Keywords:
Falls
Fractures
Dementia
Hospital admission
Alzheimer's disease
Mortality

ABSTRACT

Objectives: Investigate predictors of falls and fractures leading to hospitalization in a large cohort of people with dementia.

Design: A retrospective cohort study.

Setting and Participants: People with diagnosed dementia between January 2007 and March 2013, aged >65 years, were assembled using data from the Maudsley Biomedical Research Centre Case Register, from 4 boroughs in London serving a population of 1.3 million people.

Measures: Falls and/or fractures leading to hospitalization were ascertained from linked national records. Demographic data, cognitive test scores, medications, and symptom and functioning scores from the Health of the Nation Outcome Scales (HoNOS65+) were modeled in multivariate survival analyses to identify predictors of falls and fractures.

Results: Of 8036 people with dementia (63.9% female), 2500 (31.1%, incidence rate 125.5 per 1000 person-years) had a fall during a mean follow-up of 2.5 years and 1437 (17.7%, incidence rate 65.5 per 1000 person-years) had a fracture. In multivariable models, significant predictors of falls were increased age, female gender, physical health problems, previous fall or fracture, vascular dementia vs Alzheimer's disease, higher neighborhood deprivation, noncohabiting status, and problems with living conditions. Ethnic minority status was protective of falls (e.g., Caribbean/Asian ethnicity). Medications (including psychotropic and antipsychotics), neuropsychiatric symptoms, cognitive (Mini-Mental State Examination scores), or functional problems did not predict hospitalized falls. Predictors of fractures were similar to those predicting falls.

Implications: Over an average of 2.5 years, a third of people with dementia had a fall leading to hospitalization, necessitating action in clinical practice. Clinicians should consider that besides established demographic and physical health–related factors, the risk of hospitalization due to a fall or fractures in dementia is largely determined by environmental and socioeconomic factors. Interestingly, our data suggest that neuropsychiatric symptoms, cognitive status, functioning, or pharmacotherapy were not associated with falls/fractures.

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Falls are common in older age and associated with morbidity, reduced quality of life, increased risk of admission to long-term care facilities, health care expenditure, and premature mortality. Consequently, understanding the predictors of falls and fractures is a global health priority. Although it is established that reduced global cognition, increasing cognitive impairment, and dementia are associated with an increased risk of falls, less is known about the predictors of falls and fractures, specifically among people with confirmed dementia.

A systematic review with a search date of more than 10 years ago identified across 6 studies that motor impairments, impaired vision, type and severity of dementia-related behavioral disturbances, functional impairments, fall history, neuroleptics, and low bone mineral density were key risk factors for falls. A more recent systematic review confirmed the earlier risk factors and also found mixed results for sociodemographic risk factors, while noting that psychotropic medication (particularly benzodiazepines and antipsychotics) and orthostatic hypotension were associated with an increased risk of falls. Although these comprehensive systematic reviews have advanced the field, a number of limitations persist. First, no study has been conducted in a sample of more than 300 people with dementia, which raises questions about the generalizability of the earlier research on risk factors of falls. Second, very few studies with an adequate sample size have investigated how risk for falls varies by dementia subtype. Third, there is a lack of representative information on the respective risk for falls from commonly used medications in dementia such as benzodiazepines, anticholinergics, and cholinesterase inhibitors. Fourth, although fractures are known to be common in people with dementia and associated with adverse outcomes in this population, including premature mortality, the predictors of fractures are unclear.

Therefore, we conducted a representative cohort study investigating predictors of falls and fractures leading to hospitalization among people with clinically diagnosed dementia.

Methods

Study Setting and Data Source

A retrospective observational study was conducted using data from the South London and Maudsley NHS Foundation Trust (SLaM) Biomedical Research Centre (BRC) Case Register. SLaM is one of Europe’s largest mental health and dementia care providers, serving a geographic catchment of 4 South London boroughs (Lambeth, Lewisham, Southwark, and Croydon) with a population in excess of 1.3 million people. Data for the current study were captured from the Clinical Record Interactive Search (CRIS) application, which enables an anonymized version of SLaM’s electronic health record to be accessible for research projects within a robust and patient-led governance framework. The SLaM BRC Case Register has been described in detail and has supported a range of studies, including several longitudinal cohort studies of dementia and related mental disorders of later life. SLaM caters for most mental health and dementia care provided in this catchment area covering 1.3 million people, specifically the case register; includes representative data on people with mental health diagnoses from 4 London Boroughs; and is the largest electronic health record of mental health services in Europe. Data are currently archived in CRIS on more than 300,000 cases with a range of mental disorders, and the database has full approval for secondary analysis (Oxford Research Ethics Committee C, reference 08/H0606/71-5). Data from CRIS have been extensively supplemented through natural language processing applications using Generalised Architecture for Text Engineering (GATE) software, applying information extraction techniques to derive structured information from the extensive text fields held in the mental health record.

Participants

All SLaM patients receiving an outpatient diagnosis of dementia, coded according to ICD-10 criteria, between January 1, 2007, and March 31, 2013, were included in the current analysis. The first recorded dementia diagnosis was grouped by recorded ICD-10 code as follows: Alzheimer’s disease (F00), vascular dementia (F01), and dementia in other diseases (F02; which includes Lewy body dementias). If both Alzheimer’s disease and vascular dementia were recorded at the time of the first dementia diagnosis, they were recorded as mixed dementia. To avoid bias arising from dementia diagnoses made during general hospital inpatient stays when physical illness impedes the cognitive assessment, patients receiving care from SLaM General Hospital Liaison services within a 6-month period before and after dementia diagnosis date were not included in the analysis. SLaM patient records have been linked with Hospital Episode Statistics, which were available until March 2013. Information governance and data linkages are described in detail elsewhere.

Falls and Fractures Data (Outcome)

The primary outcome was a hospitalized fall and/or fracture from general hospital records. An admission was considered due to a fall and/or fracture if the relevant ICD-10 code was recorded as any discharge diagnosis. ICD-10 codes applied to ascertain falls were W00-W19 and fractures M80-M84, M907, S02, S12, S42, S52, S62, S72, S82, S92, S22, T02, T08, T10, T12X, T902, T911, T912, and T921. The censoring point for follow-up was either the first fall or fracture, death, or March 31, 2013 (end of time period for data collection).

Predictors

A range of measurements were extracted from CRIS and all independent variables (covariates) were derived from information recorded closest to the date of the first recorded dementia diagnosis in the records, and this first dementia diagnosis date was applied as the “index date” for all analyses. Demographic information extracted included age, gender, and index of multiple deprivation (IMD) for the neighborhood of residence for the Lower Super Output Area at the time of diagnosis. The IMD has previously been used in CRIS and takes into account area-level deprivation from Census data across several domains including income, employment, health, education, barriers to housing and services, living environment, and crime. We also used information from the Mini-Mental State Examination (MMSE) score at the time of diagnosis. Marital/cohabiting status was classified into cohabiting (civil partnership, married, cohabiting) and noncohabiting (single, divorced, civil partnership dissolved, widowed, separated) groups. Recorded ethnicity was extracted from structured fields and grouped into the following categories: white British, Irish, other white background, African, Caribbean, South Asian, and other.

Mental and physical well-being, as well as functional status, were determined from the Health of the Nation Outcome Scales (HoNOS 65+), which are routinely administered in UK mental health services and recorded as structured data on the electronic health record. Scores for each item range from 0 (no problem) to 4 (severe problem), and we extracted scores relating to overactive or aggressive behavior, nonaccidental self-injury, problem-drinking or drug taking, hallucinations or delusions, depressed mood, physical illness or disability, relationship problems, activities of daily living (ADL) problems, living conditions, and occupational and recreational activities, where these scales were completed within 6 months before or after the index date. To ease analysis and interpretation, we dichotomized the scores into “no or mild problem” (score 0-1) and “problem present” (score 2-4). We further used hospitalization records to
establish whether patients had hospitalized falls in the year before dementia diagnosis.

Medications received by participants were extracted from structured medication fields supplemented by natural language processing applications applied to free text.13 Receipt of medication in the following groups was ascertained for the period of 1 year before or after the index date: benzodiazepines, any medication with anticholinergic properties (referred to as anticholinergics), antihypertensives, antidepressants, antipsychotics, acetyl cholinesterase inhibitors, and analgesics. The total number of different medications prescribed was also calculated and a binary variable was created according to whether patients received 4 or more types of medications.15

Statistical Analysis

All statistical analyses were conducted with Stata, version 13, software. The study population was initially summarized in terms of demographic and clinical variables, followed by univariate Cox proportional hazard models for predictors affecting time to first fall leading to hospitalization as the outcome variable. Univariate analyses were repeated in the complete case sample (with no missing data on any of the variables), followed by multivariate models. In a final stage, analyses were repeated for first fracture as the outcome.

Results

In the observation period, 8036 patients with a diagnosis of dementia were identified with a mean age of 81.0 (standard deviation, 7.0) years, of whom 63.9% were female with a mean MMSE score at the time of dementia diagnosis of 19.6 (6.3). Of these, 2500 patients (31.1%) had at least 1 previous hospitalized fall in the follow-up period (incidence rate 125.5 per 1000 person-years of follow-up). Overall, 1437 (17.7%) had a fall (incidence rate 124.8 per 1000 person-years follow-up) and 1142 (18.0%) had a fracture (incidence rate 65.5 per 1000 years of follow-up). In the observation period, 8036 patients with a diagnosis of dementia were identified with a mean age of 81.0 (standard deviation, 7.0) years, of whom 63.9% were female with a mean MMSE score at the time of dementia diagnosis of 19.6 (6.3). Of these, 2500 patients (31.1%) had at least 1 previous hospitalized fall in the follow-up period (incidence rate 125.5 per 1000 person-years of follow-up). Overall, 1437 (17.7%) had a fall (incidence rate 124.8 per 1000 person-years follow-up) and 1142 (18.0%) had a fracture (incidence rate 65.5 per 1000 person-years follow-up). Overall, 1437 (17.7%) had a fall (incidence rate 124.8 per 1000 person-years follow-up) and 1142 (18.0%) had a fracture (incidence rate 65.5 per 1000 person-years follow-up). Overall, 1437 (17.7%) had a fall (incidence rate 124.8 per 1000 person-years follow-up) and 1142 (18.0%) had a fracture (incidence rate 65.5 per 1000 person-years follow-up).

Sample characteristics grouped according to the presence of falls in the follow-up period are presented in Table 1. Patients with dementia who had a fall leading to hospitalization were older, from more deprived neighborhoods, and had higher MMSE scores at diagnosis; they were less likely to be male, cohabiting, from an ethnic minority, have a diagnosis of Alzheimer’s disease, or prescribed a cholinesterase inhibitor. In terms of symptoms, function, and medication, those with a hospitalized fall were more likely to have depressed mood, worse physical health, to have problems with their living conditions, to be prescribed antidepressants and analgesics, and to have a previous hospitalized fall or fracture before dementia diagnosis.

Predictors of Falls Leading to Hospitalization

No substantial differences were detected in incidence rates and unadjusted Cox regression models between the full cohort and the complete case sample. Hazard ratios for hospitalized falls related to potential predictors are presented in Table 2. In the fully adjusted model, statistically significant demographic predictors included age, female gender, noncohabiting status, a higher index of deprivation, as well as vascular dementia, mixed-type dementia, and dementia in other diseases (all compared to Alzheimer’s disease). Caribbean, African, South Asian, and “any other white” (all compared to white

### Table 1: Sample Characteristics by Fall Status

<table>
<thead>
<tr>
<th>Risk Factors</th>
<th>Had Fall (≥1 Fracture) (n = 2500)</th>
<th>No Fall or Fracture (n = 5617)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sociodemographic status and cognitive function</td>
<td>Mean age at dementia diagnosis (SD) 82.3 (6.8)</td>
<td>80.4 (7.0)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Female gender, % 70.1%</td>
<td>61.1%</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Married or cohabiting status, % 29.9%</td>
<td>39.5%</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Mean index of deprivation (SD) 26.6 (11.6)</td>
<td>25.6 (11.7)</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Mean MMSE score at diagnosis (SD) 19.9 (6.1)</td>
<td>19.5 (6.4)</td>
<td>.022</td>
<td></td>
</tr>
<tr>
<td>Ethnicity, %</td>
<td>White British 75.5</td>
<td>64.6</td>
<td>.002</td>
</tr>
<tr>
<td>Irish 6.6</td>
<td>4.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any other white 6.2</td>
<td>8.2</td>
<td>.545</td>
<td></td>
</tr>
<tr>
<td>African 1.0</td>
<td>2.2</td>
<td>.398</td>
<td></td>
</tr>
<tr>
<td>Caribbean 6.6</td>
<td>14.2</td>
<td>.011</td>
<td></td>
</tr>
<tr>
<td>South Asian 1.9</td>
<td>3.3</td>
<td>.535</td>
<td></td>
</tr>
<tr>
<td>Other 2.2</td>
<td>4.0</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>Dementia subtype diagnosis, %</td>
<td>Alzheimer’s disease (F00) 54.9</td>
<td>59.5</td>
<td>.002</td>
</tr>
<tr>
<td>Vascular dementia (F01) 25.5</td>
<td>22.3</td>
<td>.011</td>
<td></td>
</tr>
<tr>
<td>Mixed-type dementia 15.2</td>
<td>14.2</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>Dementia in other diseases (F02) 4.4</td>
<td>4.0</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>HoNOS5 65+ symptoms/disorders, %</td>
<td>Overactive, aggressive behavior 18.3</td>
<td>18.7</td>
<td>.710</td>
</tr>
<tr>
<td>Nonaccidental self-injury 1.4</td>
<td>1.2</td>
<td>.398</td>
<td></td>
</tr>
<tr>
<td>Problem-drinking or drug taking 2.5</td>
<td>2.4</td>
<td>.613</td>
<td></td>
</tr>
<tr>
<td>Hallucinations or delusions 13.9</td>
<td>12.8</td>
<td>.223</td>
<td></td>
</tr>
<tr>
<td>Depressed mood 16.9</td>
<td>15.1</td>
<td>.039</td>
<td></td>
</tr>
<tr>
<td>Physical illness or disability 50.9</td>
<td>46.9</td>
<td>.001</td>
<td></td>
</tr>
<tr>
<td>HoNOS5 65+ functional problems, %</td>
<td>Relationship problem 16.6</td>
<td>17.3</td>
<td>.445</td>
</tr>
<tr>
<td>Activities of daily living problem 55.4</td>
<td>54.4</td>
<td>.400</td>
<td></td>
</tr>
<tr>
<td>Problem with living conditions 12.4</td>
<td>10.4</td>
<td>.009</td>
<td></td>
</tr>
<tr>
<td>Problem with occupational and recreational activities 32.3</td>
<td>31.9</td>
<td>.738</td>
<td></td>
</tr>
<tr>
<td>Medication prescription, %</td>
<td>Benzodiazepines 12.4</td>
<td>11.9</td>
<td>.545</td>
</tr>
<tr>
<td>Anticholinergics 8.4</td>
<td>8.4</td>
<td>.935</td>
<td></td>
</tr>
<tr>
<td>Antihypertensives 31.1</td>
<td>32.7</td>
<td>.151</td>
<td></td>
</tr>
<tr>
<td>Antidepressants 26.7</td>
<td>23.1</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Antipsychotics 14.4</td>
<td>14.9</td>
<td>.633</td>
<td></td>
</tr>
<tr>
<td>Cholinesterase inhibitors 29.8</td>
<td>34.6</td>
<td>&lt;.001</td>
<td></td>
</tr>
<tr>
<td>Analgesics 31.2</td>
<td>28.0</td>
<td>.003</td>
<td></td>
</tr>
<tr>
<td>Received 4 or medications 18.9</td>
<td>17.3</td>
<td>.076</td>
<td></td>
</tr>
<tr>
<td>Previous hospitalized fall or fracture, %*</td>
<td>Fall 9.3</td>
<td>5.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Fracture 5.4</td>
<td>3.4</td>
<td>&lt;.001</td>
<td></td>
</tr>
</tbody>
</table>

* t test or χ² test. | 1 At the time of dementia diagnosis. | 2 Missing data: 5%-10%. | 3 Missing data: <5%. | 4 Missing data: >10%. | 5 y before or after dementia diagnosis. | 6 Within 1 y before dementia diagnosis.

British) ethnicities were associated with a decreased risk of falls. In relation to comorbidities, functioning, pharmacotherapy, only physical health problems, previous falls and/or fractures, and problems with living conditions all remained significant predictors in the fully adjusted model.

### Predictors of Fractures in the Sample

Similar predictors for fracture were detected as for falls. In a multivariate Cox fully adjusted regression model, a significantly higher risk of fractures was associated with higher age [1-year increase, hazard ratio (HR) 1.05, 95% confidence interval (CI) 1.0-1.06], female gender (HR 1.62, 95% CI 1.40-1.88), noncohabiting status (HR 1.20, 95% CI 1.04-1.38), higher deprivation (HR 1.06 per 10-point increase, 95% CI 1.01-1.12), physical health problems (HR 1.28, 95%
CI 1.12-1.46), previous hospitalized falls (HR 1.59, 95% CI 1.32-1.90), problems with living conditions (HR 1.28, 95% CI 1.06-1.55), diagnoses of vascular dementia (HR 1.18 compared to Alzheimer’s disease, 95% CI 1.01-1.39). Lower fracture hazards were associated with Caribbean (HR 0.30, 95% CI 0.22-0.40) and South Asian ethnicity (HR 0.58, 95% CI 0.36-0.91, both compared to white British), as well as the receipt of antipsychotics (HR 0.71, 95% CI 0.57-0.88).

Discussion

In the current study over a mean 2.5 years’ follow-up, we found that approximately a third of people with dementia using secondary mental health services were admitted to the hospital due to a fall. Our data also add knowledge on the predictors of falls in people with dementia, suggesting that socioeconomic factors (eg, age, female gender, deprivation, nonwhite ethnicity), type of dementia, and environmental factors (eg, living conditions) are important risk factors. We did not find evidence that neuropsychiatric symptoms (eg, aggressive behavior) or severity of dementia at diagnosis (eg, from MMSE score) were independent predictors of falls in the adjusted models, and neither was there any independent risk associated with the medication groups analyzed.

Of the sociodemographic risk factors, older age and female gender also have been well established as risk factors for falls in the general older adult population samples. Interestingly, noncohabiting status was also associated with a slightly elevated hazard of hospitalized fall. There is increasing evidence to suggest that deprivation is associated with a range of adverse outcomes in older people; however, to our knowledge, our study is the first to suggest that it may be a falls risk factor and might, like marital status, act as a risk factor for falls or as a factor influencing the likelihood of hospitalization following a fall. Of interest, we found evidence that African, Asian, and Caribbean (vs
white British) older adults were at decreased risk of falls, leading to hospitalization. Previous researchers have noted that Caucasian older people have increased mobility compared to those from minority ethnic groups, possibly providing more opportunities to fall.23 In addition, Caucasian people have been noted to engage in balance-risk-taking behavior, and lower rates of falls have been noted in ethnic minority groups in the general older adult population.20

Our study also sheds new light on the relative risk of falls across different dementia diagnoses. Specifically, our data indicate that vascular dementia, mixed dementia, and dementia in other diseases are all associated with increased risk of falls compared to Alzheimer’s disease. In line with the general older adult population,2 we also found evidence that physical illness and disability were associated with falls. Functional dependence, as estimated from HoNOS-rated problems on activities of daily living, was not associated with falls risk in the fully adjusted model. This may reflect a stronger influence of particular health conditions rather than associated dependence, and it might also reflect lower mobility in more dependent groups. Interestingly, problems with living conditions were also a risk factor for falls. Environmental modifications, such as putting in hand rails and raising toilet seats, are important interventions that can be adapted to the individual falls risk, with established efficacy in the general older adult population.3,29 Thus, addressing such instances is a relatively easily modifiable risk factor for people with dementia. Unsurprisingly, previous fall was a predictor of a future fall in this sample, which is consistent with general population findings;2 but it also supports the importance of routine questioning for a falls history in people with dementia from the individual and other sources (eg, partner and carer).

The fact that poor cognitive function (defined by the MMSE) was not a predictor for hospital admission is of interest. A number of previous small-scale studies in the general older adult population have suggested that worse cognitive status is associated with increased falls in dementia, whereas in people without dementia, worse cognitive ability is associated with an increased falls risk.5 The reasons why we found no relationship between cognitive status and falls may be attributable to the fact that other risk factors (physical illness, living conditions, type of dementia, and various demographic risk factors) are more important, or might reflect limited first diagnoses at times of higher falls risk.

The finding that a range of commonly used medications in people with dementia, such as benzodiazepines, anticholinergics, cholinesterase inhibitors, analgesics, and antipsychotics, were not associated with falls is also novel. All of these medications have been associated with falls in the general older adult population.2,32–34 A previous large study in Japan also found some evidence that benzodiazepine hypnotics [odds ratio (OR) 1.43, 95% CI 1.19–1.73, P < .001], ultrashort-acting nonbenzodiazepine hypnotics (OR 1.66, 95% CI 1.37–2.01, P < .001), hydroxyzine (OR 1.45, 95% CI 1.15–1.82, P = .001), risperidone and perospirone (OR 1.37, 95% CI 1.08–1.73, P = .010) were associated with fractures in dementia.35 The reason for the lack of association in our sample is unclear, but it may be attributed to the identification of other risk factors that play a more prominent role in predicting hospitalized falls. We also found that taking 4 or more medications was not associated with falls in the fully adjusted models. Before firm conclusions are drawn about medication safety in dementia, more detailed analyses are needed into hospital presentations and the ways in which falls are identified and recorded, as it is possible that the disorders being treated might supervise falls when hospital discharge diagnoses are being listed and/or that falls are considered as integral to certain disorders and are not, when comorbid, separately recorded.

The proportion of people who had a fracture with their first hospitalized fall was substantial (48%). There has been a longstanding bidirectional relationship suggested between dementia and fractures, with people who have a fracture at increased risk of functional decline and cognitive impairment and ultimately dementia.36 Despite the increased awareness of the fracture risk in people with/at risk of dementia, little is actually known about predictors. Our findings suggest that the risk factors for fractures are broadly similar to falls in this sample.

Although we believe that the current data are novel and are derived from a large and detailed clinical database, some limitations should be noted. First, it was not possible to collect information on prefall/prefracture mobility, balance, and physical performance levels, which are key risk factors for falls.2 Moreover, we did not have sufficient information to investigate the underlying factors for the falls. Second, it was not possible to decipher the different types of fracture that occurred during the study. Future research is required to explore this, potentially with an emphasis on hip fractures, which are associated with particularly deleterious outcomes.10 Third, there is a need for more research into interactions between medications and treated conditions in relation to the recording of falls, which requires a more informative grouping of medications as risk predictors than the limited approach taken in this analysis, one example being an investigation into the potential differential effects of individual antipsychotic agents. Finally, we did not have information on specific physical health comorbidities, which may influence the fall and fracture risk in people with dementia.

Conclusion

We found that over an average of a 2.5-year period, a third of people with dementia experience a fall that leads to a hospitalization. Our results suggest stronger influences of sociodemographic factors, physical health, and environmental factors on falls risk in dementia compared to the severity of dementia or its pharmacotherapy, although further mechanistic investigation is required.

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