

## Intracardiac tumors: results from a single heart center

*Kalp içi tümörler: Tek kalp merkezinin sonuçları*

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### ABSTRACT

**Background:** This study aims to present the results of surgical treatment of intracardiac tumors in our cardiac surgery center.

**Methods:** Data of 21 patients with intracardiac tumors (15 males, 6 females; median age 60.9 years; range 35 to 87 years) who underwent surgery between April 2006 and May 2015 were retrospectively analyzed. The patients were diagnosed preoperatively by transthoracic echocardiography and computed tomography or magnetic resonance imaging.

**Results:** The mean follow-up was 27.85 months. Of 21 patients, 12 had benign tumors and nine had malignant tumors. Of the benign tumors, nine were myxomas, one was an intramuscular lipoma, one was an interatrial septal lipoma, and one was a papillary fibroelastoma. Of the malignant tumors, eight were metastatic tumors and one was a primary tumor. Median sternotomy was performed in all patients to access the heart. Thrombi due to a cardiac mass were detected intraoperatively in some patients.

**Conclusion:** Our study results suggest a high-degree of diagnostic confusion between intracardiac thrombi and tumors. Therefore, metastatic cardiac tumors should be considered in patients with pleural or pericardial effusion of no other identified cause.

**Keywords:** Cardiac tumor; metastasis; primary; surgery.

Intracardiac tumors are encountered rarely in cardiac surgery and are often asymptomatic with an incidence ranging from 0.0017% to 0.28%.<sup>[1]</sup> Of these tumors, 75% are benign (75% of these are myxomas) and 25% are malignant (75% of these are sarcomas). In addition, metastatic cardiac tumors are seen more frequently than primary tumors.<sup>[1]</sup> The most common

### ÖZ

**Amaç:** Bu çalışmada kalp cerrahisi merkezimizde kalp içi tümörlerin cerrahi tedavisi sonuçları sunuldu.

**Çalışma planı:** Nisan 2006 - Mayıs 2015 tarihleri arasında ameliyat edilen kalp içi tümürlü 21 hastanın (15 erkek, 6 kadın; ort. yaş 60.9 yıl; dağılım 35-87 yıl) verileri retrospektif olarak incelendi. Hastalara ameliyat öncesi transtorasik ekokardiyografi ve bilgisayarlı tomografi veya manyetik rezonans görüntüleme ile tanı kondu.

**Bulgular:** Ortalama takip süresi 27.85 aydı. Yirmi bir hastanın 12'sinde benign ve dokuzunda malign tümör tespit edildi. Benign tümörlerin dokuzu miksuma, biri intramusküler lipom, biri interatriyal septal lipom ve biri papiller fibroelastom idi. Malign tümörlerin sekizi metastatik ve biri primer tümör idi. Tüm hastalarda kalbe ulaşmak için medyan sternotomi yapıldı. Bazı hastalarda cerrahi sırasında kardiyak kitle nedeniyle trombüsler tespit edildi.

**Sonuç:** Çalışma sonuçlarımız kalp içi trombüs ve tümörlerinin tanısında önemli düzeyde bir karışıklık olduğunu göstermektedir. Bu nedenle, başka bir neden tespit edilemediğinde, plevral veya perikardiyal efüzyonlu hastalarda metastatik kardiyak tümörler akla gelmelidir.

**Anahtar sözcükler:** Kalp tümörü; metastaz; primer; cerrahi.

primary cardiac tumor in adults is myxoma, whereas rhabdomyosarcoma is the most common tumor in children.<sup>[2]</sup>

Five-year life expectancy rates are about 83% for benign, 30% for primary malignant, and 26% for metastatic cardiac tumors.<sup>[3]</sup> For benign tumors, surgery often yields good outcomes with low recurrence



Available online at  
www.tgkdc.dergisi.org  
doi: 10.5606/tgkdc.dergisi.2016.12631  
QR (Quick Response) Code

Received: November 14, 2015 Accepted: January 11, 2016

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rates.<sup>[3]</sup> In contrast, malignant tumors have a very poor prognosis with a life expectancy of 7-24 months.<sup>[3]</sup> Herein, we present the results of surgical treatment of intracardiac tumors in our cardiac surgery center.

## PATIENTS AND METHODS

Data of a total of 29 patients who underwent surgery for intracardiac tumors between April 2006 and May 2015 were retrospectively analyzed. Due to intraoperative diagnosis of thrombus, eight patients were excluded from the study. The study included 21 patients (15 males and 6 females; mean age 60.9 years; range, 35 to 87 years). Data including the demographic and clinical characteristics of the patients such as age, gender, smoking status, and comorbidities (hypertension, diabetes mellitus, peripheral artery disease, chronic obstructive pulmonary disease) were retrieved from the hospital database. Preoperative diagnosis was established using transthoracic echocardiography (TTE) and computed tomography (CT) or magnetic resonance imaging (MRI). Median sternotomy was performed in all patients during surgery. The following patient data were recorded: type and localization of the tumor, clinical signs and symptoms on admission, the length of postoperative stay in the intensive care unit and hospital, the amount of drainage and blood products transfused, the presence of atrial fibrillation (AF), mortality rate, and primary cancer diagnosis in cases with metastatic tumors.

The study protocol was approved by the Medical Faculty of Pamukkale University Ethics Committee. A written informed consent was obtained from each

**Table 1. Demographic data and clinical characteristics of patients**

	n	%
Gender		
Male	15	71.4
Female	6	28.6
Hypertension	14	66.7
Diabetes mellitus	5	23.8
Smoking	6	28.6
Chronic obstructive pulmonary disease	2	9.5
Peripheral arterial disease	1	4.8
Dyspnea	11	52.4
Palpitation	4	19
Peripheral edema	2	9.5
Cerebrovascular accident	2	9.5
Chest pain	2	9.5
Fatigue	1	4.8
Incidentally	5	23.8

patient. The study was conducted in accordance with the principles of the Declaration of Helsinki.

## RESULTS

The demographic and clinical features of the patients are presented in Table 1. Of 21 patients, 12 had benign tumors and nine had malignant tumors. Of the benign cases, nine were myxomas, one was an intramuscular lipoma, one was an interatrial septal lipoma, and one was a papillary fibroelastoma (PFE). Of the malignant cases, eight were metastatic tumors and one was a primary tumor (an angiosarcoma). Three patients had malignant epithelial tumor metastases, one had a lung adenocarcinoma metastasis, one had a malignant epithelial tumor metastasis of papillary-type renal cell carcinoma, one had a thymoma with thymic carcinoma, one had carcinoma metastasis of unknown origin, and one had a malignant mesenchymal tumor.

Tumor types and rates are shown in Table 2, The mean length of postoperative stay in intensive care unit and hospital, and the amount of drainage and blood products transfused are shown in Table 2. In patients with benign tumors, the most frequent symptoms on admission were dyspnea (52.3%) and palpitation (19%), while in malignant cases, the most frequent signs and symptoms were dyspnea (52.3%) and pericardial/pleural effusion (23.8%).

The mean follow-up was 27.85 (range, 0 to 110) months. Benign and malignant cases were followed for a mean duration of 41 months and 10.7 months, respectively. Preoperative thromboembolic phenomena were observed in two patients (9%) diagnosed with myxomas. One patient (4.7%) had left hemiplegia with mild sequelae, while one (4.7%) had a transient

**Table 2. Tumor types and rates**

	n	%
Benign		
Myxoma	9	42.9
Intramuscular lipoma	1	4.7
Interatrial septal lipoma	1	4.7
Papillary fibroelastoma	1	4.7
Malignant		
Primary		
Angiosarcoma	1	4.7
Metastatic		
Malignant epithelial tumor	4	19
Lung adenocarcinoma	1	4.7
Carcinoma	1	4.7
Malignant mesenchymal tumor	1	4.7
Thymoma with thymic carcinoma	1	4.7

**Table 3. Postoperative data**

	n	Mean±SD
Intensive care unit mean time (hour)		23.3±13
Hospitalization mean time (day)		7.2±5.2
Mean drainage (mL)		573.8±344
Mean blood transfusion (unit)		3.2±1.5
Mean ejection fraction (%)		58±6.7
Mean PAP (mmHg)		37.8±14.1
Postoperative atrial fibrillation	7	

SD: Standard deviation; PAP: Pulmonary artery pressure.

ischemic attack. Overall, AF was found in 19% of patients with benign tumors and 14.2% of patients with malignant tumors.

The in-hospital mortality rate was 33% (n=7). Of these patients, two (9%) had benign tumors and five (23.8%) had malignant tumors. One patient with a right atrial lipoma had aortic stenosis and insufficiency, mitral valve stenosis and insufficiency, and tricuspid valve insufficiency. This patient also had a permanent complete atrioventricular (AV) block with a permanent right atrial pacemaker lead. Despite the attempts to survive through tumor excision, aortic valve replacement, and mitral and tricuspid annuloplasty, the patient died due to cardiac failure in the 21<sup>st</sup> day after surgery. Another patient with a benign tumor who died had PFE. This patient presented with chest pain caused by a coronary embolism. The patient died from multi-organ and cardiac failure in the eight postoperative day.

The first patient with a malignant tumor had a primary malignant lung epithelial tumor with a left atrial metastasis. The patient underwent aortic valve replacement two years previously. The patient died from cardiopulmonary failure three days after surgery. The second patient had a malignant epithelial tumor with a papillary-type renal cell carcinoma as the primary tumor. This patient underwent nephrectomy and right atrial mass excision in the same session. The patient died in the early postoperative period due to renal failure and low cardiac output. The third patient had a malignant mesenchymal tumor with an unknown primary tumor. This patient died from low cardiac output and hepatic failure in the sixth postoperative day. The fourth patient had a primary malignant epithelial lung tumor with a left atrial metastasis. This patient suffered from an arrest during the anesthesia induction and underwent cardiopulmonary bypass surgery after resuscitation. Following resection, the patient died from low cardiac output in the early postoperative period. The fifth patient had an angiosarcoma. The

tumor had transmurally enlarged the right atrium, invading the superior and inferior vena cava, superior pulmonary vein, and the free wall of the right ventricle. The mass in the right atrium was resected extensively and the defect was closed with a pericardial patch. This patient died from pulmonary failure 29 days later following surgery. After discharge, one patient died from a cerebrovascular disorder 11 months after surgery.

## DISCUSSION

Myxomas are the most common benign cardiac tumors.<sup>[2,3]</sup> These tumors develop most commonly between the fourth and sixth decades of life in females.<sup>[4]</sup> They are most often localized in the left atrium (75%); however, they may also develop in the right atrium (15-20%) and ventricles (3-4%).<sup>[4]</sup> Genetically transmitted myxomas occurs in individuals with Carney complex, which is related to cardiac and cutaneous myxomas, endocrine hyperfunction (i.e., of the adrenals, pituitary gland, thyroid, and Sertoli cells), and cutaneous hyperpigmentation (a form of lentiginosis).<sup>[5,6]</sup> Cardiac tumors can present with intracardiac obstruction, as well as common extracardiac signs and symptoms, such as systemic embolization and fever, cachexia, arthralgia, Raynaud's phenomenon, itching, and anemia.<sup>[1]</sup> Stroke, myocardial infarction, malignant arrhythmia, and related sudden cardiac death can be the first signs of these tumors.<sup>[2]</sup>

Taş et al.<sup>[4]</sup> reported that 67.7% of patients with myxomas were females and 32.3% were males, resulting in a female: male ratio of about 2:1. Consistent with these findings, in the present study, six patients with a myxoma were females and three were males, resulting in a female: male ratio of 2:1. In our study, the tumors were localized in the left atrium in seven (77.8%) patients and in the right atrium in two (22.2%) patients. Similarly, Taş et al.<sup>[4]</sup> reported tumor localizations in the left and the right atria in 93% and 6% of their patients, respectively. The mean age was 49.8 (range, 5 to 76) years in the aforementioned study. Also, Aval et al.<sup>[7]</sup> reported a mean patient age of 50.6 (range, 13 to 76) years. Consistent with the literature data, the mean age was 55.6 (range, 35 to 73) years in our study.

Despite their benign nature, myxomas can cause serious symptoms, and complications due to their location and size.<sup>[1,4]</sup> They may cause systemic extracardiac signs, such as obstruction, peripheral/cerebral embolization, prostration, weight loss, fever, muscle pain, joint pain, and anemia.<sup>[4,8]</sup> In their study of 42 myxoma cases, Aval et al.<sup>[7]</sup> reported symptoms of

dyspnea in 54.8% of patients, dyspnea, and palpitation in 28.5%, syncope in 2.4%, and swelling in the legs in 4.8% of patients. In this study, the presenting symptoms of patients with myxomas were dyspnea and palpitation in six (66.7%) patients, syncope in two (22.2%), and swelling in the legs in one (11.1%) patient. With an increased tumor mass, myxomas may cause dilatation in the left atrium and a consequent increase in left atrial diameter; this progression ultimately decreases the left atrial volume, which may cause hemodynamic changes in blood flow from the atrium to the ventricle and rhythmic disorders (AF).<sup>[4]</sup>

Treatment options for intracardiac tumors include simple, complex, or surgical excision; total artificial heart implantation; and cardiac transplantation. For benign tumors such as myxomas, simple resection is usually sufficient.<sup>[9]</sup> Pineda et al.<sup>[10]</sup> found no significant difference in morbidity or mortality between minimally invasive surgery and median sternotomy groups. Compared to a standard median sternotomy approach, minimally invasive cardiac surgical techniques have been shown to be advantageous for the resection of benign cardiac tumors. These advantages include reduced surgical injuries, blood loss, and pain, as well as more rapid return to functional activity, shorter intensive care unit and hospital stays, and a higher level of patient satisfaction.<sup>[10]</sup> The authors found that a minimally invasive approach with right mini-thoracotomy for the resection of benign cardiac masses might be performed safely with less resource utilization. In another study including 34 patients undergoing atrial mass removal, Russo et al.<sup>[11]</sup> reported similar results. With a follow-up period of 4.8 years, they demonstrated that a minimally invasive approach to cardiac mass resection was as safe and effective as median sternotomy.<sup>[10]</sup> In the present study, all patients underwent median sternotomy and cardiopulmonary bypass.

Aval et al.<sup>[7]</sup> reported postoperative AF in 9.5% of patients, partial heart block in 7.1%, paroxysmal atrial tachycardia with heart block in 2.3%, and complete heart block in 2.3% of patients. Taş et al.<sup>[4]</sup> reported postoperative AF in 10% of patients, temporary nodal rhythm in 9%, and AV block in 4% of their cases. In this study, we observed AF in 11.1% of patients, which is consistent with previous studies. Aval et al.<sup>[7]</sup> reported a mean follow-up of 48.8 (range, 1 to 82) months, and Taş et al.<sup>[4]</sup> reported a duration of 123.4 (range, 3 to 322) months. In this study, the mean follow-up was 51.8 range, 6 to 110) months, which was similar to the results reported by Aval et al.<sup>[7]</sup> In addition, PFE was found in one patient. Consistent with

the literature findings, a 76-year-old patient presented with chest pain caused by coronary embolization. These fatal complications were due to the location of the embolization in the left cardiac chambers, near the cardiac valves. Many authors believe that the cause of embolization is tumor coverage by fibrin fibers.<sup>[12]</sup>

The most frequently observed primary malignant cardiac tumor is sarcoma. Angiosarcoma is the most prevalent sarcoma type in adults; it affects more males than females (male: female ratio, 2:1), and develops in the right atrium in 80% of cases.<sup>[13]</sup> As the tumor spreads via a hematogenous route, metastases occur rapidly and frequently, and are widespread. These tumors may metastasize in the superior and inferior vena cava, tricuspid valve, right ventricular free wall, ventricular septum, and even in the right coronary artery.<sup>[13]</sup> Early diagnosis of the tumor may be challenging, as it may cause chest pain, respiratory distress, and nonspecific extracardiac symptoms.<sup>[2]</sup> At the time of diagnosis, lung, liver, and brain metastases are present in 4 to 89% of cases.<sup>[5]</sup> In this study, the patient with an angiosarcoma had also the right atrium and vena cava involvement.

In the majority of cases, mortality is due to distant organ metastases.<sup>[6]</sup> Metastatic cardiac tumors are 100 times more frequent than primary cardiac tumors with an incidence of 10%.<sup>[6]</sup> Cardiac invasion by metastatic tumors occurs via four different routes: the direct route by mediastinal tumors and hematogenous, intracavitary (i.e., via inferior and superior vena cava), and lymphatic routes.<sup>[14]</sup> The lymphatic route is the most frequent route for secondary cardiac involvement. Malignant melanomas and thymomas are the tumors having the highest potential for cardiac metastases.<sup>[13,15]</sup> Melanomas have a high rate of cardiac metastasis (about 50%). About 30% of patients with metastatic cardiac tumors have congestive cardiac insufficiency, tachyarrhythmia, or isolated cardiomegaly symptoms. In these patients, pericardial effusion and, subsequently, cardiac tamponade may develop due to the presence of multiple lesions of metastatic invasion in the mediastinal lymph nodes. Despite the absence of symptoms, emerging pericardial effusion and cardiac tamponade indicate malignant cardiac involvement in 90% of cases.<sup>[13]</sup> Therefore, metastatic cardiac tumors and, subsequently, secondary cardiac involvement should be considered in patients with cancer who present with tachyarrhythmia, isolated cardiomegaly, symptoms of congestive cardiac insufficiency, new pericardial effusion, and cardiac tamponade. For patients with malignant tumors treated with conservative chemotherapy and radiotherapy, the

mean life expectancy is less than one year. Simple or incomplete resection prolongs the survival for only a few months in patients with malignancy.<sup>[3]</sup> Radical resection and, if necessary, chemotherapy can improve long-term results and patients' quality of life.<sup>[9]</sup>

In our series, the number of metastatic malignant tumors (38%) was higher than that of malignant primary tumors (4.7%). With regard to the localization of the tumor, 44% were localized in the left atrium, 44% in the right atrium, and 12% in the left ventricle. Three patients had malignant epithelial tumor metastases, one had a lung adenocarcinoma metastasis, one had a malignant epithelial tumor metastasis of papillary-type renal cell carcinoma, one had a thymoma with thymic carcinoma, one had carcinoma metastasis of unknown origin, and one had a malignant mesenchymal tumor.

Dias et al.<sup>[1]</sup> reported that 72% of their patients were asymptomatic on presentation to the hospital, whereas 10.9% showed systemic manifestations, such as fever (4.8%), chronic anemia (4%), weight loss (1.6%), and arthralgia (0.5%). In this study, our patients' complaints on presentation were dyspnea (52.3%), palpitation (19%), swelling in the legs (9.5%), cerebrovascular accidents (9.5%), chest pain (9.5%), and malaise (4.7%), and 23.8% of patients were diagnosed incidentally.

Vegetation, thrombus, and tumor should be considered in the differential diagnosis of an intracardiac mass. Dias et al.<sup>[1]</sup> reported that a tumor mass might be confused with a thrombus, as a thrombus could mimic a tumor in 6.4% of patients and that the differential diagnosis was possible intraoperatively. Another study documented thrombi in 15.4% of patients operated for cardiac tumors.<sup>[16]</sup> In this study, thrombi were found intraoperatively or through histopathological examination in eight (27.6%) patients who underwent surgery for cardiac tumors. On contrast, the rate at which thrombi were found in this study is higher than those reported in the aforementioned studies. One possible reason is that the study group was smaller than the groups examined by Dias et al.<sup>[1]</sup> and Strecker et al.,<sup>[16]</sup> who included 323 patients with primary cardiac tumors and reported data from a 48-year follow-up period. In addition, Elbardissi et al.<sup>[17]</sup> reported that the prognosis for malignant tumors was worse than that for benign tumors and that the mean survival time was less than one year, despite resection and aggressive adjuvant chemotherapy. Currently, the mortality and morbidity rates have been decreasing steadily in patients with cardiac tumors thanks to the developments in diagnostic methods and the more frequent use of CT and MRI in the differential diagnosis of intracardiac masses, resulting in a more accurate early diagnosis

and surgical planning. Dias et al.<sup>[1]</sup> reported that the mortality rate for an intracardiac tumor surgery improved from 16% in 1980-1998 to 6% by 2004 and 5.4% in 2014, the last year included in that publication. In this study, the mortality rate was 33.3%. This high rate is likely due the inclusion of a large number (38%) of patients with advanced metastatic tumors.

On the other hand, this retrospective study has several limitations. The major limitation of the study was its small sample size. Another limitation was the relatively high-mortality rates, as the sample included more cases of metastatic malignant tumors than malignant primary tumors.

In conclusion, metastatic cardiac tumors and associated secondary cardiac involvement should be considered in the diagnosis of patients with cancer who present with tachyarrhythmia, isolated cardiomegaly, symptoms of congestive cardiac insufficiency, emerging pericardial effusion, or cardiac tamponade. Thrombi are also seen in some patients undergoing operations for cardiac masses, suggesting a high degree of diagnostic confusion between intracardiac thrombi and tumors.

#### Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

#### Funding

The authors received no financial support for the research and/or authorship of this article.

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