Falling: should one blame the heart?

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Citation for published version (APA):
Jansen, S. (2015). Falling: should one blame the heart?

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CHAPTER SIX

ATRIAL FIBRILLATION IS ASSOCIATED WITH IMPAIRED MOBILITY IN COMMUNITY-DWELLING OLDER ADULTS
ATRIAL FIBRILLATION IS ASSOCIATED WITH IMPAIRED MOBILITY IN COMMUNITY-DWELLING OLDER ADULTS

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J Am Med Dir Assoc. 2014 Dec;15(12):929-33

ABSTRACT

OBJECTIVES
To examine the independent associations between atrial fibrillation (AF) and objectively measured mobility in a nationally representative cohort.

METHODS
Design: Wave 1 of The Irish Longitudinal Study on Ageing (TILDA), a population based study assessing health, economic, and social aspects of aging. Setting: Community-dwelling adults completed a home-based interview and a center-based health assessment. Participants: Participants aged ≥50 years, with Mini-Mental State Examination score ≥24, and who completed at least one mobility test (n=4,525). Measurements: Mobility was assessed with Timed Up-and-go (TUG) test and usual and dual task gait speed obtained using a 4.88 m GAITRite mat. AF was diagnosed using a 10 minute surface electrocardiogram recording. Linear regression analyses were performed to compare mobility in participants with and without AF, adjusting for confounders.

RESULTS
Results: In this sample (mean age 62.3 years; range 51-89), overall prevalence of AF was 3.1%, increasing to 6.7% in the over 70s (11.8% males; 2.8% females). In multivariable analysis, AF was independently associated with slower TUG (β=0.37; 95% CI=0.07, 0.71; p=0.043) and slower usual gait speed (β=-3.59; 95% CI=-7.05, -0.12; p=0.030). There was a significant age*AF interaction effect for usual gait speed (β=-0.48, 95% CI=-0.907, -0.053, p=0.028). Adults with AF walked 3.77 cm/s more slowly than adults without AF at age 70, declining by 4.8 cm/s for each additional decade.

CONCLUSION
Conclusion: AF is independently associated with lower usual gait speed in community-dwelling adults and this effect is magnified in those aged 70 and over. This may place them at increased risk of falls, hospitalisation, cognitive decline and mortality as well as stroke and heart failure. Early recognition and treatment of AF is vital to improve physical function and reduce this risk.
INTRODUCTION

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, affecting about 1-2% of the general population. It is more common in men than women and the prevalence increases steadily with advancing age, affecting 16-19% of community-dwelling men aged 80 years and over. In long-term care facilities, the prevalence is much higher, affecting 7.5-17% of residents. AF is often accompanied by cardiovascular disease such as hypertension, heart failure and valvular abnormalities. Symptoms include an irregular and fast heart rate, weakness, dizziness or fainting, shortness of breath and chest pain, although approximately one-third of patients are asymptomatic.

Regardless of whether the condition is symptomatic or asymptomatic, AF is associated with a doubled mortality rate, fivefold increased risk of stroke, increased rate of hospitalization and decreased quality of life and exercise capacity. Although it receives less attention than other outcomes, AF has also been associated with an increased risk of non-accidental falls. In support of this, AF has been associated with poorer cognitive function, depression, slower self-reported walking pace and distance, all of which are also risk factors for falls.

Research comparing objective physical performance measures in AF versus non-AF groups is limited to a small convenience sample of hospital inpatients. Commonly used tests to assess physical performance are the Timed Up-and-Go (TUG) test, timed walk test (single task gait speed) and timed walking-while-talking test (dual task gait speed). Deficits in single and dual task gait predict falls, while slower usual gait speed also predicts adverse outcomes such as hospitalisation, cognitive decline and mortality.

If AF is associated with slower gait speed and impaired mobility, this would provide novel evidence for the exploratory pathway regarding the association between AF and falls. We therefore examined the independent associations between AF and objectively measured gait and mobility performance using data from a nationally representative, community-dwelling older population.

METHODS

Study Design
The Irish Longitudinal Study on Ageing (TILDA) is a large prospective cohort study of the social, economic and health circumstances of community-dwelling adults in Ireland. This analysis is based on the first wave of data collected between January 2009 and July 2011. The study design has been described previously. Briefly, the sampling frame is the Irish Geodirectory, a listing of all residential addresses in the Republic of Ireland. A clustered sample of addresses was chosen, and household residents aged ≥50 years and their spouses/partners (of any age) were eligible to participate in the study. Ethical approval was obtained from the Trinity College Dublin Research Ethics Committee and written informed consent was obtained from 8504 participants.

Data collection involved (i) a computer-assisted personal interview (CAPI) that included detailed questions on socio-demographics, wealth, health, lifestyle, social support and participation, use of health and social care and attitudes to ageing, (ii) a self-completion questionnaire and (iii) a health assessment carried out by research nurses. The health assessment was carried out in a designated health centre, however a modified version was available in the participant’s home, if they were unable or unwilling to travel. Inclusion criteria for the present analysis was age ≥50 years, Mini-Mental State Examination (MMSE) score ≥24, participation in a health centre assessment and unaided completion of the single task gait assessment, dual task gait assessment or the TUG making 4525 participants eligible for the study.

Measurement of AF
AF was diagnosed objectively using a 10 minute surface electrocardiogram recording (Medilog Darwin) in a quiet room at ambient temperature of 21-23°C. ECG signals were sampled at 4000 Hz, filtered between 0.01 and 100 Hz and stored digitally. Data records were excluded if there was significant noise and/or artefact which made detection of AF impossible. Two clinicians independently screened the data records for AF using the ESC guidelines and any disagreement was resolved by consulting an independent cardiologist. Inter-rater agreement has previously been reported as a Cronbach’s alpha coefficient of 0.996.
Mobility and gait measurements

Mobility was assessed with the Timed Up-and-Go (TUG) test using a chair with armrests and a seat of height 46 cm. Participants were asked to rise from the chair, walk 3 m at normal pace, turn around, walk back to the chair and sit down again. No instructions were given about the use of participants’ arms. The time taken from the command ‘Go’ to when the participant was sitting with their back resting against the back of the chair was recorded using a stopwatch.

Gait assessment took place using a computerised walkway (4.88 m active area) with embedded pressure sensors (GAITRite®, CIR Systems Inc, New York, USA). Participants performed two walks at their normal pace, followed by two walks under cognitive dual task conditions where they were asked to recite alternate letters of the alphabet i.e. A-C-E, etc. Participants started and finished 2.5 m before and 2 m after the walkway to allow for acceleration and deceleration. The average gait speed was calculated from the two walks in each condition; these represented usual gait speed and dual task gait speed.

Socio-demographic data such as age, gender and education were collected. Educational level was defined as primary, secondary or tertiary corresponding to ≤8, 9-13 and ≥13 years of education respectively. Height and weight were also obtained. Global cognition was assessed using the MMSE 17. Depressive symptoms were assessed using the 8-item Centre for Epidemiological Studies Depression (CES-D) scale 18.

Respondents reported if a doctor had ever diagnosed them with high blood pressure, a heart attack, heart failure, stroke, diabetes, Parkinson’s disease, chronic lung disease, arthritis or hip fracture. They also reported all medications that they were taking. Medications were coded using the World Health Organization’s Anatomical Therapeutic Chemical (ATC) codes 19. Psychotropic use was identified from reported use of any medication with the following codes: N05A-N05C, N06A-N06C. Cardiovascular medications were similarly identified from the following codes: C01A-C01E, C02A-C02D, C02K, C02L, C02N, C03A-C03E, C03X, C04A, C07A-C07F, C08C-C08E, C08G, C09A-C09D, C09X, G04CA, S01ED. The number of psychotropic and cardiovascular medications was used in the analysis.

Indicators of behavioural health were also obtained. Respondents reported if they were a past smoker, current smoker or have never smoked. They also reported the frequency with which they consume more than two alcoholic drinks within a single day. Based on the response options, their alcohol consumption was classed as infrequent (never, not at all in the last 6 months), occasional (less than once a month, once or twice a month) and frequent (once or twice a week, 3 or 4 days a week, 5 or 6 days a week, almost every day).

AF may reflect a general decline in health status and has been independently associated with frailty status 20, therefore, we controlled for variables included in the Fried frailty phenotype 21. Grip strength was assessed using a Baseline® hydraulic hand dynamometer. Two measurements were taken on the dominant hand and the average value was used in the analysis. Physical activity was measured using the International Physical Activity Questionnaire (IPAQ). 22 Respondents indicated the frequency and duration that they took part in moderate and vigorous physical activity and walking. This was weighted to provide estimates of energy expenditure in MET-minutes per week. This was then used to categorise respondents into low, moderate or high levels of physical activity. Unintentional weight loss was identified by asking respondents ‘In the past year, have you lost 10 pounds (4.5 kg) or more in weight when you were not trying to?’ Finally, two items (‘I felt that everything I did was an effort’ and ‘I could not get going’) were used to generate a measure of exhaustion. Each item had four response options and respondents who answered ‘occasionally or a moderate amount of time (3-4 days)’ or ‘all of the time (5-7 days)’ to either of these items were considered to have ‘exhaustion’.

Statistical Analysis

Statistical analysis was carried out in Stata v12 (StataCorp LP, Texas, USA). Prevalence calculations were weighted with respect to age, sex and education to the Quarterly National Household Survey (2010) to ensure that data were nationally representative. Data were further weighted by health status and socio-demographic factors to account for those who did not attend a health assessment 23. Baseline characteristics of each group were compared. TUG was positively skewed and therefore log (TUG) was used for the analysis. Regression analysis was used to examine differences between groups using the non-AF group as the reference group. For each physical performance test, the unadjusted model is presented in Model 1. Each model was then adjusted for socio-demographic factors (age, sex, education), height and weight (Model 2). Subsequent
In this population-based sample (mean age 62.3 years; range 51-89 years), 3.1% of participants (n=112) had objectively diagnosed atrial fibrillation. The prevalence of AF increased with age from 0.8% in the 50-59 year olds to 3.2% in the 60-69 year olds, 5.4% in the 70-79 year olds and 12.2% in those aged 80 years and older. Baseline characteristics for the AF and non-AF groups are provided in Table 1.

The AF group was older, more likely to be male, to have lower levels of education, to be on more cardiovascular drugs, to exhibit signs of frailty and to have poorer behavioural health patterns compared to the non-AF group. The AF group also had a slower TUG and slower gait speed in both walking conditions compared to the non-AF group. The slower TUG and reduced usual gait speed exhibited in the AF group were also approximately 1.5 s slower in TUG and had a 13-14 cm/s slower gait speed in both walking conditions compared to the non-AF group.

The AF group had poorer mobility and gait tests compared to the non-AF group. The AF group remained significant after adjusting for age squared and other confounders, including cardiovascular conditions (Model 3, p<0.05). Dual task gait speed did not differ between groups after adjusting for confounders in Models 2 or 3.

In this section, we examined the age*AF interaction effects by adding these to Model 3 for each test. We then plotted the differences in performance between the AF and non-AF groups at each age. Complete covariate data was available for 4058 (89.7%), 4032 (89.7%) and 4004 (89.8%) participants for the TUG, normal walk and dual task walk respectively. Complete case analysis was used for multivariate analyses i.e. all missing data were treated as missing completely at random. Significance level was set at p<0.05.
TABLE 2. There was a significant age*AF interaction effect in the model for usual gait speed ($\beta=-0.480$, 95% CI=$-0.907$,$-0.053$, $p=0.028$) but not logTUG ($\beta=0.003$, 95% CI=$-0.001$,$0.007$, $p=0.157$) and dual task gait speed ($\beta=-0.287$, 95% CI=$-0.899$,$0.324$, $p=0.357$). The effect of having AF at each age on usual gait speed can be seen in FIGURE 1. Differences between the groups are significant where the 95% CI lines do not include zero. At age 70, adults with AF walk 3.77 cm/s more slowly than adults without AF, after adjusting for all confounders. This increases to a difference of 8.57 cm/s at age 80 and 12.88 cm/s at age 89 ($p<0.05$). Model fit was assessed and was good in all cases.

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<td>3.6% (35)</td>
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<td>1.2% (7)</td>
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Adjusted for age, sex, education, height, weight, MMSE, depressive symptoms, high blood pressure, heart attack, heart failure, stroke, diabetes, Parkinson’s disease, arthritis, hip fracture, chronic lung disease, smoking status, alcohol consumption, number of psychotropic medications, number of cardiovascular medications, mean grip strength, physical activity level, exhaustion, weight loss.

FIGURE 1. AF*AGE INTERACTION EFFECTS SHOWING THE DIFFERENCE IN USUAL GAIT SPEED BETWEEN RESPONDENTS WITH AND WITHOUT AF AS AGE INCREASES
Older adults with AF have poorer mobility compared to those without AF even after adjustment for socio-demographics, cardiovascular conditions, other co-morbidities, cognitive function, depressive symptoms, frailty markers and psychotropic and cardiovascular medication use. The association with slower usual gait speed is dependent on age; it is evident from age 70 onwards and becomes more pronounced with increasing age.

Limited research has examined mobility in people with AF, and to the authors’ knowledge, this is the first study to examine single and dual task gait in this group. Gait speed reflects the overall health status of an individual and relies on the function of multiple body systems including the cardiovascular and pulmonary systems. Lower usual gait speed places the AF group at increased risk of falls, hospitalization, cognitive decline and mortality along with well-known AF-related events such as stroke and heart failure.

There are several pathways which may explain the association between AF and reduced mobility. The first relates to the cardiac and physical pathway. AF is associated with decreased exercise capacity in patients with heart failure. It can lead to decreased cardiac output because of an increased ventricular rate, irregular ventricular response and loss of the atrial kick resulting in decreased gait speed and mobility due to decreased stamina on exertion. It is likely that the AF group have reduced physical function partly due to co-morbid cardiovascular or chronic conditions which may themselves lead to AF; however, chronic conditions, cardiovascular conditions and cardiovascular medications were adjusted for in the analysis so the reductions observed are unlikely to be attributable to these. AF has also been independently associated with frailty status, although the observed association with reduced gait speed remained after taking frailty measures into account.

Another potential pathway relates to cerebral function and vascular damage. Previous studies have reported that AF is associated with impaired cognition and depression, both of which can affect gait. Vascular pathology may play a role in these impairments as white matter lesions (WMLs) have been associated with depressive symptoms, gait and cognitive impairments and have also been shown to be a risk factor for recurrent falls and poorer gait in older community-dwelling adults. In support of this, AF has also been associated with increased WMLs.

There are several mechanisms through which WMLs may develop in this group. Firstly, AF is associated with a reduction in cardiac output, subsequent hypotension and reduced cerebral perfusion which may lead to the development of WMLs. In support of this, AF is associated with neurocardiovascular instability which is most commonly manifested as orthostatic hypotension, again leading to reduced cerebral perfusion. Secondly, as hypertension is a common risk factor for both AF and WMLs, it could act as a mediator in the potential causal pathway underlying this association. Finally, AF can lead to the formation of left atrial thrombi that can in turn lead to occlusion of small or large brain arteries, resulting in microinfarction (including white matter) or stroke. As MRI based brain measurements were not included in the current protocol, potential associations with WMLs could not be confirmed.

AF is also a risk factor for endothelial dysfunction which is characterised by increased oxidative stress and proinflammatory agents, and impaired nitric oxide-dependent vasorelaxation. In AF patients, important clinical correlates of this dysfunction include muscle underperfusion, premature lactic acidosis and ergoreflex oversignalling during physical activity. As these clinical correlates are likely to result in decreased gait speed, this adds a new pathophysiological explanation for the association between AF and gait speed.

The strengths of this study include the large nationally representative sample, the detailed health information obtained about these respondents allowing confounders to be taken into account and the objective assessment of AF. In addition, AF was diagnosed at the same time as the gait assessment was carried out rather than using past medical history. Most respondents with AF performed the gait tasks at speeds above 1 m/s which is the cut-off for increased risk of adverse events in older adults. However, the study sample is limited to those who attended a health assessment centre where AF could be diagnosed and the gait assessments were completed. Therefore, they are likely to be the healthier members of the population while those with more severe co-morbidities are unlikely to have been included in this study. Consequently, the results of this study potentially underestimate the associations in the overall population and specifically in subgroups such as nursing home residents. As the data is cross-sectional, we are unable to determine if individuals walked slower prior to developing AF or if it was a consequence of AF and associated conditions.
Clinical implications & conclusion

Our results highlight the need for early recognition and clinical management of AF in older adults. From our cohort, it is known that over a third of patients with AF are unaware of their diagnosis, and over half of patients with high risk of stroke receive inadequate treatment. Regular physical activity to improve overall cardiovascular health is recommended in the management of AF and these results support the need for clinicians to emphasise the importance of this. This may be of particular importance to nursing homes residents, due to the high prevalence of AF and the high incidence of falls in this group. Several studies have shown an improvement of exercise capacity in AF patients after cardioversion, suggesting that improvement of the hemodynamic changes associated with increased or irregular ventricular response in AF can be established. Early detection and treatment of AF in older adults may help to prevent stroke and other AF related cardiovascular events, while exercise-based interventions may also help to reduce the decline in physical performance and prevent falls leading to further disability.

In conclusion, AF is independently associated with lower usual gait speed in adults aged 70 years and older, placing them at increased risk of adverse events such as falls, hospitalisation, cognitive decline and mortality as well as stroke and heart failure. The early diagnosis and management of this condition is vital to reduce these risks and prevent further decline.

ACKNOWLEDGEMENTS

The authors would like to acknowledge the contribution of the TILDA participants and research team. Financial support was provided by Irish Life plc, the Irish Government and the Atlantic Philanthropies. These funders played no part in the design, methods, subject recruitment, data collection, analysis and preparation of this paper, therefore there is no conflict of interest.
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