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Original Article

Cardiac Myxomas: A single center experience and ten-years follow up

Essam Elbadry Hashim Mohamed, Ayman Mohamed Mohamed Abdel Ghaffar, Khaled Mohamed Abdelaal, Abdelrahman Adel Abdelaziz Elsayed, Mohamed AW Ezzat, Ahmed Roshdi Hamed Ahmed

Faculty of Medicine and University Hospital, Sohag University, Sohag, Egypt

Abstract

Background: Cardiac myxoma is a benign tumor that carries the risk of embolization and obstruction of the blood flow. The ideal surgical approach is still debatable. We present our experience in the surgical treatment of cardiac myxomas and its ideal surgical approach.

Methods: We retrospectively analyzed the data for all patients who underwent surgical excision of cardiac myxoma at our institution over 11 years starting from January 2006 to December 2016. Descriptive statistics were used to present preoperative, operative and postoperative data and Kaplan Meier curve to plot long-term survival.

Results: Twenty-one patients had surgical excision of a primary, single and sporadic cardiac myxoma. Thirteen patients (62 %) were females, and the mean age at operation was 55.2 years (range: 28 – 71 years). The location of myxomas was in the left atrium in 17 patients (81%) and right atrium in 4 patients (19 %). Dyspnea was the main presenting symptom (71.4%) followed by constitutional symptoms (28%), palpitations (23.8%), syncope (14.2%) and stroke (14.2%). A right atrial trans-septal incision was used in 76.5% of left atrial myxoma cases. Five patients had concomitant operative procedures (coronary artery bypass grafting (n=2), tricuspid valve repair (n=1), mitral valve replacement (n=1) and bullectomy (n=1)). Postoperative complications were reported in six patients (28.6%) (supraventricular arrhythmia (n=2), temporary conduction deficit (n=2), pulmonary atelectasis (n=1), and postoperative bleeding (n=1)). Early postoperative mortality occurred in one patient (4.76 %), and there were no late deaths related to myxoma.

Conclusion: Surgical treatment of cardiac myxoma is safe with low morbidity and mortality. The right atrial trans-septal incision is the recommended surgical approach.

KEYWORDS
Cardiac myxoma; Cardiac tumors, Sudden death, Bi-atrial approach, right atrial trans-septal incision

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Corresponding author: Essam Mohamed essam_hashem@med.sohag.edu.eg

Introduction

Cardiac myxoma is the most common benign cardiac tumor [1]. Approximately 75% to 80% of myxomas are located in the left atrium (LA), 10% to 20% are in the right atrium (RA), and from 2% to 4% in the ventricles [2]. Multicentric myxoma was reported more commonly in familial variety with autosomal dominant inheritance [1]. Myxomas occur more frequently in females, and all age groups are affected; however, they present more likely between the third and sixth decades of life [3]. Although myxomas are benign, they carry the risk of systemic embolization with subsequent cerebral or peripheral infarctions, intra-cardiac obstructions, syncope, and sudden death; therefore, once the diagnosis is established, immediate surgical resection is recommended [4]. There is a debate about the best surgical approach to intra-cardiac myxoma [5]. In this study, we present our clinical experience in the diagnosis and surgical treatment of cardiac myxomas over 10 years. Different surgical approaches were discussed to elucidate their impact on surgical outcomes.

Patients and Methods:

Study design and population:

This retrospective cohort study was conducted at our tertiary referral university hospital. All cardiac myxoma patients who underwent an operation at our Cardiothoracic Surgery Department in the period from January 2006 to December 2016 were enrolled in the study. Complete data of those patients were extracted from the department database after approval of the Ethical Committee of the University, and patients' consent was waived due to the retrospective nature of the study. The preoperative, operative and postoperative details were collected and analyzed.

Preoperative data:

Preoperative data included age, sex, main complaint, other symptoms, the time interval from the onset of symptoms to diagnosis and family history of cardiac tumors. Preoperative diagnosis was established in all patients by echocardiography (Figure 1). Preoperative coronary angiography was performed in patients older than 40 years and younger patients when suspecting coronary artery disease. Once the diagnosis of cardiac myxoma was confirmed, the patients were referred for urgent surgery.

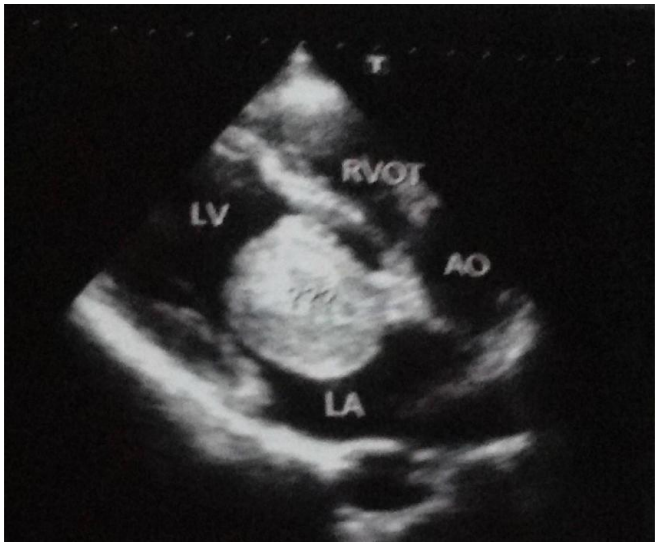

Figure 1: Trans-thoracic echocardiography of left atrial myxoma. AO: Aorta, LA: left atrium, LV: left ventricle, RVOT: Right ventricular outflow tract.

Operative data:

The tumor site, size, gross picture, attachment details, defects created, and its repair, operative events, and concomitant operative procedures were reported. All patients were operated upon through median sternotomy. Cardiopulmonary bypass was initiated using aortic and bi-caval cannulation, and moderate hypothermia was used in all patients. After aortic cross-clamp, antegrade cold blood cardioplegia was infused. Intra-operative trans-esophageal echocardiography was done routinely in all cases by anesthesiologists to evaluate the valve function after resection of the tumor and to exclude any residual lesion. The heart was not manipulated until the aorta had been cross-clamped to avoid tumor fragmentation and systemic embolization. In case of right atrial myxoma and left atrial myxoma with a shunt, pulmonary artery was included in the aortic cross-clamp to avoid pulmonary embolization. The surgical approach for left atrial myxoma was either through left atriotomy or bi-atriotomy (LA+RA) or right atrial trans-septal approach (RA+TS) (Figure 2), right atriotomy was used for right atrial myxoma (Figure 3). To avoid the recurrence of the tumor, the resection was complete with full thickness

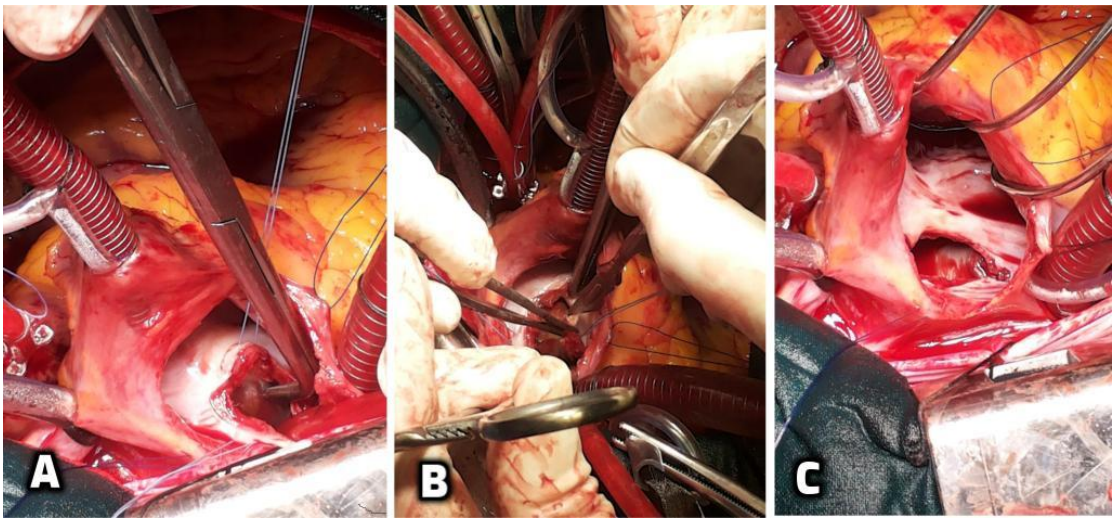

Figure 2: (A, B, C) Illustration of the excision of left atrial myxoma through a right atrial trans-septal approach

removal of the attachment of the base even if it is attached to the valve leaflets. The surgically created defect was sutured directly or repaired with an autologous pericardial patch. After excision of the tumor, the related heart chambers were irrigated by copious cold saline and suctioned by using high-speed wall suction to eliminate any loose tumor fragments that might have been dislodged during manipulation and removal of the tumor. All the removed myxomas were subjected to histopathological examination (Figure 4).

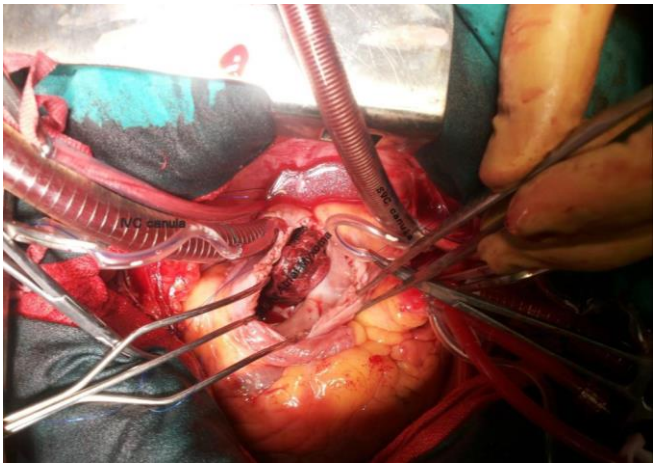

Figure 3: Excision of right atrial myxoma through right atriotomy incision. IVC: Inferior vena cave, SVC: Superior vena cava

Postoperative care:

Early postoperative all-cause morbidities and mortalities were reported. The follow-up time ranged from 5 to 120 months, and it was complete for 75% of cases at five years and 70% at ten years. Complete follow up was available for 14 patients of the operative survivors, while six patients were lost to follow up.

Statistical analysis:

Statistical analyses were conducted using the SPSS (Version 20) statistical software for Windows (IBM Corporation, Chicago, IL, USA). The data were presented as mean ± standard deviation or range for continuous variables and as numbers with percentages for categorical variables. The long-term cumulative survival analysis was plotted using the Kaplan-Meier curve.

Results

Twenty-one patients with primary cardiac myxomas were operated upon at our department during the period from January 2006 to December 2016. Thirteen patients (62%) were females, and eight patients (38%) were males. The mean age was 55.2 years (age ranged between 28 and 71 years). Ten patients (48%) were in the age group 51-60 years, and four patients (19 %) were in the age group 61-70 years. Seventeen (81%) myxomas were in the left atrium and four (19 %) located in the right atrium. The duration elapsed from the onset of symptoms to the diagnosis ranged from 1 to 8 months.

Dyspnea was the main presenting symptom (71.4%) followed by constitutional symptoms (generalized fatigue, fever, and weight loss) (28%), palpitations (23.8%), syncope (14.2%) and stroke (14.2%). Peripheral embolism, chest pain, and lower limb edema were presented equally

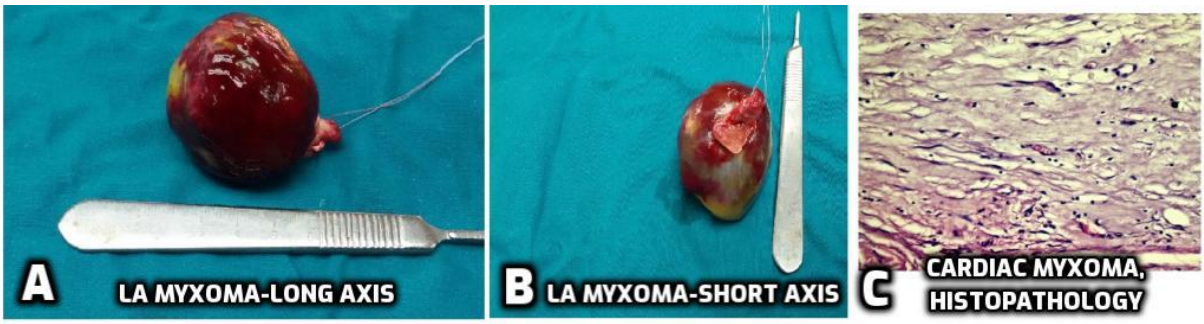

Figure 4: Gross (A, B) and microscopic picture (C) of excised left atrial myxoma

(4.76%). One patient presented by cardiogenic shock (4.76%) (Table 1).

None of the patients had a family history of myxoma. Eighteen patients (85.7%) had preoperative coronary angiography; two of them had a significant coronary artery disease and had coronary artery bypass grafting (CABG) as a concomitant procedure to myxoma resection. Sixteen out of the seventeen left atrial myxoma (94%) originated from the inter-atrial septum and one (6%) from the posterior leaflet of mitral valve.

Table 1: Demographic data and symptoms of myxoma patients. (n is the number of cases)

Total number (n= 21)			
Sex	Females	n= 13	61.90%
	Males	n= 8	38.10%
Age	Range (Years)	28.71	
	Mean age (Years)	55.2	
	20 – 30	n= 1	4.76%
	31 – 40	n= 2	9.52%
	41 – 50	n= 3	14.20%
	51 – 60	n= 10	48.0%
	61 – 70	n= 4	19.0%
	71 – 80	n= 1	4.76%
Symptoms	Dysnea	n= 15	71.40%
	Syncope	n= 3	14.20%
	Palpitation	n= 5	23.80%
	Lower limb edema	n= 1	4.76%
	Chest pain	n= 1	4.76%
	Stroke	n= 3	14.20%
	Peripheral embolism	n= 1	4.76%
	Constitutional symptoms	n= 6	28.0%
	Cardiogenic shock	n= 1	4.76%

All right atrial myxomas (100%) originated from the inter-atrial septum. After complete excision of myxomas; a pericardial patch was used to close the resulting septal defect.

Four patients with left atrial myxoma resection had concomitant procedures, 2 had CABG, one had mitral valve replacement (MVR), and one had stapler resection of emphysematous bulla of the right upper lung lobe. One case of right atrial myxoma resection had concomitant tricuspid valve repair using De-Vega annuloplasty.

The size of the excised tumors ranged from 1.5 × 2.5 cm to 5 × 7 cm. The gross appearance of the tumor was a soft, gelatinous, sessile or pedunculated mass with either a villous or smooth surface. Histopathological examination confirmed the diagnosis of myxoma in all patients.

Six patients (28.6%) had postoperative complications; supraventricular arrhythmia in 2 patients who were controlled medically, temporary conduction deficit which was managed by temporary pacing in 2 patients, pulmonary atelectasis in one patient who was managed by bronchoscopy, and postoperative bleeding in one patient who needed re-exploration.

Fourteen patients were in NYHA class I (66.7%) postoperatively compared to ten patients (47.6%) in NYHA class III preoperatively. Early postoperative mortality (defined as death occurring within 30 days of operation) was reported in one patient (4.76%). There was no myxoma related late deaths (defined as death occurring after 30 days of the operation) (Table 2 and Figure 5).

Discussion

Cardiac myxomas usually affect adults between the third and sixth decades of life and have female gender predilection [6]. In our series,

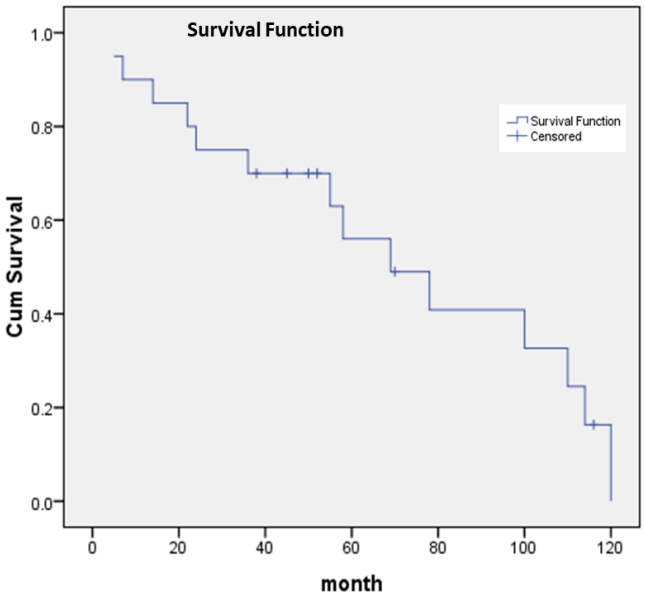

Figure 5: Kaplan-Meier cumulative survival curve for patients with cardiac myxoma who underwent surgical resection.

61.9% of the patients were females, which is similar to other published series [1]. On the other hand, female gender predominance is less pronounced in familial cardiac myxomas [7]. None of the patients in our study expressed familial inheritance.

Cardiac myxoma may arise from the left atrium, right atrium, the atrioventricular valves, the ventricles, or may rarely originate from the ventricular free wall or atrial appendages [4], All the published series in the literature showed that the left atrium is the most common site of myxoma, with the tumor base on the inter-atrial septum in 80% of the cases. [4, 8, 9]. In sporadic reported cases, the tumor was attached to the valve leaflets or in other locations in the left atrial or ventricular wall [10]. The attachment site in our cases was atrial septum except for one tumor which was attached to the posterior mitral valve leaflet.

In our patients, the location of the myxoma was in the left atrium in 17 patients (81%) and right atrium in 4 patients (19%) with no reported ventricular or multicentric myxoma. In the literature, few cases of multicentric non-familial bi-atrial myxoma were reported [11-14]. Additionally, ventricular locations of the myxoma were reported rarely in other case series. Mishra and colleagues reported the occurrence of one right ventricular myxoma in a series of 50 cases over four years [15], and Stevens and associates reported a case of left ventricular myxoma in a series of 58 cases over 25 years in Canada [16].

Microscopically, myxoma is generally a hypocellular lesion with the prominent myxoid stromal background. The neoplastic cells are frequently stellate, or spindle in shape and tend to arrange singly or less frequently in small cords or nests and intramural hemorrhage and calcification were occasionally present [4]. In our series, the histopathological diagnosis was confirmed in all patients.

Clinical presentation of cardiac myxomas is characterized by a wide range of symptoms and signs, from being asymptomatic to the life-threatening presentation. Dyspnea is the most common reported cardiac symptom; other cardiac symptoms like palpitation, syncope, congestive heart failure, and acute pulmonary edema were also reported [17]. Catastrophic presentation of acute cardiogenic shock and sudden death was reported which may be due to complete mitral valve obstruction, massive coronary embolization or massive pulmonary embolism [18]. One of our cases presented by cardiogenic shock and echocardiography revealed near-complete obstruction of the blood flow through the mitral valve by a large mobile mass. The patient was placed immediately in a steep Trendelenburg position to dislodge the tumor towards the atrial cavity and had an emergency operation. The most frequent symptom in our study was dyspnea (71.4%) followed by constitutional symptoms (28%) and palpitation (23.80%).

Trans-thoracic echocardiography (TTE) is the main tool for diagnosis of intra-cardiac tumors. Echocardiographic detection of a pedunculated, smooth mobile mass sitting in the LA is almost pathognomonic of LA myxoma [19]. Trans-esophageal echocardiography (TEE) can detect masses as small as 1-3 mm and provide more details about the exact location, dimensions, and appearance of the tumor, but it is not used routinely for diagnosis, it is reserved for cases of unsure diagnosis or intra-operative assessment [20]. In our series, the tumors were diagnosed in all cases by TTE. Intra-operatively, TEE was used in all cases as one of the standard intra-operative invasive monitoring tools; it evaluates the valve function post-tumor resection and excludes any missed tumors. Cardiac MRI and CT scanning

Table 2: Operative and postoperative data of the patients who underwent surgical resection of cardiac myxoma

Variables		Number	Percent
Myxoma Location	Left atrium	17	81%
	Right atrium	4	19%
Surgical Approach to RA myxoma	Right atriotomy	4	100%
Surgical Approach to LA myxoma			
	Uni-atrial (left atriotomy)	1	5.90%
	Bi-atrial (LA incision +RA incision)	3	17.60%
	Right atrial trans-septal	13	76.50%
Associated Procedures		5	23.80%
	CABG	2	
	Tricuspid valve repair	1	
	Mitral valve replacement	1	
	Bullectomy	1	
Postoperative Complications		6	28.60%
	AF	2	
	Atelectasis	1	
	Temporary conduction defect	2	
	Bleeding (revision)	1	
Peri-operative Mortality		1	4.76%
ICU Stay (mean± SD)	2.1±0.6 days		
Hospital Stay (mean± SD)	8.4±1.6 days		
Cross-Clamp Time (Min) (mean± SD)	20-130 (35)		
CPB Time (Min) (mean± SD)	30- 170 (55 min)		
NYHA functional class (Preoperative)			
	I	3	14.30%
	II	6	28.60%
	III	10	47.60%
	IV	2	9.50%
NYHA functional class (Postoperative)			
	I	14	66.70%
	II	5	23.80%
	III	1	4.76%
	IV	1	4.76%

. RA: Right Atrium; LA: Left Atrium; CABG: Coronary Artery Bypass Grafting; AF: Atrial Fibrillation; CPB: Cardio-Pulmonary Bypass; NYHA: New York Heart Association.

provide additional information regarding the extent of tumor within the heart or into adjacent structures. Contrast enhancement of these techniques can differentiate tumors from thrombi, and fat-suppression techniques define other benign tumors such as lipomas [21].

When the diagnosis of atrial myxomas is established, surgical excision must be performed as soon as possible to eliminate the potential risk of sudden death from complete valvular obstruction or massive embolization [1, 4, 17]. The classic concept of emergency treatment of cardiac myxoma is rarely questioned; some authors suggest that the emergency operation should be in patients with acute symptoms such as heart failure and pulmonary edema, clapper-shaped tumor intermittently prolapsing into the mitral orifice or a large lobulated tumor with a high risk of embolism [22]. Bakery and colleagues suggest that, except for real emergencies, myxoma

patients should comply with the usual recommendations and preparations like any cardiac surgery. The preoperative assessment should take 1 or 2 days, which does not constitute a high risk for stable patients but allows surgery to be performed under better conditions, particularly in elderly patients [7]. In our series, we operated upon the patients as soon as the diagnosis was established, either on the same day for unstable patients or next morning list for stable cases.

The basic principles of surgical resection of cardiac myxomas include adequate resection of the tumor, avoiding intra-operative embolization by the limitation of cardiac manipulation before aortic cross-clamping, avoiding excessive tumor manipulations to prevent fragmentation and meticulous intra-cardiac examination and irrigation to avoid leaving residual tumor [23]. In cases where the tumor is located at the close vicinity of the conduction tissue, the tumor resection is inevitably confined to the sub-endocardial level, rather than full thickness tissue removal. In these patients, close follow-up is necessary to rule out possible recurrence [24]. In our series; complete left atrial tumor resection with safety margins affected the integrity of the mitral valve in one case, where the tumor was located at the posterior mitral valve leaflet, so the procedure was accompanied by mitral valve replacement in this patient.

The routine surgical access is through the classic midline sternotomy. Recently, some authors have been tried minimal access surgery for cardiac myxoma resection; however, it was associated with longer operative time than the traditional approach. The minimally invasive approach has the advantages of shorter ICU and hospital stay, less postoperative pain and better cosmetic results. Tarui and colleagues reported a successful totally endoscopic robotic resection of left atrial myxoma in a 68-year old man using the Da Vinci Surgical System [25]. Opponents to minimal access surgery for cardiac myxoma, claim that these techniques can increase tumor manipulation; thus, increasing the possibility of local tumor seeding and systemic embolization [1]. Minimal access surgery has not been tried in our series.

The known routes for excision of the left atrial myxoma are either left atrial or bi-atrial incisions. The bi-atrial approaches included left and right atriotomy (LA + RA), a right atriotomy + trans-septal incision (RA + TS) or a left atriotomy + right atriotomy + trans-septal incision (LA +RA +TS). Right atrial myxoma can be excised through a right atrial incision only (RA) or right atrial incision plus trans-septal (TS) incision (RA+TS) [16].

In our series, we used the isolated left atrial approach in one case (5.8 %), in which the myxoma was located on the posterior mitral valve leaflet. Conversely, Jones and colleagues in their published series reported the use of left atrial approach in 34% of the cases [24]. Lee and colleagues advocated that a left atriotomy should be performed first, then the position and shape of the tumor is evaluated, and, if the tumor can be removed without manipulation, it is removed without an additional incision. If the attachment site and the margins are not obvious and excessive manipulation is expected, an additional right atriotomy is performed [23].

The bi-atriotomy approach (LA incision + RA incision ± TS) to cardiac myxomas was popularized by Cooley in 1973 [26] its advantages are excellent exposure and localization of the resection margin by direct visualization of the tumor pedicle, minimal manipulation of the tumor and it allows examination of all cardiac chambers and easy repair the septal defect [23]. On the other hand, it was criticized for being responsible for a high incidence of arrhythmias and conduction disturbances after resection of LA myxomas [28]. In our experience, bi-atrial approach (LA incision + RA incision) was used only in three cases (17.6%) with huge left atrial myxoma attached to the septum not amenable for safe resection using an isolated left atrial approach. Jones and colleagues in their published series reported the use of bi-atrial approach in 38% of their left atrial myxoma cases [24].

The Right atrial trans-septal approach facilitates wide excision of the tumor without mandating direct handling [27], permits adequate mitral exposure, allows inspection of heart chambers for concomitant tumors [28], and it allows easy repair of a single incision on the right atrium; additionally, it was associated with a low recurrence rate [1]. In our series, the right atrial

trans-septal approach was used successfully in 13 out of 17 cases (76.4%) of left atrial myxoma. On the other hand, Jones and colleagues reported the use of a trans-septal approach in 28% of their left atrial myxoma cases [24]. The risk of recurrence of cardiac myxoma after initial surgical excision is unusual with 1-3% incidence during the follow-up period [26].

Most of the reported recurrences were in the first four years postoperatively. Patients with positive family history, young males and multi-centric cases are more susceptible to recurrence [29]. The possible surgical etiologies of recurrence are incomplete resection, excessive intra-operative manipulations, fragmentation with local seeding and embolization [17]. In our series, no familial cases and no recurrence were reported.

Our results revealed that the median cardiopulmonary bypass time was 53 min, and the median aortic cross-clamp time was 36 minutes. There is wide variability in the literature in the reported cardiopulmonary bypass and ischemic times [7, 30]. This could be attributed to the variability in the concomitant procedures; in addition to the technique of myxoma resection is different from series to series, and it could be surgeon related [9, 30].

The prognosis for patients with solitary myxoma after surgical resection is excellent [7]. Concerning our postoperative status, it was found that 20 patients were alive (95.3%) and one patient had hospital mortality (4.7%). In other series, the early postoperative mortality rate was 2.0%, and the late mortality rate was 6.1% [31].

Study limitations:

Our study has several limitations. First, this is a retrospective study; however, this study design is appropriate to study rare diseases. Second, the number of cases is limited, and this is attributed to the rarity of the disease. Third, the comparison between the outcomes of the different surgical approaches was subjected to bias because most of the cases were subjected to right atrial trans-septal approach, on the other hand, the preference of this incision together with its excellent outcome should be considered as a significant observation. Last, we did not use computerized tomography (CT) study for preoperative evaluation, and further recommendations about its value can't be drawn.

Conclusion

Cardiac myxomas require surgical intervention as soon as possible after diagnosis to avoid embolic and obstructive complications. During surgery, if the principles of extensive resection and minimal manipulation of the tumor are respected, early and long-term results are excellent. Right atrial trans-septal approach fulfills the requirements of an ideal incision for excision of the left atrial myxoma with the best outcome.

Conflict of interest: The authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest.

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