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A 20-year single community-based tertiary care center's experience with cardiac myxomas

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ABSTRACT

We analyzed 54 cases of cardiac myxoma (n = 40) and non-myxoma (n = 14) diagnosed at a single community-based tertiary care center over 20 years. The data were retrospectively collected for patients between the period January 2000 and September 2020 from the hospital database. We described patient characteristics and clinical features of cardiac myxoma. In patients with diagnosis of cardiac myxoma, the median age was 64 years (range 41–78), with 58% females. Cardiac myxoma patients presented in a variety of ways, as dyspnea (42%), palpitations (20%), and chest pain (15%). Transesophageal echocardiogram was performed in 82.5% of patients. Chest computed tomography (CT) was performed in 32.5%, while cardiac magnetic resonance imaging (CMRI) was performed in 10%. Ischemic evaluation was performed in the majority of patients, primarily having cardiac catheterization. All cardiac myxomas were a single mass and the most common location was the left atrium (n = 34, 85%), followed by the right atrium (n = 6, 15%). 33 (83%) of them were larger than 2 cm. We differentiated cardiac myxoma from non-myxoma mass, which was most commonly a thrombus by histopathology. More patients with cardiac myxoma underwent surgical resection and required hospital and ICU stay than non-myxoma patients. No patients in either group experienced inpatient mortality or a mass recurrence with a median follow-up period of 2 years.

1. Introduction

Primary cardiac tumors are rare, with a frequency of about 0.02%. Of those rare occurrences, 75% are benign, with half being myxomas [1,2]. Common symptoms of cardiac tumors include weight loss, fatigue, fever, and joint pain. Other symptoms can be more life-threatening secondary to complications such as arrhythmias, valve obstruction, heart failure, and systemic emboli [2,3]. Thus, early recognition is paramount to reduce the complication rate and improve survival. In this study, we sought to investigate our institution's experience with cardiac myxomas in effort to search for similarities and discrepancies in clinical presentation, diagnosis, and management of these benign tumors and add to the current body of literature for these rare tumors.

2. Methods

This is a single-center, retrospective, observational cohort study conducted at an 881-bed tertiary care center. The study was granted institutional review board approval prior to commencement. Patients were identified using ICD-10 code for benign neoplasm of the heart (D15.1) between January 2000 and September 2020. Patients were excluded if there was a significant lack of information in the medical record. Patients included in the study were sorted into two cohorts: (1) confirmed diagnosis of cardiac myxoma, and (2) confirmed diagnosis other than myxoma (non-myxoma). Data was vetted manually by two independent physicians to ensure accuracy. The primary endpoints were to describe patient characteristics and clinical features of the myxoma group. Secondary endpoints were to describe the differences in presentation and characteristics in patients with myxoma compared to non-myxoma. These included clinical signs and symptoms at the time of presentation, diagnostic modalities, and follow up information, as well as concomitant procedures performed, and associated complications and outcomes.

Descriptive statistics, including mean with standard deviations and medians with interquartile ranges, were used to describe frequencies within each cohort. Bivariate analyses were conducted to identify

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differences in variables between groups; chi-square test was used to compare categorical variables and the Student's *t*-test or Mann Whitney-*U* test was used for continuous data, as appropriate. Correlation analysis was conducted using dichotomized variables in patients with cardiac myxoma to identify associations. Variables with potential to be associated with certain outcomes, including hospital or ICU stay and complications ($p < 0.2$) were then entered into a binary logistic regression model. Variables were removed stepwise using a backward elimination procedure until the best fit model was identified. All statistical tests were two-sided with p-values of <0.05 considered statistically significant. Statistical analyses were conducted using SPSS v27.0 (IBM, Armonk, NY).

3. Results

A total of 99 patients were identified based on our initial query using ICD-10 codes. Of those, 45 patients were excluded due to lack of information, resulting in a final study population of 54 patients (Fig. 1). There was a total of 40 patients in the 'myxoma' group with a median duration of follow-up of 2.5 years and 14 patients in the 'non-myxoma' group with a median duration of follow-up of 2 years. Of the 40 patients with the diagnosis of cardiac myxoma, 18 (45%) were histopathologically confirmed. Thrombus was the most common non-myxoma mass, followed by artifact. The median age of the whole study population was 64 (range 41–78) and 23 were female (58%). There was no documented family history of cardiac myxomas in any patient. Baseline characteristics are summarized in Table 1. Groups were similar with the exception of more patients in the non-myxoma group having a history of hypertension. Most patients with cardiac myxoma presented with one or more symptoms, including dyspnea in 18 (45%) patients, palpitations in 8 (20%), and chest pain in 6 (15%). Embolic phenomena such as stroke or transient ischemic attack was seen in 4 (10%) patients. The diagnosis was incidental in 11 (27.5%) of the myxoma cohort (see Fig. 2).

Table 2 displays the comparison between characteristics and management of the cardiac mass between groups. All patients had a single mass in both groups and the average size was 3.2 (SD 1.6) cm with no difference between groups. More patients in the myxoma group had a mass that was located in the left atrium compared to the non-myxoma group (85% vs 35.7%, respectively, $p = 0.003$). Furthermore, all patients were diagnosed by echocardiography although more patients in the myxoma group had a TEE performed. More patients in the non-myxoma group had a cardiac MRI performed. Ischemic evaluation was more commonly performed in the myxoma group than the cardiac myxoma group (85% vs 64.3%, respectively; $p = 0.033$), primarily due to more cardiac catheterizations being performed. Finally, more patients underwent surgical resection in the myxoma group compared to the non-myxoma group (85% vs 21.4%, respectively; $p < 0.001$). Other features such as mass size, performance of an ischemic evaluation, significant coronary artery disease, and other concomitant procedures were similar between groups.

Complications and outcomes of patients with cardiac myxoma compared to non-myxoma are displayed in Table 3. Atrial fibrillation was the most common post-operative complication. Patients with cardiac myxoma were more likely to require both a hospital and ICU stay compared to patients without myxoma (72.5% vs 28.6% and 52.5% vs 21.4%, respectively; $p < 0.05$). There were no differences in initial as well as follow-up complications experienced, including atrial

Table 1
Baseline Characteristics of Patients with Cardiac Myxoma vs. Non-Myxoma Mass.

Variable	Cardiac Myxoma Confirmed (n = 40)	Non-Myxoma Mass (n = 14)
Age diagnosed (years ± SD)	62.0 ± 11.0	55.9 ± 17.9
Female Gender, n (%)	23 (57.5)	10 (71.4)
Family History of Myxoma, n (%)	0 (0)	0 (0)
Past Medical History, n (%)		
Diabetes	7 (17.5)	5 (35.7)
Hypertension	22 (55)	13 (92.9)
Hyperlipidemia	18 (45)	9 (64.3)
Coronary Artery Disease	10 (25)	5 (35.7)
Presenting Symptoms, n (%)		
Dyspnea	18 (45)	5 (35.7)
Chest Pain	6 (15)	2 (14.3)
Palpitations	8 (20)	2 (14.3)
Fever	0 (0)	0 (0)
Stroke/Embolism	4 (10)	6 (21.4)
Hemoptysis	0 (0)	0 (0)
Asymptomatic	11 (27.5)	3 (21.4)
Other Cardiac Problems, n (%)		
Atrial Fibrillation	8 (20)	2 (14.3)
Congestive Heart Failure	8 (20)	2 (14.3)
Pulmonary Hypertension	3 (7.5)	3 (21.4)

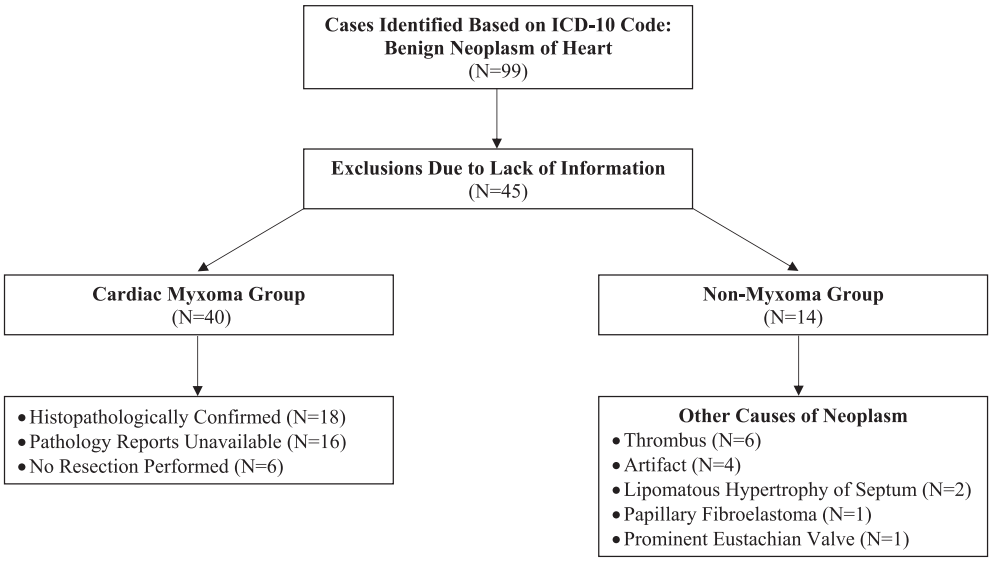

Fig. 1. Flow diagram representing study population.

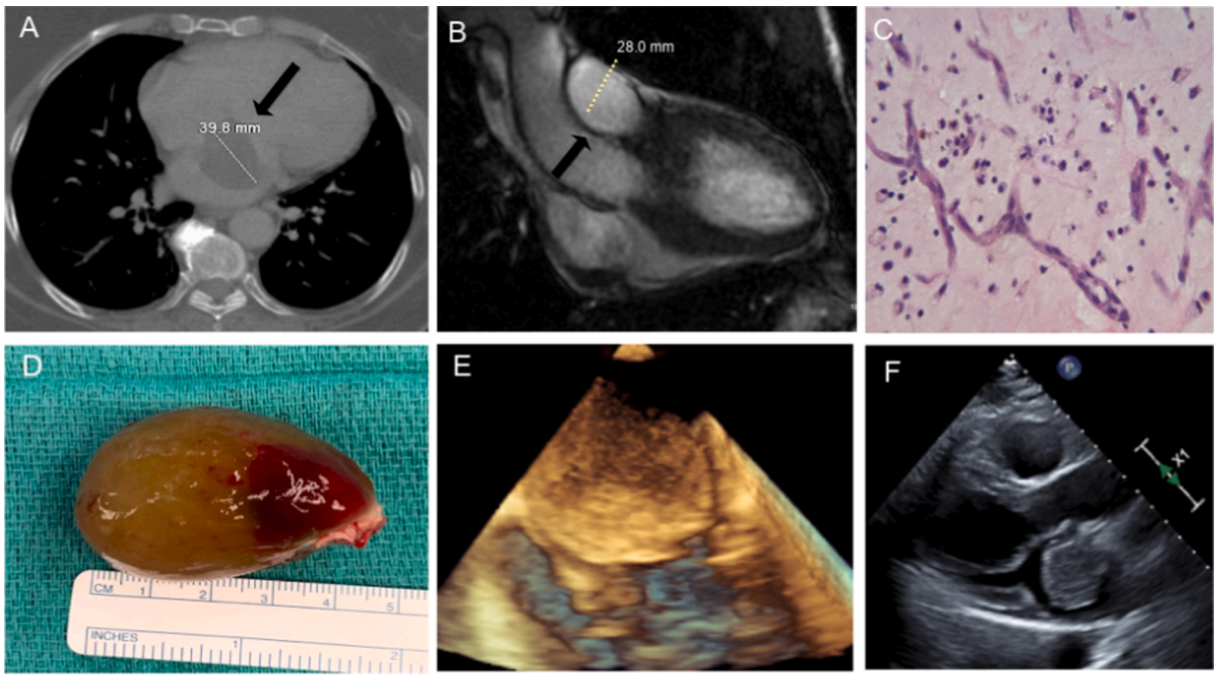

Fig. 2. (Panel A) CT chest with contrast (axial view) showing left atrial mass (arrow) measuring 39.8 mm, 27 Hounsfield units. (Panel B) MRI heart with contrast (coronal view) showing right atrium intracavitary mass (arrow) measuring 28 mm. (Panel C) Histopathology of an atrial myxoma reveals round and stellate myxoma cells with round nuclei, eosinophilic cytoplasm in a myxoid stromal background containing small blood vessels. (Panel D) Gross picture of atrial myxoma. (Panel E) Transesophageal echocardiogram showing 3D image of left atrial myxoma measuring 2.8 cm × 3.7 cm prolapsing across mitral valve. (Panel F) Transthoracic echocardiogram showing left atrial mass measuring 4.1 cm × 2.4 cm.

fibrillation, surgical site infection, and valve replacement. Finally, there were no differences in cardiac mass recurrence or inpatient mortality, which did not occur in either group.

Results of the logistic regression model for patients with cardiac myxoma revealed female gender (odds ratio [OR], 7.1; 95% CI 1.5–33.3; $p = 0.013$) as a variable associated with increased likelihood of ICU stay. Having a pedunculated mass was associated with increased risk of atrial fibrillation (OR, 28.2; 95% CI 1.5–532.6; $p = 0.026$). No other variables were significantly associated with complications or identified outcomes such as mortality and recurrence within the cardiac myxoma group.

4. Discussion

Our study examined the various clinical scenarios in which myxoma patients can present, the clinical course, differential diagnosis, and outcomes of those patients.

Myxomas are dense mesenchymal tissue, either soft or pedunculated, most commonly found in the left atrium, but they can involve any chamber of the heart, including the ventricles. With the majority of myxomas affecting atrial chambers, they pose a high risk of atrial arrhythmias and functional valve stenosis, depending on their size. They are commonly pedunculated with a stalk attached to the walls of the heart but can also be sessile at times. Myxomas can be diagnosed either incidentally or when the patient presents with complications. A myxoma on echocardiography can appear irregular in shape and can often be non-homogeneous [4]. Color flow can be helpful to determine the degree of obstruction across the mitral valve. More recently, CMRI is widely available and known to provide better details in terms of size, attachment, and even mobility with the real-time mode [5,6].

Once a cardiac mass is diagnosed, it is ideal to excise it, particularly when patients present with complications [3]. However, when myxomas are found incidentally and small in size with no hemodynamic effect, it is still unclear whether to opt for serial echocardiographic examinations or excision at the earliest [2]. When concurrent procedures such as CABG and/or valve replacement surgeries are needed, myxoma resection should be performed to avoid future complications. Confirmation of the diagnosis is uncertain until histopathology of the tissue sample is performed following surgical resection. The most common differential diagnosis of cardiac myxomas include mural thrombi which can easily be distinguished with this testing. Tissue markers such as Calretinin which is specific for mesenchymal tissue, are present in myxomas and absent in thrombi [2].

Intraoperatively, when myxomas are found arising from or attached to the interatrial septum, excision is often accompanied with septal closure due to the impending defect. And when they are found encroaching on the mitral valve, the patients might require mitral valve repair or replacement to counteract the mass effect/complication associated with the myxoma [7,8].

With various literature-to-date, it is obvious that they are easy to identify with multiple newer advancements in diagnostics, but pathology is the key to confirm it with tissue analysis as there are a handful of differentials for the myxoma mass, including fibroelastoma, thrombus or hypertrophy of the septum. Interestingly, Pinede and colleagues tried differentiating them histologically into active versus non-active myxomas based on whether they have dense or sparse infiltrate with calcification or ossification [9]. While these describe the tumor cells themselves, immunohistochemical staining serves a major part in tracing the origin that were described in the literature. Those include Vimentin, CD34 which are the most useful markers, tracing back the origin of tumor cells to primitive mesenchymal cells, while others include F8, which are characteristic of vascular endothelium (which might be absent in non-active myxomas due to necrosis and calcification) and Calretinin which has been reported in some studies from the past yet needs more evidence [2,10,11]. S-100 and cytokeratin are very rarely observed [12].

Surgical resection is associated with low mortality and excellent long-term outcomes and when preformed, patients should be followed with serial echocardiograms for a minimum of 4 years as the chance of recurrence is approximately 10–15% [13]. In our study, cardiac myxoma was surgically removed in only 85% of patients. The remaining

Table 2
Characteristics and management of cardiac masses.

Variable	Cardiac Myxoma Confirmed (n = 40)	Non-Myxoma Mass (n=14)	P-value
Echocardiography, n (%)	40 (100)	14 (100)	–
TEE, n (%)	33 (82.5)	7 (50)	0.017*
Single Mass, n (%)	40 (100)	14 (100)	–
Size of Mass, cm ± SD	3.3 ± 1.6	2.8 ± 1.5	0.452
≥2 cm, n (%)	33 (82.5)	8 (80)	0.725
≥4 cm, n (%)	10 (25)	1 (10)	0.290
≥6 cm, n (%)	4 (10)	1 (10)	0.981
Location of Mass, n (%)			
Left Atrium	34 (85)	5 (35.7)	0.003*
Right Atrium	6 (15)	6 (42.9)	
Other/Unable to Determine	0 (0)	3 (21.4)	
Pedunculated Mass, n (%)[a]	10 (35.7)	2 (100)	0.073
Additional Imaging Performed, n (%)	22 (55)	10 (71.4)	0.282
Chest CT	13 (32.5)	3 (21.4)	0.435
Cardiac MRI	4 (10)	7 (50)	0.001*
Ischemic Evaluation Performed, n (%)	34 (85)	9 (64.3)	0.033*
Cardiac CT	3 (7.5)	2 (14.3)	0.451
Cardiac Catheterization	30 (75)	6 (42.9)	0.028*
Stress Test	1 (2.5)	1 (7.1)	0.429
Significant CAD > 50%, n (%)[b]	5 (12.5)	2 (20)	0.609
Resection Performed, n (%)	34 (85)	3 (21.4)	<0.001*
Concomitant Procedure Performed, n (%)	13 (32.5)	2 (14.3)	0.190
Coronary Artery Bypass Graft	3 (7.5)	1 (7.1)	–
Valve Replacement or Repair	4 (10)	0 (0)	–
Septal Defect/PFO Closure/ Repair	6 (15)	0 (0)	–
Pulmonary Vein Isolation	2 (5)	0 (0)	–
Left Atrial Appendage Clip	2 (5)	0 (0)	–
SVC Thrombus Removal	0 (0)	1 (7.1)	–
Biventricular Pacemaker	1 (2.5)	0 (0)	–

TEE – transesophageal echocardiogram; CAD – coronary artery disease; PFO – patent foramen ovale; SVC – superior vena cava.
[a] N = 28 for 'myxoma' group and N = 2 for 'non-myxoma' group.
[b] N = 37 for 'myxoma' group and N = 10 for 'non-myxoma' group.

Table 3
Complications and outcomes of Myxoma compared to non-Myxoma patients.

Variable	Cardiac Myxoma Confirmed (n = 40)	Non-Myxoma Mass (n = 14)	P-value
Complication Experienced, n (%)[a]	15 (37.5)	3 (21.4)	0.272
Paroxysmal Atrial Fibrillation	10 (25)	1 (7.1)	0.153
Other	10 (25)	2 (14.3)	0.407
ICU Stay, n (%)	21 (52.5)	3 (21.4)	0.044*
Hospital Stay, n (%)	29 (72.5)	4 (28.6)	0.013*
<30 days	26 (65)	4 (28.6)	–
≥30 days	3 (7.5)	0 (0)	–
Follow-Up Complications, n (%)	4 (12.5)	1 (7.1)	0.751
Paroxysmal Atrial Fibrillation	3 (7.5)	0 (0)	0.292
Surgical Site Infection	0 (0)	1 (7.1)	0.088
Valve Replacement	1 (2.5)	0 (0)	0.550
Inpatient Mortality, n (%)	0 (0)	0 (0)	–
Recurrence, n (%)	0 (0)	0 (0)	–

[a] Note: some patients experiences more than one complication. Other complications included: shock, pneumothorax, mediastinitis, heart block, sinus bradycardia, ileus, adrenal insufficiency, and thrombocytopenia.

patients did not undergo surgical resection due to the presence of comorbidities or technically difficult surgeries based on location of the myxoma, deeming them ineligible for surgery. We did not identify any recurrent myxomas, possibly due to the fact that the median follow-up period was only 2.5 years and myxoma may have recurred beyond that. Unfortunately, quantification of MACE in our study was not performed due to the limited sample size and follow up of lesser duration to avoid any bias. Quality of life in our Myxoma cohort was mostly affected by the incidence of Atrial fibrillation both pre- and post-resection.

Rarely, Myxomas can be a part of an autosomal dominant disorder with defect in PRKAR1A gene known as Carney complex (CNC). Isolated cardiac myxomas in CNC are rare without other components such as cutaneous pigmentation, myxomas in skin/breast and endocrine-non endocrine neoplasia. None of our patient in the myxoma cohort had any positive family history or any non-cardiac features or presentation at younger age < 40 years or recurrence in order to suspect CNC. Hence, the patients in our myxoma cohort are more likely to have Isolated Myxoma and not part of genetic disorder [14,15].

This study has several important limitations. The retrospective design of the study introduces the potential for unmeasured confounders as well as bias with data abstraction. However, given the rareness of cardiac tumors, it may be difficult to design prospective studies. Also, we had multiple investigators vet the data as it was being abstracted. The retrospective nature also limited the inclusion of all patients identified by ICD-10 codes in one of the groups due to the lack of data available. Furthermore, in some cases, pathology results were not readily available potentially due to surgery taking place at an outside institution, transition of our health record to a different system during the study and thus potential errors in record-keeping, the fact that resection was not performed, or other causes. Although viewing pathology records would have been ideal to ensure correct categorization and diagnosis, cardiac myxoma diagnoses were carried forward on these patient profiles after resection was known to occur. In patients that were not known to undergo resection in the myxoma group, it is also difficult to determine if the cardiac mass was truly a myxoma just by imaging and might have been due to another cause (i.e., non-myxoma). These patients were included in the myxoma group given the diagnosis that was carried through on their patient record, but this limitation is important to note. The small sample size may also limit generalizability, but given the rare occurrence once again, this was expected. Small samples sizes are also seen in other studies evaluating institutional experiences with cardiac myxomas [1,3,9,11,16–21]. Despite these limitations, our study adds an up-to-date experience in the field with cardiac myxoma including the patient characteristics, management, and outcomes with these patients.

5. Conclusion

Cardiac myxomas are often non-malignant tumors that most commonly originate in the left atrium. Transthoracic, or more specifically, transesophageal echocardiography, is the ideal tool of diagnosis despite the newer technologies. However, the management yet remains a solitary decision at the physician's discretion. Our findings indicate most patients are managed with mass resection with low risk of complications, recurrence, and mortality. In conclusion, the field of cardiac myxoma still lacks integrated data in terms of standardized management. Multicentric studies across the country should be encouraged, including the pediatric population, which would be beneficial in analyzing the data to bring up guidelines.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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