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# LEFT HEART SARCOMAS

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**Introduction**

Primary tumors of the heart are uncommon, with roughly 75% benign and 25% malignant. Most of the malignant tumors are sarcomas and historically have had a very poor prognosis. These tumors tend to occur in young patients with a mean age of 40 years. Making a diagnosis of cardiac sarcoma can be difficult due to its rarity and the nature of the symptoms. For left heart sarcomas, almost all patients are symptomatic by the time the diagnosis has been made. Symptoms are dependent on the location and the extent of the tumor and are not related to tumor histology; similarly, histologic cell type has not been found to be related to prognosis in most studies. We therefore previously proposed a classification system for primary cardiac sarcoma based on anatomic location, dividing primary cardiac sarcoma into right heart, pulmonary artery and left heart sarcomas.

Left heart sarcoma presents a technical anatomic challenge: the left atrium, being the posterior heart chamber, allows somewhat limited access using routine surgical approaches. The role of chemotherapy or radiotherapy remains unclear and unproven, leaving complete surgical resection as the only mode of therapy with a proven survival benefit. Our review of the published literature showed frequent local recurrence and poor long-term survival in left heart sarcomas. Our hypothesis was that the left atrium had limited anatomic accessibility for large complex resections and reconstructions, and this led cardiac surgeons to do a more limited tumor removal with an increased chance of local recurrence and a detrimental effect on survival. To address this technical challenge, our group introduced the surgical technique of cardiac explantation, ex vivo tumor resection, cardiac reconstruction, and subsequent cardiac reimplantation or cardiac autotransplantation for left heart sarcoma in an attempt to improve the completeness of local resection, decrease local recurrence, and extend patient survival. This review discusses the approach of the cardiac sarcoma group at the Methodist DeBakey Heart & Vascular Center and the MD Anderson Cancer Center to the diagnosis and treatment of left heart sarcoma, as well as our current patient outcomes.

## Discussion

Cardiac tumors occur either as primary tumors or metastatic tumors, which are far more common. Primary tumors of the heart are quite rare, with about 25% being malignant and most of those being sarcomas.[1] The clinical presentation of patients with primary left heart sarcoma depends on the anatomic location and extent of the tumor, and is not influenced by histology. The most common presenting symptoms for left heart sarcoma, in our experience, are shortness of breath and dyspnea on exertion — both consistent with congestive heart failure (CHF), and arising from the obstruction of intracardiac blood flow. Over half of our patients had NYHA-FC III or IV CHF symptoms at presentation. Arrhythmia from local invasion, pericardial effusion and embolization occur, but are less common with left heart sarcomas than right heart sarcomas.

Constitutional symptoms such as fever, malaise and weight loss are also common.[2] The mean age of presentation is reported to be 40 years of age[3], and is 38.5 years in our current series, with a range of 20 to 57 years old.

Because most patients present with symptoms of CHF or other symptoms suggesting a cardiac problem, transthoracic echocardiography is the most common initial diagnostic test. Transthoracic echocardiography (TTE) is widely available, rapid and noninvasive, and has a high ability to identify left-sided intracardiac masses. Most primary left heart sarcomas are reported to occur in the left atrium, and this is supported by our experience in which 22 of 24 (92%) occurred in the left atrium and 2 of 24 (8%) occurred in the left ventricle. Myxoma is a far more common left-sided heart mass than sarcoma, but a number of findings on echocardiography should help the physician differentiate sarcoma from the more common myxoma. Nonseptal origin of the tumor, extension into a pulmonary vein, multiple masses, a broad attachment, and a solid or semi-solid consistency are all more common in sarcoma than myxoma. Unfortunately, this is still not always easy to interpret, and misdiagnosis of sarcoma as myxoma, only to be surprised at surgery, is relatively common. Most left atrial masses seen by cardiac surgeons are benign myxoma. Therefore, it is not too great a surprise that all cases of left atrial sarcoma referred to us had been previously operated on with a presumed diagnosis of left atrial myxoma, since few cardiac surgeons have been exposed to primary cardiac sarcoma cases. All of these cases had rapid reappearance of the left atrial tumor at the site of resection that was more consistent with regrowth of persistent, incompletely resected sarcoma than with recurrence. Intracavitary left ventricular tumors are very uncommon and usually presumed to be malignant by most physicians, and they also present a much greater technical challenge for resection. Not surprisingly, both of our cases of large intracavitary left ventricular tumors were referred without prior attempt at resection.

Once a left-sided mass suspected to be sarcoma is identified by TTE, we obtain a transesophageal echocardiogram because of its increased definition of left-sided masses. Chest and abdomen CT scan and cardiac MRI are obtained in all cases thought to be sarcoma, and are complimentary to echocardiography. CT scan allows assessment of myocardial infiltration, pericardial involvement, extra cardiac involvement, and mediastinal disease for the local tumor, as well as assessment for metastatic disease. Cardiac MRI allows tissue characterization, as well as the assessment of cardiac valvular function and intracardiac blood flow, in a dynamic fashion. This will be discussed further in a separate section by Dr. Dipan Shah (see page 4). We also obtain a PET/CT scan in all patients suspected of sarcoma to see the PET activity of the primary tumor, and look for metastatic disease that is unfortunately common with these tumors. Cardiac catheterization and coronary arteriography is individualized based on the risk of coronary involvement with atherosclerotic disease or tumor. Although a tissue diagnosis would be helpful in planning an approach to these tumors, it is very difficult to obtain from these left-sided lesions unless there is metastatic disease that can be easily biopsied. Most left-sided intracavitary cardiac masses need surgical removal even when benign due to the risk of blood flow obstruction or embolization, and most of our patients have been highly symptomatic leading up to the final tissue diagnosis usually made at surgery.

Primary cardiac sarcoma is a disease with an often dismal prognosis. When treated without surgical resection, the survival at 9 to 12 months is only 10%.[4] Most reports in the literature are either autopsy series or case reports.[5-7] Several series have been published dealing with cardiac tumors in general and containing a small number of sarcomas. These tend to highlight the technical difficulty, with operative mortality usually exceeding 20% and mean survival around 12 months.[8-10] Other series have been published that focused exclusively on primary cardiac sarcoma but did not group patients by anatomic location, as we propose. The Mayo Clinic reported 34 patients over 32 years with a median survival of 12 months.[11] A combined series from the Texas Heart Institute and the MD Anderson Cancer Center reported an actuarial survival of 14% at 2 years in 21 patients over a 26-year period.[12] We have previously used this approach and reported on our cardiac sarcomas as a combined entity using a multimodality approach; we found a median survival of 23.5 months in 27 patients over 16 years, with survival of 80.9% at 1 year and 61.9% at 2 years.[13]

The greatest determinant of long-term survival in primary cardiac sarcoma is complete resection. Complete resection is greatly affected by the anatomic location of the tumor and the structures that it infiltrates. The left atrium and left ventricle present unique anatomic challenges for the exposure needed for complete resection and reconstruction due to their anatomic location, as well as proximity, to vital structures that cannot be easily resected and reconstructed. This is evidenced by the high rate of local recurrence and secondary resections often reported in the literature.[14, 15] We hypothesized that the high rate of local recurrence

was due to the inability of the surgeon to adequately visualize the structures that needed to be removed and reconstructed, causing an inadequate resection that lead to rapid regrowth of tumor that was not completely removed, and that this could result in both secondary surgery for local recurrence and decreased survival. Typically, left atrial tumors are approached through the interatrial groove, and left ventricular tumors through the aortic valve, the mitral valve or the ventricle wall itself. Surgical approach through the interatrial groove is generally adequate for benign tumors, but limits visualization for malignant tumors, that are often larger and require a more generous margin of resection for success. We have considered complete cardiectomy and orthotopic cardiac transplantation for complete removal of these tumors. Although feasible, this approach requires the availability of a donor and post-operative immunosuppression, both of which present potential problems. Additionally, series using orthotopic cardiac transplantation for this purpose have only shown a median survival of 12 months.[16]

Left ventricular tumors can be approached through the aortic valve, through the mitral valve, or with a ventriculotomy through the ventricular wall. A transaortic valve approach works nicely for benign tumors[17], but is inadequate for malignant tumors due to their size and the amount of resection needed. A ventriculotomy through normal ventricular muscle is possible, but not preferred by the cardiac surgeon if other options exist. Our group adopted the approach of cardiac explantation, ex vivo tumor resection, and cardiac reconstruction and reimplantation of the heart — cardiac autotransplantation — to allow a radical tumor resection and accurate reconstruction in the challenging case of left heart sarcomas. Our hypothesis was that this approach would allow complete tumor resection, yielding deceased local recurrence and increased long-term survival.

The technique of cardiac autotransplantation was introduced for cardiac tumors by Cooley in 1985 to deal with a large left atrial pheochromocytoma.[18] Although this case was not successful, it introduced the senior author, Michael J. Reardon, to the technique and its potential use for cardiac tumors. Our group did the first successful cardiac autotransplant for cardiac sarcoma in 1998.[19] We have reported this for left atrial sarcoma[19] and left ventricular sarcoma.[20] Working closely with the sarcoma oncology group and thoracic surgery group at MD Anderson Cancer Center, we currently have done 28 cardiac autotransplants, with 23 of these for primary cardiac sarcoma. The surgical technique of cardiac autotransplantation has been previously addressed and will be reviewed here.[21]

## Cardiac Autotransplantation

Cardiac autotransplantation has several fundamental differences from standard orthotopic heart transplantation. In orthotopic heart transplantation, unless a domino procedure is being done, the explanted heart is not to be used and any damage to its structures is inconsequential. Therefore, the cardiectomy can be performed, leaving a wide margin of remaining tissue to use in tailoring the heart to be implanted, without regard to cutting critical structures such as the coronary sinus. Similarly, the donor heart can usually be harvested with extra tissue at its margins to be used to help tailor the implantation. In cardiac autotransplantation, the heart must be excised in a manner that does not damage any structures that cannot be repaired or replaced or are vital to cardiac function. Additionally, if the heart is simply excised and reimplanted, there is a loss of tissue to sewing, which makes reimplantation more challenging than orthotopic heart transplantation. It is therefore vital that the surgeon carefully plan the cardiac excision and reconstruction in a manner to avoid these pitfalls.

Since the heart is to be totally explanted, the first consideration is a cannulation technique that does not involve the heart itself in any way. The aorta can be cannulated in the distal ascending aorta with the standard technique used by the cardiac surgeon. The venous cannulation, however, must be directly into the superior vena cave (SVC) and inferior vena cava (ICV) just below its junction with the right atrial junction. This requires exposure and mobilization of both the SVC and IVC at the diaphragm. After commencing cardiopulmonary bypass (CPB), we further mobilize the SVC and IVC until completely free and surround each with an umbilical tape on a tourniquet. We widely mobilize the interatrial groove and circumferentially mobilize the ascending aorta and pulmonary artery. This extensive dissection facilitates both the accurate excision of the heart and its reimplantation. The ascending aorta is cross clamped, and antegrade cold blood potassium cardioplegia (10 cc/kg) is administered to achieve cardiac arrest. The left atrium is opened at the beginning of cardioplegia and a sump drain placed to decompress the heart. After cardioplegia and cardiac standstill, we widely open the left atrium to confirm pathology and the need for autotransplantation as a technique. We divide the SVC first just beyond the right atrial junction. This is followed by the IVC division, which actually has a transection line on the right atrium near its junction with the IVC. For each of these, it is important to note that the rim of tissue remaining on the body side will retract substantially towards the venous cannulae,

**Figure 1.** Cannulation and explants technique.

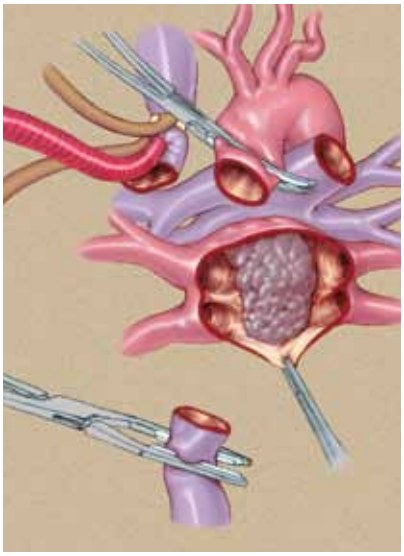


**Figure 2.** Posterior tumor as often seen. Femoral venous cannulation has been used and the IVC simply clamped.

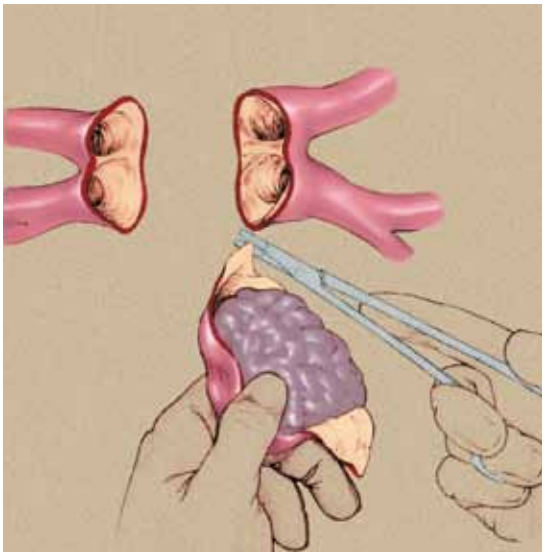


**Figure 3.** Wide excision of posterior tumor.

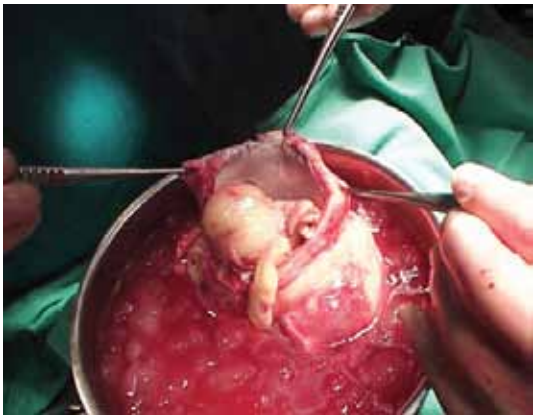


**Figure 4.** Left atrial tumor seen after heart explant.

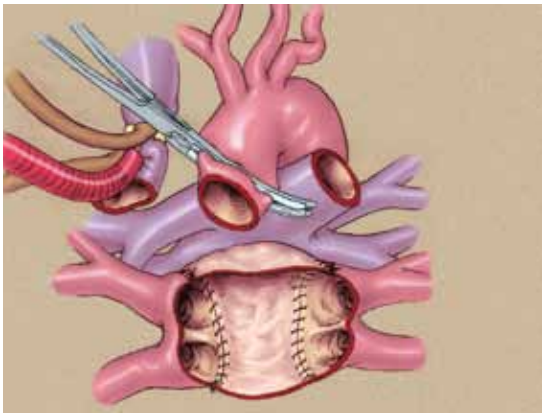


**Figure 5.** Reconstruction of posterior atrium with Bovine pericardium.

and a wide rim must be planned for during transection, or reimplantation can be exceedingly difficult, especially for the IVC. We then divide the ascending aorta about 1 cm distal to the sinotubular junction, and the pulmonary artery just proximal to its bifurcation. The left atrium transaction is then completed, dividing the atrium just anterior to the pulmonary veins, and on the left side, equal distance between the pulmonary veins and the mitral valve and left atrial appendage. This allows complete removal of the heart, which is placed into a basin on ice slush (Figure 1). The posterior left atrium is then inspected and any tumor widely excised (Figures 2 to 4). Reconstruction is with bovine pericardium, and the pulmonary veins may be individually reimplanted into openings cut in the ovine pericardium, or left as a cuff if pathology permits (Figure 5). The anterior left atrium can be removed in its entirety to include the mitral valve, leaving only a mitral annulus if necessary. Reconstruction occurs by cutting an opening in the sheet of bovine pericardium to match the mitral annulus opening. Mitral valve replacement is then done with pledgeted 2-0 Ticron sutures, with the pledgets on the left ventricular side of the annulus passing through the annulus, then through the bovine pericardium, and then through the prosthetic mitral valve. When complete, this fully seals the neo-atrial wall to the valve and annulus. The anterior and posterior bovine pericardium can then be tailored for reanastomosis (Figures 6 and 7). Reimplantation is similar to standard cardiac transplantation, with reanastomosis of the left atrium first. We then reattach the right atrium to the ICV, and then the right atrium to the SVC. At this point, the need for a wide margin of tissue remaining on the body side of the original transaction is very apparent. If either of these requires excess tension, an interposition graft of Gore-

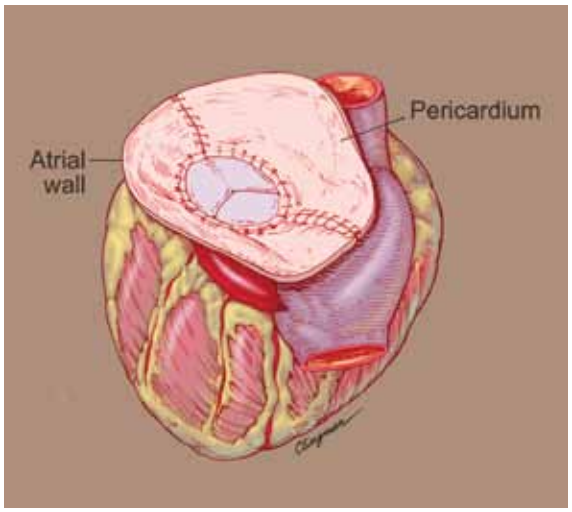



**Figure 6.** Mitral valve replacement and partial anterior left atrial wall replacement with Bovine pericardium.

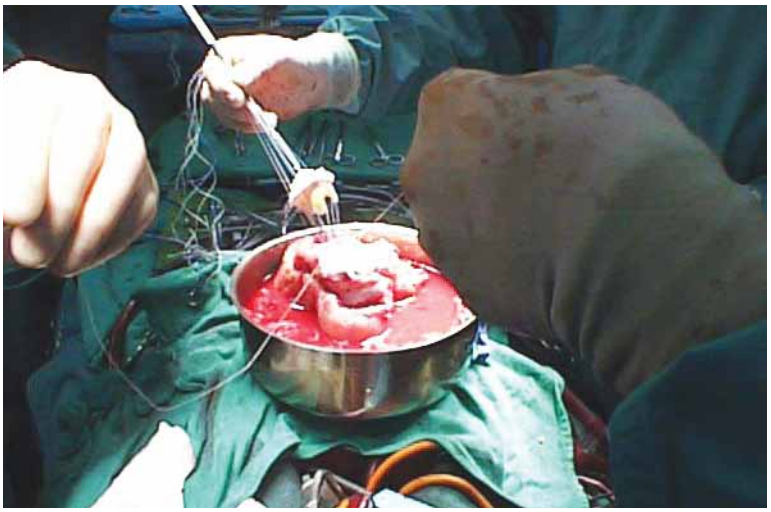


**Figure 7.** Ex vivo mitral valve replacement.

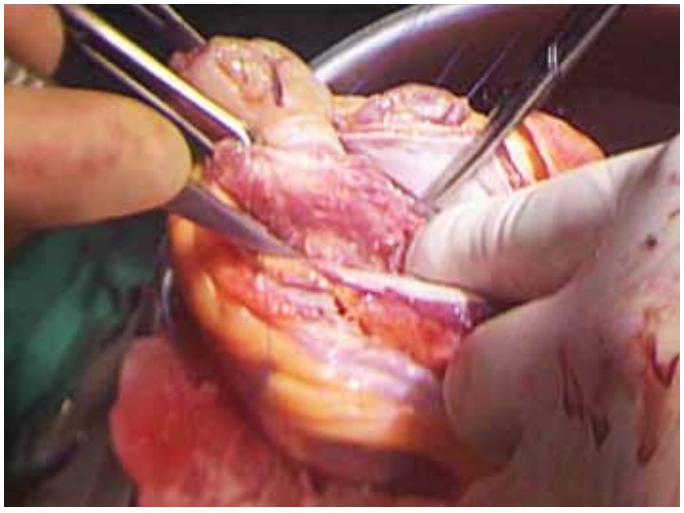


**Figure 8.** Large left ventricular tumor being removed trans mitral valve in explanted heart.

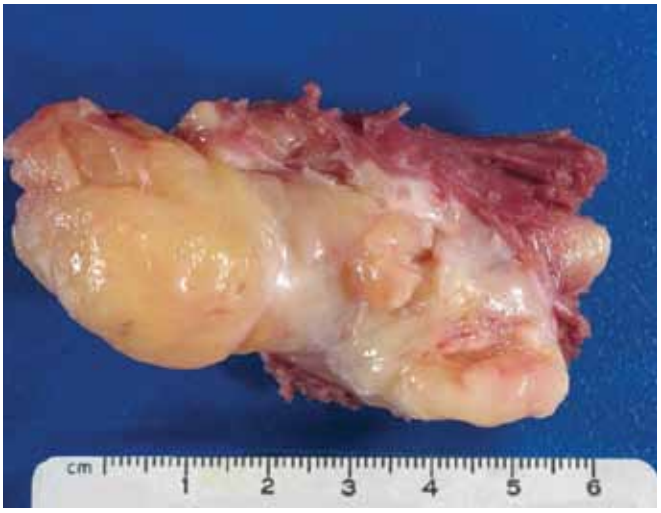



**Figure 9.** Photo of the removed left ventricular tumor showing its large size and extent that would make complete removal through convention techniques difficult or impossible.

Tex, Dacron or pericardial self-constructed tube graft can be used to bridge the defect successfully The pulmonary artery and then the aorta are reanastomosed in a standard fashion, warm blood potassium cardioplegia given antegrade, and the cross clamp is removed.

The procedure for left ventricular tumors is similar, and has required, in both of our cases, mitral valve excision due to tumor involvement and partial excision of the intracavitary interventricular septum (Figures 8 and 9). The interventricular septum was reconstructed with bovine pericardium, and valve replacement is done with a tissue valve. Although these patients are younger than the age in which we typically use a tissue valve, we would prefer to avoid Coumadin. The aggressiveness of this disease makes the risk of structural valve deterioration small.

We last presented our work in 2007 and published this experience with left heart sarcomas in 2008.[24] This work is currently done under our IRB-approved protocol, A Phase II Trial of Cardiac Tumor Resection Including Autotransplantation and Radical Resection of Cardiac Tumors. At that time, we had 20 patients who had undergone 21 cardiac autotransplants (1 also had a redo autotransplant) by the senior author. Three of these patients had complex benign disease, leaving 17 patients and 18 cardiac autotransplants for left heart sarcoma for analysis. There were 7 males and 10 females with an average age of 39.5 years and a range of 20 to 57 years. Pathology showed 7 malignant fibrous histiocytomas (MFH), 5 undifferentiated sarcomas, 3 leiomyosarcomas, 1 osteosarcoma and 1 myxoid

**Table 1.** Histologic classification of left heart sarcomas.

| | |
|---|---|
| Malignant fibrous histiocytoma | 7 |
| Undiffentiated sarcoma | 5 |
| Leiomyosarcoma | 3 |
| Osteosarcoma | 1 |
| Myxoid sarcoma | 1 |

sarcoma (Table 1). Most of the MFH cases were early in the series, and the diagnosis of undifferentiated sarcoma occurred later, suggesting a change in pathology nomenclature rather than a fundamental change in tumor types being seen. There were 11 cases that involved cardiac autotransplant, alone, and 6 that also required pneumonectomy due to extensive lung, as well as cardiac, involvement.

In the 11 cases of cardiac autotransplant alone, there were no hospital deaths and all patients were discharged to home doing well. In the 6 cases that required pneumonectomy, there were 3 hospital deaths. Each of these deaths was precipitated by severe post-operative coagulopathy requiring multiple transfusions. This volume overload led to severe unilateral pulmonary edema in the remaining lung, and subsequent right heart failure leading to death was the common pathway of loss in each of these. The survival curve for all patients with left heart sarcoma is shown in Figure 10, and the survival curve for patients with left heart sarcoma with and without pneumonectomy is shown in Figure 11. Subsequent to this publication, we have operated on 4 more isolated cardiac autotransplants for left heart sarcoma with no hospital mortality, and 1 more combined cardiac autotransplant with pneumonectomy that we lost to the same mechanism of right heart failure. We now consider the need for pneumonectomy, in addition to cardiac autotransplant, a contraindication to surgery in almost all cases. At the time of publication, 8 of 17 patients with left heart sarcomas were alive 3 to 50 months after surgery, with a mean of 22 months. All isolated cardiac autotransplants for left heart sarcomas that we operated on after this study are alive without disease. All patients are offered an adjuvant chemotherapy regimen of doxorubicin hydrochloride (75 mg/$m^2$) and ifosfamide (106 mg/$m^2$). All deaths have been related to distant metastatic disease. There have been only 2 cases of local recurrence. One was successfully treated with redo cardiac autotransplantation but died 12 months later from metastatic disease, and 1 is alive and continuing systemic chemotherapy.

**Figure 10.** Survival curve for all left heart sarcomas.

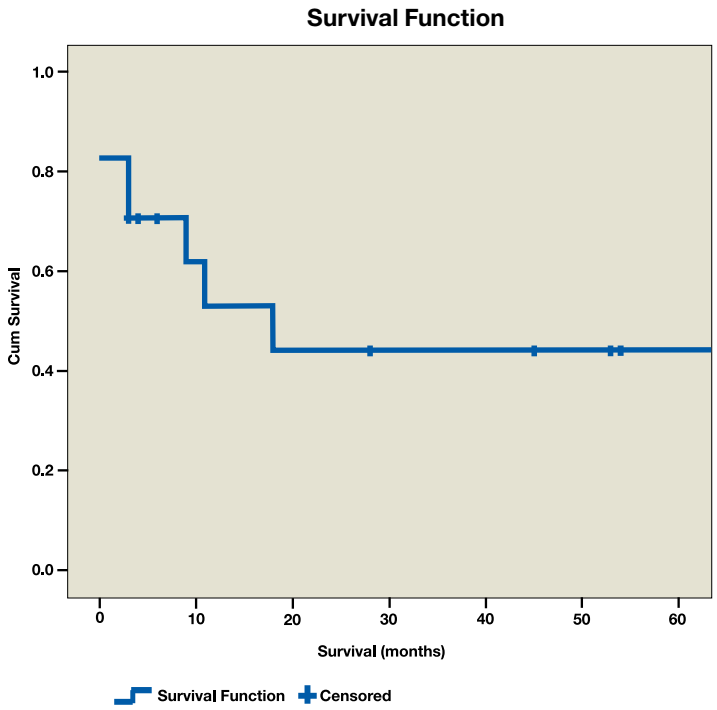
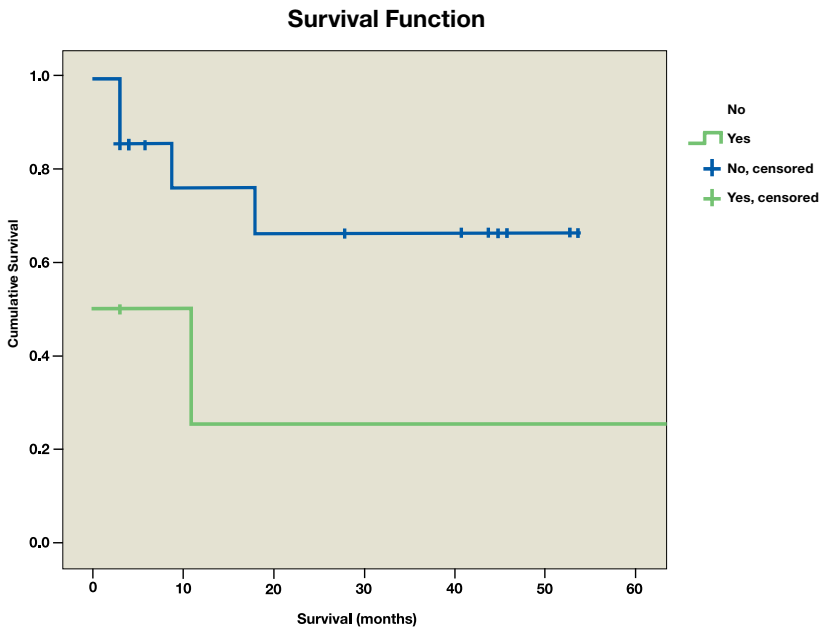


**Figure 11.** Survival curve of left heart sarcomas with and without pneumonectomy.




## Conclusion

Treatment of cardiac sarcoma is based upon complete surgical resection, and survival rates have been shown to be directly related to complete versus incomplete resection. Cardiac autotransplantation is a viable technique to achieve complete resection, despite the anatomic difficulties posed by a left heart anatomic site. This can be done with a reasonable mortality in an experienced center for cardiac autotransplantation alone. The addition of pneumonectomy to cardiac autotransplantation adds an unacceptable risk and should be avoided. If extensive pulmonary involvement would necessitate pneumonectomy in addition to cardiac resection, systemic biologic therapy alone should be considered. Survival with this approach has improved over historic controls, and further improvements will likely come from a multimodality approach and better biologic treatment options.

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