Original Article

# Diagnosis and survival analyses of patients with space-occupying cardiac lesions: a 10-year retrospective single-center study

**Lei Liu[1,2#], Aijuan Fang[1,2#^], Siyuan Cheng[1,2], Guanjun Guo[1,2], Suming Zhang[1,2], Xiaofang Chen[3], Jun Pan[3], Bugao Sun[1,2], Jing Yao[1,2]**

[1]Department of Ultrasound Medicine, Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, China; [2]Medical Image Center, Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, China; [3]Department of Cardiothoracic Surgery, Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, China

*Contributions:* (I) Conception and design: L Liu, A Fang; (II) Administrative support: B Sun, J Yao; (III) Provision of study materials or patients: L Liu, A Fang, S Cheng, G Guo, S Zhang, X Chen, J Pan; (IV) Collection and assembly of data: L Liu, A Fang; (V) Data analysis and interpretation: L Liu, A Fang, S Cheng; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

*Correspondence to:* Jing Yao; Bugao Sun. Department of Ultrasound Medicine, and Medical Image Center, Affiliated Drum Tower Hospital of Nanjing University Medical School, 321 Zhongshan Road, Nanjing 210008, China. Email: jyao@njglyy.com; sunbg06@163.com.

**Background:** Space-occupying cardiac lesions are uncommon but fatal. Echocardiography can identify diseases quickly in the clinic. This study reviews the clinical data of patients with space-occupying cardiac lesions in the past 10 years and analyzes their echocardiographic features, pathological diagnosis, and prognosis.

**Methods:** We performed a retrospective analysis of 412 patients admitted to Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing from 2011 to 2020. All patients were diagnosed with cardiac masses based on transthoracic echocardiography (TTE) and transesophageal echocardiography (TEE). We compared the diagnostic results of echocardiography and the postoperative pathological diagnosis and analyzed the characteristics of different types of space-occupying cardiac lesions. We also compared the mortality of patients with different types of space-occupying cardiac lesions through follow-up results of postoperative patients.

**Results:** The 412 patients included 189 males and 223 females. Among them, 214 patients had benign tumors (including 176 patients with myxomas), 29 had primary malignant tumors, 32 had metastatic tumors, 41 had thrombi, 92 had infectious neoplasms, and 4 patients had special types of space-occupying lesions. A total of 376 lesions were correctly characterized by TTE, with an accuracy of 91.3%. Patients with benign tumors (9/214), thrombi (4/41), infectious neoplasms (5/92), or special types of space-occupying lesions (0/4) exhibited low rates of mortality or recurrence. In contrast, patients with primary malignant tumors (16/29) or metastatic tumors (16/32) exhibited high mortality rates.

**Conclusions:** Echocardiography is a valuable tool for characterizing space-occupying cardiac lesions. It can provide important preoperative diagnostic information for cardiothoracic surgeons.

**Keywords:** Echocardiography; heart-occupying; myxoma; neoplasm; thrombus, tumor

Submitted Nov 28, 2021. Accepted for publication Jun 01, 2022.
doi: 10.21037/qims-21-1151
**View this article at:** https://dx.doi.org/10.21037/qims-21-1151

^ ORCID: 0000-0002-1492-1287.

## Introduction

There are many types of space-occupying cardiac lesions, including mural thrombi, valve tumors, pericardial tumors, and various types of primary or secondary benign and malignant tumors. It has been nearly 80 years since Beck (1) first removed a pericardial teratoma in 1942. In 1954, Crafoord (2) successfully used the cardiopulmonary bypass technique to remove a cardiac myxoma for the first time . The incidence of primary cardiac tumors is 0.001–0.3%; approximately 75% of these are benign cardiac tumors, and atrial myxomas are the most common (3). Patients with cardiac conditions usually have nonspecific clinical symptoms, such as fever, chest tightness, arrhythmia caused by palpitations, valvular dysfunction, pericardial effusion with tamponade, and peripheral embolism with systemic dysfunction (4). However, some tumors are asymptomatic and are only discovered by physical examination. Transthoracic echocardiography (TTE) significantly improves the detection rate of space-occupying cardiac lesions. It can show the location and size of a lesion and indicate whether hemodynamics are affected. In addition, TTE also exhibits high sensitivity and specificity in evaluating the extent of lesions, which is extremely valuable for a surgeon's preoperative preparation (5). Most cardiac tumors need to be surgically removed to halt disease progression and prevent serious complications. Most benign cardiac tumors can be completely removed. The first-line treatment for primary and secondary cardiac malignancies is surgical resection followed by radiotherapy and chemotherapy, which can prolong patient survival (6,7). In this study, we reviewed 412 patients with space-occupying cardiac lesions who underwent cardiac surgery from 1 January 2011 to 31 December 2020. We analyzed the locations of the space-occupying cardiac lesions, the preoperative TTE diagnoses, and the postoperative pathological results to assess the diagnostic value of TTE. We also performed an outpatient review and postoperative telephone follow-up of patients to analyze their prognoses. We present the following article in accordance with the STROBE reporting checklist (available at https://qims.amegroups.com/article/view/10.21037/qims-21-1151/rc).

## Methods

### *Study population*

We enrolled 557 patients with space-occupying cardiac lesions. These patients had all been admitted to the Department of Cardiothoracic Surgery at Nanjing Drum Tower Hospital (Nanjing University, Nanjing, China) from 1 January 2011 to 31 December 2020. The inclusion criteria were as follows: admittance to the Department of Cardiothoracic Surgery at the Affiliated Drum Tower Hospital of Nanjing University Medical School, Nanjing, China; diagnosis of space-occupying cardiac lesion(s) using TTE or TEE; and the availability of surgical treatment and pathological results. A patient was also included in the study if they had a confirmed malignant tumor elsewhere in their body and the cancer embolus had metastasized to the heart; or if clinical treatment had been effective (including treatment for thrombi) and they had yet to undergo surgery. The exclusion criteria were as follows: patients with sufficient clinical diagnoses who had not undergone heart surgery and exhibited no pathological findings; patients who were diagnosed in other departments and were not cardiothoracic surgery inpatients; patients who were diagnosed as outpatients but were not hospitalized; and patients who were lost to follow-up and could not be contacted.

As a result of screening, 412 patients with space-occupying cardiac lesions were selected for retrospective analysis (*Figure 1*). Medical records were consulted, and these patients' admission and follow-up data were obtained. There were 189 males and 223 females included. The patients were aged 13–86 years at the time of diagnosis, with a median age of 57 years. In total, 18.9% (78/412) of the patients were smokers, 6.1% (25/412) had a long-term history of excessive alcohol consumption, 16.0% (66/412) had hypertension, and 9.0% (37/412) had diabetes (*Figure 2*). In addition, 263 patients had chest tightness, shortness of breath, and palpitations as their main symptoms, while 22 patients were hospitalized due to cerebrovascular or peripheral embolisms. A further 75 patients had a history of long-term fever, and 5 patients exhibited pericardial effusion with cardiac tamponade. In total, 7 patients exhibited severe arrhythmia, 6 patients had edema of the face and lower extremities, and 34 patients had no obvious symptoms on physical examination.

### *Echocardiography*

We used GE Vivid E95, Philips EPIC 7C, and Philips iE 33 color Doppler ultrasound diagnostic equipment for echocardiography (GE Healthcare, Chicago, IL, USA; Philips Healthcare, Best, the Netherlands). The probe frequency was 1.5–5.0 MHz, and patients adopted a

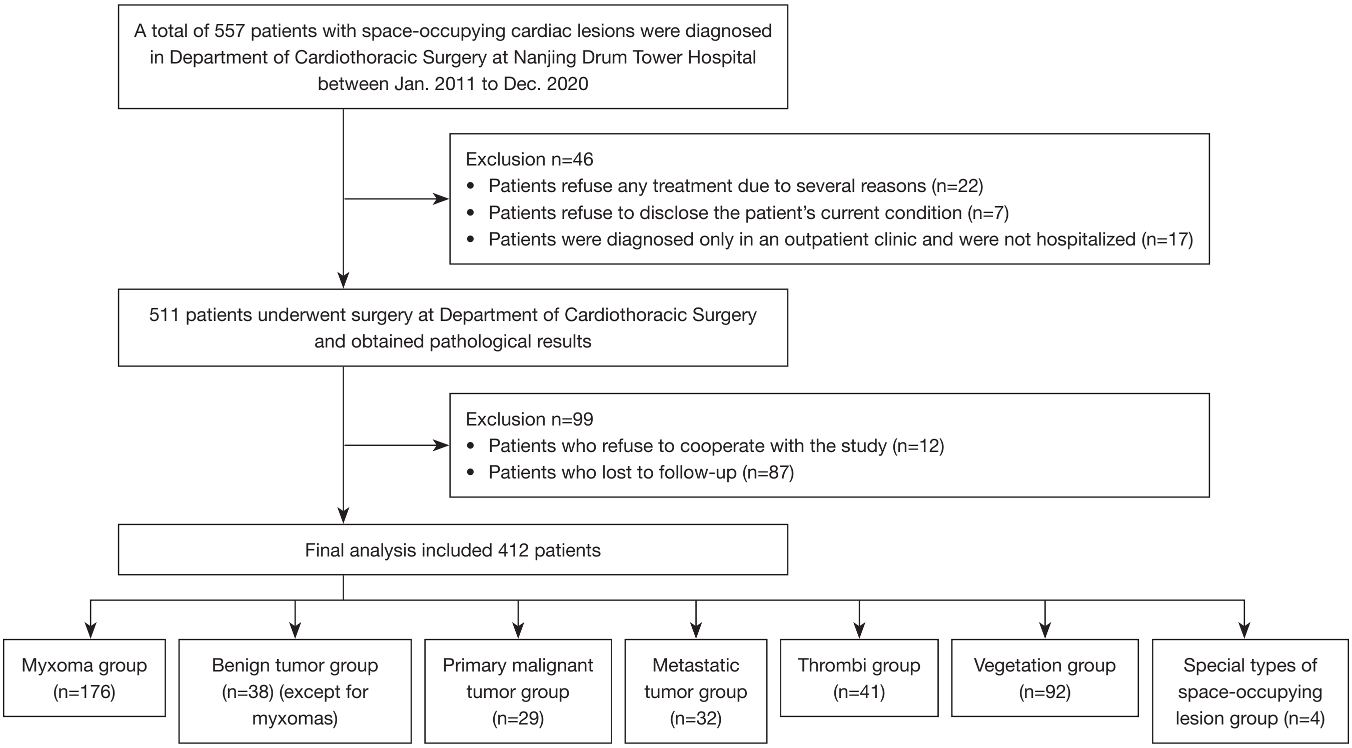



**Figure 1** Flow diagram of the case selection procedure.

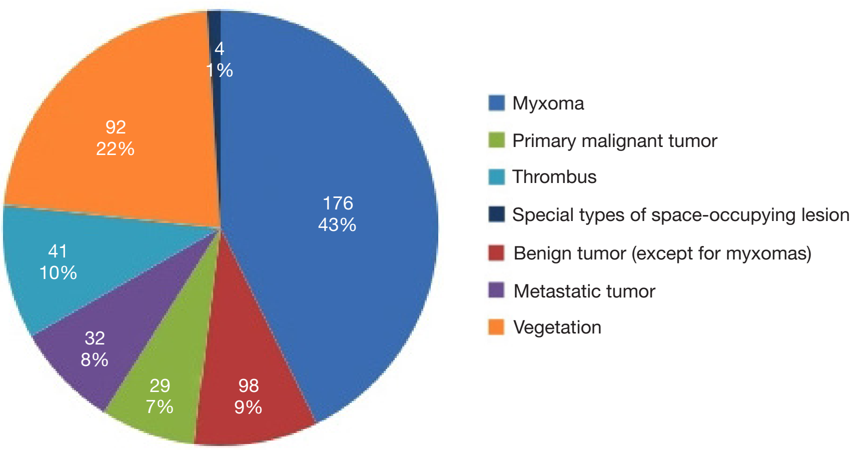



**Figure 2** The proportion of various types of space-occupying cardiac lesions.

decubitus position on their left side during the scans. We performed multiple routine standard TTE scans, with some additional non-standard scans, to record the size of each heart cavity, wall thicknesses, valve shapes, heart activity and movement, blood flow, and left ventricular ejection fractions. The standard views included a parasternal long-axis view, a short-axis view of the aorta, and apical 4-, 3-, and 2-chamber views. Non-standard views were used to record the positions, sizes, and shapes of any lesions. We recorded internal echoes, blood flow, mobility, relationships between lesions and surrounding tissues, and whether there was pericardial effusion and hemodynamic changes. We

**Table 1** Types and locations of space-occupying cardiac lesions

| Occupation type | Cases | Left atrium | Left ventricle | Right atrium | Right ventricle | Mitral valve | Tricuspid valve | Aortic valve | Pericardium | Superior vena cava | Inferior vena cava |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Myxomas[1] | 176 | 155 | 0 | 21 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Benign tumors[2] (excluding myxomas) | 38 | 2 | 7 | 13 | 8 | 0 | 0 | 0 | 11 | 1 | 0 |
| Primary malignant tumors[3] | 29 | 5 | 0 | 16 | 2 | 0 | 0 | 0 | 10 | 0 | 0 |
| Metastatic tumors | 32 | 5 | 0 | 15 | 5 | 0 | 0 | 0 | 0 | 2 | 11 |
| Thrombi | 41 | 12 | 17 | 8 | 5 | 1 | 0 | 0 | 0 | 0 | 0 |
| Infectious neoplasms | 92 | 0 | 3 | 2 | 1 | 47 | 5 | 43 | 0 | 0 | 0 |
| Special types of space-occupying lesions[4] | 4 | 0 | 3 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Total | 412 | 179 | 30 | 76 | 21 | 48 | 5 | 43 | 21 | 3 | 11 |

1, Myxomas account for a large proportion, and are counted separately from other benign tumors here. 2, Benign tumors mainly include lipoma, hemangioma, solitary fibroma, inflammatory pseudotumor, papillary elastic fibroma, pericardial cyst, and fibrous clot in the pericardium. 3, Primary malignant tumors include angiosarcoma, soft tissue sarcoma, rhabdomyosarcoma, diffuse large B-cell lymphoma, pericardial endometrial sarcoma, malignant mesothelioma, etc. 4, Multiple parts of the same type of occupancy are counted multiple times.

used echocardiography to evaluate the internal blood supply to the space inside lesions when necessary. The study was performed in accordance with the Declaration of Helsinki (as revised in 2013) and approved by the Ethics Committee of Nanjing Drum Tower Hospital (Nanjing, China). Informed consent was provided by each patient.

### *Statistical methods*

Statistical analyses were performed using the software SPSS 23.0 (IBM Corp., Armonk, NY, USA). Graphs were analyzed using GraphPad Prism 7.0 (GraphPad Software, Inc., San Diego, CA, USA). The 2 groups of data were compared using a paired 4-grid table. Differences between the 2 inspection methods were evaluated using McNemar's test. Survival analyses were performed using log-rank tests. A P value <0.05 was considered statistically significant.

## Results

### *Ultrasonographic manifestations and clinical data*

In total, 412 patients with space-occupying cardiac lesions were identified using TTE, and these findings were confirmed pathologically or clinically after surgery. Among these, 179 patients (43.4%) had lesions in the left atrium, and 76 patients (18.4%) had lesions in the right atrium. A further 48 patients (11.7%) had space-occupying lesions in the mitral valve, 43 patients (10.4%) had lesions in the aortic valve, 30 patients (7.3%) had lesions in the left ventricular space, 21 patients (5.1%) had lesions in the pericardium, 21 patients (5.1%) had lesions in the right ventricular space, 11 patients (2.7%) had lesions in the inferior vena cava, 5 patients (1.2%) had lesions in the tricuspid valve, and 3 patients (0.7%) had lesions in the superior vena cava (*Table 1*). Among the 412 patients with space-occupying cardiac lesions, 214 had benign tumors (176 patients had myxomas), 29 had primary malignant tumors, 32 had metastatic tumors, 41 had thrombi, 92 had infectious neoplasms, and 4 had special types of space-occupying lesions (*Figure 2*).

### *Comparison of TTE diagnoses of various space-occupying cardiac lesions and postoperative pathological results*

We evaluated the sensitivity, specificity, the missed diagnosis rate, and the misdiagnosis rate of TTE in diagnosing the following space-occupying cardiac lesions. For myxomas, sensitivity was 95.5%, specificity was 92.8%, the missed diagnosis rate was 4.5%, and the misdiagnosis rate was 7.2%. For benign cardiac tumors (excluding myxomas), sensitivity was 81.6%, specificity was 95.7%, the missed diagnosis rate was 18.4%, and the misdiagnosis rate was 4.3%. For cardiac malignancies, sensitivity was 82.8%, specificity was 96.3%, the missed diagnosis rate was 17.2%, and the misdiagnosis

**Table 2** Comparison of TTE on 412 cases of space-occupying cardiac diagnosis and postoperative pathological results

| Occupation type | Cases (n) | TTE diagnosis (n) | UCG sensitivity (%) | UCG specificity (%) | Missed diagnosis rate (%) | Misdiagnosis rate (%) | $\chi^2$ | P value |
|---|---|---|---|---|---|---|---|---|
| Myxoma | 176 | 168 | 95.5 | 92.8 | 4.5 | 7.2 | 2.560 | 0.110 |
| Benign tumor (excluding myxomas) | 38 | 31 | 81.6 | 95.7 | 18.4 | 4.3 | 2.783 | 0.095 |
| Primary malignant tumor | 29 | 24 | 82.8 | 96.3 | 17.2 | 3.7 | 3.368 | 0.067 |
| Metastatic tumor | 32 | 30 | 93.8 | 98.9 | 6.2 | 1.1 | 0.167 | 0.683 |
| Thrombi | 41 | 36 | 87.8 | 96.5 | 12.2 | 3.5 | 2.722 | 0.100 |
| Infectious neoplasm | 92 | 86 | 93.5 | 96.3 | 6.5 | 3.7 | 1.389 | 0.239 |
| Special types of space-occupying lesion | 4 | 1 | 25.0 | 96.1 | 75.0 | 3.9 | 7.579 | |
| Total | 412 | 376 | 91.3 | 96.3 | 8.7 | 3.7 | | 0.006* |

*P<0.05, indicating that there is a statistical difference between the TTE diagnosis results and the pathological diagnosis results. TTE, transthoracic echocardiography; UCG, ultrasonic cardiogram.

rate was 3.7%. For metastatic tumors, sensitivity was 93.8%, specificity was 98.9%, the missed diagnosis rate was 6.2%, and the misdiagnosis rate was 1.1%. For intracardiac thrombi, sensitivity was 87.8%, specificity was 96.5%, the missed diagnosis rate was 12.2%, and the misdiagnosis rate was 3.5%. For infectious neoplasms, sensitivity was 93.5%, specificity was 96.3%, the missed diagnosis rate was 6.5%, and the misdiagnosis rate was 3.7%. For special types of space-occupying lesions, sensitivity was 25.0%, specificity was 96.1%, the missed diagnosis rate was 75.0%, and the misdiagnosis rate was 3.9%. The accuracy of TTE in diagnosing the 412 patients with space-occupying cardiac lesions was 91.3% (*Table 2*).

There was a statistically significant difference between TTE diagnoses of special types of space-occupying lesions and the postoperative pathological results (P<0.05). This may be because special types of space-occupying lesions are uncommon in clinical practice, and these lesions are difficult to diagnose. There were no statistically significant differences between TTE diagnoses of other types of space-occupying cardiac lesions and the postoperative pathological or clinical treatment results (all P>0.05).

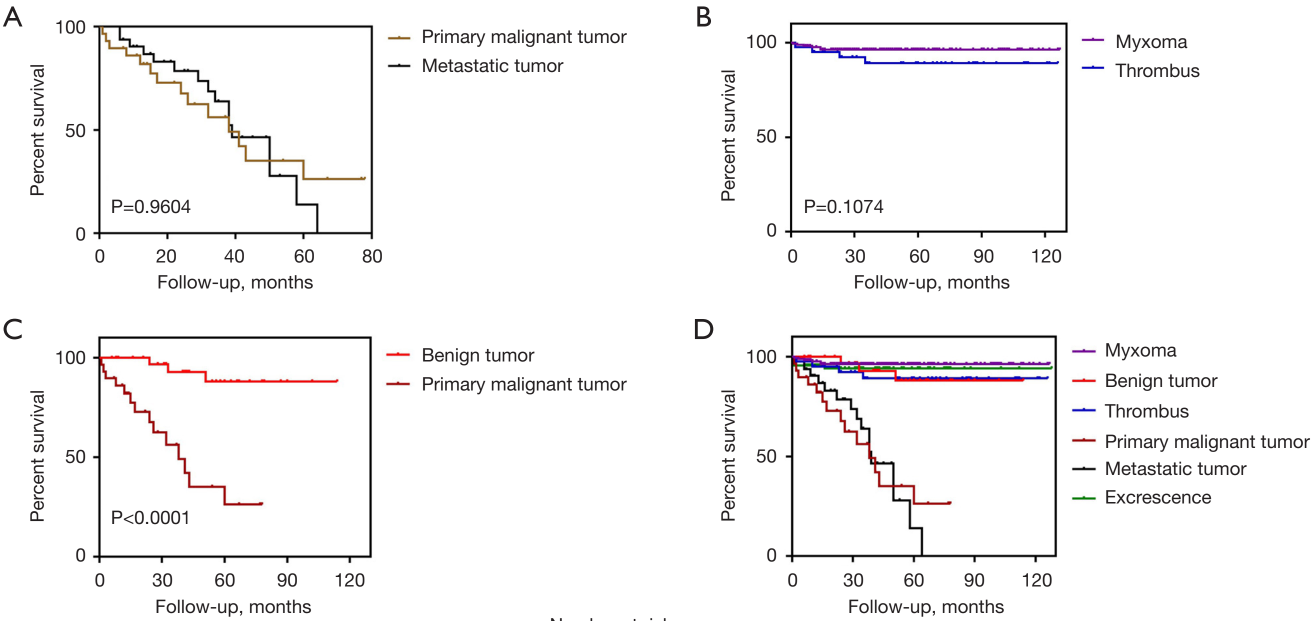
### *Prognostic follow-up of patients with space-occupying cardiac lesions*

Patients enrolled in the study were followed up as outpatients or interviewed by telephone to record postoperative outcomes. The mean follow-up time was 63.2 months, and the median follow-up time was 50.5 months. The follow-up period ended in August 2021. In total, 412 patients were followed-up, whereas 245 (36.3%) of the 657 patients who were originally enrolled were lost to follow-up and excluded from the study. The endpoints on the survival curves were patient death due to tumor-related events and recurrence of space-occupying lesions.

There were 214 patients with benign tumors, including myxomas. Among these, 7 patients died, 5 of whom were of advanced age and died from multiple organ failure. A patient died from a non-medical event, and another died from sepsis due to a postoperative infection. In addition, 2 patients experienced recurrences, at 14 and 18 months after surgery, respectively. The 10-year average mortality rate (including recurrence) was 4.20% (9/214).

There were 41 patients with thrombi. One of these patients died due to a pulmonary embolism. In addition, 3 patients experienced recurrences, 1 of which was due to a cerebroarterial embolism, and the other 2 relapses were due to peripheral vein thrombi. The 10-year average mortality rate (including recurrence) was 9.76% (4/41).

There were 92 patients with infectious neoplasms and 5 of these patients died. Among these, 2 patients died from subacute bacterial endocarditis, 1 patient died after artificial mechanical aortic valve neoplasms were diagnosed as fungal endocarditis, 1 patient died postoperatively of Pentalogy of Fallot, and 1 patient died from postoperative sepsis. The




| Number at risk | | | | | |
|---|---|---|---|---|---|
| Myxoma | 176 | 109 | 46 | 23 | 0 |
| Benign tumor | 38 | 28 | 11 | 3 | 0 |
| Thrombus | 41 | 31 | 23 | 14 | 0 |
| Primary malignant tumor | 29 | 12 | 7 | 3 | 0 |
| Metastatic tumor | 32 | 16 | 5 | 2 | 0 |
| Excrescence | 92 | 54 | 22 | 7 | 0 |

**Figure 3** Survival follow-up of space-occupying cardiac lesions. (A) Comparison of survival between primary malignant tumor and metastatic tumor. (B) Comparison of survival between myxoma and thrombus. (C) Comparison of survival between primary malignant tumor and benign tumor. (D) Comparison of postoperative survival of various types of space-occupying patients.

10-year average mortality rate (including recurrence) was 5.43% (5/92).

There were 29 patients with primary malignant tumors, and 16 of these patients died. Among these, 6 patients died of end-stage angiosarcoma, and 3 died from primary cardiac lymphoma. A patient died when an angiosarcoma recurred after surgery and invaded the pericardium, and another died from an end-stage malignant mesothelial tumor. A patient had low-grade soft tissue-derived tumors that could not be removed entirely, and this patient died 32 months after surgery. Each of the remaining 4 patients had malignant cardiac tumors; these patients refused to undergo investigative surgery, were discharged without treatment, and all died within 5 years. The 10-year average mortality rate (including recurrence) was 55.17% (16/29). The median survival time was 38.21 months.

There were 32 patients with metastatic tumors, and 16 of these patients died. Among these, 6 patients died from hepatocellular carcinomas that metastasized to the right atrium via the hepatic vein and inferior vena cava. There were 3 patients who died of end-stage lung cancer, and 3 patients died of end-stage renal cell carcinoma. A patient died from a metastatic malignant melanoma, 1 patient died of end-stage pancreatic cancer, 1 patient died of end-stage gastric cancer, and 1 patient died of end-stage thymic cancer. The 4 patients with special types of space-occupying lesions have survived to date with no signs of recurrence. The 10-year average mortality rate (including recurrence) was 50.0% (16/32). The median survival time was also 38.21 months.

During the follow-up period, there were no deaths or recurrences in the 4 patients with special types of space-occupying lesions.

The survival curve results showed that prognoses for patients with primary malignant tumors and metastatic tumors was poor (*Figure 3*). Patients who survived needed radiotherapy, chemotherapy, or immunotherapy, and their long-term life expectancy was low. By contrast, postoperative mortality and recurrence rates for patients with benign cardiac tumors, including myxomas, infectious

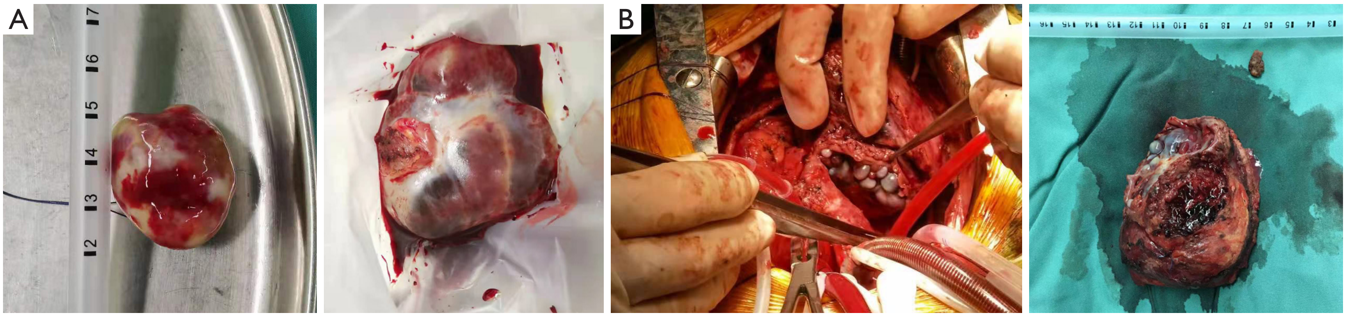



**Figure 4** Intraoperative specimens of myxoma and angiosarcoma. (A) Left atrial myxoma with a size of about 2.3 cm × 3.4 cm, with a smooth surface and a clear boundary with the heart's endometrium. (B) Right atrial angiosarcoma with a size of about 4.5 cm × 5.8 cm with a rough surface, the color is deep red, and part of it is pale "pebbles", which are not clearly demarcated from the tissue.

neoplasms, intracardiac thrombi, or special types of space-occupying cardiac lesions, were low. Pairwise comparisons showed that the survival rates of patients with benign tumors, including myxomas and infectious neoplasms, were significantly different from those of patients with metastatic or primary malignant tumors (all P<0.003; *Figure 3*).

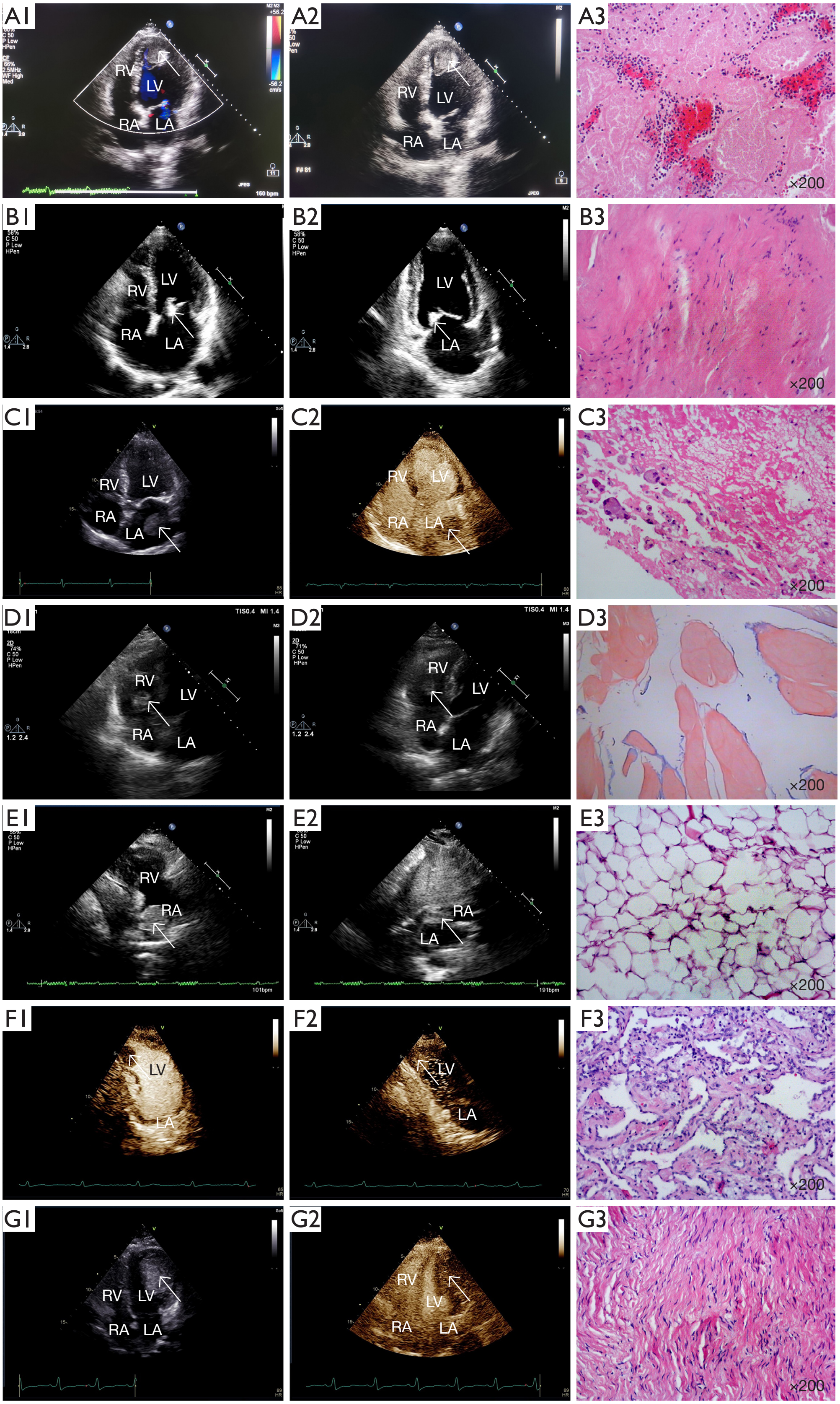
## Discussion

Space-occupying cardiac lesions are space-occupying masses that grow in the heart cavity, myocardium, and pericardium. The use of TTE has advantages in diagnosing space-occupying lesions. Two-dimensional ultrasound can clearly show the location, size, shape, boundaries, and motion of a lesion within surrounding tissues. The color Doppler mode can show internal blood flow within the lesion and any changes in hemodynamics. Although transesophageal echocardiography is indispensable for particular applications, TTE examinations are inexpensive, noninvasive, and relatively convenient for patients (8). In this study, surgeons decided whether additional TEE and cardiac magnetic resonance (CMR) examinations were needed based on clinical experience. First, they considered whether patients with cardiac malignancies had indications for surgery and required additional TEE. Second, if the nature of the mass was not clear, TEE and CMR were added depending on whether it was a thrombus or a tumor (9). Furthermore, space-occupying cardiac lesions, even benign tumors, such as myxoma, are at risk detachment at any time, so they are categorized as needing sub-emergency surgery and should be operated on as soon as possible (*Figure 4A*). Finally, TEE examination is an invasive operation examination that not every patient can adapt to it. Under the action of substantial external force, space-occupying lesions, including thrombus, vegetations, and myxoma, are at risk of detaching. Therefore, this was a carefully chosen inspection method.

In this study, TTE exhibited a sensitivity of 91.3% and a specificity of 96.3% in diagnosing space-occupying cardiac lesions, indicating a high level of detection and accuracy. Our results are similar to the results of other prospective studies (10,11). Survival curves were constructed for a follow-up period of 10 years. The death of a patient due to tumor-related events or the recurrence of space-occupying lesions were the follow-up endpoints. The results showed that 10-year mortality rates for patients with metastatic tumors or primary malignant cardiac tumors were significantly higher than those for patients with benign tumors, thrombi, and infectious neoplasms (*Figure 4B*; P<0.05).

Intracardiac thrombosis is the most common space-occupying cardiac disease observed in clinical practice (12). Our study only included a few patients with thrombi or infective endocarditis because we confirmed the presence of thrombi and infectious neoplasms by surgery, and some of these cases would have been resolved by other treatments. Cases that were not supported by sufficient evidence were excluded from the group, even if they were suspected. Cardiac thrombi often appear as irregular masses with low or medium echoes or appear during TTE as cords with almost no activity (*Figure 5A1,5A2*). They may be visualized as undeveloped clumps by contrast echocardiographic perfusion imaging (CEPI) (13). However, atypical clumps may also be visible, making diagnoses difficult. Thrombi often have a smooth gray-white cut surface and form a solid mass of necrotic tissue. This tissue may exhibit a fibrous


A1
RV
LV
RA
LA
A2
RV
LV
RA
LA
A3
×200
B1
RV
LV
RA
LA
B2
LV
LA
B3
×200
C1
RV
LV
RA
LA
C2
RV
LV
RA
LA
C3
×200
D1
RV
LV
RA
LA
D2
RV
LV
RA
LA
D3
×200
E1
RV
RA
E2
RA
LA
E3
×200
F1
LV
LA
F2
LV
LA
F3
×200
G1
RV
LV
RA
LA
G2
RV
LV
RA
LA
G3
×200

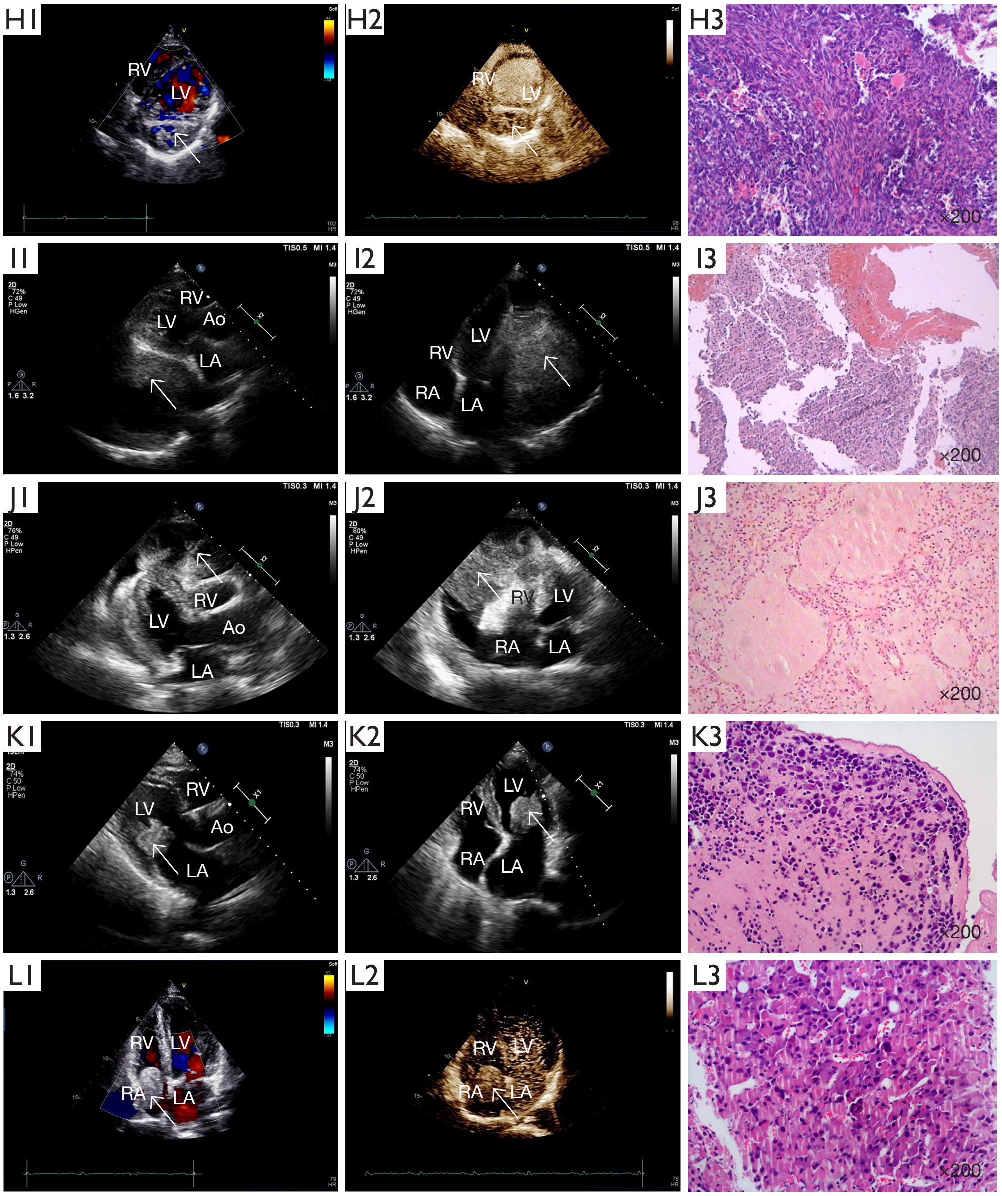



**Figure 5** Ultrasound manifestations and pathological features of various types of space-occupying patients. (A1, A2) The apical mural thrombosis of patients with a left ventricular aneurysm. (B1, B2) The formation of mitral valve infectious neoplasms in patients with infective vegetation. (C1, C2) Left atrial myxoma. (D1, D2) A papillary fibroelastoma originating from the intima of the tricuspid valve. (E1, E2) Right atrial lipomas. (F1, F2) Left ventricular hemangioma. (G1, G2) Left ventricular fibroids. (H1, H2) Left ventricular angiosarcoma (left ventricular short-axis non-standard view). (I1, I2) Left ventricular lateral wall pericardial malignant mesothelioma. (J1, J2) Right ventricular lateral wall liposarcoma. (K1, K2) Mitral primary cardiac lymphoma of the posterior leaflet of the valve. (L1, L2) The metastasis of kidney cancer tumor thrombus to the right atrium. (A3-L3) All pathological pictures are HE staining, ×200 times. HE, hematoxylin and eosin; LA, left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle; Ao, aorta.

inflammatory exudate under microscopy but shows no tumor characteristics (*Figure 5A3*). Intracardiac thrombi often occur in patients with hemodynamic abnormalities, such as left ventricular insufficiency or atrial fibrillation (14,15). Two-dimensional sound imaging showed a smoke-like blood stasis echo within the left atrium, consistent with the results observed for more than 70% of thrombi in the left heart cavity in our study. The 41 patients with thrombi exhibited 4 endpoints: 1 patient died of a pulmonary embolism, 1 patient died of a cerebral arterial embolism, and 2 patients died of peripheral venous embolisms. However, the actual mortality rate may be lower because most patients who survived thrombi and were treated with anticoagulants were not included in our study.

Infective endocarditis is an infection of the autologous or artificial heart valve, the surface of the endocardium, or an indwelling cardiac device (16). Recently, invasive surgery has become more common and the incidence of infective endocarditis has also been increasing, with a 1-year mortality rate now greater than 30% (16). The surface of the heart valve is attached to vegetation consisting of platelets, fibrin, erythrocytes, white blood cells, and infectious pathogens. Ultrasound showed medium and high echo clumps attached to the valve leaflets that oscillate during the cardiac cycle (*Figure 5B1*,*5B2*). Microscopy showed fibrous tissue proliferation associated with degenerate necrotic tissue and some acute and chronic inflammatory cell infiltration (*Figure 5B3*). This study found that only a few vegetations were attached to the intima surface of the tricuspid valve or the heart cavity. The number of infectious vegetations on the mitral and aortic valves was 35 and 31, respectively. A further 12 patients had vegetations on both the mitral and aortic valves (*Table 1*). We found that most patients with infectious neoplasms exhibited 2-leaflet aortic valve malformations (including 1 patient with a quadruple-leaflet aortic valve malformation), valve prolapse, or other structural or functional abnormalities. For example, postoperative valve infections or thrombi may occur after a valvuloplasty or valve replacement (17,18).

Primary benign and malignant tumors of the heart are clinically uncommon, and their incidence at autopsy is 0.0017–0.03% (19). In agreement with our results, international research studies have found that more than 80% of primary tumors are benign (20-22). Primary benign tumors include myxomas, hemangiomas, fibromas, lipomas, and other inflammatory pseudotumors. Among these, myxomas are the most common and account for approximately 70% of primary benign cardiac tumors (23). Samanidis *et al.* (24) reported that approximately 75% of cardiac myxomas originate in the left atrium, whereas 23% are located in the right atrium, and only 2% are located in a ventricle. In our study, the incidence of left atrial myxomas was 88.1%, and this finding informed our clinical diagnosis procedure. For primary tumors originating in the left atrium, a myxoma is the first diagnosis to consider. Under two-dimensional ultrasound, myxomas exhibited a mid-to-low echo mass with clear edges, a pedicle connected to the atrial septum, and a large degree of mobility (*Figure 5C1*). When contrast agent completely filled the left ventricle, CEPI showed that the tumor mass was only partially visible. As the contrast agent in the left ventricle dissipated, the whole mass became visible (*Figure 5C2*). Under microscopy, stellate tumor cells were visible in the mucus-like tissue (*Figure 5C3*). International studies have reported that the 30-day mortality rate after myxoma resection is as high as 10%, and the recurrence rate is approximately 5%, which exceeds the recurrence rate for several months or years after surgery (24).We followed up 176 patients with myxomas after they had surgery. Among them, 4 patients died, 2 died of heart failure, 1 died from postoperative sepsis, and 1 patient's cause of death was unrelated to cardiovascular events. A further 2 patients experienced recurrences at 14 and 18 months after surgery, respectively. These recurrence and mortality rate data show that our resection strategy for myxomas is safe and resulted in favorable prognoses.

Papillary fibroblastomas are also common primary benign cardiac tumors. These tumors often originate in the inner membrane of a heart valve, usually in isolation (25). The tumor surface is papillary with a short pedicle. Under microscopy, elastic fibers are visible along the nipple axis, and the tumor surface is covered with a single layer of flat or cube-shaped epithelial cells (*Figure 5D1*,*5D2*). The loose connective tissue comprises acidic polysaccharides, collagen fibers, elastic fibers, a few smooth muscle cells, and occasionally monocytes. The central collagen-fiber bundle is interspersed with a fine mesh of elastic fibers (*Figure 5D3*).

Primary benign heart tumors also include lipomas (*Figure 5E1-5E3*) (26), hemangiomas (*Figure 5F1-5F3*) (27), fibroids (*Figure 5G1-5G3*) (28), and cystic tumors (19). Overall prognoses for patients with these tumors were good. There were 2 patients of advanced age who died of multiple organ failure 2 years after surgery. Primary malignant cardiac tumors are rare, and many are angiosarcomas (29). Overall prognoses for patients with primary cardiac sarcomas were very poor, with a median survival time of approximately 12 months (30). We found that overall prognoses for patients with primary malignant tumors were poor. The median survival time for these patients was approximately 41 months, which was different from the median survival times reported by previous studies. Radiotherapy, chemotherapy, or immunotherapy treatment provided immediately after a diagnosis can prolong patient survival times (31). Ultrasound shows that these tumors are usually large and can highlight echogenic masses and blood flow within the tumor (*Figure 5H1*). The tumor boundary with the ventricular wall may be unclear. CEPI shows that these tumors are similar to the surrounding myocardial tissue. However, the tumours remain visible after the intracardiac contrast agent dissipates (*Figure 5H2*). Angiosarcoma tumor cells appear oval and fusiform under microscopy. They form irregular, anastomosed, slit- or branch-like vascular cavities. Except for a few fast-growing tumor cells that penetrate the basement membrane, the tumor cells are all located within the membrane (*Figure 5H3*).

Pericardial malignant mesotheliomas are relatively rare malignant cardiac tumors, which are often associated with excessive pericardial effusion or tamponade (*Figure 5I1,5I2*) (32,33). The disease has a poor prognosis, and patients have a short life expectancy (33). In our study, 1 patient with malignant pericardial mesothelioma survived for 52 months after undergoing a partial resection of the tumor body combined with radiotherapy and chemotherapy. Histopathology showed that the tumor cells within the fibrous connective tissue formed a papillary glandular tube. The tumor cells were irregular with abundant cytoplasm, and mitotic figures were observed (*Figure 5I3*) (34).

Cardiac liposarcomas are also rare primary malignant cardiac tumors. They appear as strong echoes under two-dimensional ultrasound, with fine spots, due to the presence of many mature adipocytes (*Figure 5J1,5J2*). These tumors often result in distant metastasis; therefore, complete resection is the principal treatment (35). Tonini *et al.* (36) reported that a cardiac liposarcoma that had metastasized to the abdomen measured 30 cm × 32 cm × 35 cm. Under the microscope, cardiac liposarcoma tumor cells appear as small round or oval cells with uniform morphology, and they are interspersed with adipocytes (*Figure 5J3*). These neoplastic cells exhibit different cell morphologies based on their stage of differentiation. Liposarcoma cells may show different degrees of atypia, regardless of their stage of differentiation.

Primary cardiac lymphomas are rare lymphomas that usually occur in the right atrium but can also invade the right ventricle, pericardium, left atrium, or left ventricle (5). Some of these tumors have a pedicle and intact capsule, which grow within the heart cavity (*Figure 5K1,5K2*). In some patients, the tumors infiltrate the myocardial cells and visceral pericardium. The lesions are diffuse and atypical cells are scattered within a fibrin-like exudate. These basophilic cells have irregular nuclei, a high nucleoplasm ratio, and little cytoplasm (*Figure 5K3*).

Common metastatic malignant tumors include hepatocellular metastases, renal clear cell adenocarcinomas, and other squamous cell carcinomas that have metastasized to the heart (*Figure 5L1-5L3*). These space-occupying lesions require radiotherapy and chemotherapy at the primary tumor site. After treatment, the prognosis for these patients is often poor (23,29).

A patient's medical history and imaging examinations can provide considerable diagnostic insight. Our study found that TTE exhibited a high level of detection and accuracy for metastatic malignant tumors, and the misdiagnosis rate was low. When using TTE to diagnose metastatic malignant tumors, we observed sensitivity of 93.8%, specificity of 98.9%, and a misdiagnosis rate of only 1.1%. Analyses of tumor locations showed that half of the metastatic tumors extended into the right atrium through the superior and inferior vena cava (*Table 1*). Compared with primary malignant tumors, metastatic tumors were also associated with a higher mortality rate, although the difference was not significant (P=0.960).

Among the 412 patients with space-occupying cardiac lesions, 4 patients had special types of space-occupying lesions, 1 of whom had a vascular tumor. However, the boundary between the tumor and the surrounding muscle tissue was unclear and the tumor itself was not pathological. There were 2 patients with Loeffler endocarditis, which is a cardiac manifestation of eosinophilia syndrome. This rare systemic disease is characterized by the continuous production of eosinophils, leading to organ damage (37). There was also a patient with an apparent space-occupying mass in the right atrium. However, no space-occupying manifestations, such as a thrombus or myxoma, were discovered during surgery. The muscle bundle spanning the right atrium was investigated, and the apparent mass may have been due to abnormal imaging under the ultrasound.

In this study, we integrated patient data from a variety of sources. We consulted patient medical records, followed-up with patients, and accessed echocardiographic records and postoperative pathology reports. Our results show that TTE is a valuable tool for diagnosing patients with space-occupying cardiac lesions. Echocardiography exhibits both high sensitivity and high specificity. When combined with other imaging techniques, TTE can provide cardiothoracic surgeons with important preoperative diagnostic information.

### *Limitations*

This was a single-center study, and all patients were admitted to the cardiothoracic surgery department of our hospital. Most of these patients were from the Jiangsu and Anhui provinces in China. Furthermore, surgery was the primary treatment requirement for most patients admitted to this hospital department. Therefore, many patients with cardiac thrombi or infective endocarditis who received conservative treatment in the internal medicine department were excluded from this study. Consequently, the proportion of patients in our study who had thrombi or neoplasms would have been much lower than the general population. In addition, we did not investigate the benefits of surgery by comparing our patient mortality rates with those of a population of similar patients who did not undergo surgery. Future studies should include such a control group and recruit patients from several centers across a wider geographical area.

## Acknowledgments

*Funding:* This research was funded by the National Natural Science Foundation of China (No. 81571691) and the Nanjing Medical Science and Technology Development Project (No. YKK18086).

## Footnote

*Reporting Checklist:* The authors have completed the STROBE reporting checklist. Available at https://qims.amegroups.com/article/view/10.21037/qims-21-1151/rc

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at https://qims.amegroups.com/article/view/10.21037/qims-21-1151/coif). The authors report that this research was funded by the National Natural Science Foundation of China (No. 81571691) and the Nanjing Medical Science and Technology Development Project (No. YKK18086). The authors have no other conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was performed in accordance with the Declaration of Helsinki (as revised in 2013) and approved by the Ethics Committee of Nanjing Drum Tower Hospital (Nanjing, China). Informed consent was provided by each patient.



## References

1. Beck CS. An intrapericardial teratoma and a tumor of the heart: both removed operatively. Ann Surg 1942;116:161-74.
2. Chitwood WR Jr. Clarence Crafoord and the first successful resection of a cardiac myxoma. Ann Thorac Surg 1992;54:997-8.
3. Patel J, Sheppard MN. Pathological study of primary cardiac and pericardial tumours in a specialist UK Centre: surgical and autopsy series. Cardiovasc Pathol 2010;19:343-52.
4. Ragland MM, Tak T. The role of echocardiography in diagnosing space-occupying lesions of the heart. Clin Med Res 2006;4:22-32.
5. Zhao Y, Huang S, Ma C, Zhu H, Bo J. Clinical features of cardiac lymphoma: an analysis of 37 cases. J Int Med Res 2021;49:300060521999558.
6. Barreiro M, Renilla A, Jimenez JM, Martin M, Al Musa T, Garcia L, Barriales V. Primary cardiac tumors: 32 years of experience from a Spanish tertiary surgical center. Cardiovasc Pathol 2013;22:424-7.
7. Fuchida S, Yamada N, Uchida R, Okano A, Okamoto M, Ochiai N, Shimazaki C. Malignant lymphoma presenting as a cardiac tumor and superior vena caval syndrome successfully treated by haploidentical stem cell transplantation. Leuk Lymphoma 2005;46:1517-21.
8. Jolobe OMP. Transthoracic echocardiography is a noninvasive alternative to TEE. Am J Emerg Med 2020;38:828-9.
9. Li X, Chen Y, Liu J, Xu L, Li Y, Liu D, Sun Z, Wen Z. Cardiac magnetic resonance imaging of primary cardiac tumors. Quant Imaging Med Surg 2020;10:294-313.
10. Mihos CG, Nappi F. A narrative review of echocardiography in infective endocarditis of the right heart. Ann Transl Med 2020;8:1622.
11. Sheiban I, Casarotto D, Trevi G, Benussi P, Marini A, Accardi R, Motta A, Brunelli M, Muneretto C, Tenuti A. Two-dimensional echocardiography in the diagnosis of

intracardiac masses: a prospective study with anatomic validation. Cardiovasc Intervent Radiol 1987;10:157-61.
12. Srichai MB, Junor C, Rodriguez LL, Stillman AE, Grimm RA, Lieber ML, Weaver JA, Smedira NG, White RD. Clinical, imaging, and pathological characteristics of left ventricular thrombus: a comparison of contrast-enhanced magnetic resonance imaging, transthoracic echocardiography, and transesophageal echocardiography with surgical or pathological validation. Am Heart J 2006;152:75-84.
13. Kirkpatrick JN, Wong T, Bednarz JE, Spencer KT, Sugeng L, Ward RP, DeCara JM, Weinert L, Krausz T, Lang RM. Differential diagnosis of cardiac masses using contrast echocardiographic perfusion imaging. J Am Coll Cardiol 2004;43:1412-9.
14. Antwi-Amoabeng D, Willyard CE 3rd, Gullapalli N, Keogh M. Disappearing "Myxoma": Left Atrial Thrombus Masquerading as a Myxoma. Cureus 2020;12:e8536.
15. Wanishsawad C, Roongsritong C, Sitthi-Amorn C, Puavilai W. Spontaneous echo contrast on transthoracic echocardiography and left atrial thrombus in rheumatic mitral valve disease patients: a clinicopathologic study. Clin Cardiol 1994;17:547-51.
16. Cahill TJ, Prendergast BD. Infective endocarditis. Lancet 2016;387:882-93.
17. Allen CJ, Patterson T, Chehab O, Cahill T, Prendergast B, Redwood SR. Incidence and outcomes of infective endocarditis following transcatheter aortic valve implantation. Expert Rev Cardiovasc Ther 2020;18:653-62.
18. Gürsoy MO, Kalçik M, Karakoyun S, Özkan M. The current status of fluoroscopy and echocardiography in the diagnosis of prosthetic valve thrombosis-a review article. Echocardiography 2015;32:156-64.
19. Luc JGY, Phan K, Tchantchaleishvili V. Cystic tumor of the atrioventricular node: a review of the literature. J Thorac Dis 2017;9:3313-8.
20. Kamiya H, Yasuda T, Nagamine H, Sakakibara N, Nishida S, Kawasuji M, Watanabe G. Surgical treatment of primary cardiac tumors: 28 years' experience in Kanazawa University Hospital. Jpn Circ J 2001;65:315-9.
21. Maimaitiaili A, Zhang WM, Guo YZ, Elmaik D, Tang NH, Zhang ZG. Survival of Patients with Primary Cardiac Tumors in an 11-Year Single Center Study. Heart Surg Forum 2019;22:E097-102.
22. Wang JG, Wang B, Hu Y, Liu JH, Liu B, Liu H, Zhao P, Zhang L, Li YJ. Clinicopathologic features and outcomes of primary cardiac tumors: a 16-year-experience with 212 patients at a Chinese medical center. Cardiovasc Pathol 2018;33:45-54.
23. Rahouma M, Arisha MJ, Elmously A, El-Sayed Ahmed MM, Spadaccio C, Mehta K, Baudo M, Kamel M, Mansor E, Ruan Y, Morsi M, Shmushkevich S, Eldessouki I, Rahouma M, Mohamed A, Gambardella I, Girardi L, Gaudino M. Cardiac tumors prevalence and mortality: A systematic review and meta-analysis. Int J Surg 2020;76:178-89.
24. Samanidis G, Khoury M, Balanika M, Perrea DN. Current challenges in the diagnosis and treatment of cardiac myxoma. Kardiol Pol 2020;78:269-77.
25. Vieira MJ, Craveiro N, Alves M, Pitta L. Unusual place… unusual number. Echocardiography 2020;37:467-8.
26. Maia Alves R, Gamboa C. Cardiac Lipoma of the Interventricular Septum. Eur J Case Rep Intern Med 2020;7:001685.
27. Shojaeifard M, Saedi S, Alizadeh Ghavidel A, Karimlu MR, Kasaei M, Reza Pouraliakbar H, Mozaffari K. Concomitant cardiac and hepatic hemangiomas. Echocardiography 2020;37:462-4.
28. Ascaso M, Astrosa E, Moscoso B, Fernandez A, Barriuso C, Castella M. Biventricular fibroma resection in an adult. Multimed Man Cardiothorac Surg 2019.
29. Taguchi S. Comprehensive review of the epidemiology and treatments for malignant adult cardiac tumors. Gen Thorac Cardiovasc Surg 2018;66:257-62.
30. Siontis BL, Leja M, Chugh R. Current clinical management of primary cardiac sarcoma. Expert Rev Anticancer Ther 2020;20:45-51.
31. Billan S, Kaidar-Person O, Gil Z. Treatment after progression in the era of immunotherapy. Lancet Oncol 2020;21:e463-76.
32. Farhat SB, Salah M, Milouchi S. Primary malignant pericardial mesothelioma: a case report. Pan Afr Med J 2020;36:375.
33. Matsuyama S, Imazuru T, Uchiyama M, Ota H, Iida M, Shimokawa T. Primary malignant pericardial mesothelioma presenting with cardiac tamponade. Int J Surg Case Rep 2020;73:253-6.
34. Banišauskaitė A, Jankauskas A, Šarauskas V, Aržanauskaitė M. A case report of malignant primary pericardial mesothelioma with atypical imaging appearance: multimodality imaging with histopathological correlation. Eur Heart J Case Rep 2020;4:1-5.
35. Deppe AC, Adler C, Madershahian N, Reuter H, Bangard C, Baldus S, Wahlers T, Wippermann J. Cardiac liposarcoma-a review of outcome after surgical resection. Thorac Cardiovasc Surg 2014;62:324-31.

36. Tonini V, Gozzi G, Pirini MG, Cervellera M. Giant abdominal metastasis from cardiac liposarcoma. BMJ Case Rep 2018;2018:bcr-2018-225616.
37. Polito MV, Hagendorff A, Citro R, Prota C, Silverio A, De Angelis E, Klingel K, Metze M, Stöbe S, Hoffmann KT, Sabri O, Piscione F, Galasso G. Loeffler's Endocarditis: An Integrated Multimodality Approach. J Am Soc Echocardiogr 2020;33:1427-41.

**Cite this article as:** Liu L, Fang A, Cheng S, Guo G, Zhang S, Chen X, Pan J, Sun B, Yao J. Diagnosis and survival analyses of patients with space-occupying cardiac lesions: a 10-year retrospective single-center study. Quant Imaging Med Surg 2022;12(8):4081-4094. doi: 10.21037/qims-21-1151