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The Role of Falls in Fracture Prediction

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Abstract Close to 75% of hip and non-hip fractures occur among seniors age 65 years and older. Notably, the primary risk factor for a hip fracture is a fall, and over 90% of all fractures occur after a fall. Thus, critical for the understanding and prevention of fractures at later age is their close relationship with muscle weakness and falling. In fact, antiresorptive treatment alone may not reduce fractures among individuals 80 years and older in the presence of nonskeletal risk factors for fractures despite an improvement in bone metabolism. This article will review the epidemiology of falls, and their importance in regard to fracture risk. Finally, fall prevention strategies and how these translate into fracture reduction are evaluated based on data from randomized controlled trials.

Keywords Falls · Fractures · Treatments that reduce the risk of falling · Fall risk · Fracture risk prediction

Introduction

Thirty percent of those 65 years or older and 40–50% of those 80 years or older report having had a fall over the past year [1, 2]. Serious injuries occur with 10–15% of falls, resulting in fractures in 5% and hip fracture in 1–2% [3]. As an independent determinant of functional decline [4], falls lead to 40% of all nursing home admissions [5]. The primary risk factor for a hip fracture is a fall, and over 90% of all fractures occur after a fall [6]. Recurrent fallers may have close to fourfold increased odds of sustaining a fall-related fracture compared to individuals with a single fall [7]. As the number of seniors 65 years of age and older is predicted to increase from 25–40% by 2030 [8–12], the number of fall-related fractures will increase substantially. Notably, even today 75% of fractures occur among seniors age 65 years and older [13], and by 2050 the worldwide incidence in hip fractures is expected to increase by 240% among women and 310% among men [14]. Thus, therapeutic interventions that are effective in fall prevention are urgently needed.

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Fall Definition and Inclusion of Fall Risk in Fracture Risk Prediction

Buchner et al. [15] created a useful fall definition for the common data base of the FICSIT (Frailty and Injuries: Cooperative Studies of Intervention Techniques) trials. Falls were defined as “unintentionally coming to rest on the ground, floor, or other lower level.” Coming to rest against furniture or a wall was not counted as a fall [15]. Challenging for their assessment is that falls tend to be forgotten if not associated with significant injury [16], requiring short periods of follow-up. Thus, high-quality fall assessment in older persons requires a prospective ascertainment of falls and their circumstances, ideally in short periods of time (< 3 months) [16].

Fall reports may be performed by postcards, phone calls, or diary/calendar, although the usefulness and comprehensiveness of different ascertainment methods have not been compared directly. Notably, fall assessment has not been standardized across randomized controlled trials (RCTs) or large epidemiologic data sets [17], which prevented falls to be included in the World Health Organization FRAX tool (http://www.shef.ac.uk/FRAX/) that estimates the probability of a major osteoporotic fracture in the next 10 years [17]. Based on one Australian cohort study (Dubbo study), the Garvan nomogram has been developed as an alternative fracture prediction tool that includes falling as a risk factor of fracture (www.fractureriskcalculator.com). In a comparative assessment, however, the predictive accuracy of the two tools showed similar performance in postmenopausal women [18]. One explanation for a similar predictive accuracy between FRAX and the Garvan nomogram may be the relatively long time interval of fall assessment in the Garvan nomogram (fall recall in the last 12 months), which may lead to the underreporting of falls not associated with significant injury [16]. Notably, however, there was a suggestion that the Garvan nomogram had greater fracture predictive accuracy among men compared with FRAX [18, 19].

Fall Mechanics and Risk of Fracture

Mechanistically, the circumstances [20] and the direction [21] of a fall determine the type of fracture, whereas bone density and factors that attenuate a fall (eg, better strength or better padding) critically determine whether a fracture will take place when the faller lands on a certain bone [22]. Moreover, falling may affect bone density through increased immobility from self-restriction of activities [23]. It is well known that falls may lead to psychological trauma known as fear of falling [24]. After their first fall, about 30% of persons develop fear of falling [23] resulting in self-restriction of activities [23], and decreased quality of life. In support of the concept that falling is a key determinant of fracture risk, antiresorptive treatment alone may not reduce fractures among individuals 80 years and older in the presence of nonskeletal risk factors for fractures despite an improvement in bone metabolism [25].

Further, consistent with the understanding that factors unrelated to bone are at play in fracture epidemiology, the circumstances of different fractures are strikingly different. Hip fractures tend to occur in less active individuals falling indoors from a standing height with little forward momentum, and they tend to fall sideways or straight down on their hip [22]. Conversely, other nonvertebral fractures (eg, distal forearm or humerus fractures) tend to occur among more active older individuals who are more likely to be outdoors and have a greater forward momentum when they fall [26].

Supporting the notion of bone not to be seen in isolation, fracture risk due to falling is increased among individuals with osteoarthritis of the weight-bearing joints despite having increased bone density compared with controls [27]. One prospective study found that prevalent knee pain due to osteoarthritis increased the risk of falling by 26% and the risk of hip fracture twofold [28]. A most recent study applied a biomechanical risk measure, the factor-of-risk, for the prediction of hip fracture risk [29]: it is the ratio of force on the hip in a fall to femoral strength, and 1 standard deviation increase in peak factor-of-risk was associated with a 1.88-fold increased risk of hip fracture in men and a 1.23-fold increased risk of hip fracture in women. Notably, examining the components of factor-of-risk, fall force, and soft tissue thickness were predictive of hip fracture risk independent of femoral strength estimated from bone mineral density [29].

Risk Factors for Falls

Falls are a hallmark of age and becoming frail, and falls are often heralded by the onset of gait instability, visual impairment or its correction by multifocal glasses, drug treatment with antidepressants, anticonvulsants/barbiturates, or benzodiazepines, weakness, cognitive impairment, vitamin D deficiency, poor mental health, home hazards, or often a combination of several risk factors [30, 31]. The seemingly inseparable relationship of falls to worsening health status and the complexity of factors involved in falling has led to pessimism on the part of physicians when faced with falling, especially recurrent falling. However, there is a growing body of literature that should encourage the standardized assessment of falls and application of fall prevention strategies for fracture prevention.

Fall Prevention Strategies

Fall prevention by risk factor reduction has been tested in several approaches. Multifactorial approaches, such as medical and occupational therapy assessment or adjustment in medications, behavioral instructions and exercise programs, as demonstrated in the PROFET (Prevention of Falls in the Elderly Trial) [32] and FICSIT trials [33], as well as single intervention strategies, such as Tai Chi balance training [34] and exercise [33] reduced falls by 25–50%. Multifactorial approaches may be especially useful in high-risk populations for falls, such as older individuals in care institutions [35]. Significant limitations of multifactorial interventions and exercise programs are their cost, high implementation time, and limited long-term adherence. The latter may explain the lack of data regarding fracture prevention with these interventions.

Notably, however, exercise as a strategy of fall prevention may be applied at a smaller expense when the program is instructed but unsupervised. Such a home exercise program reduced falls in a randomized trial by Campbell et al. [36] among community-dwelling elderly women age 80 years and older. Consistently, a simple unsupervised exercise home program, instructed during acute care after hip fracture repair, reduced falls significantly by 25% over 12-month follow-up among 173 senior hip fracture patients with a mean age of 84 years [37•]. Although not powered for a fracture end point, there was a suggestion that the unsupervised home exercise program contributed to reduction in repeat fractures among acute hip fracture patients (relative fracture rate difference was −56% for the exercise home program vs control; 95% CI, −82%, +9%; $P=0.08$) [37•].

Tai Chi has been successful in reducing falls among healthy older individuals [34, 38], and physically inactive community-dwelling older individuals [39], whereas frail older individuals [40] and fallers [38] may not benefit as much. Furthermore, Tai Chi may not improve bone density [41], and fracture prevention has not been explored as an end point with Tai Chi intervention programs.

As an extension of exercise, programs that support dual tasking may be valuable for fall prevention. Earlier studies suggested that fall risk is increased in seniors unable to walk while talking (stop walking when talking [42, 43]). Thus, dual tasking assessments may best identify those at the greatest risk of falling and programs that improve dual tasking may be useful in fall prevention at a higher age. This concept was tested in a recently published trial which showed that a music-based multitask exercise program improved gait and balance and reduced fall risk significantly by 39% in community-dwelling seniors [44•].

Fall Prevention Strategies with Evidence for Fracture Reduction

Two interventions among older individuals resulted in both fall and fracture reduction. One is cataract surgery with limited evidence from one trial. A total of 306 women over 70 years of age, with cataract, were randomized to expedited (~ 4 weeks) or routine (12 months wait) surgery. Over a 12-month follow-up, the rate of falling was reduced by 34% in the expedited group (rate ratio, 0.66; 95% CI, 0.45–0.96) accompanied by a significantly lower number of persons with a new fracture ($P=0.04$) [45].

With evidence from several double-blind RCTs (12 RCTs for fractures and 8 RCTs for falls) summarized in two 2009 meta-analyses, supplementation with vitamin D should reduce the risk of falls [46] and nonvertebral fractures, including those at the hip [47], by about 20%. Notably, however, for both end points, this benefit was dose-dependent and only observed at an adherence-adjusted dose greater than 480 IU per day for fractures [47], and a treatment dose of at least 700 IU per day for falls [46].

Muscle weakness is an important risk factor for falls and is a prominent feature of the clinical syndrome of vitamin D deficiency [48]. Thus, muscle weakness due to vitamin D deficiency may plausibly mediate fracture risk through an increased susceptibility to falls. The vitamin D receptor is expressed in human muscle tissue [49, 50•], and vitamin D bound to its nuclear receptor in muscle tissue may lead to de novo protein synthesis [51, 52], followed by a relative increase in the diameter and number of fast type II muscle fibers [52]. Notably, fast type II muscle fibers decline with age relative to slow type I muscle fibers resulting in an increased propensity to fall [53].

The Institute of Medicine (IOM) did a thorough review on the effect of vitamin D on fall prevention in 2010 [54••]. However, their synopsis—that the evidence of vitamin D on fall prevention is inconsistent—is in contrast to the 2011 assessment of the Agency for Healthcare Research and Quality for the US Preventive Services Task Force [55••], the 2010 American Geriatric Society/British Geriatric Society Clinical Practice Guideline [56], and the 2010 assessment by the International Osteoporosis Foundation (IOF) [57••], all three of which identified vitamin D as an effective intervention to prevent falling in older adults reviewing the same evidence. Notably, the main inconsistency raised by the IOM is based on four studies that cannot be considered reliable indicators of true treatment efficacy, as those studies used low-dose vitamin D [58], had less than 50% adherence [59], had a low-quality fall assessment [60], or used one large bolus dose of vitamin D among seniors in unstable health [61]. Further, including these four studies in a pooled analysis of a total of 12 blinded and open-design trials evaluated by the IOM, there was a significant benefit overall (odds ratio [OR], 0.89; 95% CI, 0.80–0.99), most pronounced in 6 of 12 studies that fulfilled the criteria for a high-quality fall ascertainment (OR, 0.79; 95% CI, 0.65–0.96) [54••]. As falling is a challenging end point to assess as discussed above [62], the latter analysis by the IOM restricted to the six trials with high-quality fall assessment may best reflect true treatment efficacy with a 21% fall reduction. Further, these finding support the 2009 meta-analysis of eight double-blind RCTs with a high-quality fall ascertainment, also showing a significant benefit with a 19% fall reduction based on the relative risk of individual trials that gave a higher dose of vitamin D [46].

The IOM raised several issues with the 2009 meta-analysis [54••], which were addressed by the authors in a 2011 rebuttal [63•]. In the re-analysis suggested by the IOM, the authors confirmed their earlier finding of a dose-response association: there was a significant reduction in the odds of falling based on all eight trials (OR, 0.73 [0.62, 0.87]); however, this benefit was driven by trials that tested high-dose vitamin D (700–1000 IU vitamin D per day), which reduced the odds of falling by 34% (OR, 0.66 [0.53, 0.82]), whereas low-dose vitamin D did not reduce the odds of falling (OR, 1.14 [0.69, 1.87]) [63•]. Notably, a dose-response relationship between vitamin D and fall and fracture reduction is supported by epidemiologic data showing a significant positive trend between serum 25 (OH)D concentrations and hip bone density [64] and lower extremity strength [65, 66].

Finally, it is important to note that vitamin D may address several components of the fall-fracture construct, including strength [67], balance [68], lower extremity function [65, 66], falling [69, 70], bone density [64, 71], the risk of hip and nonvertebral fractures [72], and the risk of nursing home admission [73]. In a most recent trial that tested 2000 IU of vitamin D per day to the current standard of care of 800 IU of vitamin D per day in a double-blind RCT of 173 acute hip fracture patients, the higher dose of vitamin D did not reduce the rate of falls superior to 800 IU of vitamin D [37•]. However, the higher dose compared with 800 IU of vitamin D reduced the rate of hospital readmission significantly by 39%, which was driven by a significant 60% reduction of fall-related injuries, primarily refracture [37•].

Conclusions

Fall risk reduction is a significant component of fracture prevention at older age and the public health impact of falls is significant. Falls can be reduced by several interventions, with vitamin D offering efficacy established in several RCTs extending to fracture reduction in some of the same trials. To study falls and the fall-fracture risk profile from different interventions and cohort studies better, fall definition and ascertainment need to be standardized.

Disclosure Conflicts of interest: H.A. Bischoff-Ferrari: has been a consultant for Novartis, Amgen, DSM, MSD, and Nestlé; and has received grant support from Nestlé, DSM, and MSD.

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