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Primary pulmonary sarcomas and carcinosarcomas – postoperative results and comparative survival analysis☆

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Abstract

Objective: To evaluate the early and long-term results after surgery for primary pulmonary sarcomas (PPS) and to compare them with those of patients with pulmonary carcinosarcomas (PCaSa). **Methods**: During a 20-year period, 48 patients with PPS and 15 patients with PCaSa underwent surgery. There were 40 males and 23 females with a mean age of 52.1 years (range 13–78). The histologic diagnoses in PPS group were fibrosarcoma (15), fibroleiomyosarcoma (10), leiomyosarcoma (6), rhabdomyosarcoma (6), hemangiopericytoma (3), epitheloid hemangioendothelioma (3), malignant schwannoma (1), liposarcoma (1) and undifferentiated sarcoma (3). The following curative resections were carried out: lobectomy (36), including two sleeve lobectomies (in PPS group), pneumonectomy (15) and polysegmental resections (4). In four PPS cases, these procedures were extended to the thoracic wall, diaphragm or pericardium. An atypical resection was applied in one PPS patient (the tumor was falsely classified as benign on frozen section examination). Exploratory thoracotomy was performed in five of PPS patients (11%) and in two of those with PCaSa (13%). The majority of PPS patients were with low stages I and II (76%). The PCaSa patients were predominantly with stage IIIA (39%). **Results**: No postoperative death was registered. Major complications included two localized empyemas (4.2%) in PPS and one reoperation for bronchial stump fistula (6.7%) in PCaSa groups. Local recurrences were operated on in one patient per group (2.1 and 6.7%, respectively). Follow-up was available on 57 patients and ranged from 4 to 148 months. The overall cumulative 5-year survival was 48.81% for PPS and 49.38% for PCaSa patients ($P = 0.9035$). It was better in low vs. higher stage cases, statistically significant in PPS group ($P = 0.0005$) and without significant difference in PCaSa cohort ($P = 0.11$). **Conclusions**: Complete resection of PPS and PCaSa favors an acceptable survival, especially in low stages. There is no significant difference in the survival rates between PPS and PCaSa patients, despite the greater number of cases with higher stages in PCaSa group.

Keywords: Primary pulmonary sarcoma; Pulmonary carcinosarcoma; Surgery; Survival

1. Introduction

Primary pulmonary sarcomas (PPS) are rare mesenchymal tumors. Since the lung is one of the favored metastatic sites for soft tissue sarcomas, care must be taken to exclude the possibility of an alternate primary source by means of thorough clinical history and imaging evaluation. Few publications reviewed more than 20 operated on patients with PPS [1–4]. Primary pulmonary carcinosarcomas (PCaSa), once considered to be in PPS group [9,10], are rare tumors as well [5–8]. Recently, some authors suggested that their prognosis is determined by the sarcoma component of the tumor [8].

The objective of our paper is to evaluate the early and long-term results after surgery for PPS and to compare them with those of patients with PCaSa.

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2. Patients and methods

2.1. Patients

During a 20-year period (January 1981–December 2000), 48 patients with PPS and 15 patients with PCaSa were consecutively operated on in our departments (59 patients at St Sophia University Hospital of Pulmonary Diseases and four at the University Hospital of the Thracian University). Clinical data, surgical reports, paraffin-embedded blocks and microscopic slides were available for all patients. There were 28 males (58%) and 20 females (42%) in the PPS group and 12 males (80%) and three females (20%) in the PCaSa group. The mean age was 53.3 years (range 13–78) for PPS and 51.4 years (range 38–67) for PCaSa patients.

2.2. Preoperative assessment

Complete clinical history, physical examination, complete blood cell count, biochemical profile, chest radiography, computed tomographic scan of chest, brain and upper abdomen, ultrasonography of chest and abdomen, electrocardiography, routine pulmonary function tests, arterial blood gases, bronchoscopy, mediastinoscopy and percutaneous core or fine needle biopsy composed the preoperative assessment in our patients. Differential lung perfusion scans were performed on patients with marginal pulmonary function, especially when pneumonectomy was indicated

2.3. Treatment strategies

The type of surgical procedures is presented in Table 1. Exploratory thoracotomy was performed in five of PPS patients (11%) and in two of those with PCaSa (13%). In one PPS case the tumor was falsely classified as benign on frozen section examination during the operation and an atypical resection of lingula was applied. The polysegmentectomy group consisted of resection of the left superior lobe superior division (1) and resections of superior (1) or basal segments (1) of the left inferior lobe. They were performed on patients with restricted pulmonary function and relatively small peripheral pulmonary lesion. Sleeve lobectomies were carried out in two PPS patients with endobronchial localization and negative mediastinal lymph nodes. Among four cases (three with PPS and one with PCaSa), the resections were extended to the thoracic wall in one, the diaphragm in another and the pericardium in two patients. Curative resection with clear margins was possible in 43 patients of the PPS group (89%) and in 13 patients of the PCaSa group (87%). Systematic mediastinal lymphadenectomy was completed during curative resection in all cases, but one erroneously classified as benign within the operation.

Adjuvant therapy was administered inconsistently and with changing different components, so no useful conclusions can be drawn.

Table 1
Type of surgical procedures in PPS and PCaSa groups

Type of resection	PPS		PcaSa	
	N	%	*N*	%
Lobectomy	29	60	7	47
Pneumonectomy	10	21	5	33
Polysegmentectomy	3	6	1	7
Atypical resection	1	2		
Exploratory thoracotomy	5	11	2	13

2.4. Tumor characteristics

All lesions were mainly solitary masses. In 12 of PPS cases (25%) and in one PCaSa patient (6.7%) the tumor size was less than 5 cm. It was greater than 5 cm in 36 of PPS patients (75%) and in 14 of PCaSa patients (93.4%).

In all cases experienced pathologists systematically examined routine hematoxylin and eosin stained slides. Some special stains, immunohistochemistry and electron microscopy were also performed. For the purposes of the study, one pathologist reexamined all microscopic materials. The histologic classification and the tumor grading were based on the last revision of the WHO International Histological Classification of Tumors from 1999 [11] and other sources [12,13]. Table 2 shows the histopathological types and grades of malignancy (from 1 to 3) in the PPS group.

The stage grouping in all patients was updated according to the last revision of the Union Internationale Contre Cancrum (UICC): TNM classification of malignant lung tumors from 1997 [14]. Table 3 presents the postoperative TNM stages in both PPS and PCaSa groups.

The majority of PPS patients were with stage IB (T2N0M0) – 26 (55%) and with stage IIB (T3N0M0 or T2N1M0) – 10 (21%). In 11 PPS patients (23%) positive lymph nodes were found at levels N1 (6) and N2 (5). A satellite nodule in other than primary lobe was reevaluated as M1 in one PPS patient and he was restaged as stage IV. The PCaSa patients were predominantly with higher stage: IIIA – 6 (39%).

2.5. Follow-up and statistical analysis

All patients were seen by the surgeon at least twice, at the end of the first month and at the end of the sixth month after discharge. They were followed-up either until death or up to the completion of the study (December 2000). The follow-up period ranged from 4 to 148 months. Seven patients were lost to follow-up after a period of 24–36 months. Follow-up data were collected mainly from the National Cancer Registry and by personal communications either with the

Table 2
PPS histological types and grades of malignancy

Histological type of PPS	G1	G2	G3	Total
Fibrosarcoma	2	9	4	15 (32%)
Fibroleiomyosarcoma		6	4	10 (22%)
Leiomyosarcoma		3	3	6 (12%)
Rhabdomyosarcoma			6	6 (12%)
Hemangiopericytoma			3	3 (6%)
Epitheloid hemangioendothelioma		2	1	3 (6%)
Undifferentiated sarcoma			3	3 (6%)
Malignant schwannoma			1	1 (2%)
Liposarcoma		1		1 (2%)
Total	2 (4%)	21 (44%)	25 (52%)	48

patients or with their family physicians. All deaths were attributed to malignancy.

Survival rates of the cumulative survival were obtained according to the Kaplan–Meier method [15]. Survival differences between subgroups were compared with the log–rank test. A P value less than 0.05 was considered to be significant. The computed analysis was performed using the SPSS 2001 statistical package (SPSS Inc., Chicago, IL, USA). Histology (PPS vs. PCaSa) and TNM stage (low (I + II) vs. higher (III + IV) stages) in both groups were analyzed as determinants of survival.

3. Results

3.1. Early postoperative results

There was no 30-day postoperative mortality. Major morbidity was 4.2 and 6.7% in PPS and PCaSa groups, respectively. It consisted of two localized empyemas in the first group, successfully treated with a thoracic drainage. One patient in the second group developed a bronchial stump fistula after a right pneumonectomy and was reoperated on within 3 weeks. Six months later bone metastases were diagnosed and he died 9 months after the initial operation. Minor complications, such as prolonged air leakage, wound infections and atelectasis, appeared in four patients (8.4%) with PPS and in two cases (13.3%) with PCaSa. All of them recovered after a conservative treatment.

Table 3
TNM staging of PPS and PCaSa groups

Stage	PPS	PcaSa
I A	2 (4%)	
I B	26 (55%)	4 (27%)
II B	10 (21%)	3 (21%)
III A	5 (10%)	6 (39%)
III B	4 (8%)	2 (13%)
IV	1 (2%)	

3.2. Long-term postoperative results

Local recurrences were reoperated on in one patient (2.1 and 6.7%, respectively) in both groups. A 32-year-old patient with a fibrosarcoma underwent atypical resection of lingula for a small peripheral tumor (3.5 cm) without lymph node metastases falsely classified as benign on frozen section examination during the operation. He developed a local recurrence 18 months later and a completion pneumonectomy was performed because of a lower lobe invasion. The patient passed away 18 months after the second operation. In another patient who was a 51-year-old man, a local recurrence developed 10 months after a right lower lobectomy for carcinosarcoma. A completion pneumonectomy was carried out and the patient died 8 months later with brain metastases.

All patients with exploratory thoracotomies died within 19 months in PPS and within 8 months in PCaSa groups.

3.3. Survival analysis of PPS and PCaSa patients

The overall cumulative 5-year survival of PPS group appears to be 48.81% with mean survival time of 37.87

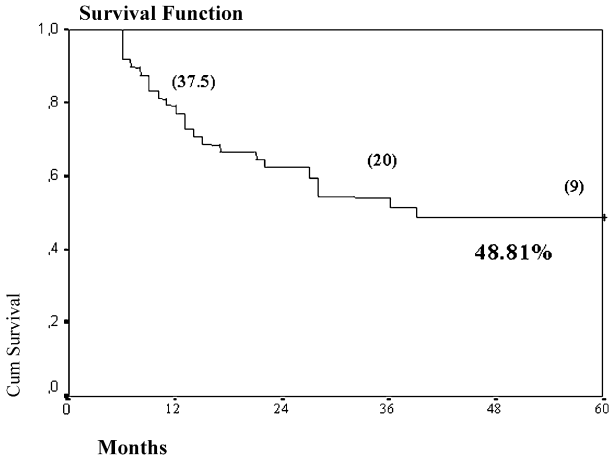

Fig. 1. Cumulative 5-year survival of 48 PPS patients (95% confidence interval 31.25–44.49 months, SE – 3.38). Number in parentheses indicates patients at risk for main intervals analyzed.

months (Fig. 1). There is no statistically significant difference between the survival of the patients with stage I compared with those with stage II ($P = 0.341$). A group of 38 cases with low stages was formed with an overall cumulative 5-year survival of 56.94% and mean survival time of 42.6 months. The second group with higher stages included 10 patients with an overall cumulative 5-year survival of 15.0% and mean survival time of 18.55 months. Statistically significant difference ($P = 0.0005$) between survivals of these two groups was found (Fig. 2).

The PCaSa group has an overall cumulative 5-year survival of 49.38% with mean survival time of 37.19 months (Fig. 3). There are seven low stage patients of this group with cumulative 5-year survival of 62.5% and mean survival time of 48 months. The rest of the eight patients with higher stages have cumulative 5-year survival of 37.5% with mean survival time of 27.5 months. Six of them died within 4, 6, 9, 10, 11 and 96 months after the operation. One is still alive 32 months after surgery and one patient was lost to follow-up. There is no statistically significant difference between the survival rates in both low and higher stage PCaSa groups ($P = 0.11$).

There is no statistically significant difference between the overall cumulative 5-year survival rates of both PPS and PCaSa groups ($P = 0.9035$).

4. Discussion

PPS were elucidated in the recent two to three decades [4,10,16,17]. The evolution of histopathological techniques promoted the introduction of new typing and grading criteria for soft tissue sarcomas (including PPS) [12,18] and changed the classification systems in use [11,13]. A series of recent publications described strictly defined groups of patients with PPS, based on immunohistochemical and

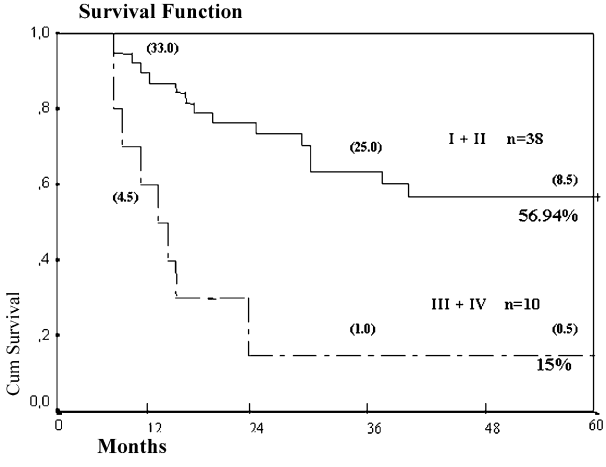

Fig. 2. Cumulative 5-year survival curves of PPS patients with low (95% confidence interval 35.65–49.57 months, SE – 3.55) and higher (95% confidence interval 6.43 – 30.67 months, SE – 6.19) stages ($P = 0.0005$). Number in parentheses indicates patients at risk for main intervals analyzed.

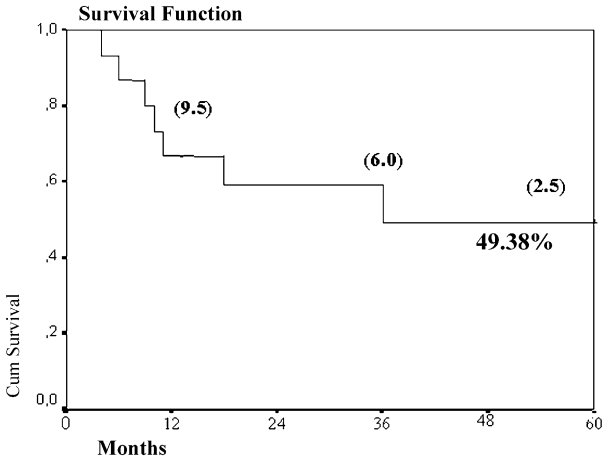

Fig. 3. Cumulative 5-year survival curve of 15 PCaSa patients (95% confidence interval 24.75–49.62 months, SE – 6.35). Number in parentheses indicates patients at risk for main intervals analyzed.

ultrastructural analysis [2–4,18–20]. Although malignant fibrous histiocytoma and synovial sarcoma are currently considered the most common histological types [1,20], there were none in our series, and fibrosarcoma was the most common tumor. We are aware of the fact that these data could be exposed to discussion. Only two of the tumors (4%) in our series were scored in grade 1 and the rest was classified in the higher grades of malignancy. Our results corroborate those of other authors [4,21].

PCaSa is also a rare, defined as bi-directional, tumor containing a mixture of carcinomatous and sarcomatous components [8]. This tumor type was included in the classification group of lung carcinomas many years ago, but most of the published series presented a small number of treated patients [6–8,24]. In fact the rarity of PPS and PCaSa makes prospective, randomized or comparative studies infeasible and conclusions about treatment results and prognosis are based on retrospective observations.

Complete surgical resection with clear margins is the largely accepted treatment for PPS and PCaSa. Our rate of resectability was 89% in the PPS group and 87% in the group of PCaSa. It is comparable to 83 and 100% complete resections in PPS [4,21], as well as 93% resectability in PCaSa [25] series. Our results outperform the reported radical resectability rates of 69 [23] and of 50% [2] in PPS patients. The tendency of these tumors to expand locally toward adjacent structures and organs led to extended resections in 33% of Porte et al. [22] cases. Bacha et al. [1] performed extended radical resection with cardiopulmonary bypass support in three of their patients. The rate of such resections was 6.2 and 6.7%,respectively, in our PPS and PCaSa groups. Conservative pulmonary resections with bronchoplasty, including carinal resection, should be used in endobronchial sarcoma when feasible [1,23], as we successfully did in two of our cases with endobronchial localization and negative mediastinal lymph nodes. Recently, more authors [4,21] reported macroscopically

complete resections, which is consistent with our results, but others found positive resection margins in six of their 23 patients [1] or no radical resection in 39% of their cases [2]. Sometimes a false negative result of frozen section examination could lead to an inappropriate operative procedure [2], as experienced in one of our cases.

In contrast to the classical statement that soft tissue sarcomas metastasize rarely by the lymphatic system [2,18], we found lymph node invasion in 11 (23%) of our PPS patients at level N1 (6) and at level N2 (5). Results of Regnard et al. [4] with positive nodes in 25% of their cases are almost the same. These findings favor the systematic lymph node dissection in all cases with PPS not only for staging purposes, but also in a curative intent [1].

In our series there is no 30-day operative mortality and the percentage of major and minor postoperative complications are acceptable. Other authors also indicated a nil operative mortality [4,21,24]. Bacha et al. [1] reported a patient (5%) in their series of 23 cases who died after extended completion pneumonectomy for recurrent leiomyosarcoma. There was 33% 30-day postoperative morbidity in Porte et al. [21] series.

Postoperative local recurrences are not so rare and are often unsuitable for operative treatment. Chemotherapy and/or radiotherapy could be administered in such cases [2]. Reoperations for local relapse were carried out in 2.1 and 6.7% of our PPS and PCaSa cohorts, respectively. Three patients (16.6%) in PPS series of Porte et al. [21] underwent repeat surgery for pulmonary metastases (2) and sarcoma of the previous thoracotomy scar. Repeat pulmonary resections for local recurrence were reported by different authors [1,3,4].

We find an overall 5-year cumulative survival rate of 48.81% in our PPS group. The mean survival time is 37.87 months with a standard error (SE) of small value and not so large 95% confidence interval, allowed by the greater number of observations in our study. Our results corroborate those reported by other authors [2,4,21]. An earlier publication of McCormak and Martini [22] presented a 36% 5-year survival, while one of the recent publications by Bacha et al. [1] registered a 69% 5-year survival rate for their completely resected patients. All these data are not thoroughly consistent, but they suggest approximately about a 50% chance for 5-year survival in the entire group of surgically treated PPS patients. Our study confirms that 'low stages of primary lung sarcoma favorably influence survival', as shown by Regnard et al. [4].

The 5-year cumulative survival of PCaSa patients was surprisingly high – 49.38% with a mean survival time of 37 months. The SE is greater and the 95% confidence interval is too large, which is attributed to the small number of patients not suitable for statistical analysis. The literature data are not consistent. Xu et al. [24] reported a 43% 5-year survival rate for their 15 operated on PCaSa patients. Davis et al. [5] registered a median survival time of 12 months in 15 patients after potentially curative resection treatment. In a large series of 66 PCaSa patients Koss et al. [25] found a 21.3% 5-year survival rate, but the number of surgically treated patients and the type of treatment are not precisely stated. Based on their own experience of seven cases Huwer et al. [8] concluded that 'the prognosis of PCaSa patients seems to depend on the sarcoma component of the tumor'. Although the survival rate is better in low stage cases, there is no significant difference compared to those with higher stages. Following our results there is no significant difference between overall survival rates of PPS and PCaSa, despite the greater number of patients with higher stages in PCaSa group.

Treatment strategies concerning conservative therapy of soft tissue sarcomas have changed over the last decade; nowadays pulmonary sarcoma patients are appropriate candidates for adjuvant and even for neo-adjuvant treatment [20]. Huwer et al. [8] believed that generally accepted modes of soft tissue sarcomas therapy should be adopted in the treatment of patients with PCaSa, because their prognosis seems to depend on sarcoma component of the tumor.

In conclusion, our results confirm the appropriateness of the initial surgical resection as a treatment of choice for PPS and PCaSa patients. The early postoperative results are quite good with an acceptable morbidity rate. The long-term follow-up demonstrates satisfactory 5-year survival rates depending on the disease stage and on how radical the surgical resection is. If survival is the endpoint of evaluation, there is no difference in the clinical outcome of PPS vs. PCaSa groups.

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