Evaluation and Management of Hip Fracture Risk in the Aged

Internal Medicine Grand Rounds

Craig D. Rubin, MD

September 10, 2010

This is to acknowledge that Craig Rubin, MD has not disclosed any financial interests or other relationships with commercial concerns related directly or indirectly to this program. Dr. Rubin will not be discussing off-label uses in his presentation.

Biographical Information:

Craig D. Rubin, MD

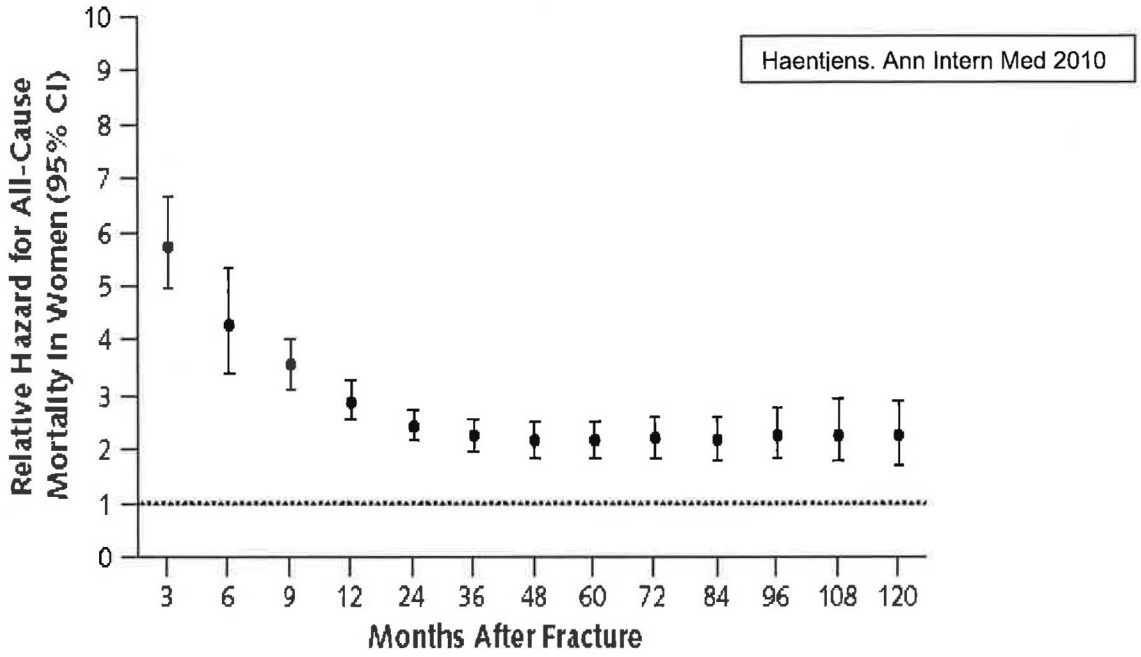
Professor Internal Medicine

Division General Internal Medicine, Chief Section of Geriatrics

Interests: Aging, Alzheimer's Disease, Osteoporosis

Introduction

Hip fractures are common and a major national health concern. According to the National Center for Health Statistics[1], in 2004, there were more than 320,000 hospital admissions for hip fractures. The first year death rate following hip fracture is approximately 30% which is above that of age-matched controls[2] and it remains elevated compared to age-matched controls even after 10 years of follow-up.



Although some studies have suggested a recent decline in the incidence and mortality related to hip fractures after adjusting for the increasing age of the U.S. population[3,4], the sheer growth in the segment of our population most vulnerable to hip fracture; those over 80-years will continue to grow more rapidly than any other segment of our population during the next three decades. By 2040 it has been estimated there will be well over 500,000 hip fractures a year in the U.S[5].

Hip fractures frequently result in a decline in functional status and a need for assistance with activities of daily living. This associated decline in function frequently results in loss of independence and requires up to 20% of patients previously living independently to move to long-term care facilities for least for a year after their fracture [6,7,8].

The direct and indirect costs for the individual, their family and the taxpayer are staggering and will only increase [6]. The CDC has estimated that by 2020 the annual direct and indirect cost of injuries related to falls will reach nearly $55 billion in 2007 dollars[9]. Therefore, hip fractures will continue to be a challenge for patients and their families, health care providers and policy makers.

The Hip Fracture Syndrome: the interaction of bone and fall-related factors.

Hip fractures occur when a force directed to the proximal femur exceeds the elastic properties of the bone. In osteoporosis research and clinical care, hip fracture prevention has largely focused on identifying patients with low bone mass and instituting therapies to increase bone density to improve bone strength. Additional important bone factors which are not clinically measured include accumulated fatigue damage, and bone microarchitecture[10], both of which also contribute to bone quality and strength. Although low bone density is a known risk factor for hip fracture, it has less ability to predict fractures[11], then other "non-bone" risk factors. In addition, the efficacy of bone active agents in reducing hip fractures is also limited with absolute risk reductions commonly at 1 % or a number- needed- to- treat (NNT) value of 100. Furthermore, their effectiveness in reducing risk of hip fracture in patients over 80 years old is not established[12]. More recently in an attempt to predict individual patient fracture risk to guide pharmacologic treatment decisions, models that include other risk factors for hip fracture have been developed. Recently the FRAX (WHO Fracture Risk Assessment Tool) index has been promoted as a means to assess risk with or without bone density measurements[13]. The FRAX algorithm incorporates 10 clinical risk factors (age, gender, BMI, previous fracture, family history of fracture, glucocorticoid use, current smoker, alcohol use of 3 units/d or more, rheumatoid arthritis, hip bone mineral density (BMD) T-score if available) and generates a 10-year risk of fracture. Treatment recommendations vary depending on which management guidelines are used[14] Recently, the US Preventive Services Task Force noted that there are simpler tools, such as age and BMD or age and fracture history that predict hip fractures as well as the FRAX[15-18]

Since more than 90% of hip fractures occur after a fall [19-21] strategies to lower fall risk are fundamental to reduce hip fractures. Interventions that rely solely on improving bone density or increasing bone strength will have only a modest effect. A shift in the clinical (and research) paradigm is required to better address the etiology, evaluation and management of hip fracture risk.

Falls are caused by a complex interaction of factors at play at the time of the fall. The factors contributing to a fall can be viewed as extrinsic (environmental) or intrinsic (i.e. postural hypotension). In addition, the direction of fall has a major influence on the likelihood of sustaining a hip fracture[22] as well as low lean body mass and height of the fall.

Observational studies have identified fall risk factors (see Table)[24]. Simple clinical assessments can identify risk factors and a linear relationship exists with the number of risk factors and the risk of falling. Furthermore, a targeted approach to reduce identified risk factors (gait and balance training, reduction in medications) has been shown to result in fewer falls in an at-risk group of older men and women living in the community[24].

Fall Risk Factors

Age-related changes in physiology -i.e. postural hypotension	Impairment in: -cognition -vision -gait and balance -muscle strength
Medication effects	
Depressive symptoms	
Advanced age	Arthritis
Treatment with four or more prescriptions medications	Use of psychoactive medications
	Environment

Even though effective strategies to evaluate risk of falls have been identified, they may be underutilized. In an attempt to translate evidence from a randomized control trial into clinical practice Tinetti et al reported[25] the results of a program to disseminate fall risk information. An intervention region in the state of Connecticut was selected and provided with multidisciplinary intervention teams which encouraged primary care clinicians and staff members involved in home care, outpatient rehabilitation, and senior centers to adopt effective risk assessments and strategies for the prevention of falls. The teams focused on six risk factors based on the results of prior randomized control trials[24,26,27]. The factors included gait and balance impairments, medication reduction, postural hypotension, sensory and perceptual deficits, foot and footwear problems and environmental hazards[25]. Geographically distinct usual care regions received none of the practice-change interventions provided to the intervention area. The rates of serious fall-related injuries and use of medical services were determined for the two regions. Over the two years following the intervention phase of the study there was a 9% lower rate of serious fall-related injuries and an 11% decline in use of fall-related medical services in the intervention region compared to the usual care region. The investigators estimated this to translate into 1800 fewer emergency department visits or hospital admission and a potential savings of $21 million in health care costs.

Over the past 20-years there have been a large number of studies to assess strategies to reduce falls. Recently two Cochrane Reviews were published identifying the best evidence of interventions designed to reduce falls[28,29]. The reviews examined randomized controlled trials conducted in nursing care facilities and hospitals and older people living in the community. These reviews were divided because of the large number of studies but also because the different environments warranted separate analysis. The characteristics of the setting in which a patient resides is an important consideration in assessing the efficacy of a particular intervention. The functional state of individuals residing in a nursing home, hospital or community varies greatly as does the environment and ability of the staff to provide services. Similar interventions applied to individuals in these different environments can have varying results. For example,

physical therapy interventions may be less effective in severely impaired nursing home residents compared to less functionally impaired patients residing in the community[30,24].

Given the many risk factors for falls it is not surprising that a variety of interventions have emerged and studied to assess their efficacy in reducing falls and thus hip fractures. Interventions have included vitamin D, physical therapy, environmental modifications, exercise, medication optimization and education. With the growing number of studies and the complexity and variety of interventions the Prevention of Falls Network Europe taxonomy has been used to better catalogued interventions.

Categories and Subcategories of Interventions (ProFaNE taxonomy)

ProFaNE Category	ProFaNE Subcategory
Exercises (supervised/unsupervised)	-Gait, balance, co-ordination, functional tasks -Strength/resistance (including power) -Flexibility -3D (tai chi, qi gong, dance, yoga) -General physical activity -Endurance -Other kind of exercises
Medication (drug target)	-Antihypertensives -Other cardiovascular agents -Vitamin D -Calcium -Other bone health medication -Drugs used in diabetes -Anti-Parkinson drugs -Other specified drugs
Surgery	-Cataract -Pacemaker -Podiatric surgery -Others
Management of urinary incontinence	
Fluid or nutritional therapy	
Psychological	-Cognitive (behavioral) interventions -Others
Environmental/assistive technology	-Furnishings and adaptations to homes and other premises/direct action -Aids for personal mobility -Aids for communication, information and signalling -Aids for personal care and protection -Other environmental inverventions
Social environment	-Staff ratio -Staff training -Service model change -Telephone support -Caregiver training -Home care services -Others
Knowledge	-Written material, videos, lectures, etc -Others

Modified from Cameron et al. *Cochrane Database of Systematic Reviews* 2010[28]

The Cochran reviews further classified studies as: 1) single interventions comprised of interventions from only one category, 2) multiple interventions comprising a combination of categories delivered to all participants, and 3) multifactorial interventions comprised of more than one main category of intervention but the interventions were determined after an assessment each individual received.

Nursing home and hospital studies

The nursing home and hospital Cochrane review included 41 trials[28]. The 30 nursing home studies found that interventions targeting single risk factors did not reduce falls, including exercise interventions. In fact pooled data from four of seven studies in nursing care facilities testing a combination of exercise types showed a significant increase in the rate of falls.

Overall, single exercise modality interventions did not reduce the rate of falls or risk of falling[28]. Pooled data from two small studies (53 participants) that included gait, balance and coordination exercises found reduction in rate of falls but not in risk of falling[31,32]. A randomized controlled trial (RCT) of Tai Chi and resistance exercise in elderly[33] in a long term care facility was not effective in reducing number of fallers or time to first fall.

Multifactorial interventions can be effective in reducing the rate of falls and risk of falling. This is particularly the case when provided by a multidisciplinary team and included exercise. If the studies were not multidisciplinary, there was no significant effect. Unfortunately, the study designs did not lend themselves to evaluation of individual components.

Seventeen studies reported on rate and risk of fractures. Only one study reported a reduction in hip fractures.

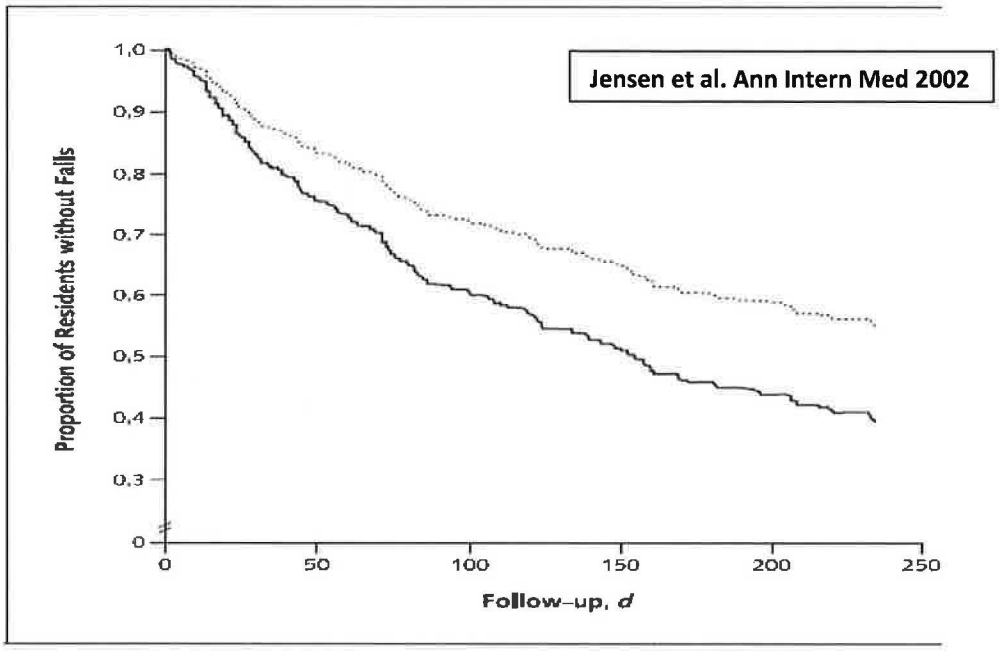
Rate and risk of fracture data for studies reporting a fracture outcome

	95% CI	N (intervention)	N (control)	Fracture type
Becker 2003	0.19 to 4.48	509	472	Hip fractures
Bischoff 2003	0.18 to 20.79	62	60	Hip fractures
Burleigh 2007	0.04 to 3.25	100	103	All fractures
Chapuy 2002	0.36 to 1.07	393	109	Hip fractures
Cox 2008	0.63 to 1.18	3315	2322	Hip fractures
Cumming 2008	0.01 to 7.78	2047	1952	All fractures
Flicker 2005	0.44 to 1.16	313	312	All, including vertebral fractures
Haines 2004	0.14 to 7.19	310	316	All fractures
Jensen 2002	0.06 to 0.94	188	196	Hip fractures
Law 2006	0.99 to 2.20	1762	1955	Non vertebral factures
McMurdo 2000	0.04 to 3.89	52	38	All fractures
Rosendahl 2008	0.01 to 3.00	87	96	Hip fractures
Rubenstein 1990	0.48 to 4.33	79	81	All fractures
Sakamoto 2006	0.04 to 10.70	315	212	Hip fractures
Schnelle 2003	0.49 to 37.42	92	98	All fractures
Shaw 2003	0.21 to 1.43	130	144	Hip fractures
Stenvall 2007	0.01 to 1.94	102	97	All fractures

Modified from Cameron et al. *Cochrane Database of Systematic Reviews* 2010[29]

Jensen et al., 2002, carried out a cluster randomized, controlled, non-blinded trial enrolling 439 older persons (median age 83 years) living in nine residential care facilities in Sweden[34]. The intervention group received an 11-week multifactorial intervention program which incorporated general as well as resident-specific tailored strategies (staff education, environmental modification, exercise, provision of hip protectors and assistive devices, medication review for high risk medications and post-fall problem-solving conferences) compared to usual care. After a 34-week follow-up period, the incidence of falls decreased a significant 12% in the intervention group compared to controls. There was also a significant reduction in femoral fractures with a

number-needed-to-treat (NNT) to prevent a fall of eight, and a NNT of 22 to prevent a femoral fracture. (Pharmacologic interventions at best have shown NNT's of 50 to 100).



Survival curves were determined by using the multiple Cox regression method with adjustment for baseline factors, unadjusted for clustering (hazard ratio, 0.66 [95% CI, 0.48 to 0.89]). The dotted line denotes the intervention group; the solid line denotes the control group.

Jensen also performed a subgroup analysis with a mini-mental state examination (MMSE) score of less or greater than 19. (The MMSE is a 30-point questionnaire used to screen for cognitive impairment.) In those with score of 19 or higher falls were reduced but not in those with a score lower than 19. However, there was a significantly reduced fracture rate in the intervention subgroup with MMSE less than 19 compared with the control subgroup with MMSE less than 19[34].

In another study, Shaw et al. enrolled cognitively impaired elderly patients who presented to the emergency room after a fall[35]. Patients were randomized to usual care or a multifactorial assessment in which risk factors were identified and interventions were designed to address identified problems. Patients were followed for a year and prospectively monitored for hospital encounters, falls and injuries. There was no significant difference between groups in number of falls or in the number of sustained femoral neck fractures

Vitamin D supplementation in nursing care facilities reduced the rate of falls but it should be noted that many of these patients were vitamin D deficient and so the findings may not be broadly applicable to other populations and settings[28].

Chapuy et al. found that in a group of elderly (85 years old) ambulatory women with secondary hyperparathyroidism as well as in a similar study group of elderly

institutionalized women that 1200mg of calcium and 800 IU of vitamin D_3 normalized serum parathyroid and vitamin D levels and pointed to a trend to reduce the risk of hip fractures[36,37] . There was no data on rates of falls and they did not find a significant reduction in risk of falling. Of the four trials reporting fracture data none reached statistical significance in fracture reduction[28].

In a RCT of 124 institutionalized Swiss women(mean age 85 years), treated over 12 weeks with 800 IU of vitamin D and 1200 mg of calcium versus 1200 mg of calcium resulted in a 49% reduction of falls ($p < 0.01$); recurrent fallers seem to benefit most by the treatment[38]. Half of the women completed a battery of musculoskeletal tests at baseline and follow-up with musculoskeletal function improving significantly in the calcium and vitamin D group ($p= 0.0094$). There was no difference in hip fractures between groups. It should be emphasized that 50% of women had 25-hydroxyvitamin D serum concentrations below 12 ng/ml and 90% below 31 ng/ml. Biochemical markers of bone turnover were reduced, and vitamin D levels were both increased significantly in those treated with Vitamin D.

In summary nursing home interventions that target multiple versus single risk factors are more likely to be effective. Single factor interventions in nursing homes that appear to be effective include vitamin D administration and evaluation for high risk medications.

The hospital setting

Eleven studies were reviewed that took place in what was categorized as a hospital[28]. Most of these settings would not be applicable to the traditional U.S. acute care hospital. Patients were generally admitted for more than six weeks (one was an acute setting, six subacute and four in both acute and subacute hospitals). The Cochrane reviewers emphasized the small number of hospital studies and variability of the studies limited the review.

Multifactorial studies in hospitals with a length of stay of at least three weeks are effective in reducing rates of falls but the interpretation is difficult because the interventions vary so that no recommendation can be made about a specific component.

A study by Sternvall[39] enrolled 199 patients randomized to comprehensive geriatric assessment and rehabilitation in a geriatrics ward following surgery for hip fracture compared with usual care in an orthopedics ward. The intervention group had a lower rate and risk of falls. They received multidisciplinary team care targeted to preventing delirium and falls, nutritional supplementation, calcium and vitamin D and staff team rating of patients fall risk. There were four new fractures in the usual care group and none in the intervention group.

Cumming reported a targeted multifactorial intervention with a length of stay shorter than 17 days that included a risk assessment of falls, staff and patient education, drug review, modification of bedside and ward environments, an exercise program, and alarms for selected patients[40]. No reductions in falls were noted between groups.

Pooled data from three subacute hospital studies showed that supervised exercise resulted in a reduction in the risk of falling. This is in contrast to nursing home studies which suggest that exercise may result in an increase in the rate of falls.

Medication reviews by a pharmacist with written report to physicians or utilization of a pharmacy coordinator for patients going from hospital to nursing home did not result in fall risk reductions.

There was no reduction in risk of falling in a RCT comparing 800 IU and 1200 mg calcium versus 1200mg of calcium alone in patients with a median age 84 years admitted to an acute geriatrics unit with a median length of stay of 30 days[95].

A number of studies have evaluated environmental or assistive technology interventions. Carpet flooring (compared to vinyl) increased rate of falls[41]; wrist bands identifying a patient at risk of falling did not reduce falls [42]; and bed exit alarms did not reduce the number of bed-related falls[43].

Preventing falls in the community

A Cochrane Review was conducted to assess interventions to reduce falls in community-dwelling older people[29]. One-hundred eleven trials (55,303 participants) were reviewed. The Cochrane investigators found that **multi-component exercise** interventions reduced the rate and risk of falling. These programs contained at least two or more of the following: strength, balance, flexibility and endurance. The review did not find evidence for a difference between targeting at risk individuals or those enrolled without known risk. Three groups of exercise appeared effective in reducing fall rate and risk. These included Tai Chi (being gait, balance and functional training) as a group exercise, multiple component group exercise and individually prescribed multiple-component home-based exercise. The review also found significantly more injuries occurred with resistance exercise training.

Multiple interventions-fixed combinations are interventions provided to all participants without individual screening or evaluation. Typically these studies combine exercise with one or more other intervention such as education and home safety. Thirteen studies of this approach were analyzed in which 11 had an exercise component. In the study by Day et al.[44] ambulatory patients were recruited by voter rolls. The intervention included exercise, vision assessment and home safety assessment. A supervised exercise program for one hour a week for 15 weeks, supplemented with home exercise for up to

12 months reduced falls[44]. The reduction in falls was associated with improved balance but also increased social interaction and awareness of falls may have contributed to the outcomes. Home modification and vision assessment did not appear to be an essential component of the intervention.

Multifactorial interventions consist of an assessment and more than one main category of intervention targeted to the individual. The evidence suggests that with this approach there is a reduction in rate of falls but not risk of falling or fracture. Additional research needs to explore the difference between programs that provide integration of assessment and intervention by a multidisciplinary team versus those that provide assessment and referral. Patient characteristics, varied health care systems and structure make comparison of studies challenging.

Vitamin D did not reduce falls in community dwelling elders[29]. A subgroup analysis found in older people selected on the basis of low vitamin D level, supplementation reduced the rate of falls and risk of falling but the authors cautioned that these findings were based on a limited number of trials (260 participants out of 21,100). In addition another recent meta-analysis based on data from 10 studies concluded that vitamin D reduced the risk of falls with a relative risk (RR) of 0.86 (95% CI=0.79-0.93); but this analysis included studies from a variety of settings; institutionalized, hospital and community[45]. These authors also acknowledge "the utility of vitamin D treatment in patients who are not deficient in vitamin D is not clear". A study by Sanders et al.[46] reported the annual oral administration of high-dose cholecalciferol (500,000 IU) annually during the winter for 3 to 5 years in 2258 community-dwelling women at least 70 years old, resulted in an increased risk of falls (RR,1.15; 95% CI,1.02-1.30; P=.03) and non-vertebral fractures (RR 1.26, 95%CI, 1,00-1.59;P=.047). Less than 3% of a subgroup of participants had 25-hydroxycholecalciferol levels lower than 25 nmol/L.

Overall, home safety interventions did not reduce falls, but may be effective in people at high risk (i.e. fall history or at least one risk factor such as severe visual impairment). For severely visually impaired patients one trial of a home safety intervention was effective in reducing rate and risk of falls[47]. In addition, accelerating (for those on a wait list) first eye cataract surgery reduced rate of falls (but not number of fallers)[96]. However, speeding the scheduling of a second cataract surgery for those on a wait list had no impact on falls[97]. Of note, two trials evaluating the effect of interventions to improve vision which included a comprehensive vision and eye assessment, with appropriate treatment increased both the rate of falls and number of participants falling (trend for more fractures but not statistically significant[48]). Although the duration of the study was up to 12 months, the authors suggested that older patients may need a considerable period of time to adjust to new eyeglasses and that they should be warned to be particularly careful during the post-op period.

The gradual withdrawal of psychotropic medication reduced the rate of falls but not the risk of falling[49]. A prescribing modification program for primary care physicians significantly reduced risk of falling in patients under their care.[50]

A randomized control trial using an anti-slip shoe device (Yaktrax Walker) reduced the rate of falls in snow and icy conditions in Wisconsin[51]. The NNT was six to prevent one non-serious injurious fall.

Pacemakers reduced the rate of falls in people with carotid sinus hypersensitivity and a history of syncope and falls[52].

Two trials providing knowledge/education programs in fall prevention to community populations found no reduction in fall risk or rate of falls.

Neurological disorders-home-based physiotherapy for people with Parkinson's disease or with stroke–related mobility problems did not reduce falls.

Tai chi

Tai chi (TC) is a balance-oriented exercise program which has been growing widely as an exercise program to prevent falls in older people. Because the movements used in TC incorporate strengthening, balance, postural alignment, and concentration, it may lead to reduced falls. Wolf et al. published in 1996 the results of a 16-week TC intervention trial in older persons; it showed a 48% reduction in the risk of falls compared to a wellness education program[53]. Subsequent studies have had inconsistent results and a variety of questions remain. There have been wide variations in the use of balance measures, differences in target populations by age and function, and the type and duration of the exercise program[54]. Based on data from 4-trials, the Cochrane reviewers estimated TC reduced the rate of falls (RR 0.63, 95% CI .52 to .78) and risk of falling (RR 0.65, 95% CI 0.51 to 0.82)[29]. TC was one of the least costly but also least studied exercise intervention.[55] Voukelatos et al[56]. enrolled relatively healthy community dwellers, mean age nearly 70 years old and 84% women. The control group received no activities. The majority of classes involved Sun style TC (83%), two classes involved Yang-style TC (3%), and the remainder involved a mixture of several styles (14%). A number of assessments of balance were made at baseline and 16 weeks with improvement noted in the TC group.

Li et al. studied physically inactive subjects with a mean age of 77 years[57]. The intervention group was taught in the Yang style of TC. The control group received stretching exercises but did not have any balance training component to their sessions. In addition to reducing falls, improvements in measures of functional balance and physical performance were reported. Wolf et al.[58] conducted a 48 week program comparing TC with a wellness group serving as control. The median age was 82 years. Those enrolled were "transitioning to frailty" and resided in congregate living. The style of TC consisted of six TC forms resulting in a progressive narrowing of lower extremity

stance. The TC group had a better sickness impact profile score and was less likely to use an assistive device at baseline. TC did not reduce the risk of falling in the intervention group compared to control but the direction of effect (CI) 50.52–1.08) was in favor of the TC group.

Woo and colleagues recruited men and women through notices in community centers[59]. Subjects were assigned to a TC, resistance exercise or a control group with no prescribed exercise. The TC group performed Yang style techniques with 24 forms. After 12 months no difference in either number of falls or balance or flexibility was seen between intervention and controls.

Not included in the Cochrane review, a recent study by Inge et al. reported[60] the results of a randomized trial to assess the effectiveness of Tai Chi Chuan on fall prevention in elderly people(mean age 77 years) living at home with a high risk of falling. The intervention group received lessons in 10 positions derived from the Yang style. The control group received usual care. The 12-month study found no differences between groups in measures of balance or fall incidence.

Cognitive impairment and dementia

Cognitive impairment is an independent risk for falls. Most studies of fall prevention and osteoporosis have excluded patients with dementia. Patients with Alzheimer's and a history of falls are at increased risk of fracture and reduced survival compared to non-fallers with the disease. The efficacy of interventions that reduce fall risk in non-cognitively impaired populations may not be applicable to those with dementia [61-63].

The mechanism underlying increased fall risk in patients with dementia is not well understood. Clarifying the mechanism of fall risk in cognitively impaired individuals is essential to devise treatment strategies to reduce fall incidence and injury.

Rapport et al. studied patients on an inpatient rehabilitation unit and reported that measures of executive function accounted for variance in falls beyond that explained by age and functional motor ability[64]. Executive function is the cognitive domain that includes the ability to plan, initiate, sequence and monitor complex goal-directed behavior.

In another study comparing the relationship between cognitive function and falls in cognitively intact older individuals, an increased risk of falls was noted in subjects with lower scores on tests of executive function and attention. In addition, overall verbal intelligence was inversely related to increased risk of recurrent falls. Memory scores were not associated with falls. The study controlled for confounding effects of gait and other fall risk factors[65].

A prospective cohort study investigating cognitive function and falls found declines in verbal ability, processing speed (used to measure executive function), and immediate

memory were associated with increases in rates of falling and fall risk.[66] Persad et al. also reported that impairment in executive function played a greater role than other areas of cognition such as memory in mobility performance [67].

Multiple cognitive factors are likely necessary to avoid falling including memory, visuospatial ability, praxis, attention and executive function. Executive function is critical to planning and to the rapid behavioral and motor responses needed to avoid a fall after an extrinsic or environmental challenge. Consideration of multiple areas of cognition is necessary to understand and develop strategies to reduce fall and fracture risk in patients with dementia.

Hip protectors have been studied as an intervention to prevent hip fractures in frail institutionalized older patients. The mechanism of fracture prevention being the placement of a foam pad or plastic shield to redirect the force generated from the fall away from the proximal femur. Early studies were very promising with findings showing reductions in hip fractures in the very high risk patients studied[69, 70]. However, these studies suffered from being designed as cluster studies with inherent methodological concerns. A RCT by Kiel et al.[71] reported their results of a trial of hip protectors in nursing home patients where each patient served as their own control wearing the hip protector on one side. They found no reduction in hip fractures. A recent Cochrane review came to the conclusion that there was no evidence of any significant effect of hip protectors on the incidence of pelvic or other fractures[68]. In addition, adherence of hip protectors has always been problematic.

Pharmacologic interventions for osteoporosis

A number of medications have been shown to reduce hip fractures in RCTs. Among bisphosphonates these include alendronate[74,75] (ARR 1.0%), risedronate[98] (AR 1.0% without prevalent fracture between age 70-79 and 3.0% ARR in patients with baseline prevalent vertebral fracture),and zolendronic acid[72,73,76] (1.1% ARR). Ibandronate has shown efficacy in reducing vertebral fractures but not in reducing hip fractures. Teriparatide [77-80],selective estrogen receptor modulators (SERM's) raloxifene[82] and lasofoxifene (in phase III trials[83]) and calcitonin have not been found to be effective in reducing hip fractures based on randomized controlled trials. Zoledronic acid reduced hip fracture in high risk patients with recent hip fractures[73]. Risedronate is reported to reduce hip fractures in one study in patients with Alzheimer's disease[84]. However, the results of this trial need to be qualified for a number of reasons; how the diagnosis of Alzheimer's was made is not clear and the enrollment of 500 subjects in a month is remarkable. The patients were vitamin D deficient at baseline and although the control group received vitamin D and calcium, reductions in markers of bone resorption were accompanied by a decline in bone density. Furthermore, the difference in hip fracture rate was seen within the first two months of therapy[84].

In the single randomized trial where hip fractures were the primary outcome risedronate reduced hip fractures in patients between the age of 70 and 79 but was not effective in reducing hip fractures in those over age 80[98]. Patients in this group were recruited by age plus an additional risk factor for hip fracture. Only a minority of participants had their bone density measured. It has been questioned whether the lack of reduction in hip fractures was because of the absence of low BMD or other risk factors (high risk of falling) although they likely all fell. In a pooled analysis of three studies with participants over the age of 80, a reduction in vertebral fractures was noted but once again a reduction hip fracture was not achieved[81].

Denosumab is a recently approved monoclonal antibody for the treatment of women with postmenopausal osteoporosis at high risk for fracture or for patients who have failed or are intolerant to other available osteoporosis therapy. High risk is defined as a history of osteoporotic fracture or multiple risk factors for fracture or patients who have failed or are intolerant to other available osteoporosis therapy. Denosumab binds to RANKL (the receptor activator of nuclear factor-κB ligand), a transmembrane or soluble protein necessary for the formation, function, and survival of osteoclasts. Denosumab inhibits RANKL from activating its receptor, RANK, on the surface of osteoclasts and their precursors. The blocking of the RANKL/RANK interaction and the resulting inhibition of osteoclast activity leads to decreased bone resorption. Denosumab is administered subcutaneously once every six months. A three year RCT[85] found the age-adjusted absolute risk reduction of hip fractures was 0.3% (P=0.04) and a NNT of 200. Twenty-seven percent (3576) of the patients in the trial were ≥ 75 years old. An analysis of efficacy of hip fracture reduction in this group is not available from the data presented. Patients are instructed by product labeling to take to take calcium 1000 mg daily and at least 400 IU vitamin D daily because of concerns of hypocalcemia. Infections are also a concern with this medication and although rare, osteonecrosis of the jaw has been reported in patients taking this medication; like bisphosphonates, a causal relationship has not yet been determined.

Calcium

Conflicting evidence[86-88] exists regarding the efficacy of calcium in reducing hip fractures. Findings from studies with low adherence and inadequate documentation of baseline vitamin D status are common methodological concerns[87,88]. In a recent meta-analysis, vitamin D was reported to be effective in reducing fractures only when given with calcium.[89] The beneficial effect of calcium on bone metabolism is related to the blunting or reversal of the age-related impairment of calcium absorption and/or insufficient intake which results in secondary hyperparathyroidism and increased bone resorption.[90] In younger or ambulatory patients who are less likely to be calcium or vitamin D deficient, supplementation is not likely to demonstrate fracture reduction. The older the patient and/or the lower the vitamin D status, the more likely calcium (and vitamin D) supplementation will show clinical benefit and reduction in fracture.[89]

Evaluation and management of hip fracture risk

Fall risk

All older patients should be asked if they have fallen during the past year and if so, the frequency, circumstances, symptoms, time of fall and consequences should be described. All patients should have a gait and balance assessment. The "Get-Up-And-Go Test" is a practical test to perform in the clinical setting[91]. Patients are asked to stand from the sitting position without use of arms (if possible), walk about 3 meters then turn and return to their chair and sit down. The ability to stand without the use of arms (arms folded) assesses proximal leg strength, stance (balance) gait width, step height, speed, symmetry, stability especially with turning and sitting provides a good overall screening assessment. The test can be timed, normal being less than 10 seconds; greater than 20 seconds is abnormal and correlates with poor functional independence and higher risk of falls.[92] However, timing the maneuver may distract the examiner from closely observing the performance of the patient. An alternative validated tool is the Tinetti balance and gait assessment tool[93] which takes 15 minutes to complete and shares many of the components of the Get Up and Go. When assessing gait and balance, older patients should not be asked to perform tandem gait since around after the age of 70 it becomes very difficult for most normal individuals.

Older persons reporting only a single fall without associated symptoms and who demonstrate no difficulty during gait and balance testing generally do not require further evaluation. For patients with more than one fall and/or difficulty performing a gait and balance assessment, a full multifactorial fall risk assessment should be performed. The overall goal of the multifactorial assessment is to identify known fall risk factors and implement a strategy to reduce or eliminate them. A common approach is to consider extrinsic (environmental factors: uneven sidewalks, poor lighting) or intrinsic factors (dizziness, weakness, poor vision). A careful review of all prescription and non-prescription medications is essential. High risk and non-essential medications should be eliminated if possible. High risk medications include psychotropic, anxiolytics and antidepressant agents and sedating agents. Careful consideration should be given to chronic medical problems as well as the possibility of new pathology. For example, a patient with diabetes developing peripheral neuropathy, a patient with BPH recently initiated on an alpha-adrenergic blocker, or a patient with hypertension with a recent addition to their antihypertensive regimen. New onset syncope or near-syncope prompts consideration of cardiac disease such as arrhythmia or carotid hypersensitivity or volume depletion.

The physical exam should focus on orthostatic blood pressure measurements, visual acuity, focal neurologic findings, muscle strength, cognition, and depression. The feet should be examined for deformities, ulcers, severe bunions. Footwear should be evaluated for excessive wear. High heels, unlaced or unbuckled shoes should be

avoided. Initial routine laboratory testing includes a complete blood count, electrolytes, BUN, creatinine, glucose, and an EKG should be performed.

Results of the initial evaluation guide the approach to manage fall risk. Problems identified should be addressed as necessary (i.e. a patient with carotid hypersensitivity should be referred for evaluation for pacemaker placement, those with visual impairment related to cataracts should have corrective surgery).

In ambulatory older patients with a history of falls, reducing unnecessary prescriptions, physical therapy interventions for those with gait and balance problems, and instructions for safe tub and toilet transfer are effective strategies. Multi-component exercise interventions reduce the rate and risk of falling. Tai chi appears to be an effective exercise strategy although more studies regarding position, intensity of exercise and target population are needed. Vitamin D administration in those who are deficient is effective in reducing fall risk and hip fractures but the routine administration in vitamin D replete individuals is in doubt. Home safety interventions may be effective in people at high risk (i.e. fall history or at least one risk factor such as severe visual impairment). If there is concern for environmental hazards the patient or family should be counseled. One small study found anti-slip shoe devices reduced falls in snow and icy conditions. Although not reported as a risk factor, patients should be cautioned regarding risk of cats and dogs as a cause of falls. General knowledge and education programs in fall prevention to community populations have not been shown to be beneficial in reducing falls. Cognitively impaired patients require a multidisciplinary assessment and approach to care. The cognitively impaired are a high risk population that has not been well studied.

In the nursing home setting multifactorial interventions can be effective in reducing the rate of falls and risk of falling. This is particularly the case when provided by a multidisciplinary team and includes exercise. Unfortunately, the individual components of existing studies have not lent themselves to evaluation and determination of which aspects of care is most beneficial. In one nursing home study, staff education, environmental modification, exercise, provision of hip protectors and assistive devices, medication review for high risk medications, and post-fall problem-solving conferences resulted in a reduction of falls and hip fracture.

Single exercise modality interventions did not reduce the rate of falls or risk of falling in nursing home populations. The initial enthusiasm for the role and effectiveness of hip protectors has waned based on more recent studies finding they were ineffective in reducing hip fractures. Single factor interventions in nursing homes that appear to be effective include vitamin D administration (likely because of the high prevalence of hypovitaminosis D) and evaluations for high risk medications.

Few fall intervention trials have been reported in the acute care setting. Most "hospital" studies were conducted in settings with a length of stay of at least three weeks.

Multifactorial strategies have suggested they result in reduced rates of falls but because interventions vary no recommendations can be made for specific components. A variety of small studies found that carpet flooring (compared to vinyl) increased the rate of falls; wrist bands identifying a patient at risk of falling and bed exit alarms did not reduce the number of falls.

Bone strength

Bone density remains the only readily available direct means of assessing bone strength and fracture risk. Other indirect factors include age, BMI, prior fracture, smoking, alcohol, steroid use and other medications known to increase risk of osteoporosis and conditions that secondarily cause bone loss. The National Osteoporosis Foundation currently (January 2010) recommends bone mineral density (BMD) testing in women age 65 and older and men age 70 and older. A recent report from the U.S. Preventive Services Task Force notes that methods to identify risk for osteoporotic fractures are available but no trials have directly evaluate screening effectiveness[17]. The decision to screen patients with advanced age should be balanced with an assessment of individual patient wishes and consideration of the patient's functional status and co-morbid conditions. As people live longer the difficult balance of competing risk of death and the time to realize the outcomes of the intervention needs to be assessed. Even with traditional survival analysis methods the benefit of an intervention may be overestimated .[94]

However, in patients under age 80 a bone active agent (bisphosphonates) should be considered in patients with a femoral neck T-score greater than -2.5. This is especially true if the patient has a pre-existing vertebral fracture or if the patient previously sustained a hip fracture. Both situations substantially increase the risk of subsequent fractures and these patients are much more likely to benefit from treatment. In patients over the age of 80; treatment benefit is much less of a certain and has not been demonstrated in RCTs.

If a pharmacologic treatment is determined to be appropriate, the bisphosphonates alendronate, risedronate and zolendronic acid have shown efficacy in reducing hip fracture. Denosumab is a recently approved monoclonal antibody that has reduced hip fracture risk in women with postmenopausal osteoporosis. No pharmacologic agents have documented efficacy in reducing hip fractures in those over 80 years old.

Conclusion

Hip fractures are a complicated interaction of fall risks and bone strength. Because 90% of hip fractures occur in the setting of a fall prior to the fracture, identifying interventions that reduce fall risk factors is essential. Fall assessment and multi-component exercise interventions that include strength, balance, and flexibility appear to reduce fall and fracture rate. Although large clinical heterogeneity exists in fall trials, research methodology can be improved. Better characterization of study populations and interventions are needed. In addition, many studies exclude subjects with impaired cognition. This is a large and growing group at risk for fractures about which very little is known.

A number of bone active agents have shown modest efficacy in reducing hip fractures but there is little evidence that a pharmacologic approach alone is effective for those over 80 years old. Nonetheless, a reduction in fall risk combined with agents that improve bone strength is a promising strategy.

The culture of modern medicine is more compatible with an emphasis on drug development which has been an enormously successful approach for many disease states. A similar scientific approach will need to be utilized to better understand the mechanism contributing to falls and thus lead to the development of successful interventions.

Finally, the multidisciplinary approach to hip fracture risk assessment and management is time consuming and difficult to achieve in our current system of care. Current proposed modifications to our health care system (i.e. perhaps the medical home) may improve our ability to assess and manage hip fracture risk.

2010 AGS/BGS Clinical Practice Guideline:
Prevention of Falls in Older Persons[23]

SCREENING AND ASSESSMENT

- All older individuals should be asked whether they have fallen (in the past year).
- An older person who reports a fall should be asked about the frequency and circumstances of the fall(s).
- Older individuals should be asked if they experience difficulties with walking or balance.
- Older persons who present for medical attention because of a fall, report recurrent falls in the past year, or report difficulties in walking or balance (with or without activity curtailment) should have a multifactorial fall risk assessment.
- Older persons presenting with a single fall should be evaluated for gait and balance.
- Older persons who have fallen should have an assessment of gait and balance using one of the available evaluations.
- Older persons who cannot perform or perform poorly on a standardized gait and balance test should be given a multifactorial fall risk assessment.
- Older persons who have difficulty or demonstrate unsteadiness during the evaluation of gait and balance require a multifactorial fall risk assessment.
- Older persons reporting only a single fall and reporting or demonstrating no difficulty or unsteadiness during the evaluation of gait and balance do not require a fall risk assessment.
- The multifactorial fall risk assessment should be performed by a clinician (or clinicians) with appropriate skills and training.
    - The multifactorial fall risk assessment should include the following:
      Focused History
    - History of falls: Detailed description of the circumstances of the fall(s), frequency, symptoms at time of fall, injuries, other consequences
    - Medication review: All prescribed and over-the-counter medications with dosages
    - History of relevant risk factors: Acute or chronic medical problems, (e.g., osteoporosis, urinary incontinence, cardiovascular disease)

Physical Examinations

- Detailed assessment of gait, balance, and mobility levels and lower extremity joint function
- Neurological function: Cognitive evaluation, lower extremity peripheral nerves, proprioception, reflexes, tests of cortical, extrapyramidal and cerebellar function
- Muscle strength (lower extremities)
- Cardiovascular status: Heart rate and rhythm, postural pulse, blood pressure, and, if appropriate, heart rate and blood pressure responses to carotid sinus stimulation
- Assessment of visual acuity
- Examination of the feet and footwear

Functional Assessment

- Assessment of activities of daily living (ADL) skills including use of adaptive equipment and mobility aids, as appropriate
- Assessment of the individual's perceived functional ability and fear related to falling
  (Assessment of current activity levels with attention to the extent to which concerns about falling are protective [i.e., appropriate given abilities] or contributing to deconditioning and/or compromised quality of life [i.e., individual is curtailing involvement in activities he or she is safely able to perform due to fear of falling])

Environmental Assessment

Environmental assessment including home safety

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