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Original article:

CLINICAL CHARACTERISTICS AND LONG TERM POST-OPERATIVE OUTCOME OF CARDIAC MYXOMA

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ABSTRACT

Background and aim: Myxoma is the most common type of primary cardiac neoplasm, but the clinical characteristics and long term outcome are less known in the elderly in China.
Methods: We analyzed medical records of 112 consecutive patients who underwent operative resection of cardiac myxoma between December 1988 and December 2010 in our hospital. Their data were retrospectively analyzed and the difference between two age groups (< 60 years, n = 87 and ≥ 60 years, n = 25) was compared.
Results: The mean age of 112 patients was 48.8 ± 12.5 (range 13 ~ 75) years, and 66 patients (58.9 %) were female. The interval from onset of symptoms to diagnosis was 12 months and the most common presenting symptoms were chest distress (66 patients 58.9 %), followed by palpitations (55 patients, 49.1 %) and dyspnea (47 patients, 42.0 %). Mitral valve diastolic murmur was heard in 67 (59.1 %) patients. The tumor was located in the left atrium in 96 (85.8 %) patients. There were no in-hospital death. During follow-up ranged between one and twenty-one (7.3 ± 5.3) years, there was no malignancy. Myxoma recurred in 3 (2.7 %) patients and deaths occurred in 5 (4.5 %) patients. The 5 and 15 years survival was 97.8 % and 89.5 %, respectively. To compare with the younger patients, the elderly have higher ratios of concomitant hypertension, fewer complaints of dyspnea and chest distress ($p < 0.05$).
Conclusion: The elderly have lower complaints of dyspnea and chest distress, surgical treatment is associated with low long-term mortality and recurrence rate even in the elder patients.

Keywords: Cardiac myxoma, clinical characteristics, outcome, the elderly

INTRODUCTION

Cardiac myxoma is not common, their prevalence ranges from 0.001 % to 0.3 % in various series (Reynen, 1995; Markel et al., 1987). However, large clinical observation studies shown that the incidence of primary cardiac tumor was as high as 0.3 %-0.81 % of all heart operations, and primary myxomas composed 40 %–96.7 % of all cardiac tumors (MacGowan et al., 1993; Sezai, 1990; Yu et al., 2007).

Although more patients present obstructtive, embolic and constitutional symptoms, the incidence of asymptomatic myxoma tended to increase and the accidental diagnosis is relatively frequent, as a result of the development of cardiac imaging, particularly echocardiography (Matebele et al., 2010; Roberts, 1997; Holley et al., 1995). Surgical resection is the only recommendation of treatment, with perioperative mortality of 0 % to 5 %, recurrence of 3 % to 8 % in sporadic cases and 20 % in familial myxomas (Gaszewska-Żurek et al., 2011; Oliveira et al., 2010).

There are few reports in China about the clinical presentation and outcome especial-

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ly in the elder patients. This retrospective study aims to describe presentations and surgical management, to assess the survival in hospital and during the long-term follow-up, and to find the possible difference in two different age groups in patients underwent cardiac myxoma resection in our hospital.

PATIENTS AND METHODS

The medical records of 125 patients who were diagnosed as cardiac tumor in the department of cardiac surgery between December 1988 and December 2010 were retrospectively analyzed. 112 patients of sporadic type were histologically diagnosed as myxoma and the difference between two age groups (< 60 years and ≥ 60 years) was compared. Patients were invited clinic visit, telephone interviews or otherwise to their door. The following information was collected: presenting symptoms, location of tumor, approach to surgical management, in-hospital mortality and long-term outcome.

The tumors were resected by median sternotomy with cardioplegia and cardiopulmonary bypass. The right atrial tumor was resected via a right atriotomy, the left atrial and left ventricle tumors were resected transeptally, the right ventricular myxoma was resected through tricuspid valve oral. In all cases, the myxoma was removed with adequate tissue margin (0.5–1 cm margin around the stalk) and full thickness excision of the base tissue, followed by closure of the remaining interatrial communication, and surgical completeness was confirmed by histopathology. During follow-up, patient survival and complication rates were analyzed and transthoracic echocardiography (TTE) was performed. Angiography was performed in 45 patients to rule out concomitant pathology such as valvular and coronary disease. The study was approved by the hospital ethics committee and all patients gave informed consent for participation in the study.

Statistical analysis

The continuous numerical values were expressed by means ± SD. The category 'variables' was expressed in percentages. The chi-square test was used for categorical variables, and the Student's t test was used for continuous variables. Long-term survival was analyzed by Cox regression and Logistical regression analysis was used for the multivariate analysis. A value of $p<0.05$ was considered significant. The analysis was performed using SPSS version 19.0 (SPSS Inc., Chicago, USA).

RESULTS

Patients mean age was 48.8 ± 12.5 years (range, 13 to 75 years) and 66 patients (58.9 %) were female. Presenting symptoms include chest distress which occurred in 66 patients (58.9 %), palpitations in 55 (49.1 %), dyspnea in 47 patients (42.0 %), cerebral embolism in 9(8.0 %), lower extremity embolism in 6 (5.4 %) including 2 coexist with cerebral embolism, syncope in 10 (8.9 %), constitutional (weakness, fever, arthralgia) in 31 (27.7 %) patients, and 7 (6.3 %) patients had no symptoms (Table 1).

The mean duration from onset of symptoms to diagnosis was about twelve months (range, 3 days to 132 months). Mitral valve diastolic murmur was heard in 67 (59.1 %) patients, atrial fibrillation was recorded in 8 (7.1 %) by electrocardiography, cardiomegaly was detected in 28 (25.0 %) patients by chest X-ray, PAH was reported in 6 (5.4 %) patients by echocardiography.

Comorbidities include CAD in 9 (8.0 %) patients, hypertension in 11 (9.8 %), diabetes in 5 (4.5 %), moderate to significant mitral insufficiency in 5 (4.5 %), moderate to significant tricuspid insufficiency in 15 (13.4 %), patent ductus arteriosus（PDA）in 1, patent foramen ovale in 5 (4.5 %) (Table 1).

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Table 1: Clinical characteristics of myxomas

	< 60 years No. (%)	≥ 60 age No. (%)	P value	Total (112 cases) No. (%)
Age (years)*	44.09 ± 9.82	65.08 ± 4.29	0.000	48.78 ± 12.48
Female	50 (57.5 %)	16 (64.0 %)	0.648	66 (58.9 %)
Symptoms:				
Symptom duration (month)*	11.01 ± 20.33	15.65 ± 31.68	0.381	12.04 ± 23.26
Dyspnea	43 (49.4 %)	4 (16.0 %)	0.003	47 (42.0 %)
Palpitation	45 (51.7 %)	10 (40.0 %)	0.367	55. (49.1 %)
Chest distress	56 (64.4 %)	10 (40.0 %)	0.038	66 (58.9 %)
Syncope	6 (6.9 %)	4 (16.0 %)	0.226	10 (8.9 %)
Embolic event	7 (8.0 %)	6 (24.0 %)	0.069	13 (11.6 %)
Cerebral embolism	4 (4.6 %)	5 (20.0 %)	0.025	9 (8.0 %)
Limb embolism	4 (4.6 %)	2 (8.0 %)	0.614	6 (5.4 %)
Weakness	12 (13.8 %)	7 (28.0 %)	0.129	19 (17.0 %)
Fever	5 (5.7 %)	3 (12.0 %)	0.374	8 (7.1 %)
Arthralgia	2 (2.3 %)	2 (8.0 %)	0.215	4 (3.6 %)
Asymptomatic	4 (4.6 %)	3 (12.0 %)	0.184	7 (6.3 %)
Mitral valve murmur	4 (4.7 %)	1 (4.0 %)	1.000	5 (4.5 %)
Atrial fibrillation	6 (6.9 %)	2 (8.0 %)	1.000	8 (7.1 %)
Cardiomegaly	19 (21.8 %)	9 (36.0 %)	0.019	28 (25.0 %)
PAH	5 (5.8 %)	1 (4.0 %)	1.000	6 (5.4 %)
Comorbidities:				
CAD	6 (6.9 %)	3 (12.0 %)	0.415	9 (8.0 %)
Hypertension	5 (5.7 %)	6 (24.0 %)	0.015	11 (9.8 %)
Diabetes	3 (3.4 %)	2 (8.0 %)	0.310	5 (4.5 %)
Patent foramen ovale	3 (3.4 %)	2 (8.0 %)	0.310	5 (4.5 %)
MVD	4 (4.7 %)	1 (4.0 %)	0.183	5 (4.5 %)
TVD	14 (16.1 %)	1 (4.0 %)	0.183	15 (13.4 %)

* continuous numerical values were expressed by means ± SD

CAD, coronary artery disease; PAH, pulmonary artery hypertension; MVD, Mitral valve deficiency; TVD,Tricuspid valve deficiency

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Tumor location was as follows: left atrium in 96 (85.8 %), right atrium in 8 (7.2 %), bi-atrium in 1(0.9 %), mitral valve anterior leaflet in 1 (0.9 %), left ventricle in 4(3.6 %) and right ventricle in 1 (0.9 %) patient. Tumor volumes were 60.05 ± 68.97 cm^3 (Table 2).

The following associated procedures were performed: mitral replacement in 1 (0.9 %) case, tricuspid replacement in 8 (7.1 %), coronary artery bypass graft in 3 (2.7 %), ligation of patent ductus arteriosis in 1 and atrial septal defect suture in 1 (Table 3).

In-hospital deaths and complications

There were no in-hospital deaths. Cerebral embolism was noted in 1 (0.9 %) patient, new atrial fibrillation was noted in 3 (3.4 %) patients and all were successfully treated pharmacologically (Table 4).

Table 2: Location and volume of tumor

	< 60 years No. (%)	≥ 60 age No. (%)	P value	Total (112 cases) No. (%)
LA septum	57 (65.5 %)	17 (68.0 %)	1.000	74 (66.1 %)
LA wall	15 (17.5 %9	5 (20.0 %)	0.763	20 (17.0 %)
LA wall & septum	2 (2.3 %)	0 (0.0 %)	0.398	2 (1.8 %)
RA septum	1 (1.1 %)	0 (0.0 %)	1.000	1 (0.9 %)
RA wall	6 (6.9 %)	1 (4.0 %)	1.000	7 (6.3 %)
RV	1 (1.1 %)	0 (0.0 %)	1.000	1 (0.9 %)
LV	3 (3.4 %)	1 (4.0 %)	1.000	4 (3.6 %)
LA & RV	1 (1.1 %)	0 (0.0 %)	1.000	1 (0.9 %)
MV anterior leaf	1 (1.1 %)	1 (4.0 %)	0.398	2 (1.8 %)
Tumor volume (cm^3)	70.05 ± 73.61	25.26 ± 30.93	0.004	60.05 ± 68.97

* continuous numerical values were expressed by means ± SD
LA, left atrial; RA, right atrial; LV, left ventricular; RV, right ventricular; MV, mitral valve

Table 3: Concominant surgical procedures

	< 60 years No. (%)	≥ 60 age No. (%)	P value	Total (119 cases) No. (%)
CABG	1 (2.3 %)	1 (4.0 %)	0.535	3 (2.7 %)
TVR	7 (8.0 %)	1 (4.0 %)	0.681	8 (7.1 %)
MVR	1 (4.0 %)	0 (0.0 %)	1.000	1 (0.9 %)
Ligation of PDA	1 (4.0 %)	0 (0.0 %)	1.000	1 (0.9 %)
Repair of ASD	1 (4.0 %)	0 (0.0 %)	1.000	1 (0.9 %)

CABG, coronary artery bypass graft; TVR，tricuspid valve replacement; ASD,atrial septal defect; PDA, patent ductus arteriosis

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Long-term follow-up

All patients received follow-up for a mean duration of 7.26 ± 5.56 (1-21) years. There were no malignancies. Myxoma recurred in 3 (2.7 %) patients whose age was < 60 years, and no variable was correlated with recurrence by logistic analysis, even though syncope was correlated positively with it on univariate analysis. In our series, 1 recurrence for four times (1 %) was detected in a 24 year old male patient after initial operation (3 year in left atrium, 8 year in right atrium, 14 and 19 years in left atrium). The original tumors located in bi-atria, the location of recurrence was in the original place. Another case of a 53 year old man was diagnosed as left ventricle myxoma and resection followed without delay. During a follow-up, a myxoma was found in the left atrium 4 years later and in the same atrium 18 months later. The third patient was a 53 year old man by whom originally a myxoma in the left atrium was found, but 15 years later multiple myxoma were found in bi-atria and right ventricle and resections of the three chamber myxoma were done simultaneously.

Death occurred in 5 (4.5 %) patients including 1 case whose age was > 60 years and 4 cases in the other age group ($p > 0.05$). Table 5 lists the positively correlated variables on logistic analysis by mortality, which includes asymptomatic, arthralgia and larger tumor volume. The death causes were cerebral hemorrhage in 1 patient, renal failure in 1 patient and progressive HF in 3 patients.

Based on the Cox regression, the proportion of patients surviving 5 and 15 years was 97.8 % and 89.5 %, respectively (Figure 1).

Table 6 shows that the complaint of weakness and syncope were positively correlated with clinical embolic events.

To compare with the younger patients, the elderly have higher ratios of hypertention, cerebral embolism and cardiomegaly, fewer complaints of dyspnea and chest distress (all $p < 0.05$). But there was no significant difference in other clinical characteristics, tumor locations, recurrence and mortality between the two age groups.

Table 4: Surgical results

Results	< 60 years No. (%)	≥ 60 age No. (%)	P value	Total (112 cases) No. (%)
In-hospital mortality	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)	0 (0.0 %)
In-hospital AF	3 (3.4 %)	1 (4.0 %)	1.000	4 (3.6 %)
In-hospital embolism	1 (1.1 %)	0 (0.0 %)	1.000	1 (0.9 %)
Late mortality	4 (4.7 %)	1 (4.0 %)	1.000	5 (4.5 %)
Recurrence	3 (2.7 %)	0 (0.0 %)	0.000	3 (2.7 %)

Table 5: Logistic analysis of variable by mortality

Variable	Death (n = 5)	Survival (n = 107)	B	P
Recurrence	2 (40.0 %)	1 (0.9 %)	5.308	0.001
Arthralgia	1 (20.0 %9	3 (2.8 %)	3.517	0.022
MW anterior leaf	1 (20.0 %)	1 (0.9 %)	4.615	0.008

All variables in Table 1 and 2 were used in the logistic analysis.

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Table 6: Logistic analysis of variable by clinical embolism

Variable	Embolism (n = 13)	No embolism (n = 99)	B	P
Dyspnea	2 (15.4 %)	45 (45.5 %)	-1.617	0.058
Weakness	5 (38.5 %)	14 (14.1 %)	2.021	0.018
Syncope	4 (30.8 %)	6 (6.1 %)	2.081	0.011
LV wall	4 (30.8 %)	16 (16.2 %)	1.355	0.087

All variables in Table 1 and 2 were used in the logistic analysis.

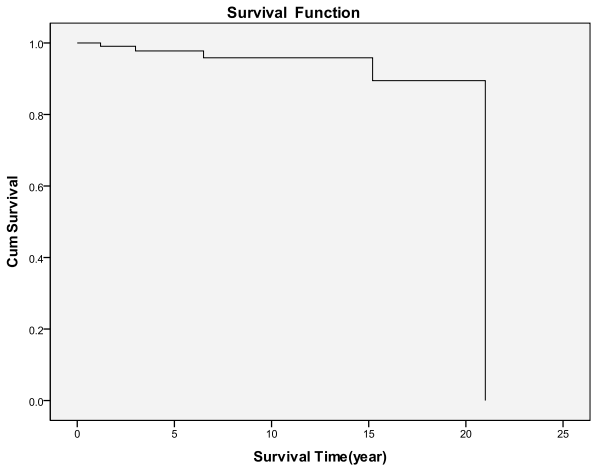

Figure 1: Based on the Cox regression, the proportion of patients surviving 5 and 15 years were 97.8 % and 89.5 %, respectively. All 112 patients completed the follow-up without censored cases.

DISCUSSION

Various studies on autopsy and surgical practice have shown different incidence of primary heart tumors including myxoma (Reynen, 1995; Holley et al., 1995). In our series, the incidence of myxoma was 0.81 % of all patients who underwent various types of cardiac surgery (data not shown), which is relatively high than reported by others.

Although myxoma occur more frequently between the age of 30 and 40 years, it's not rare in the elderly (Pinede et al., 2001). The average age ranged from 13 to 75 years old in our series, the elderly comprise 22.5 % of all the patients, while the oldest person is 95 years of age as referred by Hudson (1965).

The dominant symptom in this series is congestive heart failure due to obstruction of the mitral valve which was similar to those previously reported (Piazza et al., 2004; Attum et al., 1987; Loire, 1996). The higher incidence of cardiomegaly in the elderly may be due to more comorbidities with advanced age such as hypertension. The low complaint of dyspnea and chest distress may be due to their reluctance to complain in the elderly.

Embolic episodes are reported from 28 % to 45 % of cases and may involve the brain, kidneys or limbs (Bhan et al., 1998; Ha et al., 1999; Gabe et al., 2002). In our series, 8.0 % of the patients in < 60 year group and 24.0 % in the other group suffered from embolization, nine of them in the central nervous system, two combined with an embolus in the leg and four in the legs only. It was previously reported that smaller tumors with irregular surface more commonly result in embolic events (Oliveira et al., 2010). Furthermore, IL-6 and MMPs were considered to play a possible role in embolism formation, but the real causes are still uncertain (Orlandi et al., 2005).

Multivariate regression analysis of this sample shows that weakness and syncope were positively related with embolic events. This suggested that we should pay more attention to the patients who present the two symptoms to find the possible embolism.

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What are considered constitutional symptoms (fever, weakness, arthralgia) occurred in 27.7 % of the patients, which corresponded to that in previous reports (from 5 % to 74 %) (Gabe et al., 2002; Meyns et al., 1993).

As in previous studies (Yu et al., 2006; Perek et al., 2011), the majority of myxomas located in the left atrium, followed by the right atrium and then the ventricles.

It is reported that cardiac myxoma exhibits rapid growth, and most patients show advanced symptoms at the time of surgery (Bhan et al., 1998). But possibly due to the decreasing trends in the size and weight of myxoma, the incidence of asymptomatic myxoma has increased, which was 6.3 % in our present result, and 0 % to 26 % in other reports (Yuda et al., 2002; Grande et al., 1993).

Some authors pointed out that the clinical examination does not provide many clues to the diagnosis (Meyns et al., 1993). On auscultation, the well-described 'tumor plop' was only recorded in six patients in our series, but diastolic mitral murmur was heard in 59.1 % of the patients. So a careful listening of the heart is still a useful way leading to diagnosis.

It has been reported that TEE has led to the increase in the incidence of myxoma diagnosed preoperatively by 2 to 7 times, and the proportion of patients who underwent surgery before symptom has also increased (Yuda et al., 2002; Fyke et al., 1985). All patients in our group were diagnosed by TEE before surgery, which is consistent with that reported by others (Yuda et al., 2002). All this supports the extensive use of echocardiography for medical check-up and as preoperative screening for non-cardiovascular disease in all patients, because echocardiography is a non-invasive investigation at a minimal cost with an accuracy approaching 100 % (Perek et al., 2011; Becker et al., 2008).

It is well established that surgical removal of myxoma is related with perioperative mortality from 0 % to 7.5 % (D'Alfonso et al., 2008; Selkane et al., 2003). The zero in-hospital mortality was confirmed in our series.

The most common in-hospital complication was AF which was diagnosed in 3 patients. All of them received routine anticoagulation treatment, and no late thromboembolic complications were observed. This supports the recommendation that routine anticoagulation treatment should be used in all patients who had AF post-operatively.

The proportion of patients surviving 5 and 15 years was 97.8 % and 89.5 %, respectively, which was higher than in other series (Perek et al., 2011). A previous study reported that the leading causes of death are not related to CV disease in the long-term follow-up (D'Alfonso et al., 2008). But it's not true in our study, for 4 (80 %) deaths were attributed to CV causes, i.e. cerebral hemorrhage and progressive HF. Based on the Logistic analysis, patients who complained arthralgia or had no symptom and larger tumor volume correlated significantly with mortality.

Myxomas are usually considered benign, but recurrence rate is around 5 % to 20 % in sporadic and familial cases, which usually happens in 4 to 5 years post-operative (Becker et al., 2008; Centofanti et al., 1999). In our series, only 3 (2.7 %) patients recurred at the original location or other chamber 3 to 18 years after the initial operation. The mechanisms behind recurrence may include incomplete surgical removal, intraoperative dissemination, embolization or regrowth in another location (Oliveira et al., 2010), but we found no variable was correlated with it. To avoid the recurrence, most authors advise a full thickness resection of the base of the tumor and examined heart chambers carefully to prevent recurrence. This recommendation was not accepted by other authors who insisted that there was no difference in recurrence rates between patients who underwent an en bloc resection and a resection with only endocardial tissue attached with the tumor (Centofanti et al., 1999). In our study, the

lower recurrence rate of 2.7 % seemly supports the en bloc resection.

Although recurrence is five times more common in familial subtypes, there was no familial case found in this study group. The mixing existing of typical myxoma and malignant cell in cardiac tumor and the malignant change when it recurrs were reported by Cleveland and Kusumi separately (Cleveland et al., 1983; Kusumi et al., 2009), but there was no malignant change in our series.

CONCLUSION

Cardiac myxoma was uncommon, but it is not rare in China. Just as in younger patient, the surgical resection of myxoma in the elderly is feasible with a low perioperative mortality and low recurrence rate, so it should not be rejected merely duo to ageing. Cardiac myxomas are benign tumors, but they are considered clinically malignant tumors because of their susceptibility to embolize to distant organs. Unfortunately, few study on molecular mechanisms of tumorigenesis, recurrence and embolism have done till now.

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