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For the first fracture to be the last

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ABSTRACT

Increased longevity has made progression in the number of fractures increasingly significant. Because hip fractures give rise to high morbidity and mortality rates and have high treatment costs, their occurrence is the most important marker of effectiveness in relation to osteoporosis treatment. In countries and systems that, especially over the last decade, have been investing in the prevention of osteoporosis and its consequences, the number of hip fractures has been decreasing. What these countries have in common is secondary prevention of fractures, i.e. to avoid subsequent fractures. Given that half of the patients who present hip fractures have had a previous fracture and that the treatments available have proven to be extremely efficient for decreasing subsequent fractures, a good proportion of hip fractures are preventable. It is within this scenario that orthopedists play a leading role.

Para que a primeira fratura seja a última

Palavras-chave:
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RESUMO

O aumento da longevidade faz com que a progressão do número de fraturas seja cada vez mais expressiva. A ocorrência da fratura do quadril, pela sua alta taxa de mortalidade e morbidade e pelo alto custo de tratamento, é o mais importante marcador da efetividade no tratamento da osteoporose. Em países e sistemas que, especialmente na última década, vêm investindo na prevenção da osteoporose e de suas consequências, o número de fraturas do quadril vem diminuindo. O que eles têm em comum é a prevenção secundária de fraturas, ou seja, evitar a fratura seguinte. Visto que metade dos pacientes que tiveram uma fratura do quadril teve uma fratura prévia e que os tratamentos disponíveis provaram ser extremamente eficientes para diminuir fraturas subsequentes, boa parte das fraturas de quadril é evitável. É nesse cenário que o ortopedista desempenha um papel preponderante.

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Introduction

Osteoporosis is defined as a bone disease characterized by impairment of bone resistance, which predisposes toward increased risk of fractures.[1,2]

Fractures due to bone fragility are the greatest clinical expression of this disease.

Fractures due to fragility are defined by the World Health Organization as "fractures caused by trauma that would be insufficient to fracture normal bone and which results from reduced resistance to compression or torsion".[3]

From a clinical point of view, these fractures can be defined as resulting from minimal trauma, such as falling from a standing position or less than this, or by unidentified trauma. Fractures due to fragility typically include vertebral, proximal femoral (hip), distal radial and proximal humeral fractures.[4]

Fractures due to fragility are the strongest indicator or a risk of future fractures. Patients who have had a fracture at any site present approximately twice the risk of having a fracture in the future, in comparison with individuals who have never had such injuries. Patients with fractures due to low-energy trauma to the wrist, hip, proximal humerus or ankle present a risk of future fractures that is almost four times greater. Patients with a vertebral fracture will have new vertebral fractures within the next three years, and many will have them within the first of these years.[5–7]

Patients with vertebral fractures present a risk of having similar injuries in the future that is almost five times higher, and a risk of having hip fractures and other non-vertebral fractures that is twice as high. Patients who suffer wrist fractures present a relative risk of having hip fractures in the future that is almost twice as high.[5–7]

Secondary fractures occur rapidly after the first fracture. The risk of subsequent fractures seems to be higher just after a fracture, especially in the first year.[5–7]

Patients who have suffered a hip fracture form a group at higher risk of having fractures in the future. They need to be prioritized for assessment and for starting treatments, so as to avoid other secondary fractures.[8–10]

Contrary to what might be imagined, these patients can benefit greatly from treatment.[11,12]

Initiatives for avoiding secondary (subsequent) fractures should be offered to all men and women over the age of 50 years who have had fractures due to fragility, since these fractures may precede hip fractures in a cycle in which one fracture leads to another, in a "cascade" of fractures.[13–15]

An initial fracture due to fragility is sufficient for requesting an evaluation that includes measurement of bone mineral density, with evaluation of the risk of fractures, and for starting the treatment if there is no formal contraindication.[16,17]

Studies with the highest level of evidence have shown that osteoporosis can be treated, thus diminishing the likelihood of fractures in the future.[17]

Around 50% of all cases of hop fracture are concentrated in 16% of the postmenopausal female population, with histories of fractures. Therefore, secondary prevention presents an opportunity for intervention in around half of all hip fracture patients.[18,19]

The impact of fractures due to fragility

In Brazil, the number of people affected by fractures due fragility reaches 10 million and the expenditure on treating and caring for these cases within the National Health System (SUS) is high. In 2010 alone, around R$ 81 million was spent within SUS on attending to patients with osteoporosis and who had suffered falls and fractures.[20]

It has been estimated that the number of hip fractures per year in Brazil, which was around 121,700 in 2010, will reach 160,000 by 2050.[21,22]

A recent study conducted by the Mayo Clinic showed that between 2000 and 2011, there were 4.9 million hospital admissions due to osteoporotic fractures, 2.9 million due to acute myocardial infarction (AMI), three million due to stroke and 700,000 due to breast cancer. Osteoporotic fractures accounted for more than 40% of the hospital admissions among these four types of admission, and for the length of hospital stay. The hospital cost was greater for osteoporotic fractures (US$ 5.1 billion) than for AMI (US$ 4.3 billion), stroke (US$ 3 billion) or breast cancer (US$ 0.5 billion).[23]

Drug treatments

Drugs for treating osteoporosis can be divided into two groups: (1) inhibitors of bone reabsorption, which work through blocking the action of osteoclasts. These consist of bisphosphonates, selective estrogen receptor modulators (SERMs), calcitonin, estrogen and denosumab and (2) activators of bone formation, which work as anabolic agents, thus increasing bone metabolism, with predominance of bone formation through stimulation of osteoblasts. These comprise parathyroid hormone (PTH), teriparatide (which is similar to PTH), growth hormone (GH) and active metabolites of vitamin D (alphacalcidol and calcitriol).

Strontium ranelate presents a double mode of action, in that it both inhibits reabsorption and stimulates bone formation.

Bisphosphonates reduce occurrences of vertebral and non-vertebral fractures by 40–50%. They are indicated both for women and for men, and in cases of secondary osteoporosis induced through corticoids.[24,25]

They are available in oral and injectable forms in various frequencies of dosage: daily, weekly, monthly, three-monthly and annual use.

Raloxifene is the SERM most used for preventing and treating osteoporosis. Over a three-year evaluation on women with osteoporosis, there was an increase in bone mineral density in the spine and femoral neck, with a reduction in the risk of vertebral fractures.[26,27]

Calcitonin is available in as a nasal spray or in subcutaneous form for daily use. It gives rise to a reduction in occurrences of vertebral fractures in 36% of the patients, but without any reduction in hip fractures or any significant change in either bone mineral density or bone metabolism.[28]

Estrogen replacement therapy is indicated for preventive treatment of osteoporosis. The risks and benefits of this

option need to be discussed between the patient and her gynecologist.[29]

Denosumab is a monoclonal antibody that has been found to reduce the incidence of new vertebral fractures and hip fractures in postmenopausal women who are at high risk of suffering fractures. Its convenient form of dosage (a single subcutaneous application every six months) facilitates adherence to the treatment.[30]

The active metabolites of vitamin D (calcitriol and alphacalcidol) increase calcium absorption. They may have a direct effect on bone cells and may also reduce the incidence of fractures. Active derivatives of vitamin D have been indicated for use among debilitated elderly people with osteoporosis who are reclusive and have little exposure to the sun, at a dose of 0.5 mcg/day. However, the results relating to fracture prevention are not uniform. Alphacalcidol may diminish the myopathy consequent to aging.[31,32]

Teriparatide (PTH) has an anabolic effect. It stimulates bone reabsorption and formation, acts on the coupling mechanism of bone remodeling, promotes large gains of bone mass, diminishes the risk of vertebral and non-vertebral fractures and increases the bone mass of vertebrae, femurs and the whole body. Its use is safe and well tolerated, both for men and for women. It is indicated in cases of severe osteoporosis with fractures: it has a major effect on osteoporosis induced due to corticoids and the effects persist for six months after withdrawal. Recent studies have shown that it can be used for two years. Beyond that point, the therapy can continue with bisphosphonates or denosumab.[33,34]

Strontium ranelate acts both to inhibit reabsorption and to stimulate bone formation. It has been shown to be effective for reducing the occurrences of vertebral, non-vertebral and hip fractures.[35–37]

Physical activity, calcium and vitamin D

Peak maturation of the skeleton is attained between the ages of 20 and 30 years. With adequate nutrition and the normal levels of physical activity available to everyone, higher levels of bone mass can be attained. This forms a calcium reserve bank from which the deposits will be spent during the period of aging, thus delaying or impeding osteoporosis, especially in women. During growth, the skeleton gains bone helps to maintain the bone mass that has been acquired and, during the aging process, this diminishes the losses, maintains muscle tonus and aids in diminishing the number of falls.[38,39]

All patients presenting bone loss, or who are potentially at risk of losses, should be counseled to include calcium and vitamin D in their diets, or as supplements. Calcium absorption decreases with age. Around 75% of the calcium ingested by children is absorbed, while only 30–50% is absorbed in adults. Vitamin D activates calcium absorption in the intestine and it needs to be supplemented in elderly, sedentary or hospitalized individuals.[40]

Gaps in treatment

Despite substantial evidence that previous occurrence of a fracture results in increased risk of a subsequent fracture, fewer than 30% of postmenopausal women and fewer than 10% of men with previous fractures are treated.[41,42]

Independent of the availability of medications that reduce the risk of repeated fractures by 25–70%, the majority of patients with incidental osteoporotic fractures are neither investigated nor treated.[43,44]

Current practices have the result that 80% of patients with fractures due to fragility are neither evaluated nor treated for osteoporosis or for prevention of falls so as to reduce the future incidence of fractures. The consequence of this gap in treatments is that very many fractures occur but could have been avoided. These are an affliction among elderly people and cost millions of dollars around the world.[45,46]

Secondary prevention

Treatments that are started early on, after a primary fracture, may diminish recurrent fracture rates by between 30 and 60%.[47,48]

Anti-osteoporosis treatment implemented after repair treatment for a hip fracture caused by minimal trauma has been correlated with a reduced rate of new clinical fractures and with lower mortality and longer survival.[12,49–51]

Patients who have suffered a hip fracture are the group at highest risk of subsequent fractures. Priority needs to be given to starting their treatment, in order to avoid secondary fractures. Contrary to common assumptions, these patients may benefit greatly from this treatment.

Several studies have shown that persistence with and adherence to osteoporosis treatment is poor, and that this results in less-than-ideal effectiveness (under real treatment conditions). Non-adherent patients have been found to have more comorbidities, be more frail and have higher healthcare expenditure.[13,52–54]

For each environment reported, a fracture liaison service (FLS) is the most effective tool. The FLS is a service dedicated to treating patients subsequent to fractures due to fragility. This is perhaps the only effective means for achieving a change in the current panorama. This approach creates a continuum of care and makes it possible to surmount the gaps in investigation and intervention subsequent to fractures and the unnecessarily high incidence of fractures thereafter.

The FLS in Glasgow has already attended more than a million people since the turn of the century. A cost-effectiveness analysis has shown that for every 10,000 patients attended through the FLS, in comparison with ordinary attendance in the United Kingdom, 18 cases of fractures were avoided, including 11 cases of hip fracture, with savings equivalent to 33,600 dollars.[55,56]

The Healthy Bones program run by the health insurance company Kaiser Permanente is the biggest program for preventing fractures due to fragility in the world. It is conducted by orthopedists and is highly focused on reducing the incidence of fractures by 20% over a five-year period. The program began with hip fractures alone and, as its effectiveness became proven, more resources were injected, such that it now acts in relation to both secondary and primary prevention. In 2009, after seven years of the program integrated with Kaiser's

eleven medical centers in southern California, the hip fracture reduction rate had surpassed 40%.[57–59]

Prevrefrat – the Brazilian experience

Prevrefrat (Programa de Prevenção a Refraturas, i.e. repeated fracture prevention program) is a service destined for treating patients who have had fractures caused by low-intensity trauma such as falling from a standing position, consequent to osteoporosis.

It has been in operation for almost four years and, since 2013, it has been a worldwide reference point for prevention of new fractures.

Through its coordinator, Prevrefrat has disseminated a philosophy of secondary fracture prevention and has decisively helped in implementing other services throughout Brazil.

Prevrefrat is one of the most respected FLS in the world, and is classified as a gold standard, as demonstrated in Fig. 1.

Methodology of Prevrefrat

The first consultation consists of a brief interview to ascertain whether the case fits within the program. The next step is to register the individuals within the program, through gathering data relating to their medical history, their lifestyle habits and the fracture that occurred.

After this, lateral radiographs of the fracture and of the dorsal and lumbar spine are produced, and bone densitometry is measured.

Laboratory tests are requested: calcium, creatinine, 25(OH) vitamin D and PTH, and possibly others if needed. Another consultation is scheduled, on average four weeks later, in order to assess the tests.

If a secondary cause is detected, the patient is referred to other specialists. In cases of osteopenia or primary osteoporosis, and if there is no contraindication, an annual venous infusion of zoledronic acid is administered, or denosumab is applied subcutaneously if the creatinine clearance is less than 35.

Supplementation of calcium and vitamin D is also applied, in accordance with the criteria established through the international guidelines.

At the physician's discretion, a DVD containing 14 exercises to be performed at home is provided. The next consultation is scheduled for three weeks afterwards, on average. In the first year, the consultations take place every three months and, after this, they become half-yearly.

In the clinical profile for Prevrefrat, injectable drugs that are administered once a year or half-yearly (supplied by the Federal Hospital of Ipanema) are specified. This is because of the extremely low degree of adherence to oral drugs: more than 70% of such patients do not complete one year of treatment. Poor adherence has a decisive negative influence on the outcome with regard to avoidance of new fractures. The severity of our patients' clinical condition does not allow use of drugs with this profile of low adherence.

Studies presented at the International Osteoporosis Foundation World Congress of 2014 demonstrated adherence rates of 100% among patients with hip fractures and 85% among those with non-hip fractures.

The results that follow prove that this option is correct and effective.

Results from Prevrefrat

Over a period of three years and ten months, 450 patients were followed up and 12 cases of fractures occurred. None of these

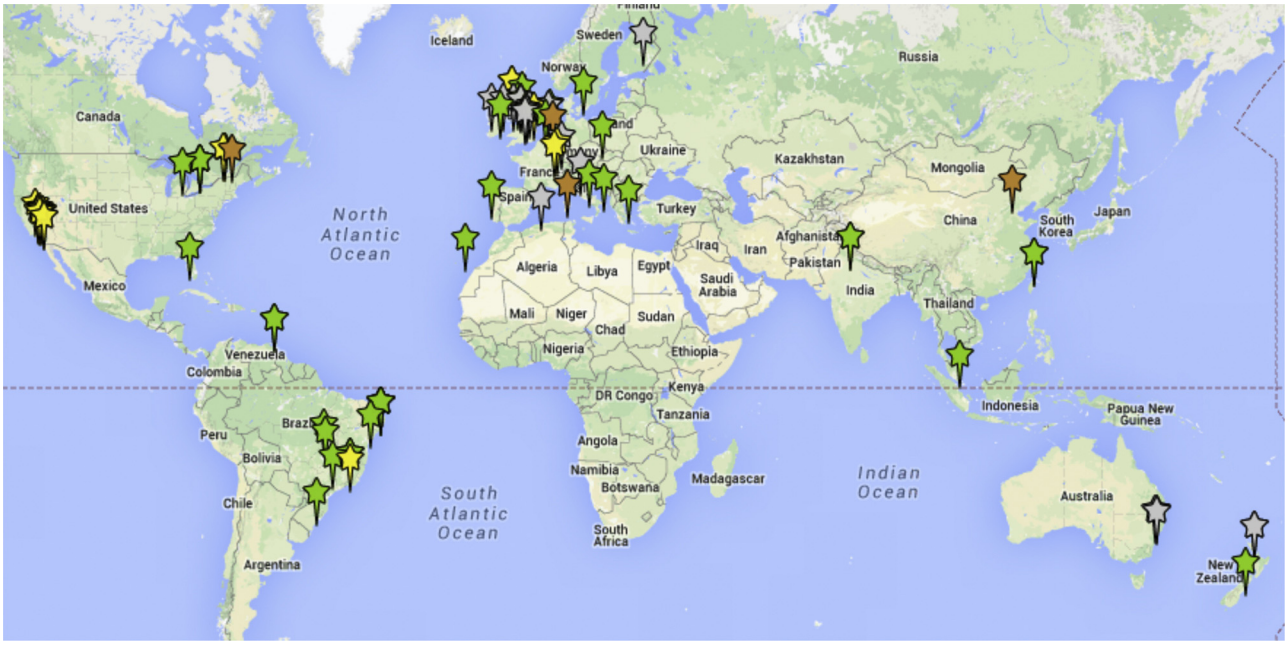

Fig. 1 – Map of good practices from the Capture the Fracture campaign of the International Osteoporosis Foundation. Source: http://www.capture-the-fracture.org/map-of-best-practice.

were hip fractures. In other words, the rate of reduction of subsequent fractures was more than 97%.

Ethical dimension of secondary prevention of fractures

Older patients usually present with their first fracture at an emergency service, or go to an orthopedist who has the skills and expertise to manage the acute condition and repair the fracture. However, there is an additional dimension: knowing that the fracture occurred in an individual with low bone resistance identifies this person as presenting higher risk of future fractures. Studies with the highest level of evidence have shown that osteoporosis can be managed to diminish the likelihood of future fractures. The data clearly demonstrate that a high proportion of secondary fractures can be avoided through appropriate management and that an initial fracture due to fragility is reason enough to ask for a complete evaluation, including measurement of bone mineral density and evaluation of the risk, and is enough for starting treatment.

It might be argued that in many cases, neither the orthopedist nor the emergency physician is the ideal person for starting this investigation and treatment. However, this does not absolve them from the responsibility for ensuring that the patient or the patient's family is fully aware of the risk and for referring the patient for appropriate evaluation and follow-up.

The underlying bone fragility and the increased risk of fractures can be managed subsequently by orthopedists, endocrinologists, rheumatologists, geriatricians and other healthcare professionals, along with collaboration from professionals involved in the rehabilitation process.

The data are sufficiently convincing to characterize appropriate referral as an obligation to do the right thing, i.e. to provide the way forward to the best result. Any conduct differing from this will certainly be below the acceptable ethical and clinical standards.[60]

Conflicts of interest

The authors declare no conflicts of interest.

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