ORIGINAL ARTICLE

Relationship between left atrial appendage morphology and thrombus formation in patients with atrial fibrillation and rheumatic mitral valve disease

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Background. **Left atrial appendage (LAA) is the main source for thrombus formation inside the heart in patients with atrial fibrillation (AF). In cases with valvular-AF other than paroxysmal AF it becomes up to 17-fold higher than expected.** ***Objective.*** **To figure out the relationship between LAA thrombus and morphology in patients with mitral valve disease and concomitant AF.** ***Material and methods.*** **We studied 100 cases operated on for mitral valve surgery and LAA resection, between 1998 and 2007. Eighty-three cases had rheumatic etiology. All cases were as long-standing persistent AF.** ***Results.*** **19% had some thrombus inside LAA. Nine (9%) showed preoperative stroke (RR= 19.18, CI 95% from 4.50 to 81.65, p= 0.0001). Morphology was cactus (38%), chicken wing (28%), windsock (18%), and cauliflower (16%). Relative risk for LAA thrombus for cauliflower was 9.37 (CI 95% from 3.69 to 23.80, p < 0.0001), cactus (RR= 0.79, CI 95% from 0.391 to 1.633, p = 0.614), Chicken wing (RR = 0.15, CI 95% from 0.022 to 1.090, p= 0.061), and Windsock (RR = 0.25, CI 95% from 0.035 to 1.769, p= 0.165).** ***Conclusions.*** **The most common LAA type in rheumatic mitral valvular patients with AF was cactus. Relative risk for thrombus formation in LAA was only important to cauliflower, with 9.37-fold higher than expected. More broadly, this could have huge implications for future percutaneous as well as surgical strategies.**

Key words: **Left atrial appendage; Left atrium; Arrhythmia; Atrial fibrillation; Stroke; Thrombus.**

Introducción. **La orejuela izquierda (OI) es la principal fuente embolígena del corazón, especialmente en pacientes con fibrilación auricular (FA), siendo de hasta 17 veces cuando es FA no paroxística de origen valvular.** ***Objetivo.*** **Determinar la relación entre la existencia de trombos en el interior de la OI y la morfología de la misma en los pacientes con enfermedad valvular mitral y FA concomitante.** ***Material y métodos.*** **Se estudiaron en forma retrospectiva 100 pacientes operados de cirugía valvular mitral y resección de la OI, de 1998 a 2007. La etiología fue reumática en 83%. La FA fue persistente de larga evolución en todos los casos.** ***Resultados.*** **19% tuvieron trombo en el interior de la OI. Nueve (9%) tuvieron embolia preoperatoria (RR= 19.18, IC 95% de 4.50 to 81.65, p= 0.0001). La morfología fue cactus (38%), ala de pollo (28%), veleta (18%), y coliflor (16%). El riesgo de trombos en OI para coliflor fue de 9.37 (IC 95% de 3.69 to 23.80, p < 0.0001), cactus (RR= 0.79, IC 95% de 0.391 to 1.633, p = 0.614), ala de pollo (RR = 0.15, IC 95% de 0.022 to 1.090, p= 0.061), y veleta (RR = 0.25, IC 95% de 0.035 to 1.769, p= 0.165).** ***Conclusiones.*** **La morfología mas frecuente de la OI en pacientes con enfermedad mitral y FA fue cactus. El riesgo relativo para desarrollar trombos en su interior fue importante solamente para coliflor, siendo de 9.37 veces mayor. Esto puede tener importancia en la toma de decisiones tanto quirúrgicas como percutáneas.**

Palabras clave: **Aurícula izquierda; Arritmia; Fibrilación Auricular; Embolia; Trombo; Orejuela izquierda.**

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One of the most important troubles in atrial fibrillation (AF) is the stroke, coming from thrombus formation inside the heart. AF is considered a disease which kills through embolism. Broadly speaking, AF causes up to 25% of all strokes. Blackshear et al. [1] showed 17% of patients with non-valvular AF have any thrombus inside the heart. Out of them, up to 91% are coming from the left atrial appendage (LAA). Working in this context, the framework can be divided into three main sections. Viz, AF causes stroke, stroke causes AF, and AF is associated with some other factors predisposing to AF [2]. LAA removal to eliminate the stroke has been postulated all the way back around 1930 and 1950 [3-6]. Blackshear et al. [1] suggested LAA elimination as prophylaxis to drop off the stroke possibility in patients with non-valvu-

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lar AF. Johnson et al. [7] have clearly stressed LAA removal is highly recommended in all cases undergoing open chest surgery, regardless whether or not AF is present. In this setting, 2017 new guidelines for AF surgery coming from Society of Thoracic Surgeons indicates that LAA resection/exclusion is recommended (indication class of recommendation IIa, level of evidence C) in all patients with AF undergoing cardiac surgery [8].

LAA is much more thrombogenic than right atrial appendage. One of the most feasible explanation is that the entrance orifice of the LAA is quite narrow compared to that on the right [9]. In addition, the LAA body is long and narrow, which favors blood stasis inside. Moreover, the blood coming from the pulmonary veins has a more direct flow towards the mitral valve than towards the LAA, which also favors a lack of washing, when compared with the right atrial appendage [9].

Little has been studied regarding the relationship between the morphology of the LAA and the incidence of internal thrombi. In this paper we have studied this relationship, taking as studied material the LAAs that were excised during the course of mitral valve surgery in a series of patients.

MATERIAL AND METHODS

From January 1998 to April 2007, 100 patients with mitral valve disease were operated on. They all had concomitant FA. LAA was fully resected in all of them. Sixty (60%) were female. The age was 57.7 ± 13.5 years-old. The etiology of mitral valve disease was rheumatic in 83%. The preoperative duration of AF was 6.5 ± 2.4 years. The left ventricular ejection fraction was 49.2 ± 6.5%. The pulmonary systolic artery pressure was 55.2 ± 13.9 mm Hg. Eleven patients (11%) had a preoperative ischemic stroke. The size of the left atrium in its largest diameter by transthoracic echocardiography was 6.5 ± 0.7 cm. All preoperative characteristics are shown in **Table 1**.

Surgical technique

In all cases, LAA was removed in the same way, according to surgical technique previously described by the author [10]. Once on cardiopulmonary bypass, with the aorta previously cross-clamped, and during the course of mitral valve surgery, the left atrium was first approached and the mitral valve was explored. At this stage, the approach was changed leaving behind the mitral valve surgery in a temporary stand-by. The heart is twisting while pulling up and out, exposing the back of the pericardial sac. A silk stitch is placed on the pericardial sac at the middle between pulmonary veins and inferior vena cava. Special care is taken into account by proceeding in two stages in order to avoid picking up the esophagus located just behind the pericardium in this area. Once the stitch is placed on, a textile strip of approximately 5 x 30 cm (obtained from a surgical pad) is knotted in the middle part to the pericardial sac. Now, the two ends of this strip are pulled up and towards surgeon's side, forming a "V" shape. Both arms of the "V" support the previously tilted heart, resting on the lateral face of the heart. All the above perfectly exposes the fully LAA including its base. In this way, it is possible to work without excessive manipulation of the LAA, which is often friable and prone to tearing due to excessive handling [10]. LAA was exposed and sectioned using scissors under direct vision from its base, preserving only no more than 1 cm in height as a stump. This stump was closed by means of a Carrell double suture using 3/0 prolene with Teflon pledgets at both ends of the base. The final appearance was of a straight suture line on the outer face of the left atrium. Finally, the textile device was removed and the heart is returned to its original anatomical position to keep continuing with mitral valve surgery in progress.

Special care should be taken to avoid leaving a stump larger than 1 cm in height, since this may be the origin of a blind *cul-de-sac* where thrombi may form after surgery [11]. It is important to emphasize that in all cases the LAA was completely resected under direct vision by this method described here [10].

Statistical analysis

All data obtained in this study were analyzed through the Xlstat (Addinsoft SARL) software for Microsoft Excel®. Univariate analysis was carried out using the Student t test and the Mann-Whitney U test for continuous variables. Categorical variables were subjected to Fisher's exact test. Continuous data are shown as mean and (±) standard deviation. Categorical data are presented as percentage values. A p value < 0.05 was considered statistically significant.

TABLE 1. Preoperative/Intraoperative Characteristics

Sample (cases)	**100**
Age (years)	**57.7 ± 13.4**
Gender M/F (%)	**40/60**
Mitral valve etiology (%)	**100**
Left ventricle ejection fraction (%)	**49.1 ± 6.5**
Pulmonary systolic artery pressure (mm Hg)	**55.1 ± 13.9**
Preoperative stroke (%)	**11**
Preoperative AF (%)	**100**
Preoperative AF duration (years)	**6.5 ± 2.4**
Preoperative left atrial size (cm)*	**6.5 ± 0.7**

** Larger diameter of the left atrium obtained by transthoracic echocardiographic study*

RESULTS

The most important finding in this study was the establishment of frequencies for the different LAA morphologies. In our study herein, we found out that, in this series of mitral patients, preferably of rheumatic origin (83%), the most frequent LAA type was cactus (38%), followed by chicken wing (28%), windsock (18%), and cauliflower (16%) (**Table 2**).

Of the total series, 19% had a thrombus inside the OI. Nine (9%) had preoperative stroke (RR = 19.18, 95% CI from 4.50 to 81.65, p = 0.0001). The relative risk for thrombus formation inside LAA for cauliflower was 9.37 (95% IC from 3.69 to 23.80, p <0.0001), cactus (RR = 0.79, 95% IC from 0.391 to 1.633, p = 0.614), chicken wing (RR = 0.15, 95% IC

TABLE 2. Intraoperative findings

Thrombus in left atrial appendage (%)	**19**
Cauliflower	**11**
Cactus	**06**
Windsock	**01**
Chicken wing	**01**
Morphology of the left atrial appendage (%)	**100**
Cactus	**38**
Chicken wing	**28**
Windsock	**18**
Cauliflower	**16**

from 0.022 to 1.090, p = 0.061), and windsock (RR = 0.25, 95% IC from 0.035 to 1.769, p = 0.165). No postoperative stroke was observed (**Table 3**).

DISCUSSION

Stroke or systemic embolism is the most common complication of AF. Patients with non-valvular AF are up to 5 times more likely to develop a brain embolic event than those in normal sinus rhythm [12], and up to 17 times more with valvular AF [13]. In these patients having AF, LAA is the most common site of thrombi inside the heart. Seventeen percent of the series of non-valvular AF present thrombi in the left atrium, of which up to 91% are located inside LAA [1]. In the case of patients with valvular AF, up to 13% have a thrombus in the left atrium, out 57% of them are located in the LAA with or without extension into left atrium [1]. In a study previously published by the author, in a series of 27 patients with AF underwent mitral valve surgery and LAA resection, postoperative stroke was practically zero [14].

When some comparison is making between both appendages, evidence seems to indicate that the LAA is infinitely superior to the right atrial appendage in terms of the thrombogenic formation in patients with any type of AF. The LAA morphology has much to do, and is perhaps the most definitive element. The LAA has a long body, narrow base, and sometimes multilobed. Contrastingly, the right atrial appendage has a wider base and small body, as well as smaller in extension than the LAA. All this means that LAA has a much greater thrombogenic power than the right atrial appendage in patients with AF [15].

As we have studied the possibility of treating AF exclusively by closing the LAA in high-risk patients for long-term oral anticoagulation, knowledge about the LAA morphology has been growing up. Several imaging techniques have highlighted the different LAA types. According to the morphology cited by Di Biase et al. [16], they reported as follows: 48% for chicken wing, 30% cactus, 19% weather windsock, and 3% cauliflower. In contrast, we figured out that the LAA morphology was cactus (38%), chicken wing (28%), windsock (18%), and cauliflower (16%). In our patients with rheumatic mitral valve disease and concomitant long-standing AF, cactus morphology was the most frequent. It is worth stressing that in our study the identification of the morphology was made under direct vision by two or more independent observers, while in the study by Di Biase it was made by imaging. Moreover, Di Biase et al. [16] found a relative risk for stroke of 8.0 for cauliflower, and practically zero for chicken wing. We had a relative risk of thrombi in LAA for cauliflower of 9.37 (95% IC from 3.69 to 23.80, p <0.0001), with a very important statistical significance with respect to the other morphologies [cactus (RR = 0.79, 95% IC of 0.391 to 1633, p = 0.614), chicken wing (RR = 0.15, 95% IC 0.022 to 1.090, p = 0.061), and windsock (RR = 0.25, 95% IC 0.035 to 1.769, p = 0.165)]. If we assume that stroke risk is directly linked to thrombus formation inside LAA, then shall we say that, despite the difference in morphology, the relative risk for thrombus formation in LAA is very similar in both studies, being larger for cauliflower, and almost zero for chicken wing.

To the best of our knowledge, there is no previous study in rheumatic mitral valve patients with AF, emphasizing the morphology of the LAA. This our study is the first focused on this particular issue.

To what extent the resection or exclusion of the OI as a measure of prophylaxis for the stroke, is a subject still under discussion. One of the best sources in this regard is located in a series of patients undergoing the Cox-maze procedure to eliminate AF. This procedure is designed to eliminate any type of FA or flutter. It was performed for the first time in humans in 1987 [17], and subsequently modified over the years, until reaching its current evolutionary state [18,19]. As part of the surgical technique, the Cox-maze procedure involves the resection of the LAA [20]. It is a well-recognized fact that the Cox-maze procedure has the lowest rate of perioperative stroke in cardiac surgery. In practice, the long-term postoperative stroke rate is comparable to the risk of stroke in the general population, indicating that this procedure eliminates the risk of stroke associated with AF [21]. Certainly, much of this success is due to the high rate of sinus rhythm conversion after the maze, accepting at least a rate of sinus rhythm conversion greater than 70% at 1-year follow-up [22]. However, another part of the success is related to the elimination of the LAA as part of the surgical technique. Cox et al. [23] reported only two cases of perioperative stroke among 306 cases (0.7%), and only one case among 265 patients operated on in

TABLE 3. Relative risk for thrombosis according to the left atrial appendage morphology

MORPHOLOGY	RELATIVE RISK (RR; CI)*	P VALUE
Cauliflower	**9.37; CI 95% from 3.69 to 23.80**	**< 0.0001**
Cactus	**0.79; CI 95% from 0.391 to 1.633**	**0.614**
Windsock	**0.25; CI 95% from 0.035 to 1.769**	**0.165**
Chicken wing	**0.15; CI 95% from 0.022 to 1.090**	**0.061**

** CI: Confidence interval.*

a follow-up at 11.5 years. We have also studied this phenomenon in a much more direct way through a series of 27 patients undergoing surgery for rheumatic mitral valve disease and long-standing concomitant AF. For several reasons, only the LAA resection was performed as a complementary procedure to mitral valve surgery. In no case the Cox-maze procedure was performed. As expected, the rate of conversion to sinus rhythm was quite low (14.8%). However, although oral anticoagulation with warfarin was only carried out for the first 3 months after surgery, there was no case for stroke in an 18 months-follow-up. Medication used after stopping warfarin was only based on aspirin [14]. This study makes very clear the extent to which the single LAA resection can be a prophylactic step for thrombus formation and stroke in patients with AF [14]. At the same time, in this series of 100 cases for LAA removal presented in this article, there was no case for postoperative stroke.

There are several studies indicating the importance of the surgical technique to eliminate LAA, and its relationship with the subsequent thrombus formation [11]. Removal of the LAA can be performed by two ways, briefly speaking: resection (cut-and-sew), and exclusion. Based on the findings of Kanderian et al [24], the best technique with maximum safety in terms of effectiveness, absence of endoleaks, reopening, etc., is resection by means of section-and-suture from outside the heart under direct vision. The exclusion of the LAA can be done by internal continuous suture, internal purse-string suture, external ligature, or by stapler. In the exclusion, the LAA remains in situ connected to the left atrium as isolated from the main bloodstream. According to this study by Kanderian et al [24], a patent LAA was observed in 5.8% of cases (0% excision, 8% exclusion suture, and 58% stapler exclusion), remnant LAA (stump more than 1 cm in height) 20% (excision with cut-and-sew 27%, internal suture exclusion 8%, and exclusion with stapler 58%), excluded LAA but with persistent flow inside 34% (surgical excision 0%, exclusion with suture 61%, exclusion with stapler 58%), successful closure 40% (surgical excision 73%, exclusion suture 23%, exclusion with stapler 0%). Of particular importance in the exclusion suture group was 61% persistent flow, and the stapler group with residual stump greater than 1 cm (58%). Partially closed LAA is more likely to cause internal thrombosis due to increased blood stasis. Arnaya et al. [25] have studied the association between incomplete ligation or closure of the LAA and the rate for stroke or embolism. In a series of 72 patients, those with stroke had a smaller neck of the remaining or persistent LAA than those without stroke (2.8 ± 1.0 vs 7.1 ± 2.1 mm, p = 0.002). In this context, the risk of embolism was 6.5% per year, increased to 14.4% when oral anticoagulation was not administered, and increased up to 19% per year in those cases with a neck diameter ≤5 mm. The possibility of stroke was 5-fold increased more than expected.

Due to these findings, we prefer to perform resection with a cut (section with scissors) and-suture of the LAA, from outside the heart, under direct vision. In this way, the possibility of complications is reduced only to the possible preservation of a stump of more than 1 cm to 27% [24]. We have observed that, when the cut is made from outside the heart, under direct vision, using scissors, leaving no more than 1 cm of tissue between the base of implantation of the LAA and the level of the surgical cut, after closing by double Carrel suture with prolene 3/0 with large needle, the possibility of a residual stump is almost null.

Through this study we have been able to know the frequency of the different morphologies of the LAA in patients with valvular AF, and the relative risk for thrombus formation according to any particular morphology. The relative risk of almost zero for thrombus formation for the chicken wing shape is striking. The same finding was repeated in the study by Di Biase [16]. It is possible that some of the observations derived from this study could be translated to the field of structural interventional cardiology.

It should be pointed out that there is no previous study in rheumatic mitral patients with AF, emphasizing the morphology of the LAA. This our study is the first one focused on this particular item.

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