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Research Article

Left atrial cardiopathy as an early predictor for atrial fibrillation in patients with cryptogenic stroke.

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Abstract

Background: Atrial cardiopathy (AC) is still one of the most important mechanisms behind cryptogenic stroke. Indeed, atrial cardiopathy may be the underlying cause of embolic stroke even in absence of AF. Thus, detection of AC has a great value for therapeutic purposes and secondary prevention of further thrombo-embolic events. The aim of the study was to evaluate the left atrial function to detect atrial cardiopathy and early predicting AF. **Methods:** The study included 62 patients who proved to have ischemic stroke of unknown etiology (CS) presented to neuropsychiatry department or out-patient clinic of Minia university hospital after exclusion of high risk patients for cardio-embolism or recognized causes of stroke. Two-dimensional Echo-Doppler study of left atrium was done and at least 48 hours rhythm monitoring during hospitalization. **Results:** AF-recorded (32%) and non-AF recorded (68%). LAVI in AF-recorded group (Mean ± SD = 46.3 ± 4.1) with p-value = 0.0001, while LV diastolic function assessment in AF-recorded group (40% with normal diastolic function) (30% with grade I LVDD) (30% with grade II LVDD) with p-value = 0.158. **Conclusion:** Evaluation of atrial cardiopathy by 2D echocardiography is important and of great clinical value for prediction of AF in patients presented with cryptogenic stroke or TIA. LAVI is a sensitive parameter for detection of AF in comparison with LV diastolic dysfunction assessment by pulsed-Doppler and tissue Doppler imaging.

Key words: cryptogenic stroke, atrial cardiopathy, dopplar echocardiograghy.

Introduction

Ischemic cerbro-vascular stroke is a common fatal disease, worldwide which is considered one of the first three leading causes of death, and the most common causes of long-term disability. Cryptogenic stroke (CS) is defined as ischemic cerbro-vascular stroke without defined cause in-spite of complete work-up. They differ from infarctions of undetermined causes, which may involve overlapping causes or an incomplete investigation [1]. There are potential mechanisms and etiologies that may be involved in CS, but atrial cardiopathy (AC) is still one of the most important mechanisms behind CS. Atrial cardiopathy includes structural, contractile or electrophysiological changes affecting the left atrium and in context leading to atrial fibrillation (AF) soon or later. So, AC is an important and independent risk factor for AF. Indeed, atrial cardiopathy may be the underlying cause of embolic stroke even in absence of AF [2]. Cryptogenic stroke 'cerbro-vascular infarctions of undefined cause' is considered challenging in medicine nowadays due to multiple possible etiologies and over-lapping mechanisms behind it. To define an

ischemic cerebro-vascular event as cryptogenic, four conditions must be excluded; (a) Small deep infarcts in the distribution of penetrating cerebral vessels (<15 mm on CT, <20 mm on MRI diffusion images). (b) Intra-cranial or extra-cranial stenosis (>50% luminal stenosis of the artery supplying the ischemic area). (c) A

defined cardio-embolic source identified by transthoracic echocardiography. Or resting electrocardiography (ECG); (d) certain defined cerebral arteritis.[3]

Embolic Stroke of Undetermined Source 'ESUS' is a subgroup of cryptogenic stroke which is defined as ischemic stroke of unknown embolic origins. The definition of ESUS returns to the year 2014 by Hart et al.,[4]. In 2017, it was reported that ESUS represents approximately 17% of whole etiologies of ischemic stroke.[5]

Three main categories must be clearly defined in the diagnostic work-up of ESUS; (a) Undetected or subclinical AF. (b) PFO and inter-atrial septal aneurysms. (c) Significant atherosclerosis of carotid arteries or atheromatous plaques of aorta.

Detection of subclinical AF after cryptogenic stroke is an important goal for secondary prevention of further thrombo-embolic episodes which mainly depends on anticoagulation therapy. Two-dimenional speckle tracking echocardiography is a novel, feasible, simple and non-invasive technique for evaluation of left atrial function and early detection of any structural, architectural, remodeling, contractile or electrophysiological deformation of LA which is defined as left atrial cardiopathy[6].

So, atrial cardiopathy is an independent risk factor for cryptogenic stroke and its detection has a great applied clinical benefit in management and secondary prevention of cryptogenic stroke.

Patients and methods

A prospective study was carried out at Cardiology Department, Minia Cardiothoracic University Hospital. The study included 62 patients who were proved to have ischemic stroke of unknown etiology (CS) presented to neuropsychiatry department of Minia University hospital. The study was approved by the ethical committee of Faculty of medicine, Minia university. Patients were admitted and signed an informed consent.

Inclusion criteria: This study was done on patients of both sexes with documented cerebrovascular ischemic stroke by a brain imaging (brain CT or MRI to exclude primary intracranial hemorrhage) or presented with transient ischemic attack.

Exclusion criteria*:* High risk patients for cardio-embolism (persistent or paroxysmal AF, metallic cardiac prostheses, more than +2 severity valvular heart disease, previous history of CAD, LV systolic dysfunction (LVEF< 50%), intra-cardiac mural thrombi by TTE, intra-cardiac shunts, Signficant > 50% carotid artery stenosis by carotid duplex ultrasonography) & definite recognized cause of cerbrovascular stroke (vasculitis, cerebral arteritis, thrombocycemia, polycythemia rubra vera, anti-phospholipid syndrome or metabolic disorders).

Methods

All Patients were subjected to a detailed history taking, full general and local cardiac clinical examination, 12 leads surface resting ECG, two-dimensional trans-thoracic Doppler-echocardiography for evaluation LV diastolic dysfunction through transmitral pulsed Doppler assessment by E/A ratio and tissue Doppler imaging by e`/a`, LA antero-posterior (AP) diameter in PLAX (Para-sternal long axis) view, LA volume in biplane view (apical 4 and apical 2- chambers views) and LA volume index (LAVI). Bilateral carotid arteries duplex ultrasonography and at least 48 hours hospitalization rhythm monitoring were performed. Patients are subdivided into two groups: - AF-recorded patients and non-AF recorded patients. Recording of AF was by at least 48 hours ECG rhythm monitoring during hospitalization. Episodes of AF more than 30 seconds were recorded. LA volume was measured in biplane view (apical 4 and apical 2-cahmbers views). LA volume index was calculated by (LA maximal volume / body surface area by m^2).

Results

The mean age of patients included was 39.8 ± 9.8 years old, 30 patients (48.4%) were males and 32 patients (51.6%) were females. Regarding modifiable risk factors of atherosclerosis, the mean body mass index (BMI) of included patients was 28.2 ± 5.4, 18 patients (29%) were diabetic, 24 patients (38.7%) were hypertensive, 18 patients (29%) were smokers.

The mean range of serum cholesterol level was 219.6 ± 45.7 mg/dl while mean range of serum triglycerides was 171.0 ± 34.2 mg/dl (table 1). AF-recorded in (32%) of participants and non-AF recorded (68%) (Figure 1). LV diastolic dysfunction was evaluated in all participants by trans-mitral pulsed Doppler assessment (E/A ratio) and tissue Doppler imaging (e`/a`). n=28 (45.1%) normal LV diastolic function, n=24 (38.7%) grade I LV diastolic dysfunction and n=10 (16.1%) grade II LV diastolic dysfunction. (Table 2).

Table (1): Patients demographic data, risk factors and co-morbidities.

Characteristics	**Cases N= 62**
Gender	
• Males	30 (48.4%)
• Females	32 (51.6%)
Age	39.8 ± 9.8
Risk factors	
• DM	18 (29.0%)
• Hypertension	24 (38.7%)
• **Other comorbidities:**	
Collagen disease	14 (22.5%)
Chronic chest disease	2 (3%)
CKD	2 (3%)
• **Smoking**	18 (29.0%)
• **Family history**	14 (22.6%)
BMI (Kg/ m²)	28.2 ± 5.4
BSA (m²)	1.9 ± 0.2
Lipid profile	
• Cholesterol	219.6 ± 45.7
• TGs	171.0 ± 34.2

Qualitative data presented as number (%), quantitative data presented as mean±SD, DM: diabetes mellitus, CKD: chronic kidney disease, BMI: body mass index, BSA: body surface area, TGs: triglycerides

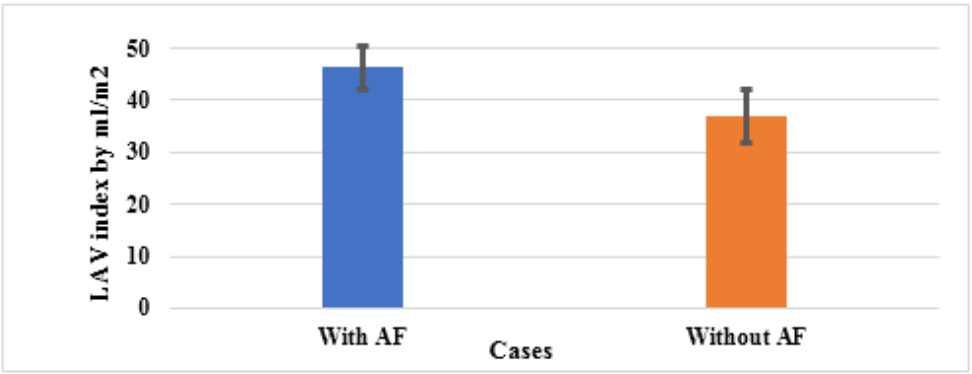

Figure (1): LA volume index (LAVI) by ml/m and incidence of AF occurrence during hospitalization.

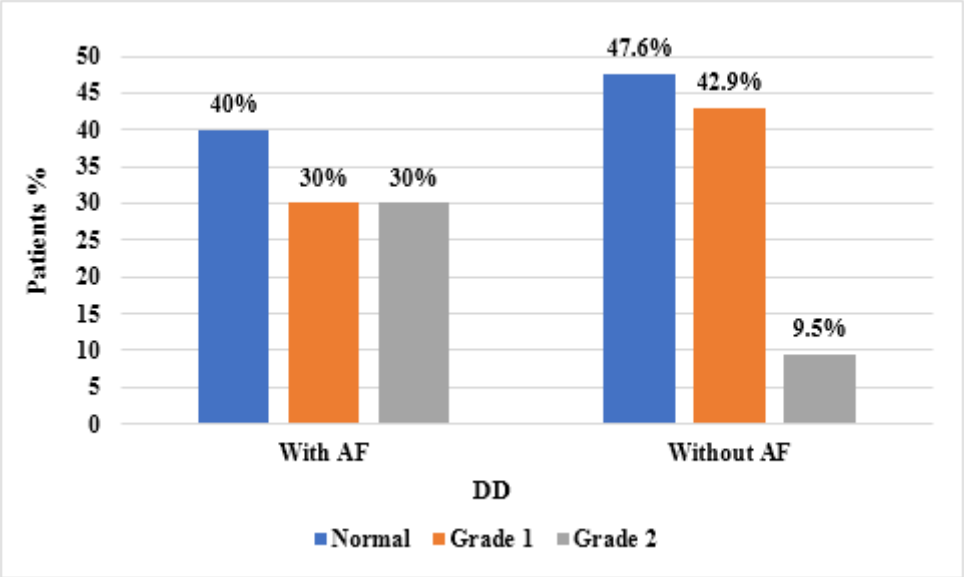

Figure (2): LV diastolic dysfunction and occurrence of AF during hospitalization.

Table (2): Comparison between LAVI and LV diastolic dysfunction as LA cardiopathy parameters for prediction of AF.

Characteristics	Cases without AF N= 42	Cases with AF N= 20	p value
LAV index	46.3 ± 4.1	46.3 ± 4.1	<0.0001*
DD			
• **Normal**	8 (40.0%)	8 (40.0%)	
• **Grade 1**	6 (30.0%)	6 (30.0%)	0.158
• **Grade 2**	6 (30.0%)	6 (30.0%)	

Independent samples t-test for parametric quantitative data between the two groups.
Chi-square test for qualitative data.
*: significant level at p value< 0.05.
AF: atrial fibrillation, DD: differential diagnosis, LAV: left atrial volume.

Discussion

The study included 62 patients presented by ischemic cerebrovascular stroke of unknown etiology (cryptogenic). These patients were examined by 2D-Doppler-echocardiography searching for atrial cardiopathy by assessment of LV diastolic dysfunction, LA volume and LAVI and then monitored for at least 48 hours during hospitalization for detection of sub-clinical atrial fibrillation.

Atrial remodeling (atrial cardiopathy) represents an alteration in atrial size and function secondary to cellular changes in the atrial tissue. Clinical observations suggest that several risk factors such as advanced age, hypertension, and diabetes mellitus may lead to atrial remodeling with the development of interstitial fibrosis and increased atrial volume[7].

Our study aims to compare the sensitivity of LA volume index and LV diastolic dysfunction assessed by trans-mitral pulsed Doppler and tissue Doppler as parameters of left atrial cardiopathy for prediction of AF.

The results show that n=28 (45.1%) of participants were with normal LV diastolic function, while n=24 (38.7%) were with grade I LV diastolic dysfunction and n=10 (16.2%) were with grade II LV diastolic dysfunction (Table 2). More than 30 seconds episodes of AF were recorded by ECG rhythm monitoring during hospitalization in 20 patients of them (32%).

The results showed that LAVI was significantly high in AF- recorded patients (Figure 2), thus this correlation demonstrates the applied clinical value of LA maximal volume index in early prediction of AF or as a direct cause for cryptogenic stroke.

Jordan et al., 2019 study which was published in AHA journal demonstrated that LAVI is associated with AF detection in patients with ESUS who underwent outpatient cardiac event monitoring. These findings highlight the important interplay between left atrial volume, atrial fibrillation, and cryptogenic stroke[8].

We also found that presence of LV diastolic dysfunction is not significantly associated with occurrence of AF. Results demonstrated that 40% of AF-recorded patients were with normal LV diastolic function, 30% were with grade I LV diastolic dysfunction, 30% were with grade II diastolic dysfunction, so, LV diastolic dysfunction is not a sensitive predictor for subclinical AF, (Figure 3).

LAVI is more sensitive parameter of atrial cardiopathy for prediction of subclinical AF in comparison with LV diastolic dysfunction assessment by Pulsed-Doppler (E/A ratio) and tissue Doppler imaging (e`/a`), (Table 2). That point was demonstrated by Olsen et al., 2020[9] study which found that classical grading of LV diastolic dysfunction by E/A ratio is not that efficient for prediction of AF.

However, an important limitation of our study requires to be mentioned, 48 hours rhythm monitoring is not enough for detection of subclinical AF. We recommend one week Holter ECG monitoring during follow up in non-AF recorded patients with significantly increased LAVI in future studies.

Conclusion

The study demonstrated the importance and great clinical value for evaluation of atrial cardiopathy by two-dimensional echocardiography in prediction of AF in patients presented with cryptogenic stroke or TIA. LAVI is a sensitive parameter for detection of AF in comparison with LV diastolic dysfunction assessment by Pulsed-Doppler and tissue Doppler imaging.

Abbreviations:

2D	Two-dimensional
AC	Atrial cardiopathy
AF	Atrial fibrillation
AP	Antero-posterior
BMI	body mass index
BSA	body surface area
CAD	Coronary artery disease
CKD	Chronic kidney disease
CS	Cryptogenic stroke
DD	Differential dianosis
DM	Diabetes mellitus
ECG	Electrocardiograghy
ESUS	Embolic stroke of undetermined source
LA	Left atrium
LAMVI	LA maximal volume index
LVEF	LV ejection fraction
N	Number
PLAX	Para-sternal long axis
SD	Standard deviation
TGs	Triglycerides
TTE	Trans-oseophgheal echocardiograghy

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