Original Research Article

Association of Epicardial Adipose Tissue Thickness with Left Atrial Size and Atrial Fibrillation.

Abstract:

Background: Atrial fibrillation (AF) is the most common cardiac arrhythmia and is associated with detrimental consequences. Epicardial fat is consistently associated with the presence, severity, and recurrence of AF **Aim**: The aim of the work was to investigate association of epicardial adipose tissue thickness with left atrial size in patients with atrial fibrillation. **Patients and methods**: This study was conducted on 25 atrial fibrillation (AF) patients and 25 subjects with normal sinus rhythm as a control group matched in body weight. All patients underwent transthoracic echocardiogram. epicardial adipose tissue thickness was measured on the right ventricular free wall of the two- dimensional parasternal long-axis view at end systole. **Results:** the results showed that there was a significant statistical difference between the two groups in waist circumference, EAT (epicardial adipose tissue) thickness , LA diameter, LA volume. Receiver operating characteristics (ROC) analysis showed that an EAT thickness of > 0.30 cm maximizes the sensitivity and specificity to predict the development of AF. **Conclusion**: increases epicardial adipose tissue is associated with the occurrence of atrial fibrillation.

Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia and is associated with detrimental consequences. Although body mass index and other clinical measures are useful indications of general adiposity, much recent interest has focused on epicardial fat, a distinct adipose tissue depot that can be readily assessed using non-invasive imaging techniques. [1]

A growing body of data from epidemiological and clinical studies has demonstrated that epicardial fat is consistently associated with the presence, severity, and recurrence of AF across a range of clinical settings. (2,3)

Atrial fibrillation (AF) is commonly associated with overweight and obesity. Epicardial fat is consistently associated with the presence, severity, and recurrence of AF across a range of clinical settings. (4,5)There are several studies that point to the role for local inflammatory processes in the pathophysiology of AF. (6,7)

Patients and Methods

This study was conducted between April 2019 and April 2020 on 25 atrial fibrillation (AF) patients and 25 subjects with normal sinus rhythm as a control group matched in body weight, hypertension, diabetes mellitus, age and sex at cardiovascular medicine department Tanta university hospital and Alexandria police hospital. Privacy of all data was guaranteed and there was a code number for every patient and include all his or her investigations. Informed written consent was obtained from all patients after full explanation of benefits and risks of the study. The diagnosis of AF was based on a single 12-lead electrocardiogram (ECG) or a 24-hr Holter. Patients with atrial fibrillation (AF) aged > 18 years old were included in the study. patients with moderate and severe valvular disease and severe heart failure, patients with acute coronary syndromes diagnosed by clinical symptoms and cardiac biomarkers, patients with malignancy, patients with any collagen or autoimmune disease, patients with recent infection or any febrile illness, patients with recent surgery and patients with chronic kidney or hepatic failure were excluded from the study. Transthoracic echocardiography: All patients underwent transthoracic echocardiogram (TTE) using **GE Vivid 7 dimensions ultrasound system** and **Philips EPIQ 7 ultrasound system**. Epicardial Adipose Tissue was measured on the right ventricular free wall of the two- dimensional parasternal long-axis view at end systole. The measurement of epicardial fat on the right ventricle was chosen for two reasons. This point is known as the highest absolute epicardial fat layer thickness.The parasternal long axis view allows the most accurate measurement of epicardial adipose tissue on the right ventricle, with optimal cursor beam orientation in each view. Left Atrial diameter: was measured from the leading edge of the posterior aortic wall to the leading edge of the posterior LA wall at M- Mode obtained from the parasternal long-axis view. Left atrial volume: was measured from the biplane method of discs (modified Simpson’s rule), using the apical four-chamber (A4C) and apical two-chamber (A2C) views as shown at figure (2) at ventricular end-systole (maximum LA size), L is measured from back wall to line across hinge points of mitral valve. Shorter L from either A4C or A2C is used in equation. Data were fed to the computer and analyzed using IBM SPSS software package version 20.0. (Armonk, NY: IBM Corp) Qualitative data were described using number and percent. The Kolmogorov-Smirnov test was used to verify the normality of distribution Quantitative data were described using range (minimum and maximum), mean, standard deviation, median and interquartile range (IQR). Significance of the obtained results was judged at the 5% level (p value for comparing between the studied groups is considered statistically significant at $p \leq 0.05$).

Results.

Patients were divided into 2 groups. **Group 1:** This group included 25 patients diagnosed with AF. **Group 2:** This group included 25 normal sinus rhythm. Patients in group 1 included 14 male (56 %) and 11 females (44%). Group 2 included 15 males (60%) and 10 females (40%). Patients in both groups were age matched. Group 1 ranged between 32-71 year with a mean of 50.84 ± 11.32, while those in group 2 ranged from 30.0 – 67.0 year with a mean of 46.52 ± 10.65 (p value 0.171). Patients in both groups were body weight matched. Group 1 weight between 59.0 – 120.0 kg with a mean of 84.08 ± 16.06, while those in group 2 ranged from 56.0 – 115.0 kg with a mean of 80.40 ± 16.01 kg (p value 0.171).Waist circumference in group 1 ranged from 65.0 – 113.0 cm with a mean of 93.86 ± 12.71. Waist circumference in group 2 ranged from 60.0 – 112.0 cm with a mean of 82.0 ± 11.44. There was a significant statistical difference between the two groups (p value < 0.001) as shown in table 1. The prevalence of HTN was higher in the AF group with 9 patients (36%) vs. 6 patients (24%) in the normal group but not statistically significant (p value 0.355). As regards to diabetes, there was also a higher preponderance in the AF group with 7 patients (28%) vs. 5 patients (20%) in the normal sinus rhythm group but not statistically significant (p value 0.742) as shown in table 2. EAT thickness in group 1 ranged from 0.30 and 1.10 cm with a mean of 0.52 ± 0.19. EAT thickness in group 2 ranged from 0.10 – 0.35 cm with a mean of 0.23 ± 0.06. There was a significant statistical difference between the two groups (p value < 0.001) as shown in table (3). Left atrial diameter in group 1 ranged from 3.80 – 6.60 cm with a mean of 4.85 ± 0.68. Left atrial diameter in group 2 ranged from 2.50 – 4.0 cm with a mean of 3.32 ± 0.32. There was a significant statistical difference between the two groups (p value < 0.001) as shown in table (4). Left atrial volume in group 1 ranged from 75.0 – 115.0 ml with a mean of 94.48 ± 11.84. Left atrial volume in group 2 ranged from 38.0 – 51.0 ml with a mean of 43.49 ± 3.22 There was a significant statistical difference between the two groups (p value < 0.001) as shown in table (3). As for LVEF, LVIDd, LVIDs, IVSd and LVPWd there was no significant statistical difference between the two groups as shown in table (4). For the prediction of those at higher risk for the development of AF, a receiver-operating-characteristic (ROC) curve (Figure 3) was applied to assign the best cutoff point for EAT thickness.

Receiver operating characteristics (ROC) analysis (Table 5) showed that an EAT thickness of > 0.30 cm maximizes the sensitivity and specificity to predict the development of AF (sensitivity of 84.0 %, specificity of 96 %, positive predictive value of 95.5 % and a negative predictive value of 85.7%).

Discussion:

Growing evidence suggests that EAT, the unique visceral fat depot of the heart, is closely implicated not only in the pathogenesis of AF through several mechanisms, but also in the AF recurrence after ablation. Studies targeting cardiac adipose tissue modulation are currently underway. [5]

In this study EAT thickness in AF group ranged from 0.30 and 1.10 mm with a mean of 0.52 ± 0.19. EAT thickness in normal sinus rhythm group ranged from 0.10 – 0.35 mm with a mean of 0.23 ± 0.0. There was a significant statistical difference between the two groups (p value < 0.001).

This agreed with Hikmet Yorgun et al., 2014 who studied A total of 618 (192 in sinus rhythm, 169 with paroxysmal AF, 133 with persistent AF and 124 with permanent AF) patients who underwent CT angiography for the evaluation of CAD or pulmonary vein anatomy before catheter ablation were enrolled in this study. Thickness of the EAT and periatrial fat were measured by CT angiography. Together with body mass index, these were examined in relation to the presence and severity of AF and left atrial (LA) diameter. Patients with AF had significantly more total EAT and periatrial fat thickness compared with patients in sinus rhythm ($p < 0.001$). EAT thickness was significantly higher in permanent, persistent, and paroxysmal AF compared with sinus rhythm group ($p < 0.001$). Multivariable multinomial logistic regression analysis comparing patients with sinus rhythm and subtypes of AF revealed a significant association between periatrial fat and total EAT thickness with all AF subtypes. Correlation analysis demonstrated that both total EAT thickness and periatrial fat thickness were significantly correlated with LA diameter ($p < 0.05$). [(8)]

Also, Dereli S et al., found that Echocardiographic EAT thickness (EEATT) was significantly higher in the AF group in whom electrical cardioversion (ECV) failed (mean 8.67 ± 1.2 mm) in comparison to those in whom sinus rhythm was successfully restored (mean 6.81 ± 0.8 mm). Thus, it was concluded that EAT could be used as a predictor for the recurrence of AF after ECV. [(9)]

On the other side, Psychari SN et al., in 2018 concluded that EAT thickness was increased in paroxysmal AF patients, yet it was decreased in those with permanent AF. They hypothesize that the latter finding could be attributed to progressive fibrosis of the epicardial pad of fat in permanent AF, with enlarging left atrium, while in paroxysmal AF, atrial remodeling alterations and epicardial fat fibrosis might be not as prominent yet. [10]

This assumption was supported by Haemers et al., demonstrated fibrosis of sub-epicardial fatty infiltrates in atrial samples obtained from both humans and sheep with AF. They found an inverse correlation between fibrotic remodeling and the amount of sub-epicardial adipose tissue and hence suggested that progressive fibrosis of fatty infiltrates occurs with permanent AF. [11]

Finally, the current study revealed that there was a significant correlation between EAT thickness and Hypertension and LA diameter and volume in AF group. Receiver operating characteristics (ROC) analysis showed that an EAT thickness of > 0.30 cm maximizes the sensitivity and specificity to predict the development of AF (sensitivity of 84.0 %, specificity of 96 %, positive predictive value of 95.5 % and a negative predictive value of 85.7%).

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

References

1. January CT, Wann LS, Alpert JS, Calkins H, Cigarroa JE, Conti JB, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. Journal of the American College of Cardiology. 2014;64(21):e1-e76.

2. Zoni-Berisso M, Lercari F, Carazza T, Domenicucci S. Epidemiology of atrial fibrillation: European perspective. Clinical epidemiology. 2014;6:213.

3. Wong CX, Sullivan T, Sun MT, Mahajan R, Pathak RK, Middeldorp M, et al. Obesity and the risk of incident, post-operative, and post-ablation atrial fibrillation: a meta-analysis of 626,603 individuals in 51 studies. JACC: Clinical Electrophysiology. 2015;1(3):139-52.

4. Lavie CJ, Pandey A, Lau DH, Alpert MA, Sanders P. Obesity and atrial fibrillation prevalence, pathogenesis, and prognosis: effects of weight

loss and exercise. Journal of the American College of Cardiology. 2017;70(16):2022-35.

5. Wong CX, Ganesan AN, Selvanayagam JB. Epicardial fat and atrial fibrillation: current evidence, potential mechanisms, clinical implications, and future directions. European heart journal. 2016;38(17):1294-302.

6. McCallum CJ, Raja DC, Pathak RK. Atrial fibrillation: an update on management. Australian Prescriber. 2019;42(6):186.

7. Schnabel RB, Yin X, Gona P, Larson MG, Beiser AS, McManus DD, et al. 50 year trends in atrial fibrillation prevalence, incidence, risk factors, and mortality in the Framingham Heart Study: a cohort study. The Lancet. 2015;386(9989):154-62.

8. Yorgun H, Canpolat U, Aytemir K, Hazırolan T, Şahiner L, Kaya EB, et al. Association of epicardial and peri-atrial adiposity with the presence and severity of non-valvular atrial fibrillation. The International Journal of Cardiovascular Imaging. 2015;31(3):649-57.

9. Dereli S, Bayramoğlu A, Yontar OC, Cerşit S, Gürsoy MO. Epicardial fat thickness: a new predictor of successful electrical cardioversion and atrial fibrillation recurrence. Echocardiography. 2018;35(12):1926-31.

10. Psychari SN, Tsoukalas D, Varvarousis D, Papaspyropoulos A, Gkika E, Kotsakis A, et al. Opposite relations of epicardial adipose tissue to left atrial size in paroxysmal and permanent atrial fibrillation. SAGE open medicine. 2018; 6(20):50-58.

11. Haemers P, Hamdi H, Guedj K, Suffee N, Farahmand P, Popovic N, et al. Atrial fibrillation is associated with the fibrotic remodelling of adipose

tissue in the subepicardium of human and sheep atria. European heart journal. 2017;38(1):53-61.

Tables and figures

Table (1): Comparison between the two studied groups according to demographic data

	AF (n = 25)		Control (n = 25)		Test of Sig.	p
	No.	**%**	**No.**	**%**		
Sex						
Male	14	56.0	15	60.0	χ^2= 0.082	0.774
Female	11	44.0	10	40.0		
Age (years)						
Min. – Max.	32.0 – 71.0		30.0 – 67.0			
Mean ± SD.	50.84 ± 11.32		46.52 ± 10.65		t=1.390	0.171
Body weight (Kg)						
Min. – Max.	59.0 – 120.0		56.0 – 115.0		t=	0.171

Mean ± SD.	84.08 ± 16.06	80.40 ± 16.01	1.390	
Waist circumference (cm)				
Min. – Max.	65.0 – 113.0	60.0 – 112.0		
Mean ± SD.	93.86 ± 12.71	82.0 ± 11.44	t= 3.468*	0.001*

χ2: Chi square test **t: Student t-test**

p: p value for comparing between the studied groups

***: Statistically significant at p ≤ 0.05**

Table (2): Comparison between the two studied groups according to risk factor

Risk factor	AF (n = 25)		Control (n = 25)		χ^2	p
	No.	%	No.	%		
HTN	9	36.0	6	24.0	0.857	0.355
DM	7	28.0	5	20.0	0.439	0.742

HTN: Hypertension.
DM: Diabetes mellitus.

Table (3): Comparison between the two studied groups according to EAT thickness

EAT thickness (cm)	AF (n = 25)	Control (n = 25)	t	p
Min. – Max.	0.30 – 1.10	0.10 – 0.35	7.131*	<0.001*
Mean ± SD.	0.52 ± 0.19	0.23 ± 0.06		

t: Student t-test
p: p value for comparing between the studied groups
*: Statistically significant at $p \le 0.05$
EAT: Epicardial Adipose Tissue

Table (4): Comparison between the two studied groups according to different parameters

	AF (n = 25)	Control (n = 25)	t	p
LA diameter (cm)				
Min. – Max.	3.80 – 6.60	2.50 – 4.0	10.135*	<0.001*
Mean ± SD.	4.85 ± 0.68	3.32 ± 0.32		
LA volume (ml)				
Min. – Max.	75.0 – 115.0	38.0 – 51.0	20.778*	<0.001*
Mean ± SD.	94.48 ± 11.84	43.49 ± 3.22		
LVEF (%)				
Min. – Max.	50.0 – 78.0	56.0 – 71.0	0.182	0.856
Mean ± SD.	63.40 ± 6.66	63.12 ± 3.82		
LVIDd (cm)				
Min. – Max.	39.0 – 86.70	38.0 – 55.0	1.893	0.064
Mean ± SD.	51.10 ± 8.96	47.32 ± 4.43		
LVIDs (cm)				
Min. – Max.	23.0 – 60.30	20.0 – 35.0	1.091	0.281
Mean ± SD.	33.49 ± 7.32	29.92 ± 3.41		
IVSd (cm)				

Min. – Max.	0.70 – 1.50	0.70 – 1.20	1.091	0.281
Mean ± SD.	1.04 ± 0.21	0.98 ± 0.15		
LVPWd (cm)				
Min. – Max.	0.70 – 1.30	0.70 – 1.30	0.986	0.329
Mean ± SD.	1.02 ± 0.16	0.98 ± 0.15		
E/E'				
Min. – Max.	10.0 – 26.0	3.50 – 9.40		
Mean ± SD.	14.42 ± 3.56	6.25 ± 1.65	10.399*	<0.001*

t: Student t-test
p: p value for comparing between the studied groups
*: Statistically significant at $p \leq 0.05$
LA: left atrium
LVEF: left ventricular ejection fraction
LVIDd: left ventricular internal diameter end diastolic
LVIDs: left ventricular internal diameter end systolic
IVSd: Interventricular septum thickness end diastole
LVPWd: left ventricular posterior wall thickness end diastole

Table (5): Agreement (sensitivity, specificity) EAT thickness to diagnose AF patients (n = 25) from control (n = 25)

	AUC	p	95% C.I	Cut off#	Sensitivity	Specificity	PPV	NPV
EAT thickness	0.970	<0.001*	0.934 – 1.007	>0.3	84.0	96.0	95.5	85.7

AUC: Area Under a Curve
p value: Probability value
CI: Confidence Intervals
NPV: Negative predictive value
PPV: Positive predictive value
*: Statistically significant at $p \leq 0.05$
#Cut off was choose according to Youden index

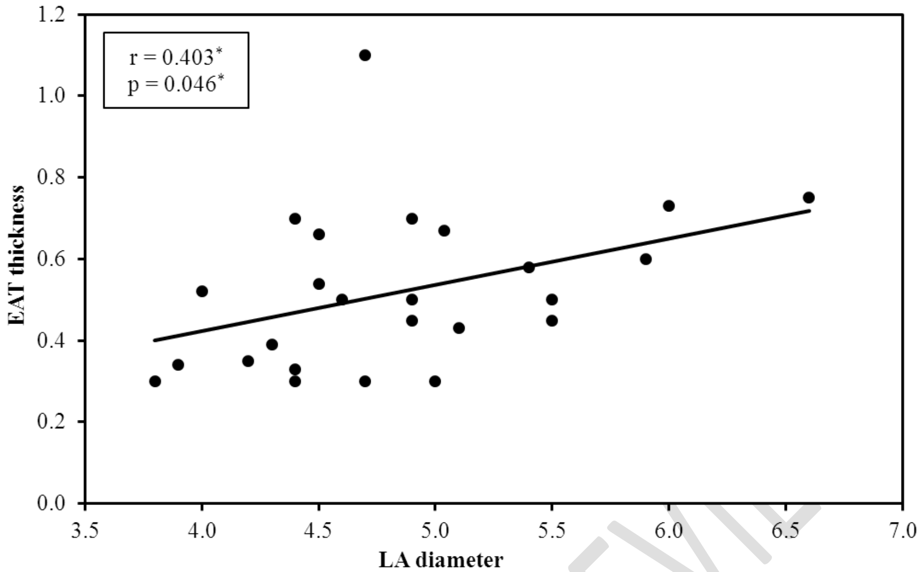

Figure (1): **Correlation between EAT thickness and LA diameter in AF group (n = 25) demonstrates that there was a significant correlation between EAT thickness and LA diameter.**

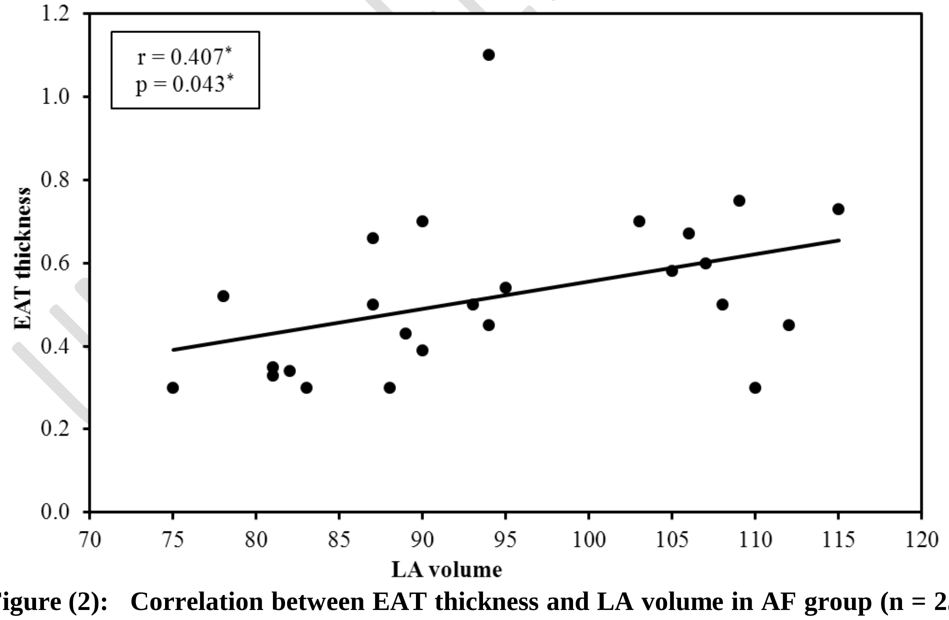

Figure (2): **Correlation between EAT thickness and LA volume in AF group (n = 25) demonstrates that there was a significant correlation between EAT thickness and LA volume.**

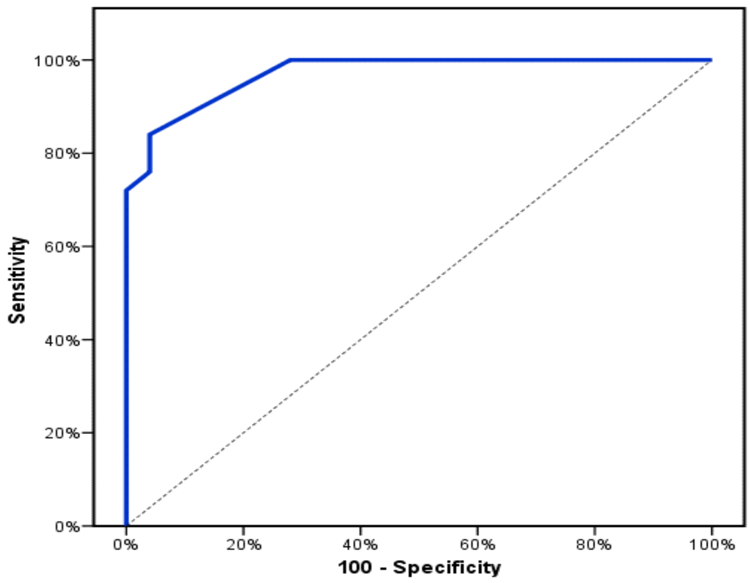

Figure (3): ROC curve for EAT thickness to diagnose AF patients (n = 25) from control (n = 25)