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Cardiac Myxoma: 10 Years Study of Presentations, Resection and Outcome

Vinod Bhan[1], Sri Satyavathi[1], Kanchumarti Sudhakar Rao[1], Velam Vanajakshamma[2]

[1]Cardiovascular Thoracic Surgery Department, Sri Venkateswara Institute of Medical Sciences, Tirupati, India
[2]Cardiology Department, Sri Venkateswara Institute of Medical Sciences, Tirupati, India
Email: v_bhan@hotmail.com

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Abstract

Background: Cardiac myxoma is a very rare heart tumor which presents as life threatening mass in cardiac chamber. The tumor may present with vague symptoms which can lead to delay in diagnosis. **Methods:** 22 patients underwent complete excision of intracardiac myxoma between January 2011 and December 2020. Majority of the patients were females (60%) with mean age of 48.9 years who presented with symptoms of dyspnea on exertion. 3 patients had significant complications due to myxoma. 2 presenting with tumor embolism and limb ischemia while 1 patient presented with pulmonary edema. All patients were diagnosed by echocardiography which helped in evaluation of size and extent of tumor. Majority of patients underwent trans-septal biatrial approach for tumor excision. **Results:** 95% of patients survived the operation. The mean tumor size excised was 5.0 ± 1.6 cm in the largest diameter. 11 patients had sessile tumor while 1 patient had dumb bell tumor occupying both atria. 15 patients were surviving the operation while 2 deaths happened after 6 years of surgery. **Conclusion:** Cardiac myxomas are rare tumors which can cause severe systemic and cardiac symptoms in patients. Early diagnosis and immediate surgical management give excellent early and long-term results.

Keywords

Cardiac Myxoma, Dyspnea, Trans-Septal Approach

1. Introduction

Primary Cardiac Tumors of heart are rare tumors with life time incidence of 0.0017% to 0.03%. Approximately 75% - 80% of primary cardiac tumors are benign with cardiac myxoma the most common amongst them. Cardiac myxomas can present in all age groups, predominantly in third to sixth decade of life and more in

females. More than 90% of these tumors are seen in left atrium arising from the Fossa ovalis of inter atrial septum [1] [2] [3]. Genetic association of these tumors has also been found in patients of Carney complex due to mutation of PRKAR1A gene.

The clinical manifestation of this tumor presents an important diagnostic challenge due to insidious onset. These patients give vague symptoms of dyspnea, chest pain and carry high risk of systemic embolization with cerebral or peripheral infarctions due to large mobile myxoma in left or right ventricle which may also cause sudden death due to prolapse through valve [4] [5] [6] [7] [8].

There is no single diagnostic test to detect them early, except for few reports of raised erythrocyte sedimentation rate (ESR) C Reactive protein (CRP) and interleukin 6 (IL6) due to inflammatory or immune features associated with this tumor [9]. Early diagnosis by echocardiography and prompt surgical intervention with complete wide excision and avoidance of residual tumor has shown good outcome in these patients. The present study summarizes 10 years of clinical experience with consecutive series of 22 patients operated for Cardiac myxomas.

2. Material and Methods

The cardiovascular surgery database of our institution was searched for records of all patients who underwent surgery for Cardiac Myxoma from Jan 2011 to Dec 2020 in the department of Cardiovascular Thoracic Surgery. Patient data was retrospectively collected from the available records of operated cases of Intra cardiac tumors out of which Non cardiac myxoma tumors of heart, secondary metastasis to heart were excluded.

Patient information on demographics, symptoms, co-morbidities was collected. 22 patients were finally included in the data of operated cases. Routine investigations like Hemogram, Renal Function Test, Random Blood Sugar and Chest xray were collected.

All patients were diagnostically worked up by echocardiography. Surgery was done by Median Sternotomy under cardiopulmonary bypass with aorta, bicaval cannulation, mild hypothermia and cold blood cardioplegia.

In majority of patients Right Atrial trans-septal approach was used in excision of tumor. In all patients fossa ovalis was excised and repaired with pericardial patch if tumor was arising from interatrial septum. If tumor was arising from other surfaces, it was excised with 5 mm of healthy tissue followed by 0.1% glutaraldehyde touch up for 5 minutes to that surface.

Postop usage of inotropes, ventilator days, ICU stay and hospital days were recorded. All cause mortality and post discharge mortality were recorded.

Continuous variables were reported as mean±standard deviation. Categorical variables were presented as percentage and frequency. Long term survival was calculated and graphically represented by Kaplan Meier graph.

3. Results

22 patients of cardiac myxoma were included in the data of operated cases. Majority of the patients were females (63%) and in age group of 40 - 60 years

(Figure 1).

The commonest symptom in patients was dyspnea on exertion in 60% patients with minimum 1 day presentation and maximum 180 days with mean duration of 21 days. In 2 patients it was an incidental finding while being worked up for other elective surgical procedure. 1 patient presented with pulmonary edema while 2 patients presented with lower limb ischemia and were taken up for emergency surgery (Table 1).

In routine investigations done in all patients, 3 patients had anemia while 12 patients had raised ESR. The commonest blood group in patients was found to be O+ ve (Table 1).

The mean bypass time in 22 patients was 72.5 ± 29.2 min while mean cross clamp time was 44.9 ± 23.2 min (Table 2).

In majority of patients Right Atrial trans-septal approach was used in excision of tumor. In 2 patients biatrial approach was used for excision in view of large tumor. In most of the patients the commonest location of tumor was interatrial septum at Fossa ovalis with average size of tumor 4.9 × 3.7 cm (Table 3).

Table 1. Clinical presentation with lab reports.

Patient	Presentation	Duration	Hbgm/dl	TLC/cu mm	ESR mm/h	Blood Group
1.	Mild Dyspnea	3 years	13.2	10,700	80	O+
2.	Acute Limb Ischemia	1 day	10.6	7300	80	O+
3.	Dyspnea on exertion (DOE)	21 days	15.6	7000	10	A1+
4.	Stroke, Left Hemiplegia	20 days	10.3	6900	48	O+
5.	DOE	21 days	10.8	12,800	30	B+
6.	Fever, DOE	15 days	10.8	18,100	109	O+
7.	DOE, Cough	6 months	9.3	13,500	32	B+
8.	DOE	2 months	13.6	10,300	14	A+
9.	Chest pain	15 days	10	21,100	64	O+
10.	DOE	1 month	11.8	13,600	10	B+
11.	Acute Limb Ischemia	1 day	13.3	8700	40	O+
12.	DOE	3 months	10.5	10,500	45	A+
13.	Chest Pain, DOE	1 day	11.7	20,800	14	O+
14.	DOE	1 month	10.8	16,800	20	B+
15.	Palpitation, DOE	15 days	7.3	10,700	120	B+
16.	DOE	5 months	12.2	14,100	22	O+
17.	Incidental finding		14	14,000	25	A1+
18.	DOE	15 days	7.2	5100	11	A1+
19.	Incidental finding		11.3	10,600	12	O+
20.	DOE, Pulmonary oedema	1 day	11.5	7200	14	A1-
21.	DOE	10 days	10.5	11,200	48	O+
22	Chest pain	1 month	9.5	14,600	35	B+

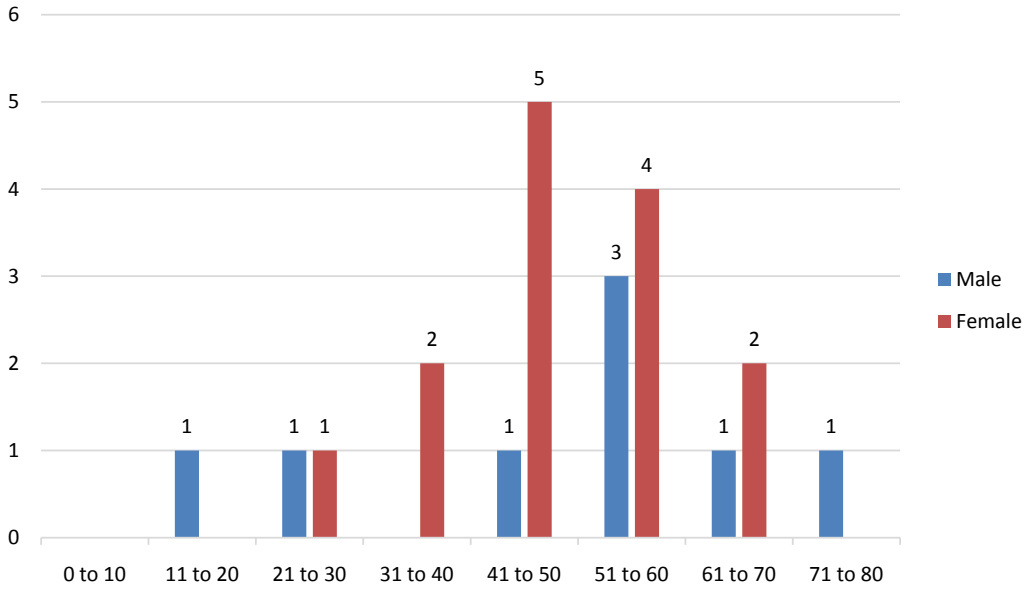

Figure 1. Age distribution of patients.

Table 2. Pump time & post op parameters.

S.No.	CPB TIME		POSTOP DAYS			
	X CLAMP	PUMP TIME	ICU	VENTILATOR	HOSPITAL STAY	INOTROPES
1.	45	65	1	1	8	1
2.	33	58	1	1	7	1
3.	61	81	1	1	12	1
4.	74	128	2	1	8	1
5.	25	42	2	1	8	1
6.	50	67	1	1	12	1
7.	45	65	1	1	10	1
8.	15	34	1	1	8	1
9.	8	19	1	1	14	1
10.	29	100	2	2	10	2
11.	45	100	3	1	13	1
12.	46	71	1	1	10	1
13.	75	120	1	1	8	1
14.	107	123	1	1	10	1
15.	72	98	2	3	12	1
16.	18	40	2	3	13	2
17.	43	72	1	1	10	1
18.	55	78	1	1	12	1
19.	49	68	2	1	16	1
20.	19	46	1	1	1	2
21.	40	65	1	1	7	1
22.	35	55	1	1	8	1

Table 3. Tumor size, surface and origin.

Patient	Size of Mass	Shape	Surface	Valve Affected
1.	3.3 × 2.5 cm	Pedunculated	RA IAS	Across Tricuspid Valve
2.	7 × 5 cm	Sessile	LA	LV Prolapsing
3.	5.2 × 3.2 cm	Pedunculated	LA	Across Mitral Valve
4.	5.2 × 3.1 cm	Sessile	LA	
5.	5.5 × 4.8 cm	Sessile	LA IAS	
6.	4 × 2 cm	Pedunculated	LA	LV Prolapsing
7.	5.9 × 3.5 cm & 10 × 8 cm	Dumb bell shaped	RA & LA IAS	Across Mitral Valve
8.	6 × 7 cm	Pedunculated	LA	Across MV
9.	2.5 × 2.5 cm	Sessile	RA	
10.	4.6 × 2.9 cm	Pedunculated	LA IAS	
11.	5 × 4 cm	Sessile	IAS Roof LA	
12.	4.6 × 5.4 cm	Sessile	LA IAS	
13.	6.5 × 5 cm	Pedunculated	LA IAS Left PV	
14.	6 × 5 cm	Sessile	LA Roof MV	Mitral Valve Annulus
15.	5.2 × 3.6 cm	Sessile	IAS LA	
16.	5.8 × 3.2 cm	Pedunculated	LA	
17.	5 × 3.5 cm	Sessile	IAS LA	
18.	5.5 × 3.5 cm	Pedunculated	LA IAS	
19.	4 × 3.5 cm	Sessile	LA MV	Ant. Mitral leaflet
20.	4.1 × 3.2 cm	Pedunculated	IAS LA	
21	2 × 1 cm	Pedunculated	LA	
22	5 × 4 cm	Sessile	LA	

Post op period was uneventful in majority of the patients with minimal ICU days except for those patients who presented as acute emergency. The mean postop hospital stay was 9.4 days except for 1 patient who expired immediately after surgery (Table 2).

The patients remained on regular hospital follow up for 1 year with no recurrence of tumor. All patients were called by phone in this study which they had provided at the time of admission. Only 17 patients phone could be contacted 15 gave no symptoms related to cardiac problem. 4 patients could not be contacted phone due to change of phone number. 2 patients expired at home, 1 patient in 6^{th} year and another in 8^{th} year. Exact details could not be elicited from attenders from phone. This data was used to predict survival based on Kaplan Meier graph (Figure 2).

4. Discussion

The first cardiac neoplasm was described in 1559 by Realdo Colombo, Vesalius'

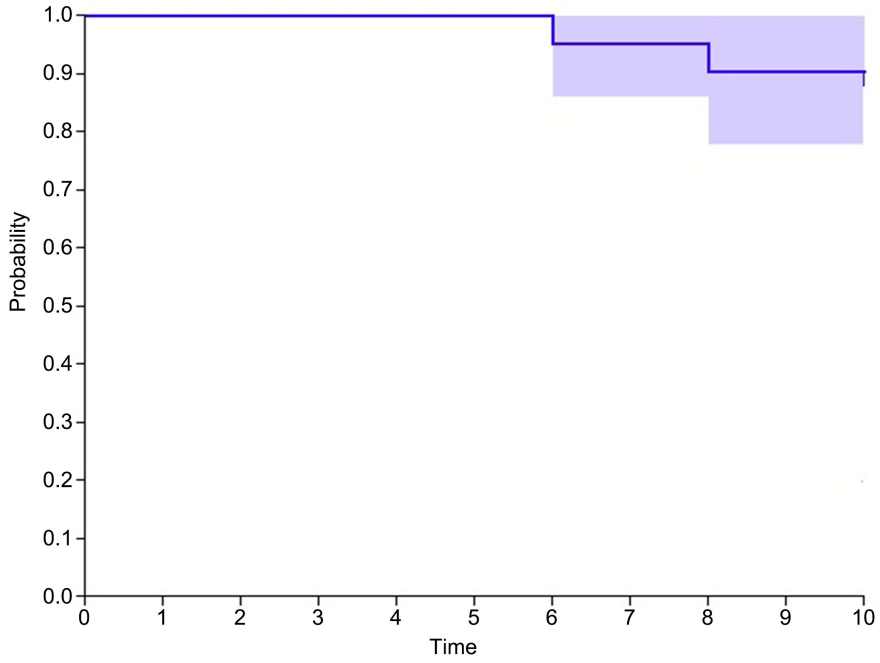

Figure 2. Kaplan Meier survival graph.

successor at Padua. The first successful attempt to remove a large cardiac myxoma was done by Bahmson and Newman in 1952 by prolapsing a large myxoma through right atriotomy under inflow occlusion. In 1954 Professor Crafoord in Sweden, removed the Left atrial myxoma, using extracorporeal circulation for the first time [10].

Primary tumors of the heart are rare with prevalence ranging from 0.0017% to 0.035% [11]. Myxoma is the most frequent benign primary tumor of the heart accounting for 0.3% of open-heart surgery.

The majority of these patients are middle-aged females. In our study, 64% of patients were females with a majority of them in the age group of 40 - 60 years of age. In Staffan Bjessino *et al.* study at Stockholm 73% of patients were females with a mean age of 51 years at operation [12], while Laurent Pinede *et al.* 64% of patients were females with 53 years median age [6], other studies have also shown female preponderance which may be related to hormonal influence [13].

The symptoms and presentation of the patients with Cardiac myxoma depend on the classic triad of 1) obstructive cardiac presentation; 2) embolic presentation; 3) constitutional or systemic manifestation [6].

Dyspnea on exertion is the commonest obstructive cardiac presentation and was seen in 60% of our patients, while in 1 patient the first presentation in the hospital was pulmonary oedema. The mean duration of symptoms ranged from 1day to 6 months with a mean of 21 days. In other similar studies mean duration of symptoms was found to be 3 - 10 months with a mean of 5.4 ± 2.3 months dyspnea was found to be the commonest presentation in 40% - 60% of patients [5] [6] [14] [15].

Changes in position may cause occasional loss of consciousness or death due

to sudden obstruction of the mitral or tricuspid valve. The size of tumor has a paradoxically inverse relationship with larger myxomas presenting late while in smaller tumors the delay in diagnosis is shorter.

In 2 patients the presentation of limb ischemia required embolectomy. Embolization presenting as vascular ischemia of limbs or brain was found to be 15% - 20% in most studies. While Karabins *et al.* in a study of 153 patients reported 4% - 6% cases of embolization [16]. He *et al.* also analyzed 162 patients and found the irregular surface of cardiac myxoma as a cause of systemic embolization [17]. The uneven surface structure and gelatinous consistency of cardiac myxoma were found to predispose to peripheral embolization.

Constitutional symptoms of anemia, fever, weight loss, fatigue, arthralgia, myalgia are rare findings and reported in 16.9% to 32.4% of patients [13] [18] [19]. In our study, 4 patients had anemia while 12 patients had raised ESR. 6 patients had a history of fever while 5 complained of generalized fatigue. These findings are nonspecific and coexist with possible pro-inflammatory or chronic inflammatory reactions.

In 2 patients of our study, it was a serendipitous discovery while evaluating by echocardiography for some other reason. 3.2% to 46.45% of patients the tumor may be asymptomatic making the diagnosis difficult [6] [13].

Diagnosing of cardiac myxoma is suspected by clinical history but transthoracic echocardiography is the best initial modality for diagnosing myxoma with the sensitivity of 95% while transesophageal echocardiography has a sensitivity of 100% [14]. All our patients were diagnosed by TTE and 2 patients also underwent TEE preoperatively due to suspicion of biatrial myxoma. TTE often defines the location, size, shape, attachment and mobility of the tumor, helping in planning the approach to tumor by surgery also. In 60% - 80% of cases tumor was found in the left atrium arising from Fossa ovalis of Interatrial septum [5] [20] [21] while in this study 81% of patients had left atrial tumor. CT or MRI are done rarely where there is suspicion of thrombus presenting as myxoma but may not be useful in all cases as both diagnoses still need surgical intervention.

Coronary angiography was done in all patients older than 40 years. None of our patients required additional coronary artery bypass along with cardiac myxoma resection.

After the diagnosis of cardiac myxoma has been made prompt surgical treatment without delay is the best option to prevent the high risk of sudden death from valvular obstruction or embolism. Resection with minimal manipulation of the heart before aortic cross-clamping and adequate resection with a negative clear margin is a cornerstone of cardiac myxoma surgery to prevent complications and recurrence. Actis Dato *et al.* in their study found that tumors of more than 10 mm have a high risk of embolization and need emergency surgery [22] while we did not find any relationship between size and embolization of tumor.

Most of our patients underwent surgery by biatrial approach through interatrial septum. Different approaches have been suggested in literature depending upon localization of the tumor, resectability and no ideal surgical approach has

been suggested. We believe that the right atrial, trans-septal approach is the best approach in most cases for complete removal of tumor, however, in large tumor occupying left atrium, separate right atrial and left atrial tumor may be necessary to prevent embolization [18] [23] [24]. In two cases we used this approach as the transeptal approach was found to be difficult due to tumor abutting septum and friable. Although this approach offers an excellent exposure, it has been criticized for being responsible for a high incidence of arrhythmias and conduction disturbance after resection of tumor [25]. In a study by Siminelakis *et al.* the ideal approach for myxomas was defined as being right atrial or both atrial incisions with excision of fossa ovalis and surrounding tissues and closure with a pericardial patch [18]. Jones *et al.* defined the advantages of the biatrial approach for direct visualization, minimal manipulation, adequate excision and inspection of all heart chambers [24]. In all patients where tumor was found to arising from the septum, we excised part of fossa ovalis and repaired it with a pericardial patch.

Most of these cases recover well after surgery with a minimal stay in ICU. In our study also ICU stay of patients was 1 - 2 days. In Yu *et al.* study the ICU stay of patients was 2.3 ± 1.3 and hospital stay 11.9 ± 7.6 days and operating these cases early prevented complications [23].

The minimal access surgery has become widespread in cardiac surgery now. Vistarini *et al.* reported that minimally invasive video-assisted surgery an effective, safe and valuable alternative approach to standard sternotomy with similar satisfactory outcomes [26]. However, there have been reports of concerns in applying this approach to myxoma resection because of increased manipulation of tumor leading to the possibility of local and systemic embolization.

The excised tumors present as pedunculated or sessile with a villous or smooth surface which are composed of stellate, fusiform, or plumb cells and have cytologically bland mesenchymal cells in a myxoid stroma. These cells are arranged in single, in cords or forms of rings. In Lee *et al.* study 67.6% were pedunculated and 32.45 were sessile tumors while in our study 45.5% were pedunculated while 50% were sessile with one case of dumb bell-shaped tumor involving both atria [27].

Most of the resections have insignificant postop complications unless patient has preop severe symptoms of pulmonary oedema due to obstructive features or neurological or limb ischemia due to tumor embolization. In our study, we had 1 mortality due to presentation of pulmonary oedema on admission while in most studies the postop early mortality has been 1% - 5% which is comparable [5] [28] [29] [30].

Cardiac myxomas can recur postoperatively especially if incomplete resection, embolization of tumor has occurred. To prevent this complication of tumor, we excised tumors completely with application of 0.1% glutaraldehyde to the excised raw surface, but the mechanism of recurrence has not been fully understood. The recurrence may occur within few months to several years but most recurrences have been found during the first four years. Atypical primary sites,

incomplete excision, metastasis, familial inheritance are all risk factors for recurrence. In large studies recurrence has been found to be 2% - 6% [13] [15] [28].

In our study, no recurrence was found in one year of follow up after surgery. The 1 death in our study occurred in the early postop period while on follow up and telephonic conversations with patient's attendees we found 2 deaths at home, 1 in 6th year another in 8th year. 4 patients were lost in follow-up and censored in the survival curve. Most of the studies show survival of 90% - 98% survival at 10 years [30] [31] [32] [33]. In our study, the survival rate was 90% on 10 years with 95% CI (Confidence Interval) which shows long term survivability after surgery (**Figure 2**).

We had no familial myxoma and this may the reason we did not get any early myxoma-related recurrence. However, we emphasize that recurrence can be prevented by planning a surgical approach to minimize manipulation of tumor and ensuring complete excision of tumor including 5 mm of normal area of clean tissue around it. The risk of smaller tumors for recurrence is more which is different from many tumors elsewhere in the body where larger sized tumors have a higher likelihood of recurrence. Although recurrence is low but endocardial resection is preferable to stalk resection to prevent recurrence [28]. Annual echocardiography is mentioned in most of the studies to detect any recurrence of tumor while patients with familial incidence require annual echo for 4 years [15]. We believe that the recurrence of tumor is rare but it may be prudent to follow up with the patient for the first 4 years in all cases, as some cases are lost in follow-up or die at home by unknown reason if follow up is advised for 1 year after surgery.

5. Conclusion

Cardiac myxomas are a rare benign tumor of the heart that can be often missed in asymptomatic patients. Any patient with dyspnea especially middle-aged females should undergo diagnostic evaluation by echocardiography to detect this potentially life-threatening condition. Surgical interventions have a low risk of complication if tumor has been picked up early and excised with minimal manipulation. The long-term outcome is good with low recurrence except in patients with a familial variant.

Limitation of the Study

Retrospective study with limited number cases due to low incidence of this tumor. Comparisons of different surgical approaches could not be done due to the lack of a control group and the limited number of cases.

Ethical Clearance

Institutional ethical clearance was taken for this study by Roc. No. AS/11/IEC/SVIMS/2017. Dt: 29.01.2021.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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