Is there any difference in mortality rates of atrial fibrillation detected before or after ischemic stroke?

Cigdem ILERI[1] , Zekeriya DOGAN[2] , Beste OZBEN[2] ,
Ipek MIDI[3] , Nevin PAZARCI[4]

[1]Kosuyolu Education and Research Hospital, Department of Cardiology, Istanbul, Turkey
[2]Marmara University School of Medicine, Department of Cardiology, Istanbul, Turkey
[3]Marmara University School of Medicine, Department of Neurology, Istanbul, Turkey
[4]Umraniye Education and Research Hospital, Department of Neurology, Istanbul, Turkey

Correspondent:
Dr. Cigdem ILERI,
Nish Adalar Sitesi 56/23
34852 Maltepe, Istanbul,
Turkey
Phone: 90 553 0109796
E-mail: cgdmileri@gmail.com
https://orcid.org/0000-0002-7974-9406

Background and purpose – Atrial fibrillation diagnosed after stroke (AFDAS) is a new term used for AF resulting from autonomic dysregulation. It is associated with a lower stroke recurrence compared to patients with known AF before a stroke (KAF). The aim of the study was to explore the characteristics and mortality rates in AFDAS patients.
Methods – 134 ischemic stroke patients (66.1±14.2 years old, n=73 male) were consecutively included in the study. While patients who had known AF with anticoagulant therapy were grouped as KAF, patients with newly documented AF rhythm (either by daily ECG or ambulatory ECG monitoring) were classified as AFDAS. All patients were followed for 1 year to obtain all-cause mortality, cardiac mortality, and neurogenic mortality.
Results – Of the 134 stroke patients, AF was detected newly in 38 patients and grouped as AFDAS. KAF patients had higher CHA_2DS_2VASc scores, hs-CRP and NT-proBNP levels, and more insular cortex involvement than the SR group. During the one-year follow-up, 35 stroke patients died. The mortality rate was significantly higher in patients with KAF (12/22; 54.5%) while the mortality rates were similar between AFDAS patients (11/38; 28.9%) and patients with sinus rhythm (SR) (12/74; 16.2%). KAF was an independent predictor when adjusted by

Van-e különbség az ischaemiás stroke előtt vagy után észlelt pitvarfibrilláció halálozási arányában?
Ileri C, MD; Dogan Z, MD; Ozben B, Prof. MD; Midi I, Prof. MD; Pazarci N, Assoc. Prof. MD

Háttér és cél – A stroke után diagnosztizált pitvarfibrilláció (AFDAS) egy új terminus, amit a vegetatív diszregulációból eredő pitvarfibrillációra használnak. Ez alacsonyabb stroke-recidívával jár a már a stroke előtt ismert AF-hez (KAF) képest. A vizsgálat célja az AFDAS-betegek jellemzőinek és halálozási arányának feltárása volt.
Módszerek – 134 ischaemiás stroke-beteget (66,1 ± 14,2 éves, n = 73 férfi) vontunk be a vizsgálatba. Míg az antikoaguláns-terápián lévő, ismerten AF-ben szenvedő betegeket a KAF-csoportba soroltuk, az újonnan dokumentált (akár napi EKG-val, akár ambuláns EKG-monitorozással) AF-ritmusú betegeket AFDAS-nak minősítettük. Minden beteget 1 éven keresztül követtünk a bármilyen okból bekövetkező halálozás, a cardialis, valamint a neurogén halálozás megállapítása céljából.
Eredmények – A 134 stroke-beteg közül 38 betegnél észleltek újonnan AF-et, és AFDAS-nak minősítették őket. A KAF-betegeknél magasabb volt a CHA_2DS_2VASc-pontszám, a hs-CRP- és NT-proBNP-szint, és nagyobb volt az insularis kéreg érintettsége, mint az SR-csoportban. Az egyéves követés során 35 stroke-beteg halt meg. A KAF-betegeknél szignifikánsan magasabb volt a mortalitás (12/22; 54,5%), míg hasonló volt a mortalitás az AFDAS-betegek (11/38; 28,9%) és a sinus-ritmusú (SR) betegek (12/74; 16,2%) között. A KAF független prediktor volt, ha az életkor,

age, sex, CHA₂DS₂VASc and NIHSS scores, and insular cortex involvement. While AFDAS had increased the mortality risk compared to SR, the difference was not significant in univariable and multivariable models.

Conclusion – AFDAS patients have similar CHA_2DS_2VASc scores and mortality rates to patients with SR, which implies that AFDAS might be a relatively benign form of AF.

Keywords: ischemic stroke, atrial fibrillation, atrial fibrillation diagnosed after stroke, AFDAS

a nem, a CHA₂DS₂VASc- és NIHSS-pontszámok, valamint az insularis kéreg érintettsége alapján korrigálták. Bár AFDAS esetén nőtt a halálozási kockázat az SR-hez képest, a különbség nem volt szignifikáns az egyváltozós és a többváltozós modellekben.

Következtetés – Az AFDAS-betegek CHA_2DS_2VASc-pontszámai és halálozási aránya hasonló az SR-betegekéhez, ami arra utal, hogy az AFDAS az AF viszonylag jóindulatú formája lehet.

Kulcsszavak: ischaemiás stroke, pitvarfibrilláció, stroke után diagnosztizált pitvarfibrilláció, AFDAS

A stroke may be the first presentation of atrial fibrillation (AF). Approximately one-fourth of ischemic stroke patients are newly diagnosed with AF[1]. The term, AF diagnosed after stroke (AFDAS) is used for both previously undetected, asymptomatic AF and poststroke AF[2].

In acute ischemic stroke, structural brain lesions, especially those with cortical involvement, may lead to autonomic dysregulation and inflammation[3]. Although the pathophysiology has not been defined clearly, autonomic dysfunction and inflammation may play a role in the development of AF by lowering the cardiac arrhythmogenic threshold[4]. AF has been detected in more than half of the cases within 3 days after admission for ischemic stroke[5]. The mean time of AF diagnosis has ranged between 3 to 77 days after stroke. Meanwhile, AF detected earlier after the stroke has been suggested to be the consequence of the stroke, not the cause of the stroke[2].

AFDAS patients are believed to have a more benign disease profile compared to patients with known AF (KAF). In a meta-analysis, it has been shown that AFDAS patients have a better vascular profile and lower comorbidities such as hypertension, diabetes, hyperlipidemia, coronary artery disease, heart failure, and previous stroke[4]. The duration of AF periods diagnosed after stroke is less than 30 seconds in approximately half of the patients, which implies that AF burden is lower in AFDAS patients[6]. Moreover, the ischemic recurrence of AFDAS is shown to be less, compared to patients with KAF before stroke[7].

The aim of our study was to investigate the characteristics and mortality differences of the patients with strokes that preceded or occurred after the diagnosis of AF.

Methods

The investigation conformed to the principles outlined in the Declaration of Helsinki. All participants gave written informed consent. The study was approved by the ethics committee of Marmara University School of Medicine.

Study population

One hundred and thirty-four patients presenting with acute ischemic stroke documented by cranial imaging were consecutively included in the study. The TOAST classification system was used to define the stroke subtypes[8]. National Institutes of Health Stroke Scale (NIHSS) scores of patients were noted at the time of hospitalization. Patients with transient ischemic attacks (TIA) were not included in our study.

Patients were evaluated for the presence of comorbidities, including hypertension, hyperlipidemia, diabetes, and coronary artery disease. Blood samples for high sensitive (hs) C-reactive protein (CRP), hs-cardiac troponin I (hs-cTnI), and N-terminal pro-brain natriuretic peptide (NT-proBNP) levels were noted. All patients underwent a transthoracic echocardiographic study by a Philips Epic echocardiography device (Philips Medical Systems, Andover, MA, USA) by an experienced cardiologist within the first three days following acute ischemic stroke. Conventional echocardiographic measurements were performed by the recommendations of the American Society of Echocardiography guidelines[9]. LVEF was assessed by biplane Simpson's method.

Electrocardiography (ECG) was obtained from each patient daily. Ambulatory ECG monitoring was performed in patients with sinus rhythm (SR) to explore

AF or other arrhythmias within the first seven days following acute ischemic stroke. The ECG recordings were analyzed by an experienced cardiologist. Patients who had newly documented AF rhythm lasting more than 30 seconds in ambulatory ECG monitoring or daily 12-lead ECG were classified as AFDAS, while patients who had known AF with anticoagulant therapy were grouped as KAF based on patient-reported medical history and prior available medical records. AFs that were detected at the time of hospitalization that had not been diagnosed and treated before this ischemic stroke event, and that also occurred during the hospitalization period were also categorized as AFDAS.

Cranial images of the patients were re-evaluated by experienced neurologists who were blind to patients' characteristics to determine whether there was an insular cortex involvement.

All patients were followed for 1 year to obtain all-cause mortality, cardiac mortality and neurogenic mortality.

Statistical analysis

Statistical analyses were performed by statistical software (SPSS 21.0 for windows, Chicago, IL). The distribution of data was assessed by using one-sample Kolmogorov–Smirnov test. Continuous data were expressed as mean ± SD while categorical data were expressed as numbers or percentages. Chi-squared test was used for the comparison of categorical variables. Student's t-test or ANOVA was used to compare the normally distributed continuous variables while the Mann-Whitney U test or Kruskal-Wallis test was used to compare the non-

parametric continuous variables. Post hoc analyses were performed using the Bonferroni test when an overall statistical significance was determined. Logistic regression analysis was performed to explore the predictors of all-cause mortality. Statistical significance was accepted as a P-value less than 0.05.

Results

One hundred and thirty-four consecutive ischemic stroke patients (66.1 ± 14.2 years old, n=73 male) were included in the study. Twenty-two patients (16.4%) had KAF while AF was detected newly in 38 patients (28.4%), who were grouped as AFDAS. The remaining 74 patients (55.2%) had SR. The general characteristics of the patients according to cardiac rhythm are shown in **Table 1**. Patients with KAF and AFDAS were significantly older compared to the patients with SR, while there was no significant difference in age between KAF and AFDAS patients. KAF patients had higher CHA_2DS_2VASc scores and more insular cortex involvement than the SR group, while CHA_2DS_2VASc scores and insular cortex involvement were similar between AFDAS and SR patients. There were no significant differences in the comorbidities and NIHSS scores among patients. Stroke patients with KAF and AFDAS were using beta-blockers more than SR patients.

The laboratory and conventional echocardiographic parameters of the patients are listed in **Table 2**. hs-cTnI was elevated in all groups while the SR group had the highest mean. hs-CRP levels were higher in KAF patients compared to patients with SR. While AFDAS patients had also higher hs-CRP levels than patients with SR,

Table 1. *The characteristics of the patients*

	KAF (n = 22)	AFDAS (n = 38)	SR (n = 74)	P
Age (years)	75.2 ± 9.3*	71.6 ± 14.7*	60.6 ± 12.6	*<0.001*
Male sex (n – %)	12 (54.5%)	18 (47.4%)	43 (58.1%)	0.558
Body mass index (kg/m²)	26.5 ± 5.7	26.6 ± 3.9	26.8 ± 4.5	0.970
CHA_2DS_2VASc	4.5 ± 1.8*	4.0 ± 1.9	3.2 ± 1.9	*0.013*
NIHSS	6.4 ± 3.9	6.1 ± 4.0	5.3 ± 4.0	0.454
Hypertension (n – %)	17 (77.3%)	29 (76.3%)	50 (67.6%)	0.507
Diabetes (n – %)	9 (40.9%)	14 (36.8%)	32 (43.2%)	0.808
Hyperlipidemia (n – %)	19 (86.4%)	27 (71.1%)	56 (75.7%)	0.404
Coronary artery disease (n – %)	9 (40.9%)	8 (21.1%)	23 (31.1%)	0.254
Insular cortex involvement (n – %)	11 (50.0%)*	12 (31.6)	14 (18.9)	*0.013*
Beta-blocker usage (n – %)	10 (45.5%)*	18 (47.4%)*	15 (20.3)	*0.005*

KAF: known atrial fibrillation, AFDAS: atrial fibrillation diagnosed after stroke, SR: sinus rhythm, NIHSS: National Institutes of Health Stroke Scale
PostHoc analysis: * denotes statistical significance versus patients with sinus rhythm

Table 2. *The laboratory parameters and conventional transthoracic echocardiographic measures of the patients*

	KAF (n = 22)	AFDAS (n = 38)	SR (n = 74)	P
Glucose (mg/dL)	108 ± 51*	121 ± 57	135 ± 53	*0.023*
Creatinine (mg/dL)	1.18 ± 0.65	0.94 ± 0.34	0.94 ± 0.46	0.364
Total cholesterol	176 ± 43+	211 ± 52	197 ± 45	*0.042*
LDL cholesterol (mg/dL)	109 ± 37+	142 ± 45*	122 ± 37	*0.017*
hs-cTnI (ng/mL)	0.08 ± 0.16*	0.09 ± 0.24*	0.11 ± 0.47	*0.005*
hs-CRP (mg/L)	41.4 ± 48.2*	27.1 ± 37.7	12.4 ± 17.6	*0.004*
NT-proBNP (pg/mL)	7298 ± 10282*	2548 ± 6200	1241 ± 4750	*<0.001*
Left atrium (mm)	45.3 ± 7.1*,+	40.9 ± 7.7*	36.2 ± 5.1	*<0.001*
LAVI (mL/m²)	39.2 ± 16.4*,+	29.3 ± 11.5*	20.9 ± 8.3	*<0.001*
LVEF (%)	54 ± 15	56 ± 11	59 ± 9	0.174
E/e'	11.6 ± 5.1*	9.7 ± 4.1	8.3 ± 3.1	*0.012*

KAF: known atrial fibrillation, AFDAS: atrial fibrillation diagnosed after stroke, SR: sinus rhythm, LDL: Low-density lipoprotein, hs-cTnI: High-sensitive cardiac Troponin I, hs-CRP: High-sensitive C-reactive protein, NT-proBNP: N terminal pro-brain natriuretic peptide, LAVI: Left atrial volume index, LVEF: left ventricular ejection fraction, E/e': the ratio of early diastolic mitral inflow velocity to early diastolic mitral annulus velocity
PostHoc analysis: * denotes statistical significance versus patients with sinus rhythm
+ denotes statistical significance versus patients with atrial fibrillation diagnosed after a stroke

the difference was not statistically significant. KAF and AFDAS patients had significantly larger left atriums compared to patients with SR. Although there were no significant differences in the left ventricular ejection fraction values of the patients, the KAF group had significantly higher NT-proBNP and E/e' compared to the SR group, while AFDAS and SR patients had similar NT-proBNP and E/e'.

During the one-year follow-up period, 35 stroke patients died (12 patients in the KAF group, 11 in the AFDAS group, and 12 in the SR group). KAF patients had significantly higher all-cause and cardiac mortality rates compared to both AFDAS patients and SR patients, while the AFDAS group had similar all-cause and cardiac mortality rates to the SR group **(Table 3)**.

The characteristics, laboratory parameters, and conventional transthoracic echocardiographic measures of stroke patients according to mortality status are shown in **Table 4**. These patients were older, had higher CHA_2DS_2VASc and NIHSS scores, hs-cTnI, and hs-CRP levels, with more insular cortex involvement, and larger left atrium.

Univariable and multivariable logistic regression analyses were modeled to explore the predictors of all-cause of mortality **(Table 5)**. Logistic regression analysis revealed KAF as an independent predictor when adjusted

Table 3. *One-year mortality rates of the patients*

	KAF (n = 22)	AFDAS (n = 38)	SR (n = 74)	p
All-cause mortality (n – %)	12 (54.5%)+,*	11 (28.9%)	12 (16.2%)	*0.001*
Neurogenic mortality (n – %)	1 (4.5%)	5 (13.2%)	5 (6.8%)	0.400
Cardiac mortality (n – %)	11 (50.0%)+,*	6 (15.8%)	7 (9.5%)	*<0.001*

KAF: known atrial fibrillation, AFDAS: atrial fibrillation diagnosed after stroke, SR: sinus rhythm
PostHoc analysis: * denotes statistical significance versus patients with sinus rhythm
+ denotes statistical significance versus patients with atrial fibrillation diagnosed after a stroke

by age, sex, CHA_2DS_2VASc and NIHSS scores, and insular cortex involvement. While AFDAS increased the mortality risk compared to SR, the differences were not significant in univariable and multivariable models.

Discussion

In our study, we explored the characteristics and mortality differences between KAF and AFDAS patients. We found that while both AFDAS and KAF patients were significantly older than the patients with SR, CHA_2DS_2VASc scores, insular cortex involvement, NIHSS scores, and comorbidities were similar between AFDAS and SR

Table 4. *The characteristics of the patients according to all-cause mortality*

	Deceased (n = 35)	Surviving (n = 99)	p
Age (years)	70.7 ± 10.9	64.5 ± 14.8	*0.026*
Male sex (n – %)	19 (54.3%)	54 (54.5%)	0.979
CHA_2DS_2VASc	4.4 ± 1.7	3.4 ± 2	*0.007*
NIHSS	6.6 ± 3.4	5.4 ± 4.1	*0.040*
Hypertension (n – %)	29 (82.9%)	67 (67.7%)	0.087
Diabetes (n – %)	18 (51.4%)	37 (37.4%)	0.146
Coronary artery disease (n – %)	15 (42.9%)	25 (25.3%)	0.050
Insular cortex involvement (n – %)	15 (42.9)	22 (22.2)	*0.019*
hs-cTnI (ng/mL)	0.19 ± 0.45	0.08 ± 0.36	*<0.001*
hs-CRP (mg/L)	34.0 ± 41.4	16.8 ± 27.1	*0.008*
LAVI (mL/m²)	30.9 ± 15.4	24.5 ±11.1	*0.016*
LVEF (%)	57 ± 12	57 ± 10	0.880
KAF (n – %)	12 (34.3)	10 (10.1)	*0.001*
AFDAS (n – %)	11 (31.4)	27 (27.3)	
SR (n – %)	12 (34.3)	62 (62.6)	

NIHSS: National Institutes of Health Stroke Scale, hs-cTnI: High-sensitive cardiac Troponin I, hs-CRP: High-sensitive C-reactive protein, LAVI: Left atrial volume index, LVEF: left ventricular ejection fraction, KAF: known atrial fibrillation, AFDAS: atrial fibrillation diagnosed after stroke, SR: sinus rhythm

patients. Interestingly, only KAF was associated with mortality in both univariable and multivariable analysis, while AFDAS patients had similar mortality rates to SR patients.

Cardiovascular diseases are more common in both ischemic stroke and AF. However, cardiovascular disease and mortality rates are not the same in every AF patient. Underlying cardiovascular diseases and one-year composite cardiovascular outcomes were observed to be higher in KAF patients than in AFDAS patients, but KAF was not found to be an independent predictor of outcomes[10]. Since comorbidities and structural heart disease are noted less in AFDAS patients, it is believed to be triggered by neurogenic mechanisms developed after stroke[3, 11]. Major factors such as autonomic dysfunction, increased catecholamine discharge, neurogenic cardiac injury, and systemic inflammation leading to atrial electrical and structural remodeling after acute stroke may facilitate the occurrence and maintenance of AF[2]. In our study, coronary artery disease and other comorbidities such as hypertension, diabetes, and hyperlipidemia were found to be similar among groups.

There are conflicting results in the literature regarding the outcome of AFDAS. For example, in a study with 5-year follow-up of stroke patients, the highest annual mortality was found in patients with newly diagnosed AF within the first 6 months after stroke[12]. Also, *Yang XM* et al showed that AFDAS patients had similar stroke recurrence and mortality rates when compared to KAF but higher than SR[13]. In our study, mortality in the AFDAS group was found to be similar to sinus rhythm patients, which may be due to the more benign vascular profile of AFDAS as we predicted. In addition, little is known about the pathophysiology of AFDAS, but in recent studies, it is thought to have two subgroups, neurogenic and cardiogenic[14]. The cardiogenic AFDAS group with pre-existing but newly diagnosed AF after stroke has atrial cardiopathy and structural heart disease[15]. In addition, in the neurogenic AFDAS group without structural heart disease, AF is thought to be triggered entirely by autonomic and inflammatory mechanisms[14]. The heterogeneity of AFDAS may explain the difference in outcome between studies.

Although it has not been revealed yet, it is hypothesized that large brain infarcts seen in moderate and severe strokes cause more autonomic dysregulation and inflammation and therefore cause more AFDAS[11, 15, 16]. We measured stroke severity, which correlates with infarct size, but we couldn't find any difference in NIHSS scores among the groups in our study. Studies about AFDAS showed a particularly remarkable involvement of the insular cortex, which plays a role in the regulation of the autonomic nervous system[3, 11]. Although there are conflicting reports on which of the right and left hemisphere

Table 5. *Univariable and multivariable logistic regression analysis showing the predictors of all-cause mortality*

	Odds Ratio	95% Confidence Interval	p
Univariable			
AFDAS versus SR	2.105	0.827 – 5.360	0.119
KAF versus SR	6.200	2.186 – 17.581	0.001
Multivariable Models			
Model 1			
AFDAS versus SR	1.755	0.637 – 4.833	0.277
KAF versus SR	4.484	1.427 – 14.089	*0.010*
Age	1.018	0.984 – 1.053	0.314
Male sex	1.073	0.469 – 2.457	0.868
Model 2			
AFDAS versus SR	1.847	0.662 – 5.156	0.241
KAF versus SR	4.518	1.406 – 14.515	*0.011*
Age	1.000	0.960 – 1.041	0.996
Male sex	1.218	0.521 – 2.843	0.649
CHA_2DS_2VASc	1.262	0.971 – 1.641	0.081
Model 3			
AFDAS versus SR	1.825	0.649 – 5.132	0.254
KAF versus SR	4.703	1.471 – 15.037	*0.009*
Age	1.019	0.984 – 1.055	0.295
Male sex	1.018	0.438 – 2.368	0.966
NIHSS	1.052	0.949 – 1.167	0.337
Model 4			
AFDAS versus SR	1.670	0.600 – 4.647	0.326
KAF versus SR	3.791	1.172 – 12.264	*0.026*
Age	1.015	0.980 – 1.050	0.405
Male sex	1.151	0.496 – 2.669	0.744
Insular cortex involvement	2.020	0.828 – 4.928	0.122
Model 5			
AFDAS versus SR	1.839	0.641 – 5.278	0.257
KAF versus SR	3.995	1.187 – 13.451	*0.025*
Age	0.998	0.957 – 1.041	0.926
Male sex	1.219	0.509 – 2.920	0.657
CHA_2DS_2VASc	1.264	0.962 – 1.662	0.093
NIHSS	1.021	0.916 – 1.138	0.708
Insular cortex involvement	2.129	0.822 – 5.514	0.120

KAF: known atrial fibrillation, AFDAS: atrial fibrillation diagnosed after stroke, SR: sinus rhythm, NIHSS: National Institutes of Health Stroke Scale

involvement increases sympathetic activity, increasing numbers of studies show that in insular cortex involvement the heart rate variability decrease and the risk of AF increase significantly[11, 17–19]. In our study, significantly higher insular cortex involvement was found in KAF patients while there was no difference between AFDAS and SR groups in terms of insular cortex involvement.

In addition, autonomic dysfunction is thought to cause not only post-stroke AF but also myocardial injury: so-called neurogenic myocardial stunning (NSM)[20]. There are opinions that myocardial damage presenting with troponin elevation after stroke may be a predictor of AF[21]. In our study, hs-cTnI was found to be high in all groups, while the SR group had the highest mean and EF values were similar between groups. Since NSM is a reversible myocardial damage diagnosed with reduced EF, regional wall motion abnormality, ECG changes, and high troponin values, it is not possible to make a conclusion based on the data available in our study[22, 23].

Approximately half of the ischemic strokes detected in the Penn Atrial Fibrillation Free study (PAFF) were detected within 6 months period before the diagnosis of AF. Most strokes occur on the day of diagnosis of AF and within the next 7 days[24]. In our study, approximately one-third of the patients were diagnosed with AFDAS, similarly in the first week. These patients had similar CHA_2DS_2VASc scores to patients with SR. However, the CHA_2DS_2VASc scores of KAF patients were higher than in the SR group. In another study investigating new AF with prolonged ECG monitoring more than one week after stroke, NIHSS and CHA_2DS_2VASc scores were found to be similar in groups with a previous diagnosis of AF and newly diagnosed AF[25]. It may be important on which day the diagnosis of AF is made after the stroke.

Limitations

First, a small sample size and a relatively short follow-up period are limitations of our study. Second, it has recently been revealed that AFDAS is a heterogeneous group and includes two different clinical entities as cardiogenic and neurogenic AFDAS. Due to the small number of AFDAS patients, we could not investigate the differences between these subgroups. Third, we excluded TIA because it was diagnosed with a subjective neurological evaluation, which might cause misdiagnosis of AFDAS. Fourth, AF might be underestimated as the patients did not undergo prolonged ambulatory ECG monitoring.

Conclusion

In summary, AFDAS patients were older but had similar insular cortex involvement, CHA_2DS_2VASc, and NIHSS

score to SR patients; the insular cortex involvement and CHA_2DS_2VASc score were higher in the KAF group than in SR patients; AFDAS patients had similar mortality rates to SR patients; KAF patients had increased mortality compared to SR patients; mortality of the KAF group was independent of age, sex, insular cortex involvement, CHA_2DS_2VASc, and NIHSS scores.

AFDAS patients have similar CHA_2DS_2VASc scores and mortality rates to patients with sinus rhythm, which supports the hypothesis that AFDAS might be a rela-tively benign form of AF. However, having a KAF diag-nosis before an ischemic stroke is an independent predic-tor of all-cause mortality.

———

CONFLICT OF INTEREST – The authors declare that they have no conflict of interest.

The study was presented as a poster presentation at the European Society of Cardiology Heart&Stroke Congress 2022 in Budapest and won the 'Best Poster Prize'.

References

1. *Sposato LA, Cipriano LE, Saposnik G, Ruíz Vargas E, Riccio PM, Hachinski V.* Diagnosis of atrial fibrillation after stroke and transient ischaemic attack: a systematic review and meta-analysis. The Lan-cet Neurol 2015;14(4):377-87.
https://doi.org/10.1016/S1474-4422(15)70027-X

2. *Wang Y, Qian Y, Smerin D, Zhang S, Zhao Q, Xiong X.* Newly detected atrial fibrillation after acute stroke: A narrative review of causes and ımplications. Cardiology 2019;144(3-4):112-21.
https://doi.org/10.1159/000502971

3. *Sposato LA, Riccio PM, Hachinski V.* Poststroke atrial fibrillation: cause or consequence? Critical review of current views. Neurology 2014;82(13):1180-6.
https://doi.org/10.1212/WNL.0000000000000265

4. *Fridman S, Jimenez-Ruiz A, Vargas-Gonzalez, JC, Sposato LA.* Dif-ferences between atrial fibrillation detected before and after stroke and TIA: A systematic review and meta-analysis. Cerebrovasc Dis 2022;51(2):152-7.
https://doi.org/10.1159/000520101

5. *Sposato LA, Klein FR, Jáuregui A, et al.* Newly diagnosed atrial fibrillation after acute ischemic stroke and transient ischemic attack: importance of immediate and prolonged continuous cardiac moni-toring. J Stroke Cerebrovasc Dis 2012;21(3):210-6.
https://doi.org/10.1016/j.jstrokecerebrovasdis.2010.06.010

6. *Sposato LA, Cipriano LE, Riccio PM, Hachinski V, Saposnik G.* Very short paroxysms account for more than half of the cases of atrial fibrillation detected after stroke and TIA: a systematic review and meta-analysis. Int J Stroke 2015;10(6):801-7.
https://doi.org/10.1111/ijs.12555

7. *Sposato LA, Cerasuolo JO, Cipriano LE, et al.* Atrial fibrillation detected after stroke is related to a low risk of ischemic stroke recurrence. Neurology 2018;90(11):e924-e931.
https://doi.org/10.1212/WNL.0000000000005126

8. *Adams HP Jr, Bendixen BH, Kappelle LJ, et al.* Classification of subtype of acute ischemic stroke. Definitions for use in a multi-center clinical trial. TOAST. Trial of Org 10172 in Acute Stroke Treatment. Stroke 1993;24(1):35-41.
https://doi.org/10.1161/01.str.24.1.35

9. *Lang RM, Badano LP, Mor-Avi V, et al.* Recommendations for cardi-ac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2015;28(1):1-39.e14.
https://doi.org/10.1016/j.echo.2014.10.003

10. *Hsieh, CY, Lee CH, Wu DP, Sung SF.* Characteristics and outcomes of ischemic stroke in patients with known atrial fibrillation or atrial fibrillation diagnosed after stroke. Int J Cardiol 2018;261:68-72.
https://doi.org/10.1016/j.ijcard.2017.11.047

11. *González Toledo ME, Klein FR, Riccio PM, et al.* Atrial fibrillation detected after acute ischemic stroke: evidence supporting the neuro-genic hypothesis. J Stroke Cerebrovasc Dis 2013;22(8):e486-e491.
https://doi.org/10.1016/j.jstrokecerebrovasdis.2013.05.015

12. *Bhatla A, Borovskiy Y, Katz R, et al.* Stroke, timing of atrial fibrillation diagnosis, and risk of death. Neurology 2021;96(12):e1655-e1662.
https://doi.org/10.1212/WNL.0000000000011633

13. *Yang XM, Rao ZZ, Gu HQ, et al.* Atrial fibrillation known before or detected after stroke share similar risk of ischemic stroke recurrence and death. Stroke 2019;50(5):1124-9.
https://doi.org/10.1161/STROKEAHA.118.024176

14. *Sposato LA, Chaturvedi S, Hsieh CY, Morillo CA, Kamel H.* Atrial fibrillation detected after stroke and transient ischemic attack: A novel clinical concept challenging current views. Stroke 2022;53(3):e94-e103. https://doi.org/10.1161/STROKEAHA.121.034777

15. *Cerasuolo JO, Cipriano LE, Sposato LA.* The complexity of atrial fibrillation newly diagnosed after ischemic stroke and transient ischemic attack: advances and uncertainties. Curr Opin Neurol 2017;30(1):28-37.
https://doi.org/10.1097/WCO.0000000000000410

16. *Paquet M, Cerasuolo JO, Thorburn V, et al.* Pathophysiology and Risk of Atrial Fibrillation Detected after Ischemic Stroke (PARA-DISE): A translational, integrated, and transdisciplinary approach. J Stroke Cerebrovasc Dis 2018;27(3):606-19.
https://doi.org/10.1016/j.jstrokecerebrovasdis.2017.09.038

17. *Zamrini EY, Meador KJ, Loring DW, et al.* Unilateral cerebral inac-tivation produces differential left/right heart rate responses. Neurol-ogy 1990;40(9):1408-11. https://doi.org/10.1212/wnl.40.9.1408

18. *Meyer S, Strittmatter M, Fischer C, Georg T, Schmitz B.* Lateral-ization in autonomic dysfunction in ischemic stroke involving the insular cortex. Neuroreport 2004;15(2):357-61.
https://doi.org/10.1097/00001756-200402090-00029

19. *Colivicchi F, Bassi A, Santini M, Caltagirone C.* Prognostic implica-tions of right-sided insular damage, cardiac autonomic derangement, and arrhythmias after acute ischemic stroke. Stroke 2005;36(8):1710-5. https://doi.org/10.1161/01.STR.0000173400.19346.bd

20. *Ileri C, Dogan Z, Bulut B, et al.* Neurogenic stunned myocardium in acute ischemic stroke. Neurogén szívizombénulás akut ischaemiás stroke-ban. Ideggyogy Sz 2022;75(1-02):15-22.
https://doi.org/10.18071/isz.75.0015

21. *Sun Y, Miller MM, Yaghi S, Henninger N.* Association of Atrial Fib-rillation Detected after Stroke with Cardiac Dysfunction and Features of Neurogenic Cardiac Injury. J Stroke Cerebrovasc Dis 2022;31(6):106445. https://doi.org/10.1016/j.jstrokecerebrovasdis.2022.106445

22. *Biso S, Wongrakpanich S, Agrawal A, Yadlapati S, Kishlyansky M, Figueredo V.* A review of neurogenic stunned myocardium. Cardio-vasc Psychiatry Neurol 2017;2017:5842182.
https://doi.org/10.1155/2017/5842182

23. *Mierzewska-Schmidt M, Gawecka A.* Neurogenic stunned myocar-dium - do we consider this diagnosis in patients with acute central nervous system injury and acute heart failure? Anaesthesiol Intensive Ther 2015;47(2):175-80. https://doi.org/10.5603/AIT.2015.0017

24. *Patel PJ, Borovskiy Y, Killian A, et al.* Optimal QT interval cor-rection formula in sinus tachycardia for identifying cardiovascular and mortality risk: Findings from the Penn Atrial Fibrillation Free study. Heart Rhythm 2016;13(2):527-35.
https://doi.org/10.1016/j.hrthm.2015.11.008

25. *Li SY, Yang XM, Zhao XQ, et al.* Newly detected atrial fibrillation is associated with cortex-involved ischemic stroke. Chin Med J (Engl) 2019;132 (17):2053-8.
https://doi.org/10.1097/CM9.0000000000000390