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Is orthostatic hypotension more common in individuals with atrial fibrillation?—Findings from The Irish Longitudinal Study on Ageing (TILDA)

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Abstract

Introduction: atrial fibrillation (AF) and orthostatic hypotension (OH) share common risk factors such as age, hypertension and cardiovascular (CV) disease. The autonomic nervous system (ANS) also plays a role in the pathogenesis of both AF and OH. The aim of this study is to assess whether individuals with AF are more likely to have OH than those without AF.
Methods: data from wave 1 of The Irish Longitudinal Study on Ageing were used. Beat-to-beat blood pressure was measured during active stand lasting 110 s. OH, defined as a drop in systolic blood pressure (SBP) ≥20 mmHg or a drop in diastolic blood pressure ≥10 mmHg at 30, 60 and 90 s was assessed. Initial OH (IOH) was assessed as a drop in SBP ≥40 mmHg or a drop in diastolic BP≥20 mmHg.
Results: in total 4,408 participants aged ≥50 had active stand and electrocardiogram data suitable for analysis. AF was identified in 101 of these. Logistic regression found participants with AF were more likely to have OH at 30 (odds ratio (OR) 1.95, 95% confidence interval (CI) 1.24–3.06) and 60 (OR 2.13, 95% CI 1.18–3.87) seconds, and IOH (OR 1.81, 95% CI 1.21–2.70). The association between IOH and OH at 30 s remained significant following adjustment for confounders (age, sex, baseline HR, education, BP, smoking, frailty, beta blocker (BB) use, anti-hypertensive use (excluding BBs) and number of CV conditions).
Conclusion: OH is more common in individuals with AF, this may reflect the role of the ANS in both AF and OH.

Keywords: *Older people, atrial fibrillation, orthostatic hypotension, falls, syncope*

Introduction

Atrial Fibrillation (AF), the most common sustained arrhythmia, is associated with significant morbidity and mortality [1]. Several mechanisms contribute to its pathogenesis, including the autonomic nervous system (ANS), which plays a role in initiation and maintenance of AF [2, 3]. Changes in heart rate variability (HRV), a marker of cardiac autonomic modulation, occur at the onset of paroxysmal AF [4] and reduced HRV has been explored as a risk factor for AF, with conflicting results [5, 6]. The incidence of AF increases with age, and is detected in 3-4% of healthy volunteers over 60, without coronary artery disease [7]. This could be due to alterations in the ANS, which changes with age [8], or due to cardiac structural and functional alterations associated with ageing [7].

The ANS also plays a role in the pathogenesis of Orthostatic Hypotension (OH). Orthostasis results in pooling of 0.5–1 L in the lower limbs and splanchnic vessels, leading to a reduction in venous return, ventricular preload and cardiac output (CO), subsequent reduction in the distension of baroreceptors and reduction in firing of baroreceptors to the cardiovascular (CV) centre in the brain stem. This leads to parasympathetic inhibition, sympathetic activation, increased heart rate (HR) and CO, and restoration of blood pressure (BP) and cerebral perfusion [9]. OH is a manifestation of autonomic dysfunction, when adaptive

mechanisms fail to compensate for this reduction in venous return that normally occurs on standing.

Prevalence of OH increases with age, and is observed in 5–30% of older people [10]. BP control progressively worsens with ageing, for reasons including impaired baroreflex sensitivity, impaired thirst, dehydration and impaired venomotor tone [9, 11]. Chronic diseases like diabetes and neurodegenerative diseases including Parkinson's disease and multi-systems atrophy also play a role in its aetiology. Polypharmacy is common in ageing, and medications are often causal in OH [9]. OH is associated with increased morbidity and mortality [12] and it may be a marker for CV risk [13].

The aim of this study was to assess whether OH is more common in individuals with AF in a community-dwelling population over the age of 50. An association between the two could pose clinical challenges given the emerging evidence linking AF to falls [14–16]. There is evidence linking AF with cognitive impairment in the absence of stroke, however the mechanism for this is debated, with proposed mechanisms including periods of cerebral hypoperfusion [17]. Emerging evidence suggests an association between OH and dementia, potentially augmenting risk of cognitive impairment secondary to cerebral hypoperfusion in individuals with AF and co-existent OH [18, 19].

Methods

Data from wave 1 of The Irish Longitudinal Study on Ageing (TILDA) were used. TILDA is a large prospective cohort study comprising of community-dwelling people ≥ 50, resident in Ireland. Details are published elsewhere [20]. Briefly, it consists of (i) a computer-assisted personal interview (CAPI), (ii) a self-completion questionnaire and (iii) a health assessment (HA). Ethical approval was obtained from the Trinity College Research Ethics committee. Participants provided written informed consent.

Evaluation of AF

Participants were invited to attend one of two health centres for HA. Those that did had a 10 min surface electrocardiogram (ECG), performed lying supine in a quiet room with ambient temperature 21–23°C. ECGs were screened for AF by two clinicians and inter-rater disagreement resolved by a cardiologist. Only objective measurements of AF were included in the study.

Measurement of OH

HA included measurement of beat-to-beat BP response to orthostasis with a Finometer© (Finapres Medical Systems BV). The assessment was performed on the same day in the same room as ECGs. Baseline BP and HR were recorded as the mean value between 60 and 30 s prior to stand. Beat-to-beat BP was measured for 110 s following stand.

Two outcomes were measured in this study—classical OH (COH) and initial OH (IOH). COH is defined as is a sustained reduction in systolic blood pressure (SBP) ≥20 mmHg or diastolic blood pressure (DBP) ≥10 mmHg within 3 min of standing [21]. COH was assessed using OH sustained at 30, 60 and 90 s post stand. IOH is defined as a transient BP decrease, within 15 s after standing of ≥40 mmHg in SBP or ≥20 mmHg in DBP [21]. IOH was measured by BP response at 10 s post stand. Data was processed using a 5 s moving average filter, therefore the 10 s value is a weighted mean from 5 to 15 s.

Statistical analysis

Statistical analysis was performed using STATA 12 (Stata Corporation). Normally distributed variables (assessed by Q-Q plots) were compared using Student's *t*-tests, non-normally distributed variables using Mann–Whitney tests and categorical variables using chi-squared tests. Univariate logistic regression was performed to assess whether participants with AF were more likely to have IOH or COH at 30, 60 or 90 s. Multivariable logistic regression was performed controlling for age, sex, baseline HR, education, mean SBP, smoking, frailty (assessed using fried frailty scale [22]), beta blocker (BB) use, anti-hypertensive medications (not BB) and self-reported CV co-morbidities.

Covariate Information

Covariate information was obtained during the CAPI and HA. Choice of covariates was based on clinically relevant variables, added to the model in succession. The order of inclusion of the variables was—age, sex, baseline HR, mean SBP, smoking, body mass index (BMI), level of education, frailty status (assessed using Fried frailty index [22]), BB use, anti-hypertensive use (excluding BBs), polypharmacy, cholesterol, self-reported hypertension, diabetes, angina, heart attack, heart failure, stroke, transient ischaemic attack (TIA) and murmur. Variables that significantly improved model fit (based on LR chi-squared) were kept. The following covariates were included in the final model: Age, sex, baseline HR, education, mean SBP, smoking, frailty (not frail or pre-frail/frail), BB use, anti-hypertensive use (excluding BBs) and number of CV conditions (0, 1 or ≥2).

Results

In total 8,175 participants were recruited to TILDA, of whom 5,035 attended for HA. A total of 4,408 had both active stand data and ECG data adequate for analysis. Of these, 101 participants had AF on ECG (2.29%). Individuals with AF were older, more likely to be male, with higher baseline HR and lower levels of education. They had higher rates of self-reported CV disease and higher levels of anti-hypertensive use (Table 1).

Results of univariate analysis (Table 2) found participants with AF were more likely to have COH at 30 (OR

Table 1. Population characteristics

Characteristics	AF (n = 101)	No AF (n = 4,307)	P value
Age, mean ± SD	69.68 ± 7.80	61.44 ± 8.20	<0.001
Female, % (n)	20.79 (21)	54.70 (2,356)	<0.001
Baseline heart rate	76.24 ± 16.50	65.01 ± 9.70	<0.001
Education, % (n)			
Primary	42.57 (43)	20.65 (889)	
Secondary	32.67 (33)	42.11 (1,813)	
Third/higher	24.75 (25)	37.24 (1,603)	<0.001
Smoking status, % (n)			
Never	28.71 (29)	46.11 (1,986)	
Past	63.37 (64)	38.87 (1,674)	
Current	7.92 (8)	15.02 (647)	<0.001
Frailty, % (n)			
Not frail	60.20 (59)	72.99 (3,076)	
Pre-frail	25.70 (1,083)	35.71 (35)	
Frail	1.31 (55)	4.08 (4)	0.004
Physical activity (IPAQ), metmins, mean ± SD	3,203.47 ± 3,887.45	3,151.638 ± 3,359.335	0.33
Body mass index (kg/m ^{2}), mean ± SD	30.30 ± 5.90	28.50 ± 4.80	0.003
MMSE, mean ± SD	28.40 ± 1.60	28.60 ± 1.80	0.0346
Disease prevalence, % (n)			
Angina	16.83 (17)	4.11 (177)	<0.001
Hypertension	47.50 (48)	32.70 (1,409)	0.002
Myocardial infarction	8.91 (9)	3.81 (164)	0.009
Heart failure	5.94 (6)	0.70 (30)	<0.001
Diabetes	14.85 (15)	6.32 (272)	0.001
Stroke/TIA	9.90 (10)	2.51 (108)	<0.001
Heart murmur	14.85 (15)	4.78 (206)	<0.001
Seated SBP, mean ± SD	126.05 ± 22.46	130.47 ± 20.55	0.12
Taking beta blockers	38.61 (39)	11.24 (484)	<0.001
Taking anti-hypertensive medications (not beta blockers), % (n)	68.32 (69)	29.39 (1,266)	<0.001
Polypharmacy (≥5 meds), % (n)	48 (48)	16.83 (722)	<0.001
Cholesterol, mean ± SD	4.41 ± 1.01	2.18 ± 1.05	<0.001

SD, standard deviation; IPAQ, International physical activity questionnaire; MMSE, mini mental state examination.

Table 2. Odds of co-existent OH in participants with AF—univariate and multivariable logistic regression

	AF on ECG		
	OR	CI (95%)	P value
Univariate analysis			
OH sustained at 90 s	1.31	0.57, 3.03	0.527
OH sustained at 60 s	2.13	1.18, 3.87	**0.013**
OH sustained at 30 s	1.95	1.24, 3.06	**0.004**
Initial OH	1.81	1.21, 2.69	**0.004**
Multivariable analysis			
OH sustained at 90 s	1.27	0.52, 3.09	0.593
OH sustained at 60 s	1.81	0.95, 3.47	0.073
OH sustained at 30 s	1.78	1.07, 2.94	**0.025**
Initial OH	2.48	1.59,3.87	**<0.001**

Values that are significant at $P < 0.05$ are presented in bold.

1.95, 95% CI 1.24, 3.06; $P = 0.004$), 60 s (OR 2.13, 95% CI 1.17, 3.87; $P = 0.013$) and IOH (OR 1.81, 95% CI 1.21, 2.69; $P = 0.004$). Results of the multivariable model are also displayed in Table 2. The association between AF and IOH (OR 2.48, 95% CI 1.59, 3.87; $P < 0.0001$) and OH at 30 s (OR 1.78, 95% CI 1.07, 2.94; $P = 0.025$) remained significant following adjustment for confounders. Participants with AF showed a strong trend towards OH at 60 s (OR 1.81, 95% CI 0.75, 3.47; $P < 0.073$) following adjustment for confounders. Results of the full multivariable model can be found in Supplementary Dataset, Table 1 in *Age and Ageing* online.

Discussion

Participants with AF are more likely to have COH at 30 and 60 s and IOH than participants in sinus rhythm. Both OH and AF share common risk factors such as age, hypertension and ischaemic heart disease, however the association between COH at 30 s and IOH and AF remains significant following adjustment for potential confounders. To our knowledge, this association has not previously been reported. Two previous studies have found that baseline OH is associated with higher incidence of AF at long term follow-up [23, 24].

Age related changes in CV structure and function may underlie the association between AF and OH independent of co-morbidities such as ischaemic heart disease [25]. Another mechanism that could underlie this association is the ANS, which plays a role in the pathogenesis of both AF and OH. Initial restoration of BP on stand is controlled by the ANS via the baroreceptors. A recent study suggests that

AF is associated with impairment of the baroreflex, and restoration of sinus rhythm improves baroreflex gain [26]. This may explain the strong association between l IOH and AF.

Clinical implications include a potential increased risk of falls and syncope. Emerging literature suggests an association between AF and falls [14–16, 27]. Previous analysis of the TILDA dataset has shown an associated between AF and impaired mobility, syncope and falls [16, 28]. Co-existent OH could further increase this, and should be considered in treatment with medications such as BBs, which have shown an association with OH on analysis of TILDA data [29].

Limitations of the current study include that only objective measurements of AF were used. Participants with paroxysmal AF may have been excluded from the AF group. The prevalence of AF was low (2.29%), which may reflect the fact that individuals with paroxysmal AF were not included in this number. Co-morbidities collected in the CAPI relied on self-reported illness.

In conclusion, this study has found that an association between OH and AF in a community-dwelling population aged over 50. A number of processes could underlie this association, such as the ANS or impairment of the baroreflex. Further analysis of the TILDA data using baseline HRV and baroreflex sensitivity and incident AF and OH at follow-up could help explore this relationship in the future.

Key points

- Orthostatic Hypotension and Atrial Fibrillation share common risk factors.
- Co-existent orthostatic hypotension could increase a risk of falls and syncope in individuals with atrial fibrillation.
- Individuals with atrial fibrillation show a strong trend towards orthostatic hypotension in the TILDA data.
- Initial OH is more common in individuals with AF and this remains significant following adjustment for potential confounders.

Supplementary data

Supplementary data are available at subscribers in *Age and Ageing* online.

Conflicts of interest

None declared.

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Objectively measured physical activity and kidney function in older men; a cross-sectional population-based study

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Abstract

Background: kidney function declines in older adults and physical activity levels are low. We investigated whether higher levels of physical activity and lower levels of sedentary behaviour were associated with lower odds of low kidney function in older men.
Methods: cross-sectional study of 1,352 men from the British Regional Heart Study, mean (standard deviation) age 78.5 (4.6) year. Physical activity and sedentary behaviour were measured using Actigraph GT3X accelerometers. Kidney function was measured by estimated Glomerular filtration rate (eGFR) using the chronic kidney disease-EPI creatinine-cystatin equation. Associations between physical (in)activity and kidney function were investigated using regression models.
Results: higher levels of physical activity and lower levels of sedentary behaviour were associated with reduced odds ratios (ORs) for lower eGFR (<45 versus ≥45 ml/min per 1.73 m^2) after adjustment for covariates. Each additional 1,000 steps, 30 min of light physical activity and 10 min of moderate/vigorous physical activity per day were associated with a lower