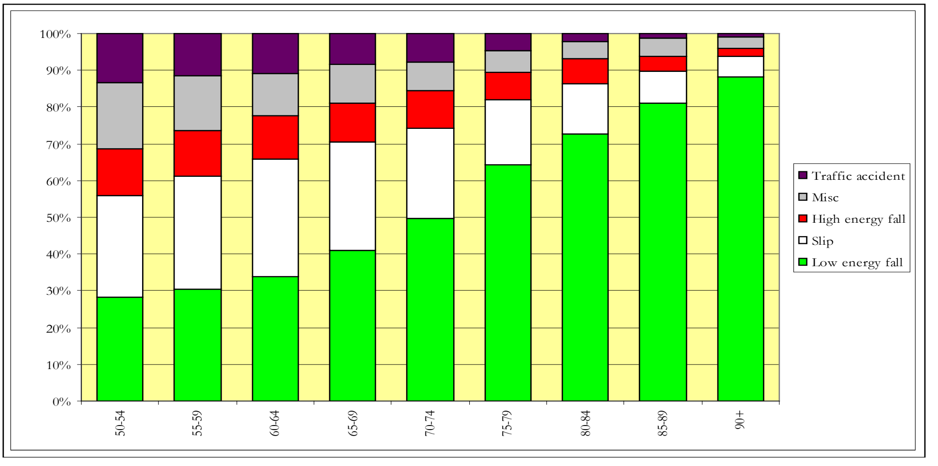


Figure 4 Anatomic fracture site and injury mechanisms

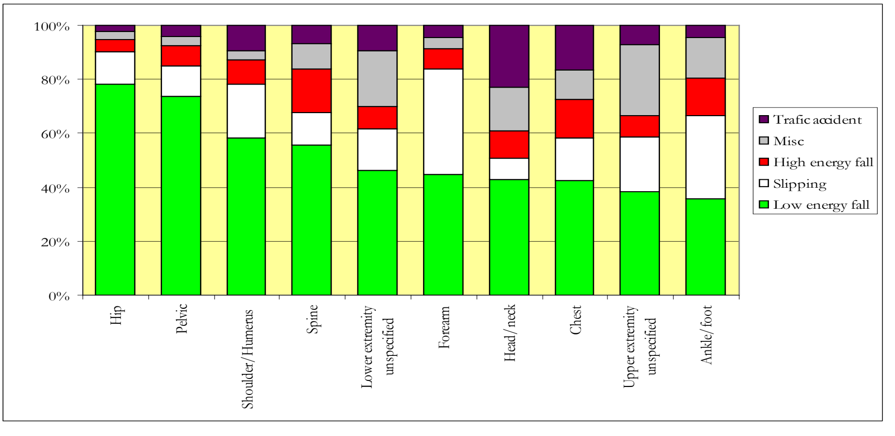


Figure 5 Anatomic fracture site in different age cohorts

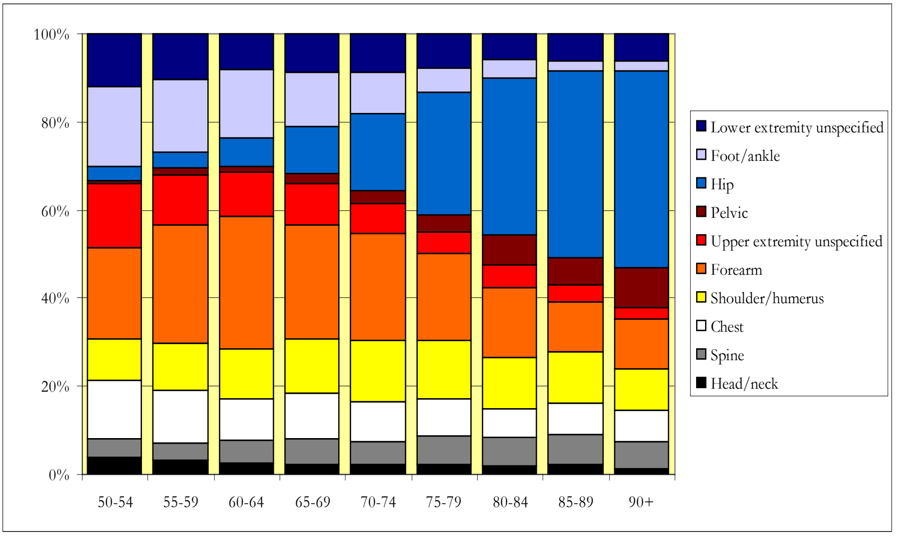
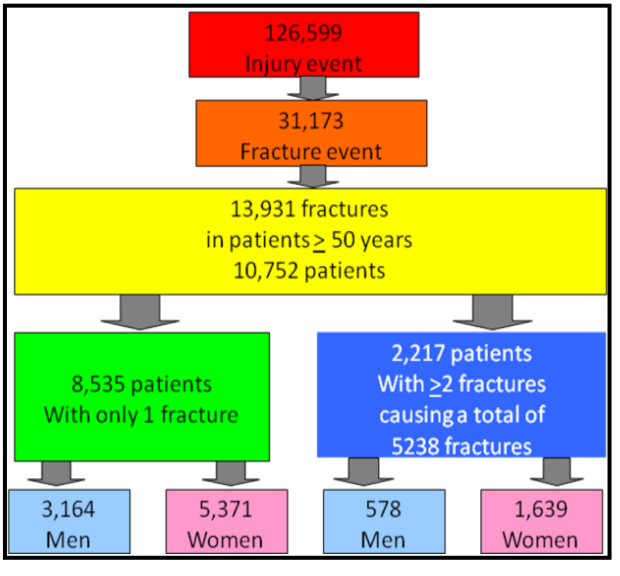


Figure 6 Flowchart of fracture recidivism ≥ 50.



The upper extremity was the dominating location for fractures in the population younger than 70 years (Fig 6). With increasing age, the lower extremity, and the hip in particular, became the predominant location for fractures.

Fracture recidivism

Characteristics

During the period 1993 – 2005 a total of 10,752 men and women aged 50 or older were involved in 13,932 fracture events (Fig 7).

Women were overrepresented in the serial fracture cohort, 74% compared with 65% in the total fracture group ≥50 years. Median age at the index fracture was 71.0 (quartile 60 – 80) years and for the re-fracture 77.0 (68 – 84) years. Mean interval to the second fracture was strongly dependent on age at first fracture. The longest interval was in the age group 60 – 69 in both men (185 weeks) and women (222 weeks). During the study period, 4,325 (40%) of the fracture patients ≥ 50 years and older had died. The median follow-up time, i.e. time from index fracture to end point (i.e. new fracture, death or Dec 31, 2005) was 231 weeks (4.4 years).

Frequences

2,217 (21%) of those having sustained two fracture events or more contributed to a total of 5,238 fractures, 38% of all fractures in this age cohort (Table 1). Hip and radius fracture were the most common ones. 20% were fractures not traditionally labelled as fragility fractures, but since more than 78% were caused by falls at the same level, most of them presumably have a fragility component. The incidence for an index fracture was 20.9/1000 person years and for a refracture 46.6/1000 person years.

Table 1 Number of people with more than one fracture

	≥2	≥3	≥4	≥5	≥6	≥7	≥8
Men	578	122	29	11	2	1	0
Women	1 639	462	121	38	11	5	2
Total	2 217	584	150	49	13	6	2

Combinations

Forearm fracture, mostly distal radius fracture, was the most common index fracture. The hip was the second most common index site and the most common subsequent one. Hip-hip fracture was the most frequent combination, no less than 8.5 % of the serial fractures (Table 2,3).

Relative risk

The total RR for a refracture was 2.2 (2.1 – 2.3 95% CI). In males the highest risk for refracture was in the age cohort 70 – 79 years (RR 2.7), in females ≥90 years (RR 3.9).

The relative risk for a second fracture increased with age, in males peak age at index fracture was 70 – 79 years, in females ≥90 years. Males had a higher risk in all age cohorts except for the oldest old (≥90 years) (Table 4, Figure 8). The risk of sustaining a refracture after an index fracture was increased for all fracture combinations. The highest RR, 6.26 (5.34 – 7.33 95% CI) for a hip fracture as a second fracture was when hip fracture also was the index fracture. Miscellaneous fracture sites and upper extremity (excluding wrist) as index fracture also conveyed an almost 3-fold risk for a subsequential hip fracture.

	Wrist	Upper extremity (excluding wrist)	Hip	Lower extremity (excluding hip)	Other	Total
Wrist	5,2	4,3	4,9	4,4	3,8	22,6
Upper extremity (excluding wrist)	3,8	4,1	4,6	3,2	3,8	19,5
Hip	2,7	3,5	7,7	2,2	4,6	20,6
Lower extremity (excluding hip)	3,5	3,1	2,7	4,1	2,5	16,0
Other	2,7	3,9	5,4	3,6	5,7	21,3
Total	17,9	18,9	25,3	17,4	20,4	100,0

Table 2 Fracture combinations in the re-fracture cohort

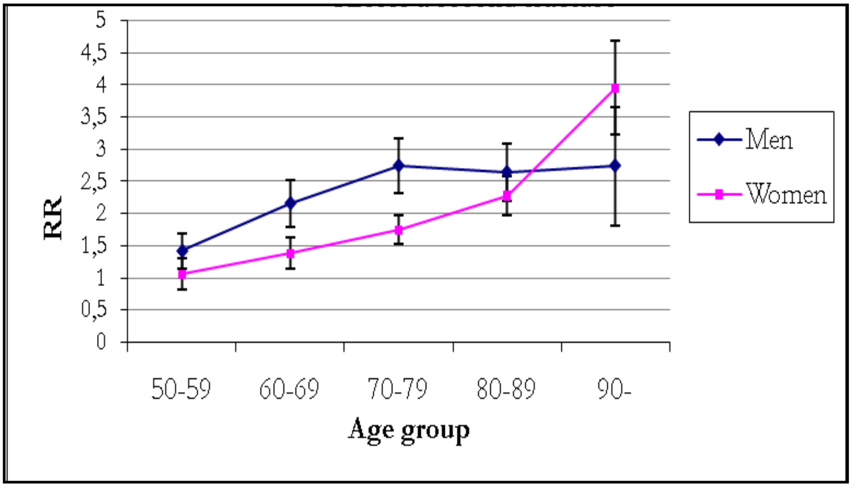
	Wrist	Upper extremity (excluding wrist)	Hip	Lower extremity (excluding hip)	Other	Total
Wrist	4,7	3,9	4,5	4,0	3,5	20,6
Upper extremity (excluding wrist)	4,1	4,5	5,0	3,5	4,2	21,3
Hip	2,9	3,7	8,2	2,3	4,9	22,0
Lower extremity (excluding hip)	3,8	3,4	2,9	4,4	2,7	17,3
Other	2,8	4,0	5,5	3,6	5,8	21,7
Total	3,7	3,9	5,2	3,6	4,2	20,6

Table 3 Fracture combinations in the total fracture cohort

Table 4 Relative risk for a second fracture

	Age cohort	Number of fracture 1	Number of fracture 2	Incidence fracture 1 Per 1000 pers yr	Incidence fracture 2 Per 1000 pers yr	Risk Ratio for a second fracture
Men	50-59	1131	93	10,9	15,5	1,42
	60-69	912	136	13,2	28,6	2,16
	70-79	885	164	17,5	47,9	2,74
	80-89	682	152	31,5	83,2	2,64
	90+	132	33	53,9	147,4	2,74
Women	50-59	1488	130	15,1	16,0	1,06
	60-69	1585	270	22,6	31,3	1,38
	70-79	1972	516	33,4	58,7	1,75
	80-89	1622	567	49,2	112,4	2,28
	90+	343	156	176,1	215,8	3,95

Figure 8 Relative risk for a second fracture in different age cohorts, men and women (95% CI)



Hip fractures

This study includes all hip fracture patients 1993 – 2005, >50 years, a total of 2,919 (31% males) admitted to Umeå University Hospital, Sweden. The annual number of hip fractures was fairly constant over time, about 220 cases per year. In males and females aged 50 or older the age-adjusted incidence showed a declining trend and was 384/10^5 in 2005 compared to an all time high in 1994 with 592 (Fig 9) (IRR 1.55 95% CI 1.37 – 1.89). Poisson regression for sex showed IRR 1.45 (95% CI 1.31 – 1.60), age IRR 1.79 (95% CI 1.75 – 1.84) and year 0.97 (95% CI 0.96 – 0.99). The most prominent decline in incidence was also seen in females where the age-adjusted incidence decreased by 35 % between 1994 and 2005, but a certain decrease could also be detected in males.

When comparing the hip fracture incidence 1993 – 96 and 2001 – 05 there were a decrease in all age groups except for females aged≥90 were the incidence increased from 2,700 to 3,860 per 100, 000 (p =0.04) 1.46 95% CI 1.03 – 2.04), i.e. 44 % (Fig 10).

Hip fracture prevalence

In males there were declining trends for both incidence and absolute numbers. The absolute annual numbers of hip fractures increased both in males from 90 years and in females already from 85 years of age. In females aged≥90, the number had more than doubled (12 – 25 hip fractures/year) (Fig 11).

Figure 7 Age-adjusted hip fracture incidence

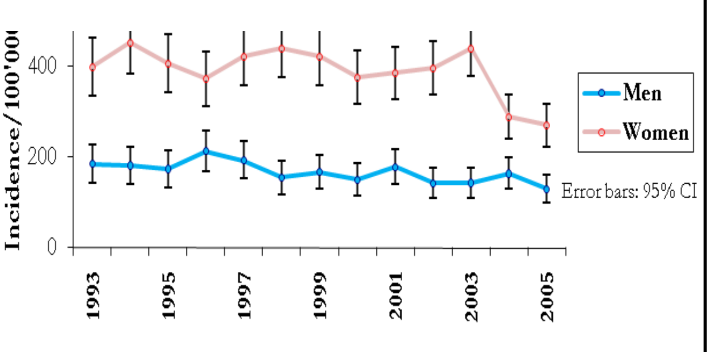
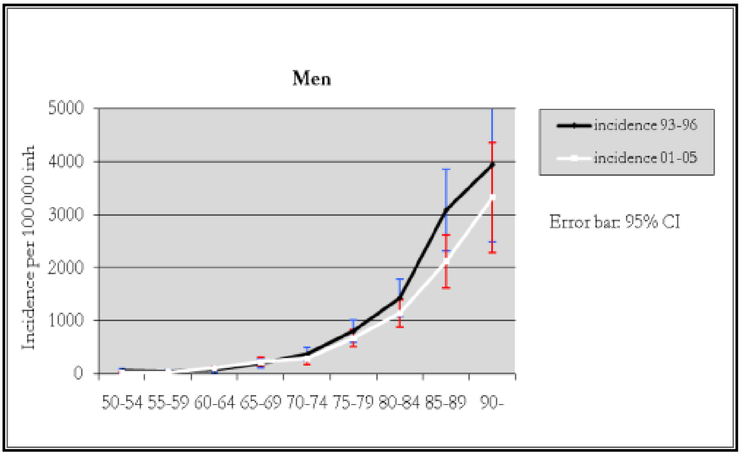


Figure 9 & 10 Hip fracture incidence in different age cohorts during the study period



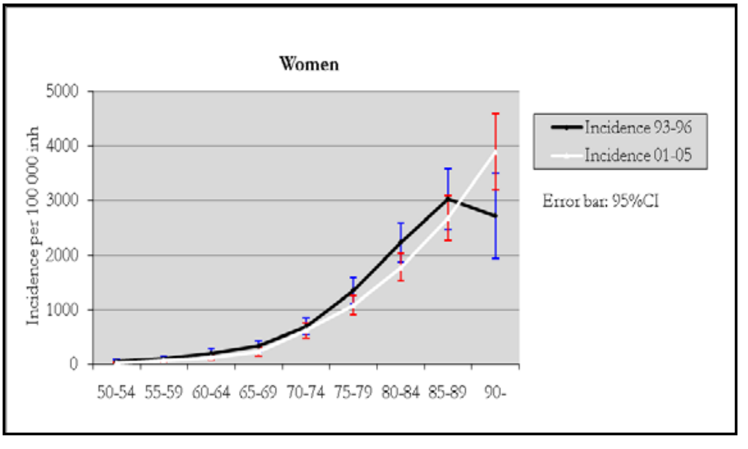
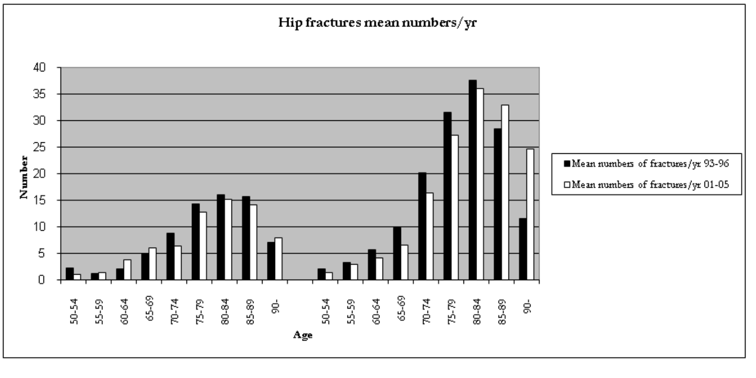


Figure 11 Hip fracture prevalence



D-vitamin

The purpose was to investigate whether plasma levels of 25 (OH) D is associated with the risk of incident hip fractures in middle-aged men and women, participating in the Umeå Fracture and Osteoporosis study (UFO) during 1993-2003.

Characteristics

106 subjects were identified as having donated blood samples to the biobank before they sustained a hip fracture. Each fracture case was compared with controls identified from the same cohort and matched for age and week of sample collection; yielding a total cohort of 314 subjects (247 women, 67 men) with a mean age at the time for sample collection of 60.4 years (range 49.4-69.8). The mean antedating time (time from blood sampling to fracture occurrence), was 5.9+/-3.6 years and the mean follow up period was 9.2 +/- 2.9 years.

Plasma 25 OH vitamin –D

The analyses were done with high-performance liquid chromatography. The prevalence of vitamin D insufficiency in our population were calculated by using the commonly used cut offs of 30nmol/l, 50nmol/l and 75nmol/l respectively. In total 1.3% of the population had plasma 25 (OH) D below 30nmol/l (moderate to severe deficiency) and 14.3 % had a mean value below 50nmol/l (insufficiency). There was a higher prevalence of 25 (OH) D insufficiencies among cases compared to controls (Table 5).

Vitamin D and hip fracture

The overall adjusted relative risk of sustaining a hip fracture was 2.7 (95%CI:1.3-5.4) in subjects with a plasma 25(OH)D below 50 nmol/l. Since age was strongly correlated with vitamin D levels, the results were also presented separately for persons less than 60 years at baseline (n=154) and for persons 60 years and above at baseline (n=160). In the oldest age group, adjusted OR of sustaining a hip fracture was 6.2 (95% CI = 1.2-32.5, $p<0.05$) for the group of individuals with a plasma 25(OH)D < 50 nmol/l, whereas no significant association was found in the youngest age group. The proportion of fractures attributable to plasma 25 (OH)D levels below 50nmol/l was 12% in the whole population.

Table 4 Plasma levels of 25 OH Vitamin-D

Plasma 25 (OH)D	Cases (n=104)	Controls (n=208)	P-value ($\chi2$)
< 30 nmol/L	2 (1.9%)	2 (1.0%)	0.606
< 50 nmol/L	23 (21.7%)	22 (10.6%)	0.010
< 75 nmol/L	76 (71.7%)	143 (68.8%)	0.606

Discussion

Fragility fractures

Extrinsic factors Fall injuries occur because of a complex interplay of almost countless extrinsic factors: e g , slippery floors as well as a decreased balance. An injury is often caused by a many factors or a chain of events – e g time pressure, dim light, slippery surface, a distracting event etc.

Low-energy trauma was responsible for the major and costliest part of the fracture panorama. In fact, almost all fractures in middle-aged and old people were caused by low-energy mechanisms. Thus, most fractures in senior citizens have a fragility component, and the contribution of osteoporosis-related fractures is therefore more important than previously thought. It is also difficult to analyze the amount of energy transferred to the skeleton. Even slips may cause a considerable force of impact since the kinetic energy is (mass x velocity^2)/2. The likelihood to sustain a fracture also depends on exposure to trauma. Therefore it is not surprising that for some types of fracture, incidence may decrease with age, because of changes in lifestyle. E g the most common one, distal radius fracture – occurring in subjects able to stretch out her hand to dampen a fall – becomes less common in the very old, because of decreased neuromuscular reflexes.

The seasonal variation in the total fracture rate was surprisingly constant in this material and the distribution of fractures occurring indoors vs. outdoors was also fairly equal irrespective of season. The role of climate (snow, ice), hours of daylight/day seems to be less important for the fracture rate in this age group.

Intrinsic factors When it comes to intrinsic factors, improvement of muscle strength and general condition is probably easier to achieve than reconditioning bone structure and skeletal sustainability–t he bone mass can hardly be affected more than a few percent per year. Impaired neuromuscular reflexes cause the patient to fall like a log, and to take the energy on the greater trochanter instead of on the hand. Likewise, ankle fracture– sometimes not considered an osteoporosis-related fracture– often lead to nasty treatment complications since the bone may be too weak to hold the osteosynthesis material.

Fractures are most common early and late in life. This no doubt reflect both extrinsic and intrinsic factors; and among the latter neurological, behavioural and musculoskeletal factors play a prominent role. As to bone structure and strength, both the growing and the senescent skeleton are porous with loci minoris resistentiae at the physes and metaphyses, respectively. The effect of menopause is clearly evident, with a breaking point between the sexes surprisingly early, around 50 years. Perhaps this is largely due to changes in life style. Furthermore, since most traumas are diverted by neuromuscular reflexes, the energy hitting the skeleton is largely dependent on the patient's agility and vigilance.

Age is also an important predictor for a recidive fracture. Old people having sustained one fracture have an extremely high risk of refracture. The number of mobile elderly with cognitive deficits is rapidly increasing. This population is at high risk for falling and subsequent fracture. Extensive use of medicinal drugs is also increasing, leading to confusion, hypotension and dizziness (Löwheim et al. 2008). A close survey of medication, tendency to falls, cognitive disabilities and adjustments in housing environment ought to be compulsory elements in the aftercare.

Other studies have indicated a high incidence of fracture recidivism in younger ages, particularly in men, for example a study from Edinburgh, Scotland, where one important factor for serial fractures in the middle-aged was drunkenness (Robinson et al. 2002). In the Umeå cohort we also found that the overall relative risk for refracture was highest in males, but the age patten was different.

Vitamin D

The importance of vitamin D in maintaining skeletal health has been known for a long time. Inadequate levels of vitamin D leads to secondary hyperparathyroidism, with increased bone turnover, bone loss and a subsequent increased risk for fractures (Lips et al. 2001). Vitamin D is also thought to play an important role for the neuromuscular function and inadequate levels have been associated with muscle weakness, poor balance and an increased fall risk, thereby increasing the fracture risk (Janssen et al. 2002).

Vitamin D deficiency becomes more common with increasing age, due to a decreased exposure to sunlight and a reduced ability to synthesize active vitamin D in the skin. It has therefore been suggested that vitamin D deficiency could be a risk factor for fragility fractures, especially in the countries with low sunlight exposure (Johnell et al. 2007). In our prospective, nested-case control study, we found a significant association between plasma 25(OH)D below 50 nmol/L and risk for hip fractures in subjects aged 60-70 years. This is in accordance with several other prospective studies (Gerdhem et al. 2005, Looker et al. 2008, Cauley et al. 2008, van Schoor et al. 2008). Subjects > 60 years with 25(OH)D levels below 50 nmol/L had a six-fold inreased risk for hip fracture compared to the counterpart. Based on this we suggest that assessment of vitamin D status (serum/plasma- 25(OHD) could be a useful marker in identifying subjects with an increased risk for hip fracture. Measurement of 25(OH)D has also recently been included in the VHU study-70 study (screening of health in subjects aged 70 years) in purpose to identify subjects with a high risk of osteoporosis/fragility fractures.

Consensus has not been reached regarding the optimal 25(OH)D concentrations needed to maintain bone health. Previously, a threshold of 50 nmol/L was thought to be representative for an insufficient level (Malabanan et al. 1998), but newer studies suggest that levels of 75-80 nmol/L are necessary for fracture prevention (Dawson-Hughes et al. 2005, Bishoff-Ferrari et al. 2005).

The vitamin D status of the Swedish population is insufficiently surveyed although multinational studies investigating vitamin D status in different countries world-wide have repeatedly found that Sweden has a very low prevalence of vitamin D deficiency and instead rather high mean values of vitamin D (Lips P et al. 2001 and 2006). This is surprising, considering that the exposure to sunlight, sufficient to produce vitamin D is limited to a few summer months in Sweden.

One explanation might be that we have a higher dietary intake of vitamin D in Sweden through the fortification of dietary products, or that we have a more common use of multivitamins. However, it should be noted that the subjects included in these multinational studies are post-menopausal women with osteoporosis and a high frequency of vitamin D supplementation. Thus, they are probably not very representative for the population in Sweden. Moreover, very few of the subjects included in these studies were living above latitude 62-63° north, where there is practically no ultraviolet light from October to February and during summer; required wavelengths of UVB is only achieved 2-3 hours per day (Bruce et al. 2007).

According to the new suggested threshold of 75 nmol/L, ~70% of our population had suboptimal vitamin D levels, which is higher than those reported in the OPRA study from Malmö, Sweden (Gerdhem et al. 2005), where 26% of the subjects were below 75 nmol/L. This supports the theory that there is a difference in vitamin D status between the northern and southern population in Sweden due to difference in sunlight exposure. It is intriguing to speculate that this may explain the higher incidence of hip fractures in the north (Johnell et al. 2002), but further studies are needed to investigate this association and to map the vitamin D status in Sweden. Today, the National Food Administration recommend vitamin D intake of 10 µg per day, with no seasonal or geographic considerations taken, but subjects living in the northern part of Sweden are perhaps in need of a higher intake to conserve their bone health.

Fracture location

Forearm fracture The relatively low incidence of forearm fractures as index fracture may be due to the cut-off bias. Many hip fracture patients may have sustained a former fracture when they were at the tender age 50 – 60 years. The importance of a fracture far back in time is unclear. Other studies have indicated that after ten years the risk for a second fracture is almost the same as the risk for a first fracture (Center et al. 2007).

Other locations Another striking observation from this study is that almost all fracture locations are associated with higher risk for refracture. No fracture locations should therefore be excluded in fracture liaisons.

Vertebral fracture One common fracture, vertebral compression fracture, is underrepresented, due to the fact that these patients seldom contact the emergency ward. Clinically it is important not to miss those fractures since they are highly associated with osteoporosis. One may suggest that a height decrease of more than 4 cm, with or without back pain, may be an indication for vertebral compressions and the patient should therefore be screened for fracture risk factors.

Hip fractures

Hip fracture is the most difficult-to-treat fracture in all age groups, in the young because of local complications, in the elderly more because of general complications. The risk of confusion, infections, healing problems and walking disabilities often contributes to change of living and a dependence of walking assistance. In the refracture cohort, hip fracture was the second most common baseline fracture, the most frequent subsequent one, and hip-hip fractures were the most common combination.

Decreasing incidence In recent studies the age-adjusted hip fracture incidence is generally declining, but there are wide variations. In Scandinavia (Kannus et al. 2006) and Canada (Jagal et al. 2005) a decline can be detected from mid 90s but even in such a small area as Scandinavia, the decline in Finland and Denmark (Nymark et al. 2006) seems to have occurred later than in Sweden (Rogmark et al. 1999) and Norway (Giversen et al. 2006). On the other hand, Paspati et al. (1998) detected an 8 % annual increase in Greece between 1977 and 1992. Hernandez et al (2006) showed that the incidence in Spain was quite stable between 1988 and 2002. The variations in the onset of the decline in hip fracture incidence may be related to the general health of the population. Cardiovascular morbidity and mortality have decreased during the 1990s. Also, the group consisting of younger old (60 – 70 years) are increasing drastically. When calculating the overall hip fracture incidence, this relatively healthy group tends to dominate, and changes in the oldest old do not stand out.

Increasing incidence Although age-adjusted incidence declines in the population >50 years, absolute fracture rate and incidence increased among the very old. We found a shift in the hip fracture panorama: an expanding group of elderly are contributing to an increasing number of fractures. Females over 90 now have the same number of hip fractures every year as those 75 – 79 years. Other studies on chronological trends in different age groups have also disclosed an increase among the oldest old from the beginning of the 21th century. Studies from Spain (Hernadez et al 2006) and Switzerland (Chevalley et al. 2007) have indicated this rise, and a recent Finnish study (Lönnroos et al. 2006) shows an 1.7- fold increase in hip fracture incidence in the oldest old (>75 years). Postponing the date of fracture and adding more "healthy" years to life is *per se* desirable. But the increasing incidence among the oldest old represents a frightening forecast of the scenario bound to occur when the age quake of World War II baby boomers will burst.

Orthogeriatrics

In a 1741 book, *L' Orthopédie*, Nicolas Andry discussed how to make children straight and beautiful – from the skull and eyebrows to the toes and nails (one should tickle the soles of rickety children to make them move). Today the bulk of musculoskeletal disorders and injuries effect middle- aged and old people. Therefore the name would more appropriately be changed to orthogeriatrics. The number of patients over 80 and 90 years has increased and will increase even more in the next 20 years. Fragility fracture now is the most frequent diagnosis in most orthopaedic wards. The change has been so slow and gradual that it has slipped our attention. Therefore we have been slow to adapt, so slow that we now are not up to the job.

The disease is fracture – not osteoporosis. Osteoporosis is just one of several risk factors, one of the strongest. The WHO definition of 1994 has been a success story, probably because that it is expressed in figures – standard deviations from the mean of a healthy young female population. Considerable emphasis has been bestowed on osteoporosis. However, osteoporosis is just one aspect of the fracture panorama, the patients have lost a similar proportion of their other organ function: they also have, e.g., “immunoporosis, myoporosis and encephaloporosis”. In fact, about one third of hip fracture patients have a substantially reduced cognitive function. The fracture is only one of the patient’s problem and sometimes even not the worst one: the reason why a tissue injury, often no more than a few cubic centimeters in extent, exerts such major impact, is the general condition of the patient, not only the injury. Other factors are concurrent diseases and drug use – most elderly people are prescribed too much medication. Interaction between different drugs in the elderly makes it almost certain that 5 – 10 drugs taken simultaneously are not working as intended. Actually, the drugs have not been tested in old sick people. The reason for this, according to one pharmaceutical company is that it is “unethical to test drugs on elderly people”. That is sheer hypocrisy if you still are selling the stuff to them.

Geriatric surgery

In early life when one also has a reduced autonomy, surgery has its own specialty. This is highly motivated because of its peculiarities in terms of surgical techniques, nursing and rehabilitation. However, apart from a few very complex conditions, most pediatric surgical cases are fairly trivial. The main issue is that these young patients are unable to take care of themselves. But from an objective point of view most children are much better off than the majority of geriatric patients. The geriatric surgical patients are much more ill, they are less able to take care of themselves; they often have no relatives or friends alive, a very loose social network and no politically strong parent organizations. Therefore, both from a quantitative and qualitative point of view there seem to be stronger arguments for a specialty in geriatric than pediatric surgery. The reason why this issue has been neglected is partly historical: 40-50 years ago there were few octa- and nonagenarians and the oldest old seldom underwent elective and even emergency surgery. Geriatric surgical units are demanding a broader skill and the participation of many specialties and professions.

FRAX

Based on several large international fracture cohorts, a new fracture risk assessment tool has recently been launched– FRAX. By combining several risk factors, fracture probability may be estimated (Kanis et al 2008 FRAX). FRAX is a computer-based algorithm that supplies models for probability for absolute fracture risk (Kanis et al 2008 FRAX, WHO Assessment 2007, Kanis on behalf of WHO 2008), and is freely available on the internet (www.shef.ac.uk/FRAX). The method uses risk factors that are easy to obtain to estimate the absolute risk of sustaining a fracture within 10 years. The probability of fracture is calculated for men and women, for different ages, different body mass index (BMI) (calculated from weight and height), and from the following risk factors:

- previous fracture
- parental hip fracture
- current smoking
- protracted use of oral corticosteroids
- rheumatoid arthritis
- other secondary causes of osteoporosis
- alcohol-consumption 3 or more units (~250 ml wine or ~500 ml beer) per day

The estimate can also be used with a measurement of BMD at the femoral neck to somewhat increase the precision of the estimate. The FRAX tool was developed by studying the relationship between risk factors for fracture and fracture outcomes in population-based cohorts from North America, Europe, Asia and Australia. The primary analysis was based on 60,000 men and women and 5,500 fractures, and it has been validated in 11 independent cohorts with a similar geographic distribution, with more than 1 million patient years of observation (Kanis et al 2007). The probability for fracture varies around the world (Kanis et al 2002). Therefore the FRAX models need to be calibrated to the different countries where the epidemiology for fracture and death is known. A model specific for Sweden has been developed.

Sex

There is a widespread misconception that women have lower bone content than men. Women are smaller than men and this is reflected in BMD – which is the projected mineral attenuation per area. Consequently, since men have some 10-15% larger bones they get a proportionally higher BMD. However, size does matter; the strength of a tube is proportional to the cube of the diameter. But there are other factors that interact, e.g. in populations – body height and femoral length have been associated with an increased fracture incidence. (So shoe size, for instance, would probably be a strong confounder!) However, there are no differences in the basic design of connective tissue between the sexes, at the menopause when women loose the bone protective estrogen effects they start loosening bone rapidly. In Figure 3 it can be seen that the incidences curves cross around 50, probably a function of the menopause, but perhaps also due to other factors, like changes in life style. In any case, the bone turnover which during childhood and early adult life has been on the positive side now changes to a negative balance, but at a similar rate compared with other organ systems. Yet, bone resorption outruns the normal turnover necessary to keep the skeleton healthy and strong. That may be one of the main reasons why antiresorptive drugs have worked so well, but it may give more complications in the future. Nevertheless women suffer more fractures than men in the latter half of their life and the fact that they also live longer makes the females dominate the fracture scene. On the other hand, men with fragility fracture tend to be more seriously ill than their female counterparts.

Future aspects

Age this is the biological and sociological factor in society that has changed dramatically during recent decades, a trend likely to accelerate in the future. In addition to age there are cohort effects. Most of today's old and very old people would not have been alive one or two generations ago. We now face a still more challenging situation when today's 50- and 60-genarians will reach old and very old age. In their turn, they will be a different population from the present octo- and nonagenarians insofar as they have already had the benefit of modern medical service. This is the paradox of modern medicine e.g. cancer and cardiology treatment has made people live long enough to render the locomotor system their weakest physical link.

What should be done?

- Our organization should be changed to better suit the needs of our sickest patients; we need a broader competence in medical treatment, nursing, rehabilitation and social work. Surgical, medical and psycohological/psychosocial cares have to be integrated.

- In an emergency situation the medical geriatric assessment and work-up should be limited to problems that can be fixed in a few days – otherwise the overall health condition will inevitably deteriorate. Therefore these patients should have a high priority, at present they are discriminated in favor of young and healthy patients.

- Evidence based therapy for our oldest old must be defined – these patients constitute a group that has been neglected, or even worse, actively excluded from trials.

- Without an economic incentive, nothing happens. It is equally important that the goals be defined: not stating maximation, not minimization of hospital days, but real measurements of quality of care.

- Surgery in elderly people is not extensively investigated. The excellent studies of Rogmark et al (2002) on hip fracture management resulted in considerably improved fracture care. However, patients with dementia and delirium were excluded, which is understandable because of the methodological difficulties – but nevertheless these patients are part of the reality in clinical fracture care.

- When performing clinical studies on drugs, patients over 80 years are often excluded and sick people will be excluded at any age. In everyday clinical practice these are the patients we are prescribing large amounts of pharmaceuticals.

- Complications due to an injury and/or surgery as well as health-related quality of life must be recorded and taken into consideration.

Conclusions

Low-energy trauma was responsible for the major and costliest part of the fracture panorama Low-energy trauma (fall <1m) caused 53% of all fractures $\geq$50 years and older. In those over 75 years low-energy trauma caused > 80 %. With increasing age, proximal fractures became more common, in both upper and lower extremities. Proximal locations were predominating in older age groups.

Although age-adjusted hip fracture incidence declined in the population >50 years, absolute fracture rate and incidence increased among the very old. In females age $\geq$90 the annual absolute number of hip fractures is the same as in those 75 – 79 years old. There was a right-shift in hip fracture distribution towards the oldest old, probably due to increased number of octo-/nonagenarians, a new population of particularly frail old that didn't exist earlier.

In this population-based study, 21% of the patients 50 years and older sustained more than one fracture. Highest estimated relative risk was in men, hip fracture as site of index fracture, increasing with age.

A plasma 25 hydroxyvitamin D < 50 nmol/l seems to be a strong and independent risk factor for hip fracture in subjects over 60 years.

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