

The Relationship Between Maximal Atrial Septal Excurtion and Left Atrial Appendix Flow in Cryptogenic Stroke Patients Without Patent Foramen Ovale

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Abstract

- Object** to examine whether a correlation exists between LAA systolic flow velocity and maximal atrial septal excurtion(MASE)In Cryptogenic stroke patients without Patent foramen ovale
- Methods** This study includes 30 patients between 18-65 aged who took cryptogenic stroke diagnosis and applied for detailed cardiac examination to neurology and cardiology clinics. ..After providing a medical history and undergoing a physical examination,each patient underwent ECG and echocardiographical examination.Two dimensional echocardiography,M-mode and Doppler studies were performed using standart techniques..In the Subkostal imaging:Atrial septal excurtion was measured by putting M-mode cursor on midseptum.After TTE,patients underwent TEE. SAA systolic flow velocity was measured by putting pulse wave doppler cursor on SAA outflow.Associations between LAA systolic flow velocity and MASE were determined by using spearman correlation coefficient.
- Results** A negative correlation was observed between LAA systolic flow velocity and MASE. When relations among ecocardiographic parametres (LADD, LVEDD, E,A,E',A', Des Time) were examined one by one, no other significant correlation was observed
- Conclusion** According to our study's results; we think that the increase of MASE may be an indicator for the decrease of LAA systolic flow velocity. This result would keep light to the other future comprehensive studies which contain other parameters which may affect and may reflect LAA function .
- Key words:** LAA systolic flow velocity, MASE, cardioemboli, cryptogenic stroke.

Öz

- Amaç** Patent foramen ovale (PFO) saptanmayan,Kritojenik İnme hastalarında; Sol atriyal appendix (SAA) sistolik akım hızı ve Atriyal septal hareket amplitüdü (MASE) arasındaki ilişki olup olmadığının incelenmesi
- Metod** Çalışmaya 18-65 yaş arası ,nedeni bilinmeyen inme tanısı almış ve kardiyembolik kaynak araştırılması amacıyla detaylı kardiyak incelemeye tabi tutulan 30 hasta alındı.Hastaların öncelikle özgeçmiş,soygeçmiş sorgulandı.Sonrasında her hasta Elektrokardiyografi(EKG) ve Transtorasik Ekokardiyografi(TTE) incelemesine alındı.2boyutlu TTE'de,standart teknikler kullanılarak M-mode ve Doppler çalışmalarını gerçekleştirildi. MASE subkostal görüntüleme penceresinde atrial mid-septuma M-mode cursoru koyarak ölçüldü TTE sonrası,hastalar Transözofageal Ekokardiyografi(TEE) e alındı ve SAA çıkış yolunda PW doppler konularak SAA sistolik akım hızı ölçüldü. Atriyal septal hareket amplitüdü (MASE) ile sol atriyal apendiks sistolik akım hızı (SAA Vel.) arasındaki ilişki spearman korelasyon katsayısı hesaplanarak belirlendi
- Bulgular** SAA akım hızı ile atriyal septal hareket amplitüdü arasında anlamlı, negatif bir korelasyon vardır. SAA ve diğer ekokardiyografik parametreler (LVDC,LADÇ,E,A,E',A',Des.Zmn) arasındaki korelasyon tek tek incelendiğinde anlamlı bir ilişki bulunmamıştır.
- Sonuç** Çalışmamızın sonucuna göre; MASE artışının, LAA sistolik akım hızındaki azalmanın bir belirteci olabileceğini düşünmekteyiz.Bu çalışma; LAA sistolik akım hızını etkileyen ve yansıtan diğer parametrelerin detaylı olarak inceleneceği daha kapsamlı çalışmalara ışık tutacaktır.
- Anahtar Kelimeler** LAA sistolik akım hızı,MASE, kardiyemboli , kriptojenik inme



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Introduction

The deaths caused by stroke are still among the most important causes of death in the world. Although detailed research, the reason of stroke can not be found in patients and it is called "cryptogenic stroke". It was understood that cardioemboli is usually underlying reason for the cryptogenic stroke. Cardioemboli is the most common reason especially among young people with cryptogenic stroke¹. LAA and inter atrial septum (IAS) are usually blamed as a potential source of these cardioembolic events.

Left atrial appendix (LAA) dysfunction is a risk factor for stroke and it is evaluated by transesophageal echocardiography (TEE)². Since TEE is an invasive procedure, it may be refused by some patients or its contraindications might prevent its usage. Therefore, there is a need for a noninvasive predictor for LAA dysfunction. However, there are limited number of studies in the literature about clinical and echocardiographic predictors for thrombosis formation in LAA. LAA systolic flow velocity is a predictor for LAA function and thrombosis formation.

Another potential source of cardioemboli associated with cryptogenic stroke is interatrial septal aneurysm (IASA)⁽³⁾. The objective diagnosis of IASA is defined with MASE measurement on TTE.^{4,5}

In this study, it is aimed to examine whether a correlation exists between LAA systolic flow velocity and maximal atrial septal excursion (MASE). At the result of study; MASE is found to be high for lower LAA systolic flow velocities. This finding may be useful to develop new strategies for patients who have contraindications for TEE (i.e. use of oral anticoagulant, esophageal varicosis, or serious lung disease) or refuse TEE. After the approval of the relation between echocardiographic parameters and LAA systolic flow velocity with large scale trials, it may also be used for healthy people who are at risk for ischemic stroke.

Methods

This study includes patients with cryptogenic stroke diagnosis who applied S.B. Dışkapı EAH Neurology and Cardiology Clinics for detailed cardiac examination. Patients with the following characteristics were excluded from the study; patients who refused TEE or have intolerance to TEE, severe valve disease, congenital heart disease, heart failure, over 65 years old and observed other reasons of stroke (organic brain diseases, hemoragic stroke). Patients in the study were aged between 18-65 years. The study was approved by the local ethic committee.

After the investigation of medical history and physical examination, each patient underwent ECG and echocardiographical examination. Two dimensional echocardiography, M-mode and Doppler studies were performed using standard techniques. Left Atrial Diameter (LADD), Left Ventricle End-Diastolic Diameter (LVEDD) and Left Ventricle End-Systolic Diameter (LVESD) and Maximal Atrial Septal Excurtion (MASE) were measured. In subcostal imaging; Atrial septal excursion was measured by putting M-mode cursor on midseptum (Figure 1). Measurements were performed using three consecutive heart beats and mean of three measurements was calculated. LVEF was calculated using Teicholz formula. Conventional and tissue-pulsed Doppler imaging included early (E) and atrial (A) peak velocities of the mitral valve, their ratio (E/A), E velocity deceleration time (Des.T), myocardial systolic velocity (Sm), early (Em) and atrial (Am) myocardial diastolic velocities obtained from the lateral mitral annulus. After TTE, patients underwent TEE. At the beginning of

TEE; orofarengal local anesthesia was applied to the patients. We examined LA and LAA morphology and existence of a thrombus or Spontaneous Echo Contrast (SEC) in standard visualization windows. LAA systolic flow velocity was measured by putting pulse wave doppler cursor on LAA outflow (Figure 2). At the end of TEE; IAS was examined with IV ajite saline injection to diagnose Patent Foramen Ovale (PFO). We diagnosed PFO when the bubbles were on the LA and LV in three beats after they reached right atrium.

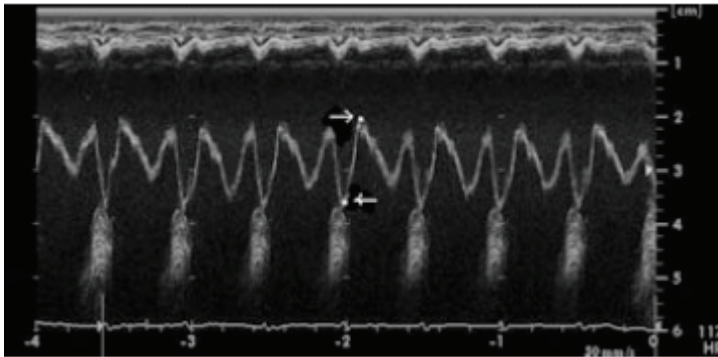


Figure 1: Measurement of Maximal Atrial septal Excursion by using M mode on TEE

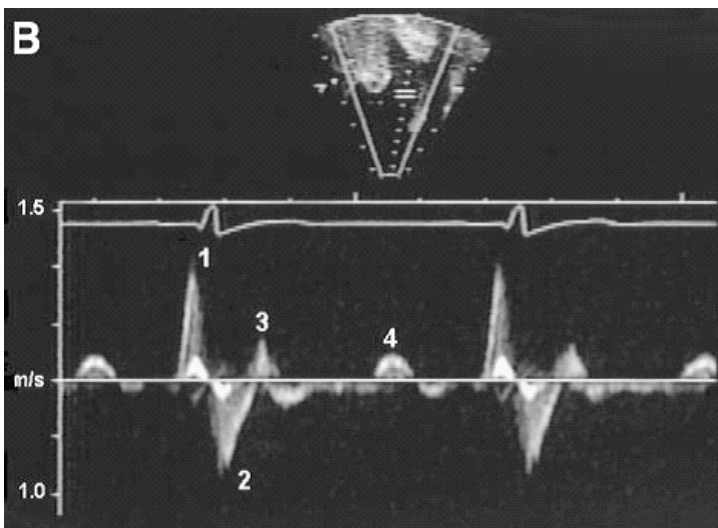


Figure 2 :LAA flow diagram on sinus rhythm . 1.LAA contraction ; 2. LAA filling; 3.systolic reflectionwaves (positive and negative); 4. early diastolic LAA outflow.

Statistics

Analysis were performed with SPSS version 17.0 . Continuous variables were expressed as mean \pm SD. Continuous variables were compared between groups using an unpaired t test (for normally distributed variables) or Mann-Whitney U test (for non-normally distributed variables). Chi square analysis was used to compare categorical variables. All reported probability values were two-tailed, and $P < 0.05$ was considered to be statistically significant. Correlation between LAA systolic flow velocity and MASE were determined by using spearman correlation coefficient.

Results

The study included 30 patients with cryptogenic stroke .They were 18-65 years old. The mean age of the participants was $52,7 \pm 8,09$ year. 21 of the patients were men (70%), 9 of the patients



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were women (%30). Cardiovascular risk factors were common in the study group; hypertension (n=15 [50%]), hypercholesterolemia (n=6 [20%]), current or previous smoking (n=11 [36%]), diabetes (n=9[30%]) and Periferic Arterial Disease (n=3 [10%]). We observed atrial fibrillation on one of patients's basal EKG (%3.3) and other patients (n=29) had normal sinus rhythm on their basal EKG. The mean LV ejection fraction was $65,4 \pm 3,5 \%$, the mean LVEDD was $4,67 \pm 0,8$, the mean LA diameter was $3,7 \pm 0,5$, the mean LAA systolic flow velocity was $48,38 \pm 23,80$. The echocardiographic characteristics of the study patients are presented in Table 1.

Table 1: Ecocardiographic parameters in the study population

Parameter	Mean	Std Dev	Minimum	Maximum
LV EF [%]	65.4667	3.55	58	75
LVEDD [cm]	4.6735	0.8359	1.5	6
LA [cm]	3.7685	0.5207	2.9	5.3
Mitral E [m/s]	0.7407	0.2424	0.4	1.4
Mitral A [m/s]	0.8917	0.2492	0.6	1.5
IVRZ [ms]	109.538	30.691	64	185
E'	7.2617	3.0491	3	15.9
A'	9.3143	2.2023	6	16
S	7.4833	1.6093	5	9.8
DES. T.	246.111	75.9356	68	371
LAA Vel. S	48.38	23.80	0.2	1.06
LAA Vel. D	0.478	0.2259	0.2	1.02

The correlation between LAA systolic flow velocity and MASE is shown in figure 3. A negative correlation was observed between LAA systolic flow velocity and MASE . No other significant correlation was observed among other echocardiographic parameters (LADD, LVEDD, E, A, E', A', Des.T.) when these parameters were examined one by one.

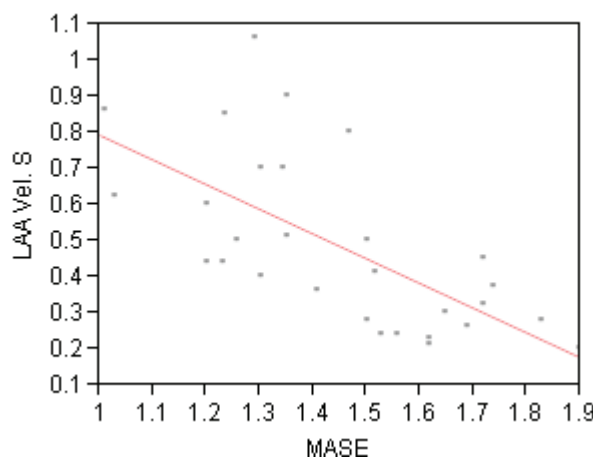


Figure 3. Relation between LAA flow velocity and MASE (Spearman $\rho = -0.7053$, $Prob > |r| = <.0001$)

Discussion

Since it has high mortality and it may be repeatable but also curable, It is very important to distinguish cardiac stroke from the other stroke etiologies⁶. When the reasons of cyriptogenic stroke in young people are examined in detail, generally cardioembolic sources are found to be the main

cause for the stroke. The more common high risk cardioembolic conditions are: impairment of LA/LAA function or interatrial septal anomalies such as PFO, increase of IAS mobility, IASA and ASD.^{7,8}

In this study, potential cardiac emboli sources were investigated with detailed cardiac examination of cryptogenic stroke patients and it was observed that there is a correlation between LAA flow velocity and MASE. The patients who have other cardioembolic sources (PFO, ASD, MVP, atrial mixoma, intracardiac thrombus) were excluded from the study. The study patients didn't have any other pathologies that may affect LAA flow velocity or other causes that may lead to stroke alone, such as mitral stenosis, atrial fibrillation, presence of SEC.

Many studies showed that TTE is insufficient to evaluate morphology and functions of LAA and to find out the potential cardioembolic sources^{9,10}. TEE is thought to be gold standard to evaluate LAA for the people with cardioembolic stroke¹¹. On the other hand, this examination is uncomfortable, expensive and semi-invasive¹². Because of these disadvantages, some of patients refuse TEE. For this reason, it becomes important at least to find out the predictor parameter for LAA dysfunction which has critical importance in terms of stroke.

In the literature, there are limited number of studies about the prediction of LAA dysfunction. Agmon at all showed that there is a weak relation between LAA discharge speed and many left atrial variables in a big patient population but TTE and TEE were performed in the different hemodynamic states in this study¹³. Nakatani at all; introduced an index in their study. It was LA dp/dtmax ($r=0,78$ $p<0,001$) which was known as a LA contraction's strong predictor and was correlated with median transmitral A wave¹⁴. In an other study, it is claimed that LA EF and Mitral flow A wave Acceleration Slope (Acc-S) were the best parameters which were correlated with LAA discharge speed and A wave Acceleration Slope (Acc-S <900 cm/sec²) shows the decrease of LAA discharge speed. There is not any study in the literature that investigates the relation between maximal inter atrial septum excursion and LAA systolic flow velocity. In our study; we investigated whether a correlation between LAA flow velocity measured by TEE and MASE measured by TTE exists or not.

As recommended usually, we measured MASE on interatrial septum by using M mode at TTE. Protrusion of interatrial septum more than 15mm into the right or left atrium with an at least 15mm diameter base of interatrial septum confirmed the diagnosis of atrial septal aneurysm.

In our study, we observed low LAA systolic flow velocities in the presence of high MASE. This relation may be caused by the increase of atrial septal excursion that may affect the mechanical functions of LA and LAA flow velocities by creating turbulent flow in left atrium. According to our study; we claimed that the increase of maximal atrial septal excursion may be an indicator for the decrease of LAA systolic flow velocity.

We expect that; this study would keep light to future comprehensive studies which include other parameters related with LAA functions. There are few studies about prescriptive indicators of LAA flow and LAA flow's contribution to thromboembolic risk. Result of our study would help to develop new strategies for the stroke patients who refuse TEE or have contraindication for TEE (osopagheal varicose veins, serious lung disease, using oral anticoagulan). Observing the etiology of stroke would be a guide for the treatment and to develop new treatment strategies.



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With future comprehensive studies, relation between echocardiographic parameters with LAA systolic flow velocity may be proved clearly and can be used among healthy people to distinguish people with high cardioembolic risk.

Our study has some limitations: since the study didn't include a control group. Measurements for normal people could not be examined. Only the correlation between LAA flow velocity and MASE is examined, but detailed examination of relations between other parameters may be performed in future comprehensive studies with larger sample sizes.

Conclusions

In this study, it is aimed to examine whether a correlation exists between LAA systolic flow velocity and maximal atrial septal excursion (MASE) and MASE is found to be high for lower LAA systolic flow velocities. This finding may be useful to develop new strategies for patients who have contraindications for TEE (i.e. use of oral anticoagulant, esophageal varicosis, or serious lung disease) or refuse TEE. After the detection and prove of the correlation between clinical and echocardiographic parameters and LAA systolic flow velocity by large scale trials, it may also be used for healthy people who are at risk for ischemic stroke.

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