Survival after pulmonary metastasectomy in soft tissue sarcoma

Prognostic factors in 214 patients

Peter F M Choong[1], Douglas J Pritchard[1], Michael G Rock[1], Franklin H Sim[1] and Frank J Frassica[2]

This retrospective study examines prognostic factors for post-metastasectomy survival in soft tissue sarcoma patients.

Between 1976 and 1992, 274 consecutive patients (median age 49 [7–96] years) with pulmonary metastatic soft tissue sarcoma of the extremity or trunk wall (31 at presentation) were managed at the Mayo Clinic. 214 underwent pulmonary metastasectomy and 163 of these also received adjuvant chemotherapy. There were 195 local excisions, 14 lobectomies, and 5 pneumonectomies. 90 patients had solitary metastases, 184 patients had 2 or more metastases. 31% of patients had MFH tumors and 88% of all tumors were high grade. Median follow-up for survivors was 8 (2–21) years.

5-year overall survival after metastasectomy was ≈40% (cf. 20% for non-metastasectomy). Age > 50, MFH tumors, ≥ 2 metastases, metastasis size > 2 cm, metastasis-free period ≤ 18 months, and the use of adjuvant chemotherapy were univariately unfavorable factors. Size of metastasis > 2 cm, number of metastases ≥ 2, and metastasis-free interval ≤ 18 months were independently unfavorable for survival. In a prognostic system, patients with 0 risk factors had a 60% 5-year survival, those with 1, 2, or 3 of these factors had 30%, 20% and 0% survival, respectively.

Departments of Orthopedics, [1]Mayo Clinic, Rochester, Minnesota and [2]Johns Hopkins, Baltimore, Maryland, U.S.A.
Correspondence: Dr. Peter F.M. Choong, Department of Orthopedics, St. Vincent's Hospital, Melbourne, Victoria 3065, Australia. Tel +61 3-92882211. Fax -92882581
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Excellent local control rates and the use of adjuvant chemotherapy have not convincingly improved survival in adults patients with soft tissue sarcomas (Harrison et al. 1993). Metastasectomy is one method of controlling pulmonary disease and 5-year post-metastasectomy salvage rates of 10–40% have been reported (Jablons et al. 1989, Casson et al. 1992, Stewart et al. 1992, Ueda et al. 1993). The rationale behind such treatment comes from studies which show that in soft tissue sarcoma the lung is often the main or only site of involvement in most patients with metastatic disease, and that solitary lesions are common (Potter et al. 1985, Huth and Eilber 1988).

We retrospectively studied post-metastasectomy survival in order to identify prognostic factors that could be helpful for designing prospective trials to clarify the role of metastasectomy in soft tissue sarcoma.

Patients and methods

From 1976 through 1991, 1216 patients with a soft tissue sarcoma of the extremity or trunk wall were treated at the Mayo Clinic. 274 with pulmonary metastases formed the basis for this study. The median age was 49 (7–96) years. The ratio of male to female was 3:2. Of the 274 tumors, 194 (71%) were located in the lower limb, 60 (22%) in the upper limb and 20 (7%) in the trunk wall. Of those situated in the extremities, 175 (69%)were proximal and 79 (31%) were distal.

Size measurements

The primary tumor size (largest diameter) was determined from measurements of fresh surgical specimens where preoperative radiotherapy was not employed. Otherwise, tumor sizes were recorded from preoperative MRI, or if this was not available, from CT. The latter two determinations have shown a close correlation with specimen measurements (Bloem et al. 1988). 9 tumors were subcutaneous,

Table 1. Frequency distribution for tumor histotypes

Histotype	Count
MFH	86
Synovial sarcoma	61
Liposarcoma	27
Fibrosarcoma	21
Leiomyosarcoma	13
Extraskel. osteosarcoma	13
Hemangiopericytoma	10
Rhabdomyosarcoma	10
Epithelioid sarcoma	9
Clear-cell sarcoma	5
Neurofibrosarcoma	4
Malignant schwannoma	3
Alveolar soft part tumor	3
Extraskel. chondrosarcoma	3
Extraskel. Ewing's sarcoma	3
Spindle cell unknown	3

with a median diameter of 6.5 (1.2–15) cm, while 265 tumors were deep-seated, with a median diameter of 8 (2–41) cm.

Histopathology

Mayo pathologists reviewed the diagnoses on all histological preparations of tumors that were excised elsewhere prior to referral (Table 1). A 4-grade system was employed (Broders et al. 1939) to classify histologic malignancy. Grades I (4) and II (28, 12%) tumors were regarded as low grade, while grades III (64) and IV (178, 88%) were regarded as high grade.

Staging of primary tumor

All patients with limb sarcomas were staged according to the surgical staging system of The Musculoskeletal Tumor Society (Enneking 1986). At presentation, there were 10 IA, 19 IB, 35 IIA, 159 IIB and 31 stage III tumors.

Metastases

Thoracic CT scans were performed at 3-monthly intervals for the first 2 years, then at 6-monthly intervals after removal of the primary tumor and also after thoracotomy. The number of metastases was determined at thoracotomy. Size determinations of the largest metastases were made from pathological measurements of the fresh sample immediately after thoracotomy, if no prior chemotherapy had been given, or from prechemotherapy CT measurements if the patient had received chemotherapy as part of the prethoracotomy treatment. CT measurements were used for all those who did not undergo thoracotomy.

The mean metastasis-free period was 13 (0–360) months. On first presentation of pulmonary metastases, 90 had solitary lesions, 44 had 2 metastases and 140 had 3 or more lesions. 19 patients had >20 metastases on discovery of the pulmonary lesion. 170 patients had unilateral pulmonary involvement (98 right, 72 left), and 104 had bilateral disease. The mean largest diameter of pulmonary metastases was 2 (0.2–10) cm. The mean number of thoracotomies per patient was 1 (1–11). 63 patients also had non-pulmonary metastases; 17 were present at the time of diagnosis of the metastasis; they did not undergo thoracotomy; while 46 were detected after thoracotomy.

Treatment

Primary tumor. Definitive surgery of the primary tumor was performed at this institution in 160 patients, while in 114 patients, this was performed elsewhere. 7 tumors were excised intralesionally (adjuvant radiotherapy 2), 54 tumors were treated with marginal margins (adjuvant radiotherapy 31), 140 had wide margins (adjuvant radiotherapy 89), 71 had radical margins (adjuvant radiotherapy 7) and 2 were only biopsied (radiotherapy 1). Radiotherapy was given preoperatively (20) or intraoperatively (2) or postoperatively (69) or pre- and postoperatively (39).

Pulmonary metastasis. All patients with local control of their primary tumor, no non-pulmonary metastatic disease and resectable pulmonary disease were considered as candidates for metastasectomy. Resectability was defined as when the size or number of pulmonary lesions permitted resection without major compromise of pulmonary function. 214 patients had local control of their disease and underwent pulmonary metastasectomy with curative intent. 13 patients were diagnosed as unresectable at the time of thoracotomy, 17 patients also had non-pulmonary metastases at the time of initial diagnosis and therefore did not undergo thoracotomy, and 30 patients elected to forego thoracic surgery. Therefore, 60 patients did not undergo resection of pulmonary disease.

Unilateral disease (150) was approached by lateral thoracotomy, while sternotomy was used for bilateral disease (64). At operation, the lungs were systematically palpated in the inflated and deflated states. Any suspicious lesions were resected with a minimum of normal pulmonary tissue. Procedures were local excision (195), lobectomy (14) or pneumonectomy (5) and all lesions were immediately examined under frozen section.

30 patients are alive and disease-free; 14 after the initial thoracotomy, 8 after 2 thoracotomies, 3 after 3 thoracotomies and 5 patients after 4 or more thoracotomies (4–11). 12 patients are alive with disease after 1 to 4 thoracotomies.

Chemotherapy

Chemotherapy as part of the treatment of the primary tumor was employed in 40 patients. In contrast, 201 patients received chemotherapy after developing metastases. Of the 214 patients who underwent metastasectomy, 163 received chemotherapy. There was a considerable variation in chemotherapy regimes given during this study. Therefore, analyses were stratified only according to whether chemotherapy had been received.

Follow-up

Follow-up was performed at the Mayo Clinic or in some cases by oncologists in the patients' home cities. Information on follow-up undertaken elsewhere was given to the Mayo Clinic at regular intervals by the patients' treating physicians or by regular questionnaires sent to the patient and their physicians by the Mayo Clinic Cancer registry. Survival times were calculated from the time of diagnosis of the primary to the last follow-up or death. Metastasis-free survival was taken from the time of diagnosis up until the time when the metastasis was observed. Survival after the metastasis was estimated from the time of diagnosis of the metastasis to death or last follow-up if alive, in patients who did not undergo thoracotomy, and from the time of thoracotomy to death or last follow-up in those who did undergo thoracotomy. The median follow-up for survivors from the time of diagnosis was 97 (22–258) months.

Statistics

The nonparametric Mann-Whitney U-test was employed to compare the ranked means of 2 groups. Contingency table analyses were used to determine the relationship between 2 nominal variables.

Table 2. Post-metastasectomy survival related to patient, tumor and metastasis variables

Variable		n	5-year survival (%)	10-year survival (%)	P -value univariate analysis
Patient					
Age	≤ 50	115	28	19	0.04
	> 50	99	16	13	
Sex	Male	129	22	18	0.9
	Female	85	23	11	
Primary tumor					
Location	Trunk wall	16	19	19	0.9
	Lower limb	155	25	16	
Diameter (cm)	≤ 5	44	30	24	0.5
	> 5	163	20	13	
Malignancy grade	High	188	22	17	0.9
	Low	26	28	11	
Histotype	MFH	68	20	10	0.07
	Non-MFH	146	24	18	
Metastases					
Number	1	78	32	23	0.005
	> 1	136	17	12	
Size (cm)	≤ 2	122	30	24	0.0002
	> 2	78	14	6	
Metastasis-free period (mo)	≤ 18	122	17	15	0.08
	> 18	92	30	17	
Treatment primary tumor					
Surgical margin	Intralesional	7	25	0	0.8
	Marginal	45	27	20	
	Wide	205	17	13	
	Radical	57	28	15	
Radiotherapy	Yes	102	17	17	0.6
	No	112	26	15	
Chemotherapy	Yes	27	16	14	0.5
	No	187	22	16	
Treatment metastasis					
Thoracotomies	≤3	186	20	13	0.02
	>3	28	38	30	
Adjuvant chemotherapy	Yes	158	17	10	0.002
	No	56	42	35	

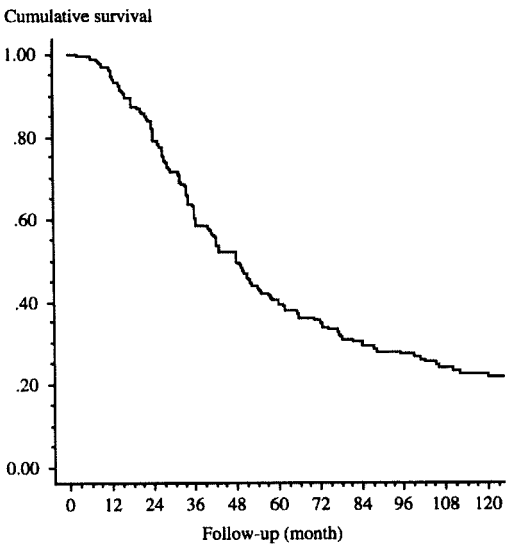

Figure 1. Overall survival of 214 patients who underwent pulmonary metastasectomy.

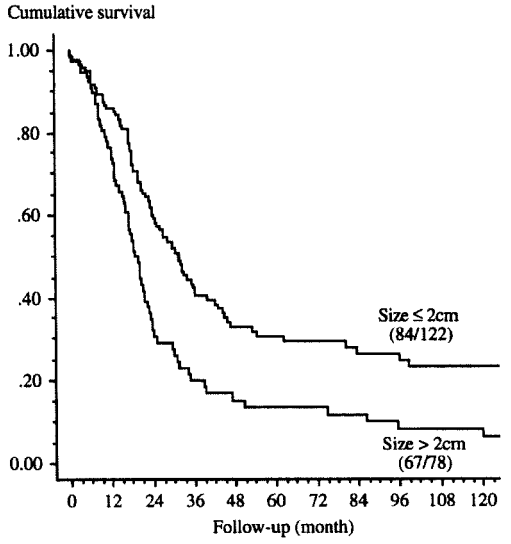

Figure 2. A. Post-thoracotomy survival related to size of first pulmonary metastasis, p < 0.0002. Numbers in parentheses represent events/patients.

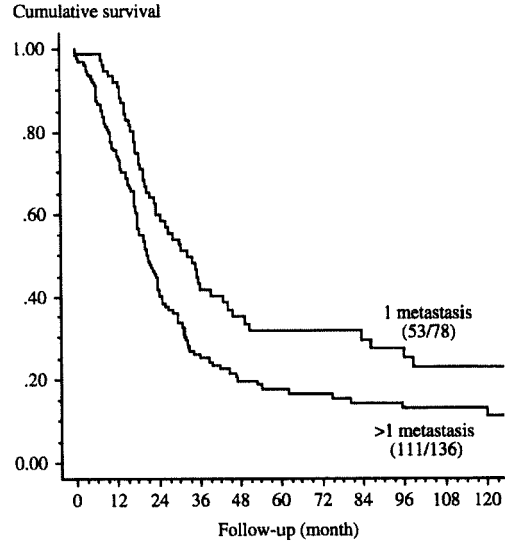

Figure 2. B. Post-thoracotomy survival related to number of pulmonary metastases, p < 0.005. Numbers in parentheses represent events/patients.

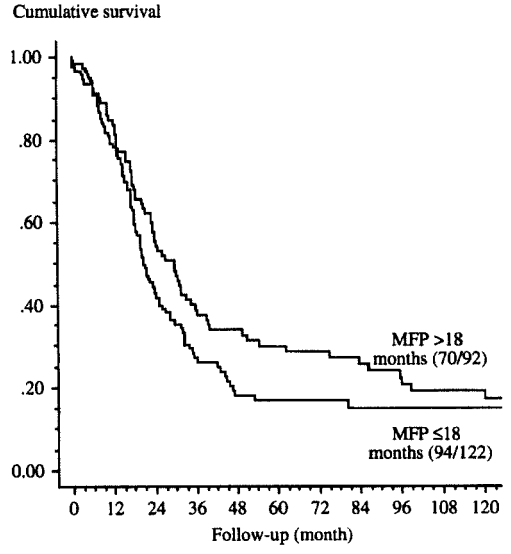

Figure 2. C. Post-thoracotomy survival related to metastasis-free period (MFP), p 0.08. Numbers in parentheses represent events/patients.

Survival curves were generated using Kaplan-Meier methods and differences compared with the log rank test. Deaths from causes other than tumor were classified as censored. Univariately significant variables were entered into a Cox proportional hazards model to determine the influence of each variable on survival and independent factors were compared using the Wald statistic. $P < 0.05$ was regarded as significant.

Results

Univariate analysis of survival after thoracotomy (Table 2)

The overall 5- and 10-year survival of patients undergoing pulmonary metastasectomy was 40% and 20%, respectively (Figure 1).

Patient variables. Patients younger than 50 years had a better survival rate than those who were older. Gender did not influence survival.

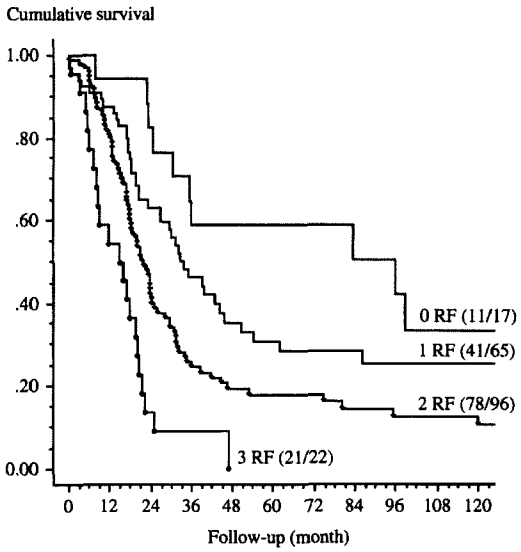

Figure 3. Post-thoracotomy survival based on the number of risk factors (RF) present - number of metastases > 1, size of metastasis > 2 cm, MFP ≤ 18 months, p < 0.0001. Numbers in parentheses represent events/patients

Primary tumor variables. Size, depth, location, grade and stage of the primary tumor did not correlate with survival. When post-thoracotomy survival was stratified according to 5 classifications of histotype—namely, MFH, synovial sarcoma, liposarcoma, fibrosarcoma and others—there were no differences between groups. If, however, the tumors were reclassified as MFH or non-MFH tumors, MFH tumors had a poorer survival.

Pulmonary metastatic tumor variables. The number of pulmonary lesions resected correlated with survival. Those with a solitary nodule had a better survival than those who had 2 or more lesions. Size of metastasis greater than 2 cm correlated with a poorer survival than smaller lesions. Patients with a metastasis-free interval greater than 18 months had a more favorable survival rate than those whose metastases occurred within 18 months (Figure 2).

Treatment variables. Surgical margins, the use of adjuvant radiotherapy and/or chemotherapy in the treatment of the primary tumor did not affect the outcome after pulmonary metastasectomy. Patients with more than 3 thoracotomies had a better survival rate than those with fewer attempts at curative metastasectomy. Patients who received adjuvant chemotherapy with pulmonary metastasectomy had a less favorable survival rate. There were no differences in the primary tumor size, grade, histotype, number of metastases or metastasis-free period between the chemotherapy and non-chemotherapy groups. There was a trend indicating that patients treated by chemotherapy had slightly larger metastases (2.5 cm vs. 2.0 cm, p 0.06).

Multivariate analysis

Age (≤ or > 50), histotype (MFH or non-MFH), number of metastases (1 or >1), size of metastasis (≤ or > 2 cm), and metastasis-free period (≤ or > 18 months) were entered as nominal covariates into a Cox proportional hazards model (200 patients) (Table 3). Size of metastasis greater than 2 cm, 2 or more lesions and a metastasis-free period less than 18 months were independently unfavorable prognostic factors. Age of the patient and histotype lost their univariate significance. Although the number of thoracotomies and the use of chemotherapy were univariately significant factors, they were excluded from the multivariate analysis because they were time-dependent variables, occurring after the detection of metastases.

Prognostic system

The number of metastases > 1, a metastasis-free period ≤ 18 months, and size > 2 cm were regarded as high risk factors. The patients were then classified according to the number of these factors characterizing their condition. Thus, a 4-level prognostic system based on the number of high risk factors (0, 1, 2, or 3) was constructed. The best survival rate was seen in patients who had no high risk factors, while the incremental addition of these factors was accompanied by a decrease in survival (Figure 3).

Table 3. Multivariate analysis of factors related to post-thoracotomy survival

Covariate	Coefficient	Standard error	P-value	Relative risk
Size of metastasis > 2 (cm)	0.72	0.17	0.0001	2.1
Metastases > 1	0.45	0.17	0.009	1.6
Metastasis-free period < 18 (mo)	0.49	0.18	0.006	1.6
Age > 50 yr	0.25	0.18	0.16	1.3
MFH tumors	0.091	10.9	0.63	1.1

Wald statistic p < 0.0001. Analysis perfomed on 200 patients with complete data on all 5 variables

Table 4. Clinicopathological features of patients with post-metastasectomy survival of 10 years or more

Case	Age	Sex	Histotype	Grade	Site [a]	Metastasis		Laterality	Surgery [b] (n)	Chemo-therapy	Post-thoracotomy survival (yr)	Status [c]
						n	cm					
1	42	M	Liposarcoma	Low	L	15	2.5	B	2	Yes	10	DOD
2	26	M	MFH	High	L	2	1.0	U	1	Yes	11	ANED
3	41	F	Fibrosarcoma	High	L	1	2.3	U	5	Yes	11	ANED
4	28	M	Synovial sarcoma	High	L	3	0.5	B	6	Yes	11	ANED
5	17	M	Synovial sarcoma	High	U	1	1.2	U	1	No	12	ANED
6	23	F	Fibrosarcoma	Low	T	1	1.0	U	3	Yes	12	DOD
7	55	M	MFH	High	L	2	1.2	U	1	No	13	DNED
8	36	F	Liposarcoma	High	L	1	1.5	U	1	No	13	ANED
9	40	M	Liposarcoma	High	L	1	1.5	U	11	No	14	ANED
10	45	M	Synovial sarcoma	High	L	3	2.0	B	2	No	14	ANED
11	45	M	Liposarcoma	Low	L	1	1.5	U	5	Yes	15	DNED
12	13	M	Synovial sarcoma	High	L	1	6.0	U	1	Yes	15	ANED
13	29	M	Ewing's sarcoma	High	L	12	2.0	B	5	No	16	DOD
14	21	M	Chondrosarcoma	High	L	3	0.3	U	4	Yes	17	ANED
15	31	F	Fibrosarcoma	High	U	10	4.0	B	1	No	19	ANED

[a] U upper limb, L Lower limb, T trunk.
[b] Metastasectomy local excision in all cases except case 12 where pneumonectomy was performed.
[c] ANED alive no evidence of disease, DNED died, no evidence of disease, DOD died of disease.
Only case 13 had metastasis on presentation.

Clinicopathological characteristics of 15 survivors more than 10 years post-metastasectomy (Table 4)

Only 1 patient was over 50 years of age and the majority were male. There were only 2 MFH tumors. All but 3 of the tumors were high grade. 3 patients had 10 or more metastases removed and 5 had bilateral disease. The mean number of thoracotomies was 3 (1–11), and the mean size of the largest metastasis was 1.9 (0.3–6.0) cm. The mean post-metastasectomy survival was 13 years.

Discussion

Many have reported the beneficial effect of pulmonary metastasectomy in soft tissue sarcoma (Morrow et al. 1980, Casson et al. 1992, Van Geel et al. 1994). Our study concurs with these by demonstrating that in patients deemed to be curable, an overall 5-year post-thoracotomy survival of almost 40% was possible. It is clear, however, that some patients still succumb to pulmonary disease despite apparently curative surgery. Therefore, it would be advantageous to identify prognostic factors which could distinguish subsets of patients in whom thoracotomy would be more efficacious, in order to rationalize the use of this modality.

Several metastatic variables from our study had prognostic importance for post-thoracotomy survival. The strongest variable was the size of the largest metastasis when pulmonary disease was first diagnosed. Metastatic size as a prognostic variable has not been highlighted by other studies. Gadd et al. (1993) found that size variations did not correlate with differences in survival. Their results, however, were based on 78 patients. Small series may be one reason why this variable has not gained prognostic significance in the past. Another variable found to be independently significant was the number of metastases. This accords with the study by Casson et al. (1991) who also found that 2 or more pulmonary metastases were associated with a significant decrease in median survival. A study from the National Cancer Institute has also shown that the number of pulmonary nodules affected survival (Roth et al. 1985). Their analyses demonstrated that those with 3 or fewer nodules had a better survival than those with more nodules. However, in a later series (Jablons et al. 1989) they reported that patients in whom all disease could be resected, the number of nodules did not appear to influence long-term survival. This finding differs from ours as we have found that, despite the removal of all known metastases, patients with solitary lesions still survived far longer than those in whom 2 or more lesions were removed. Our finding of a better survival in those who had a longer metastasis-free period agrees with Creagen et al. (1979) and Jablons et al. (1989) and, like the latter, we were able to demonstrate that this variable was independently prognostic.

Casson et al. (1992) reported that patients with MFH tumors had twice the median survival of those with other histotypes, and this factor was independently prognostic. While the results of our univariate

analysis concurred with theirs, we failed to demonstrate any independence on Cox modeling. The histological heterogeneity of MFH tumors is well known and may lead to diagnostic differences between institutions. This may be one reason for the difference in prognostic strengths of histotype between the two series. Some authors have even questioned the existence of MFH tumors (Fletcher 1992). In this regard, both results should be interpreted with caution.

Histologic grade in this study was not found to be prognostic for survival after thoracotomy. Studies by Gadd et al. (1993) and Casson et al. (1992) corroborate our findings. Van Geel et al. (1994), however, analyzed 67 patients and found that, on multivariate analysis which included grade, metastasis-free interval, thoracotomy, pulmonary nodules, radicality of surgery and age, the only factor significantly related to disease-free survival was grade. The apparent disparity in these observations may relate to differences in grading criteria.

Age of the patient had univariate prognostic significance but the outcome in older patients which may be attributable to the theoretical decrease in host immunity, decreased DNA repair, oncogene activation or amplification, and defects in tumor-suppressor genes with advancing age (Cohen 1994), on multivariate analysis, was just beyond the level of significance. This suggests a covariation with one or more of the other factors tested. Jablons et al. (1989) also analyzed age as a prognostic factor, but could not detect any significance.

Repeated thoracotomies may be curative. Patients in our series who developed multiple episodes of metastases tolerated multiple thoracotomies, and this correlated with prolonged survival. Van Geel et al. (1994) reported a longer median survival in those who underwent at least a second thoracotomy. Pogrebniak et al. (1991) also found that 31 of 43 patients who underwent 2 or more thoracic explorations could be rendered free of disease at the second thoracotomy. Although our results suggest that patients who had more than 3 thoracotomies had a better outcome than those who had 3 or less, this should be interpreted with caution. Clearly, if a patient is cured after his or her first thoracotomy, then the result is better than for those who develop multiple pulmonary recurrences that may require multiple thoracotomies. Our observations probably reflect the fact that thoracotomy has permitted patients to survive long enough to develop further metastases, which are then treated by repeated surgery. Therefore, in patients destined to experience multiple pulmonary metastases, repeated thoracotomy can increase longevity.

Our patients who survived for at least 10 years after metastasectomy demonstrate that high grade tumors with bilateral disease need not be a barrier to longevity, and that multiple metastases and numerous subsequent thoracotomies for their management can be tolerated. The majority of patients with small metastases (≤ 2 cm) who were treated with local excision and the fact that as many as 214 of 274 patients underwent thoracotomy reflect our philosophy of early and aggressive surgery. Another important point raised by this subset of patients is that it demonstrates the imperfection in current malignancy grading systems, where patients with apparently low grade tumors may have recurrent and multiple metastases, while other patients with apparently high grade tumors are able to survive, despite the aggressiveness predicted by their grade.

The results of adjuvant chemotherapy on survival after pulmonary metastasectomy are unclear. Mountain (1994) examined the outcome after planned surgery and chemotherapy versus surgery alone, and could not demonstrate a difference in survival. Lanza et al.'s (1991) review of 26 patients with pulmonary metastases who received preoperative chemotherapy, followed by resection, did not show a correlation between chemotherapy and survival, but this may be due to their method of response evaluation. Despite implying a survival hazard from chemotherapy, our results do not allow for a complete evaluation of the possible impact of chemotherapy. There is a need for controlled trials to ascertain the role of chemotherapy in the management of pulmonary metastasis.

An earlier study from our institution (Creagen et al. 1979), which could identify only short disease-free intervals and extrathoracic recurrence as being prognostically unfavorable, reported a post-thoracotomy 5-year survival of 29%. The authors could not decide whether the use of thoracotomy in metastatic disease was therapeutically worthwhile. While the retrospective nature of our study has clear weaknesses, we believe that our data strongly indicate that surgery prolongs survival. We have identified prognostic factors which can be employed in a prognostic system that differentiates between good and poor survivors. This may be useful for selecting patients who may be candidates for controlled studies of pulmonary metastasectomy.

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References

Bloem J L, Taminiau A H M, Eulderink F, Hermans J, Pauwels E K J. Radiologic staging of primary bone sarcoma: MR imaging, scintigraphy, angiography, and CT correlated with pathologic examination. Radiology 1988; 169: 805-10.

Broders A C, Hargrove R, Meyerding H W. Pathological features of soft tissue sarcoma. Surg Gynecol Obstet 1939; 69: 267-80.

Casson A G, Putnam J B, Natarajan G, Johnston D A, Mountain C, McMurtrey M, Roth J A. Efficacy of pulmonary metastasectomy for recurrent soft tissue sarcoma. J Surg Oncol 1991; 47 (1): 1-4.

Casson A G, Putnam J B, Natarajan G, Johnston D A, Mountain C, McMurtrey M, Roth J A. Five-year survival after pulmonary metastasectomy for adult soft tissue sarcoma. Cancer 1992; 69 (3): 662-8.

Cohen H J. Biology of aging as related to cancer. Cancer 1994; 74 : 2092-2100.

Creagen E T, Fleming T R, Edmonson J H, Pairolero P C. Pulmonary resection for metastatic non-osteogenic sarcoma. Cancer 1979; 44: 1908-12.

Enneking W F. A system of staging musculoskeletal neoplasms. Clin Orthop 1986; 204: 9-24.

Fletcher C D. Pleomorphic malignant fibrous histiocytoma: fact or fiction? A critical reappraisal based on 159 tumors diagnosed as pleomorphic sarcoma. Am J Surg Pathol 1992; 16 (3): 213-28.

Gadd M A, Casper E S, Woodruff J M, McCormack P M, Brennan M F. Development and treatment of pulmonary metastases in adult patients with extremity soft tissue sarcoma. Ann Surg 1993; 218: 705-12.

Harrison L B, Franzese F, Gaynor J J, Brennan M F. Long-term results of a prospective randomized trial of adjuvant brachytherapy in the management of completely resected soft tissue sarcomas of the extremity and superficial trunk. Int J Radiat Oncol Biol Phys 1993; 27 (2): 259-65.

Huth J F, Eilber F R. Patterns of metastatic spread following resection of extremity soft tissue sarcomas and strategies for treatment. Semin Surg Oncol 1988; 4: 20-6.

Jablons D, Steinberg S M, Roth J, Pittaluga S, Rosenberg S A, Pass H I. Metastasectomy for soft tissue sarcoma. Further evidence for efficacy and prognostic indicators. J Thorac Cardiovasc Surg 1989; 97 (5): 695-705.

Lanza L A, Putnum J B, Benjamin R S, Roth J A. Response to chemotherapy does not predict survival after resection of sarcomatous pulmonary metastases. Ann Thorac Surg 1991; 51: 219-24.

Morrow C E, Vassilopoulos P P, Grage T B. Surgical resection for metastatic neoplasms of the lung. Cancer 1980; 45: 2981-5.

Mountain C F. Surgical treatment of soft tissue sarcoma pulmonary metastasis. In: Soft tissue sarcomas. Diagnosis and treatment. Raaf J H (Ed.). Mosby. St. Louis 1994; 344-5.

Pogrebniak H W, Roth J A, Steinberg S M, Rosenberg S A, Pass H I. Reoperative pulmonary resection in patients with metastatic soft tissue sarcoma. Ann Thorac Surg 1991; 52: 197-203.

Potter D A, Glenn J, Kinsella T, Glatstein E, Lack E E, Restrepo C, White D E, Seipp C A, Wesley R, Rosenberg S A. Patterns of recurrence in patients with high-grade soft-tissue sarcomas. J Clin Oncol 1985; 3 (3): 353-66.

Roth J A, Putnam J B, Wesley M N, Rosenberg S A. Differing determinants of prognosis following resection of pulmonary metastases from osteogenic and soft tissue sarcoma patients. Cancer 1985; 55: 1362-6.

Stewart J R, Carey J A, Merrill W H, Frist W H, Hammon J W J, Bender H W J. Twenty years' experience with pulmonary metastasectomy. Am Surg 1992; 58 (2): 100-3.

Ueda T, Uchida A, Kodama K, Doi O, Nakahara K, Fujii Y, Komatsubara Y, Ono K. Aggressive pulmonary metastasectomy for soft tissue sarcomas. Cancer 1993; 72 (6): 1919-25.

Van Geel A, Van Coevorden F, Blankenstein J D, Hoekstra H J, Schuurman B, Bruggink E D M, Taat C W, Theunissen E B M. Surgical treatment of pulmonary metastases from soft tissue sarcomas: A retrospective study in The Netherlands. J Surg Oncol 1994; 56: 172-7.