Association of stressful life events with incident falls and fractures in older men: the Osteoporotic Fractures in Men (MrOS) Study

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Abstract

Background: small, retrospective studies suggest that major life events and/or sudden emotional stress may increase fall and fracture risk. The current study examines these associations prospectively.

Methods: a total of 5,152 men aged ≥65 years in the Osteoporotic Fractures in Men study self-reported data on stressful life events for 1 year prior to study Visit 2. Incident falls and fractures were ascertained for 1 year after Visit 2. Fractures were centrally confirmed.

Results: a total of 2,932 (56.9%) men reported ≥1 type of stressful life event. In men with complete stressful life event, fall and covariate data (n = 3,949), any stressful life event was associated with a 33% increased risk of incident fall [relative risk (RR) 1.33, 95% confidence interval (CI) 1.19–1.49] and 68% increased risk of multiple falls (RR = 1.68, 95% CI = 1.40–2.01) in the year following Visit 2 after adjustment for age, education, Parkinson’s disease, diabetes, stroke, instrumental activities of daily living (IADL) impairment, chair stand time, walk speed, multiple past falls, depressive symptoms and antidepressant use. Risk increased with the number of types of stressful life events. Though any stressful life event was associated with a 58% increased age-adjusted risk for incident fracture, this association was attenuated and no longer statistically significant after additional adjustment for total hip bone mineral density, fracture after age 50, Parkinson’s disease, stroke and IADL impairment.

Conclusions: in this cohort of older men, stressful life events significantly increased risk of incident falls independent of other explanatory variables, but did not independently increase incident fracture risk.

Keywords: accidental falls, fractures, life change events, psychological stress, prospective studies, aged, male, men, older people

Introduction

One-third of community-dwelling adults aged ≥65 years fall at least once annually, half of whom have multiple falls [1–3]. Two to six percent of falls result in fractures [1–4].

While demographics, medical conditions, physical function, medications and sensory impairments are established predictors of falls [5–7] and fractures [8, 9], limited data suggest that stressful life events also may predict these outcomes [10, 11].
Many studies have examined the association between psychological stress and adverse health outcomes. According to the allostatic load model, environmental stress may trigger a neurohormonal response, leading to physiological dysregulation and adverse health outcomes [12]. However, perceived stress and physiological stress response may vary according to individual and social/environmental factors. Some but not all prospective studies report a positive association between stressful life events, such as death of a spouse, job loss or change in residence, and incident cardiovascular disease or mortality [13–17]. Numerous indices of allostatic load, combining inflammatory and metabolic biomarkers, have predicted increased risk of impaired physical function [12]. Two retrospective studies, including one conducted in long-term care residents, reported that major life events and sudden emotional stress increased risk of falls and fractures [10, 11].

We are unaware, however, of any studies that prospectively examined the effect of stressful life events on falls and fractures in community-dwelling adults, while effectively accounting for important confounding variables, including comorbid conditions, and measures of physical function and social integration. This, therefore, is the aim of the current study.

### Methods

#### Participants

A total of 5,994 community-dwelling men aged ≥65 years enrolled in the Osteoporotic Fractures in Men (MrOS) study at six US sites (March 2000 to April 2002): Birmingham, AL; Minneapolis, MN; Palo Alto, CA; Monongahela Valley near Pittsburgh, PA; Portland, OR and San Diego, CA. Exclusion criteria included inability to walk without assistance from another person or bilateral hip replacement. Written informed consent was obtained from all participants. Institutional review boards at all centers approved the study protocol, and procedures were conducted in accordance with the ethical standards for human subjects research described in the Helsinki Declaration. MrOS study design and recruitment are detailed elsewhere [18, 19].

A total of 5,152 MrOS participants participated in a second study visit (March 2005 to May 2006) and reported complete data on a history of stressful life events in the prior year (fracture cohort). A further subset of 4,981 reported complete data on incident falls for 1 year after the second study visit (fall cohort) (see Supplementary data available in Age and Ageing online, Appendix Figure S1).

#### Stressful life events

At MrOS study Visit 2, participants were asked their marital status, and, if widowed, their spouse’s date of death. In addition, they were asked to report occurrence of any of several stressful life events in the past year: serious illness or accident of wife or partner; death of other close relative or close friend; separation from child, close friend or other relative on whom participant depends for help; loss of pet; given up important hobby or activity; serious financial trouble and/or move or change in residence. Because of questionnaire wording, each type of stressful life event could be counted only once per participant.

### Falls and fractures

Following study Visit 2, all MrOS participants (or, if deceased, participant’s contacts) were queried by mail every 4 months for 1 year regarding incident falls or fractures. Overall response rates exceeded 99%, including 97% complete ascertainment for falls. Fractures were confirmed by central review of radiographic reports.

#### Covariables

Race and education were reported at MrOS baseline. Other covariables were first assessed, or were updated, at study Visit 2. Physical activity was measured using the Physical Activity Scale for the Elderly (PASE) [20]. Medical history included self-reported comorbid conditions, fractures since age 50, and number of falls in the previous year. Depressive symptoms were assessed using the 15-item Geriatric Depression Scale [21]. A medication inventory was used to classify medications used within the preceding 30 days into categories by their ingredients, including antidepressant and other psychotropic medications [22]. Health status was assessed as impairment in instrumental activities of daily living (IADLs). Weight was measured using a balance beam or digital scale. Participants were timed walking 6 m taking ≤2 deviations outside a 20-cm narrow path. Time to complete five chair stands also was measured. Total hip bone mineral density (BMD) (g/cm²) was measured with dual energy X-ray absorptiometry (QDR 4500 W, Hologic, Inc, Waltham, MA, USA).

We calculated change between MrOS baseline and Visit 2 for weight, self-reported co-morbid conditions, PASE score, IADL impairment, walk speed and chair stands. We also estimated scores at Visit 2 for several measures of social integration [23] (living arrangement [alone, with spouse/partner, with other], social network score [1 point each for having ≥3 living children versus ≤2, and for having ≥1 confidants versus none], and social engagement score [1 point each for working, caregiving, and participating in non-religious and religious social groups]) and change in these scores compared with MrOS baseline.

#### Statistical analyses

For each participant, the number of types of stressful life events was categorized as any, none, one, two, three or more, or as the sum of types of stressful events. Differences in characteristics between participants with and without any stressful life event were assessed using Chi-square tests for dichotomous variables and t tests for continuous variables.

For 1 year following study Visit 2, incident falls were categorized as ≥1 versus none, and ≥2 versus zero or one. Risks
of ≥1 incident falls, multiple incident falls and incident fracture were assessed using log binomial regression or Poisson regression with robust variance estimators, with results expressed as relative risks (RRs) with 95% confidence intervals (CIs) [24]. All models were adjusted for age. Additional covariables were included if, after age-adjustment, they were significantly \( (P < 0.05) \) associated with any stressful life event, and with incident falls (fall models) or incident fracture (fracture models). To investigate the impact of recent changes in health status on the association between stressful life events and falls, measures of change between MrOS baseline and Visit 2 in weight, physical activity, IADL impairment, walk speed, chair stands and newly reported comorbid conditions were separately added to multivariable models and included if statistically significant \( (P < 0.05) \).

We next examined whether several individual measures of social integration (i.e. living arrangement, social network, social engagement) or changes in these individual measures moderated the association between stressful life events and falls. We considered a variable a moderator if its interaction term was statistically significant in multivariable models \( (P < 0.05) \) [23].

Finally, to explore the association between different types of stressful life events and fall risk, separate age-adjusted models were created for each type of stressful life event.

All analyses were performed with SPSS, version 17 (Chicago, IL, USA).

**Results**

Of 5,152 MrOS participants with complete stressful life events data in the year before study Visit 2 (fracture cohort), 2,932 (56.9%) reported ≥1 type of stressful life event, including 37.1% with one, 14.1% with two and 5.7% with ≥3 types of events (Table 1). Frequency of stressful life events was similar in the fall cohort (data not shown). Compared with other MrOS enrollees not included in the fracture and fall cohorts, respectively, those in these cohorts were younger, more educated, had less IADL impairment, more physical activity, better physical function and fewer had comorbid conditions or past fractures (data not shown).

Within the fracture and fall cohorts, compared with men with zero stressful events, those with ≥1 stressful life event were older, more often reported comorbid conditions and past fractures, had more IADL impairment and had worse physical function (see Supplementary data available in *Age and Ageing* online, Appendix Table S1). Compared with men included in multivariable-adjusted fall models, those excluded because of missing covariable data had poorer self-reported health (data not shown).

**Stressful life events and falls**

Among 4,981 men with complete stressful life event and falls data, 27.7% fell and 14.7% fell multiple times during the year after Visit 2. Among men with 0, 1, 2 and ≥3 types of stressful life events, incident falls occurred in 21.9, 29.9, 35.5 and 39.9%, respectively.

In age-adjusted analyses, any stressful life event was associated with a 41% increase in risk for incident fall (RR = 1.41, 95% CI = 1.28–1.55) and a nearly 2-fold increase in risk for multiple incident falls (RR = 1.87, 95% CI = 1.61–2.18) (Table 2). Further adjustment for education, Parkinson’s disease, diabetes, stroke, IADL impairment, chair stand time, walk speed, multiple past falls, depressive symptoms and antidepressant use modestly attenuated these results. Results also suggested dose–response relationships between the number of types of stressful life events and fall risk. Effect estimates were not altered by further adjustment for measures of change between MrOS baseline and Visit 2 in weight, physical activity, IADL impairment, walk speed, chair stands, or newly diagnosed comorbid conditions, nor by adjustment for any social integration variables (data not shown).

However, the interaction between social network score and stressful life events was significant \( (P = 0.019) \) when added to the final multivariable model predicting incident falls. Stratified analyses suggested that fall risk associated with stressful life events may be inversely related to social network score, from RR = 2.18 (95% CI = 1.24–3.82) in those with a score of 0, to RR = 1.42 (95% CI = 1.20–1.68) and RR = 1.18 (95% CI = 1.01–1.38) in those with scores of 1 and 2, respectively.

Age-adjusted risk for incident falls appeared increased for most individual types of stressful life events. (see Supplementary data available in *Age and Ageing* online, Appendix Table S2) Few men experienced the death of their wife or partner.

**Stressful life events and fractures**

During up to 1 year after Visit 2, 109 (2.1%) men experienced ≥1 incident fractures, including 75 (2.6%) men with ≥1 types of stressful life events and 34 (1.5%) men with no stressful life events. Any stressful life event was associated with a 58% increase in age-adjusted risk for incident clinical

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Table 1. Proportion of men with stressful life events in the year prior to study Visit 2

<table>
<thead>
<tr>
<th>Stressful life event type</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any stressful event</td>
<td>2,932 (56.9)</td>
</tr>
<tr>
<td>1 type of stressful event</td>
<td>1,913 (37.1)</td>
</tr>
<tr>
<td>2 types of stressful events</td>
<td>727 (14.1)</td>
</tr>
<tr>
<td>3+ types of stressful events</td>
<td>292 (5.7)</td>
</tr>
<tr>
<td>Wife/partner death</td>
<td>75 (1.5)</td>
</tr>
<tr>
<td>Wife/partner illness/accident</td>
<td>915 (17.8)</td>
</tr>
<tr>
<td>Death other close relative/friend</td>
<td>1,809 (35.1)</td>
</tr>
<tr>
<td>Separated from child, friend or relative you depend on</td>
<td>134 (2.6)</td>
</tr>
<tr>
<td>Loss of important activity/hobby</td>
<td>670 (13.0)</td>
</tr>
<tr>
<td>Moved/changed residence</td>
<td>281 (5.5)</td>
</tr>
<tr>
<td>Serious financial trouble</td>
<td>166 (3.2)</td>
</tr>
<tr>
<td>Loss of pet</td>
<td>281 (5.5)</td>
</tr>
</tbody>
</table>

*Results for 5,152 men who completed the stressful life events questionnaire at study Visit 2.*
Table 2. Association of stressful life events with risk of incident falls in 1 year after study Visit 2, RR (95% CI)

<table>
<thead>
<tr>
<th>Model</th>
<th>No stressful events</th>
<th>Any stressful event</th>
<th>1 Stressful event type</th>
<th>2 Stressful event types</th>
<th>3+ Stressful event types</th>
<th>Sum of types of stressful events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incident falls*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.0 (ref.)</td>
<td>1.41 (1.28–1.55)</td>
<td>1.11 (0.97–1.28)</td>
<td>1.39 (1.21–1.60)</td>
<td>1.71 (1.49–1.95)</td>
<td>1.13 (1.10–1.15)</td>
</tr>
<tr>
<td>MV1b</td>
<td>1.0 (ref.)</td>
<td>1.38 (1.23–1.55)</td>
<td>1.14 (0.97–1.34)</td>
<td>1.39 (1.18–1.63)</td>
<td>1.66 (1.41–1.95)</td>
<td>1.12 (1.08–1.16)</td>
</tr>
<tr>
<td>MV2c</td>
<td>1.0 (ref.)</td>
<td>1.33 (1.19–1.49)</td>
<td>1.13 (0.96–1.32)</td>
<td>1.35 (1.15–1.59)</td>
<td>1.46 (1.24–1.72)</td>
<td>1.08 (1.04–1.12)</td>
</tr>
<tr>
<td>Incident multiple falls*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td>1.0 (ref.)</td>
<td>1.87 (1.61–2.18)</td>
<td>1.29 (1.02–1.62)</td>
<td>1.87 (1.50–2.33)</td>
<td>2.57 (2.07–3.18)</td>
<td>1.20 (1.16–1.24)</td>
</tr>
<tr>
<td>MV1b</td>
<td>1.0 (ref.)</td>
<td>1.80 (1.50–2.16)</td>
<td>1.26 (0.97–1.64)</td>
<td>1.72 (1.32–2.24)</td>
<td>2.28 (1.76–2.96)</td>
<td>1.18 (1.12–1.24)</td>
</tr>
<tr>
<td>MV2c</td>
<td>1.0 (ref.)</td>
<td>1.68 (1.40–2.01)</td>
<td>1.21 (0.94–1.57)</td>
<td>1.62 (1.25–2.10)</td>
<td>1.85 (1.43–2.40)</td>
<td>1.13 (1.07–1.19)</td>
</tr>
</tbody>
</table>

RR, relative risk; CI, confidence interval; IADL, instrumental activities of daily living; MV1, multivariable model 1; MV2, multivariable model 2.

*aResults for any stressful event and falls available for 4,981 participants in age-adjusted models, 3,977 in MV1 models and 3,949 in MV2 models. Results for sum of types of stressful events and number of stressful events available for 4,959 participants in age-adjusted models, 3,966 in MV1 models and 3,933 in MV2 models.

bMV1 models adjusted for age, education, Parkinson’s disease, stroke, IADL impairment, chair use and time spent on the toilet.

cMV2 models adjusted for MV1 variables as well as for multiple falls in the year before V2, depressive symptoms, and antidepressant medication use.

Table 3. Association of stressful life events with risk of incident clinical fracture in 1 year after study Visit 2, RR (95% CI)

<table>
<thead>
<tr>
<th>Model</th>
<th>Any stressful event</th>
<th>Sum stressful event types</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>1.58 (1.05–2.36)</td>
<td>1.04 (0.91–1.18)</td>
</tr>
<tr>
<td>MV1b</td>
<td>1.32 (0.82–2.13)</td>
<td>1.06 (0.90–1.25)</td>
</tr>
<tr>
<td>MV2c</td>
<td>1.12 (0.72–1.74)</td>
<td>0.95 (0.81–1.11)</td>
</tr>
</tbody>
</table>

RR, relative risk; CI, confidence interval; BMD, bone mineral density; IADL, instrumental activities of daily living; MV1, multivariable model 1; MV2, multivariable model 2.

aMV1 models adjusted for age, V2 total hip BMD, fracture after age 50, Parkinson’s disease, stroke and IADL impairment.

bMV2 models additionally adjusted for multiple falls in the year before V2, depressive symptoms and antidepressant medication use.

cMV2 models adjusted for MV1 variables as well as for multiple falls in the year before V2, depressive symptoms, and antidepressant medication use.

fracture (Table 3). Results were attenuated and no longer statistically significant after additional adjustment for BMD, fracture after age 50, Parkinson’s disease, stroke and IADL impairment.

Discussion

In this cohort of community-dwelling older men, stressful life events were independently associated with increased risk of future falls. Fall risk increased further for men with more types of stressful events. Exploratory analyses suggested that fall risk subsequent to stressful events may be moderated by social network. By comparison, the age-adjusted association of stressful life events with increased risk of incident fractures did not appear independent of other explanatory factors.

To our knowledge, this is the first prospective study to examine the association between stressful life events and risk of incident falls in community-dwelling older adults and to account for multiple confounders of this association. However, our finding of no independent association between stressful life events and risk of fracture contradicts an earlier case–control study [11]. In the prior study, fracture cases had significantly more stressful events in the past year than did control subjects, but the control group was younger, and results were not adjusted for comorbidities, health status or BMD. Further, because stressful events data were collected after fracture, these earlier results were more prone to recall bias. In another study, elderly long-term care residents who recently had undergone the major life event of changing residence were at increased falls risk [25]. Although our results could be interpreted as validating this earlier study, since the prior study did not account for possible confounders, it is uncertain whether its findings can be attributed to the life event itself.

The association between stressful life events and falls observed in the current study appears moderate in strength, similar in magnitude to that associated with sedative use or urinary incontinence, but smaller than the risk associated with gait or cognitive impairment [5]. However, the mechanism connecting stressful life events to falls is uncertain. One possible explanation, suggested by the allostatic load model, is that stressful life events trigger a neuroendocrinological response, causing stress hormone release and multi-system physiological dysregulation, leading to adverse health outcomes such as falls [12]. Some data suggest that inflammation, a potential indicator of physiological stress, could lead to loss of muscle mass [26] and impaired physical function. Alternatively, sudden emotions, possibly triggered by a stressful life event, could transiently impact balance or visual attention, leading to a fall [10]. Some studies also suggest that stressful life events might lead to worsened clinical outcomes by adversely impacting self-care behaviour [27, 28]. Our exploratory finding that fall risk associated with stressful life events appeared greater in men with a lower social network score suggests that stressful life events could lead to increased social isolation, which plausibly could lead to decreased physical activity, strength and balance, thereby increasing fall risk. Though we found no evidence that results were impacted by changes in physical activity or function between MrOS baseline and Visit 2, we had no data on changes in these measures between the stressful life event and MrOS Visit 2 to more directly investigate this pathway.

This study has numerous strengths. It provides the strongest evidence to date supporting stressful life events as a risk factor for falls. As a prospective cohort study in which participants were recruited from population-based sources, were...
not selected on the basis of stressful life event history, and in which stressful life events were ascertained prior to follow-up for falls and fractures, results regarding the association between stressful life events and incident falls and fractures were less subject to selection bias than those from prior studies. Additional strengths included the nearly complete follow-up for incident falls and fractures, and the accounting for a comprehensive set of possibly confounding variables.

However, this study had several limitations. First, because recall of stressful life events is retrospective and stressful life events and falls are self-reported, both are susceptible to error. Secondly, because the timing of discrete stressful life events was not precisely known, analyses were limited in their ability to estimate the duration of their effect on falls. Thirdly, self-reported life events may not be equally stressful to all individuals, and no data were available to estimate participants’ resiliency or coping style and no measures of perceived stress or physiological stress were available to correlate with these life events. Fourthly, this study had limited power to examine the association between stressful life events and hip fractures, to examine dose relationships between stressful life events and fractures and to examine associations of specific types of stressful life events with falls and fractures. Fifthly, despite accounting for a comprehensive set of possibly confounders, we cannot exclude the possibility of residual confounding. For example, because of the timing of data collection, we could not account for whether changes in psychotropic medication use in the year after MrOS Visit 2 impacted risk of falls during that period. Finally, because men included in these analyses were community-dwelling, largely healthy men, even compared with other MrOS participants, study findings are prone to selection bias and may not apply to other populations.

In conclusion, we found that within this prospective cohort of community-dwelling older men, those with stressful life events in the past year had a significantly increased risk of falls and multiple falls during the subsequent year. Future studies are needed to confirm these findings and to investigate the mechanism that may underlie this association. Additional studies may explore whether clinical screening of older men with recent stressful life events for fall reduction interventions and/or a social network intervention will reduce falls.

Key points
- A recent history of one or more stressful life events increased risk of future falls in older, community-dwelling men, independent of multiple confounding factors.
- Though the association between stressful life events and falls observed in the current study appears moderate in strength, the mechanism is uncertain.
- Stressful life events did not independently increase incident fracture risk.

Conflicts of interest
None declared.

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Supplementary data
Supplementary data mentioned in the text is available to subscribers in Age and Ageing online.

References


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