

# Comparison between patients with atrial fibrillation in cardiac surgery with and without left atrial appendage excision

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**Background.** Atrial fibrillation is the most common arrhythmia in patients older than 40 years-old, and it significantly increases the risk of stroke. In patients with atrial fibrillation, the left atrial appendage excision during cardiac surgery is one of the suggested surgical procedures to avoid thrombus formation and risk of systemic embolization. **Objective.** To determine prevalence of stroke after cardiac surgery with or without left atrial appendage excision in patients with atrial fibrillation. **Material.** Thirty-one patients with atrial fibrillation underwent cardiac surgery from January, 2020 and July, 2021 were included. They were divided into two study groups, with and without left atrial appendage excision. Relevant variables between groups were: Postoperative major bleeding, stroke and death. Results were analyzed by descriptive statistics, X<sup>2</sup> and Student's t-distribution. **Results.** Ten patients were included in the excision group and 21 in non-excision group. The indications for cardiac surgery were mainly valvular surgery, especially mitral valve operations. Two patients without left atrial appendage excision (9.5%) developed stroke, but none of the patients in the excision group ( $p=0.320$ ). Patients with excision developed more events such as postoperative major bleeding and mortality, though without statistically significant difference. **Conclusions.** There was no statistically significant difference regarding occurrence of stroke in patients with atrial fibrillation undergoing cardiac surgery with or without left atrial appendage excision. A limitation of this study is the small sample size; therefore, we recommend to continue this study including a mayor number of patients.

**Key words:** Atrial fibrillation; Left atrial appendage, excision, resection; Stroke.

**Antecedentes.** La fibrilación auricular es la arritmia más común en pacientes mayores de 40 años, y aumenta significativamente el riesgo de accidentes cerebro-vasculares. Una alternativa quirúrgica para evitar eventos tromboticos y accidente cerebro-vascular es la escisión de orejuela izquierda durante cirugía cardiaca en pacientes con fibrilación auricular. **Objetivo.** Determinar la prevalencia del accidente cerebro-vascular posterior a cirugía cardiaca con o sin escisión de orejuela izquierda en pacientes con fibrilación auricular. **Material.** Se incluyeron 31 pacientes con fibrilación-auricular sometidos a cirugía cardiaca durante el periodo comprendido entre enero del 2020 y julio del 2021. Se dividieron en dos grupos, con y sin escisión de orejuela izquierda. Las variables relevantes entre grupos fueron: sangrado posquirúrgico, accidente cerebro-vascular y muerte. Los resultados se analizaron mediante estadística descriptiva, X<sup>2</sup> y T de student. **Resultados.** Diez pacientes se incluyeron en el grupo de escisión y 21 sin escisión de orejuela izquierda. Las indicaciones para cirugía fueron principalmente cirugía valvular, predominantemente mitral. Presentaron accidente cerebro-vascular 2 pacientes (9.5%) que no fueron sometidos a escisión de orejuela izquierda, pero ningún paciente con escisión de orejuela izquierda ( $p = 0.320$ ). Los pacientes con escisión de orejuela izquierda presentaron mas eventos de sangrado postquirúrgico y mortalidad, aunque sin diferencia estadísticamente significativa. **Conclusiones.** No hubo diferencia significativa con respecto a accidente cerebro-vascular en pacientes con fibrilación auricular sometidos a cirugía cardiaca con y sin escisión de orejuela izquierda. Una limitación de este estudio es la cantidad de pacientes. Por lo tanto, sugerimos continuar este estudio con mayor número de pacientes.

**Palabras clave:** Fibrilación auricular; Orejuela izquierda, escisión, resección; Accidente embólico vascular cerebral.

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Atrial fibrillation (AF), is the most common arrhythmia in population older than 40 years; these patients have 5 times more risk of developing stroke, mainly

consistent in thromboembolic events due to blood flow anomalies related with left atrium stasis [1]. Clinical and diagnostic evidence show that at least 70% of all events of stroke in patients with atrial fibrillation have a cardioembolic cause, originated in the left atrium of which 90% are specifically formed in the left atrial appendage (LAA). This fact has been evidenced by echocardiographic reports and necropsy studies [2,3].

It is important to mention the involvement of thrombin in cardiovascular disease and in inflammatory phenomena associated with systemic atherosclerosis, coagulation disorders, platelet activation increase and formation of atherosclerotic plaques in the aortic root. All these previous elements induce a pro-coagulant status increasing the probability of developing embolism and thrombus sources in addition to LAA, aorta, right ventricle and brain vessels [4]. These previous situations derived in the interest of LAA management by occluding it either with mechanical devices or with interventional procedures [4,5].

Left atrial appendage excision (LAAE) by means of cut and sew is one additional procedure performed in some patients with AF submitted to cardiac surgery. Nevertheless, it is not a standard procedure because there are studies indicating LAAE has no clear benefit [7,8].

It has been demonstrated in a clinical trial that in patients with AF, synergy of oral anticoagulants administration in combination with LAAE, the risk of developing major adverse cardiovascular events is significantly reduced up to 30% of all cases [9].

## MATERIAL

With the previous approval of local committee of ethics and local research, a retrospective review was performed with clinical records of patients with AF who underwent cardiac surgery in the period between January 2020 and July 2021 in our institution.

Patient groups were divided for their analysis: those submitted to cardiac surgery with LAAE and those without LAAE. The variables studied were: age, gender, chronic, preoperative left ventricle ejection fraction (LVEF), pre and postoperative use of oral anticoagulants, performed cardiac surgery and complications such as major postoperative bleeding, stroke and death.

We utilized descriptive statistics (absolute numbers and percentages) and median with standard deviation. In order to compare groups X2 was used for qualitative variables and Student's t-distribution for quantitative variables, taking in consideration  $p \leq 0.05$  as statistical significance.

## RESULTS

Thirty-one patients were included obtaining a median of age of  $59.5 \pm 10$  years, from which 18 (58%) were females, and 13 (42%) males. Regarding to comorbidities, 11 (35.4%) had type 2 diabetes mellitus, 24 (77.4%) systemic arterial hypertension, 10 (32.2%) obesity, 5 (16.1%) hypercholesterolemia, 3 (9.6%) venous insufficiency. Median preoperative LVEF was  $51 \pm 11\%$ . Preoperative oral anticoagulants were present in 15 (48.3%), and postoperative in 23 (74.5%). Six patients (19.3%) were also receiving antiplatelet drugs. Primary cardiac surgery indication was 2 (6.4%) coronary artery bypass grafting, 4 (12.9%) surgical aortic valve replacement, 14 (45%) surgical mitral valve replacement, 1 (3.2%) surgical tricuspid valve replacement; 10 (32.2%) underwent two or more simultaneous cardiac procedures. Postoperative major bleeding occurred in 6 patients (19.3%), stroke in 2 (6.4%), and death in 3 (9.6%). (Table 1).

A comparison between clinical features and evolution in patients with AF who underwent cardiac surgery with LAAE (n=10) and without LAAE (n=21) was made. Median age was  $59 \pm 8.9$  years  $60 \pm 13$  years, respectively ( $p=0.567$ ). In this sample, female gender predominated, without statistical difference between groups ( $p=0.589$ ). In relationship with comorbidities, type 2 diabetes mellitus were present in 6 patients (60%), systemic arterial hypertension in 9 (90%), obesity in 3 (30%), hypercholesterolemia in 2 (20%), venous insufficiency in 1 (10%) in patients with LAAE; in patients without LAAE (23.8%) had type 2 diabetes mellitus, 15 (71.4%) systemic arterial hypertension, 7 (33.3%) obesity, 3 (14.2%) hypercholesterolemia, 2 (9.5%) venous insufficiency, without statistical difference between both groups.

Patients with LAAE that used preoperative oral anticoagulants were 2 (20%), antiplatelet drugs 2 (20%); and those without LAAE, 11 (52%) were using preoperative oral anticoagulants, and 4 (19%) were using preoperative antiplatelet drugs ( $p=0.525$  and  $p=0.950$ , respectively). Postoperative oral anticoagulants were indicated in 2 (20%) of the patients submitted to LAAE in contrast with 21 (100%) of those who were not submitted to LAAE ( $p=0.000$ ).

Surgeries performed in patients with LAAE were: 1 (10%) surgical aortic valve replacement, 6 (60%) surgical mitral valve replacement, and in 3 (30%) there were performed more than one simultaneous procedure, while in patients without LAAE 2 (9.5%) underwent coronary artery bypass grafting, 3 (14.2%) surgical aortic valve replacement, 8 (38%) surgical mitral valve replacement, 1 (4.7%) surgical tricuspid valve replacement, 7 (33.3%) two or more simultaneous cardiac procedures ( $p=0.686$ ). Major postoperative bleeding developed in 4 (40%) of patients with LAAE and in 2 (9.5%) without LAAE [ $p=0.048$  (odds ratio, 6.3; confidence interval 95%, 0.7-69)]. In postoperative evolution, 2 patients without LAAE developed stroke (9.5%), but none with LAAE developed this event ( $p=0.320$ ). Two (20%) of the patients with LAAE died, in contrast with one patient (4.7%) without LAAE ( $p=0.186$ ). (Table 2).

**Table 1. Clinical features and evolution of 31 patients with atrial fibrillation submitted to cardiac surgery.**

| VARIABLE                             | N = 31     |
|--------------------------------------|------------|
| Age (years)                          | 59.5 ± 10  |
| Gender                               | 18 (58%)   |
| Female                               | 13 (42%)   |
| Male                                 |            |
| Type 2 Diabetes mellitus             | 11 (35.4%) |
| Systemic arterial hypertension       | 24 (77.4%) |
| Obesity                              | 10 (32.2%) |
| Hypercholesterolemia                 | 5 (16%)    |
| Venous insufficiency                 | 3 (9.6%)   |
| LVEF* (%)                            | 51 ± 11    |
| Preoperative oral anticoagulation    | 15 (48.3%) |
| Postoperative oral anticoagulation   | 23 (74.2%) |
| Preoperative antiplatelet therapy    | 6 (19.3%)  |
| Cardiac surgery performed            |            |
| Coronary artery bypass grafting      | 2 (6.4%)   |
| Surgical aortic valve replacement    | 4 (12.9%)  |
| Surgical mitral valve replacement    | 14 (45.1%) |
| Surgical tricuspid valve replacement | 1 (3.2%)   |
| Two or more simultaneous procedures  | 10 (32.2%) |
| Major postoperative bleeding         | 6 (19.3%)  |
| Stroke                               | 2 (6.4%)   |
| Mortality                            | 3 (9.6%)   |

\* LVEF: Left ventricle ejection fraction. Values expressed in absolute numbers and percentages.

## DISCUSSION

Atrial fibrillation is the most common arrhythmia in people older than 40 years and it has been strongly related to the risk of stroke. This is why it has been important to decrease this risk by using prophylactic drugs, interventional procedures or surgery [10]. Pharmacological therapy as prophylaxis in stroke consists in the administration of oral anticoagulants [11]. In surgical field, LAEE is performed mainly as a concomitant procedure in cardiac surgery. Nevertheless, this procedure has not an absolute indication to be performed systematically, due to a discrepancy in clinical trials and case reports that analyze the possible benefit of this procedure in order to avoid stroke [13]. Our research study had the main objective of inquire whether left atrial appendage excision (additional to the main indicated cardiac surgery and associated with postoperative oral anticoagulants administration) has a significant impact by decreasing the risk of stroke.

Comorbidities also play an important role in this regard. In Mexico, there has been an increase of people with systemic arterial hypertension, type 2 diabetes mellitus and obesity in recent decades. In a research study that included 33,366 Mexican adults older than 20 years it was shown that 43.2% had systemic arterial hypertension, and there was correlation among systemic arterial hypertension, body mass index, obesity and previous diagnosis of type 2 diabetes mellitus and hypercholesterolemia [14]. In other research study performed in 1,040 Mexican patients who

had stroke, it was possible to demonstrate that the main risk factors were systemic arterial hypertension, obesity and diabetes, and 18% were associated with cardioembolism [15]. Therefore, it is rational to expect that more than 77% of our patients with AF had also systemic arterial hypertension and one third had diabetes and obesity, which increase the risk of stroke.

In a study of 28,044 patients with AF, the clinical behavior in patients receiving warfarin and antiplatelet drugs therapy was analyzed; the risk of developing stroke was found in 64% and 22%, respectively. Therefore, we can conclude that warfarin therapy is more effective to reduce the risk of stroke. However, the risk of intracranial hemorrhage with the use of anticoagulant/antiplatelet therapy should always be considered. Hence, it is important to monitor the attachment of the patients to this therapy, so the risk of hemorrhage can be diminished [16]. In this series of cases, almost the half of patients were receiving anticoagulant therapy before cardiac surgery. Also, more than 70% of them received oral anticoagulants and about 20% antiplatelet drugs in the postoperative period.

There is still a debate whether or not LAEE should be performed in a prophylactic way in all patients submitted to cardiac surgery to avoid risk of stroke. Nevertheless, in patients with AF who will be submitted to coronary artery bypass grafting, aortic

**Table 2. Comparison between clinical features and evolution of patients with atrial fibrillation submitted to cardiac surgery with and without left atrial appendage excision.**

| VARIABLE                                     | With LAEE (n=10) | Without LAEE (n=21) | P value |
|--|------------------|---------------------|---------|
| Median Age (years) ± Standard deviation      | 59 ± 8.9         | 60 ± 13             | 0.567   |
| Gender                                       |                  |                     |         |
| Female                                       | 7 (70%)          | 11 (52%)            | 0.589   |
| Male   | 3 (30%)          | 10 (48%)            |         |
| Type 2 Diabetes mellitus                     | 6 (60%)          | 5 (23.8%)           | 0.052   |
| Systemic arterial hypertension               | 9(90%)           | 15 (71.4%)          | 0.255   |
| Obesity                                      | 3(30%)           | 7 (33.3%)           | 0.855   |
| Hypercholesterolemia                         | 2(20%)           | 3 (14.2%)           | 0.690   |
| Venous insufficiency                         | 1(10%)           | 2 (9.5%)            | 0.967   |
| LVEF (%)                                     | 52 ± 13          | 49 ± 9.9            | 0.367   |
| Preoperative oral anticoagulation            | 4 (40%)          | 11 (52%)            | 0.525   |
| Postoperative oral anticoagulation           | 2 (20%)          | 21 (100%)           | 0.000   |
| Preoperative antiplatelet therapy            | 2 (20%)          | 4 (19%)             | 0.950   |
| Cardiac surgery performed                    |                  |                     |         |
| Coronary artery bypass grafting              | 0                | 2 (9.5%)            |         |
| Surgical aortic valve replacement            | 1 (10%)          | 3 (14.2%)           |         |
| Surgical mitral valve replacement            | 6 (60%)          | 8 (38%)             | 0.686   |
| Surgical tricuspid valve replacement         | 0                | 1 (4.7%)            |         |
| Two or more simultaneous procedures          | 3 (30%)          | 7 (33.3%)           |         |
| Reoperation for major postoperative bleeding | 4 (40%)          | 2 (9.5%)            | 0.048   |
| Stroke                                       | 0                | 2 (9.5%)            | 0.320   |
| Mortality                                    | 2 (20%)          | 1 (4.7%)            | 0.186   |

LAEE: Left atrial appendage excision. LVEF: Left ventricle ejection fraction. Values expressed in absolute numbers and percentages. X2, statistical significance p < 0.05.

or mitral valve replacement, LAEE could be potentially beneficial. It is important to mention that external resection and suture is the method that assures success in this procedure given that other surgical could course with a residual communication between left atrial appendage and left atrium [17]. All of the patients included in our research study had AF, and they were submitted to several cardiac surgery procedures, mainly mitral valve surgery. Out of all 31 patients in this study, only 10 (32.2%) underwent LAEE, since this is not a systematic procedure in our hospital. However, in recent years there has been more statistical evidence in favor of LAEE in patients with AF [9,18,19]. Surgical treatment of AF was first performed in 1987 by Cox et al. known as Cox-maze procedure I [20], and later improved in a definite way as Cox-maze III [21]. This technique is characterized by being a “cut and sew” procedure. To highlight, LAEE is part of this surgical procedure. However, due to its technical complexity, the procedure has not gained worldwide acceptance in real life. Therefore, simpler alternatives have been proposed in order to overcome technical difficulties of this surgery, such as Cox-maze IV procedure. The Society of Thoracic Surgeons has developed their own guidelines for the management of surgical ablation for AF patients [10]. Even so, current trends in surgical ablation for AF in USA indicates that less than 50% underwent surgical ablation [22].

LAEE is a simpler surgical procedure, that could take only few additional minutes during cardiac surgery. Current clinical guidelines recommend that isolated AF surgery (in absence of an underlying cardiac disease) should only be performed in specific cases: symptomatic refractory patients or intolerant to antiarrhythmic drugs, failed interventional ablation, or that the patient prefers a surgical procedure. Nonetheless, in patients in which cardiac surgery is already indicated for another cause, LAEE is recommended [10,18].

Previous clinical experience suggests that traditional techniques of LAEE could be ineffective due to left atrium recanalization. Therefore, excision should be performed in order to avoid a cul-de-sac mechanism [23]. A meta-analysis analyzed 7 studies including 3,653 patients (1,716 with LAEE and 1,937 without LAEE), and it was found that incidence in stroke was lower in patients with LAEE compared with those ones without LAEE, while major bleeding and need of reintervention were similar between groups [19].

LAAOS (Left Atrial Appendage Occlusion Study) III clinical trial included 4,770 patients with AF that underwent cardiac surgery comparing patients with LAEE (N=2379) and patients without LAEE (N=2391). Stroke and systemic embolism occurred in 114 patients (4.8%) in LAEE group and in 168 (7%) without LAEE group, with statistically significant difference [9]. In our series, we observed two events of stroke in patients without LAEE, and no cases with LAEE; however, because of the

small sample we could not find statistically significant difference. Need for reintervention because of major postoperative bleeding was more frequent in patients with LAEE and mortality too, though without statistically significant difference.

In our research study, there were three deaths: one of them was discharged from hospital but came back to hospitalization 3 months later complicated with empyema and died with septic shock, another patient underwent cardiac surgery with cardiopulmonary bypass time of 300 minutes due to a failed mitral valve repair that required biological mitral valve replacement and died in postoperative period by vasoplegic shock, and the other patient developed acute kidney failure and died in the postoperative period. None of the patients developed stroke. Therefore, we cannot attribute their mortality to this complication.

This is a retrospective observational study in which information about 31 patients with AF that underwent cardiac surgery with and without LAEE was collected. This additional procedure was performed according to each cardiac surgeon's judgement. Despite stroke occurred in 2 patients without LAEE and none in patients with LAEE, statistically significant difference was not found due to the small number of patients, given that in larger research studies it does have been possible to document the benefit of to diminish the risk of stroke in patients with AF submitted to cardiac surgery.

Regarding the increased requirement of reintervention because of major postoperative bleeding in patients with LAEE, it is convenient to analyze the technical features of surgical procedures and consider an opportunity area in this matter to improve the results and avoid this complication that prolong hospital stay and endanger the patient's life. One of the main limitations in this research study is the small number of patients.

As a conclusion, there was not statistically significant difference in evolution of patients with AF submitted to cardiac surgery with LAEE compared to surgery without LAEE in relation to frequency of stroke. There were more postoperative major bleeding events in those patients with LAEE, and the mortality in this group was also higher, although without statistically significant difference. One of the main limitations of this research study is the small sample of cases analyzed. Hence, we suggest to continue this study to include a larger number of patients, preferably in a prospective way and with longer follow-up.

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