

## Relation between Epicardial Fat Thickness and Acute Ischemic Stroke in Patients with Atrial Fibrillation

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### ABSTRACT

**Background:** Cerebrovascular disease is the second most common cause of death after coronary artery disease (CAD) and remains a major health problem worldwide. Cardioembolic stroke is the most common predicted cause of cryptogenic stroke, and atrial fibrillation (AF) is the most frequent cause of cerebral cardio-embolism.

**Objective:** The aim of this study was to evaluate the performance of epicardial fat thickness (EFT) as a risk factor of acute ischemic stroke in patients with AF.

**Patients and Methods:** This was a case-control study at Cardiology Department, Zagazig University Hospitals and Nasser Institute for Research and Treatment, conducted on 60 patients: (20) AF patients with acute ischemic stroke (AIS), (20) AF patients without AIS and (20) controls without AF or AIS.

**Results:** The current study showed that, AF patients with AIS have mean of age ( $66.15 \pm 9.12$ ). Our recent study revealed that, males with AF with AIS were more than females (65.0%; 35.0% respectively). The current study showed that, there were statistically significant difference between the studied groups regarding smoking and hypertension (HTN). Regarding echo finding, mean value of EFT was statistically higher among AF patients with AIS than AF patients without AIS. Mean value of EFT was statistically higher among AF patients with AIS than controls group. Mean value of EFT was statistically higher among AF patients without AIS than controls group.

**Conclusion:** EFT is an independent predictor for the development of acute ischemic stroke in patients with AF.

**Keywords:** Epicardial Fat Thickness, Acute Ischemic Stroke, Atrial Fibrillation.

### INTRODUCTION

Accurate classification of stroke etiology is crucial for optimizing stroke management. Cardio-embolic stroke is the most frequently predicted cause of cryptogenic stroke; the most frequent cause of cerebral cardio-embolism is atrial fibrillation (AF), including paroxysmal AF. AF is the most common etiology of ischemic stroke; the incidence of stroke in individuals with non-valvular AF is estimated to be 5 times higher than in individuals without AF. The prevalence of AF in the whole stroke population has been reported to range from 17%–25.6%. The risk for stroke and thromboembolism in patients with AF has been shown to escalate proportionally with combined vascular risk factors<sup>(1)</sup>. However, by routine arrhythmia screening methods, it is difficult to detect the short and usually asymptomatic presentations of paroxysmal AF (also called occult AF)<sup>(2)</sup>.

There is evidence that abnormal levels of plasma free fatty acids (FFAs) are associated with an increased risk of myocardial disease, including AF and heart failure. Adipose tissue covers a significant portion of the epicardial surface, and myocyte-adipocyte cross linking is known to be important in the physiological function of the normal myocardium. Myocardial injury and ischemia are followed by changes in the levels of adipocyte-derived biomarkers (FFAs and adipokines) and adipose deposition. Fat can accumulate around the heart in epicardial adipose tissue or inside the heart as lipid droplets. The mechanism by which fatty infiltration promotes arrhythmogenicity is not well characterized. Recent studies have shown that increased epicardial adiposity can directly modulate the

electrophysiological properties of the heart and ion currents, causing higher arrhythmogenesis in left atrial myocytes, which contributes to an increased risk of AF<sup>(3)</sup>.

Epicardial fat is a metabolically active tissue; echocardiography is a useful technique for measuring epicardial fat thickness (EFT). Previous studies have demonstrated associations between EFT and coronary artery disease, carotid atherosclerosis, metabolic syndrome, and obesity. In addition, increased EFT has been shown to be associated with the presence and chronicity of AF<sup>(4)</sup>.

The aim of this study was to evaluate the performance of EFT as a risk factor of acute ischemic stroke in patients with AF.

### PATIENTS AND METHODS

This case control study was conducted in the period from January 2021 to January 2022. It included 60 patients and was done at Zagazig University Hospitals and Nasser Institute for Research and Treatment.

#### Ethical consent:

All patients gave an informed consent to participate in the study. The study was approved by Ethical Committee of the Institutional Review Board at Faculty of Medicine, Zagazig University Hospitals. This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

**Study patients were divided into 3 groups: Group 1** (AF patients with acute ischemic stroke [AIS]): 20

patients, **Group 2** (AF patient without AIS): 20 patients, and **Group 3** (controls without AF or AIS): 20 patients.

**Inclusion criteria:**

Patients who were admitted to the hospital with AIS (defined as a focal neurologic deficit of sudden onset and of presumed ischemic origin that lasts at least 24 hours and is not associated with hemorrhage on computed tomography (CT) or magnetic resonance imaging (MRI) of the brain)<sup>(5)</sup> and AF and referred to the cardiology outpatient clinic for echocardiographic evaluation. We also included AF patients without acute stroke and controls without AF or AIS. Those patients were also being among referrals to outpatient clinic for echocardiography assessment and for further management.

**Exclusion criteria:**

Paroxysmal AF: AF that terminates spontaneously or with intervention within 7 days of onset. Valvular AF: refers to patients with moderate/severe mitral stenosis and those with mechanical prosthetic heart valve(s)<sup>(6)</sup>. AF patient on long-term anticoagulant drugs. Acute Heart Failure. Hematological disease. Cancer. Severe renal or liver disease. Ongoing infection or systemic inflammatory conditions and autoimmune disease, and patients with transient ischemic attacks in which the neurologic deficit cleared completely in less than 24 hours were also excluded.

**Operational design:**

**A) Type of study:** Case-control study.

**B) Steps of performance and techniques used:**

**1-Complete history taking:** Demographic data (age and sex), family history of cerebrovascular disease, and smoking status.

**2-Physical examination:** Full general and local examination with special emphasis on initial vital signs and trends for heart rate and blood pressure, and body mass index (BMI; weight [kg]/height squared [m<sup>2</sup>]).

**3-Diagnostic tools**

**Echocardiographic assessment of EFT:**

Epicardial fat was defined as the echofree space between the outer wall of the myocardium and the visceral layer of the pericardium. The EFT was measured at the point on the free wall of the right ventricle along the midline of the ultrasound beam, perpendicular to the aortic annulus at the end of systole in parasternal long axis view<sup>(7)</sup>.

**Statistical analysis**

The data were coded, entered and processed on computer using Statistical Package for the Social Sciences (SPSS) (version 18). The results were represented in tabular form then interpreted. Mean, standard deviation, range, frequency, and percentage were use as descriptive statistics. Chi-Square test (X<sup>2</sup>) was used to test the association of variables for categorical data. ANOVA (F test) was used for normally quantitative variables and post hoc test (LSD) for pairwise comparisons. P value < 0.05 was considered significant.

**RESULTS**

There was statistically significant difference between the studied groups regarding age, gender, family history, smoking and HTN. There was no statistically significant difference between AF patients with AIS and AF patients without AIS regarding age. Mean value of age was statistically higher among AF patients with AIS than controls group. Mean value of age was statistically higher among AF patients without AIS than controls group (**Table 1**).

**Table (1): Comparison between the studied groups regarding demographic data and medical history**

		AF patients with AIS (20 Pts)	AF patients without AIS (20 Pts)	Controls group (20 Pts)	F. test	P. value	LSD
Age (years)	Mean ± SD	66.15± 9.12	62.25± 11.43	49.10± 12.82	12.653	<0.001	P1=0.277 P2<0.001 P3=0.001
	Gender	Male	No.	13	10	19	X <sup>2</sup> 10.000
%			65.0%	50.0%	95.0%		
Female		No.	7	10	1		
		%	35.0%	50.0%	5.0%		
Family history	No	No.	4	8	15	12.525	0.002
		%	20.0%	40.0%	75.0%		
	Yes	No.	16	12	5		
		%	80.0%	60.0%	25.0%		

P1 between AF patients with AIS and AF patients without AIS; P2 between AF patients with AIS and controls group; P3 between AF patients without AIS and controls group.

There was no statistically significant difference between the studied groups regarding BMI and vital data (Table 2).

**Table (2): Comparison between the studied groups regarding examination**

		AF patients with AIS (20 Pts)	AF patients without AIS (20 Pts)	Controls group (20 Pts)	F. test	P. value
<b>BMI kg/m<sup>2</sup></b>	<b>Mean ± SD</b>	27.20± 2.76	29.45± 2.96	28.25± 3.49	2.657	0.079
<b>SBP (mmHg)</b>	<b>Mean ± SD</b>	125.25± 11.05	127.70± 14.32	120.50± 10.50	1.836	0.169
<b>DBP (mmHg)</b>	<b>Mean ± SD</b>	83.50± 8.28	85.25± 12.71	81.50± 10.39	0.624	0.539
<b>HR (bpm)</b>	<b>Mean ± SD</b>	83.65± 9.09	86.90± 12.12	81.80± 6.20	1.492	0.234

BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate

Mean value of EFT was statistically higher among AF patients with AIS than AF patients without AIS. Mean value of EFT was statistically higher among AF patients with AIS than Controls group. Mean value of EFT was statistically higher among AF patients without AIS than Controls group (Table 3).

**Table (3): Comparison between the studied groups regarding EFT**

		AF patients with AIS (20 Pts)	AF patients without AIS (20 Pts)	Controls group (20 Pts)	F. test	P. value	LSD
<b>EFT (mm)</b>	<b>Mean ± SD</b>	5.75± 1.20	5.04± 1.14	2.39± 0.59	58.435	<0.001	P1=0.034 P2<0.001 P3<0.001

P1 between AF patients with AIS and AF patients without AIS; P2 between AF patients with AIS and Controls group; P3 between AF patients without AIS and Controls group.

## DISCUSSION

The current study showed that, AF patients with AIS have mean of age (66.15± 9.12) years. Similarly, **Goel et al.** <sup>(8)</sup> who aimed to clarify prevalence of persistent/paroxysmal AF in stroke patients from single center hospital-based study. They reported that AF was more common in the age group of >60 years. The study from Ludhiana (Punjab) to describe risk factors, clinical features, and short-term outcomes of stroke patients with AF, showed that 10% of patients of stroke had AF and these patients had higher age group <sup>(9)</sup>.

Our study revealed that, males with AF with AIS were more than females (65.0% and 35.0% respectively). AIS had a higher prevalence per 100,000 admissions in males than females (2097 cases per 100,000 admissions in males and 1618 cases per 100,000 admissions in females) <sup>(10)</sup>. In their study of prediabetes, **Andes et al.** <sup>(11)</sup> found a higher incidence in male patients.

This disagreed with **Goel et al.** <sup>(8)</sup> who showed that AF was significantly more common in females with ischemic stroke. Also, this disagreed with **Otite et al.** <sup>(12)</sup> who aimed to evaluate trends in atrial fibrillation (AF) prevalence in acute ischemic stroke (AIS) and transient ischemic attack (TIA) in the United States. They reported that, prevalence of comorbid AF in AIS was greater among Caucasians and women. This disagreement could be attributed to small sample size in our study and due to ethnic differences as well.

The current study showed that, there were statistically significant difference between the studied groups regarding smoking and HTN. According to **Cosansu and Yilmaz** <sup>(13)</sup>, who aimed to evaluate the effectiveness of EFT on prediction of AIS in patients with AF; they reported that, there was a significant difference between the AIS group and the control group in terms of factors that may affect EFT such as AF, HTN, smoking.

Regarding echo finding, mean value of **EFT** was statistically higher among AF patients with AIS than AF patients without AIS. Mean value of **EFT** was statistically higher among AF patients with AIS than controls group. Mean value of **EFT** was statistically higher among AF patients without AIS than controls group. This agreed with **Haberka et al.** <sup>(14)</sup> who aimed to evaluate the predictive values of major ultrasound indices of carotid artery and fat depots for stroke in patients with high and very high cardiovascular (CV) risk. They showed that increased EFT (> 2.8 mm) was predictive for stroke in a prospective follow-up. **Cosansu and Yilmaz** <sup>(13)</sup> found a significantly higher EFT in patients with acute ischemic stroke compared to control groups. They showed that increased EFT was an independent predictor of AIS in patients with AF

Noteworthy, increased EFT was also found in young patients with embolic stroke of undetermined source. **Cho et al.** <sup>(2)</sup>, who aimed to assess the performance of echocardiographic epicardial fat thickness (EFT) and plasma FFA level in identifying

patients with ischemic stroke and AF, showed that patients with ischemic stroke and AF had higher EFT compared to subjects with stroke, but without AF.

## CONCLUSION

EFT is an independent predictor for the development of acute ischemic stroke in patients with AF.

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