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Cardiac Myxomas: Clinical spectrum, investigation findings, and surgical treatment based on our 25-year-experiences

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ABSTRACT

Objectives: The aim of this study was to describe the clinical spectrum, investigation findings, and surgical treatment of cardiac myxomas.

Patients and methods: Between November 1991 and July 2016, 229 patients (99 males, 130 females; mean age 37.1 years; range 7 to 63 years) with a primary or recurrent intra-cardiac myxoma underwent surgical excision at our institute. The diagnosis was made by transthoracic and transesophageal echocardiography. The basic surgical principle of complete wide excision was applied, and either unicameral (right or left atrial approach) or bicameral (both atria opened) surgical approach was used. Myxomas originating from the valve or valve annulus required a special attention. Postoperative echocardiograms were obtained in all patients before discharge. All patients were followed at three and 18 months, and five years postoperatively.

Results: The most common presenting symptoms were dyspnea and palpitation. There were 197 left atrial, 27 right atrial, two left ventricular, and one each of right ventricular, right ventricular outflow tract and multiple myxomas. There were three early death events; however no late mortality was seen. During follow-up, all patients were in the New York Heart Association Class I and echocardiography showed good ventricular functions with normal pulmonary artery pressure. Seven patients developed sporadic recurrence of myxoma. The valves were competent in the patients who underwent valve repair.

Conclusion: Based on our experience, we recommend the left atriotomy approach for left atrial myxomas and the right atriotomy approach for dumbbell-shaped left atrial and right atrial myxomas. Biatrial approach should be used in large and unusually located left atrial myxomas, while individualized approaches should be performed for others. To prevent recurrence, the surgical excision must include a substantial portion of normal endocardium near the base of implantation. The early mortality is commonly seen due to coronary embolism, and the late survival of patients after myxoma excision is usually excellent.

Keywords: Biatrial approach; cardiac tumor; left atrium; myxoma; recurrence.

Primary cardiac tumors are uncommon and represent only 5 to 10% of all neoplasms of the heart and pericardium.[1] About 80% of primary cardiac tumors are benign and, of these, more than half are myxomas.[2,3] The incidence of cardiac myxomas is between 0.0013 to 0.005%.[4] The majority of the data originate from small series of patients in developed countries. In this article, we report our 25-year experiences and describe the clinical spectrum, investigation findings, and surgical treatment of cardiac myxomas.

PATIENTS AND METHODS

Between November 1991 and July 2016, a total of 229 patients (99 males, 130 females; mean age: 37.1 years; range, 7 to 63 years) underwent complete and wide excision of primary or recurrent intra-cardiac myxomas at our institute.

Operative technique

All patients were referred for surgery and conventional median sternotomy approach was used. The cardiopulmonary bypass was established by aortic and bicaval cannulation. The myocardial protection was achieved by antegrade root cardioplegia. A special care was taken to avoid a forceful manipulation of the heart before the aorta was cross-clamped. Various unicameral (either right or left atrial approach) or bicameral (both atria opened for big tumors, particularly for the left atrial tumors) approaches were used.

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Statistical analysis

Statistical analysis was performed using SPSS version 10.0 software (SPSS Inc., Chicago, IL, USA). The Fisher's exact and chi-square tests were used to analyze statistical significance between variables. For continuous variables, the unpaired Student t-test was used. A p value of less than 0.05 was considered statistically significant.

RESULTS

Clinical findings

The common presenting symptoms were dyspnea and palpitation. One patient who had a huge right atrial myxoma developed hypoxia and cyanosis due to right-to-left shunting through atrial septal defect. Detailed clinical presentation is described in the Table 1. The laboratory findings showed an elevated erythrocyte sedimentation rate (ESR) in 171, anemia in 103, eosinophilia in 55, elevated WBC count in 39, and elevated serum globulin levels in all patients. A familial occurrence of the disease was excluded in the first-degree relatives. Initial chest radiography showed cardiomegaly with a cardiothoracic ratio of 55 to 70%, pulmonary congestion in 84, and left atrial enlargement in 47 patients. Electrocardiography showed left atrial enlargement in 79, right atrial enlargement in 21, right axis deviation in 44, left axis deviation in nine, right ventricular hypertrophy in 42, left ventricular hypertrophy in 11, and right bundle branch block in 16 patients. Two-dimensional transthoracic and transesophageal echocardiography were done in all patients and was the main diagnostic tool (Figures 1, 2). Of 229 patients, there were 197 left atrial, 27 right atrial, two left ventricular, and one each of right ventricular, right ventricular outflow tract, and multiple myxoma. These myxomas ranged from 3 to 16 cm in size at their greatest diameter. Preoperative right ventricular systolic pressure (RVSP) was less than 30 mmHg in 29 patients, between 30 and 60 mmHg in 55 patients, and higher than 60 mmHg in 56 patients. In the remaining patients, RVSP was unable to be calculated. Mild right ventricular (RV) dysfunction was present in 10 patients, and moderate and severe RV dysfunction were seen in three and two patients, respectively. Isolated mild left ventricular (LV) dysfunction was present in two patients, while mild to moderate biventricular dysfunction was seen in three and global hypokinesia was detected in one patient. The remaining patients had good biventricular functions.

Table 1
Clinical characteristics of patients

	n	%
Cardiac symptoms		
Dyspnea	199	86.9
Palpitation	128	55.9
Chest pain	64	27.9
Syncope	46	20.1
Orthopnea/paroxysmal nocturnal dyspnea	12	5.2
Cyanosis	1	0.4
Embolic symptoms		
Central nervous system	12	5.2
Peripheral	1	0.4
Coronary	1	0.4
Systemic symptoms		
Fever	54	23.6
Fatigue	43	18.8
Weight loss	32	14
Others		
Pedal edema	19	8.3
Miscelleneous	9	3.9
Auscultation		
Mid diastolic murmur	153	66.8
Tumor plop	114	49.8
Pansystolic murmur	71	31.0
Loud pulmonary second sound	62	27.1
Other signs		
Edema	9	3.9
Hepatomegaly	7	3.1
Clubbing	4	1.7

In addition, there were few associated lesions such as mild mitral regurgitation (MR) in 117, moderate MR in 21, severe MR in six, mild to moderate mitral stenosis in four, mild tricuspid regurgitation (TR) in 49, moderate TR in 10, severe TR in five and ostium secundum type of atrial septal defect (ASD-OS) in one patient. Coronary angiography was performed in patients above 40 years of age to rule out coronary artery lesions. One patient showed recanalized obtuse marginalis, while another patient had right coronary artery disease. In two patients, angiogram showed tumor blush from the right coronary artery and from the left coronary artery in another patient (Figure 3).

Operative findings

Complete excision of the tumor with a cuff of surrounding tissue was the basic principle of excision (Figures 4, 5a, b). Myxomas originating from the posterior mitral annulus required quadrangular

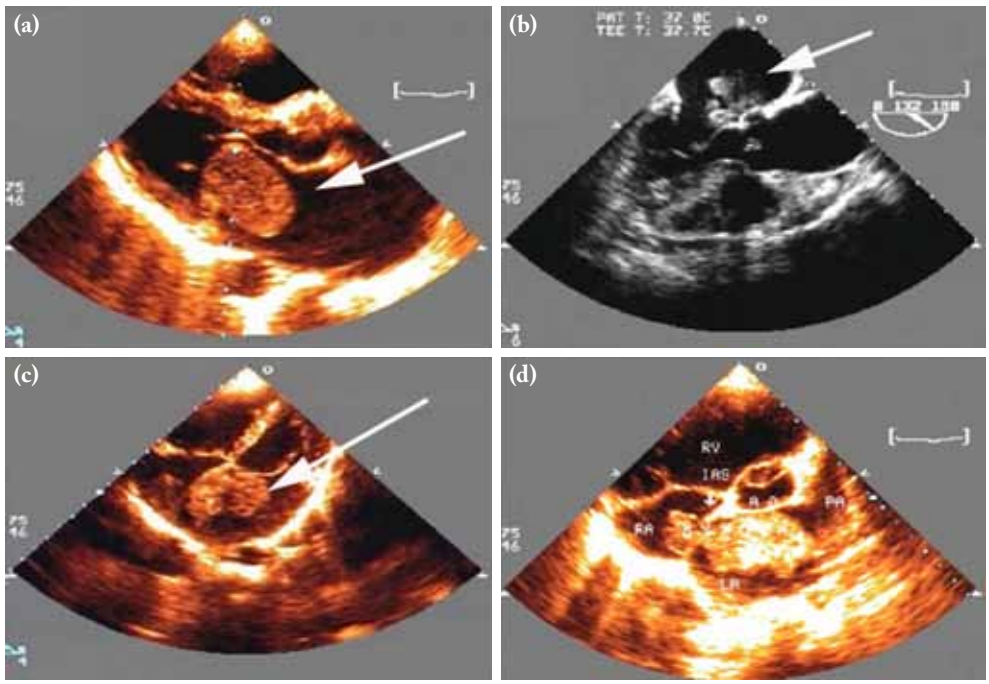

Figure 1. Transthoracic and transesophageal echocardiography images showing **(a)** a typical left atrial myxoma attached to the fossa ovalis of interatrial septum (arrow); **(b)** a multi-headed left atrial myxoma attached to the fossa ovalis of interatrial septum (arrow); **(c)** a left atrial myxoma attached to the interatrial septum and mitral valve-mimicking vegetation (arrow); and **(d)** a dumbbell-shaped myxoma, primarily in left atrium.

resection and prosthetic ring annuloplasty in six patients. Mitral valve repair was required in another 13 patients and repair was performed with anterior mitral leaflet chordal shortening and ring annuloplasty using prosthetic ring in seven patients and commissural annuloplasty in the remaining six patients. Myxomas arising from the tricuspid annulus were shaved off and modified DeVega's annuloplasty was done. In a patient with a myxoma arising from the right ventricular out flow tract involving the pulmonary valve leaflet required excision of the two leaflets. Details of surgical findings, approach, and technique are described in Table 2. Weaning from the cardiopulmonary bypass was done in a usual way. Transesophageal or epicardial echocardiography was done in the patients with valve regurgitation.

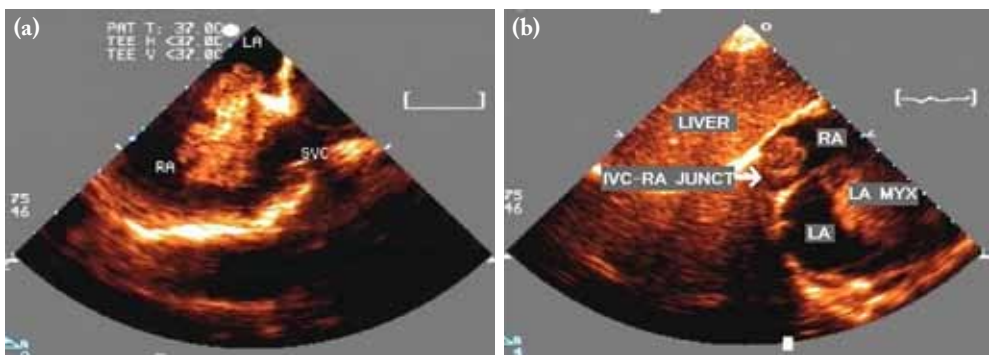

Figure 2. Transesophageal echocardiography images showing **(a)** a right atrial myxoma attached to the fossa ovalis of interatrial septum; and **(b)** a right atrial myxoma at inferior vena cava-right atrial junction.

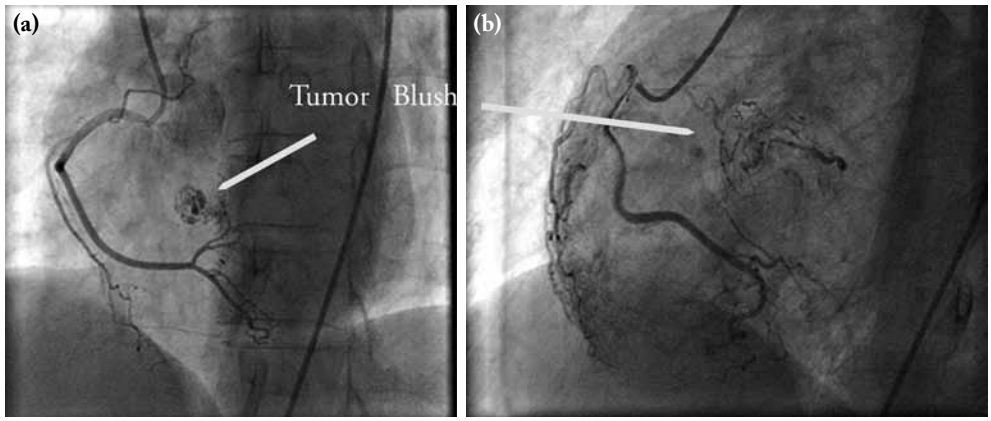

Figure 3. **(a, b)** A right-sided coronary angiogram showing tumor blush from right coronary artery (arrow).

Postoperative outcomes

There were three early mortalities in our entire series due to acute severe left ventricular dysfunction and multi-organ failure, probably secondary to coronary embolism. There was no late mortality. One patient developed convulsion postoperatively and cranial computed tomography (CT) showed an old parietal lobe infarct. The patient was recovered and discharged uneventfully. One patient also developed cerebral hypoxia due to cyanosis caused by right-to-left shunting across the ASD, secondary to right atrial outflow obstruction caused by a huge right atrial myxoma. The patient required prolonged ventilation; however, he recovered and was uneventfully discharged. All patients underwent transthoracic echocardiography on the day of surgery in the intensive care unit and before discharge to evaluate the ventricular functions, valve repair status, and possibility of residual tumors. Echocardiography revealed no residual myxoma in all patients (n=229), good biventricular functions in 224 patients, mild to moderate right ventricular dysfunction in two patients, and severe left ventricular dysfunction in three patients. Three patients also developed mild to moderate MR, one patient developed severe MR requiring mitral valve repair, and one patient developed severe TR, which was medically managed. Postoperatively, the right ventricular systolic pressure was less than 30 mmHg in 87 patients, between 30 and 60 mmHg in 41 patients, and higher than 60 mmHg in two patients. None of the patients had pulmonary embolism. The mean length of intensive care unit stay was 6 (range: 2 to 9) days and the mean length of hospital stay was 9 (range: 5 to 18) days. Follow-up was done at three months, one and five years, and 6 to 17 years. A total of 226 patients survived after the operation, and 203 of them (90%) attended to follow-up at three months. However, the remaining 23 patients (10%) were lost to follow-up. Of the patients, 40.3% (n=66) attended to the follow-up at one year, 30.5% (n=69) at five years, and 24.3% (n=55) between 5 to 17 years. All patients were in the New York Heart Association (NYHA) Class I and echocardiography showed that all patients had good ventricular functions with normal pulmonary artery pressures. However, there were six patients with moderate MR, one with severe MR, and two with moderate to severe TR during follow-up. One patient developed right parietal area infarct leading to left hemiparesis. The patient with severe mitral regurgitation was advised mitral valve replacement. There were seven patients with a recurrent myxoma (Figure 5c) in our entire series, and the mean time to recurrence was 7.2 (range: 2 to 13) years. Apart from one case of multiple myxomas, the remaining six patients developed recurrence at the same site or adjacent area, probably due to inadequate excision or tumor sidling. In a patient with multiple myxomas, a left ventricular myxoma which was developed was thought to be due to multi-centric foci. The location at the initial surgery, recurrence period and site of recurrence are described in Table 3.

DISCUSSION

Although primary tumors of the heart are rare, myxomas are the most frequent benign primary heart

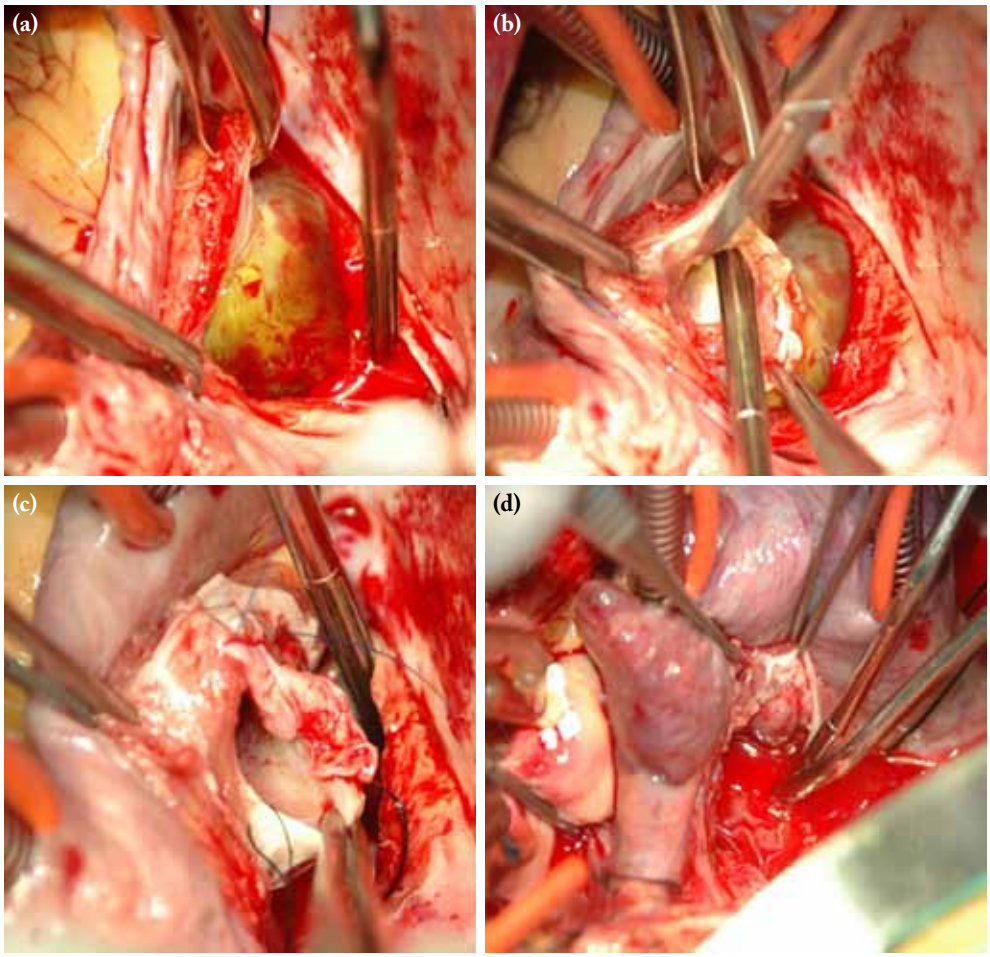

Figure 4. An intraoperative view of left atrial myxoma excision through left atriotomy approach. **(a)** Left atrial approach showing myxoma attached to the interatrial septum; **(b)** left atrial myxoma along with interatrial septum excised; **(c)** a septal defect closure using an autologous untreated pericardial patch; and **(d)** a completed septal closure and checking for suture line leakage.

tumors, which account for 0.3% of open heart surgery worldwide. The clinical presentation in the majority of the patients includes significant hemodynamic symptoms related to the blood flow obstruction and embolic phenomena. Cardiac myxomas can be challenging to diagnose, due to their rare occurrence and varying clinical presentation. The mean age was 37.1 years at the time of diagnosis in our study,

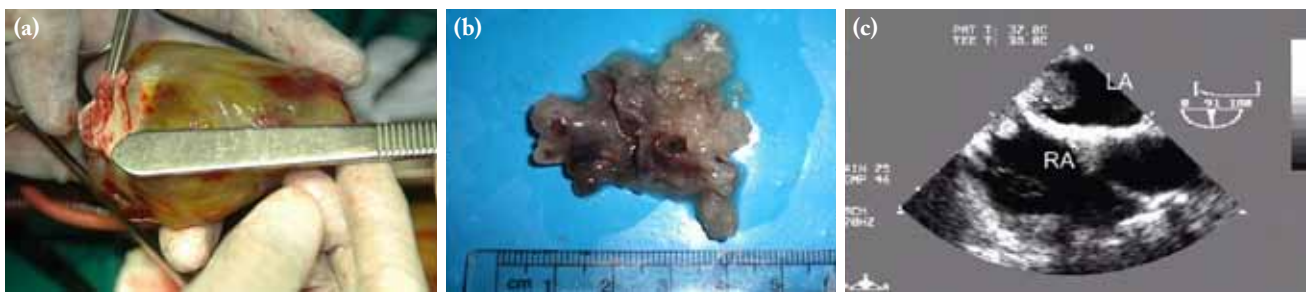

Figure 5. An excised myxoma and postoperative echocardiography showing **(a)** an excised left atrial myxoma; and **(b)** an excised multi-headed myxoma. **(c)** Postoperative transesophageal echocardiography showing a recurrent biatrial myxoma.

Table 2
Operative findings and approaches and techniques applied

LA myxoma			**RA myxoma**			**Others**		
Site of attachment	n	%	Site of attachment	n	%	Site of attachment	n	%
Fossa ovalis (IAS)	170	86.3	Fossa ovalis	23	85.2	LV apex	2	50
LA roof	17	6.6	IVC-RA junction	3	11	RV-IVS	1	25
PML annulus	6	3.0	Tricuspid annulus	1	3.7	Conal septum & PV cusps	1	25
Pulmonary veins	3	1.3				LA, RA, RVOT	1	25
Base of LAA	1	0.5						
Approach			**Approach**			**Approach**		
LA	145	73.6	RA	27	100	LA & aortic	2	50
RA	27	13.7				RA & PA	2	50
Biatrial	25	12.7				PA	1	25
Technique			**Technique**			**Technique**		
WE + direct closure	155	58.4	WE + pericardial patch closure	23	85.2	WE	3	75
WE + pericardial patch closure	57	28.9	Excision & fulguration	4	14.8	WE + pericardial patch closure	1	25
Excision & fulguration	23	11.7						
WE + Dacron patch closure	2	1.0						
Additional procedures			**Additional procedures**			**Additional procedures**		
Mitral annuloplasty	19	9.6	Tricuspid annuloplasty	10	37.0	Pulmonary valvectomy	1	25
CABG & mitral annuloplasty	1	0.5						

LA: Left atrium; RA: Right atrium; IAS: Interatrial septum; LV: Left ventricle; IVC: Inferior vena cava; IVS: Interventricular septum; PML: Posterior mitral leaflet; PV: Pulmonary valve; RVOT: Right ventricular outflow tract; LAA: Left atrial appendage; PA: Pulmonary artery; WE: Wide excision; CABG: Coronary artery bypass grafting.

which is significantly lower than in most Western countries where the mean age is 50 to 55 years.[5-7] In addition, dyspnea was the most common symptom in our patients as the obstructive pathology. Patients may also present with cyanosis and cerebral hypoxia produced by right-to-left shunting secondary to the right ventricular inflow obstruction caused by a huge right atrial myxoma associated with patent foramen ovale or ASD, as in one of our patients. A higher risk of embolization has been also reported and events occur in 30 to 45% of the patients.[5-10] In our series, the embolization was less

Table 3
Recurrence data

Location at first surgery	Recurrence period (years)	Site of recurrence
Right atrium (IAS, fossa ovalis)	13	Biatrial (IAS)
Left atrium (IAS)	13	Biatrial & extending to right atrium wall
Right atrium (Lower end of fossa ovalis)	9	LA (IAS)
Left atrium (IAS)	7	RA (IAS)
Multiple (LA, RA, RVOT) IAS & RVOT	5	Left ventricle apex
Left atrium (IAS)	2	Roof of left atrium & IAS
Biatrial (IAS)	2	Biatrial (IAS)

IAS: Interatrial septum; LA: Left atrium; RA: Right atrium; RVOT: Right ventricular outflow tract.

frequent than the Western series. In our series a total of 14 patients developed embolization preoperatively and three patients developed tumor embolization postoperatively. Of 14 patients, 12 patients had central nervous system (CNS) embolization and one each had peripheral arterial and coronary artery embolization. Of three patients with postoperative tumor embolization, two developed in the early postoperative period and one patient developed in the late postoperative period. All these patients had CNS embolization. Anemia and elevated ESR are non-specific markers of several diseases and are significantly more common in our study. The presence of systemic symptoms was positively correlated with elevated ESR. Systemic symptoms, anemia, and elevated ESR could be due to the systemic effects of interlukin-6, the cytokine implanted in generating a generalized inflammatory response in patients with myxomas. There were also elevated serum globulin levels in all patients with reversal of albumin-globulin ratio in our series.

Echocardiography is currently the most main diagnostic modality available for imaging cardiac tumors. It is non-invasive and allows a preoperative diagnosis with accuracy and can quantitate the tumor size, shape, attachment, and mobility.[11,12] It can also screen the other chambers of the heart for additional tumors. In addition, transesophageal echocardiography has an increased sensitivity and specificity for the diagnosis, particularly in patients with poor transthoracic echo window.[11,12] In our series, the two-dimensional transthoracic and transesophageal echocardiography were successful primary tools for the diagnosis of cardiac tumors. Magnetic resonance imaging (MRI) and CT are not the first-line diagnostic tools for myxomas, although more and more cases are diagnosed by these technologies. These modalities are helpful to detect benign and malignant tumors, when transthoracic and transesophageal echocardiography offer limited tissue characterization and confident distinction between thrombi.[11-14] In addition, prolapse through the mitral valve orifice on CT is a reliable discriminative finding indicating a myxoma,[11-14] while the absence of both first-pass and delayed contrast enhancement on MRI is suggestive of a thrombus.[11-14]

Cardiac CT is also useful to detect metastases in suspected malignancies, particularly when coupled with 18 F-fluorodeoxyglucose (FDG) positron emission tomography (PET). However, if a mass has a typical echocardiographic appearance and is located as a left atrial myxoma, additional images with CT or MRI are unnecessary. Surgical excision is the treatment and must be undertaken immediately to avoid the complications, such as systemic embolization and valvular obstruction or incompetence.

The first successful surgery of a myxoma was performed by Crafoord in Stockholm, Sweden in 1955, on cardiopulmonary bypass.[1-19] Since then, many approaches have been described in the literature, such as left atriotomy, right atriotomy and biatrial approach.[11-19] In our series, the approaches used for left atrial myxomas are left atriotomy in 73.6% (n=145), right atriotomy in 13.7% (n=27), and biatrial approach in 12.7% patients (n=25). Based on our findings, we found that the left atriotomy approach was much more convenient, simple, rapid, and safe approach for the excision of the left atrial myxomas. The right atriotomy approach was used for dumbbell-shaped left atrial myxomas. The biatrial approach was used in large and unusually located left atrial myxomas. The right atrial myxoma was approached through right atriotomy, while other types of myxoma were approached either through right atrium and pulmonary artery for the right ventricular outflow tract myxomas and left atriotomy and transaortic approach for the left ventricular myxomas. A wide excision with direct closure of the defect was also done in 58.4%, pericardial patch closure of the defect in 28.9%, excision and fulguration of the raw area in 11.7%, and the use of a Dacron patch in 1% patients of left atrial myxomas. For the right atrial myxoma excision, a pericardial patch was used in 85.2% patients and excision with fulguration was done in 14.8% patients. Myxomas attached to the chamber wall apart from the interatrial septum, such as the right ventricular septum, left ventricular apex, and tricuspid valve annulus require wide excision alone or excision with fulguration. Myxomas attached to the pulmonary valve require excision of the valve leaflet, while those attached to the posterior mitral leaflet can be excised with the quadrangular resection of the leaflet with myxoma, followed by prosthetic ring annuloplasty. Myxomas attached to the anterior mitral leaflet require treatment according to the involvement of the leaflet area. If a small portion of the leaflet is involved, myxoma can be shaved off the leaflet, or a small portion of the leaflet can be excised, and the defect can be repaired with an autologous pericardial patch. However, if the major portion of the leaflet is involved, it may require mitral valve replacement. To prevent recurrence, there

is a consensus that surgical excision must include a substantial portion of the normal endocardium near the base of implantation.[16-19] Recurrence can be due to inadequate resection, intraoperative implantation, embolization or multi-centric growth.[5,6] In our series, the recurrence rate was 3.1%, which is comparable to the international standard of 5%.[16,17,19] The recurrence was mainly found in left atrial myxomas, excised through right atriotomy approach, probably due to inadequate excision or intraoperative implantation. In one case of multiple myxomas, recurrence was seen at a different location, probably due to the multi-centric growth. There were also three early mortalities in our entire series, due to acute severe left ventricular dysfunction and multi-organ failure, probably secondary to coronary embolism. There was no late mortality or pulmonary embolism.

In conclusion, cardiac myxomas are the most common benign cardiac tumors in adults and the left atrium is the commonest chamber involved. Transthoracic and transesophageal echocardiography is the optimal diagnostic modalities for myxomas. The diagnosis of a cardiac myxoma is an indication for an urgent surgery, due to the high risk of sudden death from a thromboembolism or valvular obstruction. Therefore, we recommend the left atriotomy approach for the left atrial myxoma excision in view of convenience, simplicity, and safety and right atriotomy approach for dumbbell-shaped and right atrial myxomas. The biatrial approach can be used in large and unusually located left atrial myxomas, while individualized approaches can be used for the treatment of for other types of myxoma. To prevent recurrence, the surgical excision must include a substantial portion of the normal endocardium near the base of implantation. The early mortality is most commonly due to coronary embolism and the late postoperative survival is usually excellent.

Declaration of conflicting interests

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