Early Cognitive Impairment in Middle-Aged Patients with Atrial Fibrillation:a Neuropsychological Study with Echocardiographic Correlates

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Article

Early Cognitive Impairment in Middle-Aged Patients with Atrial Fibrillation: A Neuropsychological Study with Echocardiographic Correlates

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Abstract

Objectives: Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia and has increasingly been associated with cognitive impairment and dementia. Structural remodelling of the left atrium may contribute to early cognitive decline in patients with AF.This study aimed to evaluateearly cognitive impairment in middle-aged patients withAFusing comprehensive neuropsychological testing and to explore its association with conventional echocardiographic parameters of left atrial structure and function. **Methods**: Between 2023-2024, fifty-six consecutive outpatients with AF aged 45–65 years underwent clinical evaluation, transthoracic echocardiography, and comprehensive neuropsychological assessment using the Montreal Cognitive Assessment (MoCA) and the Consortium to Establish a Registry for Alzheimer's Disease battery (CERAD). A control group of 58 age group-matched individuals without known cardiovascular disease was included in comparative cognitiveanalyses. **Results**: Patients with AF demonstratedearly cognitive deficits, particularly in episodic memory and visuospatial functions, detectable even in individuals with normal MoCA scores. Patients with abnormal MoCA results exhibited more pronounced and widespread cognitive impairment. No statistically robust associations were observed between cognitive performance and conventional echocardiographic parameters of left atrial structure and function. These findings may reflect limited statistical power or the need for more sensitive markers of atrial remodeling. **Conclusions**: Early cognitive impairment in AF may be present before abnormalities are detectableby brief cognitive screening tools. The combined use of comprehensive neuropsychological assessment and echocardiographic evaluation may enhance early identification of cognitive vulnerability in this population. Further prospective studies are warranted to clarify the clinical relevance of atrial structural remodeling in this context.

Keywords: atrial fibrillation; mild cognitive impairment; dementia; neuropsychological assessment; echocardiography; left atrial remodelling

1. Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, with an estimated global prevalence of approximately 37.5 million individuals [1]. The burden of dementia,another major public health concerns, had grown toaround 55 million people worldwide[2]. The prevalence

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of both AF and dementia is expected to increase substantially in the coming decades, largely driven by population aging [3].

Accumulating evidence indicates a strong association between AF and cognitive impairment. Several epidemiological studies have demonstrated that AF is an independent risk factor for cognitive decline, even after adjustment for traditional vascular risk factors [4].Data from large population-based cohorts have shown that patients with AF experience poorer cognitive outcomes compared with individuals in sinus rhythm [5].This increased risk is further amplified in the presence of comorbid conditions such as heart failure, diabetes mellitus and chronic kidney disease. Importantly, cognitive impairment and various forms of dementia may occur in patients with AF irrespective of other established risk factors. While AF contributes to cognitive decline, modification of cardiovascular risk factors remains a cornerstone of dementia prevention [6,7].

Mild cognitive impairment is defined as a decline in one or more cognitive domains—including attention, executive function, memory, language and visuospatial abilities—relative to previous performance, without significant impairment of daily functioning [8]. This early stage of cognitive decline represents a critical window for intervention and preservation of brain health [9].Consequently, regular cognitive monitoring in patients with AF is essential for timely identification and management of mild cognitive impairment .

Cognitive assessment in patients with AF is typically performed in a stepwise manner [10]. Initial cognitive screening can be conducted by clinicians in routine outpatient settings using brief, validated instruments. Individuals who screen positive should undergo more detailed neuropsychological evaluation using standardized tools such as the Montreal Cognitive Assessment (MoCA) or the Mini-Mental State Examination (MMSE) [11]. Although these instruments do not establish a definitive diagnosis, they allow risk stratification and facilitate referral for specialized assessment. MoCA has demonstrated higher sensitivity for vascular cognitive impairment than MMSE, making it particularly suitable for patients with AF. Given that patterns of cognitive dysfunction vary across dementia subtypes, complementary neuropsychological instruments are often required to detect subtle early deficits [12,13].

Structural and functional remodelling of the left atrium, commonly referred to as left atrial myopathy, frequently develops in patients with AF and has been implicated in the pathogenesis of cognitive impairment [14]. Atrial fibrosis represents a key pathological substrate and results from a complex fibrogenic process involving inflammatory activation, fibroblast proliferation, and excessive extracellular matrix deposition. Central molecular mechanisms include activation of the transforming growth factor-β1 signalling pathway and the RAAS (renin–angiotensin–aldosterone system) [15].Experimental studies have demonstrated that increased activity of these pathways is associated with atrial dilatation and fibrosis, which may contribute to impaired cerebral perfusion, microembolization, and chronic inflammatory responses [16].AF has additionally been associated with an increased risk of Alzheimer's disease, with proposed mechanisms including cerebral hypoperfusion due to irregular cardiac rhythm, atherosclerosis, and subsequent amyloid-β deposition [17].

Some studies have further suggested sex-related differences in the incidence of AF, dementia and stroke hasalso been reported. While men exhibit a higher incidence of AF, women with established AF appear to have a higher long-term risk of dementia [18].

The aim of the present study was to perform a neuropsychological assessment of patients with atrial fibrillation using selected cognitive tests for early detection of impairment across multiple cognitive domains. Additionally, the study sought to investigate the association between conventional echocardiographic parameters of left atrial structure and function, and cognitive impairment in this patient population.

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2. Materials and Methods

2.1. Study Design and Participants

This study was conducted between 2023 and 2024 at the University Hospital "St. George", Plovdiv, Bulgaria. A total of 56 consecutive outpatients with AF were recruited from the Departments of Cardiology and Neurology. All participants underwent a comprehensive clinical and neurological examination, laboratory testing, electrocardiography, transthoracic echocardiography and neuropsychological assessment.

Eligible participants were aged 45–65 years. To minimize potential confounding effects on cognitive performance, enrolmentin the studyrequired the absence of severe somatic or neurological diseases. Exclusion criteria were:history of cerebrovascular accidents; traumatic brain injury with loss of consciousness exceeding one hour; epilepsy; malignant disease; substance use disorders; major psychiatric illness; decompensated chronic diseases (cardiovascular, endocrine, renal, hepatic, or pulmonary); alcohol abuse; neurodegenerative disorders (including Parkinson's disease, Alzheimer's disease, and vascular dementia); or inability to provide informed consent.

All patients completed a questionnaire and underwent neuroimaging, blood tests, echocardiography and neuropsychological evaluation at baseline. One year after the initial assessment, all patients underwent repeat neuropsychological testing. For the present cross-sectional analyses, we use the baseline information as echocardiographyexamination was only performed at baseline.

For selected analyses, a control group of 58 age-matched individuals without cardiovascular disease, diabetes mellitus, dyslipidemia, or chronic kidney disease was included. We re-used a subsample recruited during routine preventive examinations at the Cardiology Clinic and from ambulatory care settings [19]. None of the control participants had a history of vascular risk factors or other relevant comorbidities. Controls were included onlyin selected analyses due to the absence of echocardiographic data.

The study protocol was approved by the Ethics Committee of the Medical University of Plovdiv (Approval No. P-1516/27.06.2022). Written informed consent was obtained from all participants prior to enrolment.

2.2. Questionnaire and Clinical Variables

At the initial visit, participants completed a structured questionnaire administered by a trained researcher. The questionnaire collected information on sociodemographic characteristics (age, sex, ethnicity, educational leveland marital status), lifestyle factors (physical activity, smoking status and alcohol consumption), medication use, comorbidities, and history of COVID-19 infection.

Symptoms of anxiety and depression were assessed using the Patient Health Questionnaire-4 (PHQ-4) [20]. Responses were rated on a four-point Likert scale ranging from 0 to 3. Height and weight were self-reported based on recent measurements.

2.3. Neuropsychological Assessment

To exclude structural brain pathology, all participants underwent either computed tomography or magnetic resonance imaging of the brain at the University Hospital "St. George" or at the Translational Neurosciences Complex, Medical University of Plovdiv. No pathological findings were identified.

Neuropsychological testing was performed by an experienced clinical neuropsychologist. Cognitive function was assessed using the MoCA [21] and the CERAD [22] neuropsychological battery. TheMoCA assesses seven cognitive domains, with a maximum total score of 30 points, including executive function, visuospatial abilities, attention, language, abstraction, delayed recall and orientation [23,24].Based on MoCA scores, patients with AF were categorized into two subgroups: normal cognitive performance (≥27 points) and abnormalcognitive performance (<27

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points). A higher than the commonly used (≥26 points) MoCA cut-off was applied to increase sensitivity for detecting very early and subtle cognitive changes in this relatively young and clinically active population. Previous validation studies have demonstrated that higher cut-off values may be more appropriate when the primary aim is early detection of mild cognitive impairment, particularly in populations with high educational attainment or vascular risk factors, where the standard cut-off of <26 may underestimate early cognitive decline [25].

Comparisons between theMoCA-definedgroups were performed using CERAD subtest scores. The CERAD battery includes the Verbal Fluency Test, Boston Naming Test (BNT), Word List Recall, Word List Recognition and Constructional Praxis. Subtest scores were summed according to standard scoring procedures to obtain a total score with established sensitivity for distinguishing mild cognitive impairment from normal cognition [26].

2.4. Echocardiographic Assessment

Transthoracic echocardiography was performed at baseline in accordance with contemporary recommendations of the American Society of Echocardiography and the European Association of Cardiovascular Imaging [27,28]. Standard two-dimensional, M-mode and Doppler imaging were obtained using a commercially available ultrasound system. The evaluation focused on conventional parameters of left atrial (LA) structure and left ventricular (LV) systolic and diastolic function. LA anteroposterior diameter was measured in the parasternal long-axis view. LA volume was calculated from apical four- and two-chamber views using the biplane method of disks (modified Simpson's method) and indexed to body surface area to obtain the left atrial volume index (LAVI).

LV end-diastolic and end-systolic volumes were measured using the biplane Simpson's method, and left ventricular ejection fraction (LVEF) was derived automatically by the system software.

Diastolic function was assessed using pulsed-wave Doppler of transmitral inflow to measure peak early (E) and late (A) velocities, E/A ratio, and deceleration time. Tissue Doppler imaging of the septal and lateral mitral annulus was performed to obtain early diastolic velocities (e'), and the average E/e' ratio was calculated as an estimate of LV filling pressure [28].

Advanced imaging techniques, including speckle-tracking strain analysis and left atrial deformation imaging, were not performed in the present study.

All echocardiographic examinations were acquired and interpreted by an experienced cardiologist blinded to the neuropsychological assessment results. In patients examined during atrial fibrillation, Doppler and volumetric measurements were averaged over multiple consecutive cardiac cycles to account for beat-to-beat variability.

Data were screened for missing values and summarized using descriptive statistics. Between-group differences were assessed using Welch's t-test, one-way and two-way analysis of variance (ANOVA) with Tukey's post hoc test, and Pearson's chi-square test, as appropriate.

Statistical analyses were performed using JASP version 0.19.2.0 and Stata MP version 19. Statistical significance was defined as a two-tailed p-value < 0.05.

3. Results

3.1. Participant Characteristics

The study sample consisted of 56 patients with AF, including 24 women (42.9%) and 32 men (57.1%), with a mean age of 56.9 ± 6.6 years. Twenty-six patients experienced a first episode of AF. Based on MoCAscores, 26 patients demonstrated normal cognitive scores, whereas 30 patients (53.6%) scored below the predefined normal threshold. Patients with abnormal MoCA scores tended to have a lower level of formal education (Table 1).

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Table 1. Descriptive characteristics of the patients with normal and abnormal MoCA scores.

Characteristics	Normal MoCA (n=26)	Abnormal MoCA (n=30)	P
Age	56.08 ± 5.90	57.60 ± 6.20	0.351
Sex			
Male	14 (53.85%)	18 (60%)	0.643
Female	12 (46.15%)	12(40.0%)	
Bulgarian ethnicity	26 (100%)	29 (96.67%)	0.348
Education			
Primary	0 (0%)	2 (6.67%)	0.016
High school	13 (50%)	25 (83.33%)	
Bachelor's	6 (23.08%)	1 (3.33%)	
Master's	6 (23.08%)	2 (6.67%)	
PhD	1 (3.85%)	0 (0%)	
Marital status			0.165
Married	23 (88.46%)	22 (73.33%)	
Divorced	0 (0%)	4 (13.3%)	
Single	2 (7.69%)	1 (3.33%)	
Widowed	1 (3.85%)	3 (10%)	
Income adequacy perception			0.431
Very easy	0 (0%)	2 (6.67%)	
Easy	4 (15.39%)	6 (20%)	
Rather easy	11 (42.31%)	7 (23.3%)	
Rather difficult	8 (30.77%)	12 (40%)	
Difficult	3 (11.54%)	3 (10%)	
Risk factors			
IHD	19 (73.1%)	21 (70%)	0.799
Hypertension	25 (96.2%)	28 (93.3%)	0.640
Diabetes	4 (15.4%)	4 (13.3%)	0.827
Dyslipidemia	7 (26.9%)	6 (20%)	0.541
CKD	1 (3.8%)	1 (3.3%)	0.918
Atrial fibrillation type			0.774
Persistent	12 (46.15%)	15 (50.00%)	
Paroxysmal	14 (53.85%)	15 (50.00%)	
CHA_2DS_2-VASc score	2.38 ± 0.70	2.47 ± 0.73	0.670
Anticoagulant use			0.799
No	7 (26.92%)	9 (30.00%)	
Yes	19 (73.08%)	21 (70.00%)	

Abbreviations: CKD – chronic kidney disease;IHD – ischemic heart disease;MoCA – Montreal cognitive assessment.

3.2. Neuropsychological Performance

Comparisons were conducted among three groups: healthy controls, patients with AF with normal MoCA scores and patients with AF with abnormal MoCA scores (Figure 1). Statistically significant differences were observed in CERAD total ($F_{(2, 66.00)} = 83.17$, $p < 0.001$, $\eta^2_p = 0.61$) and subtest scores, including the BNT ($F_{(2, 59.26)} = 4.31$, $p = 0.018$, $\eta^2_p = 0.09$), Word List Recall ($F_{(2, 65.53)} = 154.33$, $p < 0.001$, $\eta^2_p = 0.74$), and Word List Recognition ($F_{(2, 47.33)} = 200.63$, $p < 0.001$, $\eta^2_p = 0.79$), andConstructional Praxis ($F_{(2, 65.53)} = 71.15$, $p < 0.001$, $\eta^2_p = 0.22$).Conversely, there were no between-group differences in Verbal Fluency ($F_{(2, 66.31)} = 2.71$, $p = 0.073$, $\eta^2_p = 0.03$).In post-hoc comparisons, patients with normal versus abnormal MoCA scores differed significantly only in semantic memory performance, as assessed by the BNT(mean difference 0.45, SE = 0.15, p = 0.009). The other CERAD subtest scores did not differ between the two groups with abnormal MoCA. These findings indicate early memory and visuospatial deficits even in patients with atrial fibrillation who exhibit normal global cognitive

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screening results.The most pronounced impairments were observed in episodic memory, semantic memory, visuospatial abilities and overall cognitive performance.

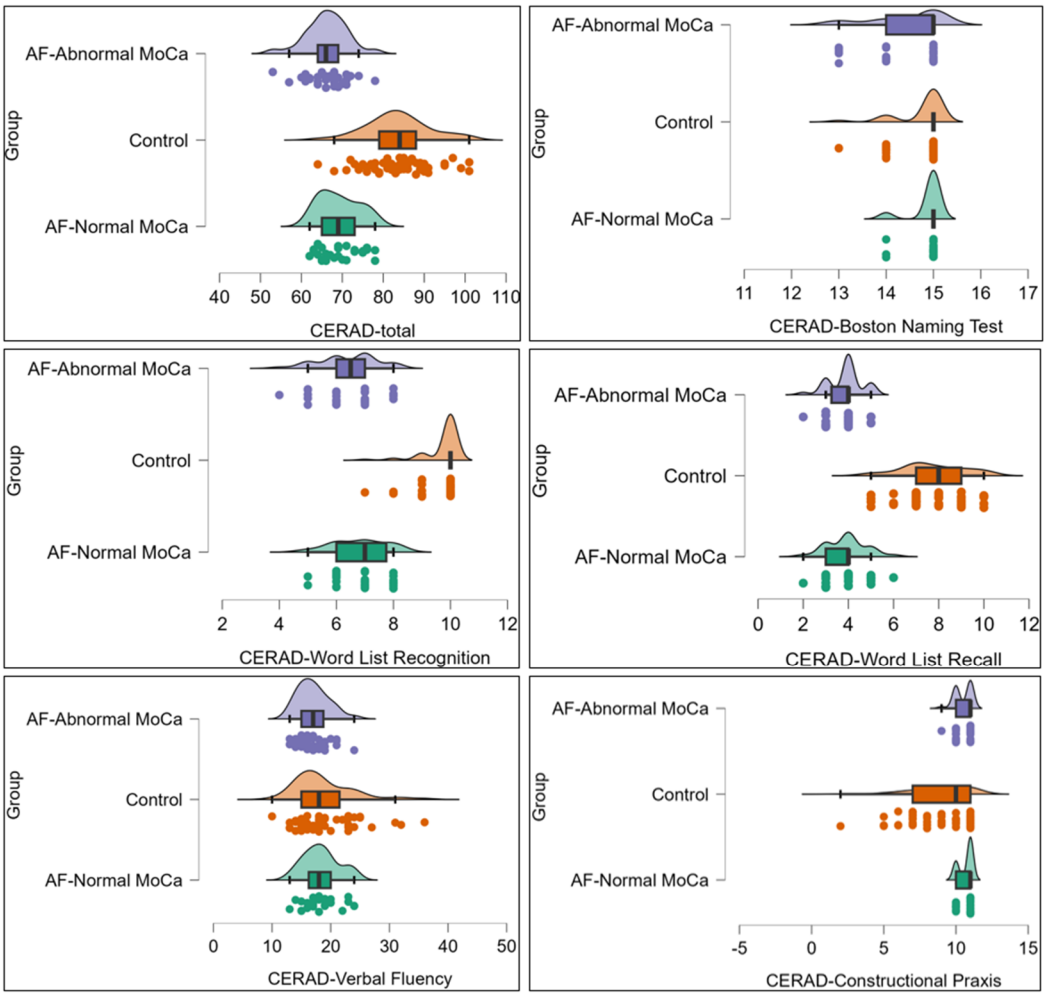

Figure 1. Comparison of CERAD total and select subtest scoresbetween participant groups defined by participants' MoCA scores and AF status.

3.3. Echocardiographic Parameters Across MoCA Groups

Conventional echocardiographic parameters of left atrial structure and left ventricular function were compared between patients with normal and abnormal MoCA scores (Table 2). No statistically significant differences were observed in LAVI, absolute left atrial volume, left ventricular volumes or left ventricular ejection fraction between cognitive groups. Exploratory analyses suggested an interaction between sex and cognitive status with respect to LVEF and LVESV, and a potential interaction between sex and cognitive status for LAVI; however, the latterfinding did not reach robust statistical significance. Diastolic parameters, including transmitral E and A velocities, E/A ratio, deceleration time, and average E/e' ratio, did not differ significantly between cognitive groups. Overall, conventional echocardiographic measures of left atrial structure and left ventricular function were not independently associated with cognitive performance in this cohort.

Table 2. Comparison of conventional echocardiographic parameters according to MoCA group and sex.

Echocardiographic parameters				Comparisons P-values [1]		
Normal MoCA (n=26)		Abnormal MoCA (n=25)		Normal vs. abnormal MoCA	Male vs. Female	MoCA* Sex
Male (n=14)	Female (n=12)	Male(n=15)	Female(n=10)			

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LAVI(mL/m²)	27.67 ± 7.72	25.86 ± 9.99	27.30± 8.09	33.50 ± 7.53	0.133	0.361	0.098
Left atrial volume (mL)	57.97± 17.18	50.75 ± 20.48	57.67 ± 16.71	58.11 ± 12.91	0.471	0.490	0.435
LVEF (%)	47.97 ± 7.85	55.00 ± 9.88	53.87 ± 10.50	45.83 ± 6.38	0.522	0.843	0.005
LVEDV (mL)	104.14 ± 23.50	110.75 ± 17.38	105.40 ± 24.66	111.60 ± 18.35	0.865	0.302	0.974
LVESV (mL)	54.21 ± 14.90	49.67 ± 12.74	48.20 ± 14.90	60.00 ± 9.45	0.575	0.349	0.038
E velocity (m/s)	0.75± 0.23	0.87 ± 0.21	0.68 ± 0.18	0.71 ± 0.16	0.059	0.190	0.514
A velocity (m/s)	0.71 ± 0.19	0.65 ± 0.32	0.64 ± 0.23	0.66 ± 0.23	0.733	0.656	0.550
E/A ratio	1.05± 0.54	1.43 ± 0.93	1.37 ± 0.85	1.30 ± 0.95	0.686	0.511	0.344
Deceleration time (ms)	231.57 ± 36.40	245.75 ± 110.97	205.40 ± 63.65	303.60 ± 96.32	0.483	0.016	0.067
Septal e′ (cm/s)	10.21 ± 2.15	8.98 ± 3.16	8.50 ± 3.98	9.30 ± 3.30	0.450	0.812	0.274
Lateral e′ (cm/s)	11.57 ± 2.85	10.69 ± 3.14	9.13 ± 2.92	11.20 ± 4.16	0.520	0.297	0.114
Average E/e′ ratio	7.33 ± 3.13	9.43 ± 3.80	8.42 ± 3.06	7.69 ± 3.14	0.726	0.464	0.136

Abbreviations: A velocity - late diastolic ventricular filling caused by atrial contraction; E velocity - peak speed of early mitral inflow into the left ventricle during diastole; E/A ratio - left ventricular diastolic function and filling pressure; Lateral e′ - mitral annulus movement toward the apex during early diastole; LVEDV – left ventricular end-diastolic volume; LVEF – left ventricular ejection fraction; LVESV – left ventricular end-systolic volume; MoCA – Montreal cognitive assessment LAVI – left atrial volume index; Septal e′- early diastolic mitral annular velocity at the interventricular septum.[1]Two-way Welch's ANOVA comparisons.

4. Discussion

The present study found that subtle cognitive deficits in specific domains can be detected in patients with atrial fibrillation (AF) even when global cognitive screening results, as assessed by the MoCA, remain within the conventionally defined normal range. In particular, impairments in episodic memory, visuospatial abilities and overall cognitive performance were observed in patients with AF, who scored within the normal range on the MoCA, underscoring the limited sensitivity of brief screening instruments for identifying very early cognitive changes in relatively young and clinically active populations. These findings align with contemporary evidence that AF is associated with cognitive dysfunction and dementia risk beyond shared vascular risk factors and even in the absence of overt stroke, and they support the use of detailed domain-specific neuropsychological testing to complement brief screening in AF [29,30].

Our findings are in line with other studies that found AF to be an independent risk factor for impaired cognition [31–33]. Some studies show that rhythm control therapy may be associated with a significantly reduced risk of dementia in AF patients and even may lead to improvement in patients' cognitive functions. For example, Rosman et al. found that patients, who experienced early AF recurrence after ablation did not show significant cognitive improvement in comparison to those who did [34]. Another study showed that cognitive impairment in patients with AF correlates with parameters related to the left atrium. It is suggested that left atrial diameter may be an independent predictor of cognitive impairment [35]. The prospective Rotterdam study found that prevalent AF increased the risk of dementia [36]. In the Whitehall II study incident dementia was more frequent in patients with AF compared with those without AF [37]. Kalantarian et al. [38] investigated the association of AF with cognitive decline and dementia, and suggested that AF was significantly associated with a higher risk of cognitive impairment independent of a history of stroke. An important finding of this study is the suggestive association between echocardiographic parameters of left atrial remodeling and cognitive performance [39].

Although the present study did not demonstrate statistically robust associations between cognitive performance and conventional echocardiographic parameters, accumulating evidence

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suggests that subclinical cardiac abnormalities may play a role in early cognitive decline [40,41]. The predominance of preserved or mildly reduced LVEF in this cohort further suggests that overt systolic dysfunction was unlikely to explain the observed cognitive findings. However, a significant interaction between sex and cognitive status was observed for LVEF and left ventricular end-systolic volume (LVESV). While mean systolic function remained largely preserved overall, women with abnormal MoCA scores demonstrated lower LVEF and higher LVESV compared with cognitively preserved women, whereas an opposite tendency was observed in men. This cross-over interaction may indicate subtle, sex-specific differences in ventricular remodeling associated with cognitive vulnerability. Importantly, no main effect of cognitive status on LVEF was identified, and the magnitude of differences was modest, suggesting that global systolic dysfunction is unlikely to represent a primary mechanistic driver. Given the limited subgroup sizes and exploratory nature of these analyses, this finding should be interpreted cautiously and considered hypothesis-generating.

Structural and functional alterations of the left atrium, broadly conceptualized as atrial cardiomyopathy, have been increasingly recognized as potential contributors to cerebrovascular and neurocognitive outcomes. In our cohort, conventional echocardiographic indices did not indicate a high prevalence of markedly elevated left ventricular filling pressures. Mean E/e' values were largely within normal or mildly increased ranges, and advanced diastolic dysfunction was not systematically observed. Given the limitations of transmitral flow assessment in atrial fibrillation, tissue Doppler parameters and indexed left atrial volume were considered more informative. Although LAVI was variably increased, structural enlargement alone was not significantly associated with cognitive performance. These findings suggest that overt diastolic dysfunction, as assessed by standard echocardiographic measures, is unlikely to be the primary driver of early cognitive impairment in this relatively stable AF population.

Atrial structural remodeling may influence cognitive function through several pathophysiological pathways, including impaired cerebral perfusion due to irregular ventricular response and reduced cardiac output, cerebral microembolization arising from a thrombogenic atrial substrate, endothelial dysfunction, and chronic inflammatory activation. In this context, atrial fibrillation may represent not only an arrhythmia, but also a marker of an underlying "thrombogenic atrium," predisposing to both overt and subclinical cerebral injury.

Large population-based cohorts, including the ARIC study, have demonstrated associations between measures of left atrial structure and function and incident ischemic stroke and dementia [42]. Importantly, more sensitive markers of atrial function—such as left atrial strain (reservoir, conduit and contractile function), emptying fraction, and other deformation indicesappear to show stronger associations with cognitive outcomes than structural enlargement alone [43]. Similarly, electrophysiological markers of atrial remodeling, including advanced interatrial block and abnormal P-wave indices, have been linked to increased dementia risk.

These findings support the concept that atrial cardiomyopathy may contribute to cognitive impairment independently of clinically apparent stroke, possibly through chronic cerebral hypoperfusion or recurrent subclinical embolic events. Given that the present study evaluated conventional echocardiographic parameters without strain-based assessment of atrial function, it is plausible that subtle functional abnormalities were not fully captured.

It is noteworthy that the present study used a higher MoCA cut-off (27 points) to define normal cognitive function. This may be seen as a deliberate methodological choice, but the aim was to increase sensitivity for detecting early cognitive impairment. While the original validation studies proposed a cut-off of <26 points, accumulating evidence suggests that this threshold may underestimate early or subtle cognitive deficits, particularly in middle-aged individuals and in populations at risk for vascular cognitive impairment. Thomann et al. [15] proposed a revised cut-off approach for the MoCA, demonstrating that higher thresholds improve diagnostic accuracy for early neurocognitive disorders by enhancing sensitivity, albeit at the expense of specificity. Such an approach is appropriate when the primary objective is early detection and risk stratification rather than definitive diagnosis. Support for this strategy is further provided by the findings of Gagnon et

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al. [19], who demonstrated that mild cognitive impairment in middle-aged adults may remain undetected by standard screening thresholds, despite clear deficits on more comprehensive neuropsychological testing. Their results highlight the vulnerability of brief cognitive screening tools to false-negative findings in populations with preserved functional independence and relatively high baseline cognitive reserve. This is particularly relevant in atrial fibrillation, where cognitive impairment may develop insidiously and precede overt clinical manifestations. In the present study, the appropriateness of a higher MoCA cut-off is reinforced by the observation that patients with atrial fibrillation and normal MoCA scores nonetheless exhibited significant impairments on the CERAD neuropsychological battery, particularly in episodic memory and visuospatial domains. These findings indicate that reliance on standard MoCA thresholds alone may fail to capture early cognitive decline and support the combined use of sensitive screening cut-offs and detailed neuropsychological assessment for comprehensive cognitive evaluation.

Several limitations of the present study should be acknowledged. The relatively small sample size and single-center design may have limited statistical power to detect modest associations between cognitive performance and echocardiographic parameters and may also restrict the generalizability of the findings. In addition, the cross-sectional nature of the analysis precludes causal inference regarding the relationship between atrial fibrillation, atrial remodeling and cognitive impairment. Only conventional echocardiographic parameters of left atrial structure and left ventricular function were assessed, as advanced imaging techniques such as speckle-tracking–derived left atrial strain were not available; these methods may offer greater sensitivity for detecting subtle atrial dysfunction associated with cognitive decline. Although efforts were made to minimize confounding differences in educational attainment between cognitive groups may have influenced neuropsychological performance. Furthermore, atrial fibrillation was analyzed as a clinical entity without detailed assessment of AF burden or longitudinal rhythm variability, factors that may also affect cognitive outcomes. Larger prospective studies incorporating advanced atrial functional imaging and longitudinal cognitive assessment are warranted to further clarify these relationships

Despite these limitations, the present study suggests thatcomprehensive neuropsychological assessment, combined with echocardiographic evaluation may provide valuableinsights into early cognitive impairment in patients with atrial fibrillation, particularly in relatively younger populations. The integration of sensitive cognitive screening with comprehensive neuropsychological testing and assessment of left atrial structural remodelling may enhance recognition of individuals at increased risk for cognitive decline. Earlydetectionof subtle cognitive changes couldfacilitate timely intervention, optimization of cardiovascular risk factor management, and potentially improved long-term outcomes.

5. Conclusions

Atrial fibrillation and cognitive impairment represent major and growing public health challenges. The present study foundthat early cognitive impairment in patients with atrial fibrillation predominantly affects episodic memory and visuospatial functions, while semantic memory appears relatively preserved in the initial stages. Importantly, evenin patients with normal global cognitive screening results, subtle deficits may be detected through more comprehensive neuropsychological batteries.Exploratory analyses suggested possible sex-specific differences in certain echocardiographic parameters; however, these findings require confirmation in larger cohorts. The combined use of detailed neuropsychological assessment and conventional echocardiographic assessmentmay enhance early identification of cognitive vulnerabilityin this patient population. Further prospective studies with larger sample sizes and longer follow-up periods are required to clarify the role of atrial structural remodelling in the pathogenesis of cognitive impairment and to determine its potential value in risk stratification and early intervention strategies for patients with atrial fibrillation.

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Abbreviations

The following abbreviations are used in this manuscript:

A velocity - late diastolic ventricular filling caused by atrial contraction;
AF – Atrial fibrillation; BNT - Boston Naming Test;
CERAD - Consortium to Establish a Registry for Alzheimer's Disease battery;
CKD - Chronic kidney disease;
E velocity - peak speed of early mitral inflow into the left ventricle during diastole;
E/A ratio - left ventricular diastolic function and filling pressure;
Lateral e' - mitral annulus movement toward the apex during early diastole;
LVEDV – left ventricular end-diastolic volume;
LVEF – left ventricular ejection fraction;
LVESV – left ventricular end-systolic volume;
MMSE – Mini mental state examination;
MoCA – Montreal cognitive assessment LAVI – left atrial volume index;
PHQ - Patient health questionnaire;
Septal e' - early diastolic mitral annular velocity at the interventricular septum.

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