

BRIEF REPORT

Thirteen years follow-up of heart myxoma operated patients: what is the appropriate surgical technique?

Stavros Siminelakis¹, Alexandra Kakourou¹, Alexandra Batistatou², Stelios Sismanidis¹, Alexandra Ntoulia², Kosmas Tsakiridis¹, Theodora Syminelaki², Eleftherios Apostolakis¹, Paul Zarogoulidis², Theodora Tsiouda³, Nikolaos Katsikogiannis⁴, Ioanna Kougioumtzi⁴, Georgios Dryllis⁵, Nikolaos Machairiotis⁴, Andreas Mpakas¹, Thomas Belevlis⁶, Konstantinos Zarogoulidis¹

¹Department of Cardiothoracic Surgery and Department of Pathology, University Hospital of Ioannina, 45500 Greece; ²Pulmonary Department-Oncology Unit, "G. Papanikolaou" General Hospital, Aristotle University of Thessaloniki, Thessaloniki, Greece; ³Internal Medicine Department, "Theageneio" Anticancer Hospital, Thessaloniki, Greece; ⁴Surgery Department (NHS), University General Hospital of Alexandroupolis, Alexandroupolis, Greece; ⁵Internal Medicine Department, Regional Hospital of Syros, Syros, Greece; ⁶Cardiology Department, "Saint Luke" Private Hospital, Thessaloniki, Greece

ABSTRACT

Background: Cardiac myxoma is a benign neoplasm that represents the most prevalent primary tumor of the heart. If not treated with the right surgical technique recurrence occurs. Aim of our study is to present our surgical approach and the histology of the tumors resected.

Methods: All patients, except for one, underwent extracorporeal circulation and mild hypothermia, right atrial or both atrial incision and excision of the fossa ovalis, followed by prosthetic patch suturing. All specimens were submitted for microscopic evaluation (haematoxylin-eosin). We contacted personally each patient and asked them to complete a standardized questionnaire, concerning their peri-operative characteristics.

Results: Six cases were "active" myxomas, 3 were "mildly active" and 3 were "inactive". "Normal differentiation" was seen in 6, "medium" in 1 and "poor" in 5 cases. In our series there were no recurrences recorded during the follow-up period.

Conclusions: The ideal approach, according to our experience is right atrial or both atrial incision as described by Shumacker and King, with excision of the fossa ovalis and the surrounding tissues and closure with a pericardial patch. Such a technique provides an excellent long-term survival in these patients.

KEYWORDS

Surgery of myxomas; atrial myxoma; cardiac surgery

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Introduction

Cardiac myxoma represents the most common type of primary cardiac tumor. Typically it is regarded as a benign neoplasm (1)

Correspondence to: Paul Zarogoulidis. Pulmonary Department, "G. Papanikolaou" General Hospital, Aristotle University of Thessaloniki. Thessaloniki, Greece. Email: pzarog@hotmail.com.

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and although it can occur in almost any age, usually patient ages range from 30-60 years, with a female predilection. Clinically myxomas may present with a variety of symptoms such as obstructive cardiac, embolic and constitutional.

Obstructive cardiac signs include dyspnea, thoracic pain, cough, dizziness and heart failure due to tumor prolapse into the mitral orifice (2) mimicking heart failure symptoms (3). Embolic manifestations can occur in any organ (4) and usually present with peripheral or pulmonary emboli or stroke. Constitutional symptoms include arthralgia, myalgia, fever, rash, weight loss, cachexia, fatigue, Reynaud's phenomenon and they are believed to be related with IL-6 production by tumor cells (5).

Cardiac myxoma most commonly occurs in the left atrium,

Table 1. Patients' characteristics diagnosed with heart myxoma during the 13 years period.

No	Age	Sex	Clinical presentation	Postoperative complications	Follow-up (months)	Follow-up findings
1	76	F	Stroke	nil	154	Neurologic residue
2	63	F	Dyspnea	nil	135	nil
3	48	M	Peripheral embolism	nil	114	nil
4	71	M	Random finding	AF	113	nil
5	72	F	Syncope	AF	65	nil
6	70	M	Stroke	AF	14	Death from accident
7	57	F	Random finding	nil	43	nil
8	71	F	Random finding	nil	41	nil
9	73	F	Dyspnea	nil	38	nil
10	43	M	Stroke	nil	23	nil
11	28	F	Fever, rash, fatigue	nil	19	nil
12	72	F	Stroke	Inoperable	62	nil
13	20	F	Stroke	nil	3	nil

F, female; M, male; AF, atrial fibrillation.

originating from the interatrial septum near or on the fossa ovalis. However, it can arise in any of the heart chambers. Most myxomas are single and sporadic although familiar cases are also well known. (Carney syndrome represents the majority of familiar cases).

The diagnosis is usually based on transthoracic and transesophageal echocardiography (better approach to the tumor's location and characteristics). Surgical resection under cardiopulmonary bypass and cardiac arrest is the commonest treatment, regardless of tumor size. There have been many reports of postoperative local recurrence and of distant metastases with aneurysmal changes of vessel walls and independent growth (6-10).

The aim of our study is to present our surgical technique that is characterized by total removal of heart myxoma without heart block and no recurrences during a follow-up period of 13 years. Moreover we attempted to associate the histopathologic findings and the clinical presentation of myxomas.

Patients and methods

In the Cardiothoracic Surgery Department of our University Hospital we treated 13 cardiac myxomas (Table 1). The patients' age was between 20-76 years. More particularly the study group included 9 women (69.23% of the whole population, range, 20-76 years) and 4 men (30.76% of the whole population, range, 43-71 years).

We reviewed these 13 cases and collected data concerning: (I) the clinical manifestations of cardiac myxoma; (II) the serologic alterations; (III) the patients' medical history; (IV)

their treatment; (V) post-operative course; (VI) the detailed histopathologic features of each case and (VII) the follow-up findings. Follow-up was achieved by contacting each patient personally and completing a standardized questionnaire.

In particular, they were asked if they had a regular follow-up and what the findings were, if they had any disturbances in their everyday life or any changes towards a healthier lifestyle and if they had been hospitalized again after their heart surgery.

Surgical resection with bicaval extracorporeal circulation and mild hypothermia was performed in all cases, except for one patient to whom surgery was refused due to high risk of cerebral bleeding from systemic heparin administration during the extracorporeal circulation (11). The approach was achieved with right atrial incision and excision of the fossa ovalis, followed by prosthetic patch suturing. In addition to this in cases where the tumor was occupying the majority of the left atrium another approach was selected as described by Shumacker and King (12). The incision starts from the right pulmonary vein continues vertically to the interatrial septum and free wall of the right atrium (Figures 1-3). With this method the left atrium opens wide (Figure 4) and it is impossible to escape a remnant of the tumor.

Histopathologic analysis (haematoxylin-eosin) was possible in all cases. For detailed microscopic analysis modification of a previously published sub typing was employed (5). Briefly, myxomas were differentiated as "active", with increased cellularity of myxoma cells, "mildly active", with areas of variable cellularity and "inactive", with low cellularity. Furthermore, based on the architecture of the lesions, "normal differentiation" was

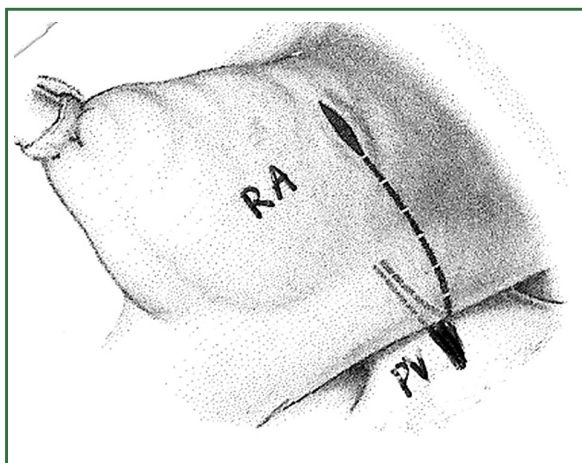


Figure 1. Incision line from pulmonary vein to the free wall of atrium.

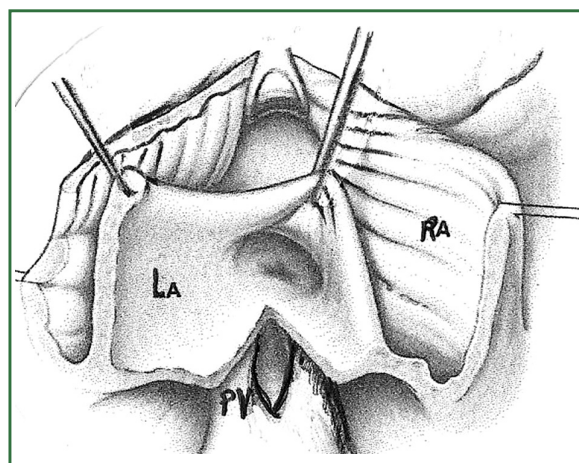


Figure 3. Final view of the approach to both atria.

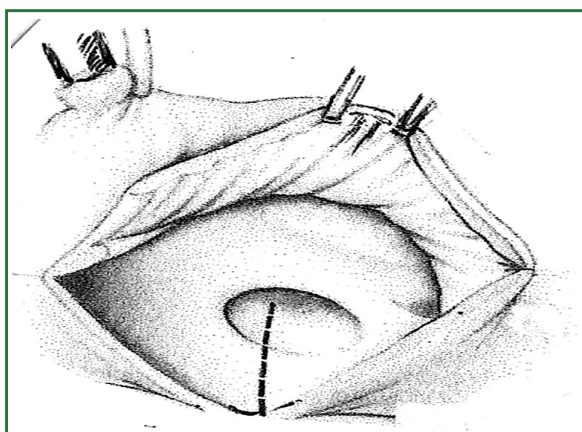


Figure 2. Incision line to the interatrial septum.

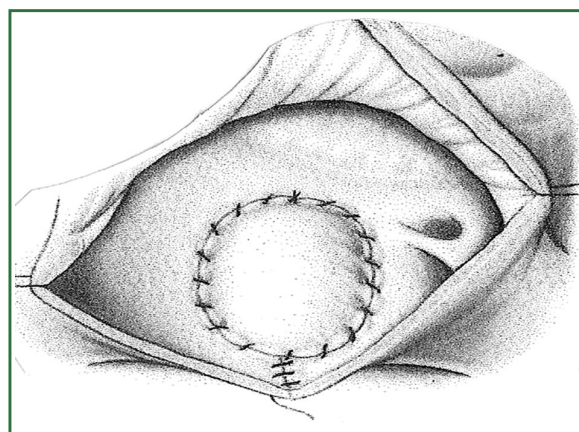


Figure 4. Final view of the repaired atria.

considered when rudimentary or well-developed vessels were surrounded by cells and then by matrix, “poor differentiation” when cells were singly dispersed, or in rows within matrix and “medium differentiation” for cases with intermediate features between the two.

Results

The predominant clinical manifestations (Table 2) were embolic (stroke and peripheral embolism) in 46.15% of the patients, followed by cardiovascular (dyspnea, cough, dizziness, chest pain) in 23.07% and constitutional (fever, rash and fatigue) in 7.69%. In three cases (23.07% of the patients) the myxoma was diagnosed accidentally, during regular echocardiographic control. Only four patients presented laboratory abnormalities. In all four of them elevated E.S.R >20 mm/hr was found and anemia was observed in two of them.

All tumors were located in the left atrium, attached to the atrial septum (fossa ovalis). No tumors were located in the right atrium or the ventricles. The size of the tumors ranged between 2 cm × 2 cm and 4.2 cm × 5.9 cm. Two of them were attached to the interatrial septum and were pediculate. All specimens were submitted in total for microscopic evaluation. The surface of the tumor was evaluated in all tumors (Table 2). It was covered by a single layer of cuboidal, endothelial-like cells and was smooth in 10 cases (#1, #2, #4, #5, #7, #8, #9, #10, #11, #13) and villous in 2 cases (#3, #6) (Figure 5). Ossification was observed in one case (#4) and calcification in none.

Six cases (46.15%) were “active” myxomas, 3 were “mildly active” (23.07%) and 3 were “inactive” (23.07%). “Normal differentiation” was seen in 6 cases (46.15%), “medium” in 1 (7.69%) and “poor differentiation” in 5 (38.46%) (Figure 6). The myxoma case with “medium” differentiation was also “mildly” active. Three out of 6 “active” myxomas (50%) showed

Table 2. Patients' histology divided to 2 groups of clinical presentation.

No	Clinical presentation	Laboratory tests (+)	Tumor surface	Histologic classification	Architecture of lesions
1	Stroke	E.S.R	Smooth	Active	Poor differentiation
3	Peripheral embolism	nil	Villous	Mildly active	Medium differentiation
5	Syncope	nil	Smooth	Mildly active	Poor differentiation
6	Stroke	nil	Villous	Active	Normal differentiation
10	Stroke	nil	Smooth	Active	Poor differentiation
12	Stroke	nil	Inoperable	Inoperable	Inoperable
13	Stroke	E.S.R, anemia	Smooth	Active	Poor differentiation
2	Dyspnea	E.S.R	Smooth	Mildly active	Normal differentiation
4	Random finding	nil	Smooth,ossification	Inactive	Poor differentiation
7	Random finding	nil	Smooth	Active	Normal differentiation
8	Random finding	nil	Smooth	Inactive	Normal differentiation
9	Dyspnea	nil	Smooth	Inactive	Normal differentiation
11	Fever, rash, fatigue	E.S.R, anemia	Smooth	Active	Normal differentiation

E.S.R, erythrocyte sedimentation rate.

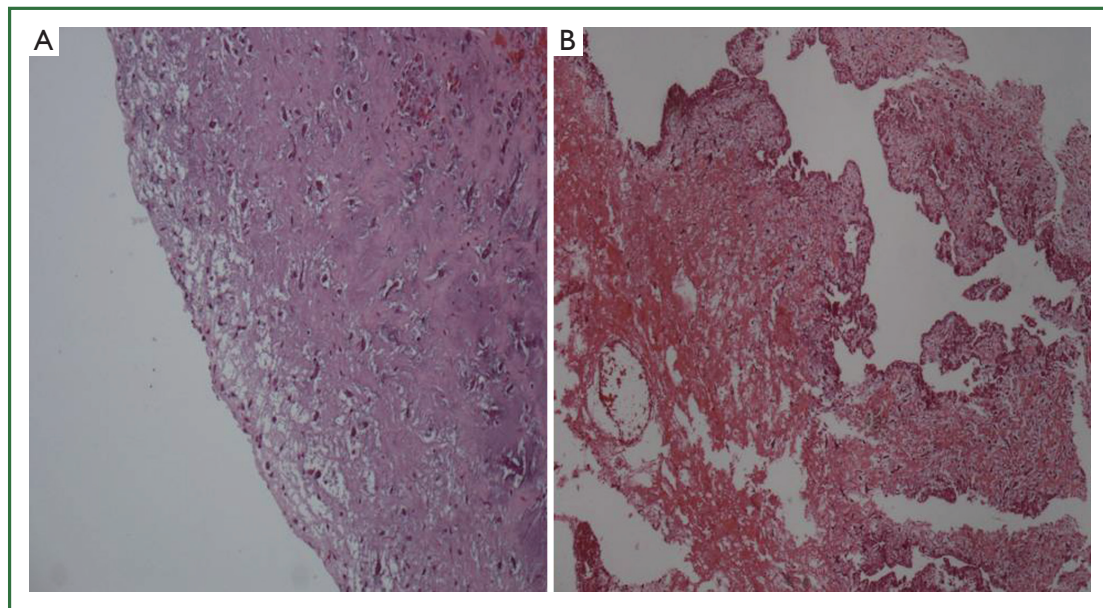


Figure 5. Surface of the excised myxomas, covered by a single layer of flattened endothelial-like cells. (A) Smooth surface, (haematoxylin-eosin $\times 100$); (B) Villous surface with multiple, friable villous extensions, (haematoxylin-eosin $\times 100$).

“normal differentiation”, while three were “poorly differentiated”.

One third of the mildly active myxomas were normal differentiated, one third medium differentiated and one third poorly differentiated. Two thirds of the “inactive” myxomas were “normally differentiated”, and one “poorly”.

All patients, apart from one, underwent surgery. The only postoperative complication was atrial fibrillation in 3 patients

(20%), which was treated with Amiodarone.

Follow-up was between 3-154 months. In our series there was only one death during the follow-up period, which was not related with the patient's medical history of heart myxoma. All cases recovered fully except for one patient who had suffered preoperatively a stroke (as the initial symptom of heart myxoma) and has a neurological residue after the excision of the heart

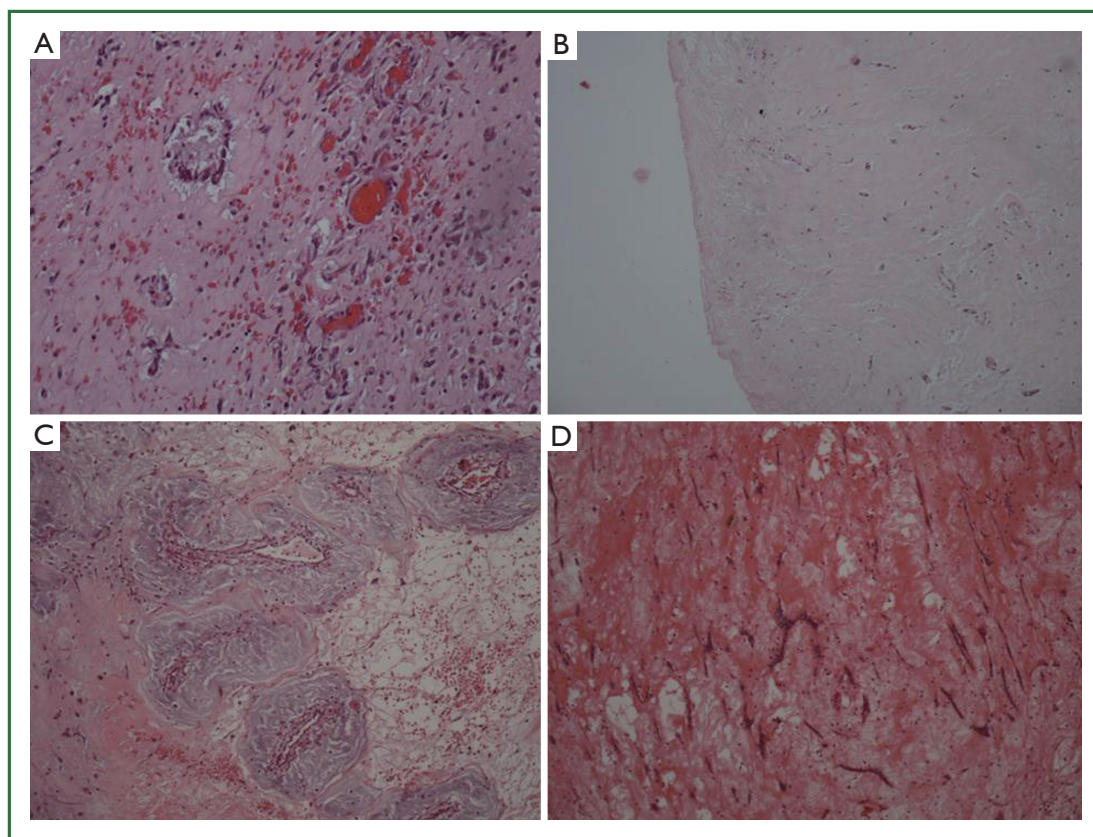


Figure 6. Histologic characteristics of myxomas. (A) Active myxoma with normal differentiation. Increased cellularity of myxoma cells, which form rudimentary vascular structures, (Haematoxylin-eosin $\times 200$); (B) Mildly active myxoma with medium differentiation—Variable cellularity of myxoma cells that form vascular structures, (Haematoxylin-eosin $\times 200$); (C) Inactive myxoma with normal differentiation—Low cellularity of myxoma cells, which form rudimentary vascular structures, (Haematoxylin-eosin $\times 200$); (D) Inactive myxoma with poor differentiation—Low cellularity of myxoma cells, dispersed or lepidic, which form short chains, (Haematoxylin-eosin $\times 200$).

tumor (case #1 has difficulties in the movement of the right arm and in speech). No recurrences were recorded.

Discussion

Myxomas represent the most common primary cardiac tumors. They can appear in almost all age groups but most commonly between the third and the sixth decades of life with a female predilection. In our series the patients' mean age was 58.76 years and 69.23% of the whole group was women. Myxomas can originate from any of the heart chambers, most commonly from the left atrium. Right atrial myxomas (13) and heart valve myxomas (14) are rare but still there have been reported such cases.

It appears that the clinical features of these tumors are not pathognomonic for the diagnosis of myxoma. Actually in a few cases there were no symptoms at all and the tumors were discovered incidentally during regular echocardiographic

examination. The most common symptoms though are obstructive, embolic and constitutional. This classic triad of symptoms depends on the tumor's location, size, mobility and its surface. Embolism (mainly affects the central nervous system) was the most frequent clinical manifestation in our series, occurring in 46.15 % of the patients in our study. Cerebral emboli may lead to numerous aneurysms, as in one patient (11) in our study, to whom surgery was refused, but his long-term outcome was finally good without having any disturbances or ever being hospitalized again (case #12). Obstructive symptoms (cardiovascular) occurred in 23.07% of patients in our series with manifestations such as dyspnea, cough, chest pain and dizziness and they are related with mechanical interference with the mitral valve. Finally, constitutional signs were observed only in one patient in our series who presented fever and rash. There are cases though in literature where cardiac myxoma was presented only with dermatologic lesions (purpuric macules on palms and

soles) (15).

Diagnosis was initially achieved by TTE, which was then complemented by TOE. Both diagnostic methods and especially TOE are excellent for characterizing the tumor's appearance, location and dimensions. Most myxomas measure a few centimeters, however there have been reported cases of huge atrial myxomas (16,17).

According to histopathologic features the tumor's surface is either villous and friable or smooth. It appears that the presence of a villous surface is associated with cerebral and peripheral embolism (cases #3 and #6) whereas smooth surfaced tumors can appear either as a random finding (cases #4, #7, #8) or with cardiovascular manifestations (cases #2, #5, #9) or with embolic manifestations (cases #1, #10, #13). No immediate correlation was detected, between the histologic differentiation-architecture of lesions and the clinical manifestations. There could be though some type of correlation with the recurrence rate, but since no recurrences were recorded in our study, no such relation could be estimated.

Urgent surgical resection with median sternotomy and the patient placed on bicaval cardiopulmonary bypass under mild hypothermia and cardioplegic cardiac arrest is the treatment of choice. Such an operation is safe and curative with a low peri-operative risk. Resection of the tumor and the area of endocardium that is attached plus a margin of safety (18) should be complete and it is necessary to prevent recurrence, since incomplete resection (19), along with peri-operative manipulations causing detachment of tumor pieces, are definitely risk factors for post-operative recurrence.

According to literature recurrence of sporadic myxoma develops in about 3% of tumors (20,21). It may occur several months after the first operation or even years later. Ricardo Oliveira *et al.* (21) presented a study where among the 19 patients, to whom follow-up was achieved, in a mean follow-up period of 5.2 ± 3.7 years, there were 2 recurrences (10.5% recurrence rate).

Sheng Wen-Bo *et al.* (19) had 5 recurrences (4.67% recurrence rate) in their series, G. Samanidis *et al.* (18) presented a study where during a mean follow-up period of 3.1 ± 3.2 years there were two recurrences. Finally in Laurent Pinede *et al.* series (5), in a median follow-up period of 3 years there were 6 recurrences recorded (5% recurrence rate). Malignant heart tumors are sarcomas and they relapse but occur preferentially in the right side of the heart. An exception to this rule is leiomyosarcoma (22), a rare form of primary cardiac sarcoma that occurs predominantly in the left atrium, as does cardiac myxoma.

In our series follow-up was up to 13 years. All patients who underwent surgical excision of heart myxoma were reached personally and follow-up was achieved in all of them. No recurrences

were recorded during the follow-up period (0% recurrence rate). We consider that the total excision of the interatrial septum is strongly related with no recurrences. Recurrence involves two main risks: the risk of a re-operation which is more difficult and causes more suffering to the patient and off course the risk of the clinical manifestations of the tumor itself. The surgeon should therefore not hesitate to remove totally the tumor.

According to our experience the ideal approach is right atriotomy with excision of the fossa ovalis and the surrounding tissues and closure with a pericardial patch. In addition to this in cases where the tumor is occupying the majority of the left atrium we suggest another approach as described for congenital surgery by Shumacker and King (12). The incision starts from the right pulmonary vein continues vertically to the interatrial septum and the free wall of the right atrium. With this method the left atrium opens wide and it is impossible to escape a remnant of the tumor. The worst approach is through the left atrium, because this technique does not allow us to see properly the base and the petiole of the myxoma (there could be remaining tissues). Surgical excision of the tumor provides an excellent long-term survival in most patients, compared to other primary cardiac tumors (20).

Conclusions

Heart myxoma is the most common primary cardiac tumor which is usually located in the left atrium. Operative treatment is urgently required. The best approach is through the right atrium with excision of the fossa ovalis plus a margin of safety, followed by sewing a prosthetic patch. In addition to in cases where the tumor is occupying the majority of the left atrium in order to avoid the possibility of recurrence we suggest another approach as described by Shumacker and King. Regarding histopathologic features the tumor's surface is either villous and friable or smooth. It appears that the presence of a villous surface is associated with cerebral and peripheral embolism whereas smooth surfaced tumors can appear either as a random finding or with cardiovascular manifestations.

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