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Resection of advanced thoracic malignancies requiring cardiopulmonary bypass☆

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Abstract

Objectives: Patients with malignancies involving cardiac structures have limited therapeutic options and significant risk of mortality. The decision to offer radical palliative or curative resection must be made only after consideration of the substantial surgical risks. The purpose of this retrospective study was to determine the feasibility and benefits of resection with cardiopulmonary bypass (CPB) of metastatic or non-cardiac primary malignancies extending directly into or metastasizing to the heart in select patients. Our results were examined to assess the risks and benefits of such radical therapy. **Methods**: We retrospectively reviewed patient charts and identified all patients with malignancies involving the cardiac chamber or great vessels (excluding renal carcinomas with caval extension) or with substantial cardiac compression who had undergone resection with CPB at The University of Texas M.D. Anderson Cancer Center between January 1995 and July 2000. We evaluated demographic data, symptomatology, tumor characteristics, and outcomes. **Results**: Nineteen patients (six males and 13 females; median age of patients, 47 years; age range, 17–67 years) were included in the study. Eleven patients underwent surgery with curative intent, and eight underwent surgery with palliative intent. Seventeen patients had tumors that required CPB because their tumors directly involved the heart and/or great vessels (nine sarcomas, seven epithelial carcinomas, and one unclassified), and two patients (both with sarcomas) required CPB to relieve tumor tamponade. The technique included CPB ($n = 5$), CPB with diastolic arrest ($n = 12$), and CPB with hypothermic circulatory arrest ($n = 2$). Five patients underwent concomitant pneumonectomy, and three underwent lobectomy. Two patients (11%) died in the hospital after resection with palliative intent. Of the 11 patients who underwent resection with curative intent, ten (91%) had complete resections. The median time in the intensive care unit was 5.3 days (range, 0–37 days) and the median length of hospital stay was 17.2 days (range, 0–107 days). Major complications occurred in 11 patients (58%); the most common major complications were pneumonia ($n = 7$ patients), mediastinal hematoma ($n = 4$ patients), and acute respiratory distress syndrome ($n = 2$ patients). The median follow-up duration was 27 months. The overall 1- and 2-year survival rates were 65 and 45%, respectively. **Conclusions**: Extensive thoracic tumors involving cardiac structures can be resected with acceptable risk. When resection was performed with curative intent, excellent 1- and 2-year cumulative survival rates were achieved. Although resection with palliative intent was associated with greater mortality rates, some patients survived for 1 and 2 years. The use of CPB in selected patients with thoracic malignancies should be considered, especially when complete resection can be achieved.

Keywords: Metastasis; Cardiac tumors; Cardiopulmonary bypass

1. Introduction

Primary cardiac tumors, although rare, can be resected surgically, often with excellent results. However, primary cardiac tumors make up only a small percentage of tumors involving cardiac structures. Intrathoracic tumors that extend into cardiac structures or extrathoracic tumors metastatic to the heart are 20–40 times more common than primary cardiac tumors [1]. Metastases involve the pericardium, epicardium, myocardium, and endocardium, in approximately that order of frequency [2].

Cardiac involvement by direct extension or metastasis is uniformly fatal. Treatment options for these patients are severely limited, often consisting of palliative pericardial drainage [3]. Except in cases of minor involvement of the left atrium, intrathoracic tumors extending into cardiac structures are usually deemed unresectable, and surgical resection of metastatic disease to the heart is not standard therapy.

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However, other tumors without cardiac involvement that previously were not considered surgically approachable are now being resected in select cases, with some long-term survival as well as effective palliation. Examples include Pancoast tumors involving the vertebral body or subclavian vessels and isolated adrenal or brain metastases from non-small cell lung cancer [4–6]. The ability to resect these advanced tumors while maintaining acceptable morbidity and mortality rates is largely the result of careful patient selection, better surgical technique, and improved perioperative and postoperative management. In light of these improved results in non-cardiac cases by using aggressive surgical techniques for patients whose disease was formerly thought to be unresectable, we have offered aggressive surgical resection to a select group of patients with intrathoracic tumors extending into cardiac structures. The purpose of this retrospective study was to determine the feasibility and benefits of resection with cardiopulmonary bypass (CPB) of metastatic or non-cardiac primary malignancies extending directly into or metastasizing to the heart in select patients.

2. Methods

We retrospectively reviewed patient records and identified all patients who had undergone CPB at The University of Texas M.D. Anderson Cancer Center from January 1995 to July 2000. Only patients with malignancies involving cardiac chambers or great vessels or with significant cardiac compression necessitating CPB for tumor extirpation were included. Patients were excluded from the study if they had undergone a non-malignant pulmonary embolectomy or resection of inferior vena cava tumor thrombi secondary to renal cell carcinoma. Follow-up data were available on all patients who were included in the study.

Data on a number of variables, including demographics, symptoms and signs at presentation, and any preoperative therapy, were collected. Tumor characteristics, including location, histologic features, and the presence of metastases, as well as operative details were collected. All complications were noted, along with overall survival duration.

The decision to proceed with resection had been determined after evaluating the results of computed tomography (CT), magnetic resonance imaging (MRI), and transthoracic or transesophageal echocardiography. Patients had been presented at multidisciplinary conferences before undergoing resection. The decision to proceed in each case had been based on a number of tumor-related and patient-related factors, which included tumor biology (indolent vs. aggressive), availability of active chemotherapeutic agents to achieve cytoreduction and hence improve resectability, disease-free interval in cases involving metastatic lesions, the presence and severity of symptoms, and the physiologic status of the patient.

The requirement for CPB had been based on any one of three general indications: direct invasion of cardiac structures, great-vessel involvement necessitating CPB for resection or significant cardiac compression requiring CPB to allow manipulation of the tumor during resection. In our study, surgery was considered curative in cases in which an R0 resection was achieved and the patient was free of extracardiac metastases. The operation was considered palliative in cases in which the cardiac resection was classified as R1 or R2 or in which synchronous extracardiac metastases were present at the time of resection.

Survival curves were calculated using the method of Kaplan and Meier [7]. The statistical test to compare survival was the log rank test.

3. Results

3.1. Preoperative evaluation

Nineteen patients who had undergone resection with CPB were included in the study. The mean age of the patients was 45 years (range, 17–67 years). Females outnumbered males 2:1 (13:6). The primary symptoms at presentation were dyspnea (12 of 19 patients; 63%) and pain (four of 19 patients; 21%); one patient (5%) presented with recurrent laryngeal nerve palsy, one (5%) presented with phrenic nerve palsy, and one (5%) presented with a cerebrovascular accident. Most patients (12 of 19; 63%) had a chest X-ray abnormality. CT was the primary mode of evaluation in all cases. Transthoracic and transesophageal echocardiography was performed on 17 of 19 patients (89%) and 15 of 19 patients (74%), respectively. A full radiographic metastatic work-up of primary intrathoracic tumors was also performed. Data on preoperative therapy and the histologic features and location of tumors are summarized in Table 1.

3.2. Intraoperative

The operative approaches were sternotomy (13 of 19 cases; 68%), posterolateral thoracotomy (three of 19 cases; 16%), and clamshell incision (three of 19 cases; 16%). Arterial cannulation was aortic in 16 of 19 cases (84%) and femoral in the remaining three cases. Various venous cannulation sites, dictated by the location of the tumor, were utilized. These included bi-caval (eight of 19 cases; 42%), atrial (five of 19 cases; 26%), uni-caval (three of 19 cases; 16%), femoral (two of 19 cases; 11%), and intra-abdominal caval (one of 19 cases; 5%). CPB with cardiac arrest was performed in 12 cases (63%), simple CPB in five cases (26%), and CPB with hypothermic circulatory arrest in two cases (11%). Every effort was made to achieve primary repair when feasible; however, reconstruction with autologous pericardium, bovine pericardium, Dacron (Hemeshield®, Meadox Boston Scientific Corp., New Jersey) grafts, or Gore-Tex (Gore-Tex® Acuseal Cardiovascular Patch and Gore-Tex® Vascular Graft, W.L. Gore & Associates, Arizona) patch/graft was required

Table 1
Clinical features, preoperative therapy, and survival of 19 patients with advanced cardiac malignancies who underwent resection with CPB[a]

Patient no.	Histologic diagnosis	Site of primary	Cardiac structure involved	Other sites of disease	Pre-op chemo	Survival (months)	Present status
1	Undifferentiated carcinoma	Med.	PA, LA	No	Dox, I	1.5	Alive
2	Angiosarcoma	Cavo-atrial junction	RA, IVC	No	Dox, I	16.7	Alive
3	Melanoma	Unknown	LA	No		62.7	Alive
4	Oncocytic carcinoma	L adrenal	IVC	No		19.0	Alive
5	Myxoid sarcoma	Med.	PA	Yes	Dox, I	6.4	Alive
6	Leiomyosarcoma	PA	PA, LPA, RPA	No		16.5	Alive
7	Leiomyosarcoma	Lung	PA	Yes		4.4	Alive
8	Intravascular leiomyomatosis	Uterus	IVC, RA, RV	No		2.4	Alive
9	Squamous cell lung cancer	Lung	DTA	No		25.0	Alive
10	Leiomyosarcoma	IVC	IVC, RA	No	P	19.6	Alive
11	Ewings sarcoma	Lung	LA	No	Dox, I	18.8	Dead
12	Unclassified malignant tumor	Uterus	IVC, RA	Yes	Dox, I	10.3	Dead
13	Melanoma	Unknown	LA	No	P, E	2.3	Dead
14	Leiomyosarcoma	Uterus	PA	Yes	Dox, I	0.00	Dead
15	Thymic carcinoma	Thymus	SVC, RA	No	P, T, E	2.9	Dead
16	Synovial cell sarcoma	Extremity	LA	Yes	Dox, I	19.4	Dead
17	Leiomyosarcoma	Uterus	Comp.	Yes	C, T, E	0.03	Dead
18	Hepatocellular carcinoma	Liver	RA	Yes		62.4	Dead
19	Sarcomatoid carcinoma	Extremity	RV	Yes		1.4	Dead

[a] Med., mediastinum; PA, pulmonary artery; LA, left atrium; Dox, doxorubicin; I, ifosfamide; RA, right atrium; IVC, inferior vena cava; LPA, left pulmonary artery; RPA, right pulmonary artery; RV, right ventricle; DTA, descending thoracic aorta; P, cisplatin; E, etoposide; SVC, superior vena cava; T, paclitaxel; Comp., cardiac compression; C, carboplatin.

in eight patients (42%). The time on CPB averaged 105 ± 9 min (range, 58–175 min). In cases in which cardiac arrest was employed, the duration of arrest was 54 ± 10 min (range, 14–137 min). The total circulatory arrest time in the two patients who underwent CPB with circulatory arrest was 27 and 28 min. Additional procedures, performed in 58% of patients, were pneumonectomy (five cases; 26%), pulmonary lobectomy (three cases; 16%), resection of a mediastinal mass (two cases; 11%), and radical nephrectomy (one case; 5%).

3.3. Resectability

In 11 patients, the only site of disease was intrathoracic. A complete (R0) resection was performed in ten of these patients (91%), while the remaining patient had residual microscopic disease only (R1 resection). Eight patients had synchronous extracardiac disease. In five of these patients (63%), the intracardiac tumors were completely resected; in the other three, gross residual cardiac disease remained after attempted resection of the intracardiac tumor (R2 resection). Therefore, the overall resectability of tumors from cardiac structures only was R0 in 15 cases (79%), R1 in one case (5%), and R2 in three cases (16%).

3.4. Postoperative course

The average hospital stay was 18.3 ± 4.1 days, with 6.7 ± 2.4 days spent in the intensive care unit and 4.8 ± 2.4 days spent with the patients on a ventilator. Complications occurred in 11 patients (58%) and are detailed in Table 2. Two patients (11%), both of whom underwent palliative resection, died during the in-hospital or 30 day postoperative period.

3.5. Survival

The median follow-up duration was 27 months. Fig. 1 demonstrates the overall survival. The median survival was 62.4 ± 25.4 months. Fig. 2 demonstrates the survival based on the intent of resection. The median survival duration has not yet been reached for the patients who underwent resection for cure and was 10.3 ± 8.6 months for the patients who underwent resection for palliation.

Table 2
Postoperative morbidity in 19 patients

Complication	No. of patients (%)
Pneumonia	7 (37)
Supraventricular tachycardia	5 (26)
Mediastinal hematoma	4 (21)
Urinary tract infection	3 (16)
Tracheostomy	3 (16)
Coagulopathy	2 (11)
Acute respiratory distress syndrome	2 (11)
Wound infection	2 (11)
Myocardial infarction	1 (5)
Cerebrovascular accident	1 (5)
Ileus	1 (5)
Phrenic nerve injury	1 (5)

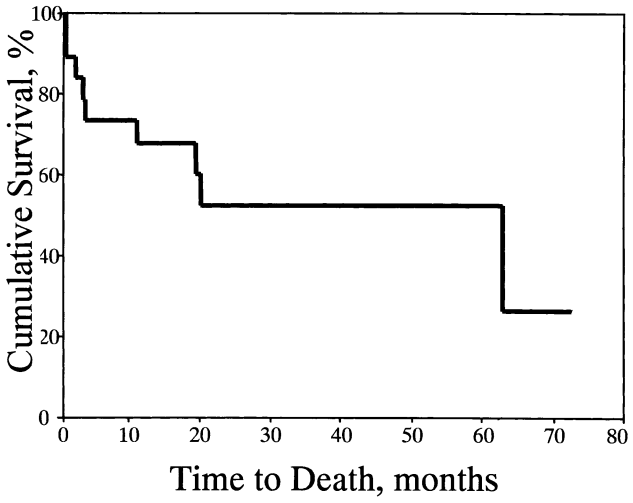

Fig. 1. Overall survival after resection for all 19 patients.

4. Discussion

Use of CPB for the resection of tumors that invade or originate in cardiac structures is not new. In 1954, Crafoord successfully resected an atrial myxoma from the left atrium. As advances in diagnostic methods were developed, increasing numbers of atrial myxomas were identified and removed [1]. They remain the only cardiac tumor for which resection is curative. However, atrial myxomas represent a small percentage of malignancies involving cardiac structures. The incidence of metastases to the heart is 20–40 times higher than that of primary tumors of the heart. In

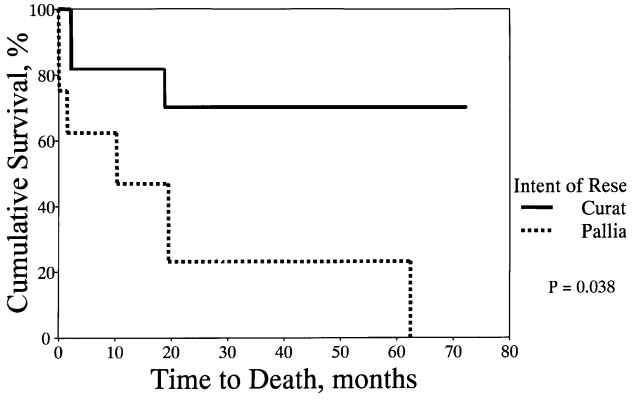

Fig. 2. Survival based on the intent of resection. Patients who underwent a curative resection had no other sites of disease other than their cardiac involvement. They were rendered free of disease after complete resection of their cardiac disease. Patients who underwent a palliative cardiac resection had extracardiac disease at the time of their cardiac operation. Even after complete resection of their cardiac disease, these patients had persistent disease elsewhere.

addition, primary intrathoracic tumors or metastasis can infrequently invade cardiac structures by direct extension.

The most common sites of metastasis to the heart are the pericardium and epicardium. These metastases commonly present as pericardial effusions and are not amenable to resection. Infrequently, however, the patient may develop an isolated cardiac or intrathoracic metastasis that involves the heart by direct extension. Primary mediastinal and intrathoracic tumors may also extend into cardiac structures. Treatment options for these patients are limited. The rare occurrence of these metastases results in only sporadic anecdotal reports of successful treatment [8–11].

Even in cases in which the tumors are localized to the heart, treatment options other than surgery (i.e. chemotherapy, radiation therapy, and transplantation) have had only sporadic success [12–15]. Some reports of resection of non-small cell lung cancer involving great vessels or the left atrium, tumors formerly felt to be unresectable, demonstrate that survival following resection is higher than that following non-surgical treatment [6]. Likewise, aggressive repeated resections of pulmonary metastases have also led to long-term survival in some cases. Thus, an aggressive surgical approach employing CPB for resection of these tumors can be justified in a highly select group of patients.

4.1. Patient selection

The patients reviewed in this study were a highly select group. The decision to proceed with surgery was made on an individual basis after multidisciplinary assessment. Factors addressed included biologic features of the tumor (i.e. the tumor's aggressiveness, responsiveness to chemotherapy, and resectability), symptomatology, and performance status of the patients. The mean age of the patients was 45 years. Preoperative assessment was thorough and included transthoracic and transesophageal echocardiography in most patients. Patients considered for palliative surgery had either considerable symptoms or impending cardiac compromise or were believed to have extracardiac disease that could be resected at a later date.

4.2. Technical

A wide variety of techniques must be employed to successfully resect these tumors. Our 19 patients required various combinations of incisions, cannulation sites, and methods of CPB (alone or in combination with cardiac or circulatory arrest). Because each tumor has its own unique attributes requiring surgical adaptation, no standard approach to these tumors exists. In some operations, a second surgical team was involved to assist with resection of the intra-abdominal portion of the tumor. A coordinated effort between the surgeon, anesthesiologist, and perfusionist is required. Each member of this team should be prepared to modify his planned approach on the basis of intraoperative findings.

4.3. Feasibility

An R0 resection was achieved in 79% of these tumors. The morbidity rate associated with these operations was acceptable, considering the proportion of patients who received simultaneous pulmonary resections. Likewise, the mortality rate was also acceptable. Although this was a highly select group of patients, it is apparent that with careful preoperative assessment complete resection can be obtained with acceptable risk.

4.4. Outcome

Generalization of the results seen in this group of patients is difficult because of the heterogeneity of the tumors and the highly select patient population examined. However, it is evident that with careful multidisciplinary assessment of patients, the use of CPB to obtain a complete resection can help to achieve long-term survival. The trend toward increased mortality combined with the significantly diminished long-term survival among patients who underwent palliative resection makes the indiscriminate use of this technique for palliation unjustified. In these patients, careful assessment of the severity of the patient's symptoms and the extent of their non-cardiac disease is mandatory before any attempted resection.

In conclusion, our review of patients requiring CPB to resect a predominantly metastatic group of cardiac tumors showed that the procedure was performed without significant increases in morbidity or mortality rates. Most patients were able to undergo complete clearance of their cardiac disease. Although only a small group of patients were studied and follow-up was moderate, with careful patient selection, long-term survival was achieved in a large proportion of the group rendered free of all disease at the completion of surgery. Patients with simultaneous extracardiac disease obtained palliation but, as expected, with greatly diminished survival.

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Appendix A. Conference discussion

Professor A. Yim (*Shatin*, *Hong Kong*): Obviously among these patients with such locally advanced tumor, patient selection is very important. What sort of modalities and criteria do you use to select patients for surgery? I presume everybody will have mediastinoscopy, but do you go for PET scan or other imaging modalities to select out those patients who will not receive this aggressive therapy?

Dr Vaporciyan: PET scanning, unfortunately, was just recently introduced at our institution. We were doing PET scans at outside institutions. Most of the patients received CT scanning, of specific regions, bone scanning, CT of the brain, MRI, and an aggressive work-up for any evidence of metastatic lesions. In addition, to determine resectability, all the cardiac patients received a transthoracic echocardiogram, and a majority, about 85%, received a transesophageal echocardiogram, along usually with an MRI of the mediastinum.

Dr Yim: I am focusing more on the nodal metastases.

Dr Vaporciyan: The nodal metastases were aggressively worked up with just conventional radiographic imaging and any additional tests that were indicated. PET scanning at our institution has only been available for about the last two years.

Dr Yim: How about mediastinoscopy?

Dr Vaporciyan: Mediastinoscopy was utilized for nonsmall cell lung cancers, of course, but for the sarcomatous metastases that were isolated to the lung without evidence of mediastinal nodes, we still resected those patients if we could get clearance of their disease. Most of our patients with metastatic sarcomas usually do not involve the mediastinal nodes.

Dr P. Macchiarini (*Hanover*, *Germany*): I have one very short technical question and one oncological question.

First, a technical question. I saw that you never used fibrillation, and cardiopulmonary bypass you did either such or as a diastolic arrest or with circulatory arrest, and you might I think take all the steps to resect the tumor and then do it under fibrillation and avoid therefore the very high incidence of respiratory complications you had, probably related to such strategy.

Dr Vaporciyan: The tumors here that were presented were only the ones that failed any other modality and required cardiopulmonary bypass for resection. There were numerous tumors that involved either the main left or right pulmonary artery trunk that could be resected with fibrillation and a clamp or atrial structures that we could fibrillate and resect with a clamp. The ones presented here, however, surpassed all those possible techniques. As you can see, only three or so of the patients could be done on simple bypass. The majority had, on average, a 50-minute arrest time and so their tumors were not technically resectable with simple fibrillation.

Dr Macchiarini: The second and last question is, from an oncological point of view, you showed an 11% survival in the palliative group, which makes, however, a 25% mortality, which makes no oncological sense. Do you have any explanation?

Dr Vaporciyan: Well, this was a palliative group as well as an extremely selected group. They were felt to be in immediate danger of death due to the location of their tumor or were experiencing significant changes in quality of life. They were also patients who probably already had long-term survival with their disease. For example, one was a leiomyomatosis with an extensive IVC thrombus up into the right ventricle. Despite the ability to perform only an R1 resection she was afforded considerable relief of her dyspnea. Some of the other patients also underwent additional resective procedures of their extracardiac metastases later. One was a young 28-year-old girl with an angiosarcoma of the heart who then underwent lobectomy to clear the rest of her disease, and is still free of disease over a year and a half later.