

## Mortality and Embolic Potential of Cardiac Tumors

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### Abstract

**Background:** Cardiac tumors are rare, mostly benign with high embolic potential.

**Objectives:** To correlate the histological type of cardiac masses with their embolic potential, implantation site and long term follow up in patients undergoing surgery.

**Methods:** Between January 1986 and December 2011, we retrospectively analyzed 185 consecutive patients who underwent excision of intracardiac mass (119 females, mean age  $48 \pm 20$  years). In 145 patients, the left atrium was the origin site. 72% were asymptomatic and prior embolization was often observed (19.8%). The diagnosis was established by echocardiography, magnetic resonance and histological examination.

**Results:** Most tumors were located in the left side of the heart. Myxoma was the most common (72.6%), followed by fibromas (6.9%), thrombi (6.4%) and sarcomas (6.4%). Ranging from 0.6cm to 15cm (mean  $4.6 \pm 2.5$ cm) 37 (19.8%) patients had prior embolization, stroke 10.2%, coronary 4.8%, peripheral 4.3% 5.4% of hospital death, with a predominance of malignant tumors (40%  $p < 0.0001$ ). The histological type was a predictor of mortality (rhabdomyomas and sarcomas  $p = 0.002$ ) and embolic event (sarcoma, lipoma and fibroelastoma  $p = 0.006$ ), but not recurrence. Tumor size, atrial fibrillation, cavity and valve impairment were not associated with the embolic event. During follow-up (mean  $80 \pm 63$  months), there were 2 deaths (1.1%) and two recurrences 1 and 11 years after the operation, to the same cavity.

**Conclusion:** Most tumors were located in the left side of the heart. The histological type was predictor of death and preoperative embolic event, while the implantation site carries no relation with mortality or to embolic event. (Arq Bras Cardiol. 2014; 103(1):13-18)

**Keywords:** Heart Neoplasms / mortality; Heart n/ surgery; Embolism / complications.

### Introduction

Primary cardiac tumors are uncommon and often asymptomatic with an incidence ranging from 0.0017% to 0.28%<sup>1</sup>. The differential diagnosis of cardiac masses includes vegetations, thrombi, and tumors. It may involve the endocardium, myocardium or epicardium. Secondary involvement of the heart by extra-cardiac tumors is rare. Benign tumors constitute 80% of primary cardiac neoplasms and myxomas are the prevalent type<sup>2</sup>. Angiosarcoma is the most frequent malignant cardiac tumor and is characterized by rapid growth, local invasion and distant metastasis<sup>3</sup>.

The clinical findings of cardiac tumors vary. They may mimic either cardiac or systemic diseases, and, therefore, should be

considered in the differential diagnosis of distinct heart diseases. In addition, as surgical therapy is curative in most cases, early diagnosis is required to prevent complications. In patients with primary cardiac neoplasm, tumors location and cells type are important in determining clinical presentation, therapy options, and outcomes<sup>4,5</sup>.

The aim of this study is to correlate the histological type of cardiac masses with their embolic potential, implantation site and long term follow up in patients undergoing surgery.

### Methods

Between January 1986 and December 2011, we retrospectively analyzed 185 consecutive patients (118 females - 64%), with age ranging from 1 month to 86 years (mean age  $48 \pm 20$  years), who were operated on at our Institution for primary cardiac mass.

The diagnosis was established by echocardiography, magnetic resonance and histological examination.

Patients' characteristics, as well as demographic distribution, are listed in tables one to three. The most frequent primary cardiac tumors origin site was the left atrium (Table 1), most of the patients were asymptomatic (72%) and when with symptoms, dyspnea was the most common clinical presentation. Embolization was often observed (19.8%) especially to the central nervous system (Table 2).

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Complete patients' follow-up was collected by chart review and patients' phone interview to assess late functional status.

### Statistical Analysis

All data were initially descriptively analyzed. Analysis of the minimum and maximum values, calculation of means, standard deviations and median were done for quantitative variables. For qualitative variables were calculated absolute and relative frequencies. The continuous variable studied was tumor size, the others were categorical (recurrence, embolism, origin site, histological type, atrial fibrillation, valve disease, death and hospital death).

For comparison of means of two groups (variable tumor size) it was used the Student t test (normal data distribution). The test of proportions of the categorical variables were performed using the chi-square or Fisher's exact test (when expected frequencies less than 5%). Long-term cumulative evaluations were assessed by means of Kaplan-Meier analysis and curves were compared with the log-rank test. A p value less than 0.05 was considered statistically significant. Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 16.0 for Windows (IBM Corporation Armonk, New York).

This study was approved by our Institutional Ethics Committee / Review Board, which waived the requirement for informed patient consent due to the retrospective design of this study.

### Results

One hundred seventy four patients (93.6%) had benign cardiac tumors. Their preferred implantation site was the left side of the heart (88%). 78% were in the left atrium, 8% in the left ventricle, 13% in the right atrium and 2% in the right ventricle. Myxoma was the most common histological type (72.6%), followed by fibroma (7%) and intracardiac thrombus (6.5%); the remaining types are listed in table 3.

Hospital mortality was 5.4%: four for patients with benign tumors (2.3%) and six malign (50%). Two infants with rhabdomyoma developed untreated low output syndrome

despite high-dose inotropic support due to surgical resection and reconstruction of involved cardiac cavity. The third patient was a 12 year-old young girl who died of unknown cause during recovery of a 2,5cm left atrial thrombus and ductus

**Table 1 – Classification of 185 patients with intracardiac tumors according to implantation site**

Origin Site	Nº of patients (%)
Left atrium	143 (77.3%)
Right atrium	23 (12.4%)
Left ventricle	15 (8.1%)
Right ventricle	4 (2.2%)

**Table 2 – Preoperative clinical profile of 185 patients with cardiac tumors**

Symptom Cardiac	Nº of patients
Dyspnea	52 (28%)
Atrial fibrillation	50 (26.9%)
Palpitation	17 (9.1%)
Syncope	18 (9.7%)
<b>Embolic</b>	
CNS	19 (10.2%)
AMI	9 (4.8%)
Peripheral	9 (4.8%)
<b>Systemic</b>	
Fever	9 (4.8%)
Anemia	7 (3.8%)
Weight loss	3 (1.6%)
Arthralgia	1 (0.5%)

CNS: Central nervous system; AMI: Acute myocardial infarction.

**Table 3 – Institutional experience with cardiac tumors resection**

Type of tumor	Nº of patients (%)	Male/Female	Mean age (years)	Size (mean) (cm)
Myxoma	135 (72.6%)	45 / 90	52 ± 16	1-12.5 (4.7 ± 2.1)
Fibroma	13 (7%)	8 / 5	38 ± 37	0.6 – 11 (3.9)
Thrombus	11 (5.9%)	3 / 8	35 ± 22	1.8 – 5.7 (2.9)
Sarcoma	7 (3.8%)	3 / 4	55	2.5 – 6.4 (4.6)
Papillary Fibroelastoma	4 (2.2%)	2 / 2	46	0.6 – 1.8 (1)
Lipoma	4 (2.2%)	2 / 2	45	1.5 – 8.3 (4.7)
Rhabdomyoma	4 (2.2%)	1 / 3	0.03	2.2 – 10 (4.3)
Angiosarcoma	3 (1.6%)	1 / 2	40	2.5 – 3 (2.7)
Osteosarcoma	2 (1.1%)	0 / 2	13.5	4.5 – 5.5
Hemangioma	1 (0.5%)	1 / 0	67	2.5
Meningioma	1 (0.5%)	1 / 0	19	9

arteriosus resection, and necropsy was not allowed. The fourth was a 42-year-old woman with coronary embolization prior to her myxoma resection, who died of untreated low output syndrome after surgery. The six patients with malignant tumors died early during the postoperative period due to rapidly disease progression (54.5%).

When comparing hospital mortality with cells type, more deaths related to malign tumors ( $p = 0.002$ ) were observed. The histological type was predictor of mortality (rhabdomyomas, sarcomas and angiosarcomas;  $p < 0.001$ ) (Figure 1) but not of recurrence ( $p = 0.182$ ). There was no relation between implantation site and mortality ( $p = 0.346$ ) (Figure 2).

Preoperative thromboembolic event occurred in 37 patients (19.8%) (Table 2), mainly to the central nervous system (10.2%), but also to coronary arteries (4.8%), to lower limbs (4.3%) and to pulmonary territory (0.5%). The tumor size ( $p = 0.132$ ), pre-operative atrial fibrillation ( $p = 0.206$ ) and implantation site ( $p = 0.121$ ) were not associated with embolic event. Nevertheless, the histological type was predictor of embolic event (osteosarcoma, angiosarcoma, papillary fibroelastoma and lipoma;  $p = 0.006$ ).

During follow up (mean  $87 \pm 51.9$  months) there were two patients with prior myxoma resection who died 60 and 27 months after surgery of unknown cause and cerebrovascular accident respectively. Actuarial survival was 100%, 98.8% and 98.8% at 1, 5 and 10 years respectively. There were two recurrences to the same cavity; one left atrial mixoma recurrence 11.2 years after the surgical resection and a right atrial osteosarcoma 11 months after the operation. Both were operated on and had an eventful

recovery. One neurological embolic event was observed at 27 months follow up but not related to intracardiac mass.

## Discussion

In this study it was observed that the histological type was a predictor of mortality and embolic events.

Malignant tumors (sarcomas) were predictors of hospital mortality. Angiosarcoma is the most common malignant tumor of the heart and is characterized by rapid growth, local invasion, and distant metastasis with reserved prognosis. Patients with non metastatic cardiac sarcoma amenable to complete resection experienced improved survival<sup>6</sup>. However, the high overall rates of disease progression and mortality, highlight the need for more effective local and systemic treatments that may be used in conjunction with surgery to improve patient outcomes<sup>7</sup>. Some authors recommend, in order to reducing mortality, multimodal therapy (surgical resection, radiofrequency ablation, or radiation treatment). They achieved reasonable survival for patients with resected cardiac sarcomas (mean 47 months). Patients with local tumor recurrence or metastatic disease may still benefit from aggressive treatment<sup>8</sup>.

Elbardissi et al<sup>5</sup> in 48 years of experience in 323 patients with primary cardiac tumors found that patients with malignant tumors have a dismal prognosis and despite aggressive adjuvant chemotherapy after resection, the median survival rates of these patients were less than 1 year.

We observed a decrease in mortality over time. In the period between 1980 and 1998 we had 16% of mortality<sup>9</sup>. At that time,

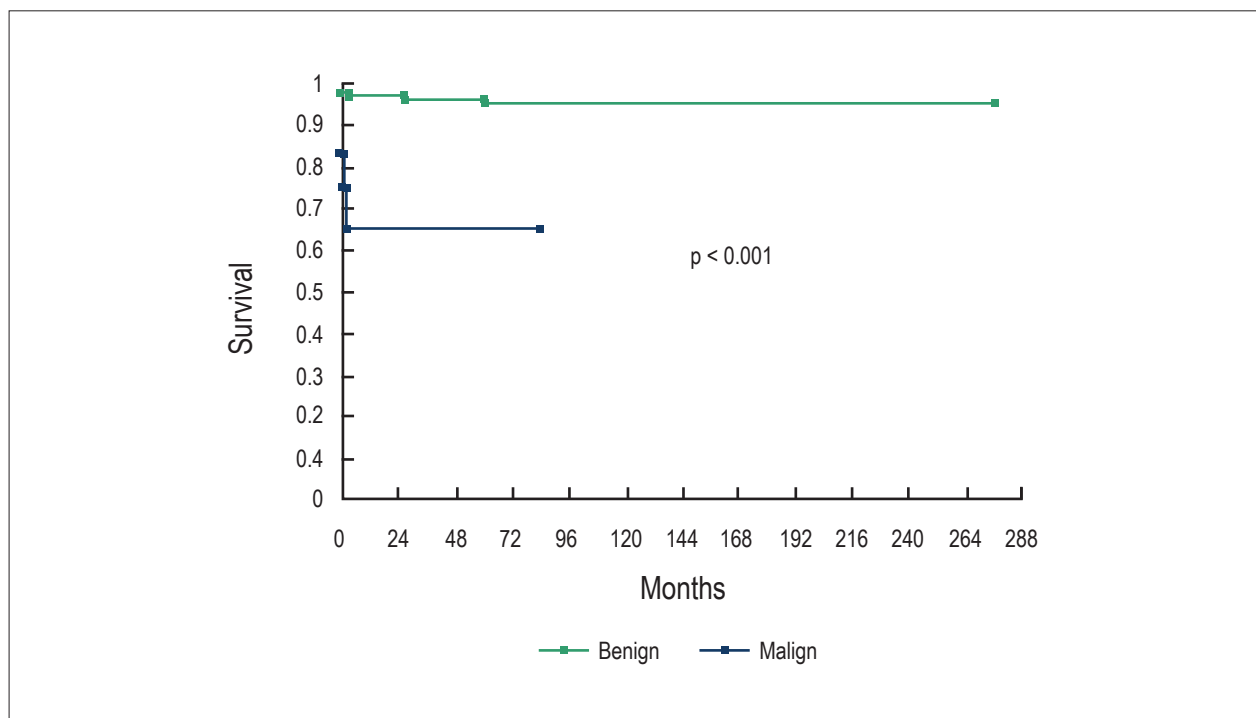


Figure 1 – The tumors' histological type was related with higher mortality.

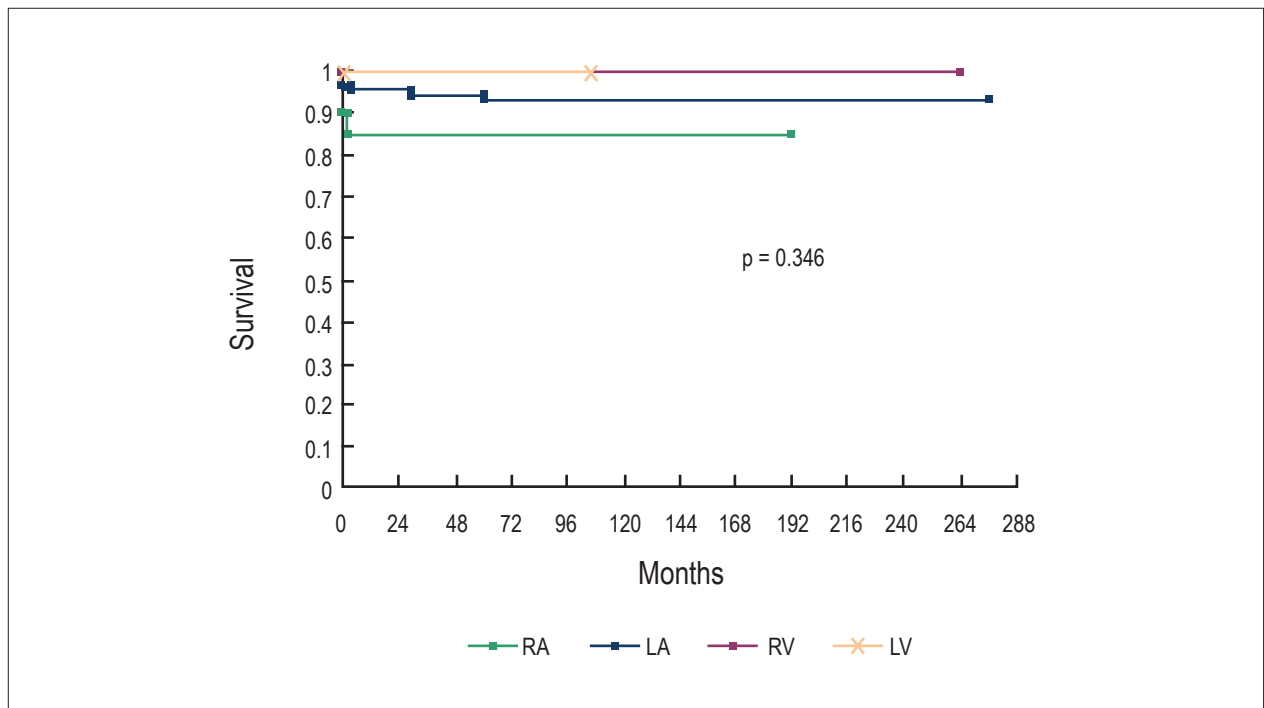


Figure 2 – The tumors' implantation site did not interfere with survival (RA: right atrium; LA: left atrium; RV: right ventricle; LV: left ventricle).

the great majority of patients were diagnosed belatedly and, with the advent of routine use of additional methods, such as echo complemented with MRI, the diagnosis can be performed early and avoid complications. In the subsequent period up to 2004, the mortality dropped to 6%<sup>10</sup>. In this study, the hospital mortality of 5.4% is still considered high, although mainly due to the malignant tumors aggressive behavior.

As it has been written, the majority of cardiac tumors are benign and cardiac myxomas are the most frequent ones (over 70%). Myxoma is the most prevalent cardiac tumor in the adult population, predominating in the female sex, with a gelatinous and transparent gross appearance. Myxoma is usually a single tumor, preferably located in the left atrium and inserted close to the oval fossa. They are considered benign tumors, even though they may behave in a malignant way with local relapse, invasion of the thoracic wall, and embolism<sup>11</sup>.

The clinical presentation of cardiac tumors is usually divided into cardiac, embolic and systemic manifestations, such as fever, cachexia, arthralgia, Raynaud's phenomenon, rash, and anemia, which are attributed to the production of certain cytokines, such as interleukin-6<sup>12</sup>, and symptoms related to metastasis. In our series, systemic manifestations were present in 10.9% of the patients, and were reported as fever (4.8%), chronic anemia (4%), weight loss (1.6%) and arthralgia (0.5%).

Despite the fact that 72% of our patients were asymptomatic, cardiac manifestations may be related to tumor's size, because as they grow, they can progressively obstruct cardiac chambers mimicking valve disease. So, dyspnea may be followed by others symptoms of heart failure, as happened in our series.

In order to avoid complications such as intracavity obstruction or embolic events, the treatment of choice for primary cardiac tumors is resection<sup>13</sup>.

Primary cardiac tumors should be considered as a possible diagnosis for all patients with embolization, although in our casuist, we had 12 patients (6.4%) with thrombus mimicking primary cardiac tumors. Cardiac imaging has difficulty in categorizing intracardiac mass and some patients may have their mass classified as thrombus after pathological evaluation. Two of these patients were subsequently diagnosed as having antiphospholipid syndrome. There are several cases in literature of atrial and ventricular thrombus related to antiphospholipid syndrome mimicking primary cardiac tumors<sup>14</sup>. Another recent study<sup>4</sup> found a prevalence of cardiac thrombus in 13 of 84 (15.4%) patients with cardiac tumors. They showed thrombotic masses of variable age, occasionally with features of organization and typical concentric fibrinous layers. One case showed evidence of early peripheral calcification. None of the cases contained areas suggestive of residual myxoma or other-type neoplasm.

Most patients, in whom tumor was diagnosed and later confirmed thrombus by pathology, belonged to our initial series in which the diagnosis was established only by echocardiography. We have currently used, to all cardiac masses, transthoracic echo at first, followed by transesophageal echo and resonance to confirm the diagnosis.

Recurrence develops in about 3% of tumors, although the rate is higher with familial cardiac myxomas. Our study showed tumor recurrence in two cases. One of them was a myxoma 11 years after initial surgical treatment. It was observed that the cumulative myxoma recurrence was as high as 13%, and has

increased steadily up to 4 years after which there was a low hazard of tumor recurrence. There was no association between the method of surgical excision and the incidence of tumor recurrence. Patients who experienced a myxoma recurrence were younger than those who did not (mean 42 years versus 57 years). The site of recurrence was at the location of the original tumor in 81% of cases. These authors recommended, based on this finding, all patients (especially younger patients) who undergo tumor resection should be followed closely with echocardiography semiannually for 4 years after resection<sup>5</sup>.

## Conclusion

Our analysis shows that most tumors were located in the left side of the heart, most of intracardiac mass is benign and myxoma is the most common histological type. And also the histological type was a predictor of death and preoperative embolic event while the implantation site carries no relation to mortality or to embolic event.

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## Author contributions

Conception and design of the research and Acquisition of data: Dias RR; Analysis and interpretation of the data: Dias RR, Fernandes F, Ramires FJA; Writing of the manuscript: Dias RR, Fernandes F; Critical revision of the manuscript for intellectual content: Mady C, Albuquerque CP, Jatene FB.

## Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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## Study Association

This study is not associated with any thesis or dissertation work.

