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The Complex Interplay of Depression and Falls in Older Adults: A Clinical Review

Andrea laboni, M.D., D.Phil., F.R.C.P.C. and Alastair J. Flint, M.B., F.R.C.P.C., F.R.A.N.Z.C.P. Department of Psychiatry, University of Toronto (AI, AJF), Department of Psychiatry and Geriatric Rehabilitation Program, University Health Network (AI, AJF), and the Toronto Rehab and Toronto General Research Institutes (AJF), Toronto, Ontario, Canada

Abstract

Depression and falls have a significant bidirectional relationship. Excessive fear of falling, which is frequently associated with depression, also increases the risk of falls. Both depression and fear of falling are associated with impairment of gait and balance, an association that is mediated through cognitive, sensory, and motor pathways. The management of depression in fall-prone individuals is challenging, since antidepressant medications can increase the risk of falls, selective serotonin reuptake inhibitors may increase the risk of fragility fractures, and data are lacking about the effect of fall rehabilitation programs on clinically significant depression. Based on the current state of knowledge, exercise (particularly Tai Chi) and cognitive-behavioral therapy should be considered for the first-line treatment of mild depression in older fallers. Antidepressant medications are indicated to treat moderate to severe depression in fall-prone individuals, but with appropriate precautions including low starting dose and slow dose titration, use of psychotropic monotherapy whenever possible, and monitoring for orthostatic hypotension and hyponatremia. To date, there have been no recommendations for osteoporosis monitoring and treatment in individuals prescribed antidepressant medications, beyond the usual clinical guidelines. However, treatment of the older depressed person who is at risk of falls provides the opportunity to inquire about his or her adherence with osteoporosis and fracture-prevention guidelines.

Keywords

Antidepressants; depression; falls; fear of falling; fractures

One-third of community-dwelling seniors fall each year, with half of these individuals falling more than once. Ten percent of all falls result in a major injury, which can lead to institutionalization and death. Falls often result in a fear of further falls, leading to fear-related restriction of activities: this activity restriction has been associated with subsequent impairment in balance, mobility, and disability. 2,3

Send correspondence and reprint requests to Alastair J. Flint, M.B., F.R.C.P.C., F.R.A.N.Z.C.P., Toronto General Hospital, 200 Elizabeth St., 8 Eaton North–Room 238, Toronto, ON M5G 2C4, Canada. alastair.flint@uhn.on.ca.

This clinical review examines falls from the perspective of depression and its treatment, as well as associated anxiety. Like falls, depression is common in old age, with 15% of community-dwelling seniors reporting clinically significant depressive symptoms. There is a close relationship between anxiety and depression in old age, making it difficult to examine their effects independently. Fear of falling and worries about the consequences of falling are common manifestations of anxiety in older adults and are associated with a variety of avoidance and safety behaviors. This article aims to provide a selected overview of literature most pertinent to the clinician and will highlight gaps in the evidence and areas for future research.

DEPRESSION AND FALLS

Depression and falls are frequently associated. A recent meta-analysis summarized the findings of 17 prospective studies and found an odds ratio for the association of depression with falls of 1.63 (95% CI: 1.36–1.94).⁶ The relationship between depression and falls is complex and bidirectional (Figure 1). Depression is an independent risk factor for falls. In one prospective study, there were four determinants of recurrent falls: postural sway, history of falls, handgrip strength, and depressive symptoms.⁷ Individually, symptoms of depression may have a direct role in promoting falls. Older women with insomnia and sleep fragmentation have an increased risk of falling, even when controlling for the use of sedatives.⁸ Poor appetite and weight loss are commonly seen in geriatric depression and nutritional deficiencies in vitamin D and folate may be related to falls.⁹ In addition, cross-sectional studies have identified an association between lower vitamin D levels and symptoms of depression but it is not known whether low vitamin D levels are a cause, consequences, or indirect correlate of depression.¹⁰

Depression is also associated with a characteristic pattern of cognitive deficits, affecting mainly attention, executive function, and processing speed. Walking is a complex process in which the motor, sensory, and cognitive functions interact. In particular, the cognitive domains of attention and executive function are central to gait performance. In general, older adults need to allocate greater attention to walking to compensate for changes in their sensory and motor function. When walking with distractions, depressive symptoms and deficits in executive function are associated with increased unsteadiness. Balance-impaired individuals with depression are slower when given a cognitively challenging gait task, and this correlates with measures of executive function. Depression is thus associated with neurocognitive changes in the ability to attend to one's environment and to coordinate motor output.

Psychomotor slowing is a common feature of major depression: related gait disturbances have been found in depression. In particular, individuals with depression walk slowly with a shorter stride length, longer standing phase, and increased gait variability. ^{15,16} These gait patterns characteristic of depression have been shown to be associated with falls. ^{17,18}

The complex relationship between depression, cognitive performance, motor performance, and risk of falls is illustrated by a recent study that found that the association between depression and slowed choice stepping reaction time (which is a composite measure of fall

risk) was mediated by two paths: one through quadriceps strength and the other through executive function, with both mediating variables then influencing choice stepping reaction time via simple reaction time and balance. ¹⁹

Depression and falls are also linked indirectly through several common risk factors. Functional decline, history of falls, and cognitive impairment have been separately linked to both depression and falls.²⁰ Poor physical health is also a notable risk factor for both falls and depression. Vascular disease, in particular, and its related burden of white matter lesions, may produce concurrent changes in balance, gait, and mood.²¹

The interaction between depression and falls may also be self-perpetuating. Depressive symptoms are particularly high in those who are recurrent fallers, ²² which may be related to the demoralizing effect of repeated falling. In a prospective study over an 8-year period, increase in depressive symptoms was associated with an increased rate of falls. ²³ Conversely, a lower rate of falls was associated with improvement in morale scores over the follow-up period. ²³ Depressive cognitive–affective symptoms seen in repeat fallers include a lower sense of self-efficacy and negative expectations of the future. Activity restriction and decreased social participation can be a complication of recurrent falls ²⁴: the resulting social isolation is known to be a significant risk factor for depression in older adults. ²⁵

FEAR OF FALLING

Fear and anxiety is another significant cognitive—affective response to falling. Fear of falling can be an expected and adaptive response to having experienced a fall. However, fear of falling can be excessive and disabling, to the point where an individual may be agoraphobic. It is not always easy to distinguish between an adaptive and an unhealthy fear of falling. For example, in a study of hospitalized fallers, only 1 of 48 individuals with moderate to severe fear of falling felt that this fear was excessive or unreasonable, even though the fear frequently resulted in avoidance of activities. However, a clear discrepancy between perception of fall risk and objectively determined fall risk (as determined by history of falls, balance and gait performance, lower extremity strength, and physical conditions such as visual impairment and Parkinson's disease that increase the risk of falls) points to fear of falling as being excessive. Delbaere et al. ²⁷ found that community-dwelling residents who had low "physiologic" fall risk but high perceived fall risk were significantly more likely to have depressive symptoms, neurotic personality traits, and impaired executive functioning compared with persons whose perceived risk was congruent with physiologic risk.

The term "fear of falling" is often used interchangeably with low falls self-efficacy. Nevertheless, it is becoming clearer that fear of falling, although related to falls efficacy, is a distinct concept. ²⁸ Falls self-efficacy reflects an individual's cognitive appraisal of his or her abilities and has been found to be related to one's functional abilities. ²⁹ On the other hand, fear of falling is an emotional response that can be measured physiologically in threatening situations ³⁰ and is associated with neuroticism and trait anxiety. ^{31,32}

Fear of falling is common in community-dwelling seniors, with most studies reporting a prevalence of 25%–50%; about half of those who are fearful will curtail their activities as a

result.^{33,34} The incidence of fear of falling over a 2-year period was found to be 45% in a community sample and was associated with female gender, falls, gait abnormalities, and depressive symptoms³⁵ Fear of falling is persistent, with 80% of affected seniors continuing to report fear of falling over a 3-year follow-up.³⁶

Given the close relationship between depression and anxiety in late life, it is not surprising that depression is closely linked to excessive fear of falling. In hospitalized fallers who had moderate to severe fear of falling, 38% met criteria for a depressive disorder, compared with 4% of those who were not fearful: depressive disorder accounted for more of the explained variance in fear of falling than other known risk factors for this fear. Individuals with moderate to severe depressive symptoms are more likely to be severely afraid of falling than those without depression (OR: 2.74; 95% CI: 1.69–4.47). Depressive symptoms predict the persistence of fear of falling and whether someone will restrict their activity level. In a prospective study, activity restriction in the nondepressed was most strongly associated with physical factors such as balance, strength, and vision. In the depressed group, activity restriction was associated only with fear of falling, suggesting that psychological factors were more at play.

Fear of falling is associated with an increased risk of future falls, ³⁹ possibly through an effect on gait and balance. Fearful or cautious gait is a common gait disturbance in older adults. Anxious elders walk more slowly, take shorter strides, have a wider base, and have a longer double limb support time and higher gait variability. ^{40,41} Those who are most concerned about falling tend to make disproportionate adjustments to gait speed in response to postural threat. ³⁰ There is some evidence that a slowed gait is maladaptive and reduces, rather than improves, stability. ⁴² Fearful gait may improve when the fearful person feels more secure; for example, handholding, while not offering any objective support of gait, can temporarily decrease fear of falling with simultaneous improvement in gait. ⁴³ Balance and postural control are also affected by fear. Abnormal fear-related protective responses take different forms including stiffening and postural over adjustment. ^{44,45} Thus, while a certain amount of caution is appropriate for someone who is fall-prone, there is likely an individual optimal range of arousal and vigilance for falls.

ANTIDEPRESSANTS AND FALLS

Antidepressants are a commonly prescribed medication in older adults, in 9% of community-dwelling seniors to as high as 31% of nursing home residents. He is the has been associated with falls. A recent meta-analysis found that the odds ratio of falls with antidepressants was 1.68 (1.47–1.91), he is imilar to the risk associated with benzodiazepines and antipsychotics. These data are based on pharmacoepidemiologic studies, which are subject to "confounding by indication," that is confounding by the clinical condition for which the drug is prescribed. Notwithstanding this important caveat, risk of falls has been reported with tricyclic antidepressants and selective serotonin reuptake inhibitors (SSRIs); other specific antidepressants have not yet been studied. The highest risk of falls appears to be within the first few weeks after initiation of an antidepressant. There is little known about whether there are differences between individual medications in the SSRI class and whether there is a dose effect.

Multiple antidepressant-related adverse effects have been implicated in falls (Figure 1). In a study of paroxetine, 38% of subjects fell during the 21-week trial. Orthostatic changes in blood pressure during treatment and memory impairment at baseline were associated with falls. ⁴⁹ Hyponatremia, a common and potentially serious adverse event complicating the use of SSRIs in older adults, has been implicated in fractures in a small case—control study. ⁵⁰ Antidepressants may also directly impair postural control. Increased postural sway was noted in depressed patients in the first week of treatment with sertraline, when compared with nortriptyline and controls. ⁵¹ However, in a similar study, there was no change in balance over the course of 6 weeks of treatment with paroxetine or nortriptyline. ⁵²

From a clinical point of view, it can be difficult to weigh the risk of falls from untreated depression against the risk of falls associated with antidepressant medication. Unfortunately, there are no prospective controlled data available to offer guidance. In a small uncontrolled study, antidepressant treatment after 10 weeks improved both depressive symptoms and gait parameters, including gait speed, variability, asymmetry, and stride length.⁵³ However, this study did not directly assess for gait changes during the higher-risk early treatment period.

DEPRESSION, ANTIDEPRESSANTS, AND FRACTURES

SSRI antidepressants have been found to be associated with fragility fractures, more so than other classes of psychotropic medications.^{54,55} This association was first observed in a series of case–control studies using large administrative databases^{54–56} but has since been replicated with prospective cohort studies.^{57,58} In a multivariate analysis, controlling for such factors as depressive symptoms, falls history, visual and cognitive impairment, comorbidities, postural hypotension, other medications, alcohol and smoking, the risk of fragility fracture over 8 years with current SSRI use was found to be 2.35 (1.3–4.2).⁵⁷

SSRIs also have been found to have a dose relationship with fractures.^{54,58} Similar to the risk for falls, the risk of fracture associated with SSRI use is the highest in the first 2 weeks of treatment (OR: 6.30; CI: 2.65–14.97) but remains elevated with continuous antidepressant use beyond the first month of use (OR: 1.32; CI: 1.19–1.48).⁵⁹ This pattern is in contrast to the risk of fractures with tricyclic antidepressants, which is highest with a new prescription, but decreases significantly with continuous use.⁵⁶

Older adults are thus at highest risk for falls and fractures shortly after starting an SSRI antidepressant but break bones at a higher rate throughout their treatment. The role of serotonin in bone metabolism may be a mechanism for this long-term association between fractures and SSRI use. Serotonin transporters are known to be present on bone cells, and central serotonin has a role in regulating bone mass through sympathetic outflow. In animal studies, the disruption of the serotonin transporter gene decreases bone density, as does administering SSRI medication. In date, clinical evidence for an association between SSRIs and bone loss is striking but somewhat inconsistent—while some have observed a significant decrease in bone mineral density in patients taking SSRIs, this has not been confirmed in other large studies.

As is the case with studies of antidepressants and falls, studies of SSRIs, bone loss, and fractures are subject to "confounding by indication." Depression itself has been associated with decreased bone mineral density⁶³ and has also been associated with fractures.⁶⁴ Multiple factors may be involved in the loss of bone density and fractures in depression, including the effects of inactivity, hypercortisolemia, inflammatory processes associated with depression, smoking, and alcohol abuse. Interestingly, the only study to specifically examine the effect of treatment of depression with an SSRI on bone turnover (albeit in premenopausal women) found that improvement in severity of depression was significantly associated with suppression of markers of bone turnover, although whether this finding translates to a reduced risk of fracture is not known.⁶⁵ Other uses for SSRI antidepressants may also confound this research. In particular, SSRIs are being more frequently used in cognitively impaired and institutionalized older adults,⁴⁶ presumably for neuropsychiatric symptoms of dementia. Behaviorally disturbed individuals with dementia are at increased risk of fractures.

Fractures themselves are associated with the development of depression. Hip fractures are a particular threat to independence and well-being, leading to institutionalization in 20%–30% and with a 1-year mortality rate of 26%.⁶⁶ In the period after a hip fracture, 15% of older adults meet criteria for major depression, and half will have elevated depressive symptoms. ⁶⁷ In some individuals, a high level of distress immediately after the injury improves over time.⁶⁸ In a smaller proportion, depressive symptoms seem to arise as their recovery plateaus and they are faced with enduring deficits.⁶⁹

Depression is associated with a slower recovery, poorer functional status, and higher levels of disability after a hip fracture. When depressed, persons who have suffered a hip fracture are less likely to participate in rehabilitation activities and recover more slowly.⁷⁰ Improvement in level of disability during rehabilitation is associated with improved mood.⁷¹

Age, medical comorbidity, level of disability before and after the fracture, apathy, delirium, cognitive impairment, and poor social support are all risk factors for the development of depression after hip fracture.⁶⁷ Use of an antidepressant at baseline, perhaps an indicator of a history of depression, is also a risk factor.⁶⁷ Gene polymorphisms in serotonin transporter and 5HT-1A receptor, markers of vulnerability to stress, have also been implicated in the development of depression and impaired function after a hip fracture.^{72,73} The presence of depressive symptoms prefracture may also be a risk factor for loss of functional status.⁷⁴

DEPRESSION, FEAR OF FALLING, FALLS PREVENTION, AND EXERCISE

Preventative programs for falls are now widespread, often incorporating some or all of the components of falls risk assessment, education, and exercise to improve balance and strength. A recent meta-analysis reported that fall-prevention programs are effective in reducing falls by an average of 14% over at least 5 months of observation. An earlier Cochrane Review, however, found significant heterogeneity in the outcomes of falls-prevention interventions, with some randomized controlled trials reporting a 30% reduction in the rate of falls.

Exercise has been found to have modest short-term benefit in the treatment of mild-moderate depressive disorder, including older individuals. Theorem fall-prevention programs, which usually incorporate an exercise component, have not shown a beneficial effect on depression rating scale scores. Although clinically significant depressive symptoms are common in community-dwelling fallers, they tend to be less frequent in clinical trials of fall-prevention programs; this may represent a selection bias in individuals presenting to and participating in these programs or studies. Thus, the apparent lack of benefit of fall-prevention programs on depression may be due to the paucity of clinically depressed persons in the studies that have examined this question. In addition to a selection bias, there is also the issue of program non-adherence and dropouts; individuals with depression and/or fear of falling are less likely to adhere to a falls or exercise program, and they drop out at a higher rate.

Cognitive-behavioral approaches tailored to fear of falling have been designed and implemented with some success. Through cognitive restructuring and behavioral changes, these programs aim to reduce fear of falling by improving self-efficacy and the sense of control over falling. This approach has shown improvement in fear of falling and falls efficacy, although mixed results in preventing falls and increasing activity levels. 81,82 Unfortunately, there have not been any studies examining the effect of these interventions on concurrent depressive symptoms. Given the fact that antidepressant medications have been associated with an increased risk of falls, and the depression associated with fear of falling is often of mild-moderate severity, further research in psychotherapeutic interventions is warranted.

DEPRESSION AND FALLS: CLINICAL IMPLICATIONS

An overall assessment for falls risk is important when starting psychotropic medication in fall-prone individuals. This would include an assessment of other falls promoting medications, checking for drug interactions, observing gait and tone, and inquiring about falls history. Given that most falls occur early in treatment and may potentially be doserelated, SSRI medications should be started at a low dose and increased slowly in older adults to minimize their effect on falls. Cognitive impairment, orthostatic hypotension, extrapyramidal effects, and hyponatremia should be monitored during treatment. Given the possibility of skeletal changes with long-term use of SSRIs, it is important for the risk—benefit of antidepressant treatment to be evaluated on an ongoing basis.

To date, there have been no recommendations for osteoporosis monitoring and treatment in individuals prescribed SSRI medications beyond the usual clinical guidelines. However, individuals with depression make less use of preventative services. ⁸³ No studies have specifically looked at adherence to osteoporosis screening and treatment in depressed older adults. When prescribing an SSRI, it is therefore useful to inquire about the older patient's adherence with osteoporosis and fracture-prevention guidelines. These vary internationally but tend to include a recommendation for screening dual-energy x-ray absorptiometry in those older than 65 years, the use of bisphosphonates in individuals with diagnosed osteopenia or osteoporosis, and repeat dual-energy x-ray absorptiometry scans every 2 years. ⁸⁴ Recommended lifestyle modifications include adequate elemental calcium (1000 mg/day)

and vitamin D (400–800 IU/day), for which supplements are often required, stopping smoking, decreasing caffeine intake, and regular weight-bearing exercise.

FUTURE DIRECTIONS

As this review indicates, research evidence suggests that both depression and antidepressant medication are associated with falls and fractures. Moreover, while exercise and cognitive behavioral therapy have benefit in treating mild-moderate depression in the general older adult population, there are currently no data pertaining to the efficacy and feasibility of these interventions in persons who both are at high risk of falls and are clinically depressed. Thus, clinicians currently find themselves between Scylla and Charybdis in deciding on the optimal management of this group of patients. Confounding biases are arguably the main limitation in interpreting pharmacoepidemiologic data pertaining to the contribution of antidepressant medication to falls and fractures. It is unlikely that adequately powered randomized controlled trials that are specifically focused on the use of antidepressants in persons at high risk of falls will be conducted. We believe that incorporating falls as an adverse outcome into clinical trials that study antidepressants in older persons should be standard practice, but biases in the types of patients selected for these studies (which typically focus on cognitively intact, medically stable, young-old patients without comorbid neurologic conditions) will likely mean that the risk of falls will be low. A more feasible line of research will be to examine the effect of antidepressants on sophisticated measures that are valid "markers" for increased risk of falls and fractures, in well-designed RCTs that not only account for potential confounding variables but also explore the interaction between the antidepressant and these variables. This line of research should examine not only whether antidepressant use per se independently predicts risk of falls and fractures but also whether and how the method of use of antidepressants, such as starting dose, speed of dose titration, and concomitant use of anxiolytics and hypnotics in the early stage of treatment, affects the risk of falls.

There is also a need for research in nonpharmacologic interventions. Given that the presence of a depressive disorder and/or severe fear of falling may interfere with a person attending a falls-prevention program, cost-effective home-based interventions for depressed and anxious older fallers warrant investigation. There is also the need to determine whether the presence of clinically significant depressive symptoms has a moderating effect on the treatment of fear of falling and whether depression contributes to persistence in fear of falling, despite improvement in falls efficacy.

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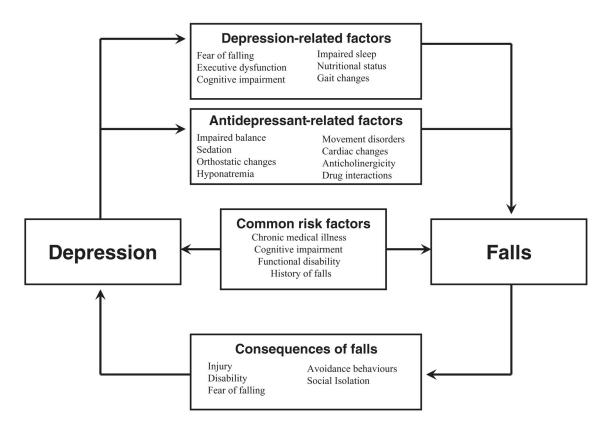


FIGURE 1.

The association between depression and falls involves factors related to the symptoms of depression, the treatment of depression, and the effect of falls on mood. The interaction is further complicated by common risk factors for falls and depression in older adults.

TABLE 1

Practice Points

Depression and fear of falling are independent risk factors for falls, each mediated through multifactorial pathways.

Antidepressant medications are associated with a 70% increased risk of falls; SSRIs are associated with risk of fractures. These findings are, however, limited by the possibility of confounding biases, such as the reason for initiation of the antidepressant.

Antidepressant medications are indicated to treat moderate to severe depression in fallers, but be wary of the potential increased risk of falls and prescribe accordingly (e.g., low starting dose, gradual titration, avoid more than one psychotropic at a time whenever possible, monitor orthostatic blood pressure and serum sodium).

Consider exercise, particularly Tai Chi, and cognitive-behavioral therapy for the first-line treatment of mild depression in older fallers.

When treating the older depressed patient, inquire about his or her adherence with osteoporosis and fracture-prevention guidelines.