Published in final edited form as:
Pacing Clin Electrophysiol. 2015 February ; 38(2): 178–186. doi:10.1111/pace.12543.

Atrial Fibrillation Exacerbates Cognitive Dysfunction and Cerebral Perfusion in Heart Failure

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Abstract

Background—Heart failure (HF) increases risk for cognitive impairment in part due to the negative effects of cardiac dysfunction on cerebral perfusion. Atrial fibrillation (AF), an independent risk factor for cognitive impairment, often accompanies HF and is associated with lower systemic perfusion. However, no study has examined the associations among AF, cognitive function, and cerebral perfusion in patients with HF.

Methods—187 HF patients completed neuropsychological testing and underwent transcranial Doppler ultrasonography. Cerebral blood flow velocity of the middle cerebral artery (CBF-V) operationalized cerebral perfusion. A medical chart review ascertained AF.

Results—32.1% of HF patients had a history of AF. HF patients with AF exhibited worse global cognition, memory, and CBF-V relative to patients without AF. These effects remained after HF severity and other demographic and medical factors were taken into account. Partial correlations controlling for possible confounds showed decreased CBF-V predicted worse cognition in multiple domains in the overall sample ($r = 0.13$ to 0.15, $p < 0.05$) and in the subgroup of HF patients with AF ($r = 0.26$ to $r = 0.28$, $p < 0.05$), but not among HF patients without AF.

Conclusions—AF exacerbates cognitive deficits in HF possibly through its association with decreased cerebral perfusion. Longitudinal studies are needed to determine whether AF accelerates cognitive decline in HF and whether medical (e.g., ablation) and lifestyle interventions (e.g., exercise programs) that target cerebral perfusion improve cognitive outcomes in patients with HF and AF.

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Conflict of Interest The authors declare no conflict of interest.

Author Contributions Concept/Design: MA, JG, MBS
Data Analysis/Interpretation: MA, MBS, JG, LHS, RJ, JH
Drafting Article: MA, MBS, JG, LHS, RJ, JH
Approval of Article: All authors
Statistics: MA, MBS, JG

Keywords

Heart failure; atrial fibrillation; cognitive function; cerebral blood flow

Introduction

Heart failure (HF) affects over 800,000 new individuals each year and is associated with an array of poor outcomes, including recurrent hospital readmissions and premature death.[1,2] In addition to these traditional prognostic indicators, HF is also known to increase risk for neurological outcomes like Alzheimer's disease, vascular dementia, as well as structural and functional brain abnormalities.[3-6] Impairments on cognitive testing can also be found in up to 80% of persons with HF[7] with prevalent deficits noted in the domains of attention/ executive function, memory, and psychomotor speed.[8] Cognitive impairment may in part explain many of the negative outcomes associated with HF such as elevated mortality risk.[9]

Recent work has sought to clarify the etiology of cognitive impairment in HF. Cardiac dysfunction and subsequent reductions in cerebral perfusion is believed to be the primary underpinning of poor neurocognitive outcomes in this population.[10,11] Medical conditions that often accompany HF (e.g., obesity, hypertension, diabetes, sleep apnea) also play a key role in the development of cognitive impairment (for a review, see Alosco et al., 2013)[12] possibly through known adverse effects on cerebral perfusion.[13-16] For example, many vascular risk factors in HF (e.g., obesity, hypertension) have indeed been shown to interact with altered cerebral hemodynamics to exacerbate cognitive impairment in this population.[17,18]

Although not yet examined, atrial fibrillation (AF) is an important vascular correlate of HF that may also be linked with poor cognitive outcomes in this population. AF is the most prevalent cardiac arrhythmia in the general population[19] and can be found in approximately 50% of patients with advanced HF.[20] AF increases risk for all-cause mortality and hospital readmissions in HF[21] and may also be an important modifier of the relationship between cerebral hypoperfusion and cognitive impairment in this population. As an example, AF is associated with reduced cardiac output and cerebral blood flow reductions in patients with HF.[19,22] AF is also a known correlate of ischemic-related brain injury,[23] and an independent risk factor for dementia[24] and cognitive dysfunction.[23,25]

Despite these findings, the associations among AF, cognitive function, and cerebral blood flow remain poorly understood and no study has examined the interrelationships among these variables in a sample of older adults with HF. The purpose of the current study was to determine the impact of AF on cognitive function and cerebral perfusion among older adults with HF. Based on past work, we hypothesized that HF participants with AF would exhibit worse cognitive function and greater cerebral blood flow reductions than their non-AF counterparts.

Methods

Participants

This sample consisted of a total of 187 participants with HF that were enrolled in an National Institutes of Health (NIH) study examining neurocognitive outcomes in older adults with HF. Strict inclusion/exclusion criteria were implemented to reduce possible confounds that influence cognitive outcomes. Specifically, the inclusion criteria were age of 50-85 years, English as a primary language, and a diagnosis of New York Heart Association (NYHA) class II, III, or IV at the time of enrollment. Exclusion criteria entailed a history of significant neurological disorder (e.g., dementia, stroke, multiple sclerosis, etc.), head injury with >10 minutes loss of consciousness, severe psychiatric disorder (e.g. schizophrenia, bipolar disorder), past or current substance abuse/dependence, and stage 5 chronic kidney disease. All participants in this sample had complete cognitive and cerebral blood flow data. Participants averaged 68.50 (SD = 8.81) years of age and were 30.5% female. See Table 1 for demographic and medical information.

Measures

Cognitive Function—A brief neuropsychological test battery assessed cognitive function in multiple domains. All cognitive measures used in the current study exhibit excellent reliability and validity. The domains and neuropsychological tests administered are as follows:

- Global Cognitive Function: Modified Mini-Mental State Examination (3MS)[26]
- Attention/Executive Function: Trail Making Test A and B,[27] Digit Symbol Coding,[28] and Frontal Assessment Battery.[29]
- Memory: The California Verbal Learning Test-II (CVLT-II) long delay free recall and total recognition hits.[30]
- Language: Boston Naming Test (BNT)[31] and Animal Fluency test.[32]

Cerebral Blood Flow—Transcranial doppler (TCD) ultrasonography, under an expanded Stroke Prevention Trial in Sickle Cell Anemia (STOP) protocol,[33] examined cerebral blood flow velocity in the major brain arteries. TCD is a valid indicator of cerebral perfusion, as it demonstrates strong associations with neuroimaging modalities that directly examine blood perfusion at the level of the brain tissue (e.g., arterial spin labeling).[34] Mean cerebral blood flow velocity of the middle cerebral artery (CBF-V) operationalized global cerebral perfusion in this study. The middle cerebral artery irrigates much of the cerebrum important for cognitive functions, including aspects of the frontal, temporal, and parietal lobes. CBF-V of the middle cerebral artery has been shown to demonstrate reliable associations with changes in cerebral blood flow and exhibit higher blood flow velocity relative to the other major arteries (e.g., anterior and posterior cerebral artery).[35]

Demographic and Medical History—Demographic and medical characteristics were ascertained through participant self-report and a medical chart review. Specifically, all participants first completed a medical history questionnaire and a medical record review was

then performed by a trained research assistant to supplement and corroborate participant's self-report. Through these methods, a physician diagnostic history of AF (i.e., yes or no) for all participants was obtained along with a history of other demographic (e.g., age, sex, race) and medical characteristics (e.g., hypertension, diabetes, sleep apnea). AF status in this sample consisted of all participants with any form of AF (e.g., persistent, paroxysmal, permanent). Medications were also ascertained via medication lists that were provided by the participants. For the current study, we categorized medications into anticoagulants and beta-blockers according to the American Heart Association classification guidelines.

Procedures

The local Institutional Review Board (IRB) approved the study procedures and all participants provided written informed consent prior to study enrollment. All participants completed demographic and medical history self-report measures and a medical chart review was performed. A brief neuropsychological test battery was then administered to assess global cognitive status, attention/executive function, memory, and language. At a separate study session, but within 2-weeks of cognitive test administration, all participants underwent TCD that was performed by a trained hospital technician.

Statistical Analyses

Raw scores of the neuropsychological measures assessing attention/executive function, memory, and language were transformed to T-scores (a distribution with a mean of 50, and a standard deviation of 10) using normative data that adjusts for age. Memory scores were corrected for gender. Attention/executive function, memory, and language composite scores were computed that consisted of the mean of the T-scores of cognitive measures that make-up their respective domain.

A series of separate analysis of variance's (ANOVA) first examined the impact of AF on each cognitive domain (e.g., global cognitive status, attention/executive function, memory, and language) and CBF-V. The grouping variable included AF (i.e., positive or negative history). To determine the independent effects of AF on cognitive function and CBF-V, these analyses were repeated using analysis of covariance (ANCOVA) with left ventricular ejection fraction (LVEF) and diagnostic history of hypertension, diabetes, and sleep apnea entered as covariates. These medical variables are prevalent in HF and well known to influence cognitive outcomes in this population. We did not adjust for age for analyses examining the cognitive composites given that the cognitive variables were transformed to T-scores that already take into account the effects of age; however, analyses that examined CBF-V included age as a covariate. Lastly, one more set of the above analyses were repeated with anticoagulant and beta-blocker status also entered as covariates in order to explore possible confounding effects of medications. Due to missing data on medications, these analyses were reduced to 171 participants.

Partial correlation analyses were then performed to examine the association between CBF-V and cognitive function in each domain among the overall sample of patients with HF (i.e., those with and without AF). These analyses also controlled for LVEF, hypertension, diabetes, and sleep apnea. We then investigated the association between CBF-V and

cognitive function after restricting the sample to HF patients with AF and then to patients without AF.

Results

Sample Medical Characteristics

A medical chart review showed that participants in this sample exhibited an average LVEF of 40.31 (SD = 14.41). Of the sample, 32.1% (n = 60) of patients with HF had a comorbid history of AF. Other medical variables were also common in the overall sample, including hypertension (66.3%), type 2 diabetes mellitus (34.8%), and sleep apnea (24.1%). Of the sample, 15.5% were prescribed an anticoagulant and 42.2% beta-blockers. Independent samples *t*-tests and chi-square analyses showed that HF patients with AF were significantly older, exhibited worse HF severity, and were more likely to be prescribed an anticoagulant relative to patients without AF ($p < 0.05$ for all). There were no differences between HF patients with and without a history of AF on other demographic (e.g., education, sex) or medical variables (e.g., hypertension, type 2 diabetes mellitus, sleep apnea, beta-blocker status). See Table 1.

Cognitive Test Performance in the Overall Sample

Refer to Table 2 for cognitive test performance in the overall sample and among HF patients with and without AF. Cognitive dysfunction was common, as the sample demonstrated an average 3MS score of 92.74 (SD = 5.39) and 21.4% scored below a 90 on this measure of global cognitive status. When using a T-score cutoff of 35 to define cognitive impairment (i.e., 1.5 SD below the normative mean), impairments were particularly prevalent in attention/executive function and memory. Specifically, 16.6% demonstrated impaired performance on CVLT-II recognition hits and 17.6% and 24.6% had a T-score < 35 on the Trail Making Test part B and the FAB, respectively.

AF and Cognitive Function

Chi-square analyses showed HF patients with AF exhibited significantly greater impairments in cognitive function. Specifically, 31.7% of HF patients with AF scored below a 90 on the 3MS relative to 16.5% of those without AF (χ^2 (N = 187, df = 1) = 5.55, p = 0.02). When using a T-score cutoff of 35, impairments on CVLT recognition hits (χ^2 (N = 187, df = 1) = 8.83, $p < 0.01$) were also more common in patients with AF versus those without AF. Although impairments were noted to be more prevalent on nearly all cognitive measures in AF patients, between group differences did not reach statistical significance at the $p = 0.05$ level for any other tests. See Table 2.

Unadjusted ANOVA analyses first examined differences between HF patients with and without AF on each cognitive domain. Relative to patients without AF, HF patients with AF exhibited worse performances on the 3MS ($F(1, 185) = 7.12$, $p = 0.01$, partial eta-squared = 0.04) and in memory ($F(1, 185) = 4.86$, $p = 0.03$, partial eta-squared = 0.03). According to normative T-score standards, a history of AF resulted in a drop in memory performance from the average to the low average range. There were no significant between group differences for attention/executive function or language ($p > 0.10$ for all).

After accounting for medical variables ANCOVA analyses continued to show that HF patients with AF exhibited worse cognitive function in the same domains than those without AF: 3MS ($F(1, 181) = 6.34$, $p = 0.01$, partial eta-squared = 0.03) and memory ($F(1,181) = 4.86$, $p = 0.03$, partial eta-squared = 0.03). No such pattern emerged for attention/executive function or language ($p > 0.10$ for both). The association between AF and 3MS remained significant after adjustment for anticoagulant and beta-blocker status ($F(1,163) = 4.58$, $p = 0.03$, partial-eta squared = 0.03) and there was a trend for memory ($F(1,163) = 2.98$, $p = 0.086$, partial eta-squared = 0.02). Figure 1 displays between mean group differences in cognitive function and CBF-V using means from analyses that included covariates in the full sample (N = 187).

AF and Cerebral Blood Flow

Unadjusted ANOVA analyses showed significant between group differences on CBF-V ($F(1, 185) = 10.30$, $p < 0.01$, partial eta-squared = 0.05). This effect remained after controlling for age, HF severity, and comorbid medical conditions ($F(1, 180) = 8.30$, $p < 0.01$, partial eta-squared = 0.04). In each case, AF was associated with greater reductions in CBF-V relative to HF patients without AF. See Figure 1. AF continued to negatively impact CBF-V when anticoagulant and beta-blocker status were entered as covariates ($F(1,162) = 14.07$, $p < 0.001$; partial eta-square = 0.08).

Cerebral Blood Flow and Cognitive Function: Overall Sample

Partial correlations controlling for LVEF, hypertension, type 2 diabetes mellitus, and sleep apnea showed significant associations between CBF-V with memory ($r(181) = 0.15$, $p = 0.046$) and language ($r(181) = 0.15$, $p = 0.046$). There was also a trend for attention/executive function ($r(181) = 0.13$, $p = 0.09$). In each case, lower CBF-V was associated with worse cognitive function. CBF-V was not associated with 3MS scores ($p > 0.10$).

Cerebral Blood Flow and Cognitive Function: AF and non-AF HF patients

After restricting the sample to only HF patients with AF (n = 60), partial correlations controlling for the above-listed medical variables revealed that decreased CBF-V was associated with worse attention/executive function ($r(54) = 0.28$, $p = 0.04$), memory performance ($r(54) = 0.26$, $p = 0.05$), and language abilities ($r(54) = 0.28$, $p = 0.04$). CBF-V was not associated with 3MS performance ($p > 0.10$). Interestingly, among individuals without AF (n = 127), CBF-V did not demonstrate significant associations with any of the cognitive domains ($p > 0.10$) and all correlation coefficients were < 0.10.

Discussion

Cognitive dysfunction was common and associated with reduced cerebral blood flow in this sample of patients with HF. Many comorbid medical conditions (e.g., obesity, hypertension, type 2 diabetes mellitus) have previously been shown to contribute to cerebral hypoperfusion and cognitive impairment in HF (see Alosco et al., 2013 for a review).[12] The current study is the first to examine the associations among AF, cognitive function, and cerebral perfusion in patients with HF and identifies AF as a possible contributor to cerebral hypoperfusion and cognitive dysfunction in this population.

We found that AF was associated with additive deficits in global cognitive status and memory abilities in older adults with HF. AF is a known risk factor for cognitive impairment even in the absence of stroke or transient ischemic attacks.[36] The current association between AF and worse memory performance is consistent with past work.[36] Our findings also appear to be clinically meaningful, as memory performance in HF patients without AF decreased from average relative to normative standards to low average in HF patients with AF. These findings are noteworthy given the increased risk for dementia in HF, including Alzheimer's disease.[3] Indeed, AF is associated with a 1.5X greater risk for developing Alzheimer's disease[37] and may also contribute to the onset of vascular dementia in patients with HF through its associated risk for clinical and subclinical strokes.[38] Clinician awareness of AF progression may indeed be warranted in the serial monitoring of memory over time in order to intervene with appropriate medical treatment to help slow and/or accommodate cognitive worsening. The current findings between AF and worse 3MS scores in this study is also consistent with past work that suggests AF may accelerate age-related cognitive decline. For example, individuals with AF have been shown to exhibit a drop in approximately 10 points on the 3MS between the ages of 80 to 85 years relative to a 6 point decrease in individuals without AF.[39] Nonetheless, the between group difference in 3MS scores in this sample was relatively modest (i.e., approximately 2 points lower in HF persons with AF) and prospective studies are needed to clarify the clinical implications of our findings and examine whether AF accelerates cognitive decline and increases risk for dementia in HF.

Reduced cerebral blood flow was associated with worse cognitive function in the overall sample and in HF patients with AF. Such findings suggest that reduced cerebral blood flow may be one possible mechanism by which AF contributes to cognitive dysfunction in HF. Cerebral perfusion declines with worsening cardiac function in HF[40] and additional cardiac damage from AF may further suppress blood flow output[19] to worsen cerebral hypoperfusion. This pattern is unfortunate, as neurocognitive impairment in HF is theorized to in part stem from white matter hyperintensities due to decreased blood supply and oxygenation to the brain.[11] Interestingly, cerebral blood flow was not associated with cognition in the subgroup of individuals without AF. These findings raise the possibility that AF may exacerbate HF severity and subsequent cerebral blood flow reductions beyond a critical threshold necessary to produce brain abnormalities that manifest impairments in cognitive function. This hypothesis seems plausible given the independent association between AF with thromboembolisms and silent and clinically meaningful cerebral ischemic infarcts.[23,41,42] Cerebral hypoperfusion also plays a key role in the pathogenesis of Alzheimer's disease[43] and AD-related neuropathology is found in both AF and heart disease patients,[41,44] suggesting that the combination of these medical conditions may accelerate dementia-related pathology (e.g., amyloid beta accumulation). Future work that employs advanced neuroimaging (e.g., arterial spin labeling MRI) is needed to elucidate the mechanisms of AF-related cognitive impairments, particularly as it involves cerebral perfusion and the cerebral structure.

If confirmed by larger studies that employ objective assessments of AF, our findings may have several therapeutic implications. Medical treatment for HF and AF overlap and often involve interventions that target ventricular rate control and cardiac rhythm restoration,[19]

including pharmacological therapy, cardiac transplantation, and/or structured exercise programs. Past work shows that each of these interventions improve cerebral perfusion likely through increases in cardiac function.[10,45,46] While medication treatment to prevent stroke (e.g., warfarin, Aspirin) is a common treatment prescription in AF that may attenuate poor neurocognitive outcomes, a recent case-controlled trial revealed no effects of warfarin and Aspirin on cognitive outcomes over a 3-year time period.[47] Thus, more specific treatments for AF such as radiofrequency ablation and/or ventricular pacing may be more effective in improving cognitive outcomes. These interventions improve cardiac output[48] and yield clinical benefits in HF, including increased physical fitness and exercise tolerance.[49] It is possible that vascular benefits from the above medical and lifestyle interventions translate to better cognitive function. Supporting this notion is past work that demonstrations ablation and pacing in patients with AF improve both brain perfusion and cognitive function, including better memory abilities.[50] Interestingly, AF is associated is a known cause of ischemic lesions and cerebrovascular insult and ablation procedures may attenuate the impact of such pathology on cognitive outcomes. As an example, two past studies shows that paroxysmal AF patients exhibit new ischemic lesions following ablation that persist; however, in each case the brain lesions did not impact cognitive performance.[51,52] Cardiac rehabilitation has also been shown to increase CBF-V and improved cognitive abilities in patients with cardiovascular disease.[46] Future work is needed to identify the most optimal and safe interventions for improving cardiac function in HF patients with comorbid AF and determine whether such interventions benefit cerebral blood flow levels to possibly attenuate cognitive impairment or even delay onset of dementia.

Because the primary purpose of the larger parent study was to examine neurocognitive outcomes in HF, detailed assessments of AF were not performed and the use of self-report to ascertain a global AF diagnosis deserves brief discussion. Self-report is practical and often relied on in both clinical and research settings to collect medical information; however, it presents with some limitations in this study. Specifically, the rhythm rate and exact diagnostic status (i.e., paroxysmal, persistent, or permanent) of the sample is unclear and thus may be a possible confound. Some individuals may have been in sinus rhythm and these participants possibly exhibit less cognitive impairments relative to paroxysmal, persistent, and permanent AF patients.[53] For instance, chronic atrial fibrillation is associated with a 3-6% risk of thromboembolic events and this rate is significantly higher than those AF individuals with sinus rhythm.[54] However, it is unlikely that participants of the current sample are in sinus rhythm given HF is a significant predictor of AF progression.[55] There are also differences between persistent and paroxysmal AF patients, as thromboembolic complications and cognitive impairments have been suggested to be more severe in persistent AF relative to paroxysmal AF.[23,54] Unfortunately, the current study was unable to examine between diagnostic group differences and future studies that employ objective assessments (e.g., 24-hour Holter monitors) to directly quantify cardiac physiology (e.g., ventricular rate) and also identify the etiology of AF are needed to help shed further light on the additive effects of AF on cognition and cerebral blood flow.

Several other limitations of the current findings deserve further review. First, we examined cross-sectional data and thus the directionality and exact nature of the relationships among HF, AF, cognition, and cerebral blood flow remain not well understood. For example, it is

unclear in this sample whether AF preceded or developed after the diagnosis of HF, which is a common controversy.[19] In addition, HF and AF may ultimately be manifestations of vascular risk factors such as hypertension, diabetes, and obesity.[19] Thus, HF and AF may serve as mediators between these medical comorbidities and cognitive impairment and longitudinal studies that employ model-based approaches (e.g., structural equation modeling) will help to clarify this possibility. Case-controlled prospective studies are needed to confirm the directionality proposed in the present study. AF and HF are also both associated with structural brain abnormalities, likely a consequence of cerebral hypoperfusion. Thus, it is possible that patients with comorbid AF in this sample exhibited greater structural brain alterations due to exacerbation in cerebral blood flow reductions and such pathology may ultimately underpin the between group differences in cognitive test performance. Future work should implement neuroimaging modalities to clarify the mechanisms between AF and cognitive impairment in HF.

Conclusions

In brief summary, the current study suggests that AF exacerbates cognitive dysfunction in older adults with HF possibly via greater reductions in cerebral blood flow. AF is a significant risk factor for brain abnormalities and dementia and longitudinal studies are needed to determine the impact of AF on cognitive decline in HF. Future work should also examine whether medical (e.g., ablation) and/or lifestyle interventions (e.g., exercise programs) that target cardiac function and cerebral blood flow can improve cognitive outcomes in patients with HF and AF.

Acknowledgements

Support for this work included National Institutes of Health (NIH) grants DK075119 and HL089311.

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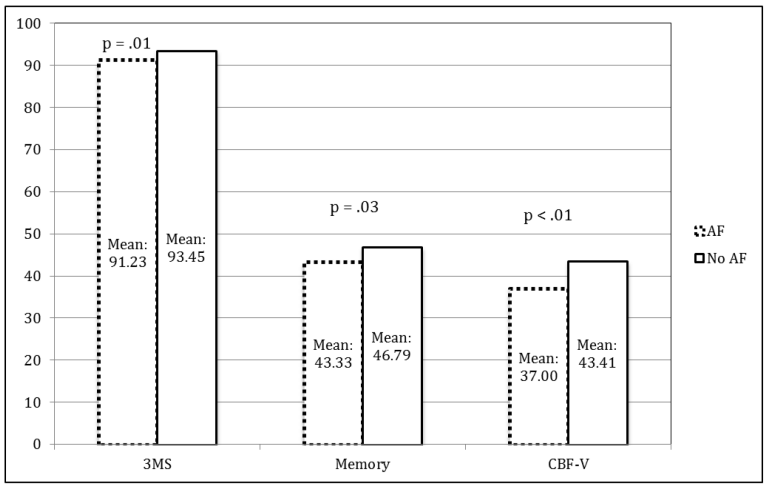

Figure 1.

The Negative Impact of Atrial Fibrillation on Cognitive Function and Cerebral Blood Flow in Patients with Heart failure

Figure Note. 3MS is based on raw scores and memory scores are T-scores; CBF-V units are cm/s; all variables displayed represent significant between group differences after adjusting for left ventricular ejection fraction, hypertension, type 2 diabetes mellitus, and sleep apnea; analyses examining CBF-V were also adjusted for age

3MS = Modified Mini-Mental State Examination; CBF-V = Cerebral blood flow velocity of the middle cerebral artery

Table 1

Demographic and Medical Characteristics of Heart Failure Patients with and without Atrial Fibrillation

Demographic Characteristics	Total Sample	Heart Failure w/ AF	Heart Failure w/o AF	χ^2/*t* statistic
N	187	60	127	--
Age, mean (SD) years	68.50 (8.81)	70.98 (8.59)	67.33 (8.71)	2.69*
Sex (% Women)	30.5	26.7	32.3	0.61
Years of Education, mean (SD)	13.61 (2.67)	13.18 (2.57)	13.82 (2.70)	−1.53
Medical Characteristics				
LVEF, mean (SD)	40.31 (14.41)	37.08 (15.72)	41.84 (13.55)	−2.02*
Hypertension (%)	66.3	71.7	63.8	1.14
Type 2 diabetes mellitus (%)	34.8	41.7	31.5	1.86
Sleep Apnea (%)	24.1	30.0	21.3	1.70
Anticoagulant (%, N = 171)	15.5	43.3	2.4	49.85**
Beta-blocker (%, N = 171)	42.2	38.3	44.2	1.18

Note. LVEF = Left Ventricular Ejection Fraction; AF = Atrial Fibrillation;

* $p < .05$;

** $p < 0.001$

Table 2

Cognitive Test Performance (N = 187)

	Total Sample		HF w/ AF		HF w/o AF	
	Mean (SD)	**% T < 35**	**Mean (SD)**	**% T < 35**	**Mean (SD)**	**% T < 35**
Global Cognition						
3MS	92.74 (5.39)	--	91.23 (5.83)	--	93.45 (5.04)	--
Attention/Executive Function						
Trail Making Test A	49.62 (11.05)	9.1	49.16 (11.26)	10.0	49.84 (10.99)	8.7
Trail Making Test B	44.13 (17.40)	17.6	41.93 (19.22)	20.0	45.16 (16.45)	16.5
Frontal Assessment Battery	43.01 (22.13)	24.6	40.22 (24.60)	28.3	44.32 (20.83)	22.8
Digit Symbol Coding	47.73 (9.13)	8.6	47.08 (9.44)	8.3	48.03 (9.00)	8.7
Memory						
CVLT-II LDFR	46.90 (10.36)	8.6	45.67 (11.14)	11.7	47.48 (9.96)	7.1
CVLT-II recognition hits	44.47 (12.99)	16.6	41.00 (14.40)	28.3	46.10 (11.98)	11.0
Language						
Boston Naming Test	49.36 (13.94)	12.3	48.63 (12.46)	10.0	49.71 (14.64)	13.4
Animal Fluency	54.54 (10.72)	2.1	52.90 (9.67)	5.0	55.47 (11.13)	0.8

Note. 3MS = Modified Mini-Mental State Examination; CVLT = California Verbal Learning Test; LDFR = Long delay free recall; means and SD are T-scores