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Perspective Article

Hip fractures in the elderly without osteoporosis

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Abstract

In clinical practice, hip fracture is a very common reason for hospital admission in the elderly. Most subjects over the age of 65 years, experience an injury at the hip mostly after a fall. Many elderly persons suffer from osteoporosis, which is characterised by loss of bone mass and deterioration of bone microarchitecture thus increasing the susceptibility to fracture. Osteoporosis is defined by WHO as a Bone Mineral Density (BMD) of 2.5 standard deviations (SD) below that of a young adult as assessed by dual energy x-ray absorptiometry (DXA). It has been shown that some patients with a hip fracture have either normal or "osteopenic" hips as defined by DXA (-2.5 <T-score<1). Other diseases that usually affect the elderly population may constitute independent risk factors for falls and fractures, such as diabetes mellitus, neurologic conditions, sarcopenia, use of medication. The clinician's role apart from treating osteoporosis is also to address secondary causes related to increase risk of fracture including falls in order to decrease the incidence of hip fractures. This article addresses some common pathological conditions that have been shown to predispose for hip fractures individuals regardless of their DXA BMD status.

Keywords: Hip fractures, Bone Mineral Density, Falls, Osteoporosis

Introduction

In developed countries, hip fractures remain a common event that is associated with high rates of morbidity and mortality, annually[1]. The cost for the healthcare systems, for hospitalization, surgical procedures, and rehabilitation of patients suffering from these fractures is alarmingly high, worldwide. In United States 150,000 hip fractures occur every year and account of 7% of all osteoporosis related fractures[1].The annual cost is estimated between $10.3 and $15.2 billion[1]. National Health Service (NHS) in UK is burdened with £1.1 billion for osteoporotic hip fractures, annually[2]. Prevention of fragility fractures can increase the savings for health care systems. The Glasgow Fracture Liaison (FLS) reported that for every 1000 patients experiencing osteoporotic hip fractures, 11 can be prevented, decreasing the annual cost around £120,604[3]. The surgical treatment of hip fractures is expensive due to the high cost implants. A study by Iorio et al., showed that the calculated cost for hip fractures surgical treatment was US $20,000-24,000 per case either with internal fixation, hemiarthroplasty or total hip arthroplasty[4]. Rehabilitation may be prolonged until the patient regains his previous physical and mobilization status. Rates of mortality of elderly patients after a hip fracture within the first year vary between 6 and 27 percent, while about 50 percent remain unable to have the previous range of motion, walking only with help[5-9].

Osteoporosis is defined as a chronic disease characterised by reduced bone mass and deterioration of bone microarchitecture, thereby reducing bone strength and increasing the risk of fractures after a fall[8,9]. Starting from menopause in women and advanced age in men, bone absorption performed by osteoclasts increases, while bone formation also gradually declines, thereby producing a negative balance of bone mass[9]. Bone mechanical strength is minimised and elderly people may experience a hip fracture caused only by a relatively low force imposed on the bone after a fall[9]. Dual-energy x-ray absorptiometry (DXA) is predominantly used for the diagnosis of osteoporosis. The World Health Organization (WHO) defined osteoporosis based on BMD by using T-scores, i.e., the number of

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standard deviations below the mean BMD for young adults and T<-2.5, is the definition to characterise a patient as suffering from osteoporosis[10]. "Osteoporotic" fractures could therefore be strictly defined as those occurring in patients with osteoporosis as predicted by their DXA T-score. Nevertheless, the majority of hip fractures occur in "osteopenic" hips (-2.5 <T-score<-1) and some of them in normal hips (T-score >-1)[11,12]. It has been shown that fifty percent (50%) of hip fractures occur in a group of people with a T-score higher than -2.5 and six percent (6%) in individuals with a normal BMD (T-score>-1)[9]. Although the risk for a hip fracture increases as the T-score decreases, the majority of fractures have been shown to occur in the "osteopenic" than in the "osteoporotic" group, as the interval -2.5<T-score<-1 contains much more people than the group of people with a T-score<-2.5[11-13]. Pasco JA et al, followed 616 postmenopausal women aged 60-94years and presented the incidence of hip fractures for a median of 5.6 years[14]. Based on DXA-criteria 37.6% of these women had "normal" BMD, 48% had osteopenia and only 14.5% had osteoporosis[15-18]. Consequently, there are data to suggest that hip fractures occur commonly in individuals, especially elderly, without osteoporosis as defined by DXA. Age is a very important factor for fragility and as the life expectancy rises dramatically, numbers of elderly people are increasing worldwide. It's believed that in the year 2050 about 12% of entire population will be over 85 years old[13]. By the year 2040, we expect 512,000 hip fractures to be recorded in the elderly population in USA[14]. A more pessimistic prediction by Schneider and Guralnik in 1990 refers to 840,000 hip fractures in 2040[13,15].

Fractures at the hip occur mainly from a fall at the lateral side of the femur. Hayes et al. in a study published in 1993, showed that elderly people who live in nursing homes have a 20 fold risk and elderly people who live at their own home and have a better health status have a 6 fold risk to experience a low energy fall and a fracture[7]. Osteoporosis is not the etiology of the falls that cause a fracture. Many other independent and significant risk factors lead to a fall. Some of them are neuromuscular impairment, side effects of medication, vision and hearing deficits, other co morbidities like postural hypotension, peripheral neuropathy within diabetes mellitus etc[7]. This article explores the occurrence of hip fractures in elderly populations without osteoporosis. The aim is to evaluate risk factors that contribute to falls and prevent fractures in non-osteoporotic elderly persons.

Medication that decrease BMD but increase the risk of fractures exponentially

Drugs with intent to treat a wide range of diseases are independent risk factors for fragility fractures despite a sometimes rather small effect on BMD as measured by DXA. Glucocorticoids are widely used to treat chronic diseases, like asthma, rheumatoid arthritis, inflammatory bowel diseases, autoimmune diseases and other pathologic conditions[19]. Long-term use of glucocorticoids at doses >5 mg prednisolone per day, alters the metabolic environment and decrease cortical bone thickness and trabecular quality leading in bone loss of femur neck[19]. Patients receiving glucocorticoids have significantly lower total, cortical, and trabecular BMD and thinner cortices, fewer, thinner, wider, and irregularly spaced trabecular, fewer trabecular plates, fewer axially aligned trabecular, and lower trabecular connectivity[19]. Glucocorticoids produce thus important alterations to the bone strength not only by decreasing BMD, and the risk for a bone fracture after a fall is much more elevated[19]. Van Staa et.al in a meta-analysis of the epidemiology of glucocorticoid-induced osteoporosis, showed that patients receiving glucocorticoids had higher risk for a vertebral fracture compared to non-users despite only 0.79SD decrease in lumbar spine BMD[20]. Vertebral fracture incidence is higher in any level of BMD in the group of people using glucocorticoids for treatment of a disease compared with those not using glucocorticoids, as analyzed by Van Staa et al.[20]. The relative rate of fracture for elderly people receiving oral glucocorticoids, compared to non-users, is 1.61 for hip fracture and 2.6 for vertebral fracture, even if BMD is not much decreased[20,21]. Kanis et al. (2004) in an article published in Osteoporosis International showed that not only vertebral but also hip fracture risk at a specific BMD, is greater for an elderly patient receiving glucocorticoid therapy than the same BMD in a non-glucocorticoid-treated person[21,22].

Aromatase inhibitors (AIs) are drugs used for the treatment of estrogen-dependent breast cancer in women by blocking the biosynthesis of estrogen[23]. Estrogen production in peripheral tissues is blocked by these pharmaceutical drugs and the three third generation AIs (anastrozole, letrozole and exemestane) reduce the levels of circulating estrogens. Bone loss is accelerated and the risk for a fracture is elevated, after a fall[24]. It must be noted that bone matrix is composed 70% of inorganic mineral in the form of calcium hydroxyapatite and 30% of collagen and non-collagen proteins. AIs may change the orientation and quality of these proteins which give elasticity to the bone[24]. DXA does not provide evidence concerning the quantity and quality of collagen in bones. Most of the hip fractures occur in women under AIs who have DXA-based osteopenia and may not receive therapy for osteoporosis[25]. Edwards et al presented important conclusions based on the impact of AI's on the rate of hip fractures[24]. Based on their investigations, first hip fractures in women who survived from breast cancer occurred in earlier age (sixth decade of life) compared with the control group (eight decade of life)[24]. Additionally, first hip fractures reported in breast cancer women under AIs who had osteopenia based on DXA[24]. Despite the fact that AIs are used in middle aged women with breast cancer, increasing the hip fracture incidence, we believe that further studies have to be carried out in order to observe the impact of AIs

in elderly women over 65 years and whether hip fractures occur more often in women with osteopenic or osteoporotic DXA-scores.

The impact of type 2 Diabetes Mellitus on hip fracture risk

In the US about 25% of citizens over 65 years old have type 2 diabetes mellitus T2DM[26].The mortality following a hip fracture of a diabetic person has been shown to increase five to eight times fold for the first 3 months after diagnosis and remain elevated for 5 years after[26].The risk for a hip fracture among elderlies with T2DM is 40-70% higher compared with normoglycemic individuals in the same age group[27]. Hyperglycemia decreases secretion of osteocalcin from osteoblasts and adiponectin from fat cells[28]. Type 2 Diabetes Mellitus (T2DM) increases osteoclastogenesis due to low osteocalcin secretion and restricts proliferation, differentiation and mineralization of osteoblastic cells due to low concentration of adiponectin in blood, leading in bone loss[28]. The altered quality and strength of bones in patients with T2DM increase the hip fracture risk but BMD is minimally affected in many cases[26]. Patients suffering from diabetes may have normal or mild decrease on BMD but increased risk of hip fractures as the disease affects the bone mineralization and turns bones in a poorer quality status[29,30]. BMD T-score values around -1.5 have been associated with hip fractures in these groups of patients that are not categorized as osteoporotic[29-31]. T2DM is accompanied with high BMI giving high Z-scores of 0.27 at the hip by DXA-method, reported by a meta-analysis from Vestergaard P.[27]. Despite of the fact that older white women (but not men or black women) with T2DM have increased BMD by DXA, it is reported that they lose bone rapidly at the femoral head and total hip[32]. This is the reason why they have increased fracture risk after a fall[32]. A meta-analysis by Schwartz AV published in Diabetes Care has reported that there is an increased rate of falls in patients with T2DM (HR 1.19 [95% CI 1.08-1.31]) and even higher fall rate in insulin-treated patients with T2DM[33]. A white woman with T2DM with a BMD T-score at femoral head of -1.9 has the same fracture risk with a non-diabetic woman with a BMD T-score of -2.5[31].

Sarcopenia is strictly associated with hip fractures in elderly people

The European Working Group on Sarcopenia (EWGSOP) has defined the term sarcopenia as the presence of low muscle mass and strength[34]. Muscle weakness and the prevalent of sarcopenia (sarks as flesh and penia as poor) increase the amount of people in danger of a hip fracture, although the BMD interpreted by DXA is not dramatically reduced in those persons[35]. People with sarcopenia have 3-fold increased risk for a fall[35,36]. The prevalence of hip fracture is higher in elderly with reduced muscle mass index and sarcopenia[37]. Sarcopenia usually affects older people as they consume lower concentrations of proteins, due to catabolic situation of inflammatory disease they face and low appetite[38]. The risk factor of muscle weakness associated with a hip fracture in elderly is determined not only by the total body muscle mass decrease but by the rate of muscle lose too[38]. Whole body DXA is one of the quantitative tools proposed to estimate sarcopenia[39]. Several studies have observed the effect of sarcopenia in hip fracture. One study among Hong Kong Chinese geriatric patients has described a prevalence of 73.6% in men and 67.7% in women with hip fracture according to the Asian Working Group for Sarcopenia[39]. Based on European Working group on Sarcopenia, pre-sarcopenia (low muscle mass without change in muscle strength or performance) was 20.8% in male and 12.4% in female elderlies39. Hida et al. in a study published in 2013, supported that 44.7% of elderly male has sarcopenia and 81.1% of elderly women population[40]. All studies have shown the important role of sarcopenia for the incidence of hip fractures among elderly people, even if osteoporosis is not presented on DXA T-scores.

A fall, but not osteoporosis is the necessary condition for a hip fracture to occur

Hip fractures in the elderly are usually attributed to the sphere of a subsequent decreased BMD. Nevertheless, a hip fracture occurs not spontaneously, but mainly after a fall. As a consequence, it has been suggested that the main reason for a hip fracture is not osteoporosis but a fall[7]. Surely, an osteoporotic hip becomes more fragile and more prone to a fracture after a fall, but other factors for falls do play a role. Increased life expectancy has burdened elderly people with many co-morbidities, disabilities and loneliness. An elder person that suffers a hip injury may also be affected by peripheral neuropathy, ocular or inner-ear balance problems, heart disease, fainting episodes, and sensory impairments of a previous stroke, hypotension, sarcopenia or receive drugs with subsequent sensor complications[7]. Falls and fall mechanics are the leading cause of a hip injury in elderly people. The location of the fall impact, the degree of soft tissue that surrounds the hip especially the muscle tissue, the property of the hitting surface, the geometry of the hip, the body mass and other parameters that affect the fracture risk. Ninety percent (90%) of all hip fractures happening every year, translated in 300,000 people in real numbers are associated with a fall[7]. Hayes et al. (1993) have shown that a fall on the side of the femur increases the risk of a hip fracture 20-fold in nursing elderly patients and 6-fold in home fallers[7]. Fractures after falls are thought by some authors to be prevented by the use of hip protectors which are plastic shields (hard) or foam pads (soft), fitted in pockets on the trochanteric side bilaterally, in specially designed underwear. It has been shown that the acceptance and adherence of this protecting method by elderly people can reduce the risk of hip fractures either in nursing care and residential care settings[41].

Neurologic conditions increasing the incidence of hip fractures

Either a gait or balance deficits are important risk factors for a fall. Fallers with a past medical history of a stroke have a significant high risk for a traumatic hip fracture[42]. The prevalence of stroke has increased these last decades due to the expanded average survival of humans[43]. The incidence of hip fractures in such patients may be due to the fact that post stroke life expectancy has improved[44]. Overall fracture rates in general elderly population is approximately 5%[45], similar to fracture rates in persons with stroke (0.6-8.5%)[46-48]. But a large proportion of fractures at about 45-59% involve the hip in the stroke-group[49,50], on the paretic side, usually[51]. Falls in patients with a stoke history are more likely to cause a hip fracture due to decreased bone mineral density, especially on the affected side[52]. Additionally these individuals are more susceptible to experience a hip rather than a wrist fracture as they can't stretch their arm end break a fall[53,54]. It has been shown that polyneuropathy, dementia and Parkinson's disease are further underlying causes of fall-induced hip fractures. Among 32 patients with mean age of 78 years old, 25% had polyneuropathy, 15.6% had dementia and 9.4% had Parkinson's disease[55]. Additionally, anatomic neurological changes in the elderly population such as degeneration of the frontal lobes and basal ganglion, the presence of hydrocephalus and lesions on cerebellum associated with brain atrophy are neurologic conditions that can lead to a fall and a hip fracture[56].

Discussion

Hip fractures that occur in the elderly population are not a simple disease as this big part of the society has much comorbidities that make the prognosis, treatment and rehabilitation of these injuries difficult to address. The term "osteoporotic" fracture strictly refers to patients with a T-score <-2.5 but we have shown various examples where hip fractures may occur in patients without an osteoporotic BMD. One of the main aims of a clinician in our view, apart from treating osteoporosis, is to reduce the number of falls by means of preventive medicine. Many diseases contribute to the high prevalence of falls like ocular and ear impairments, medications, and systemic illnesses like diabetes mellitus type 2, strokes, Parkinson's disease peripheral neuropathy, sarcopenia and others. Certainly osteoporosis is a major subsequent threat but it has been proved that the vast majority of hip fractures occur in the range of osteopenic and normal femur necks based on DXA measurements. Orthopaedic surgeons and other medical practitioners have to realise that giving a surgical treatment for a hip fracture in an older patient is not adequate. In most cases, a deeper analysis of the main etiology of that injury would be advisable so that a recurrent fracture in the healthy hip should be avoided. Additionally, further clinical studies have to be done in elderly individuals with other secondary factors for bone fragility[57], which may cause minimal decrease on BMD but on the other hand produce major alterations in bone strength thereby increasing the risk and incidence of hip fractures, so that these fractures may be avoided.

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