Original Article

The Role of Serum Lipoprotein(a) in Increasing the Risk of Thrombus Formation in Patients with Atrial Fibrillation

Ali Kazemi Saeed, MD[1*], Gholamreza Namadanian, MD[2], Darioush Kamal Hedayat, MD[3]

[1]Tehran Heart Center, Medical Sciences / University of Tehran, Tehran, Iran.
[2]Behshahr General Hospital, Medical Sciences / University of Tehran, Tehran, Iran.
[3]Shariati Hospital, Medical Sciences / University of Tehran, Tehran, Iran.

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Abstract

Background: *Atrial fibrillation (AF) is prevalent among cardiac patients; and as the risk of thromboembolism is high in this arrhythmia, discrimination of the effective risk factors in producing left atrial (LA) thrombosis is clinically important. The molecular structure of lipoprotein(a) [Lp(a)] is very similar to plasminogen , so it can be hypothesized that the high level of Lp(a) is a compromising factor for the prevention of fibrinolysis (thrombogenesis).*

Methods: *This case-control study was conducted in patients with chronic AF. Most of the subjects had mitral stenosis. LA thrombosis was confirmed by transthoracic and transesophageal echocardiography.*

Result: *The study group consisted of 50 chronic AF patients mostly with mitral stenosis. Half the patients had LA thrombosis (patient group or P) and the other half did not (control group or C). The mean age of the control group (C) and patient group (P) was 45±11 y and 57±9 y, respectively. There was no significant correlation between sex and LA gradient and existence of LA thrombus. LA size was 49±5 mm (C) and 56±9 mm (P), respectively. Left atrial blood velocity was 12±2 cm/sec (C) and 5±3 cm/sec (P), and Lp(a) concentration was 30±6.7 mg / dl (C) and 55±2.75 mg / dl (P). There was a significant correlation ($p<0.001$) between age, LA blood velocity, LA size, and serum concentration of Lp(a), which was confirmed by t-test.*

Conclusion: *There has been a great deal of research into the classic risk factors of LA thrombosis in chronic AF, but the study on the effect of Lp(a), which is an atherosclerosis risk factor, on the formation of LA thrombosis is almost new. According to the results of the present study, Lp(a) should be measured in all chronic AF patients. We can assume that lowering Lp(a) serum level may decrease the risk of LA thrombosis in chronic AF patients.*

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Introduction

Atrial fibrillation (AF) is the most common arrhythmia and involves more than %5 of normal population older than 69 years.[1,2] The prevalence of AF is %9.1 in patients with cardiovascular disease and %4.6 in subclinical status, and it

[*]**Corresponding Author:** ***Ali Kazemi Saeed,*** *Assistant Professor of Cardiology, Tehran Heart Center, Tehran University of Medical Sciences, Tehran, Iran. 1411713138. Tel: +98 21 88029620. Fax: +98 21 88029637. E-mail: Alikasaeid@yahoo.com.*

is higher in men than women.[3]

The high frequency of AF-induced stroke and the consequent disabilities warrants the importance of the management of this problem. One study reported that the risk of stroke occurrence in AF patients was 5 times more than that in a control group and that the probability of stroke in patients with AF due to mitral stenosis (MS) was 17 times higher.[4]

Given the AF-induced burden, the recognition and elucidation of the predisposing risk factors of thrombus formation is crucial.[5,6] Therefore, an evaluation and assessment of probable factors that aggravate clot formation should be in the core of attention.[7,8]

Methods

The study was performed between January 2003 and January 2005 in Shariati hospital. During this study fifty patients with AF and moderate-to-severe MS requiring transesophageal echocardiography (TEE) were recruited. The subjects comprised patients with AF and MS who were candidates for percutaneous transvenous mitral commissurotomy (PTMC), patients with AF and MS who had a history of thromboembolism, and patients who were candidates for cardioversion.

Following definitions were defined for important variables.

Atrial fibrillation defined as the absence of p- wave in surface electrocardiogram and irregularity in rhythm and f-waves, which are seen better in leads II, III, and avf.

Mitral stenosis defined as mitral valve area less than 1 cm^2/m^2 by transthoracic echocardiography (TTE) using pressure half time (PHT) and planimetry methods.

Left atrial thrombosis considered as recognition of a mass in left atrium (LA) or left atrial appendage (LAA) that is attached to the atrial wall with different echogenicity.

LAA velocity considered as the velocity of blood in 1/3 proximal portion of LAA in basal short axis view of TEE.

SEC (Spontaneous Echo Contrast) considered as circulatory or turbulent movement in LA or LAA, which was classified as no echogenicity (0), little echogenicity in LA or LAA (+1), turbulent flow in LAA and with less intensity in LA (+2), severe turbulent flow in middle part of LA with low velocity (+3). LA diameter was measured by TTE in long axis parasternal view.

In this analytic case-control study, patients with AF and moderate-to-severe MS who had indication for TEE were assessed by TTE for an evaluation of mitral valve area using planimetry and PHT methods. In addition, LA diameter, ejection fraction (EF), transmitral valve gradient, and TEE were performed for them.

Blood sampling was carried out immediately after TEE, and lipoprotein (a) was measured in one week by the immunoturbidimetric method. The normal value was less than 30 mg/dl for both sexes.

All the patients had the indication of TEE, and no extra expense was imposed on them. All the patients gave us written consent for their blood samples, and all of them were informed that the blood sampling was not relevant to their treatment procedures.

Results

Half of our patients had thrombosis in LA and the other half did not.

Mitral valve area in the case group (with LA thrombosis) and control group (without LA thrombosis) was 1.02±0.20 cm^2 and 1.02±0.26 cm^2, respectively, with no significant statistical difference. Also, there was no statistical difference between the two groups in terms of prothrombin time.

The respective mean age of the control and case groups was 45±11.4 years and 57±9.7 years. There was a significant relationship between the increase in age and thrombus formation (P<0.001). The results were similar in both sexes (P>0.05) (Table 1).

Table 1. Demographic variables*

variables	control group (N=25)	case group (N=25)	p value
Age (y)	45±11.4	57±9.7	<0.001
Sex (M/F)	3/22	6/19	>0.05
LAA velocity	12±2 cm/s	5±3 cm/s	<0.001
Lp(a) serum level	30±6.7 mg/dl	55±2.7 mg/dl	<0.001
LA size	49.3±5.9 mm	56.2±9.0 mm	<0.05

LA, Left Atrium; LAA, Left atrial appendage
* Data are presented as mean±standard deviation

LAA velocity was 5±3 cm/sec and 12±2 cm/sec in the case and control groups, respectively, which indicated a significant relationship between LAA velocity and LA thrombosis. LA size was 49.3±5.9 mm for the control group and 56.2±9 mm for the case group. The relationship between LA thrombosis and LA size was significant P<0.05. The serum level of lipoprotein (a) in the case and control groups was 55±27.5 and 30±6.7 mg/dl, respectively, which revealed a meaningful relationship between Lp(a) serum level and probability of LA thrombus formation (p<0.05).

The echo findings in Spontaneous Echo Contrast (SEC) had a significant relationship with LA thrombosis, which was confirmed by chi-square test (P<0.001) (Table 2).

Table 2. Spontaneous echo contrast (SEC) and left atrial clot relationship

SEC	Status (n)		Total
	Clot+	Clot -	
Mild	1	19	20
Moderate	4	6	10
Severe	20	0	20
Total	25	25	50

Discussion

This study showed that the patient's age, LA size, blood flow velocity in LAA, SEC,[9] and lipoprotein (a) serum level are all the influencing factors on LA thrombosis formation. Regarding the relationship between LA thrombosis with LA size and the patient's age, it can be assumed that an increase in LA size with age will result in an increase in the risk of thrombus formation. Nevertheless, this association has not been confirmed by previous studies.[10]

Lp(a) serum level was higher in our case group (1.8 fld); and although similar findings have been reported elsewhere,[11] further research is required to determine whether it is an independent finding.

SEC also showed a statistical relation with LA thrombosis in the case group, which is again compatible with previous studies.

There was also a significant statistical difference in LA blood velocity between the two groups.

The main conclusion to be drawn is that the measurement of Lp(a) serum level in patients with AF can predict the risk of clot formation and thromboembolization.[12] But whether a reduction in the Lp(a) serum level can prevent the risk of LA thrombus formation needs further studies.[13]

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