RESEARCH ARTICLE

Cardiac tumors—sex-related characteristics and outcomes after surgical resection

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Abstract
Objectives: Cardiac tumors represent a rare and heterogeneous pathological entity, with a cumulative incidence of up to 0.02%. Gender was previously reported to influence outcomes after tumor surgery. This study aimed to investigate for gender-related differences in outcomes after cardiac surgery.

Methods: Between 2009 and 2021, 95 male and 88 female patients underwent surgery for tumor extirpation in our center. Preoperative baseline characteristics, intraoperative data, and long-term survival were analyzed. The diagnosis was confirmed postoperatively by (immune-)histopathological analysis.

Results: There were no significant differences in baseline characteristics and survival. Myxoma was the most common tumor type overall and was more diagnosed in women (n = 36 vs. n = 62, p ≤ 0.001). Sarcoma was the most common malignant tumor type (n = 5). Tumor location at the atrial septum was more likely in women (n = 26 vs. n = 16, p = 0.041), whereas ventricular localization was more common in male patients (n = 20 vs. n = 7, p = 0.001). Minimally invasive tumor extirpation was significantly more often performed in women, and in-hospital stay was shorter in female patients.

Conclusion: The localization and dignity of cardiac tumors differ between genders, not affecting survival. Surgical tumor extirpation remains the gold standard of treatment for cardiac tumors in both genders as it is highly effective and associated with good long-term survivorship.

KEYWORDS
cardiac masses, cardiac surgery, cardiac tumors, fibroelastoma, gender study, metastases, myxoma

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1 | INTRODUCTION

Cardiac tumors are a rare entity with incidences between 0.17 and 0.19%. The majority of which is benign. Nevertheless, patients with malignant primary cardiac tumors face a poor prognosis. Due to their rarity, clinicians may only see a few cases during their professional careers, and the majority of scientific literature is based on case studies and descriptions. Over the last decades, there has been a rise in the prevalence of benign and malignant cardiac tumors related to improved imaging modalities. Concerning preoperative diagnostics, echocardiography is the primary diagnostic tool in most cases. Transesophageal echocardiography (TEE) enables the assessment of size, location, mobility, and pericardial involvement. Also, it shows hemodynamic effects of the suspected mass and can detect even small masses (<1 cm). Transesophageal echocardiography (TEE) is used when valvular involvement is suspected in patients with atrial involvement or mobile masses. After a cardiac mass is suspected, patients may be referred to magnetic resonance imaging (MRI) for an exact evaluation of the cardiac chambers and the pericardium to enable exact surgical planning. Besides MRI, computed tomography (CT) offers a diagnostic alternative that is optimal for detecting calcified masses and assessing chest and lung tissue as well as corresponding vascular structures and enables the exclusion of obstructive coronary artery disease in the same setting.

Gender disparities have been reported in the face of other cardiovascular diseases, such as coronary artery disease or valvular heart disease. The relationship between gender and cardiac tumor outcomes has been investigated; this analysis focuses on intraoperative details to improve the understanding and patients outcome after surgical tumor resection. Although sex differences have already been reported in the case of cardiac tumors, survival differences after surgical resection, with long-term follow-up, are lacking.

We used our clinical database—one of the largest single-center databases of cardiac tumors to evaluate sex differences in cardiac tumor prevalence and survival after surgical resection between 2009 and 2021.

2 | METHODS

The local ethics commission board approved the retrospective analysis of consecutive cases treated at our institution. All relevant perioperative data were obtained from our clinical software systems. Between 2009 and 2021, 183 consecutive patients with cardiac masses were identified and included to be analyzed retrospectively with respect to sex-related differences.

2.1 | Variables of interest

The retrospective analysis was performed using an institutional patient database. The variables evaluated in this study include preoperative baseline characteristics (Table 1), heart tumor characteristics (Table 2), and characteristics of tumors in other locations than the heart (Table 3), as well as intra- and postoperative characteristics (Table 4).

2.2 | Statistical analysis

The statistical analysis was performed using Statistical Package for Social Sciences, version 23.0 (SPSS IBM). All data were presented as continuous or categorical variables. Categorical data were expressed as total numbers and percentages. Continuous
data were evaluated for normality using a one-sample Kolmogorov–Smirnov test and were expressed as the mean ± standard deviation (SD) in cases of normally distributed or median (interquartile range) in cases of non-normally distributed continuous variables. Univariate analysis was performed using either Student t or Mann–Whitney U test for normally and non-normally distributed continuous variables, respectively. Pearson’s χ² or Fisher exact tests were used for comparison of categorical data depending on the minimum expected count in each cross-tab. p values <0.05 were considered statistically significant. The percentages were not always calculated by the total of 183 patients due to the absence of some follow-up data. Long-term survival was calculated and graphically presented using Kaplan–Meier plots, with Log-rank and Breslow tests to confirm statistical significance. Multinomial regression analysis was applied to examine independent predictive factors among significantly correlated variables, described by the odd’s ratio (OR) and 95% confidence interval (CI).

### RESULTS

The mean follow-up of our analysis was 56.6 ± 44.1 months. Overall 35 patients of the whole cohort were lost of follow-up due to a variety of reasons.

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**TABLE 2** Heart tumor characteristics.

| % (n) | Male (n = 95) | Female (n = 88) | p  |
|-------|---------------|-----------------|----|
| Left atrium, n (%) | 49 (52) | 67 (76) | <0.001 |
| Right atrium, n (%) | 24 (25) | 17 (19) | 0.335 |
| Atrial septum, n (%) | 16 (17) | 26 (30) | 0.041 |
| Ventricular, n (%) | 20 (21) | 7 (8.0) | 0.013 |
| Pericardial, n (%) | 1 (1.1) | 0 (0.0) | 1.000 |
| Mediastinal, n (%) | 3 (3.2) | 0 (0.0) | 0.247 |
| Involvement of heart valves, n (%) | 17 (18) | 11 (13) | 0.311 |
| Tumor prolapse through the tricuspid valve, n (%) | 11 (4.2) | 1 (1.1) | 0.370 |
| Tumor prolapse through the mitral valve, n (%) | 4 (4.2) | 9 (10) | 0.113 |
| Infiltrative, n (%) | 7 (7.4) | 1 (1.1) | 0.066 |
| Malignancy, n (%) | 10 (11) | 4 (4.5) | 0.128 |
| Total resection, n (%) | 86 (91) | 86 (98) | 0.041 |
| Myxoma, n (%) | 36 (38) | 62 (70) | 0.001 |
| Fibroelastoma, n (%) | 13 (14) | 8 (9.1) | 0.330 |
| Other benign tumors, n (%) | 34 (36) | 16 (18) | 0.008 |
| Sarcoma (primary and secondary), n (%) | 3 (3.2) | 2 (2.2) | 1.000 |
| Other malign tumors, n (%) | 2 (7.4) | 2 (2.2) | 0.172 |

Note: Bold values indicate p < 0.05.

**TABLE 3** Tumors in other location.

| % (n) | Male (n = 95) | Female (n = 88) | p  |
|-------|---------------|-----------------|----|
| Malignant, n (%) | 12 (13) | 12 (14) | 0.632 |
| Breast cancer, n (%) | 0.0 (0) | 5 (5.7) | 0.024 |
| Cervical cancer, n (%) | 0.0 (0) | 2 (2.3) | 0.230 |
| Prostate cancer, n (%) | 3 (3.2) | 0.0 (0) | 0.247 |
| Colon cancer, n (%) | 1 (1.1) | 0.0 (0) | 1.000 |
| Lymphoma, n (%) | 1 (1.1) | 1 (1.1) | 1.000 |
| Melanoma, n (%) | 1 (1.1) | 0.0 (0) | 1.000 |
| Sarcoma, n (%) | 0.0 (0) | 2.3 (2) | 0.230 |
| Renal cancer, n (%) | 2 (2.1) | 1 (1.1) | 1.000 |
| Lung cancer, n (%) | 4 (4.2) | 1 (1.1) | 0.370 |
| Benign, n (%) | 1 (1.1) | 0.0 (0) | 1.000 |

Note: Bold values indicate p < 0.05.

**TABLE 4** Intraoperative and postoperative data.

| % (n) | Male (n = 95) | Female (n = 88) | p  |
|-------|---------------|-----------------|----|
| Sternotomy, % (n) | 63 (66) | 63 (49) | 0.017 |
| Clamshell thoracotomy, % (n) | 1 (1.1) | 0.0 (0.0) | 1.000 |
| Minimally-invasive, % (n) | 29 (31) | 45 (51) | 0.005 |
| Bi-caval cannulation, % (n) | 23 (24) | 25 (28) | 0.519 |
| Two-stage cannulation, % (n) | 32 (34) | 16 (18) | 0.017 |
| Femoral cannulation, % (n) | 33 (35) | 44 (50) | 0.042 |
| Simple tumor extirpation, % (n) | 43 (45) | 52 (59) | 0.061 |
| Tumor removal from any heart valve, % (n) | 28 (29) | 28 (32) | 0.751 |
| Concomitant procedures, % (n) | 28 (51) | 28 (39) | 0.106 |
| Aortic valve replacement, % (n) | 8 (8.4) | 4 (4.5) | 0.290 |
| Mitral valve replacement, % (n) | 2 (2.1) | 2 (2.2) | 1.000 |
| Mitral valve repair, % (n) | 3 (3.2) | 7 (8.0) | 0.200 |
| Tricuspid valve repair, % (n) | 2 (2.1) | 2 (2.2) | 1.000 |
| Length of hospital stay, days | 12 ± 7.9 | 11 ± 4.5 | <0.001 |
| All-cause mortality, % (n) | 17 (18) | 8 (9.1) | 0.083 |

Note: Bold values indicate p < 0.05.
3.1 Preoperative characteristics of male and female patients with a cardiac tumor

Baseline characteristics are displayed in Table 1. The mean age was 60 ± 16 years in both groups, the body mass index was comparable between male and female patients (27 ± 6.6 vs. 26 ± 5.6 kg/m²), p > 0.05. The number of male patients (n = 95, 52%) and female patients (n = 88, 48%) were balanced.

Male and female patient’s medical history with chronic lung disease (7.4% vs. 5.7%), prior stroke (15% vs. 23%), prior transitory ischemic attack TIA (5.3% vs. 8.0%), hypertension (55% vs. 52%), diabetes mellitus with insulin (18% vs. 13%), peripheral vascular disease (8.4% vs. 15%), atrial fibrillation (23% vs. 22%), coronary artery disease (42% vs. 32%), prior percutaneous coronary intervention (11% vs. 10%), previous heart surgery (13% vs. 9.1%), current smoker (23% vs. 20%), and former smoker (14% vs. 13%) were well balanced, p > 0.05. The preoperative clinical presentation with New York Heart Association NYHA class 3 (28% vs. 35%), dyspnea or angina pectoris or palpitations (48% vs. 35%), fever (4.2% vs. 1.1%), previous syncope (2.1% vs. 8.0%), and dizziness (3.2% vs. 3.4%) was comparable between male and female patients, reaching no statistically significant difference. The preoperative left ventricular function (LV-EF) was analyzed and compared for LV-EF < 30% (male = 34% vs. female = 48%), LV-EF 30%–45% (male = 12% vs. female = 10%) and LV-EF < 30% (male = 12% vs. female = 2.3%, p = 0.019), showing a significant difference regarding the reduced LV-EF with less than 30% between groups.

3.2 Heart tumor characteristics of male and female patients with a cardiac tumor

Table 2 shows the heart tumor characteristics for male and female patients concerning the localization of the cardiac mass, functional impairment of heart valves, and dignity. Most heart tumors were localized in the left atrium. Female patients showed 76% of cases significantly more often a heart tumor in the left atrium than male patients with 52%, p < 0.001. Inline, females showed tumors in the atrial septum more often than men (30% vs. 17%, p = 0.041). The numbers of tumor localization in the right atrium were comparable between male and female patients (25% vs. 19%, p = 0.335).

In contrast, the male population suffered more often from ventricular tumors with 21% than the female with 8.0%, p = 0.013. Pericardial (1.1% vs. 0.0%, p = 1.000) and mediastinal (3.2% vs. 0.0%, p = 0.247) localization were comparable between male and female patients. The tumor involved heart valves in 18% in the male population and in 13% of females, p = 0.311, tumor prolapse through the tricuspid valve was recognized in 4.2% in males and 1.1% in females, p = 0.370, whereas a prolapse through the mitral valve was diagnosed in 4.2% and 10%, p = 0.113. In 7.4% of cases, male heart tumors infiltrated the surrounding tissue, compared to 1.1% in females, p = 0.066.

Malignancy of the heart tumor was diagnosed in 11% of male patients and 4.5% in females, p = 0.128. The overall number of total tumor resections was high in both groups but still showed a significantly different with a higher number in females (98%) versus males (91%), p = 0.041. With 70% versus 38%, a myxoma occurred significantly more often in the female sex, p < 0.001. A fibroelastoma occurred in 14% of males and 9.1% in females, p = 0.330. Other benign dignities of heart tumors were diagnosed in 36% of male and 18% of female patients, p = 0.008. Sarcomas occurred in 3.2% vs. 2.2%, p = 1.000 and other malign tumors with 7.4% versus 2.2%, p = 0.172 in male vs. female.

3.3 Characteristics of tumor in other locations, male versus female patients with a cardiac tumor

The frequency and characteristics of tumors in other locations within the analyzed patient cohort suffering from heart tumor are displayed in Table 3. Overall, 13% of male and 14% of female patients were operated for a malignant tumor, p = 0.632. Logically, female patients suffered significantly more often from breast cancer (5.7% vs. 0.0%, p = 0.024) and cervical cancer also only occurred in female sex (2.3% vs. 0.0%, p = 0.230). In 3.2% of cases men had prostate cancer in medical history (female = 0.0%, p = 0.247). Anal cancer (0.0% in both groups), colon cancer (male = 1.1% vs. 0.0% female), lymphoma (1.1% in both groups), melanoma (1.1% in male vs. 0.0% in female), sarcoma (0.0% male vs. 2.3% female), renal cancer (2.1% male vs. 1.1% female), lung cancer (42% in male patients and 1.1% in female), as well as leukemia/myeloproliferative syndrome or thyroid cancer or a histiocytoma (0.0% each in both groups) were comparable between sexes, p > 0.05. Only one case of other benign tumor with was diagnosed in the male population (1.1% vs. 0.0%, p = 1.000).

3.4 Intra- and postoperative characteristics of male and female patients with a cardiac tumor

As displayed in Table 4. Male patients underwent significantly more often a full sternotomy (66%) than female patients (49%), p = 0.017. In one case (1.1%) of male patients a clamshell thoracotomy was carried out (female = 0.0%, p = 1.000). In line, female patients were operated significantly more often via minimally invasive surgery (male = 1.1% vs. female = 0.0%, p = 0.005). Types of cannulation were as follows: bi-caval (male 24% vs. female 28%, p = 0.519), two-stage (male 34% vs. 18%, p = 0.017) and femoral cannulation (male 35% vs. 50%, p = 0.042). A simple tumor extirpation was carried out more often in female (59%) than in male (45%), without reaching a statistically significance p = 0.061.

Tumor removal from any heart valve was realized in 29% of male patients and 32% of female patients, p = 0.751. Concomitant procedures with 51% in male and 39% in female (p = 0.106) were: coronary artery bypass surgery (CABG) (24% vs. 18%, p = 0.320), aortic valve replacement (8.4% vs. 4.5%, p = 0.290), mitral valve replacement (2.1% vs. 2.2%, p = 1.000), mitral valve repair (3.2% vs. 8.0%, p = 0.200), and tricuspid valve repair (2.1% vs. 2.2%, p = 1.000). The length of overall hospital was significantly
longer for male with 12 ± 7.9 days than for female with 11 ± 4.5 days, \( p < 0.001 \). In total, all-cause mortality was 18% for male and 9.1% for female, \( p = 0.083 \), showing no significant difference (Figure 1).

### 3.5 Multinominal regression analysis for gender

To further evaluate gender-related differences in the occurrence of cardiac tumors, we performed a multinominal regression analysis (Table 5). Where gender was shown to have a significant effect on the development of myxoma in patients (OR: 3.93, CI: 95% 2.10–7.33, \( p = 0.03 \)).

### 4 DISCUSSION

Analyzing 183 patients that underwent cardiac surgery due to a cardiac tumor at our center and focusing on gender-related differences, we found no significant differences between male and female patients regarding demographic data but detected significant differences in tumor location (Table 1). While cardiac tumors were most likely found within the left atrium in male patients, a large percentage of female patients presented with tumors located at the atrial septum. However, there was no significant difference between tumor entity or histopathological tumor type and overall survival (Figure 1).

Myxomas were the most common type of cardiac tumors in our analysis, and they are more common in women, which is in accordance with other studies in this field.\(^{13-15}\)

The most common type of malignant tumor in our analysis was sarcoma. Angiosarcoma is the dominating cardiac sarcoma subtype in literature, followed by leiomyosarcoma. Intimal sarcoma, rhabdomyosarcoma, and synovial sarcoma are important differential diagnoses. Metastasis of sarcoma into cardiac locations is very rare.\(^{16}\) Noteworthy, the prognosis of survival can be correlated for noncardiac sarcomas to the histologic grading, which is not possible for cardiac sarcomas.\(^{17}\) Malignant tumors accounted for 7.7% of the whole collective, lower than other collectives.\(^{18,19}\) Overall, solid neoplastic tumors were found in 13% of patients, which undermines the speculation that patients with other neoplasms are more likely to develop cardiac tumors. Other studies report that up to 80% of malignant cardiac tumors show distant metastasis upon first clinical presentation.\(^{20}\)

The surgical approach depended on tumor size and location. In the case of isolated benign tumors, with no need for concomitant surgical procedures, we tried minimally invasive surgery with right anterior thoracotomy, which our group previously described as feasible and safe.\(^{21}\) Using this approach, a tumor located in the left or right atrium is essential. Even with the infiltration of the tricuspid or mitral valve, skilled surgeons may use this approach, enabling the surgeon to reconstruct or replace the valve.\(^{22,23}\) During minimally invasive surgery, we used femoral and jugular cannulation for CPB.

**Table 5** Multinominal regression analysis regarding gender.

| Variable       | OR   | CI 95%     | \( p \) value |
|----------------|------|------------|---------------|
| Fibroelastoma  | 4.27 | 0.39–46.5  | 0.23          |
| Myxoma         | 3.92 | 2.10–7.33  | 0.03          |
| Primary sarcoma| 3.51 | 0.28–43.7  | 0.33          |
| Other malignancy| 1.57 | 0.11–22.34 | 0.74          |

Note: Bold values indicate \( p < 0.05 \).

**Figure 1** Kaplan–Meier survival.
which explains the higher rates of femoral cannulation in our cohort. In conditions with infiltrative tumor growth, the need for CABG, and expected complex surgery, median sternotomy with bicaval cannulation was performed.

Concerning the dignity of the tumors, patients with benign cardiac tumors showed a significantly better short- and long-term outcomes than those with malignant tumors. This is an expected outcome based on the overall worse general condition of patients with malignant tumors in this cohort. In general, malignant cardiac tumors are associated with poor outcomes. The all-cause mortality in this group was 36%, according to another analysis of malignant cardiac tumors.

Surgical removal of malignant tumors is the most effective therapy for malignant cardiac tumors, in some cases in combination with adjuvant therapy (radiation/chemotherapy). Regarding neoadjuvant radiation therapy, the elevated risk for radiation-induced cardiac toxicity should be considered essential but possibly devastating. Using the current modern planning techniques, like intensity-modulated radiation therapy and volumetric-modulated arc therapy, it is possible to reach a higher dose for the tumor or the tumor bed with sparing the organs at risk like the (not involved) heart and large vessels. However, the role of adjuvant treatments after surgery remains unclear. A retrospective review of 15 patients undergoing adjuvant chemotherapy after surgery found that this kind of treatment failed to modify the natural course of the disease. Other studies came to similar conclusions. One study by Burke and colleagues demonstrated an advantage of adjuvant therapies for the treatment of cardiac tumors. This underlines the importance of a multiprofessional interdisciplinary treatment team for cardiac tumors to find the optimal, individually tailored treatment for each patient.

Given the rarity of cardiac tumors, compared to the overall case volume of a large cardiac surgery center in combination with only about half of the patients presenting with specific symptoms, a high degree of suspicion during initial investigations is needed to detect cardiac tumors. As symptoms may be absent or vary and cardiac tumors may sometimes not be distinguished from infectious endocarditis, the importance of image modalities should be mentioned and underlined to detect and distinguish the type of tumor or mass before surgery.

Overall, this large cohort of cardiac tumors demonstrates good surgical results and undermines cardiac surgery as the first-line therapy for benign and malignant cardiac tumors in an interdisciplinary treatment model.

5 CONCLUSION

Cardiac tumors are rare, and accurate diagnostics are complex due to various cardiac masses. Cardiac myxomas can more often be found in women, and minimally invasive resection is often a feasible treatment option. Surgical excision is feasible and safe for cardiac tumors with good long-term survival and relatively low complications and thus remains the gold standard for therapy. Nevertheless, gender-related modalities should be investigated to ensure the best preoperative planning and therapy.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Raw data were generated at the University Hospital of Cologne, Department of Cardiac Surgery. Derived data supporting the findings of this study are available from the corresponding author Christopher Gaisendrees on request.

ETHICS STATEMENT

The investigation was approved by the institutional review board of the University of Cologne (Trial-Number: 20-1419) and conformed to the principles outlined in the Declaration of Helsinki.

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