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Cognitive Screening in Geriatric Patients with Atrial Fibrillation Evaluated for Falls

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Abstract

Background: Atrial fibrillation (AF) is associated with cognitive decline and dementia. This study investigates whether the Montreal Cognitive Assessment (MoCA) detects more cognitive decline than the Mini Mental State Examination (MMSE) in patients with AF. Secondary aims were to assess the rate of white matter hyperintensities (WMH) and mesotemporal atrophy (MTA) in patients with AF.

Methods: Observational cohort study. Patients of 65 years and older that visited the Fall and Syncope Clinic were eligible. Patients were included if both a MoCA and MMSE were completed. In patients of whom an MRI was performed WMH were assessed with the Fazekas score and MTA was assessed with the MTA score. To assess frailty a Frailty Index (FI) was calculated.

Results: 428 patients were included. Mean age was 80 years, 66% was female. The mean FI was 0.28 (CI 0.11 to 0.45), indicative of severe frailty. In 90 patients AF was known and in 9 patients it was first diagnosed, overall prevalence 23%. Cognitive impairment was found with the MoCA in 80% of patients with persistent AF, versus in 33% with the MMSE. Patients with paroxysmal AF had more WMH than patients with SR (p 0.04). No differences were found in relevant MTA between patients with AF or SR.

Conclusion: Cognitive decline in patients with AF is better detected using the MoCA than the MMSE. This means that in daily clinical practice, the MOCA should be used instead of the MMSE for patients with AF.

Introduction

Atrial fibrillation (AF) is an arrhythmia associated with severe outcomes such as stroke, heart failure, and death [1]. Furthermore, there is an increasing amount of evidence that shows an association between atrial fibrillation (AF) and dementia [2-9]. Several studies describe possible mechanisms and pathways through which AF could cause or contribute to cognitive decline and dementia [5, 7, 8, 10, 11]. AF is associated with both vascular dementia and Alzheimer's disease [5, 7, 8, 10, 11].

The three main hypotheses on the relationship between AF and cognitive decline are that: 1. AF leads to a prothrombotic state and subsequent thromboembolisms, 2. AF leads to cerebral hypoperfusion through reduced cardiac output, and 3. AF results in malfunctioning of cerebrovascular regulation through systemic inflammation.

Key Words

Cognition, Frailty, Geriatric cardiology.

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The prothrombotic state can cause vascular or post-stroke dementia [11]. Studies show that thromboembolism related cognitive decline may be prevented by the use of oral anticoagulation (OAC) [12, 13]. An association between AF and dementia exists also in patients without clinical stroke [4, 7], which suggests other etiologic mechanisms.

The second suggested mechanism is cerebral hypoperfusion, mainly through the development of heart failure and consequently lower cardiac output, as well as through beat to beat variations in perfusion [14]. Patients with AF indeed have a lower cerebral blood flow and brain perfusion than those with SR, and this seems more pronounced in patients with persistent AF compared to those with paroxysmal AF [15]. Chronic cerebral hypoperfusion and hypoxia may lead to a reduced clearance of amyloid-beta and form a stimulus for the phosphorylation of tau, leading to Alzheimer-like neuropathological changes [7, 10].

Thirdly, systemic inflammation possibly leads to malfunctioning of cerebrovascular regulation which has been associated to Alzheimer's and vascular dementia [7], and AF is also associated with chronic, low grade systemic inflammation [5, 11].

Table 1: Baseline characteristics

	Total	SR	Persis AF	PAF	p1	p2	p3
n (%)	428	329 (76.9)	46 (10.7)	53 (12.4)			
Female, n (%)	284 (66.4)	227 (69.0)	23 (50.0)	34 (64.1)	0.01	0.48	0.16
Age in years , mean (std.)	79.6 (6.6)	79.2 (6.5)	81.6 (7.1)	80.4 (6.3)	0.02	0.20	0.39
Number of morbidities, mean (std.)	10.7 (5.3)	10.0 (4.9)	13.8 (6.0)	12.3 (6.3)	<0.01	<0.01	0.24
Number of drugs, mean (std.)	6.7 (3.6)	6.4 (3.6)	7.9 (3.4)	7.9 (3.8)	<0.01	<0.01	0.99
Polypharmacy (>5 drugs), n (%)	266 (62.1)	191 (58.1)	36 (78.2)	39 (73.6)	0.01	<0.01	0.59
Hypertension, n (%)	294 (68.7)	215 (65.3)	39 (84.8)	40 (75.5)	0.01	0.15	0.25
Hypercholesterolemia, n (%)	129 (30.1)	95 (28.9)	18 (39.1)	16 (30.2)	0.16	0.85	0.35
Diabetes mellitus, n (%)	87 (20.3)	65 (19.8)	9 (19.6)	13 (24.5)	0.98	0.42	0.55
Stroke or TIA, n (%)	99 (23.1)	67 (20.4)	15 (32.6)	17 (32.1)	0.06	0.06	0.96
Ischemic heart disease, n (%)	108 (25.2)	73 (22.2)	19 (41.3)	16 (30.2)	0.01	0.20	0.25
Congestive heart failure, n (%)	44 (10.3)	16 (5.0)	16 (34.9)	12 (22.6)	<0.01	<0.01	0.18
Valvular disease, n (%)	53 (12.4)	33 (10.0)	10 (21.7)	10 (18.9)	0.02	0.06	0.72
CHA2DS2VASc, mean (std.)	4.0 (1.5)	3.8 (1.4)	4.7 (1.4)	4.5 (1.5)	<0.01	<0.01	0.54
HAS-BLED, mean (std.)	2.9 (1.1)	2.8 (1.1)	2.9 (0.9)	3.0 (1.2)	0.73	0.46	0.74
Chronic respiratory disease, n (%)	88 (20.6)	64 (26.8)	14 (30.4)	10 (18.9)	0.09	0.91	0.18
Chronic kidney disease, n (%)	52 (12.1)	30 (9.1)	9 (19.6)	13 (24.5)	0.03	<0.01	0.55
Thyroid disease, n (%)	61 (14.3)	44 (13.4)	8 (17.4)	9 (17.0)	0.46	0.48	0.96
Alcohol daily use, n (%)	212 (49.5)	160 (48.6)	25 (54.3)	27 (50.9)	0.77	0.66	0.69
Smoking or former smoker, n (%)	181 (42.3)	134 (40.7)	24 (52.2)	23 (43.4)	0.14	0.71	0.38
History of fractures, n (%)	171 (40.0)	135 (41.0)	19 (41.3)	17 (32.1)	0.97	0.22	0.34
Osteoporosis, n (%)	65 (15.2)	51 (15.5)	6 (13.0)	8 (15.1)	0.66	0.94	0.77
Parkinson's disease, n (%)	16 (3.7)	14 (4.3)	1 (2.2)	1 (1.9)	0.50	0.41	0.92
Parkinsonism other cause, n (%)	29 (6.8)	23 (7.0)	2 (4.3)	4 (7.5)	0.50	0.88	0.51
Dementia (all forms), n (%)	14 (3.4)	10 (3.0)	3 (6.5)	1 (1.9)	0.23	0.64	0.24

Abbreviations: SR: Sinus Rhythm, Persis AF: persistent AF, PAF: paroxysmal AF. 1Persistent AF versus Sinus Rhythm, 2Paroxysmal AF versus Sinus Rhythm, 3Persistent AF versus Paroxysmal AF.

Patients with cognitive decline or dementia are often frail, have a higher risk of falling, polypharmacy, dependency in daily activities, and difficulty managing their medications [16]. Cognitive decline can have an important impact on the compliance to treatment and overall prognosis [17]. To diagnose cognitive disorders can be difficult and often requires the expertise of a neurologist or geriatrician. Common screening tools are the Mini Mental State Examination (MMSE) and the Montreal Cognitive Assessement (MoCA) [18, 19]. The MoCA was developed to detect mild cognitive impairment (MCI), a condition that the MMSE can detect with less accuracy [19]. Also, since the MoCA has items testing executive functions, it might be more sensitive to vascular cerebral damage [20, 21]. Vascular cerebral damage can be detected with a MRI of the brain, scoring white matter hyperintensities (WMH) with the Fazekas score [22].

Recently we have shown that in a group of elderly patients with falls or syncope the MoCA is more sensitive to cognitive decline than the MMSE [23]. Taking the possible mechanisms into account through which AF could cause cognitive decline, our hypothesis is that the MoCA is more sensitive to cognitive decline than the MMSE in geriatric patients with AF. The primary objective of this study is to assess whether the MoCA detects more cognitive decline than the MMSE in patients with AF who are referred to a Falls and Syncope Day Clinic (FSC). Secondary objectives are to investigate the relationship between AF and white matter hyperintensities (WMH) and mesotemporal atrophy (MTA) as found on MRI scanning of the brain.

Methods:

We conducted an observational cohort study at a Fall and Syncope day Clinic (FSC), North West Clinics Alkmaar, The Netherlands. Including consecutive patients aged ≥65 years that visited the FSC from November 2011 until the end of May 2017 in whom cognitive function was screened with both the MMSE and MoCA. Patients were excluded if no 12 lead electrocardiogram (ECG) or 24 hour Holter monitor were performed.

The FSC is a two-day diagnostic program that evaluates elderly patients with unexplained falls with or without transient loss of consciousness (TLC). It is conducted by a multidisciplinary team led by a geriatrician and includes a physiotherapist, nurse practitioners, cardiologist and neurologist. Details and outcomes of this two-day program have been reported earlier [23, 24, 25]. In brief, all patients underwent a comprehensive geriatric assessment including laboratory testing, a 12 lead ECG, and assessment of mental, cognitive and functional state. Cognitive function was screened using Dutch validated versions of both the MMSE and MoCA [19, 26, 27]. If cognitive dysfunction was found with either the MMSE or

Table 2: Cognitive and functional state

	Total	SR	Persis AF	PAF	p1	p2	p3
MMSE score, mean (std.)	27.2 (2.4)	27.3 (2.4)	26.5 (2.3)	27.3 (2.4)	0.02	0.95	0.08
MoCA score, mean (std.)	23.7 (3.8)	23.7 (3.9)	22.6 (3.2)	24.2 (3.4)	0.06	0.40	0.02
MMSE below 26 points, n (%)	78 (18.2)	57 (17.3)	15 (32.6)	6 (11.3)	0.01	0.27	0.01
MoCA below 26 points, n (%)	278 (65.0)	209 (63.5)	37 (80.4)	32 (60.4)	0.02	0.66	0.03
Fazekas score, mean (std.)	1.9 (1.0)	1.8 (1.0)	2.1 (1.0)	1.9 (0.9)	0.22	0.65	0.53
MTA score, mean (std.)	1.7 (0.8)	1.7 (0.8)	2.1 (0.7)	1.6 (0.7)	0.02	0.43	0.01
MTA score, above cut-off*, n (%)	120 (38.1)	95 (37.8)	11 (36.7)	14 (41.2)	0.90	0.71	0.71
Frailty Index, mean (std.)	0.28 (0.1)	0.27 (0.1)	0.34 (0.1)	0.31 (0.1)	<0.01	0.01	0.19
Low handgrip strength, n (%) (n=304)	207 (68.1)	159 (68.2)	20 (64.5)	28 (70.0)	0.68	0.83	0.62
Gait disturbance, n (%)	69 (16.1)	51 (15.5)	7 (15.2)	11 (20.8)	0.96	0.34	0.48
Abnormal Tinetti score (n=391), n (%)	257 (65.7)	196 (65.3)	29 (72.5)	32 (62.7)	0.37	0.72	0.33
Dependent in ADL, n (%)	80 (18.7)	61 (18.5)	12 (26.1)	7 (13.2)	0.01	0.35	0.14
Dependent in instrumental ADL, n (%)	136 (31.8)	102 (31.0)	17 (37.0)	17 (32.1)	0.42	0.88	0.61
Use of a walking aid, n (%)	216 (50.5)	158 (48.0)	27 (58.7)	31 (58.5)	0.18	0.16	0.98
Visual impairment, n (%)	189 (44.2)	145 (44.1)	19 (41.3)	25 (47.2)	0.72	0.67	0.56
Institutionalized, n (%)	22 (5.1)	15 (4.6)	4 (8.7)	3 (5.7)	0.23	0.73	0.56

Abbreviations: SR: Sinus Rhythm, Persis AF: persistent AF, PAF: paroxysmal AF. MMSE: Mini Mental State Examination, MoCA: Montreal Cognitive Assessment, MTA: mesotemporal atrophy, ADL: Activities of Daily Living. 1Persistent AF versus Sinus Rhythm, 2Paroxysmal AF versus Sinus Rhythm, 3Persistent AF versus Paroxysmal AF. *Age adjusted cut-off.

MoCA patients were offered an analysis of cognitive function by a neuropsychologist, but outcomes of that analysis were not available for this study. Patient consent and ethical board approval were not required, since this study used archival data of standard geriatric evaluations and had no implications on therapeutic decisions.

Baseline characteristics were collected from all patients including their gender, age, medical history and medication use. All baseline ECGs were assessed by an experienced cardiologist (JR), to determine if patients had sinus rhythm (SR) or AF. To determine the rhythm on the Holter monitor the judgement of the clinically consulted cardiologists was retrieved from the medical files. A frailty index (FI) was created based on the accumulation of deficit model, as proposed by Searle and colleagues, and Rockwood and colleagues [17, 28]. In this study, we created a FI using a total of 45 deficits, comprised of 29 somatic items, 3 items of cognitive function and 13 items of basic daily functioning. Patients were considered frail at an FI of 0.18 to 0.24, and severely frail with an FI of 0.25 or higher.

Patients were classified as having SR if they were not known with AF and both their ECG and Holter monitor showed SR. Patients were classified as having persistent AF if their medical history notes AF and both the ECG and Holter showed AF as well. Paroxysmal AF was defined as having AF in the medical history, but either or both the ECG and Holter showed SR. In the case of first diagnosed AF, it was considered persistent when both the ECG and Holter showed AF, and was classified as paroxysmal when either the ECG or Holter showed SR.

The scores of the MMSE and MoCA were compared between the groups (SR, persistent AF and paroxysmal AF). Also whether patients scored below the common threshold for cognitive impairment was compared between these groups. For both the MMSE and MoCA this threshold is less than 26 out of 30 points. There were several reasons to perform an MRI of the brain, such as abnormalities in the neurological examination, walking disorders, suspected epilepsy and cognitive deficits, see also the published description of the FSC protocol [23, 24]. If an MRI of the brain was available, WMH were assessed with the Fazekas score, a categorical visual rating scale with a range from 0 to 3 points [22]. Furthermore, mesotemproal atrophy (MTA) was assessed using a categorical visual rating score with a range from 0 to 4 [29]. Age adjusted cut-off scores were used to identify patients with relevant MTA [30].

Statistical analysis

Analyses were performed using SPSS for Windows, version 20 (SPSS, Inc, Chicago, IL). Categorical variables were expressed as counts and percentages, continuous variables as mean value with standard deviation. Comparisons between participants were conducted using the Pearson Chi square for categorical variables and T test for continuous variables. P values of 0.05 or smaller were considered statistically significant. Possible confounders were analysed using the Mantel-Haenszel test for conditional independence.

Results

Participants

In total, 518 patients aged 65 years or older visited the FSC. In 493 patients a MMSE was performed and in 428 patients also a MoCA was performed. In all of these 428 patients both an ECG and a 24 hour Holter monitor was performed and consequently these 428 patients were included in this analysis. An MRI was performed in 332 patients. The medical history is shown in Table 1. The mean age was 80 ± 7 years, 66% were female and cardiovascular disease was very prevalent. Patients were on average known with 11 ± 5 morbidities

Table 3: Medication use

	Total	SR	Persis AF	PAF
ACE or ARB, n (%)	192 (44.9)	136 (41.3)	26 (56.5)	30 (56.6)
Beta blocker, n (%)	142 (33.2)	98 (29.8)	22 (47.8)	22 (41.5)
Anti platelet agent, n (%)	143 (33.4)	131 (39.8)	4 (8.7)	8 (15.1)
Vitamin K antagonist, n (%)	93 (21.7)	15 (4.6)	39 (84.8)	39 (73.6)
Diuretics, n (%)	141 (32.9)	102 (31.0)	19 (41.3)	20 (37.7)
Lipid lowering drugs, n (%)	202 (47.2)	151 (45.9)	20 (43.5)	31 (58.5)
Dihydropyridines, n (%)	71 (16.6)	53 (16.1)	8 (17.4)	10 (18.9)
Anti arithmetic, not Beta blocker, n (%)	62 (14.5)	14 (4.3)	24 (52.2)	24 (45.3)
Proton pump inhibitor, n (%)	178 (41.6)	136 (41.3)	23 (50.0)	19 (35.8)
Pulmonary agents, n (%)	74 (17.3)	56 (17.0)	9 (19.6)	9 (17.0)
Vitamin supplements, n (%)	183 (42.8)	139 (42.2)	18 (39.1)	26 (49.1)
Thyroid hormone, n (%)	42 (9.8)	30 (9.1)	6 (13.0)	6 (11.3)
Bisphosphanate, n (%)	34 (7.9)	28 (8.5)	4 (8.7)	2 (3.8)
Oral antidiabetics, n (%)	65 (15.2)	49 (14.9)	8 (17.4)	8 (15.1)
Insulin, n (%)	24 (5.6)	17 (5.2)	2 (4.3)	5 (9.4)
Pain relievers, n (%)	116 (27.1)	88 (26.7)	12 (26.1)	16 (30.2)
Benzodiazepine, n (%)	82 (19.2)	62 (18.8)	8 (17.4)	12 (22.6)
Antidepressants, n (%)	61 (14.3)	52 (15.8)	3 (6.5)	6 (11.3)
Antipsychotics, n (%)	9 (2.1)	7 (2.1)	1 (2.2)	1 (1.9)

Abbreviations: SR: Sinus Rhythm, Persis AF: persistent AF, PAF: paroxysmal AF. 1Persistent AF versus Sinus Rhythm, 2Paroxysmal AF versus Sinus Rhythm, 3Persistent AF versus Paroxysmal AF.

and used 7 ± 3 different drugs. 90 patients were known with AF and 9 patients were first diagnosed with AF, constituting to an overall prevalence of AF of 23%. Of all AF cases, 53 were paroxysmal AF (54%) and 46 were persistent AF (46%). Patients with persistent and with paroxysmal AF were known significantly more often with heart failure (35% and 23% respectively, versus 5% in patients with SR, p <0.01) and chronic kidney disease (20% and 25% respectively, versus 9% in patients with SR, p 0.03 and p <0.01).

Functional state and frailty

Functional and cognitive state is shown in Table 2. The mean FI was 0.28 (95% CI of the mean 0.11 to 0.45), indicative of severe frailty in the entire cohort. In total only 26 patients (6%) were not frail, with an average FI of 0.13, and all of these 26 patients were known with SR. Patients with persistent AF were the frailest, with an FI of 0.34 (95% CI of the mean 0.16 to 0.51). Those with paroxysmal AF had an FI of 0.31 (95% CI of the mean 0.15 to 0.48), and patients with SR an FI of 0.27 (95% CI of the mean 0.11 to 0.44). Both the patients with persistent and paroxysmal AF had a significantly higher FI than the patients with SR (p <0.01 for persistent AF versus SR, p 0.01 for paroxysmal AF versus SR). The Tinetti test for gait and balance was abnormal in 66% of all patients and a gait disorder was present in 16% [31]. Furthermore, 51% uses a walking aid. For their age and gender, handgrip strength was less than expected in 68% of patients. Most of the patients live at home, 5% live in an elderly or nursing home, 19% need help performing activities of daily living (ADL) and 32% are dependent on others in respect to the instrumental ADL. In 20% of the patients there was a risk for malnourishment, 20% had problems hearing and 44% were known with visual impairment.

Cognitive state

At baseline, 14 patients (3%) of the studied cohort were known with dementia and 60 patients (14%) with mild cognitive impairment (MCI). The rate of known dementia or MCI was not statistically different between patients with SR, paroxysmal AF or persistent AF. Overall, the mean score of the MMSE was 27 points, and of the MoCA 24 points. In general, cognitive decline was found with the MMSE in 17% of patients with SR, 11% of patients with paroxysmal AF and in 33% of patients with persistent AF. With the MoCA, cognitive decline was found in 64% of patients with SR, 60% of patients with paroxysmal AF and 80% of patients with persistent AF. Supplementary Table A shows the associations between morbidities and cognitive decline as found on the MMSE or MoCA. Cognitive decline was found with the MMSE more often in patients known with persistent AF (33%, p = 0.01), parkinsonism (36%, p = 0.003), and chronic kidney disease (33%, p = 0.007). With the MoCA, cognitive decline was found more often in patients with persistent AF (80%, p = 0.02), chronic kidney disease (81%, p = 0.013), heart failure (77%, p = 0.094), and parkinsonism (78%, p = 0.069). Since both heart failure and chronic kidney disease are associated with cognitive decline, they are possible confounders in the association between AF and finding cognitive decline on the MMSE or MoCA. Controlling for confounding shows that in patients with paroxysmal AF finding cognitive decline on the MMSE or MoCA is independent of the presence of heart failure or chronic kidney disease (Mantel-Haenszel test p = 0.107 and p = 0.219 respectively). However, in patients with persistent AF, finding cognitive decline on the MMSE is dependent on the presence of heart failure or chronic kidney disease (Mantel-Haenszel test p = 0.021), but with the MoCA it is not (Mantel-Haenszel tests of conditional independence p = 0.103).

Imaging outcomes

In 332 patients (78%) an MRI of the brain was performed, the mean Fazekas score was 1.9 ± 1.0 points and the mean MTA score was 1.7 ± 0.8 points. In patients with SR the Fazekas score was 1.8 points, and in patients with either paroxysmal AF or persistent AF the Fazekas score was higher, respectively 1.9 and 2.1 points (p = 0.22 and p = 0.65, respectively, compared to SR). Heart failure, comprised of both heart failure with reduced ejection fraction and with preserved ejection fraction, was present in 26 of the patients that underwent MR imaging. In patients with heart failure the Fazekas score was 2.2 ± 0.9 and in those without 1.8 ± 1.0 (p = 0.07). And in patients with chronic kidney disease the Fazekas score was 2.1 ± 0.9, compared to 1.8 ± 1.0 in those without (p = 0.15).

The MTA score was significantly higher in patients with persistent AF compared to those with SR (2.1 vs 1.7, p 0.02), and compared to those with paroxysmal AF (2.1 vs 1.6, p<0.01). Relevant MTA was present in 95 patients with SR (38%), 11 patients with persistent AF (37%) and 14 patients with paroxysmal AF (41%). No statistically significant differences were found in the rate of relevant MTA between patients with AF or SR.

Patients with a MMSE below the cut-off had a significantly higher MTA score (2.1 vs 1.6, p = <0.001), but not a higher Fazekas score (2.1 vs 1.8, p = 0.11). Patients with a MoCA score below the cut-off

too had a significantly higher MTA score (1.8 vs 1.6, p = 0.01), but not a higher Fazekas score (1.9 vs 1.8, p = 0.53). Also, patients with a MMSE below the cut-off had more relevant MTA (53 vs 35%, p = 0.02) but patients with a MoCA below the cut-off did not have relevant MTA more often (40 vs 36%, p = 0.55).

Discussion

As hypothesized, the sensitivity to detect cognitive decline in geriatric patients with AF is much higher for the MoCA than for the MMSE. Of patients with paroxysmal AF 60% score abnormally on the MoCA, and of those with persistent AF 80% score abnormally on the MoCA, compared to an abnormal score on the MMSE in only 11 and 33% respectively. Both the MMSE and MoCA are validated instruments to identify cognitive decline, but the MoCA is known has a higher sensitivity for identifying MCI compared to the MMSE [19,20]. It is therefore likely that the MoCA produced a better estimate of the prevalence of cognitive decline in this cohort than the MMSE.

In patients with persistent AF, cognitive decline can be identified with the MoCA independently of the presence of heart failure or chronic kidney disease, while our analysis suggests that to identify patients with persistent AF and cognitive decline with the MMSE was dependent on the presence of heart failure or chronic kidney disease. For patients with paroxysmal AF, finding cognitive decline on the MMSE was not dependent on the presence of heart failure or chronic kidney disease. This indicates that the MoCA is better suited to detect cognitive decline in patients with AF than the MMSE, possibly due to its higher sensitivity to subcortical vascular damage compared to MMSE [20].

In this cohort of very elderly and severely frail patients, we found no differences in prevalence of dementia at baseline between those with and without AF, and the prevalence of dementia was low. Probably this is explained by a referral and selection bias. Cognitive disorders can contribute greatly to an individual's risk of falling [32-34], but cognitive decline itself might not have been noticed by caretakers or diagnosed by the general practitioner before visiting the FSC. To find a high rate of cognitive decline in a population referred specifically because of falling is therefore not surprising.

The studied cohort has a high average Fazekas score, indicative of that most patients had relevant WMH. We found small differences on MR imaging were found between patients with SR or AF. More WMH were found in patients with paroxysmal or persistent AF, compared to patients with SR, but these differences were not statistically significant. In patients with cognitive decline as found on either the MMSE or the MoCA, more MTA was found, but not more WMH. Only in patients with a MMSE below cut-off significantly more relevant MTA was found. Since MTA is a biomarker for Alzheimer's disease, the combination of relevant MTA and cognitive decline found by means of a MMSE, could be suggestive for the presence of dementia in these patients. This is in contrast with the patients who scored below the cut-off of the MoCA, in whom relevant MTA was not seen more often. Most likely, this is explained by the MoCA being more sensitive to MCI compared to the MMSE [19,20]. Since both patients with persistent or paroxysmal AF were significantly more often known with heart failure, and patients with heart failure in general had more WMH in this cohort, it is possibly hypoperfusion as consequence of heart failure that lead to WMH.

The study of Glotzer and colleagues found a higher rate of adverse events in patients with a high burden of AF [35]. Also our findings show that cognitive outcomes of patients with persistent or paroxysmal AF are different, and we encourage that future research to study the influence of the burden of AF on cognitive outcomes.

This study has several limitations. The cross-sectional design only allows a description of the population and possible associations between patient characteristics, but cannot provide conclusions about causality. Only the cognitive screening tests were used in this study and not the outcomes of a full multidisciplinary cognitive assessment that often include biomarkers, and therefore we could only detect cognitive decline. Nonetheless, both the MMSE and the MoCA are screenings tools for the identification of patients with cognitive decline [18-20]. They can aid the physician with the selection of patients that should be referred for a full cognitive assessment. Our results most of all show the need to assess cognitive function in elderly patients with AF, but is not a reliable reflection of the prevalence of cognitive disorders within this population.

The data describes the patients' health status up until the moment of inclusion but follow up data of adverse events were not available. This study used the medical history as it was reported by the referring physician, combined with what was retrieved from the hospital files and therefore might be incomplete or otherwise imprecise. It is possible that a higher prevalence of white matter hyperintensities is found in the very elderly in general because of cardiovascular disease [36], which is reflected in the high mean Fazekas score of 1.9 points in the studied cohort.

Conclusion

In this study we found that cognitive decline in patients with AF is better detected using the MoCA than the MMSE. Based on these findings we urge physicians to screen their AF patients for cognitive decline, preferably using the MoCA instead of the MMSE.

The marked differences between patients with persistent or paroxysmal AF could suggest that the burden of AF influences long term cognitive outcomes, possibly in interaction with heart failure, which should be addressed in future research.

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Supplementary Tables

Table A: Factors associated with cognitive decline

		MMSE < 26 points, n (%)	p	MoCA < 26 points, n (%)	P
Sinus Rhythm	present	57 (17,3)	0,376	209 (63,5)	0,281
	absent	21 (21,2)		69 (69,7)	
Paroxysmal AF	present	6 (11,3)	0,187	32 (60,4)	0,447
	absent	72 (19,2)		246 (65,6)	
Persistent AF	present	15 (32,6)	0,014	37 (80,4)	0,022
	absent	63 (16,5)		241 (63,1)	
Hypertension	present	54 (18,4)	1,000	197 (67,0)	0,192
	absent	24 (17,9)		81 (60,4)	
Diabetes mellitus	present	17 (19,5)	0,756	62 (71,3)	0,208
	absent	61 (17,9)		216 (63,3)	
Ischemic heart disease	present	22 (20,4)	0,564	74 (68,5)	0,415
	absent	56 (17,4)		204 (63,7)	
Heart failure	present	8 (18,2)	1,000	34 (77,3)	0,094
	absent	70 (18,2)		244 (63,5)	
Parkinsonism	present	16 (35,6)	0,003	35 (77,8)	0,069
	absent	62 (16,2)		243 (63,4)	
Chronic kidney disease	present	17 (32,7)	0,007	42 (80,8)	0,013
	absent	61 (16,2)		236 (62,8)	
Gait disorder	present	16 (23,2)	0,238	50 (72,5)	0,170
	absent	62 (17,3)		228 (63,5)	

Abbreviations. AF: Atrial fibrillation.

Table B: Cognitive screening and cognitive disorders among patients using beta blockers.

	Beta blocker			Persis AF Beta blocker			PAF Beta blocker		
	No (n=286)	Yes (n=142)	p	No (n=24)	Yes (n=22)	p	No (n=31)	Yes (n=22)	p
MMSE below 26, n (%)	49 (17.1)	29 (20.4)	0.406	6 (25.0)	9 (40.9)	0.250	3 (9.7)	3 (13.6)	0.654
MoCA below 26, n (%)	180 (62.9)	98 (69.0)	0.215	19 (79.2)	18 (81.8)	0.821	17 (54.8)	15 (68.2)	0.328
MCI diagnosis, n (%)	39 (13.6)	21 (14.8)	0.746	3 (12.5)	1 (4.5)	0.339	3 (9.7)	1 (4.5)	0.486
Dementia diagnosis, n (%)	8 (2.8)	6 (4.2)	0.434	0 (0.0)	3 (13.6)	0.061	1 (3.2)	0 (0.0)	0.395

Abbreviations: Persis AF: persistent atrial fibrillation, PAF: paroxysmal atrial fibrillation. MMSE: Mini Mental State Examination, MoCA: Montreal Cognitive Assessment, MCI: Mild Cognitive Impairment.