

Known and newly discovered atrial fibrillation in correlation with outcome after stroke

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ABSTRACT:

Background: Atrial fibrillation (AF) is one of the most important risk factors for ischemic stroke. Atrial fibrillation in stroke patients can be classified as: 1. previously known atrial fibrillation that was detected before the stroke occurred and 2. newly diagnosed atrial fibrillation, detected after the stroke occurred (AF de novo). The aim of this study is to analyse the severity and outcome of stroke in patients with newly diagnosed AF and those with known AF.

Materials and Methods: A retrospective analysis was made of 98 patients with acute stroke with AF hospitalised at the University Clinic for Neurology in Skopje, North Macedonia - at the Department of Urgent Neurology in the period from 2019 to 2022. Inclusion criteria for the study were patients with AF, in all age groups, diagnosed with stroke. In the analysis, we also included other parameters such as neurological deficit quantified by NIHSS (National Institutes of Health Stroke Scale), state of consciousness quantified by GCS (Glasgow Coma Scale/Score) and degree of disability quantified by mRS (Modified Rankin Scale).

Results: The results of this study showed that group 1A (known AF) patients had a predominance of moderate to severe stroke (quantified by NIHSS score), moderate disability (quantified by mRS score), low GCS score, compared to group 1B (AF de novo) patients with a predominance of mild stroke, mild disability, but without proven statistical significance ($p > 0.05$).

Conclusion: We found that stroke severity and scores quantified by NIHSS, GCS, and mRS in patients with newly diagnosed AF did not differ from those in patients with known AF.

KEYWORDS: atrial fibrillation, stroke, NIHSS, GCS, mRS

SAŽETAK:

KORELACIJA ISHODA NAKON MOŽDANOG UDARA I NOVOOTKRIVENE ILI RANIJE POZNATE FIBRILACIJE ATRIJA

Uvod: Fibrilacija atrijske (FA) jedan je od najvažnijih čimbenika rizika za ishemijski moždani udar. Fibrilacija atrijske u bolesnika s moždanim udarom se može klasificirati kao: 1. Ranije poznata FA koja je dijagnosticirana prije moždanog udara i 2. Novootkrivena FA. Cilj ove studije je analizirati težinu i ishode moždanog udara u bolesnika s novootkrivenom i od ranije poznatom FA.

Materijali i metode: Provedena je retrospektivna analiza 98 bolesnika s akutnim moždanim udarom i FA hospitaliziranih u Sveučilišnoj klinici za neurologiju u Skopju, Sjeverna Makedonija, na Odjelu hitne neurologije u periodu od 2019. Do 2022. Godine. Uključni kriteriji su bili FA, svih dobnih

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skupina, dijagnosticiranih s moždanim udarom. U analizi uključeni su i drugi pokazatelji poput neurološkog deficita kvantificiranog NIHSS skalom (engl. National Institutes of Health Stroke Scale), stanje svijesti procijenjeno GCS zbrojem (engl. Glasgow Coma Scale/Score) i stupanj neurološkog deficita kvantificarnog pomoću mRS (engl. Modified Rankin Scale).

Rezultati: Ovo istraživanje pokazalo je da su bolesnici skupine 1A (poznata FA) češće imali srednje težak do težak moždani udar (prema NIHSS zbroju), srednje težak neurološki deficit (prema mRS zbroju) i nizak GCS zbroj naspram bolesnika iz skupine 1B (novonastala FA) kod kojih je češće bio blaži moždani udar i manji neurološki deficit, ali bez statističkog značaja ($p > 0.05$).

Zaključak: Prema našim rezultatima, težina moždanog udara i zbrojevi NIHSS, GCS i mRS se nisu razlikovali u bolesnika s novonastalom FA naspram onih s od ranije poznatom FA.

KLJUČNE RIJEČI: fibrilacija atriya, moždani udar, NIHSS, GCS, mRS

INTRODUCTION

Atrial fibrillation (AF) is one of the most important risk factors for ischemic stroke. It is known that patients with AF have a 5 times higher risk of having a stroke than those without AF. With the availability of modern cardiac monitoring technologies, detection of AF after stroke or transient ischemic attack (TIA) has improved significantly [1]. Atrial fibrillation in stroke patients can be classified as: 1. previously known atrial fibrillation that was detected before the stroke occurred and 2. newly diagnosed AF, detected after the stroke occurred (AF de novo) [1]. Among acute ischemic stroke patients with AF, 7.8% to 36.2% were first diagnosed with AF after a registered stroke [2]. Ischemic stroke that occurs in patients with AF is likely to be severe or fatal. Half of patients with AF are asymptomatic, therefore detection of AF and subsequent anticoagulant therapy is crucial for stroke prevention [2]. Patients with newly diagnosed AF and those with known AF have different characteristics. However, differences in stroke severity and outcome have not been sufficiently evaluated [2][3].

AIM

The aim of this study is to analyse the severity and outcome of stroke in patients with newly diagnosed AF and those with known AF.

MATERIALS AND METHODS

A retrospective analysis was made of 98 patients with acute stroke with AF hospitalised at the University Clinic for Neurology in Skopje, North Macedonia - at the Department of Urgent Neurology in the period from 2019 to 2022.

Inclusion criteria for the study were patients with AF, in all age groups, diagnosed with stroke (ischemic, hemorrhagic). Depending on whether it is known AF or newly diagnosed AF, we divided the patients into two groups: 1A known AF and 1B newly diagnosed AF (AF de novo).

According to the localization of the stroke registered on computed tomography, we divided the patients into two groups: 2A

patients with a stroke in the anterior circulation, 2B patients with a stroke in the posterior circulation.

In the analysis, we also included other parameters such as neurological deficit quantified by NIHSS (National Institutes of Health Stroke Scale), state of consciousness quantified by GCS (Glasgow Coma Scale/Score) and degree of disability quantified by mRS (Modified Rankin Scale). Depending on the NIHSS score, we divided stroke patients into 3 categories: mild stroke (1-5 points), moderate stroke (5-14 points), severe stroke (15-42 points). Depending on the GCS result, we divided the patients according to the level of consciousness into 3 groups: best response (15-9 points), coma (8-4 points), completely unresponsive (< 3 points). Depending on the mRS score, we divided the patients according to the degree of disability into: patients with mild disability (1-2 points), patients with moderate disability (3-4 points), patients with severe disability (5 points).

STATISTICAL ANALYSIS

The data were analysed using IBM SPSS Statistics (chi square test) and the (chi-square) test was used, which is expressed in numbers and percentages. The results are presented tabular and graphically. Statistical significance was set at $p < 0.05$.

RESULTS

In our study, 98 patients aged 49-89 years were analysed, of which 53.1% (52) were women and 46.9% (46) were men. 72.5% (71) of the patients had an ischemic stroke, 7.1% (7) had a hemorrhagic stroke, and 20.4% (20) had an ischemic stroke with hemorrhagic transformation. (figure 1).

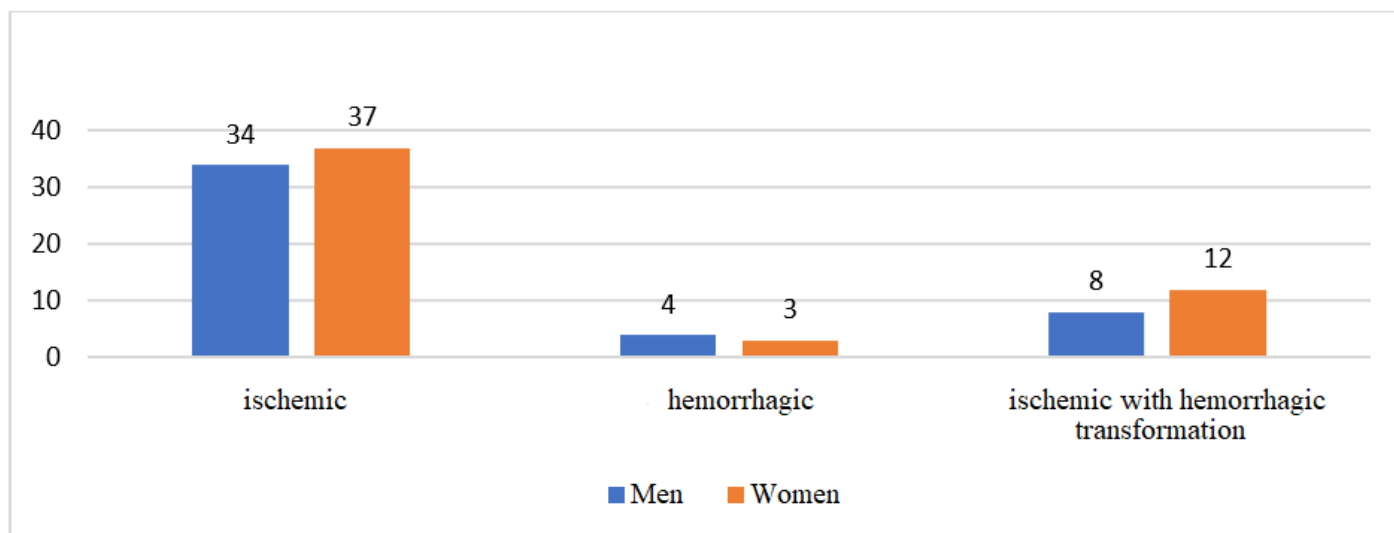


Figure 1. Distribution of the total number of patients according to gender and type of stroke

According to the localization of the stroke, 78.6% (77) of the patients had a stroke localized in the anterior circulation, and 19.4% (19) had a stroke localized in the posterior circulation. (table 1)

Table 1. Localization of the stroke and the number of patients

Localization of stroke Gender	1 –Anterior circulation		2 –Posterior circulation		3 - Thrombolysed		In total No.	In total %
	No.	%	No.	%	No.	%		
1 -Male	36	36,7%	8	8,2%	2	2,0%	46	46,9%
2 -Female	41	41,8%	11	11,2%		0,0%	52	53,1%
Total sum	77	78,6%	19	19,4%	2	2,0%	98	100,0%

Out of a total of 98 patients, 63.3% (62) had known atrial fibrillation (group 1A), of which 26.5% (26) were men, and 36.7% (36) were women. In 36.7% (36) of the patients, atrial fibrillation was newly diagnosed during hospitalisation (group 1B), of which 20.4% (20) were men, and 16.3% (16) were women. (Figure 2).

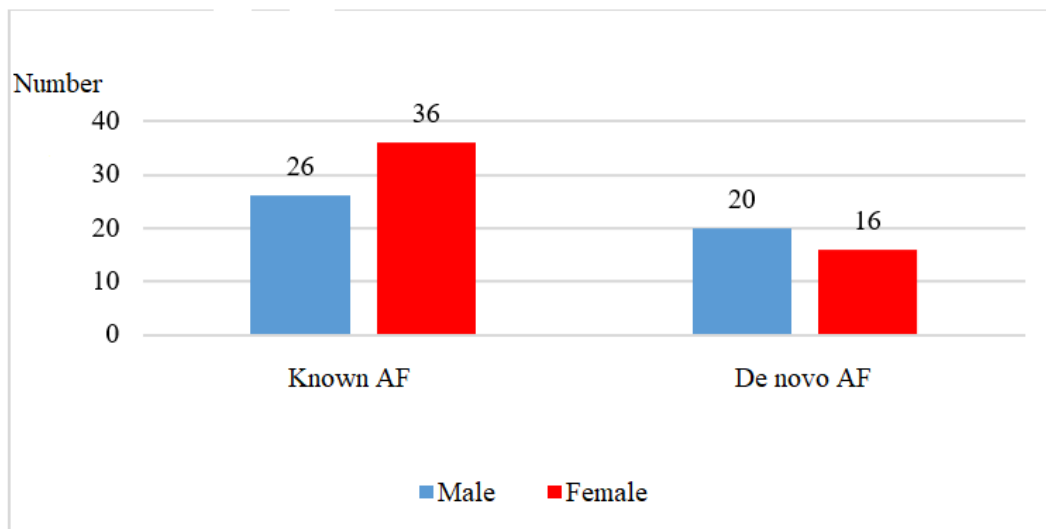


Figure 2. Patients with known versus newly diagnosed AF

$X^2=1,696 < X^2(1 \text{ and } 0,005)=3,841$ and $p>0,05$

H_0 (null hypothesis) is accepted. There is no association between AF and gender.

According to the score obtained from NIHSS; 25% of subjects from group 1A (known AF) had a mild stroke, 65% had a moderate stroke, 64.8% had a severe stroke. 75% of the individuals from group 1B (AF de novo) had a mild stroke, 35% a moderate stroke and 35.2% a severe stroke. (table 2, figure 3).

Table 2. NIHSS score (at discharge) of patients with known versus newly diagnosed AF.

		Mild stroke	Moderate stroke	Severe stroke	Total
Known AF	Count	1	26	35	62
	% within NIHSS	25,0%	65,0%	64,8%	63,3%
De novo AF	Count	3	14	19	36
	% within NIHSS	75,0%	35,0%	35,2%	36,7%
Total	Count	4	40	54	98
	% within NIHSS	100,0%	100,0%	100,0%	100,0%

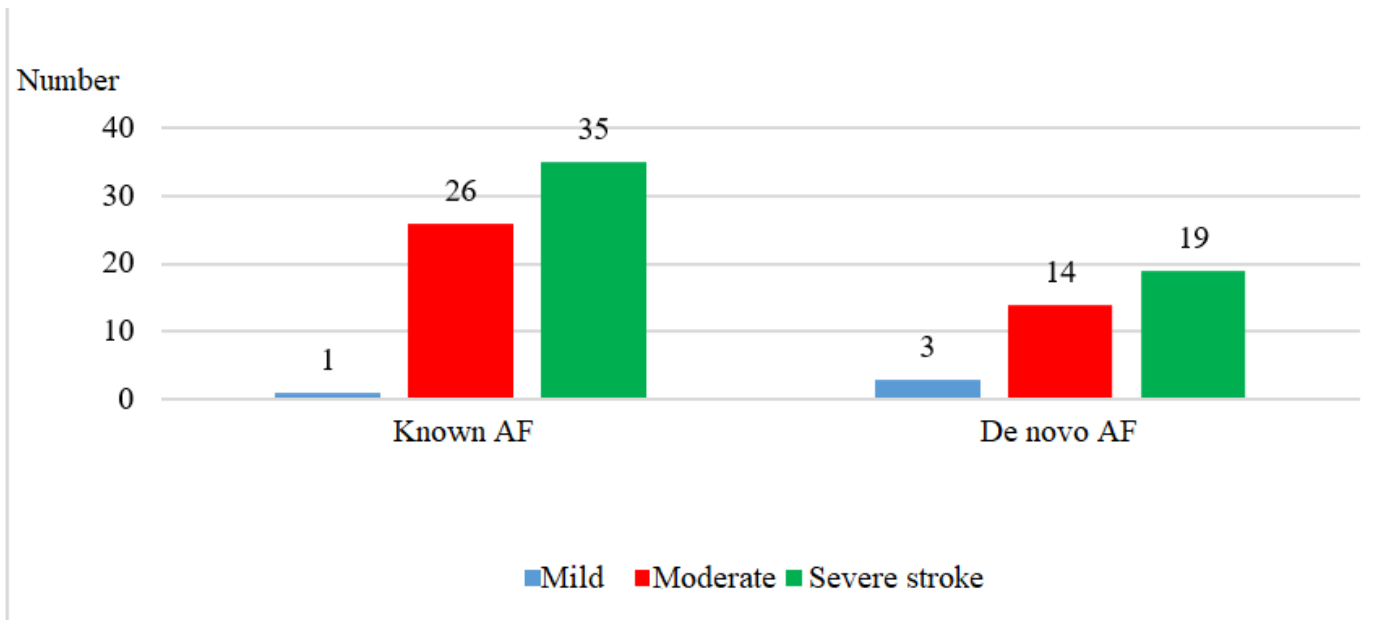


Figure 3. NIHSS score (at discharge) of patients with known versus newly diagnosed AF

$X^2=2,628 < X^2(2 \text{ and } 0,05) = 5,991$ and $p > 0,05$

H0 (null hypothesis) is accepted. There is no association between AF and NIHSS.

According to the result obtained by GCS, 62% of subjects from group 1A (known AF) had the best response, 70.8% were in coma, 33.3% were completely unresponsive. 38.0% of the patients from group 1B (AF de novo) had the best response, 29.2% were in a coma, 66.7% were completely unresponsive. (Table 3, Figure 4).

Table 3. GCS result (at discharge) of patients with known versus newly diagnosed AF

		Best response	Coma	Completely unresponsive	Total	
AF	Known AF	Count	44	17	1	62
		% within GCS	62,0%	70,8%	33,3%	63,3%
AF	De novo	Count	27	7	2	36
		% within GCS	38,0%	29,2%	66,7%	36,7%
Total		Count	71	24	3	98
		% within GCS	100,0%	100,0%	100,0%	100,0%

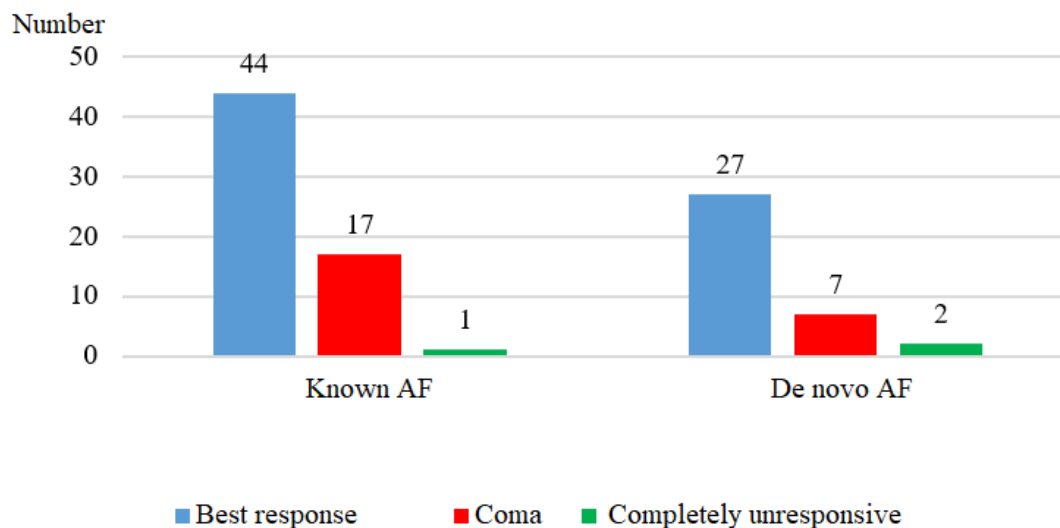


Figure 4. GCS result (at discharge) of patients with known versus newly diagnosed AF

$\chi^2=1,799 < \chi^2 (2 \text{ and } 0,05)= 5,991$ and $p>0,05$

H0 (null hypothesis) is accepted. There is no association between AF and GCS.

According to the result obtained from the mRS, 50.0% of the respondents from group 1A (known AF) had light disability, 66.7% moderate disability, 62.9% severe disability. 50.0% of the respondents from group 1B (AF de novo) had mild disability, 33.3% moderate disability, 37.1% severe disability. (Table 4, Figure 5).

Table 4. mRS result (at discharge) of patients with known versus newly diagnosed AF

		Light disability	Moderate disability	Severe disability	Total
Known AF	Count	2	16	44	62
	% within mRS	50,0%	66,7%	62,9%	63,3%
De novo AF	Count	2	8	26	36
	% within mRS	50,0%	33,3%	37,1%	36,7%
Total	Count	4	24	70	98
	% within mRS	100,0%	100,0%	100,0%	100,0%

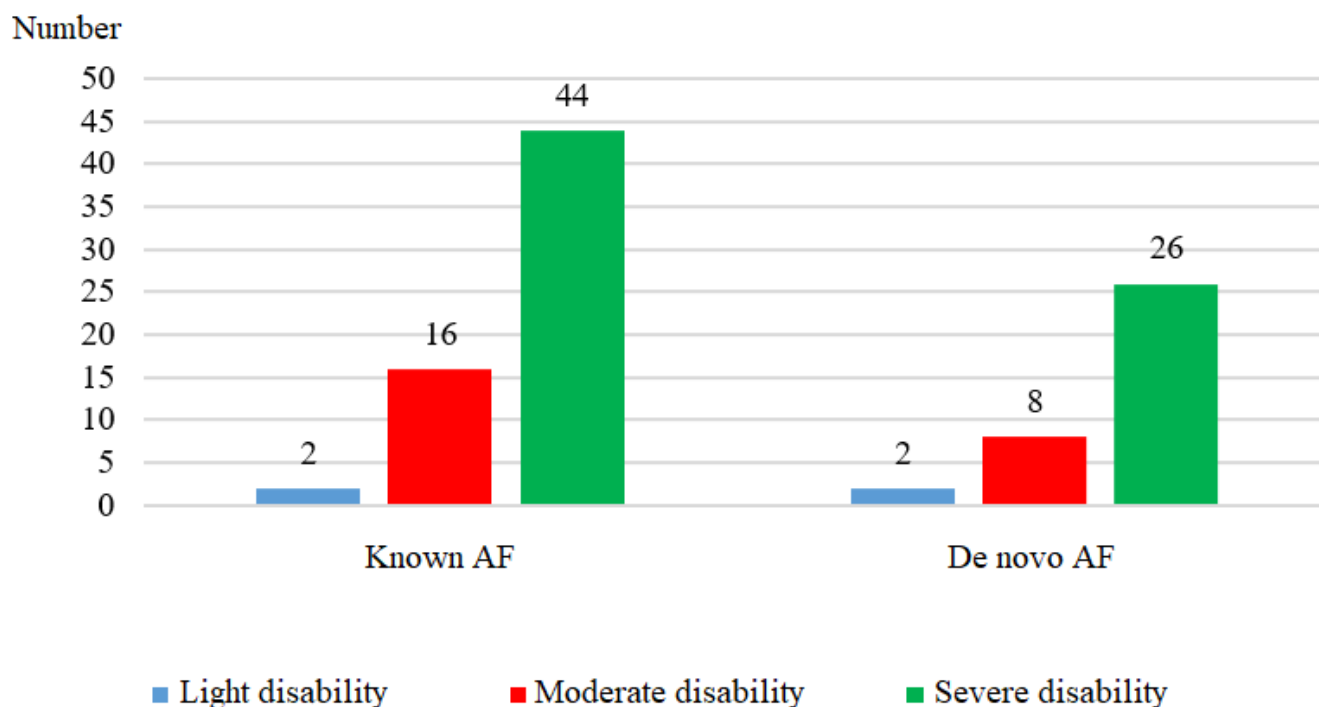


Figure 5. mRS result (at discharge) of patients with known versus newly diagnosed atrial fibrillation

$X^2=0,427 < X^2 (2 \text{ and } 0,05)= 5,991$ and $p>0,05$

H_0 (null hypothesis) is accepted. There is no association between AF and mRS.

DISCUSSION

In our study, in the period from 2019 to 2022, 98 patients with AF were hospitalised and treated at the Department of Urgent Neurology, due to a registered acute stroke. This study includes patients with AF. Other risk factors for acute stroke, such as diabetes mellitus, hypertension, hyperlipidemia, were not analysed in the study. Also, the results obtained with NIHSS, GCS and mRS were obtained when the patients were discharged from the hospital. The results showed that 36.7% (36) of the subjects were diagnosed with atrial fibrillation for the first time. The largest number of patients had ischemic stroke (72.5%), but the rate of patients with ischemic stroke with hemorrhagic transformation (20.4%) is also significant. In our group of patients dominates a stroke in anterior circulation (78.6%).

The results of this study showed that group 1A (known AF) patients had a predominance of moderate to severe stroke (quantified by NIHSS score), moderate disability (quantified by mRS score), low GCS score, compared to group 1B (AF de novo) patients with a predominance of mild stroke, mild disability, but without proven statistical significance ($p>0.05$).

In a study published in 2021, it was concluded that: Stroke severity and in-hospital outcomes in patients with newly diagnosed AF did not differ from those in patients with known AF after adjustment for clinically relevant factors [2].

The difference between our study and the study by Watanabe K et al, is that in their study NIHSS scores were obtained at hospital admission, but also in their study patient comorbidities were taken into account. In their study, mRS scores were measured at hospital discharge, which supports our study.

That study also emphasises the administration of anticoagulant therapy to patients with known atrial fibrillation and the importance of detection of latent AF and subsequent anticoagulation

in preventing severe stroke should be further emphasised [2]. A meta-analysis of 21 studies comparing known atrial fibrillation and newly diagnosed AF also takes stroke reversibility into account. A study by Fridman S et al claims that patients with AF detected after stroke (AFDAS) may have a lower prevalence of cardiovascular comorbidities and lower risk of stroke recurrence than AF known before stroke (KAF). They found significant differences in the prevalence of vascular comorbidities, structural heart disease, and stroke recurrence rates between AFDAS and KAF, suggesting that they constitute different clinical entities within the AF spectrum [5].

A study from Wang et al. also takes stroke reversibility into account, but it is suggested that the rate of stroke recurrence did not differ significantly. On the other hand, as Fridma et al. study, it claims that AF de novo patients had a lower prevalence of coronary artery disease, heart failure, and sustained AF, but higher rates of large vessel occlusion compared to known AF patients. NIHSS scores were lower in patients on pre-stroke anticoagulation [8]. In our study NIHSS score between patients with known AF and AF de novo did not significantly differ, compared to Wang et al. study.

In a study that compares known AF, AF diagnosed after stroke and sinus rhythm is said that patients with newly diagnosed AF had a higher proportion of brain infarcts and a higher frequency of insular involvement [7]. The results of Toledo et al study are in agreement with our research, as we concluded that a bigger number of strokes are in the anterior circulation. The difference is that, in this study, the results were compared between patients with AF and patients with sinus rhythm.

In one study, the distribution of ischemic lesions was described in a large series of patients with AF suffering their first ischemic stroke. It was concluded that the timing of AF diagnosis or the CHA2DS2-VASc score did not affect the lesion localization. Although some differences in lesion localization were observed according to oral anticoagulant use, the distinctions in absolute terms were small and do not seem meaningful. Strokes classified as embolic or thrombotic were more often located within the anterior cerebrovascular territory in comparison to strokes of other or undetermined aetiology. Anterior territory strokes were slightly more often located within the left hemisphere, but the observed difference was so small that its clinical significance is questionable [4].

This study on localization of strokes in patients with AF is in agreement with ours. But, Jaakkola J et al's study also determines the effects of CHA2DS2-VASc score, oral anticoagulant (OAC) use, and timing of AF diagnosis on lesion localization.

It is concluded that AF de novo had similar risk of 1-year ischemic stroke recurrence and mortality when compared with known AF and higher risk when compared with sinus rhythm. The potential risk of AF de novo should be given more emphasis, and appropriate treatment is needed to achieve reduction in the incidence of stroke recurrence and mortality [1].

In a cohort study from Borowsky et al it is stated that nearly one in 5 AF-related strokes occurred without a pre-stroke AF diagnosis [6]. AF was readily diagnosed using standard rhythm monitoring. This emphasises the importance of timely diagnosis of AF.

There are many studies examining the effects of anticoagulant and antiplatelet therapy when comparing known atrial fibrillation and atrial fibrillation diagnosed after stroke. National Institutes of Health Stroke Scale scores varied according to preceding antithrombotic therapy ($P < 0.001$). It was higher in patients who did not receive antithrombotics than in those who received antiplatelets or anticoagulants. Favourable outcome at discharge (modified Rankin Scale score, 0–2) was more prevalent in patients who received antiplatelets or anticoagulants ($P < 0.001$). Use of antiplatelets and anticoagulants was associated with a mild initial neurological deficit (National Institutes of Health Stroke Scale score ≤ 5) in patients with acute ischemic attack with AF [9].

We should acknowledge the various limitations of this study. First, this was a retrospective observational analysis. Unlike randomised studies, the selection of patients and undocumented confounding factors could affect the validity of our findings. However, it was impossible to randomise patients with stroke and AF. Secondly, there were no studies that examine the GCS score on patients with known AF and AF de novo.

CONCLUSION

We found that stroke severity and scores quantified by NIHSS, GCS, and mRS in patients with newly diagnosed AF did not differ from those in patients with known AF. Given the severity of stroke in patients with AF, it should be further emphasised that detection of latent AF and subsequent anticoagulation is crucial to prevent severe stroke.

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