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ORIGINAL ARTICLE

Cardiac tumors: a retrospective multicenter institutional study

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Summary

Purpose: *Primary cardiac tumors are uncommon but not extremely rare. Cardiac tumors, mostly intracavitary, include benign and malignant tumors that arise from the endocardium, heart valves or myocardium. This retrospective study summarizes the experience of the Cardiac Surgery Departments of three tertiary Hospitals in this field, and particularly in cardiac myxomas, over the last 29 years. Herein, we present the results of cardiac tumors excision in relation to postoperative morbidity and mortality.*

Methods: *Between 1985 and 2014, 117 patients, aged from 16 to 82 years, underwent resection of a cardiac tumor.*

Results: *Ninety one of the tumors (77.78%) were myxomas, 15 of them (12.82%) were other primary cardiac tumors, 7 of them (5.98%) were infra-diaphragmatic tumors and the remaining 4 tumors (3.42%) were benign intracavitary masses (thrombi). Patients operated on for a cardiac tumor had a 30-day mortality rate of 3.29%. Atrial fibrillation appeared in 21 out of 91 patients (23.07%) operated on for cardiac myxoma, while neurological complications were observed in 3 patients (3.29%). Re-exploration for bleeding was performed in 5 out of 91 cases (5.49%) and recurrence occurred in 4.39% of myxomas.*

Conclusions: *Despite being rare, primary cardiac tumors require open heart intervention soon after their diagnosis in order to prevent complications and achieve low mortality rates.*

Key words: *cardiac tumors, heart cancer, heart neoplasms, intracavitary cardiac tumors, myocardial tumors, myxoma*

Introduction

Cardiac masses include vegetations, thrombi, and tumors [1]. Cardiac tumors are rare, constituting only 0.001–0.28% of autopsy cases [2]. They are divided into primary cardiac tumors, metastatic cardiac tumors [3] and intracardiac tumors originated from infra-diaphragmatic organs [4]. Metastatic cardiac tumors are 40 to 100 times more frequent than primary cardiac tumors [3,5]. Primary cardiac tumors can be either benign or malignant neoplasms arising from endocardium, heart valves or myocardium.[6-9] Seventy-five percent of cardiac tumors are benign [5,10]. The most common benign type is myxomas consisting 50% to 80% of the tumors [1,5,10-13]. On the other hand angiosarcoma is the commonest malignant cardiac tumor [14,15]. Generally, cardiac surgery to excise a cardiac tumor is rare. Its incidence is one in 500 cardiac operations [16]. The majority of surgeons will rarely face primary cardiac tumors except for cardiac myxomas during their surgical career [16-18]. However, heart tumors have a high morbidity due to peri-operative embolic events. Herein, we are describing our experience in surgical treatment of cardiac tumors presenting 117

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Table 1. Classification of cardiac tumors

Tumor	*Patients*	
	N	%
Myxoma	91/117	77.78
Primary cardiac tumor (benign or malignant)	15/117	12.82
Infra-diaphragmatic tumor	7/117	5.98
Benign intra-cardiac mass (thrombi)	4/117	3.42
Total	117	100

Table 2. Primary (benign and malignant) cardiac tumors

Histological type	*Patients*		*Location*
	N	%	
Benign			
Rhabdomyoma	2/15	13.33	LV & RA
Lipoma	1/15	6.66	RV
Fibroma	1/15	6.66	IAS
Malignant			
Angiosarcoma	3/15	20	RA+RV &RV & LV
Rhabdomyosarcoma	2/15	13.33	RA & RV
Fibrosarcoma	2/15	13.33	RV & LV
Leiomyosarcoma	2/15	13.33	RA & LA
Malignant lymphoma	1/15	6.66	RV
Melanoma	1/15	6.66	RA
Total	15	100	-

LV:left ventricle, RA:right atrium, RV:right ventricle, IAS:interatrial septum, LA:left atrium

cases of heart tumors treated in the cardiac surgery departments of three tertiary Greek hospitals during the last 29 years.

Methods

Data from January 1985 to December 2014 were collected by the registries of Cardiac Surgery Departments of three Greek tertiary hospitals (General Hospital of Athens "Evangelismos", University Hospital of Ioannina and University Hospital of Patras). A total of 117 patients, aged 16 to 82 years were subjected to cardiac surgery due to a cardiac tumor. Patients were referred for elective operations. Surgical excision of the tumor through median sternotomy was carried out under extracorporeal circulation and moderate hypothermia. The tumor was completely excised together with an adjacent cuff of endocardium or along with a part of the interatrial septum. When required the septum was replaced with pericardial patch. Macroscopically, the gelatinous tissue of these tumors appeared as a yellow-brownish to yellow-greenish myxoid stroma, which is typical of myxomas.

Results

Ninety-one cardiac tumors (77.78%) were myxomas, 15 (12.82%) concerned other primary benign or malignant cardiac tumors, 7 (5.98%) were infra-diaphragmatic tumors expanding into the heart chambers and 4 of them (3.42%) were other benign intra-cardiac masses (thrombi) preoperatively misdiagnosed as cardiac tumors (Table 1). Rhabdomyoma, lipoma and fibroma were the histologic types of the primary benign cardiac tumors operated, whereas angiosarcoma, rhabdomyosarcoma, fibrosarcoma, leiomyosarcoma, lymphoma and melanoma were the primary malignant cardiac tumors operated. Patient age in this group ranged between 29 and 60 years old (Table 2). With regard to intracardiac thrombi, one of them was located in the right atrium (RA) as a result of the presence of a pacemaker wire and endocarditis, 2 of them were in the left atrium (LA) caused by mitral valve stenosis and another one was located in the left ventricle (LV) as a consequence of a recent myocardial infarction. Finally, 7 patients (5 males-71.43% and 2 females-28.57%), aged from 65 to 71 years, were postoperatively diagnosed with infra-diaphragmatic tumors (Table 1). Six of them (85.71%) had a renal cell carcinoma and the other one (14.28%) had a hepatocellular carcinoma. These carcinomas were initially diagnosed as cardiac tumors but it was finally revealed that they had expanded into the right atrium through the inferior vena cava.

Fever, weight loss and general weakness were the clinical symptoms on presentation in 65 out of 91 patients with cardiac myxomas. Diabetes mellitus was present in 8.79% of them and peripheral embolism symptoms appeared in 28% of them. One patient had a simultaneous lung cancer with a myxoma of the left atrium. White blood cell increase was found in 37.36%, increased erythrocyte sedimentation rate (ESR) and/or increased C reactive protein (CRP) were found in 34.06% and thrombocytopenia was present in 9.89% of the cases. As far as the exact location of cardiac myxomas was concerned, 80.22% of them were found in the LA and 15.38% were located in the RA. Half of the remaining 4.40% cases were myxomas of the LA and of the right ventricle (RV) and half of them were myxomas of the right chambers. Familial correlation was reported in only 6.59% of the cases (Table 3).

Table 3. Characteristics of myxoma patients

Characteristics	*Patients*	
	N	%
Location		
Right atrium	14/91	15.38
Left atrium	73/91	80.22
Left atrium and right ventricle	2/91	2.20
Right atrium and right ventricle	2/91	2.20
Clinical presentation		
Systemic illness symptoms (fever, muscle pain, bone and articulation pain, weakness, weight loss)	65/91	71.42
Systemic embolism	21/75	28
Mitral valve regurgitation	18/75	24
Tricuspid valve regurgitation	5/16	31.25
Syncope	10/91	10.98
Lab findings		
White blood cell increase (>10000/mm^3)	34/91	37.36
Thrombocytopenia (<150000/mm^3)	9/91	9.89
Increase of ESR and/or CRP	31/91	34.06
Abnormal X-ray	12/91	13.18
Comorbidities		
Atrial fibrillation	16/91	17.58
Diabetes mellitus	8/91	8.79
Lung cancer	1/91	1.09
Familial correlation	4/91	6.59

ESR: erythrocyte sedimentation rate, CRP: C-reactive protein

Table 4. Postoperative complications after cardiac myxoma resection

Complications	*Patients*	
	N	%
Atrial fibrillation	21/91	23.07
Ectopic ventricular systole	11/91	12.08
Neurological complications	3/91	3.29
Myocardial infarction (embolus in RCA)	1/91	1.09
Sternal would infection	3/91 (1 reoperation)	3.29
Renal dysfunction	2/91	2.19
Reoperation (re-exploration for bleeding)	5/91	5.49
Lung dysfunction, respiratory insufficiency	8/91 (3ARDS)	8.79

RCA: right coronary artery, ARDS: acute respiratory distress syndrome

Most cardiac tumors were myxomas arising from the LA. Postoperative complications included cardiac and respiratory dysfunction, already reported in the international literature after an open heart operation. Similar complication rates to these of the majority of open heart interven-

Table 5. Intraoperative data of cardiac myxomas resection

Intraoperative data	*Minutes*	*Mean ± SD (min)*
Cross-clamp time (L)	14-82	33±16
Cross-clamp time(R)	0-80	25±11
CPB time (L)	30-174	68±24
CPB time (R)	26-119	86±27
Cross clamp time (R+L)	37-80	60±11
CPB time (R+L)	71-128	110±16
	Patients	*%*
Inotropic support	29/91	31.86
IABP support	1/91	1.09

L: tumors localized in left chambers, R: tumors localized in right chambers, IABP: intraaortic balloon pump, SD: standard deviation

tions were reported. Atrial fibrillation developed in 23.07% of the patients and ectopic ventricular systole was reported in 12.08% of the patients, sternal wound infection occurred in 3.29% of them, 3.29% of the patients experienced neurological complications, lung dysfunction in 8.79% of the cases and renal dysfunction presented in 2.19% of the cases. One patient suffered a myocardial infarction due to an embolus of the right coronary artery bed. Finally, reoperation due to bleeding was required in 5.49% of the patients (Table 4).

According to our intraoperative data, no ischemic time was required for the surgical resection of right atrium-sided myxomas in 5 patients. Longer cross-clamp and cardiopulmonary bypass (CPB) time were reported in patients treated for left-sided or double chamber cardiac myxomas. Intraortic balloon pump (IABP) was necessary only in 1 patient (1.09%) in order to wean from CPB, while 29 patients (31.86%) required inotropic support (Table 5).

Surgical resection of primary cardiac tumors, and particularly of myxomas, was associated with excellent long-term survival rates which were not significantly inferior to those of the general population. In our series, total 30-day mortality after cardiac sarcoma resection was 3.29%. There was no death related to uncomplicated myxoma resections but the mortality rate of those with double chamber myxomas was quite high (25%). Intensive Care Unit (ICU) stay was similar to that of other open heart surgical procedures (Table 6).

Finally, total recurrence rate of cardiac myxomas was 4.39%. However, cases with familial correlation were more prone to recurrence (50%), whereas only 2.77% of LA sporadic myxomas recurred (Table 7).

On the other hand, cardiac surgery for the resection of a cardiac tumor other than myxoma was associated with a significantly higher mortality (40%). Other data about this group of patients did not significantly differ from operated myxomas or other cardiac diseases (Table 8).

Concerning the 4 intracardiac masses (thrombi), preoperatively misdiagnosed as myxomas, no 30-day mortality occurred and the other operative characteristics were excellent (Table 9).

Finally, 7 infra-diaphragmatic tumors were misdiagnosed as an RA tumor. There were 6 renal cell carcinomas and one hepatocellular carcinoma extended into the RA through the inferior vena cava. Major complications could have appeared during RA cannulation or soon after decannulation. Intraoperatively, the hepatocellular carcinoma was excised up to its part in the inferior vena cava. Therefore, the excision was not radical and the patient died during the first postoperative hours in the ICU due to massive lung embolism. A large tumor was removed from the RA during the operation. We did not observe any tumor remnant in the inferior vena cava but a large embolus due to our manipulations caused pulmonary embolism and subsequent death. An upper abdomen ultrasonography or an abdomen computed tomography (CT) or a magnetic resonance imaging (MRI) might have prevented us from performing these operations (Table 10).

Discussion

Primary cardiac tumors are much less common than metastatic lesions [3]. Cardiac myxoma is the most common primary cardiac tumor. Its incidence is 0.5 per million per year [4,18,19]. In a large series of 323 patients who underwent surgical resection of primary cardiac tumors, 163 (50%) were myxomas, 83 (26%) were papillary fibroelastomas, 18 (6%) were fibromas, 12 (4%) were lipomas, 28 (9%) were other primary benign cardiac tumors, and 19 (6%) were primary malignant tumors [18]. Myxoma may be located in any heart cavity or on any heart valve. The majority of them (70–80%) occur in the LA, 15–20% in the RA, 4% in the RV, 4% in the LV, and 2.5% are biatrial [20,21]. Left atrial myxomas originate from the interatrial septum (IAS) near the fossa ovalis in 90% of the cases [22,23]. whereas ventricular myxomas originate from the free ventricle wall. Posterior atrial wall location of a cardiac mass is typical of malignancy [24]. More than 90% of myxomas are sporadic [10,25] and less than 10%, are familial

Table 6. 30-day mortality and Intensive Care Unit stay after cardiac myxoma resection

Location	*Mortality, N*	*Mortality, %*	*ICU-stay (days, range)*	*Mean±SD (days)*
Right atrium	1/14	7.14	1-5	1.4±1.1
Left atrium	1/73	1.37	1-8	1.6±1.2
Left or right atrium and right ventricle	1/4	25	1-5	1.6±1.3
Total mortality	3/91	3.29	-	-
Total ICU stay	-	-	1-8	1.5±1.3

ICU: Intensive Care Unit, SD: standard deviation

Table 7. Recurrence of myxomas

Type	*Patients*	
	N	*%*
Left atrium sporadic	2/72	2.77
Familial	2/4	50.0
Total	4/91	4.39

as part of the Carney syndrome, including cardiac and cutaneous myxomas, endocrine hyperfunction [10] (adrenals, hypophysis, thyroid, Sertoli cells) and spotty skin pigmentation [26]. There is a female predilection of myxomas which mainly happen in the middle age [10,27,28]. Familial myxomas present another image as they are often multicentric and affect equally younger men and women. Moreover, they arise from other than the IAS sites and are more prone to recurrence [27,28]. In our series, 6.59% of the patients had a familial pattern and 50% of them recurred.

Patients with cardiac tumours may be free of symptoms for a long period of time [5]. Even at the time of diagnosis, 10-15% of the patients with cardiac myxomas have no symptoms, so they are incidentally diagnosed [27,28]. Possible clinical symptoms include cardiac, embolic and systemic manifestations [1]. Fever, weakness, arthralgia, weight loss, Raynaud's phenomenon, rash, anemia and thrombocytopenia are some of the systemic manifestations related to cardiac tumors [1,4,19]. As far as cardiac manifestations are concerned, they depend on the tumor size. The bigger the tumor is, the more it obstructs the relative valve orifice mimicking valve disease. Hence, dyspnea, or other symptoms of heart failure [1] or syncope due to the obstruction of blood flow through cardiac chambers may occur [4]. Intramural neoplasms can also produce arrhythmias and cause heart bundle branch blocks while pericardial tumors may cause cardiac tamponade [29]. A stroke, an embolism of the peripheral vasculature or a pulmonary artery embolism can also be the onset symptom of a cardiac tumor [22,27,30,31]. On the other hand, primary malignant cardiac tumors may manifest symptoms by the organs to where a metastasis has happened [28].

Provided the increased availability and technical progress in heart imaging armamentarium including transthoracic (TTE) or transesophageal echocardiography (TEE), CT and MRI, cardiac neoplasms are diagnosed early, contributing thus to curative intervention in the majority of the cases [4,14]. First of all, an intracardiac thrombus or a vegetation must be excluded when a cardiac tumor is suspected [10,28]. TTE and TEE are first-choice diagnostic tools towards the diagnosis of cardiac tumors [32]. Important information about tumor location, origin, size, shape, attachment, mobility and about the extent of valve compromise and hemodynamic consequences can be obtained by TEE and TTE [27]. However, despite their accuracy in diagnosing cardiac myxomas, TEE and TTE are not able to distinguish myxomas from valvular vegetations or atrial thrombi [13]. Moreover, they are not the appropriate tools to indicate if an intracardiac tumor is benign or malignant [33]. If echocardiography fails to accurately identify a cardiac tumor, CT or MRI can play a significant role [34,35]. MRI is able to provide additional, detailed data with regard to cardiac anatomic structures thanks to superior tissue contrast [36]. Malignant cardiac tumors are distinguished from benign ones with the use of CT as it achieves a 80% sensitivity and 100% specificity [37]. High sensitivity and specificity is also related to CT with regard to atrial thrombus diagnosis [38]. Mural thrombi can be associated with underlying valvular disease, myocardial infarction or dysfunction and atrial fibrillation [39]. In our cohort there were 4 such cases that were initially operated for cardiac tumors. Apart from thrombotic lesions and vegetations, differential diag-

Table 8. Operative results in other-than-myxoma cardiac tumors

	Primary benign and malignant cardiac tumors		*Infra-diaphragmatic cardiac tumors*		*Intracardiac masses (thrombi)*
	Patients		*Patients*		*Patients*
	N	*%*	*N*	*%*	*N (%)*
Mortality	6/15	40	1/7	14.28	0/4 (0)
	Minutes	*Mean±SD*	*Minutes*	*Mean±SD*	*Minutes*
Cross clamp time	0-82	39±18	26-88	45±15	0-35
CPB time	50-120	76±27	124-212	188±24	42-62
	Days, range	*Mean±SD*	*Days, range*	*Mean±SD*	*Days, range*
ICU stay	2-5	-	1-3	1.4±1	1-2
Hospital stay	6-15	8.2±2.2	6-26	10±3	4-7

CPB: Cardiopulmonary bypass, ICU: Intensive Care Unit, SD: standard deviation

Table 9. Operative results in 4 patients operated for intra-cardiac masses (thrombi)

Factors assessed	*Results*
Cross clamp time (min)	0-35
CPB time (min)	42-62
Mortality, N(%)	0/4 (0%)
ICU stay (days)	1-2
Hospital stay (days)	4-7

CPB: Cardiopulmonary bypass, ICU: Intensive Care Unit, min: minutes

nosis includes invasion of the heart by tumors, like pheochromocytoma, renal and hepatocellular carcinoma through the inferior vena cava. Seven patients (5.98%) of our series were misdiagnosed as having cardiac tumors, while they were hepatic and renal tumors expanding into the RA. This is another reason why it is important to perform an upper abdomen ultrasonography or a CT or an MRI in case of a tumor in the RA.

A patient with a cardiac tumor should be operated as soon as possible following diagnosis [10] in order to avoid complications such as intracavity obstruction or embolic events and prevent recurrence of the tumor [1,10,13,28,32]. Urgent surgical excision of a cardiac tumor is the method of choice for primary cardiac tumors [1,10,28,32,40,41]. A median sternotomy under cardiopulmonary bypass is routinely performed [41]. Radical resection in healthy tissue margin of a typical myxoma and careful inspection of all heart chambers intraoperatively is a sine qua non in order to prevent missed diagnosis and myxoma recurrence [13]. However, palliative tumor debulking may be required in case of a large non-resectable tumor or if difficulties regarding cardiac reconstruction arise [13,28,41]. Autotransplantation, removing the heart out of the body constitutes a possible approach so as to completely remove the tumor and anatomically reconstruct the heart [10,42]. Additionally, some primary malignant cardiac tumors are managed with surgical resection and adjuvant chemotherapy, whereas chemotherapy with or without radiotherapy is our therapeutic choice in cardiac lymphomas [43]. Finally, patients with unresectable malignant non-metastatic cardiac tumors may be candidates for heart transplantation [28].

Surgical excision of primary benign cardiac tumors linked with an excellent prognosis [31,44]. Radical surgical resection can be curative in case of a myxoma [5] clearly improving the patients' functional status [45]. Morbidity in terms of tumor embolization, valvular obstruction and recurrence is significantly decreased [4,46]. Surgical excision of an atrial myxoma is related to a 4% overall hospital mortality [4,19,47]. Similarly, benign cardiac tumor resection is usually associated with low morbidity and excellent long-term results. However, malignant cardiac tumors have poor prognosis and metastatic heart tumors should not be operated, unless successful relief of symptoms is possible [4,19,48]. As far as primary malignant cardiac tumors are concerned, inability for radical excision, local spread of the tumor or its recurrence, high metastatic potential and ineffectiveness of adjuvant chemo- or radiotherapy lead to the poor results observed [5]. Conservative treatment using adjuvant therapies without surgery results in less than a year average survival, whereas palliative partial excision extends it by only a few months [34,49]. Nevertheless, according to Look et al. complete excision of non-metastatic cardiac sarcoma improves survival [50]. Moreover, the combination of radical resection

Table 10. Operative results in 7 patients operated for infra-diaphragmatic cardiac tumors

Factors assessed	*Minutes*	*Mean±SD*
Cross clamp time	26-88	45±15
CPB time	124-212	188±24
Arrest time	13-29	21±8
	Days	*Mean*
ICU stay	1-3	1.4±1
Hospital stay	6-26	10±3
	Patients	*Rate (%)*
30-day mortality	1/7	14.28

CPB: Cardiopulmonary bypass, ICU: Intensive Care Unit, SD: standard deviation

of the tumor and adjuvant chemotherapy contributes to better long-term outcomes with a good quality of life [25]. A total of 181 patients with cardiac tumors (139 patients with benign tumors, 26 patients with malignant tumors and 16 patients having cardiac metastases) were treated at the Center for Cardiac Surgery of Münster University Hospital between 1989 and 2012. Malignant tumors were treated with surgical resection and adjuvant chemotherapy. The 5-year overall survival rates were 83% for benign tumors, 30% for malignant tumors and 26% for cardiac metastases whereas the 10-year survival rates were 75, 22 and 26%, respectively [10]. Bakaeen and colleagues observed a 47-month average survival in patients with cardiac sarcomas treated by surgical resection combined with radiofrequency ablation or radiation treatment [51]. However, Elbardissi et al. [18] examining 323 patients with primary cardiac tumors during 48 years observed that patients with malignant tumors survived less than a year on average, although they were aggressively treated with surgical resection and adjuvant chemotherapy.

Benign tumors rarely recur [13]. Myxoma, though benign, is related to a 1-4% recurrence rate for sporadic cases and a 12-22% recurrence rate for familial cases after surgical resection [28,52-54]. Atypical primary site, multicentricity, familial inheritance, malignant features, partial excision, and metastasis are all risk factors for recurrence after surgical excision of a myxoma [55]. According to Sheng et al. [13] 5 out of 107 patients operated on for a cardiac myxoma during 18 years recurred during a follow-up of 1–15 years. The recurrence rate was 4.67% and the time interval from initial surgical excision to recurrence ranged from 5 months to 6 years [13]. Similarly, total recurrence rate of cardiac myxomas in our study was 4.39%. However, the recurrence rate of familial cases was as high as 50%, whereas only 2.77% of sporadic myxomas recurred.

In conclusion, primary cardiac tumors are rare but an urgent open heart surgical intervention is required soon after their diagnosis in order to prevent complications such as embolic events or mitral orifice obstruction. Myxoma is the most frequent intracardiac tumor, but several other benign or malignant tumors can develop in the heart chambers or on the heart valves. Infradiaphragmatic tumors (mainly renal or hepatocellular carcinomas) extending into the right cardiac chambers through the vena cava are also possible and they may constitute a pitfall for the cardiologist and the cardiac surgeon. Thrombi in the heart chambers can also mimic cardiac tumors. Finally, it is observed that if a cardiac tumor is treated early, low mortality can be achieved, although recurrence is possible.

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