Are foot and ankle characteristics associated with falls in people with rheumatoid arthritis? A prospective study

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Short Title: Foot and ankle fall risk factors in RA

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ABSTRACT

Objective: To determine whether foot and ankle characteristics are associated with falls in people with rheumatoid arthritis (RA).

Methods: Two hundred and one adults with RA were recruited from rheumatology outpatient clinics in Auckland, New Zealand. Clinical characteristics, common fall risk factors, and foot and ankle variables were measured. Participants were prospectively studied for 12 months, to record the occurrence of falls using falls diaries. Logistic regression analysis identified baseline variables which were independent predictors of falls over the 12 months.

Results: Eighty-four (42%) participants fell at least once and 39 (19%) experienced multiple (>1) falls over the 12-month follow-up period. In logistic regression analysis, including age and significant baseline variables in bivariate analysis but not baseline fall history, presence of foot or ankle tender joints (odds ratio (OR) 1.95, \( P=0.034 \)) and psychotropic medication (OR 2.35, \( P=0.025 \)) were independent predictors of prospective falls. However, when baseline fall history was included in the analysis, psychotropic medication (OR 2.34, \( P=0.025 \)) and baseline fall history (over the preceding 12 months) (OR 2.27, \( P=0.008 \)) were independent predictors of prospective falls.

Conclusion: Foot and ankle characteristics are not associated with falls in people with RA, independent of prior falls. Enquiry about prior falls and psychotropic medications may assist in identifying patients with RA who are at high risk of future falls.
SIGNIFICANCE & INNOVATIONS

- Adults with rheumatoid arthritis (RA) are at high risk of falling.
- The foot and ankle are frequently affected in RA.
- This is the first prospective study to assess foot and ankle characteristics as potential fall risk factors in adults with RA.
- Psychotropic medications and baseline fall history, but not foot and ankle characteristics, are independent predictors of future falls in people with RA.
Falls are a common and potentially serious problem affecting the health and quality of life of older adults worldwide [1]. Falls are the leading cause of injuries sustained by adults over 65 years old and account for two-thirds of accidental deaths [1]. As such, falls represent an important burden to healthcare resources and treatment of fall related injuries accounts for a significant portion of healthcare spending [2]. People with rheumatoid arthritis (RA) are at greater risk of falling than healthy older adults, with previous prospective studies reporting fall incidence ranging between 35% to 50% [3]. Falls are multisystem events and the inflammatory nature of RA, and significant mechanical and systemic effects, may contribute to an increased fall risk. Indeed, RA disease-specific fall risk factors have been reported in addition to fall risk factors common to older adults. These include 28 joint Disease Activity Score (DAS28) [4], tender joint count [4, 5], swollen joint count [6], pain intensity [4, 7], use of corticosteroids, psychotropic medications, decreased lower extremity muscle strength [4], impaired standing balance [4, 6] and activity limitation; assessed by the Health Assessment Questionnaire (HAQ) [4, 5]. Falls in this vulnerable group can be devastating with RA-related reduced bone mass resulting in a threefold risk of fall-related hip fracture [8]. Therefore, falls awareness and prevention of falls are important in the management of people with RA.

The aetiology of falls is multifactorial and can result from complex interactions between intrinsic, behavioural or environmental factors [1]. As such, falls are not purely random events and can be predicted through assessment of known risk factors. Previous studies in older adults have identified a plethora of fall risk factors enabling clinicians to identify people at increased risk and implement strategies to prevent falls [1]. Risk factors
consistently found to be associated with falls include history of a prior fall(s), general pain, impaired balance, gait problems, poor muscle strength, visual impairment, psychotropic and antiepileptic medications, multiple drug use, arthritis, diabetes mellitus, Parkinson’s disease, vertigo, impaired cognition, urinary incontinence and walking aids [1].

Previous studies have suggested that age-related foot problems are also associated with falls in the general population [9-13]. Foot-related fall risk factors include disabling foot pain [9, 11, 13], pes planovalgus foot-type [9], reduced ankle range of motion [11], severe bunion deformity [11], lesser toe deformity [12], decreased toe strength [11, 12], reduced plantar sensitivity [9, 11] and increased peak plantar pressures and pressure-time integrals [13]. The feet are commonly affected in RA [14] and RA-related foot problems may be risk factors for falls. In a cross-sectional study of adults with established RA, we found elevated midfoot peak plantar pressures and self-reported foot impairment were associated with a fall in the preceding 12 months [15]. However, prospective evidence is lacking. Therefore, the aim of this 12-month prospective study was to determine whether foot and ankle characteristics are associated with future falls in people with RA.

PATIENTS AND METHODS

In this 12-month prospective observational study, eligible participants were recruited from three rheumatology outpatient clinics in the wider Auckland region of the North Island, New Zealand. All participants were English speaking adults (18 years and older) with RA according to the 2010 American College of Rheumatology/European League Against Rheumatism classification criteria [16]. Participants were excluded if they were non-ambulatory, could not attend a study visit at a specified clinic or research facility, or were unable to provide...
informed consent. Based on a previous falls study involving 176 older adults [11], an a priori sample size calculation, based on a 15% dropout rate, 80% power, and a significance level of 5%, indicated that 200 participants were needed. The study was conducted with the approval of the Northern X Regional Ethics Committee (reference NTX/11/12/114) and the Auckland University of Technology Ethics Committee (reference 12/47). The study was registered with the Australia New Zealand Clinical Trial Registry (trial ACTRN12612000597897).

Data collection

All participants attended a single baseline study visit and clinical assessments were completed by a single researcher (ABR) with five years’ experience in clinical podiatric assessment. Participant characteristics were recorded including age, gender, ethnicity, weight, height and BMI. Medical records were accessed to confirm RA diagnosis, disease duration, presence of erosive foot disease (on plain radiography), previous foot surgery, blood tests, medications and co-morbid conditions. Use of visual aids and assistive devices were also recorded. Fall history, for the preceding 12 months, was recorded by asking, “In the past 12 months, have you had any fall including a slip or trip in which you lost your balance and landed on the floor or ground or lower level?” [2].

A 100mm visual analogue scale (VAS) was used to record patient self-reported general pain, foot pain and patient global assessment of current health. Foot pain was also recorded as a dichotomous variable (present/absent) for either foot. Other patient-reported measures included activity limitation, assessed using the HAQ-II [17], fear of falling [18] and foot-related disability and impairment [19]. Current RA disease activity was determined by
assessment of joints for tenderness and swelling and calculation of the four variable DAS28-CRP [20]. The DAS28 is commonly used in clinical practice and is the ‘gold standard’ tool endorsed by the American College of Rheumatology and European League Against Rheumatism for assessing disease activity in clinical trials [21]. The DAS28 does not include the joints of the feet. Therefore, presence (yes/no) of any tender foot or ankle joint, and any swollen foot or ankle joint, was additionally recorded.

Specific foot and ankle assessments included foot-type, foot problem score (FPS), plantar sensation, foot and ankle muscle strength, ankle range of motion, toe strength, gait speed, peak plantar pressure, postural stability and footwear. Foot-type was determined through calculation of the arch index [22] and recorded as high, normal or low arch (reported as pes planovalgus foot-type). FPS was calculated based on hallux valgus severity, lesser digit subluxation, hyperkeratotic lesions, bony prominences and presence of foot pain [10]. Plantar sensation was assessed at six sites using a 10 g monofilament (fine touch) and biothesiometer (vibration perception) [23, 24]. Foot and ankle muscle strength (dorsiflexion, plantarflexion, inversion, eversion) was assessed manually using a hand-held dynamometer [25]. Ankle range of motion was assessed in weight-bearing using a modified lunge test [26]. Toe strength was assessed using the Paper Grip Test, a manual assessment whereby the patient grips a business card while an assessor attempts to pull it out from underneath the hallux and lesser digits [11]. Gait speed was determined using the 6-m walk test [10]. Peak plantar pressure was recorded using a TekScan MatScan® (TekScan Inc, South Boston, USA) portable pressure mat. Participants were tested in bare feet using a 2-step protocol [13]. The MatScan® was also used to assess postural stability which was measured as postural sway in an antero-posterior (AP) and medio-lateral (ML) direction, in quiet standing.
Participants were tested in bare feet, with eyes open and eyes closed, for 30 s [27]. Footwear was assessed as the type of footwear worn to the study visit and grouped as good, average or poor [28].

Fall data ascertainment

The primary outcome measure for the study was falls experienced over the 12-month period following the baseline study visit (prospective falls). Prospective falls were recorded using monthly falls calendars and follow-up telephone calls in accordance with the Prevention of Falls Network Europe (ProFaNE) guidelines [2]. The ProFaNE definition of “an event that results in a person coming to rest unintentionally on the ground or other lower level” was used to identify falls. We did not include falls which were the result of syncope or an external force, such as being pushed or knocked over. In order to identify these types of falls we used a modified fall definition by adding, “not as a result of a major intrinsic event or an overwhelming hazard” [11]. Fall incidence was reported in accordance with the ProFaNE guidelines [2].

Statistical analysis

Participants were grouped as ‘fallers’ or ‘non-fallers’ based on falls experienced during the 12-month follow-up period. Comparisons between groups were made using independent samples student’s t tests for normally distributed variables and Mann-Whitney U tests for ordinal or non-normally distributed data. Chi-square tests of trend were used as appropriate to examine differences between groups on categorical variables. To identify predictors of falls, a logistic regression model was created using prospective falls as the dependent variable. A limited number of predictor variables were selected based on statistical
significance of $P<0.15$ on bivariate analysis. Where multicollinearity ($r \geq 0.5$) was present, the variable with the lowest $P$ value, or of greatest clinical relevance, was retained. 12-month fall history was initially excluded as a predictor variable due to the likelihood that it would be highly correlated with other variables in the model. Multivariate binary logistic regression analyses were conducted including the selected predictor variables and controlling for age. The backward elimination method was used to remove the variable with the highest $P$ value, in a stepwise approach, until all remaining variables were significant at $P<0.05$. The logistic regression analyses were then repeated, including baseline fall history (over the preceding 12 months) as a predictor variable, to determine the effect of baseline fall history on the other variables in the model. Statistical analysis was performed using Statistical Package for Social Sciences V22.0 (IBM Corp., New York, USA).

RESULTS

Participant characteristics

Two hundred and one participants completed the baseline assessment and 196 (98%) completed follow-up to 12 months. One participant withdrew after the baseline assessment and four participants died during the study year. Available fall data for the participants who died was included in the analysis. Baseline clinical characteristics, common fall risk factors and foot and ankle characteristics, for the entire group, have been previously reported [15]. Participants were predominantly female ($n=150$, 75%). The mean (SD) age of participants was 65 (11) years. Most (80%) identified as European and had well established RA, with mean (SD) disease duration of 16 (14) years. Sixty-nine percent had co-morbid conditions, the most common being hypertension ($n=73$, 36%) and osteoporosis ($n=39$, 19%). Most participants ($n=175$, 87%) were taking non-biologic disease modifying anti-rheumatic drugs
(DMARDs) and over one third (n=74, 37%) were taking prednisone. Anti-hypertensive medication (n=96, 45%) was also common. On the day of the study visit, participants had moderate disease activity and reported mild to moderate disability, with mean (SD) scores: DAS28 3.38 (1.26) and HAQ-II 0.89 (0.62).

Foot disease was prevalent; 62% (n=112) had foot erosion on radiograph, 65% (n=130) had bunion deformity and 34% (n=68) had pes planovalgus foot-type. Seventy-three percent (n=147) reported foot pain in the past week, with a mean (SD) 100mm VAS score of 32 (29). Half of the participants failed the paper grip test for the lesser toes (n=102, 50%) and hallux (n=101, 50%) and 43% (n=85) had a vibration perception above 26 mV, indicating presence of neuropathy. On examination, 63% (n=125) presented with tender, and 29% (n=58) presented with swollen, joints in the feet. On the day of the study visit, participants reported moderate levels of foot impairment and disability and just under half (n=99, 49%) wore footwear classified as ‘average’ or ‘poor’.

Falls over the 12-month follow-up period

In total 177 falls were reported over 198 person years, with a fall rate of 891 per thousand person years or 0.89 falls per person. Of the 200 participants who were prospectively followed, 84 (42%) fell at least once and 39 (19%) experienced multiple (>1) falls.

Bivariate analysis comparing fallers and non-fallers over the 12-month follow-up period

The results of bivariate analysis comparing non-fallers and fallers over the 12-month follow-up period are presented in Table 1. Compared to non-fallers, those who fell had higher tender joint count ($P=0.005$), took more medications ($P=0.039$) and were more likely to
receive anticoagulant ($P=0.009$) and psychotropic ($P=0.028$) medication. Fallers were also more likely to use an assistive device ($P=0.007$) than non-fallers. The probability of a 1-year follow-up fall significantly increased if the participant had a history of falling ($P=0.009$) during the preceding 12 months. Specifically, of those with a 1-year history of falls preceding the baseline study visit, 59 (50%) reported a 1-year follow-up fall, whereas of those with no 1-year history of falls, only 25 (30%) reported a 1-year follow-up fall. In terms of foot and ankle characteristics, fallers were more likely to have the presence of foot or ankle tender joints ($P=0.028$) and increased antero-posterior (AP) sway ($P=0.040$) and medio-lateral (ML) sway ($P=0.042$) in eyes-closed conditions. No other foot and ankle characteristics were significantly different between the two groups.

Multivariate analysis of predictive risk factors for falls over the 12-month follow-up period

We initially analysed predictive risk factors for falls over the 12-month follow-up period excluding baseline fall history in logistic regression analysis (Table 2). Ten variables, plus age, were entered into the model including: number of medications, opiates, psychotropic medication, cardiovascular disease, patient self-reported pain (VAS), use of an assistive device, fear of falling, presence of foot or ankle tender joints, presence of foot or ankle swollen joints and eyes-closed AP sway. To avoid an underpowered model, anticoagulants and diabetes mellitus variables were excluded due to small numbers. To avoid multicollinearity, taking four or more medications, depression or bipolar disorder, tender joint count, eyes-open and eyes-closed ML sway and 12-month fall history, were excluded from the model. The final model contained two variables; psychotropic medication (OR 2.35, $P=0.025$) and presence of foot or ankle tender joints (OR 1.95, $P=0.034$) which were independent predictors of prospective falls.
Table 3 shows the results for the logistic regression modelling with baseline fall history (over the preceding 12 months) included as a predictor variable. The inclusion of 12-month fall history resulted in the variable ‘presence of foot or ankle tender joints’ being removed from the model, as it was no longer statistically significant at $P<0.05$. The final model contained two variables; psychotropic medication (OR 2.34, $P=0.025$) and baseline fall history (over the preceding 12 months) (OR 2.27, $P=0.008$) which were independent predictors of prospective falls.

**DISCUSSION**

Disease-related impairments and reduced functioning contribute to fall risk in adults with RA [3]. The current study adds to existing evidence for fall risk factors in older adults with established RA. In our study, joint tenderness in the feet or ankles was associated with increased fall risk; when excluding baseline fall history. Tenderness in the foot and ankle is generally indicative of synovitis associated with active RA [29]. In the current study of older people with most longstanding RA, tenderness in the feet may also be indicative of chronic inflammation due to increased mechanical loading on deformed and prominent joints [29]. However, when controlling for baseline fall history, presence of foot or ankle tender joints was removed as an independent predictor. This may be due to multicollinearity between the two variables with fall history, being the more powerful predictor, remaining in the model. Stanmore [4] demonstrated a similar effect, whereby ‘psychotropic medications’ was removed from a predictive model of fall risk factors in adults with RA, when controlling for fall history.
In general, we found that foot and ankle characteristics are not associated with falls in people with RA, independent of prior falls. One explanation for the non-significant findings could be the prevalence and severity of foot problems in people with RA compared to the general older adult population [29]. That is, the presence and severity of age-related foot problems that are associated with falls in older adults is greater in adults with established RA. Hence, there may not have been enough variation in the measures of foot and ankle function to discriminate fallers from non-fallers in the current study. Indeed, the fall incidence and prevalence of foot problems in our sample was higher than the general older population [11].

We found that psychotropic medication is an independent predictor of future falls. Psychotropics are commonly prescribed as an adjunct therapy for chronic arthritic pain as well as depression [30]. In the current study, 18% of participants were taking psychotropic medication and, of those, 59% experienced one or more falls during the prospective 12-month study period. Psychotropic medications cross the blood-brain barrier and act directly on the central nervous system causing impairments in dynamic and static postural control [31]. This is in addition to the known adverse effects of cognition impairment and muscle relaxation which are likely to be a mediating factor in falls [31]. Withdrawal from psychotropic medication has been shown to decrease the risk of falls in older adults [32].

Baseline fall history (over the preceding 12 months) was also an independent predictor of future falls. This finding is in agreement with previous prospective studies in RA cohorts [3] as well as studies in older adults [1]. Fall history is essentially a combination of fall risk factors. Therefore, having a history of falls is considered to be a powerful predictor of future
falls, over and above all other potential fall risk factors [1]. However, fall history as a predictor of future falls will not identify an individual who has not previously fallen but may still be at increased fall risk. In addition, fall history cannot be modified or mitigated in order to prevent future falls. This suggests that although fall history has a limited explanatory value in understanding falls in people with RA, it assists in the prediction of future falls.

The limitation of this study is the risk of recruitment bias, noting that participants were aware that they were being recruited into a study examining falls. Therefore, the recruitment strategy may have been biased towards participants with a history of falls. The consequences of a fall, such as injury or fear of falling, increase the risk of experiencing another fall [1]. Therefore, it is likely that our estimate of fall incidence in the follow-up period is higher than the general RA population. Strengths of this study include the prospective analysis, the use of a falls diary, a clear fall definition and the inclusion of a comprehensive range of validated foot and ankle measures. In addition, using a single experienced podiatrist to conduct all baseline foot and ankle assessments ensured accuracy and consistency of measurements.

In summary, psychotropic medications and baseline fall history, but not foot and ankle characteristics, are independent predictors of future falls in people with RA. Enquiry about prior falls and psychotropic medications may be beneficial in identifying patients with RA who are at high risk of future falls.

COMPETING INTERESTS

The authors declare that they have no competing interests.
ACKNOWLEDGEMENTS

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REFERENCES


Table 1: Bivariate analysis of non-fallers and fallers*. Data are presented as mean (SD) unless specified.

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Non-fallers</th>
<th>Fallers</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of medications</td>
<td>3.8 (2.1)</td>
<td>4.5 (2.3)</td>
<td>0.039</td>
</tr>
<tr>
<td>Anticoagulants, n (%)</td>
<td>2 (2)</td>
<td>9 (11)</td>
<td>0.009</td>
</tr>
<tr>
<td>Psychotropic medication, n (%)</td>
<td>15 (13)</td>
<td>22 (26)</td>
<td>0.028</td>
</tr>
<tr>
<td>Tender joint count</td>
<td>9 (11)</td>
<td>14 (14)</td>
<td>0.005</td>
</tr>
<tr>
<td>Use of an assistive device, n (%)</td>
<td>24 (21)</td>
<td>33 (39)</td>
<td>0.007</td>
</tr>
<tr>
<td>Baseline fall history (over the preceding 12 months), n (%)</td>
<td>59 (51)</td>
<td>59 (70)</td>
<td>0.009</td>
</tr>
<tr>
<td>Foot and ankle characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presence of foot or ankle tender joints, n (%)</td>
<td>65 (56)</td>
<td>60 (72)</td>
<td>0.028</td>
</tr>
<tr>
<td>Eyes-closed antero-posterior sway, mm</td>
<td>27.7 (10.6)</td>
<td>31.8 (15.5)</td>
<td>0.040</td>
</tr>
<tr>
<td>Eyes-closed medio-lateral sway, mm</td>
<td>16.1 (7.6)</td>
<td>19.2 (11.9)</td>
<td>0.042</td>
</tr>
</tbody>
</table>

*Comparisons with P<0.05 are shown
Table 2: Stepwise logistic regression analyses comparing non-fallers (n=116) and fallers (n=84) on all predictor variables, excluding baseline fall history, and adjusting for age*

<table>
<thead>
<tr>
<th>Predictor Variable</th>
<th>Odds ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of foot or ankle tender joints</td>
<td>1.95 (1.05-3.62)</td>
<td>0.034</td>
</tr>
<tr>
<td>Psychotropic medication</td>
<td>2.35 (1.11-4.95)</td>
<td>0.025</td>
</tr>
</tbody>
</table>

*Associations with P<0.05 are shown

Variables included in the model: age, number of medications, opiates, psychotropic medication, cardiovascular disease, patient self-reported pain (VAS), assistive device, fear of falling, presence of foot or ankle tender joints, presence of foot or ankle swollen joints and eyes-closed antero-posterior sway.
Table 3: Stepwise logistic regression analyses comparing non-fallers (n=116) and fallers (n=84) on all predictor variables, including baseline fall history, and adjusting for age *

<table>
<thead>
<tr>
<th></th>
<th>Odds ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychotropic medication</td>
<td>2.34 (1.11-4.94)</td>
<td>0.025</td>
</tr>
<tr>
<td>Baseline fall history (over the preceding 12 months)</td>
<td>2.27 (1.24-4.16)</td>
<td>0.008</td>
</tr>
</tbody>
</table>

*Associations with P<0.05 are shown

Variables included in the model: age, number of medications, opiates, psychotropic medication, cardiovascular disease, patient self-reported pain (VAS), assistive device, fear of falling, presence of foot or ankle tender joints, presence of foot or ankle swollen joints, eyes-closed antero-posterior sway and baseline fall history.