What are the Differences between Cardiac Angiosarcoma and Other Cardiac Sarcomas?

February 2017 - April 2022
Patients underwent surgery for cardiac sarcomas
- Angiosarcoma: 24 patients
- Other sarcomas: 16 patients

R0 resection and a Ki-67 index <50 are significantly associated with better survival.

Angiosarcoma differs from other subtypes in terms of clinical symptoms, tumor location, and surgical techniques used. R0 resection is the only independent predictor of postoperative survival.
Title Page

Surgery for Angiosarcoma and Other Cardiac Sarcomas: A Single-Institution Experience

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Ethics Statement
The study was approved by the Peking Union Medical College Hospital institutional review board (approval number: 2021-A0201-79, approval date: 2021-07-04). All study participants provided written informed consent.

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Central Picture:

Central Picture Legend:

Each subtype of cardiac sarcoma had a predilection for anatomic location and extent.

Central Message:

Angiosarcoma is the predominant histological subtype and differs from other cardiac sarcomas in terms of clinical symptoms, tumor location, surgical technique used, and prognosis.

Perspective Statement:

By reviewing our experience of surgical treatment for cardiac sarcoma, this study demonstrated that angiosarcoma differs from other subtypes in terms of clinical symptoms, tumor location, surgical techniques used, and prognosis. Early surgery is needed regardless of subtype. R0 resection is the only independent predictor of postoperative survival, and gross total resection is usually achievable.
Abstract:

Background: Cardiac sarcomas are rare malignancies with a poor prognosis. Although angiosarcoma is the most common histological subtype, its features are poorly characterized. This study aimed to compare the clinical characteristics of the various cardiac sarcomas and the surgical techniques used and to identify factors influencing the prognosis.

Methods: Forty patients underwent surgery for cardiac sarcomas were included. Sixty percent of them had angiosarcoma. Clinical characteristics, tumor location, surgical techniques used, and the prognosis were compared between patients with angiosarcoma and those with other subtypes. Kaplan-Meier curves and multivariable Cox regression were used to identify predictors of postoperative survival.

Results: Angiosarcomas were more likely than the other subtypes to present as pericardial effusion (85% vs 50%, P=0.014). Early surgery was done (median 24.0 days) regardless of histological subtype. The surgical technique varied according to histological subtype. Mean postoperative survival was 10 months. A positive margin (P=0.13), high Ki-67 index (P=0.19), younger age (P=0.86), and angiosarcoma (P=0.87) were identified to be potentially poor prognostic factors in univariate analyses. Cox regression identified R0 resection to be the only significant independent predictor of the prognosis after surgery (hazard ratio 0.423, P=0.039).

Conclusions: Angiosarcoma differs from other subtypes of cardiac sarcoma in terms of clinical symptoms, tumor location, surgical techniques used, and prognosis. Early surgery is needed regardless of subtype. R0 resection is the only independent predictor of postoperative survival, and complete resection is usually achievable. The prognosis may be poorer in patients with a
positive margin, high Ki-67 index, younger age, and angiosarcoma.

Keywords:
Cardiac neoplasm, cardiac sarcoma, angiosarcoma, surgery.

Graphical Abstract:

February 2017 - April 2022
Patients underwent surgery for cardiac sarcomas
- Angiosarcoma: 24 patients
- Other sarcomas: 16 patients

Anatomic location and extent are different. Different surgical techniques are needed.

R0 resection and a Ki-67 index <50 are significantly associated with better survival.

Angiosarcoma differs from other subtypes in terms of clinical symptoms, tumor location, and surgical techniques used. R0 resection is the only independent predictor of postoperative survival.

Introduction:
Primary cardiac sarcomas are extremely rare. Approximately one quarter of all primary cardiac tumors are malignant and three-quarters are sarcomas [1]. Cardiac sarcoma accounts for 0.005% of malignant tumors from any tissue origin and has an incidence rate of approximately 0.22 per billion person-years [2]. The prognosis of primary cardiac sarcoma is very poor, with a reported
median survival of less than 1 year [2-4]. Cardiac sarcoma can be classified according to tissue of origin into even rarer tumors, including angiosarcoma, synovial sarcoma, malignant fibrous cytoma, leiomyosarcoma, rhabdomyosarcoma, intimal sarcoma, osteosarcoma, chondrosarcoma, and others. According to the literature, angiosarcoma is the predominant subtype. However, its characteristics are different from those of the other subtypes and are not well described. The aims of this study were to summarize the characteristics of cardiac angiosarcoma that differ from those of the other cardiac sarcomas, including clinical manifestations, imaging features, tumor location, and surgical techniques used, and to identify factors that predict the prognosis.

Study Methods:

Patients and data
The study had a single-center, retrospective, observational cohort design and was approved by the Peking Union Medical College Hospital institutional review board (approval number: 2021-A0201-79, approval date: 2021-07-04). All study participants provided written informed consent. Forty patients underwent surgery for primary cardiac sarcoma (angiosarcoma, n=24; other cardiac sarcoma, n=16) at our institution between February 2017 and April 2022. Information on these patients was collected from our surgical database and reviewed. Additional data were collected during routine postoperative follow-up visits and telephone calls.

Clinical Management
We have been performing radical surgical resection for patients with primary cardiac sarcoma
since 2015. During our study period, all surgeries were performed by either of two cardiac surgeons who were skilled in complex reconstruction of the heart. The principal aim of surgery was complete removal of all visible tumor and abnormal tissue followed by reconstruction of the defect, (See Video 1). Femoral artery and/or femoral vein were cannulated when the ascending aorta and/or the inferior vena cava was involved by the tumor. All cardiac sarcomas could be macroscopically completely resected except for one case in which there was extensive left ventricular involvement. However, because of restrictions on cardiopulmonary bypass time, it is impossible to wait for negative margin pathology to determine the extent of resection. We can only confirm that the tissue at the margin is macroscopically normal. After resection, we have performed various reconstruction techniques involving the right atrium, superior and inferior vena cava, tricuspid valve annulus, right ventricular inflow and outflow tracts, main pulmonary artery, atrial septum, left atrial roof, pulmonary veins, mitral valve annulus, posterior wall of the left ventricle, aortic root, and ascending aorta. Valves were evaluated for repair or replacement when the annulus and/or sub-valvular apparatus were involved and resected. When coronary artery was involved and resected, we performed in situ coronary artery reconstruction or traditional bypass using saphenous vein afterwards. Orthotopic autologous heart transplantation was used when tumor involved the posterior wall of left atrium, pulmonary vein ostial, or near the posterior part of the mitral annulus, when in situ resection is technically very difficult. All patients in our study received various forms of adjuvant treatment after surgery.

Analysis of Data

We summarized the demographics, clinical manifestations, and surgical information for the full
study population, with particular focus on the surgical techniques used for reconstruction of
the various cardiac structures. By recording the specific location and extent of each individual
sarcoma, we plotted a distribution map for the different subtypes of cardiac sarcoma on a model
of a heart (Fig. 1). We then compared the characteristics of angiosarcoma with those of the
other subtypes. Finally, we sought predictors of the prognosis after surgery for cardiac sarcoma
in a multivariable Cox proportional hazards model.

Statistical Analysis
Continuous variables are presented as the mean and standard deviation if they were normally
distributed and as the median and interquartile range if not. Categorical variables are shown as
the number (percentage). Continuous variables were compared between groups using the
independent two-tailed Student’s t-test if normally distributed and the Mann-Whitney U test if
not. The chi-squared test was used for between-group comparisons of categorical variables
(Fisher’s exact test was used when the estimated value in any of the cells in the contingency
table was <5). The probability of survival was analyzed using the Kaplan–Meier method. The
log-rank test was used to compare the survival distributions in the two groups. Variables with
a P-value <0.1 in univariate analyses were included in the multivariate survival analysis, which
was performed using a Cox proportional hazards model. The results are presented as hazard
ratios (HRs) with 95% confidence intervals and P-values. The statistical analyses were
performed using SPSS statistical software package version 26.0 (IBM Corp., Armonk, NY,
USA). A P-value of <0.05 was considered statistically significant.

Results:
**Patient demographics and clinical characteristics**

The mean patient age was 40.4 years and the male to female ratio was 0.82. The most common symptom of cardiac sarcoma was pericardial effusion (29 patients, 72.5%). Fifteen patients (37.5%) had acute pericardial tamponade and 25 (52.5%) had a history of pericardial drainage. Other symptoms included obstructive shock (n=4, 10%), syncope (n=3, 7.5%), edema (n=2, 5%), vomiting (n=2, 5%), and hemoptysis (n=2, 5%). The median interval between onset of symptoms and diagnosis was 25.5 days (14.0, 60.0). Ten patients (25%) had metastasis (mainly pulmonary) at the time of diagnosis.

The median interval between diagnosis and surgery was 24.0 days (12.8, 60.8). Pericardial adhesion was encountered during sternotomy in 26 patients (65%). Cardiopulmonary bypass was established by femoral artery cannulation in 5 patients (12.5%), and femoral vein drainage was performed in 11 (27.5%). The distribution map on the heart model demonstrated that some subtypes had a predilection for location and extent (Fig. 1) that was consistent with their typical imaging features (Fig. 2). There were 20 R0 resections (50%), 18 R1 resections (45%), and two R2 resections (5%) according to margin pathology. After resection, various techniques were used for reconstruction of the heart (Fig. 3), including patch repair of the right atrium (n=26, 65%) or left atrial roof (n=9, 22.5%), coronary artery bypass grafting (n=9, 22.5%), repair or replacement of the tricuspid valve (n=8, 20%), repair of the right ventricular inflow tract (n=5, 12.5%), reconstruction of the tricuspid annulus (n=5, 12.5%), repair of the inferior vena cava (n=5, 12.5%), atrial septum (n=3, 7.5%), or pulmonary vein (n=3, 7.5%), and repair or replacement of the mitral valve (n=3, 7.5%). Other structures were also reconstructed, including the right ventricular outflow tract, superior vena cava, main pulmonary artery,
ascending aorta, aortic root, pulmonary valve annulus, mitral valve annulus, posterior wall of
the left ventricle, and pulmonary valve. One patient underwent orthotopic autologous heart
transplantation (Fig. 4). Closure after heart reconstruction was delayed in 13 patients (32.5%)
and one needed extracorporeal membrane oxygenation. Four patients (10%) died in hospital.
During follow-up, in situ recurrence developed in 9 patients (22.5%), two (22.2%) of whom
underwent reoperation. The mean overall survival was 10 months.

Comparison between angiosarcoma and other subtypes

The preoperative characteristics are shown according to subtype in Table 1. There was no
significant between-group difference in age, sex, or the timeliness of diagnosis and surgery.
However, pericardial effusion (85% vs 50%, \(P=0.014\)) and pericardial tamponade (50% vs
18.8%, \(P=0.046\)) were significantly more common in patients with angiosarcoma, as was the
need for pericardial drainage before surgery (70.8% vs 25%, \(P=0.004\)). The distributions of
other symptoms were not significantly different between the groups.

There were some differences in the surgical reconstruction techniques used for angiosarcoma
and those used for other types of cardiac sarcoma. Patients with cardiac angiosarcoma were
more likely to require reconstruction of the right atrium \(P<0.001\), right coronary artery
\(P=0.044\), right ventricular outflow tract \(P=0.071\), and tricuspid valve annulus \(P=0.071\). In
contrast, patients with other types of cardiac sarcoma were more likely to undergo repair of the
left atrial roof \(P=0.018\), pulmonary vein \(P=0.057\), or mitral valve \(P=0.057\). Closure tended
to be delayed less often in patients with angiosarcoma (20.8% vs 50%, \(P=0.086\)).

In terms of margin pathology, the two groups had similar R0 rates. Immunohistochemical
analysis demonstrated that angiosarcoma had a higher mean Ki-67 index (50.4 vs 35.0,
P=0.053), which was borderline for significance.

In-hospital mortality and the recurrence in situ rate were similar between the two groups. Survival of patients with angiosarcoma tended to be poorer than that of those with other subtypes (9 months vs 17 months, P=0.087).

Factors influencing survival: Cox regression analysis

The Kaplan-Meier curves for patients with angiosarcoma and those with other histological types showed significant associations of survival time with R0 resection (17 months vs 10 months, P=0.013) and a lower Ki-67 index (23 months vs 10 months, P=0.019) (Fig. 5). Although differences were not statistically significant, survival time tended to be poorer in patients aged younger than 40 years (10 months vs 17 months, P=0.086) and in those with angiosarcoma (9 months vs 17 months, P=0.087). There was no significant association between postoperative survival and metastasis at the time of diagnosis (P=0.185) or male sex (P=0.287).

Of the four variables identified to be potentially significant in the Cox proportional hazards model, namely, R0 resection, a lower Ki-67 index, younger age, and angiosarcoma, only R0 resection was an independent predictor of postoperative survival time in the Cox regression model (hazard ratio 0.423, 95% confidence interval 0.187–0.958, P=0.039; Fig. 6).

Discussion:

Cardiac sarcoma is an extremely rare and lethal neoplasm. According to the literature, angiosarcoma is the most common subtype and accounts for 41%–46% of all cardiac sarcomas [2, 3, 5]. In the present study, 60% of all cases were angiosarcoma. Therefore, it is reasonable to believe that angiosarcoma is the predominant histological subtype of cardiac sarcoma. This
study revealed differences in symptoms, tumor location, surgical techniques used, and the prognosis between angiosarcoma and other subtypes and identified factors influencing survival after surgery.

In our study, the mean age at diagnosis was 40.4 years and there was no predilection for sex. These findings are in accordance with the literature [2, 3, 6]. The clinical manifestations of cardiac sarcoma were nonspecific. However, our patients with angiosarcoma were more likely than those with other subtypes to develop bloody pericardial effusion and to present with chest tightness or pericardial tamponade. Pericardial drainage was needed in many cases. The mean intervals between onset of symptoms and diagnosis and between time of diagnosis and surgery were both less than a month, with no significant between-group differences. These results indicate that once symptoms arise, cardiac sarcomas need early surgery regardless of histological subtype. Metastasis was found preoperatively in 25% of patients, which is at the lower limit of the rates of 25%–80% reported in the literature [4, 6, 7].

Previous studies found that cardiac angiosarcoma was more likely to develop in the right side of heart [3, 7, 8]. In the present study, we documented in detail the location and extent of each cardiac sarcoma, plotted a distribution map of the different subtypes on a model of the heart (Fig. 1), and found that some subtypes had a predilection for a specific site in the heart. Angiosarcomas were most likely to involve the right atrium, right atrioventricular groove, superior and inferior vena cava, atrial septum, and left atrial roof. Malignant fibrous cytoma tended to develop in the left atrium, pulmonary veins, left atrioventricular groove, and the posterior wall of the pulmonary artery. Synovial sarcoma was more likely to involve the right ventricular outflow tract and the anterior wall of the pulmonary artery. Theoretically, the
distribution of neoplasms is related to the histological origin, microenvironment, and mechanism of tumorigenesis [9]. Since completing the present study, we have performed single-cell sequencing for the subtypes of cardiac sarcoma, and the results regarding molecular mechanisms will be reported in the future.

Because of the time limit on cardiopulmonary bypass, it is impossible for cardiac surgeons to wait for the results of margin pathology before deciding on the extent of resection. In our cases, we simply confirm that the tissue at the margin is macroscopically normal intraoperatively and re-evaluate the margin when the pathology report becomes available after surgery. Our R0 rate was 50%, with no significant difference between group, and is in line with the literature [6, 10]. Nevertheless, macroscopic complete resection is achievable for cardiac sarcoma, regardless of histological subtype.

However, surgery for cardiac sarcoma is difficult because of the need for reconstruction after resection. In this study, we documented in detail the surgical techniques used for reconstruction and found them to vary between angiosarcoma and the other subtypes, probably because of their different anatomic locations. One patient underwent orthotopic autologous heart transplantation. This surgical technique was previously described by Dr Michael J. Reardon, et al. [11, 12] Knowledge of these surgical techniques can help surgeons to be more prepared for what they encounter on the operating table.

In-hospital death happened in 4 patients (10%). Two of them (50%) died after left pneumonectomy for hilar involvement. One died from surgery related inferior vena cava obstruction. The other underwent a complex reconstruction for the aortic root, right ventricular outflow tract, tricuspid annulus, right ventricle, right coronary artery, left atrial roof, and atrial
septum (Fig. 3). This patient underwent a difficult but smooth recovery, he was already weaned from mechanical ventilation when his family chose to abandon further treatment due to financial burden.

The prognosis of cardiac sarcoma is poor, with a reported median survival time after diagnosis of 6–9 months [2, 3]. A retrospective study from the Cleveland Clinic found that the prognosis was better in patients who underwent surgery than in those who received adjuvant therapy alone [8]. All patients in the present study underwent surgery, and the overall median postoperative survival was 10 months.

Some studies have found that patients with left-sided cardiac sarcomas have a better prognosis [3, 7, 8], and the authors of one report assumed that this was because left-sided tumors were discovered earlier [3]. In our study, there was no difference in the timeliness of diagnosis between the subtypes. However, we found that survival was poorer in patients with angiosarcoma, which rarely involved the left side of the heart, than in those with other subtypes. This may explain the longer survival in patients with left-sided cardiac sarcoma. Moreover, studies from other centers have also found poorer median survival for angiosarcoma [2, 6], which is in agreement with our results.

Age is frequently associated with the prognosis in patients with malignant neoplasms. In the case of osteosarcoma, older patients usually have a worse prognosis [13]. However, in the present study, we found that patients younger than 40 years had significantly poorer postoperative survival than their older counterparts. This finding is probably related to the mechanisms of tumorigenesis and progression. The results of our single-cell sequencing in patients with cardiac sarcoma may shed some light on this phenomenon in the future.
We found a strong association between R0 resection and a better prognosis, which is consistent with the literature [4, 6]. Moreover, only R0 resection was an independent predictor of the prognosis after surgery in our Cox regression model, which underscores the importance of complete surgical resection of cardiac sarcoma.

An early pathological study found that cardiac sarcoma with a high mitotic count had a poor prognosis [3]. However, nowadays, cell proliferation in malignant neoplasms is usually evaluated by the Ki-67 index [14]. In our study, a Ki-67 index >50 was associated with poor postoperative survival.

In a study from the Houston Methodist DeBakey Hospital and the MD Anderson Cancer Center, researchers obtained a biopsy specimen for all right-sided heart sarcomas before surgery and give neoadjuvant chemotherapy. Surgery was considered for patients with an adequate response. Theoretically, effective neoadjuvant chemotherapy will increase the R0 resection rate, therefore improve postoperative survival. One of the limitations of our present study is that we have not yet established a safe method to obtain preoperative biopsies. However, we chose early surgery for all patients with suspected cardiac sarcoma for two reasons. Firstly, over a third of our patients had experienced pericardial tamponade and over half of our patients had undergone pericardial drainage when first seen, thus the risk of recurrent tamponade was evaluated as high. Secondly, almost all patients had various degrees of tumor related obstruction. Early surgery can prevent early death of recurrent pericardial tamponade or obstructive shock. Postoperative survival was also acceptable, according to our results.

However, better designed clinical trials are needed to prove which is the best option for this deadly and rare disease.
All patients in our study received various forms of postoperative adjuvant treatment, none of which had any significant efficacy. There is no evidence in the literature to suggest that postoperative adjuvant treatment has a significant impact on survival in patients with cardiac sarcoma. More research is needed to identify novel therapeutic targets.

**Conclusion:**

Cardiac sarcoma is a rare and lethal malignancy. Angiosarcoma is the predominant histological subtype and differs from other cardiac sarcomas in terms of clinical symptoms, tumor location, surgical technique used, and prognosis. Early surgery is essential once symptoms arise, regardless of histological subtype. Complete resection is usually achievable. A positive margin, high Ki-67 index, younger age, and angiosarcoma subtype may herald a poor prognosis. However, in this study, R0 resection was the only independent predictor of postoperative survival.

**Acknowledgment**

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**Funding Statement**

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Conflict of interest

None of the authors reports a conflict of interest.

Data availability statement

The data used to support the findings of this study are available from the corresponding author upon request.

References:


5. Parenzan L, Bianchetti L: [Intrapericardial anastomosis between the ascending


12. Ramlawi B, Al-Jabbari O, Blau LN, Davies MG, Bruckner BA, Blackmon SH, Ravi V,


**Figure 1:**

**Figure 2:**
Figure 5:

- **Age**
  - P = 0.086
  - CI: 95%
  - Age > 40 yrs
  - Age < 40 yrs

- **Sex**
  - P = 0.287
  - CI: 95%
  - Female
  - Male

- **Metastasis**
  - P = 0.185
  - CI: 95%
  - Without Metastasis
  - With Metastasis

- **Angiosarcoma**
  - P = 0.087
  - CI: 95%
  - Other sarcomas
  - Angiosarcoma

- **R0 Margin**
  - P = 0.013
  - CI: 95%
  - R1 or R2 Margin
  - R0 Margin

- **Ki-67 index**
  - P = 0.019
  - CI: 95%
  - Ki-67 index < 50
  - Ki-67 index > 50
# Table 1. Clinical Characteristics of Cardiac Angiosarcoma and Other Cardiac Sarcomas

<table>
<thead>
<tr>
<th></th>
<th>Total (N=40)</th>
<th>Angiosarcoma (N=24)</th>
<th>Other Sarcomas (N=16)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Male</strong></td>
<td>18 (45%)</td>
<td>12 (50%)</td>
<td>6 (37.5%)</td>
<td>0.436</td>
</tr>
<tr>
<td><strong>Age (years)</strong></td>
<td>40.4±16.5</td>
<td>40.0±17.8</td>
<td>41.8±14.9</td>
<td>0.854</td>
</tr>
<tr>
<td><strong>Symptom to diagnosis (days)</strong></td>
<td>25.5 (14.0, 60.0)</td>
<td>24.0 (13.3, 55.8)</td>
<td>27.5 (17.5, 63 3)</td>
<td>0.672</td>
</tr>
<tr>
<td><strong>Diagnosis to surgery (days)</strong></td>
<td>24.0 (12.8, 60.8)</td>
<td>24.0 (15.0, 22.3)</td>
<td>36.0 (12.0, 81.8)</td>
<td>0.633</td>
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<tr>
<td><strong>Symptoms</strong></td>
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<tr>
<td>Pericardial effusion</td>
<td>29 (72.5%)</td>
<td>21 (87.5%)</td>
<td>8 (50%)</td>
<td>0.014*</td>
</tr>
<tr>
<td>Pericardial tamponade</td>
<td>15 (37.5%)</td>
<td>12 (50%)</td>
<td>3 (18.8%)</td>
<td>0.046*</td>
</tr>
<tr>
<td>Pericardial drainage history</td>
<td>21 (52.5%)</td>
<td>17 (70.8%)</td>
<td>4 (25%)</td>
<td>0.004*</td>
</tr>
<tr>
<td>Obstructive shock</td>
<td>4 (10%)</td>
<td>1 (4.2%)</td>
<td>3 (18.8%)</td>
<td>0.283</td>
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<tr>
<td>Syncope</td>
<td>3 (7.5%)</td>
<td>3 (12.5%)</td>
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<td>0.262</td>
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<tr>
<td>Edema</td>
<td>2 (5%)</td>
<td>0</td>
<td>2 (12.5%)</td>
<td>0.154</td>
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<tr>
<td>Vomiting</td>
<td>2 (5%)</td>
<td>1 (4.2%)</td>
<td>1 (6.3%)</td>
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<tr>
<td>Hemoptysis</td>
<td>2 (5%)</td>
<td>1 (4.2%)</td>
<td>1 (6.3%)</td>
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<tr>
<td>Metastasis at diagnosis</td>
<td>10 (25%)</td>
<td>4 (16.7%)</td>
<td>6 (37.5%)</td>
<td>0.159</td>
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</table>

*Statistically significant difference, P<0.05.
**Table 2. Surgical Information on Cardiac Angiosarcoma and Other Cardiac Sarcomas**

<table>
<thead>
<tr>
<th>Reconstruction techniques</th>
<th>Total (N=40)</th>
<th>Angiosarcoma (N=24)</th>
<th>Other Sarcomas (N=16)</th>
<th>P-value</th>
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<tr>
<td>Pericardial adhesions</td>
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<td>Femoral artery cannulation</td>
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<td>Femoral vein drainage</td>
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<tr>
<td>Right atrium</td>
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<tr>
<td>CABG</td>
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<td>Left atrial roof</td>
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<td>Tricuspid repair or replacement</td>
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<td>RVIFT</td>
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<td>Atrial Septum</td>
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<td>Pulmonary vein</td>
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<td>Mitral repair or replacement</td>
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<td>Delayed closure</td>
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<td>ECOO</td>
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<td>Resection Margin</td>
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<td>R0</td>
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<td>R1</td>
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<td>R2</td>
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<td>Ki-67 index</td>
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<td>Reoperation</td>
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<td>Estimated survival</td>
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*Statistically significant difference, P<0.05. $^5$Indicates a potentially statistically significant difference, 0.05 < P < 0.10
Figure Legends:

Figure 1: Schematic illustrations showing that each subtype of cardiac sarcoma had a predilection for anatomic location and extent. Angiosarcomas (red) were most likely to involve the right atrium, right atrioventricular groove, superior and inferior vena cava, atrial septum, and left atrial roof. Malignant fibrous cytomas (blue) usually involved the left atrium, pulmonary veins, left atrioventricular groove, and posterior wall of the pulmonary artery. Synovial sarcomas (green) were more likely to involve the right ventricular outflow tract and the anterior wall of the pulmonary artery.

Figure 2: Contrast-enhanced computed tomography scans showing the typical features of the different subtypes of cardiac sarcoma. A. Angiosarcoma, which usually involved the right atrium, right atrioventricular groove, right coronary artery, and right ventricular inflow tract. B. Synovial sarcoma, usually seen as a cystic mass compressing the right ventricular outflow tract. C. Malignant fibrous cytoma, which often involved the left atrium and pulmonary veins.

Figure 3: An intraoperative photograph demonstrating the complexity of reconstructive surgery for cardiac sarcoma. This patient had angiosarcoma and required reconstruction of the aortic root, ascending aorta, right atrium, tricuspid valve annulus, right ventricular inflow and outflow tracts, and bypass grafting for right coronary artery. Ao, aorta; RA, right atrium;
RVOT, right ventricular outflow tract; RVIFT, right ventricular inflow tract

Figure 4: An intraoperative photograph obtained during orthotopic autologous heart transplantation. The explanted heart was preserved in a solution consisting of iced saline and histidine-tryptophan-ketoglutarate solution. The posterior annulus of the mitral valve and the posterior wall of the left atrium was reconstructed using bovine pericardium.

Figure 5: Kaplan-Meier curves showing that R0 resection (P=0.013) and a Ki-67 index <50 (P=0.019) were significantly associated with better survival. Patients aged younger than 40 years (P=0.086) and those with angiosarcoma (P=0.087) tended to have a poorer prognosis. There was no significant association of postoperative survival with metastasis at the time of diagnosis (P=0.185) or male sex (P=0.287).

Figure 6: Cox regression analysis identified four potentially significant prognostic variables (R0 resection, a higher Ki-67 index, younger age, and angiosarcoma). However, R0 resection was the only independent predictor of postoperative survival (hazard ratio 0.423, 95% confidence interval 0.187–0.958, P=0.039)

Video Legend:

Video 1: In this surgical record, we completely resected the tumor and all abnormal tissue until the margin was macroscopically normal. During the procedure, the involved portion of the RCA was dissected from the epicardial fat and removed. The right coronary artery is reconstructed
orthotopically using a segment of the saphenous vein. A trimmed bovine pericardial patch was used to
reconstruct the RA. The patch was sutured directly onto the epicardial fat lateral to the reconstructed
RCA. After weaning from cardiopulmonary bypass, no anastomotic bleeding was seen.
<table>
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<th>Variable</th>
<th>Hazard Ratio</th>
<th>CI</th>
<th>P-value</th>
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<td>Ki 67 index &gt; 50</td>
<td>1.830</td>
<td>(0.812–4.127)</td>
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<td>R0 margin</td>
<td>0.423</td>
<td>(0.187–0.958)</td>
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<tr>
<td>Angiosarcoma</td>
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<td>(0.666–3.035)</td>
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<td>Age &lt; 40 yrs</td>
<td>1.401</td>
<td>(0.618–3.179)</td>
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