



Associations between cardiac arrhythmia, incident disability in activities of daily living and physical performance: the ILSA study

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Abstract

Background Cardiac arrhythmias are common conditions in older people. Unfortunately, there is limited literature on associations between cardiac arrhythmias and physical performance or disability. We therefore aimed to prospectively investigate associations between cardiac arrhythmias and changes in disability and physical performance during 8 years of follow-up, using data from the Italian Longitudinal Study on Aging (ILSA). **Methods** Cardiac arrhythmias diagnosis was posed through a screening phase, confirmed by a physician. The onset of disability in activities of daily living (ADL) and the changes in several physical performance tests during follow-up were considered as outcomes. Fully-adjusted and propensity-score Cox Proportional Hazard models and mixed models were used for exploring associations between cardiac arrhythmia and the outcomes of interest. **Results** The prevalence of cardiac arrhythmia at baseline was 23.3%. People reporting cardiac arrhythmia at the baseline were significantly older, more frequently male, smokers and reported a higher presence of all medical conditions investigated (hypertension, heart failure, angina, myocardial infarction, diabetes, stroke), but no difference in dementia, Parkinsonism, cognitive or mood disorder. Cardiac arrhythmia at baseline was significantly associated with the incidence of disability in ADL (HR = 1.23; 95% CI: 1.01–1.50; $P = 0.0478$ in propensity score analyses; HR = 1.28; 95% CI: 1.01–1.61; $P = 0.0401$ in fully adjusted models). Cardiac arrhythmia at baseline was also associated with a significant worsening in balance test ($P = 0.0436$). **Conclusions** The presence of cardiac arrhythmia at baseline was associated with a significant higher risk of disability and of worsening in some physical performance tests, particularly those relating to balance. Screening and frequently assessing physical performance in older people affected by cardiac arrhythmia can be important to prevent a loss of physical performance, with further, potential, complications of medical management.

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1 Introduction

Cardiac arrhythmia are common conditions in older people, and atrial fibrillation (AF) is the most frequent. The estimated number of individuals with cardiac arrhythmia in the world in 2010 was 33.5 million.^[1] It is well known that these cardiac conditions are associated with several negative outcomes in older people, including stroke,^[2] heart failure,^[3] and mortality.^[4]

Cardiac arrhythmias, in particular AF, represent a significant public health problem, and novel estimates suggest that this condition accounts for 1% of the National Health Service budget in the United Kingdom^[5] and \$16 to 26 billion of annual US expenses.^[6]

Even if of epidemiological importance, there is limited literature regarding the impact of cardiac arrhythmias on disability and physical performance in older people. In a large epidemiological Italian study, AF was significantly and strongly associated with physical disability, but these findings were cross-sectional.^[7] In the Health, Aging, and Body Composition Study, participants with AF had a significantly greater 4-year upper and lower limbs decline than those without AF.^[8] However, this longitudinal study is one of the few investigating this topic. To the best of our knowledge, in fact, there is no clearly defined association

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between cardiac arrhythmias and functional capacity and the adjustment for potential confounders (such as age, sex, race, socioeconomic level, other cardiac diseases, and medication use) is often not considered.^[9]

Given this background, we aimed to prospectively investigate associations between cardiac arrhythmias and changes in disability and physical performance during eight years of follow-up in a large Italian cohort of older people.

2 Methods

2.1 Participants

This study is based on the Italian Longitudinal Study on Aging (ILSA), a prospective, community-based cohort study.^[10] An initial sample of 5632 individuals aged 65 to 84 years, stratified by age and sex using an equal allocation strategy, was identified on the demographic lists of the registry offices of eight municipalities (urban, suburban, rural).

The ILSA study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects were approved by the Ethics Committees of the participating centers.

The ILSA cohort was firstly examined in 1992 (baseline assessment) and re-examined in two waves in 1996 and 2000.

2.2 Baseline assessments

The baseline evaluation had screening and clinical confirmation phases of several chronic conditions. In particular, the screening phase (all participants participated in this phase) included a fasting blood sample; a personal interview during which the participants were asked about health problems and specific risk factors; a physician's examination including tests such as the Mini Mental State Examination (MMSE),^[11] the Geriatric Depression Scale (GDS),^[12] the Activities of Daily Living (ADL),^[13] spirometry, electrocardiography, the examination of heart, lungs, pulses and bruits and a neurological examination. Anthropometric measures were also evaluated and data on medications used were collected.

The clinical confirmation phase was administered by specialists only to participants who screened positive for medical chronic conditions, through a standardized clinical examination. The criteria for diagnoses and the method to calculate prevalence rates have been published elsewhere.^[14]

2.3 Disability in ADL

Each ADL item was originally scored between 1 and 3, with 1 indicating complete independence and 3 indicating total dependence. An adjusted total score, varying between

0.33 and 1, was obtained dividing the total score of the answered items by the sum of scores of these items in the assumption of complete dependency. A score of 0.33 means that the subject was completely independent (no disability), a score between 0.33 and 0.56 revealed a dependency in a maximum of two ADLs (mild disability), a score between 0.56 and 0.78 a dependency in a maximum of three ADLs (moderate disability), and a score between 0.78 and 1 dependency in four or more ADLs (severe disability).

2.4 Exposure: cardiac arrhythmia diagnosis

The presence of cardiac arrhythmia was diagnosed in two steps: phase 1 (screening). (a): positive questionnaire (self-reported diagnosis and medical treatment or pacemaker) or (b). diagnostic electrocardiography (computerized diagnosis). The screening phase was further confirmed by a phase 2 (medical confirmation). A physician reviewed clinical records (electrocardiography, 24-h Holter monitoring) and the diagnosis of cardiac arrhythmia was confirmed by the participant's physician and by the clinical evaluation of the ILSA internists.^[14] Details related to the diagnosis of cardiac arrhythmia are available in supplemental Table S1.

2.5 Outcomes: incident disability and changes in physical performance during follow-up

Several outcomes of our interest were included. First, the onset of disability in ADL during follow-up,^[13] second, the changes in physical performance tests, such as chair stands time^[15] and gait speed (over 5 m).^[16]

2.6 Statistical analysis

To generalize the ILSA sample to the Italian population, a set of weights defined according to the sex, the age distribution of the reference population (Census 1991, available at demo.istat.it) and the sample fraction, was applied to the analyses.

The association of baseline characteristics and the presence of arrhythmia at baseline was evaluated using the χ^2 or exact test for categorical variables, or generalized linear model, testing for homoscedasticity through Levene's test for quantitative variables.

Propensity scores were estimated by logistic regression models including cardiac arrhythmia as dependent variable and unbalanced features (exceeding 10% of difference at univariate analysis) as independent variables.

Incidence of disability in ADL, defined as the transition from no disability at baseline to mild, moderate or severe disability during follow-up, was evaluated through Cox proportional hazard models, with death as competing risk, adjusting (a) only for age and sex, (b) for other covariates

associated with the outcomes with $P < 0.10$ at the univariate analysis and for incidence of stroke between baseline and follow-ups, (c) with propensity-score as covariate. The proportional hazard assumption was verified considering Schoenfeld's residuals of the covariates, and interactions between variables were evaluated. Incidence of disability in physical performance tests defined as the transition from baseline to follow-ups from < 2 s (without hand) to ≥ 2 s (with or without hands) for chair stands, and as a transition from ≥ 0.8 m/s to < 0.8 m/s for gait speed, were evaluated following the same procedure.

Mixed models were finally defined to estimate the differences in physical performance tests results according to the presence of cardiac arrhythmia, adjusting for baseline score, age, sex and propensity-score.

All analyses were two-sided, and $P < 0.05$ was considered significant. The analyses were performed using SAS statistical package, release 9.4 (SAS, Cary, NC).

3 Results

Among 5,632 older people initially included in the ILSA study, 4,277 were included in this research. The mean age was 72.4 ± 5.6 years and participants were predominantly female (58.5%). The main characteristics of the population included during follow-up are reported in Table S2.

Table 1 shows the baseline characteristics of the included population, by the presence or not of cardiac arrhythmia. People reporting cardiac arrhythmia at the baseline ($n = 996$, 23.3%) were significantly older, more frequently male, smokers, wine drinkers, and had lower mean BMI levels than those without arrhythmia ($n = 3,282$) (Table 1). People with cardiac arrhythmia reported significantly higher values of creatinine, but significantly lower values for serum cholesterol and fibrinogen. As reported in Table 1, people with cardiac arrhythmia reported a significant higher presence of all medical conditions investigated (hypertension, heart failure, angina, myocardial infarction, diabetes, stroke), but no difference in dementia, Parkinsonism, cognitive or mood disorder. Participants with cardiac arrhythmia reported a higher median number of medications used and a higher prevalence of antithrombotic agents use.

People reporting cardiac arrhythmia did not report any difference in ADL disability ($P = 0.4396$) at baseline. People with arrhythmia scored significantly worse in chair stands time ($P = 0.0351$), but not in 5-m gait speed ($P = 0.1907$) (Table 1).

Table 2 shows the association between presence of cardiac arrhythmia at baseline and the outcomes of our interest

during eight years of follow-up. Cardiac arrhythmia at baseline was significantly associated with the incidence of disability in ADL (HR = 1.23; 95% CI: 1.01–1.50; $P = 0.0478$ in propensity score analyses; HR = 1.28; 95% CI: 1.01–1.61; $P = 0.0401$ in fully adjusted models), whilst no significant association was observed for incident impairment in gait speed or in chair stands time (Table 2).

Supplemental Figure S1 and Table S3 report the association between arrhythmia at baseline and changes in physical performance tests during follow-up time according to mixed models. Arrhythmia at baseline was associated with a significant worsening in one leg stand ($P = 0.0436$) and with a borderline significant worsening in number of steps necessary for a rotation of 180° ($P = 0.0547$).

4 Discussion

In this paper, with a mean follow-up period of 8 years, it was shown that the presence of cardiac arrhythmia at baseline was significantly associated with the onset of disability and to a worsening in some physical tests, particularly those that regard balance. To the best of our knowledge, this is one of the few cohort studies reporting these potential associations.

Prior works investigating cardiac arrhythmias (in particular AF) and physical frailty (a stage often preceding disability) in older adults are still limited. A cross-sectional study of older adults living in the community reported a significant association between AF and impaired gait speed,^[17] but did not assess the prospective association of AF to gait speed impairment. Studies among hospitalized older people have reported increased frailty risk in older adults with AF, but relied on self-reported disability and did not use a validated definition of frailty.^[18,19] Finally, in one cohort study among American older people living in the community, the authors found that the presence of AF was associated with an increased risk of decline in some physical performance tests, such as the short physical performance battery.^[8] However, they did not explore the potential association between cardiac arrhythmias and the onset of disability as in the current study.

It can be hypothesized that associations between cardiac arrhythmias and decline in physical performance and disability are strongly interrelated. It is widely known that cardiac arrhythmias can have both cardiovascular and non-cardiovascular clinical manifestations and that, for example, cardiovascular diseases are strongly associated with the development of frailty.^[20,21] Moreover, some risk factors (such as obesity and diabetes) are common between cardiac

Table 1. Baseline characteristics of participants considered in the analysis (weighted data).

	Overall (<i>n</i> = 4277)	Arrhythmia		<i>P</i> -value
		No (<i>n</i> = 3282)	Yes (<i>n</i> = 996)	
General characteristics				
Age, yrs	72.4 ± 5.6	72.0 ± 5.6	73.2 ± 5.4	< 0.0001
Sex, females	2503 (58.5%)	1980 (60.3%)	523 (52.5%)	< 0.0001
Marital status, married or cohabiting	2491 (58.3%)	1910 (58.3%)	581 (58.4%)	0.9496
Education, elementary school or less	3011 (71.4%)	2329 (77.3%)	682 (69.2%)	0.0825
Smoking status, current/former smoker	1813 (42.7%)	1348 (41.5%)	465 (46.8%)	< 0.0001
Wine drinker	3182 (75.0%)	2413 (74.2%)	769 (77.8%)	0.0200
BMI, kg/m ²	27.1 ± 4.6	27.3 ± 4.7	26.8 ± 4.2	0.0032
Abdominal circumference, cm	97.4 ± 12.2	97.5 ± 12.7	97.1 ± 10.8	0.2541
Bio-humoral parameters				
Creatinine, mg/dL	1.02 ± 1.53	1.01 ± 1.79	1.03 ± 0.42	< 0.0001
Cholesterol, mg/dL	222.0 ± 43.7	223.5 ± 43.9	217.9 ± 42.9	0.0002
Triglycerides, mg/dL	150.9 ± 82.1	151.1 ± 85.1	150.4 ± 74.0	0.7270
HDL, mg/dL	49.6 ± 13.7	49.7 ± 14.4	49.2 ± 11.4	0.6704
Fibrinogen, mg/dL	357.6 ± 98.4	359.5 ± 100.9	352.3 ± 91.8	0.0461
Glycaemia, mg/dL	105.9 ± 35.2	106.0 ± 37.3	105.6 ± 29.5	0.7173
Medical conditions				
Hypertension	2684 (63.2%)	1992 (61.3%)	691 (69.5%)	< 0.0001
Heart failure	296 (6.9%)	141 (4.3%)	154 (15.5%)	< 0.0001
Angina	326 (7.6%)	186 (5.7%)	140 (14.1%)	< 0.0001
Myocardial Infarction	331 (7.8%)	193 (5.9%)	138 (13.9%)	< 0.0001
Diabetes	581 (13.7%)	419 (12.9%)	162 (16.4%)	0.0052
Stroke	290 (6.9%)	202 (6.2%)	88 (9.0%)	0.0023
Dementia	208 (6.3%)	156 (6.4%)	52 (6.0%)	0.6751
Parkinsonism	123 (2.9%)	94 (2.9%)	29 (3.0%)	0.9358
MMSE (range 0–30)	26.8 ± 3.1	26.8 ± 3.1	26.7 ± 3.1	0.4793
GDS (range 0–30)	9.3 ± 6.3	9.1 ± 6.4	9.5 ± 6.2	0.4088
*Medications used, antithrombotic agents	553 (13.4%)	340 (10.7%)	212 (22.2%)	< 0.0001
Total number of medications used, median (Q1, Q3)	1 (1, 2)	1 (1, 2)	2 (1, 2)	< 0.0001
Disability items				
ADL				0.4396
No disability	2198 (67.3%)	1634 (67.8%)	567 (65.9%)	
Mild disability	863 (26.4%)	620 (25.8%)	242 (28.1%)	
Moderate disability	129 (4.0%)	94 (3.9%)	35 (4.1%)	
Severe disability	76 (2.3%)	60 (2.5%)	16 (1.9%)	
Physical performance tests				
Chair stands test				0.0351
Not possible	265 (8.1%)	204 (8.5%)	61 (7.1%)	
With hands, ≥ 2 s	112 (3.4%)	70 (2.9%)	42 (4.9%)	
With hands, < 2 s	163 (5.0%)	120 (5.0%)	43 (5.0%)	
Without hands, ≥ 2 s	117 (3.6%)	81 (3.4%)	36 (4.2%)	
Without hands, < 2 s	2608 (79.9%)	1931 (80.3%)	678 (78.7%)	
Gait speed (5-m) test				0.1907
Not possible	392 (12.0%)	300 (12.5%)	92 (10.7%)	
< 0.8 m/s	1402 (43.0%)	1086 (45.3%)	377 (43.8%)	
≥ 0.8 m/s	1462 (44.9%)	1010 (42.2%)	391 (45.5%)	

Data are presented as mean ± SD or *n* (%). ADL: activities of daily living; BMI: body mass index; GDS: geriatric depression scale; MMSE: mini-mental state examination. *Anatomic Therapeutic Classification code B01 (antithrombotic agents).

Table 2. Multivariable models.

	Model (a)			Model (b)			Model (c)		
	HR	95% CI	P-value	HR	95% CI	P-value	HR	95% CI	P-value
*Incidence of disability in ADL									
Arrhythmia	1.17	0.98–1.41	0.0818	1.28	1.01–1.61	0.0401	1.23	1.01–1.50	0.0478
#From Gait Speed ≥ 0.8 m/s to < 0.8 m/s									
Arrhythmia	1.12	0.91–1.38	0.2801	1.14	0.89–1.45	0.3088	1.16	0.92–1.47	0.2074
†From Chair Stands without hands < 2 s to ≥ 2 s or with hands									
Arrhythmia	1.18	0.94–1.48	0.1641	1.38	1.04–1.83	0.0238	1.09	0.84–1.42	0.4966

Model (a): adjusted only for age and sex; model (b): adjusted for age, sex and other covariates associated with the outcome with $P < 0.10$ at univariate analysis (marital status, education, smoking status, hypertension, heart failure, myocardial infarction, diabetes, stroke, dementia, Parkinsonism, incident stroke between baseline and follow-ups, use of antithrombotic agents, creatinine at the baseline, cholesterol at the baseline); model (c): propensity-score as covariate (estimated by logistic regression models including arrhythmia as dependent variable and unbalanced features as independent variables). *Incidence of disability in ADL: from none disability in ADL at baseline to disability in at least one ADL at follow-ups (1995–1997 or 2000–2001). Results from a Cox proportional Hazard model (death as competing risk) among participants with no disability in ADL at baseline ($n = 670$ had mild, moderate or severe disability at follow-ups; $n = 210$ died at follow-ups; $n = 1167$ had no disability at follow-ups). #From Gait Speed ≥ 0.6 m/s to < 0.6 m/s: results from a Cox proportional Hazard model (death as competing risk) among participants with Gait Speed ≥ 0.6 m/s at baseline ($n = 247$ had a Gait Speed < 0.6 m/s at follow-ups; $n = 247$ died at follow-ups; $n = 929$ had a Gait Speed ≥ 0.6 m/s at follow-ups). †From Chair Stands without hands < 2 s to ≥ 2 s or with hands: results from a Cox proportional Hazard model (death as competing risk) among participants with Chair Stands without hands < 2 s at baseline ($n = 372$ had a Chair Stands ≥ 2 s or with hands at follow-ups; $n = 288$ died at follow-ups; $n = 1153$ had a Chair Stands without hands < 2 s at follow-ups). ADL: activities of daily living.

arrhythmias and the worsening of physical performance and disability.^[22,23] Other sub-clinical cardiovascular disease (e.g., coronary calcifications) and inflammation may also be associated with cardiac arrhythmias and declining physical performance/disability.^[24] Silent cerebral infarcts often secondary to cardiac arrhythmias were not available in the ILSA study, but may also affect physical performance in older adults.^[25]

Moreover, cardiac arrhythmias might contribute directly towards the decline in physical performance and the onset of disability. All cardiac arrhythmias, in fact, may alter atrial structure and performance, modify atrial refractoriness, reduce atrial transport (in systolic phase), and probably promote the onset of atrial fibrosis.^[26] Moreover, irregular heart rates diminish left ventricular filling and cardiac output, with a consequent less vascularization of the muscles.^[27] These structural and electrical cardiac changes may ultimately impair peripheral perfusion and diminish capacity for activities of daily living.^[28]

Finally, we would like to observe that our study suggests that the presence of cardiac arrhythmias is significantly associated with an impaired balance during the follow-up period. In our opinion, this finding is of great clinical importance since people with cardiac arrhythmias usually take oral anticoagulants and the risk of falls in these subjects is likely increased by the presence of cardiac arrhythmia itself, further strengthening the necessity of a strict medical monitoring (also in terms of falls) in these people.

The findings of our study should be interpreted within light of its limitations. First, the definition of cardiac arrhythmias did not differentiate between AF and the other common forms observed in the elderly. This fact could be relevant because cardiac arrhythmias can have significantly different clinical weights, with AF representing a major determinant of quality of life and a relevant source of morbidity and mortality among older patients.^[29,30] Second, a consistent part of people originally included in the ILSA study were lost during follow-up evaluations, but this finding is common in cohort studies including older people.

In conclusion, our study suggests that, in older community-dwelling individuals, the presence of cardiac arrhythmias predicts disability development, particularly in balance function. Since cardiac arrhythmias are common in the elderly, the screening and the monitoring of patients with rhythm disturbances is needed to prevent a loss of physical performance, with further, potential, complications of medical management.

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Disclosure statement

The authors declare no conflict of interest.

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