Adult Soft Tissue Sarcomas

A Pattern of Care Survey of the American College of Surgeons

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A nationwide survey of the clinical presentation, pathology, and management of soft tissue sarcomas in adults was carried out under the auspices of the Commission on Cancer of the American College of Surgeons. Two separate 2-year periods were used to allow assessment of changes in patterns of care. Data were obtained from 504 hospitals in 1977–1978 (2355 patients) and 645 institutions in 1983–1984 (3457 patients). Pretreatment findings of interest included some evidence of physician delay in diagnosis, overuse of excisional biopsy as opposed to the generally preferred approach of incisional biopsy, a low rate of usage of the American Joint Committee for Cancer Staging (AJCSS) system, and major reliance on CT for pretreatment patient evaluation. Operation was the primary treatment, with or without adjuvant therapies, in approximately three fourths of the patients. The other one fourth were primarily patients with distant metastasis at the time of diagnosis. Some increase in multimodal therapy did occur in the second period but the rate of amputation was low (approximately 10%) in both periods studied. Survival curves support the prognostic validity of the AJCCS system and the value of complete resection of soft tissue sarcomas. Adverse prognostic factors included positive surgical margins, large tumors, retroperitoneal or mediastinal primary sites, some histologic types, and the perceived need for adjuvant therapy. Patients receiving adjuvant radiation or chemotherapy had less favorable survival data than those treated by operation alone due to criteria used for selecting patients for these therapies. Approximately one half of the treatment failures in the 1977–1978 series were locoregional, whereas 18% were limited to lung metastasis. Salvage therapy for these two forms of treatment failure yielded 61% and 21% 5-year survival rates.

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SOFT TISSUE SARCOMAS are uncommon cancers that represent only 1% of all malignant neoplasms (excluding skin) in adults. It has been estimated that only 4800 sarcomas of the soft parts are diagnosed each year in the United States.[1] The relative rarity of sarcomas in individual institutions, the great variability in histologic and clinical presentation of sarcomas, and increasing interest in multimodality treatment and limb-sparing approaches led to planning for a nationwide survey under the auspices of the Commission on Cancer of the American College of Surgeons. The network of hospital cancer programs approved by the Commission on Cancer provided a capability for collecting enough data to give a broad view of this heterogeneous group of neoplasms as well as characterizing treatment practices and results in the United States.

A stated purpose of this study of soft tissue sarcomas was to document the clinical presentation, pathology, and management used nationwide during two separate 2-year periods (1977–1978 and 1983–1984). Another goal was to evaluate the impact of multiple clinical, pathologic, and treatment factors on treatment success or failure in patients in the earlier interval (long-term study). Still another goal was to assess any changes that occurred between these two periods (the long-term and short-term studies) in terms of clinical presentation, evaluation and staging, and the overall management approach. The nature of these two surveys did not allow any randomized comparisons between groups, or a comparative study of specific therapeutic interventions, but the large data base obtained has suggested answers to a number of specific questions that were posed at the initiation of these retrospective studies.

Methods of Procedure

Cancer committees of hospitals with American College of Surgeons-approved cancer programs were invited on a voluntary basis to participate in both a long-term and short-term study of soft tissue sarcomas in adult patients

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TABLE 1. *Anatomic Site Distribution of Sarcomas (Data from Both Surveys Combined)**

Anatomic Site	N	%
Head and neck	406	8.9
Trunk	814	17.9
Upper extremities	594	13.1
Lower extremities	2110	46.4
Retroperitoneum	568	12.5
Mediastinum	58	1.3
Total	4550	100.0

* "Other," "Unknown," or multiple sites not included.

first diagnosed and/or treated at their institutions from January 1, 1977 through December 31, 1978 (long-term study) and January 1, 1983 through December 31, 1984 (short-term study). Selective criteria for patient entry included age (patients 18 years or older) and histologic confirmation of sarcoma diagnosis before or after admission to the reporting hospital. Anatomic site exclusions for the purpose of this study were sarcomas of bone, lymphoid organs and lymph nodes, viscera, and the central nervous system. Also excluded were patients with Kaposi's sarcoma (including AIDS) because the clinical presentation and management of this disorder differs from that of other soft tissue sarcomas.

The data forms for this patient care study were developed by members of the Patient Care and Research Committee of the Commission on Cancer. A series of questions believed answerable by such a large retrospective study was first decided on. The data items on both the long-term study and short-term study forms were those relating to these questions regarding clinical presentation, pathology, and clinical management. In addition, the long-term study forms requested information on treatment results and secondary treatments used. The deadline for receipt of the best information available from either the tumor registries or hospital charts was May 1, 1985.

After local review of the data collected from the Tumor Registry by the Cancer Committee of the participating institution, the data were presented to and processed by the Cancer Department of the American College of Surgeons. Statistical tabulations were performed at Roswell Park Memorial Institute in Buffalo, NY. The survival and recurrence rates were calculated by the actuarial (life-table) method.[2,3] Patients who died of causes other than soft tissue sarcoma were treated in the same manner as patients lost to follow-up care.

Results

Five hundred and four hospitals volunteered reorts on 2355 patients in the long-term study and 645 institutions reported on 3457 patients in the short-term study. Hospitals participating in each study were widely distributed geographically. Both in the long-term and short-term studies, reports were received from 49 states, Puerto Rico, and the District of Columbia.

Clinical Presentation

Sex. There was a slight male predominance in both the long-term and short-term studies with a female to male ratio of 1.0:1.1. This ratio in the entire U.S. population is 1.0:0.95.

Race. In both the long-term and short-term studies, 86% of the patients were white and 10% were black. Orientals constituted 1% of the patients. This is the race distribution in the U.S. population.

Age. The surveys specifically excluded sarcoma patients under age 18 because of the great differences in histologic type, site distribution, and response to therapy in the childhood sarcoma group (primarily childhood rhabdomyosarcoma). The age distribution of soft tissue sarcomas in this adult population for which age was recorded was: 20.7% of patients were under 40 years; 27.6% of patients were 40–60 years; and 51.8% of patients were over 60 years.

Anatomic site. The distribution of soft tissue sarcomas by anatomic site is shown in Table 1. The data were combined since they were virtually identical for the short-term and long-term surveys. More than half of these primary lesions were on the extremities in the long-term and short-term studies (59.5%), and the lower extremity had the preponderance of lesions. Next in frequency were lesions of the trunk, then retroperitoneum, and then the head and neck region.

Symptoms. The major presenting symptom in both the long-term and short-term surveys was the presence of a mass (64%), whereas one third of the patients had pain or discomfort as the initial symptom.

Family history. In this population of sarcoma patients, the family history of sarcoma in other relatives was rare (0.8% in both the long-term and short-term studies). Family history of other cancers was not unusually high (29.1% in the long-term study and 34.5% in the short-term study) and, considering inaccuracies that must occur with this type of question on such surveys, it is difficult to differentiate this pattern from that of the population of the U.S. as a whole.

Delay in diagnosis. To evaluate any delay between the onset of symptoms and diagnosis, this interval was assessed as well as the interval between initial physician contact and establishing the actual diagnosis. The median delay was 4 months for the former and only 1 month for the latter in both periods surveyed. However, 18% of patients in the earlier period and 21% in the more recent

period had a "physician delay" in diagnosis of 6 or more months, and roughly one half of the patients in both surveys had a delay of 2 or more months between initial physician visit and diagnosis. There was no improvement in these figures between the two surveys. On the presumption that sarcomas in some anatomic sites might be more subtle in their clinical presentation than in other sites, physician delay was examined by site also. Little difference in delay by site was observed.

Diagnosis

Biopsy. The frequencies of the various types of biopsy procedures used to establish the diagnosis of sarcoma are shown in Table 2. Despite the oft-stated concept that incisional biopsy for these generally large soft tissue lesions usually is preferable to excisional biopsy, roughly one half of the sarcomas were biopsied by *excision* during both periods studied. Only one fifth of the lesions were diagnosed by incisional biopsy, with a minimal increase in this approach between these two periods studied. A small increase in frequency of needle biopsy also was observed between the long-term and short-term studies, but this approach was rarely used and was not a preferred one for initial diagnosis.

Histologic diagnosis. The histologic types of sarcoma recorded in both the long-term and short-term studies are shown in Table 3. Liposarcoma and malignant fibrous histiocytoma were the most frequent types in both intervals with the latter diagnosis increasing in frequency over the two periods. Malignant fibrous histiocytoma was only first described in 1961[4] but now has become the single most frequent histologic variety of soft tissue sarcoma.

Relationship of histology to age group. Trends in histologic classification in terms of patient age were observed. Alveolar soft part sarcoma, malignant schwannoma, and synovial sarcoma were more frequent in the younger group (<40 years). Angiosarcoma, leiomyosarcoma, liposarcoma, and malignant fibrous histiocytoma were more frequent in the older group (>60 years). Other histologic varieties did not show a striking association with patient age.

Microscopic grade. Because the clinical diagnostic and postsurgical resection pathologic staging schemas described by the American Joint Committee for Cancer (AJCC) are dependent on the microscopic grade of the sarcoma,[5] this information was sought in these surveys. In the earlier series, only 45% of the patient entries had microscopic grade recorded. Little improvement in this figure was seen in the more recent data (51% had grade recorded). The distribution of microscopic grades when recorded was similar in both surveys with approximately one third of patients classified as grade 1 and roughly one half of patients classified as grade 3.

TABLE 2. *Biopsy Techniques Used for Sarcoma Diagnosis*

	1977–1978		1983–1984	
Type of Biopsy	N	%	N	%
None	319	13.5	380	11.0
Needle	114	4.8	311	9.0
Incisional	466	19.8	753	21.8
Excisional	1210	51.4	1644	47.6
Other	139	5.9	278	8.0
Unknown	107	4.5	91	2.6
Total	2355	100.0	3457	100.0

Pretreatment Evaluation and Staging

Diagnostic studies used. Clinical diagnostic staging requires various laboratory and radiologic evaluations. An attempt was made to characterize the tests used during these two intervals and to detect any trends that may have developed (Table 4). The major change in use of tests observed between the two intervals was a marked increase in use of computerized tomographic scans (CT) for both the primary site and the chest. There was a corresponding decrease in usage of liver scans and chest tomograms. Angiography and lymphangiography were rarely used in both periods.

Clinical staging. Responding institutions were asked whether the AJCC clinical diagnostic stage was recorded either in the tumor registry record or the hospital record. Despite professional education efforts for physicians regarding the value of recording stage, this information was not recorded in over 50% of the patient charts in the long-term study. There was little improvement in recording stage between the long-term and short-term studies with 47% of the latter having no stage recorded.

TABLE 3. *Distribution of Sarcoma Patients by Histologic Type**

	1977–1978		1983–1984	
	N	%	N	%
Alveolar soft part sarcoma	10	0.4	20	0.6
Angiosarcoma	48	2.0	103	2.9
Fibrosarcoma	262	11.1	228	6.6
Leiomyosarcoma	324	13.8	513	14.8
Liposarcoma	547	23.2	611	17.7
Malignant fibrous histiocytoma	348	14.8	897	25.9
Malignant mesenchymoma	32	1.4	36	1.0
Malignant schwannoma	76	3.2	138	4.0
Rhabdomyosarcoma	167	7.1	124	3.6
Synovial sarcoma	87	3.7	126	3.6
Extra skeletal chondrosarcoma	29	1.2	42	1.2
Extra skeletal osteosarcoma	10	0.4	21	0.6
Sarcoma, Nos	127	5.4	186	5.4
Other types	332	14.1	441	12.8

* Some patients reported more than one histologic type, therefore the total exceeds 100%.

TABLE 4. *Frequency of Various Pretreatment Evaluations Used in these Studies*

	1977–1978		1983–1984	
	% Done	% Abnormal Results*	% Done	% Abnormal Results*
Angiogram	11.4	73.2	11.7	71.9
Bone marrow	7.2	14.5	5.6	19.7
Bone scan	32.9	35.0	30.7	37.4
CEA	8.5	23.5	9.8	12.5
Chest tomograms	19.4	22.7	10.9	20.9
Chest x-ray	85.4	14.5	83.5	14.8
CT scan of chest	5.4	23.4	24.9	30.8
CT scan of primary	11.4	76.9	43.6	87.3
Liver function studies	51.1	19.0	51.2	22.0
Liver scan	34.3	13.4	17.5	16.2
Lymphangiogram	4.1	25.8	2.1	10.7
Skeletal x-ray	16.5	24.7	11.6	27.9
Sonogram	11.0	73.2	10.8	65.8
X-ray of tumor	26.0	75.5	26.2	77.1

* Percentages of abnormal results are for patients on whom the test was performed.

The breakdown of clinical stage for those patients either actually staged by the AJCC classification *or* calculated from the staging elements listed is shown in Table 5. The relative proportion of patients assigned to each stage varied little between the intervals studied. An attempt to correlate sex and race of the patient to clinical diagnostic stage similarly showed no differences for these factors, but there were trends in stage distribution based on histologic classification of the sarcoma. Lower stage, less-advanced sarcomas included a preponderance of fibrosarcomas and liposarcomas, whereas angiosarcoma, leiomyosarcoma, malignant fibrous histiocytoma, rhabdomyosarcoma, and synovial sarcoma tended to be in more advanced stage.

Specific clinical features of interest, and major determinants of stage, are regional nodal metastases and clinically involved distant metastatic sites. Only 230 of 2355 patients in the long-term study had histologic examination of regional lymph nodes (9.8%). This is due perhaps to the corresponding low frequency of clinical evidence of lymph node involvement. There was a slightly higher proportion of patients in the later survey who had histologic examination of regional lymph nodes (13.3%). The proportion of patients with proven regional nodal metastases was low in both studies (2.2% and 4.0%), but these must be considered minimum figures since biopsies were limited mainly to patients with clinically suspicious or involved lymph nodes. However, these data show that lymphatic spread is not a prominent feature of soft tissue sarcomas at the time of diagnosis. The frequency of nodal involvement was low for all histologic types as seen in Table 6.

TABLE 6. *Status of Regional Lymph Nodes of Sarcoma Patients According to Histologic Category (Data from Both Surveys Combined)*

Histologic Category	No. with Involved Nodes/ Total with Histology	%
Alveolar soft part sarcoma	1/30	3.3
Angiosarcoma	8/151	5.3
FIbrosarcoma	9/489	1.8
Leiomyosarcoma	24/837	2.9
Liposarcoma	26/1158	2.2
Malignant fibrous histiocytoma	44/1246	3.5
Malignant mesenchymoma	0/66	0
Malignant schwannoma	3/214	1.4
Rhabdomyosarcoma	12/293	4.1
Synovial sarcoma	10/214	4.7
Other	52/1289	4.0

Distant metastatic sites were identified at the time of initial diagnosis in 558 of 2355 patients in the long-term study (23.4%) and 807 of 3457 patients in the short-term study (23.3%). The distribution of the anatomic sites for metastases in such patients is shown in Table 7. The lung was the most frequent single site but accounted for only one third of the metastatic lesions.

Accuracy of staging. The survey forms in both surveys asked for clinical diagnostic stage and surgical pathologic

TABLE 5. *Clinical Stage of Sarcoma Either Recorded and/or Calculated from Staging Elements*

	1977–1978		1983–1984	
	N	%	N	%
I	449	19.1	668	19.3
II	166	7.0	316	9.1
III	250	10.6	435	12.6
IV	330	14.0	465	13.4
Unknown	1160	49.3	1579	45.6
Total	2355	100.0	3463	100.0

TABLE 7. *Clinically Involved Distant Metastatic Sites at Time of Diagnosis of Sarcoma*

	1977–1978		1983–1984	
	N	%	N	%
Bone	126	22.6	191	23.7
Lung	186	33.3	275	34.1
Liver	83	14.9	126	15.7
Brain	19	3.4	22	2.7
Other	144	25.8	193	23.9
Total	558	100.0	807	100.0

TABLE 8. *Relationship of Clinical Stage of Sarcoma to Initial Treatment Used*

Clinical Stage	I		II		III		IV		Total	
	N	%	N	%	N	%	N	%	N	%
Initial treatment, surgery only										
1977–78	253	63.0	76	45.8	84	33.6	47	14.2	4010	42.9
1983–84	388	58.1	110	34.8	122	28.0	68	14.6	1418	40.9
Surgery and adjuvant therapy										
1977–78	134	29.8	79	47.5	135	54.0	144	43.6	956	40.6
1983–84	238	35.6	170	53.8	253	58.2	192	41.3	1488	43.0
Nonsurgical treatment only										
1977–78	13	2.9	7	4.2	21	8.4	115	34.8	268	11.4
1983–84	19	2.8	16	5.1	45	10.3	153	32.9	359	10.4
Other										
1977–78	19	4.2	4	2.4	10	4.0	24	7.3	121	5.2
1983–84	23	3.4	20	6.3	15	9.3	52	11.1	198	5.7

stage to be listed, but the individual elements for this staging (G [grade], T [tumor], N [nodes], M [metastasis]) were requested as well. This allowed computation of AJCC stage from these individual elements and comparison with the actual stage recorded. Incomplete listing of individual elements of the staging system, particularly G, or the absence of a listed summary stage reduced the number of patients for which this comparison could be made. However, there were 669 patients in the long-term study and 1139 patients in the short-term study in whom both the individual staging elements and the summary stage were recorded. There was good general agreement between the recorded stages and those computed from the GTNM elements.

Treatment

The choice of treatment for potentially curable soft tissue sarcomas in this study was operation, with or without nonsurgical adjuvant therapy (radiation and/or chemotherapy), but nonsurgical therapy was often chosen as the only treatment for patients with metastatic disease. The entire series was used for many prognostic comparisons. However, to judge the surgical approach from the curative standpoint, data from the subpopulation of patients in the total series that had no metastases were analyzed. This group consisted of 1679 patients in the long-term study and 2490 patients in the short-term study (or roughly three fourths of the entire series). All analyses of operation as the primary treatment use these slightly smaller groups from the two studies.

The distributions of treatment modalities according to stage for all patients in the long-term and short-term studies are shown in Table 8. There is a slightly higher frequency of combined surgical and nonsurgical therapy in the later survey, when compared with the earlier survey (43.0% *vs.* 40.6%), but there was no major change in the overall distribution of treatment approaches in the two periods. Radiation therapy was shown to be effective against soft tissue sarcomas and was used as the only locoregional treatment, particularly if distant metastases were present or if the primary lesion was not resectable. There appeared to be a similar rationale for systemic chemotherapy as the only treatment when metastases were present. Both of these nonsurgical methods were used as the only primary treatment in a very small population of patients in both the long-term and short-term studies.

Treatment by clinical stage. As already noted, the GTNM staging system developed by the AJCC was recorded or could be calculated for approximately one half of the patients. The correlation of treatment chosen with the clinical stage, when known, shows some interesting trends (Table 8). Two thirds of stage I lesions were treated by surgery alone, whereas one fourth of these patients had other treatments in addition. As the stage increased, there was a corresponding increase in the use of radiation therapy and/or chemotherapy combinations with surgery as well as an increase in the use of either radiation therapy

TABLE 9. *Type of Surgical Procedure Used in Sarcoma Patients without Metastases at Time of Diagnosis*

	1977–1978		1983–1984	
	N	%	N	%
Wide local resection	879	52.4	1412	56.7
Limited local resection	455	27.1	583	23.4
Anatomic compartmental resection	168	10.0	249	14.8
Amputation	108	6.4	138	8.2
More than one type of surgery	69	4.1	108	6.4
Total	1679	100.0	2490	100.0

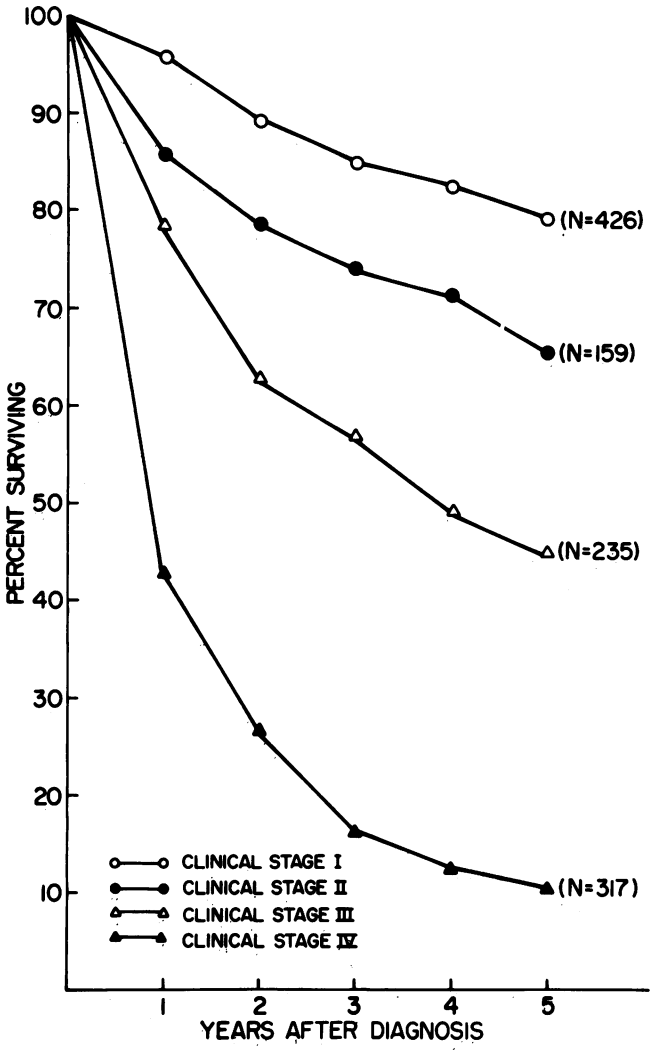

FIG. 1. Survival according to clinical stage (AJCC).

or chemotherapy alone. There was a slight overall increase in combination therapy, as opposed to surgery alone, in the more recent series.

Choice of operative procedure. The range of operative procedures used for patients without metastases is shown in Table 9. There was little change in these choices between the two intervals studied. Wide local resection was the most frequent approach; however, it was not possible to specifically determine the gross margins implied by any of these procedures.

Postsurgical resection pathologic stage. As with the clinical diagnostic stage, recording of postsurgical resection pathologic stage (AJCC) was incomplete in the data recorded. In the earlier series, pathologic stage was not recorded in 60% of the patients, but some improvement occurred by the time of the more recent survey (46% not recorded). The elements of staging that were recorded did allow surgical pathologic staging to be completed for 56% of the patients in the long-term study and 63% in the more recent study.

Treatment Results

Survival by stage. Five-year survival curves according to AJCC stage demonstrate prognostic value for this system (Fig. 1). Similar orderly separation of survival curves occurred when outcomes were differentiated by postsurgical resection pathologic stage (Fig. 2).

Survival by treatment. The survival data for surgery, surgery plus adjuvant radiation and/or chemotherapy, and radiation and/or chemotherapy without surgery were examined to detect any trends. Most patients who did not have complete gross surgical resection were in a more advanced stage, often with distant metastases, and this group had a much poorer survival (Fig. 3).

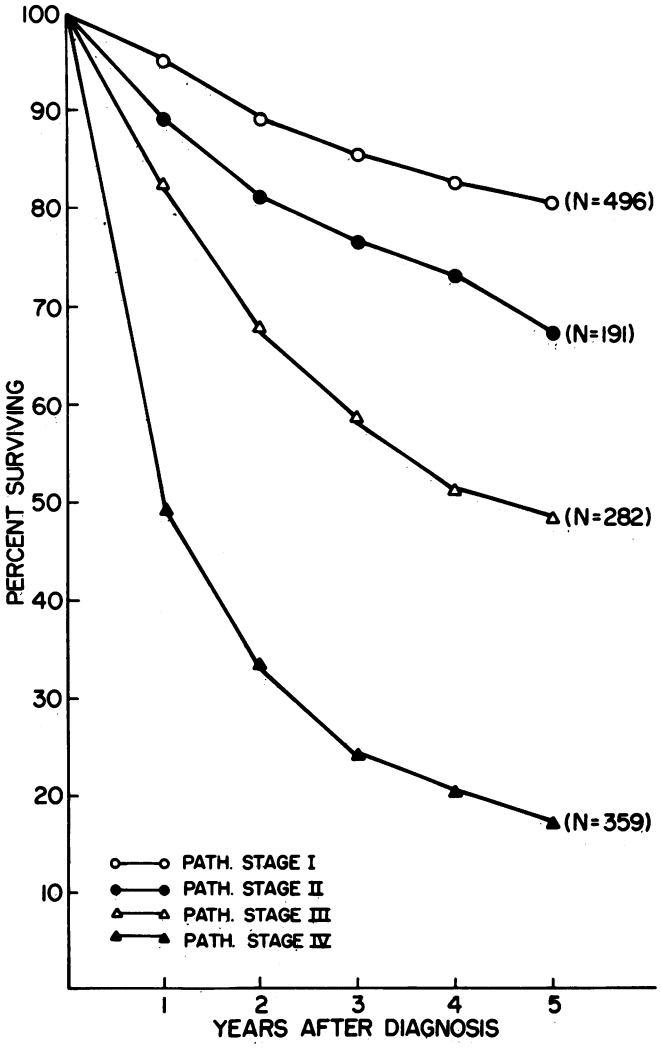

FIG. 2. Survival according to postsurgical pathologic stage (AJCC).

Curative resection. To determine the impact of the status of the surgical margin, tumor size, the anatomic primary site, the histologic type, and the presence or absence of adjuvant therapy, the subpopulation of patients without metastases but with total gross resection was used for additional analysis. For patients with total gross resection for whom precise information was available regarding the presence or absence of microscopic tumor involvement at the surgical margin, 14.5% of patients in the long-term study had "positive margins." This had an adverse effect on recurrence-free survival (Fig. 4) but no effect on overall survival. For patients with all gross tumor resected and no metastases, tumor size was a significant prognostic variable. The 5-year survival rate was 82% for tumors 5 cm or less, whereas this figure was 58% for tumors larger than 5 cm ($p < 0.05$).

Effect of anatomic site on prognosis. Using the same population of patients who had all gross tumor resected and no metastases, the anatomic site of the sarcoma was related to the prognosis in terms of 5-year disease-free survival. The retroperitoneal and mediastinal sites had a considerably worse prognosis than all other anatomic groups (Table 10), but the differences between the other sites were quite small.

Survival by histology. Five-year survival was examined according to the histologic type of soft tissue sarcoma in patients with total gross resection and no metastases. It is apparent that there is some variation on the basis of this factor (Table 11). Whether the differences noted actually are secondary to differences in histologic grade rather than presumed histogenetic site of origin is unclear from these data, but this is a reasonable potential explanation for the differences noted.

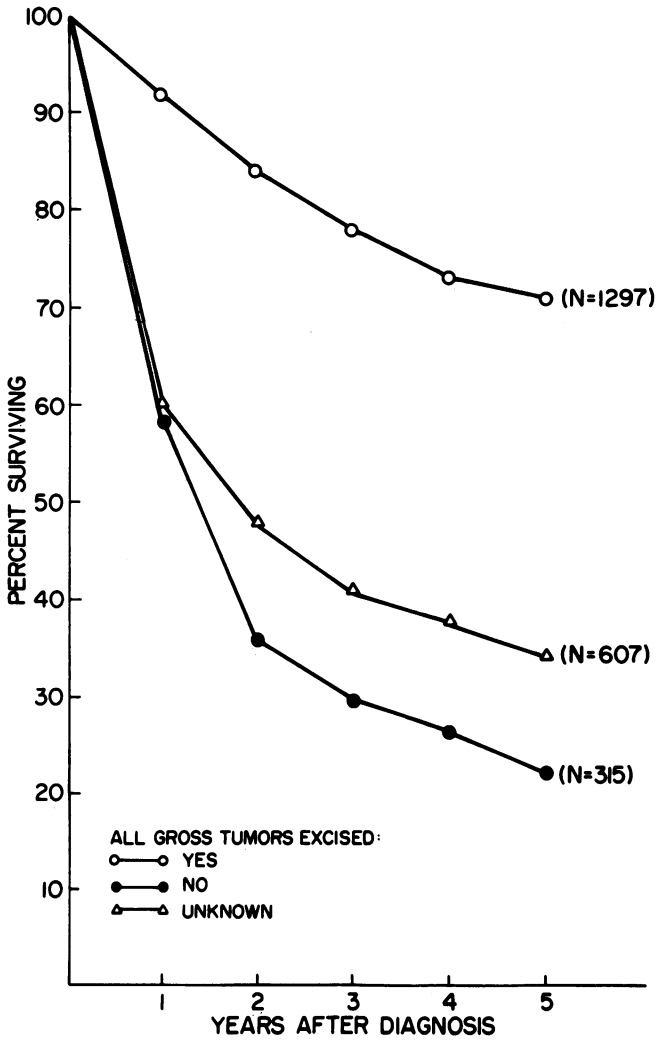

FIG. 3. Survival with or without total gross resection of sarcoma.

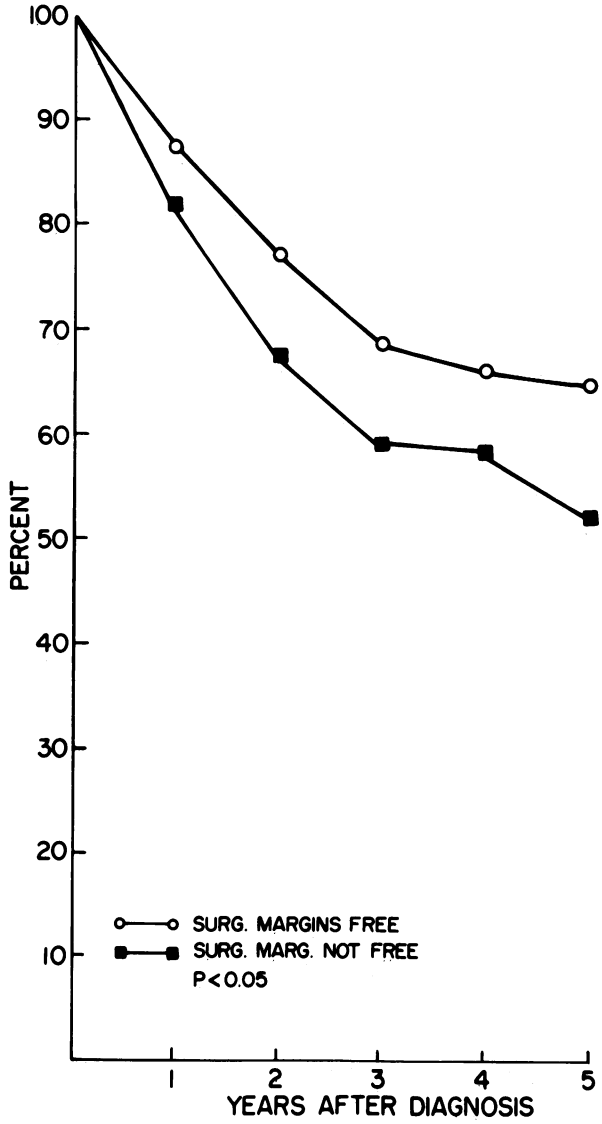

FIG. 4. Percent free of recurrence for soft-tissue sarcoma.

TABLE 10. *Five-year-Survival Data Regarding Anatomic Primary Site in Sarcoma Patients without Metastasis in Whom all Gross Neoplasm was Resected*

	Per cent Surviving 5 Years*	N†
Lower extremities	70.6	464
Upper extremities	84.0	143
Head and neck	81.0	83
Trunk	81.4	184
Retroperitoneum	48.1	69*
Mediastinum	33.3	3*
More than one site	72.7	11*

* Standard errors for these rates are greater than 5%.
† Number of patients at the beginning of the follow-up period.

Adjuvant therapy. The subpopulation of sarcoma patients without distant metastases and with grossly complete resection of the primary sarcoma was examined from the standpoint of added radiation treatment. There were 1229 patients in the long-term study for whom it was known that radiation was or was not applied as part of the initial treatment. There were 1910 such patients in the more recent short-term study. In the former group, 398 patients (32.4%) received adjuvant radiation, whereas 780 patients (40.8%) of the more recent study (1983–1984) received radiation. This adjuvant radiation was administered after operation (rather than before operation) in 93% of patients in the earlier study and 89% of patients in the more recent study.

Although the patient groups receiving radiation were not randomly assigned this adjuvant treatment, local treatment failure and 5-year survival data were compared for these groups that did or did not receive adjuvant radiation in the long-term study. There was a small difference in frequency of both local recurrence and 5-year survival in favor of the group receiving no adjuvant radiation, but this had no meaning since those patients selected for radiation therapy tended to have a more advanced clinical stage.

TABLE 11. *Five-year Survival Data Regarding Histologic Type in Sarcoma Patients Without Metastasis in Whom all Gross Neoplasm was Resected*

Histologic Type	Per cent Surviving 5 Years*	N†
Alveolar soft part sarcoma	40.0	5*
Angiosarcoma	64.7	17*
Fibrosarcoma	83.0	143
Leiomyosarcoma	69.5	147
Liposarcoma	82.8	329
Malignant fibrous histiocytoma	72.3	197
Malignant mesenchymoma	33.7	20*
Malignant schwannoma	65.7	37*
Rhabdomyosarcoma	54.6	63*
Synovial sarcoma	61.8	49*
Extraskeletal chondrosarcoma	69.2	13*
Extraskeletal osteosarcoma	60.0	5*
Sarcoma, Nos	61.4	39*

* Standard errors for these rates are greater than 5%.
† Number of patients at the beginning of the follow-up period.

A similar approach was taken with the data regarding adjuvant chemotherapy. There were 1225 patients in the earlier long-term study and 1892 patients in the more recent study who had no distant metastases, had complete gross tumor resection, and had definitive and reliable information regarding administration of adjuvant chemotherapy. There were 202 patients (16.5%) in the earlier long-term study who received adjuvant chemotherapy, whereas 318 patients (16.8%) received adjuvant chemotherapy in the recent period. As with adjuvant radiation, the survival curves for the patients in the long-term study with or without adjuvant chemotherapy had small differences in favor of those not receiving adjuvant chemotherapy. These will not be interpretable due to the stages not being comparable in these two nonrandomized groups.

Treatment Failures

Later treatment failure in patients without metastases at initial diagnosis and with total gross resection of the soft tissue sarcoma occurred in 452 of 1209 patients (37%) for whom adequate data were available. The patterns of treatment failure for this group are shown on Table 12. More than half demonstrated locoregional recurrence as the only initial site of treatment failure, and only 18% had lung metastasis as the only initial site of recurrence.

The results of salvage treatment of patients developing recurrence or metastasis after earlier definitive, and hopefully curative, treatment were analyzed. Five-year survival rate after salvage therapy for purely local treatment failure was 60.5%, whereas 20.8% of patients with lung metastasis as the only site of recurrence actually survived 5 years. If lung metastasis and other metastatic sites were both present, there was a 9.8% 5-year survival rate after secondary treatment.

Discussion

Patterns of care studies using the tumor registry data volunteered to the Commission on Cancer are particularly useful for the study of less common cancers in our population. That this study included a large proportion of the soft tissue sarcomas diagnosed in the United States is evident from the fact that the annual nationwide incidence is estimated by the American Cancer Society to be only 4800.[1] The clinical presentation of soft tissue sarcomas in regard to sex distribution, race, symptoms, and ana-

tomic site in these two large series reported herein is quite similar in the two intervals, and similar as well to previous smaller reports from individual institutions.[6,7] One important observation, in terms of the clinical presentation in both the long-term and short-term studies, was that there appeared to be a longer physician delay, in terms of diagnosis, than might be considered ideal. It should be stressed to physicians not already aware that a new soft tissue mass deserves prompt diagnostic investigation.

Most experienced surgeons consider an *incisional* biopsy preferable to a limited excisional biopsy for diagnosis of soft tissue tumors.[8] Most soft tissue sarcomas are large when first diagnosed, and a limited excisional biopsy may compromise the pathologic margins that might ultimately be achieved in a definitive resectional procedure. In view of the fact that this point has been stressed in recent years, it is surprising that excisional biopsy continued to be frequently used in the short-term survey. Needle biopsy has become a more frequent diagnostic approach for other forms of cancer, but it appears to be used rarely for the diagnosis of soft tissue sarcomas unless distant metastases are evident at the initial clinical presentation. This is fortunate due to the need for a greater amount of pathologic material for adequate histologic classification and grading of this type of neoplasm than that needed for more common cancers. It appears from this study that the optimal biopsy approach to soft tissue masses may be an important topic for education programs for practicing surgeons.

Distribution of sarcomas in terms of histologic type showed some changes between the earlier and more recent surveys, mainly an increase in use of the category malignant fibrous histiocytoma. There were similar age differences in both surveys in terms of the proportion of cases with the various histologic types when the data were separated into three major age groups, but the age trends noted have been appreciated in the past. Also, histologic categorization in terms of grade was much less frequently recorded than histologic type in both surveys. This deficiency in recording grade of the sarcoma may be related to a widespread dissatisfaction with microscopic grading among many surgical pathologists due to the lack of established uniform criteria. It does point out the clear-cut need for developing reproducible criteria for grading sarcomas.

The data obtained on the diagnostic workup used for assessing the extent of disease in these sarcoma patient populations showed an increasing dependency on CT scans of both the primary site and the thorax. Other complex radiographic procedures, such as angiography, lymphangiography, and radionuclide scans, are now uncommonly used despite brief earlier periods of enthusiasm for these tests. However, the most disappointing finding in the clinical approach to workup in both the long-term and short-term studies was the infrequent usage of the AJCC staging system. Emphasis on the use of the TNM system for staging in general and the GTNM for sarcomas, by both the AJCC and the Commission on Cancer, does not appear to have had much impact on these patterns of practice in the United States. Concerns regarding microscopic grading, alluded to previously, may well be the major deterrent to the use of this staging system. This is another area of focus for future medical education programs. For those patients in whom the clinical diagnostic stage could be determined, however, the prognostic value of the AJCC system was clearly confirmed with the larger number of patients than that used in the original formulation of this staging system.

TABLE 12. *Pattern of Initial Treatment Failure in Terms of Anatomic Site*

Site of Recurrence	Patient #	% Patients Undergoing Resection	% Patients with Treatment Failure
Locoregional only	236	19.5	52.2
Distant metastases	216	17.9	47.8
Lung only	83	6.9	18.4
Other sites only	91	7.5	20.1
Lung plus other sites	42	3.5	9.1
All sites	452	37.3	100.0

The trends in prognosis relating to size, histologic type, microscopic grade, and microscopic involvement of the surgical margin that could be determined in the study were in substantial agreement with findings previously reported by others. Also, the importance of different anatomic sites of origin was negligible except for the poorer prognosis observed for those lesions arising in the retroperitoneum.

Classically, clinical and histologic evidence of regional lymph node spread of cancer is an important prognostic indicator in the TNM staging systems, both clinical diagnostic and pathologic. For soft tissue sarcomas in adults, however, regional lymph node spread generally has been considered an uncommon event in earlier small series with a few exceptions being related to histologic type or grade.[9] The data from both surveys confirm this impression regarding infrequent regional lymphatic spread, despite the fact that biopsy for histologic study was infrequently performed. Regional lymph node involvement was identified rarely for all histologic types of soft tissue sarcoma.

Distant metastases from soft tissue sarcomas are known to occur in the lungs and this site has received the most emphasis in the past, both in terms of pretreatment evaluation and in terms of later treatment strategies.[10–12] It was a somewhat surprising finding in both of these surveys

that patients presenting with distant metastases at time of diagnosis had involvement of nonpulmonary sites more often than usually is appreciated. Only 18% of the patients with treatment failure after an operation with curative intent demonstrated metastatic spread to the lungs as the only site of recurrence. However, this did represent almost half of the patients who had distant metastasis without locoregional recurrence.

The distribution of treatment modalities revealed the expected increasing use of nonsurgical methods with increasing stage. For those patients with distant metastases, use of radiation and/or chemotherapy was the highest, as one might expect, whereas surgical resection with or without radiation and/or chemotherapy was used when it was feasible to completely excise the primary sarcoma.

Since surgical resection is considered the primary curative approach to soft tissue sarcomas, the subpopulation of patients without distant metastases and in whom all gross tumor was excised was separately analyzed to assess the importance of other factors. Among these it was found that the majority were treated by wide local resection, as generally recommended. The frequency of amputation was low in both periods. There has been recent publicity concerning the use of limb-sparing approaches,[13] but this is clearly much more of a recent innovation for osteosarcomas than it is for soft tissue sarcomas. One concern regarding the choice of operative approach, however, is the fact that surgical excision of soft tissue sarcomas with *limited* margins occurred in 27% of the patients in the earlier long-term study. This figure decreased only to 23% in the more recent period. Nevertheless, survival data for patients categorized in this survey as having limited margins at the time of resection were not particularly different from those following more extensive resectional procedures. The small subpopulation of patients with actual microscopic margin involvement did have a higher local failure rate than patients with clear margins, which should encourage surgeons to continue to adhere to the principle of wide local resection for soft tissue sarcomas if feasible.

Because limited resection margins are actually required in some clinical settings, particularly if amputation is to be avoided, the problem of possible local recurrence with limited margins has been addressed, often by using radiation therapy to supplement local operation.[14,15] In these reports, resection with limited margins was associated with control equal to that of wide radical resection if radiation therapy was added to the operative field. In this series, the end results with or without radiation were evaluated to see if there was evidence of therapeutic benefit from this adjuvant. The fact that these selected, nonrandomized treatment groups demonstrated a diminution in both recurrence-free and overall survival with administration of adjuvant radiation is not interpretable for obvious reasons. Factors affecting overall prognosis were undoubtedly used to help select patients for adjuvant radiation, thereby obscuring any possible benefit of this added therapy.

The beneficial effect of systemic chemotherapy as an adjuvant to resection is still unclear despite a number of randomized clinical trials. Multiple trials of various agents, many that include Adriamycin®, have shown no survival benefit despite the established palliative effectiveness of some agents in patients with advanced or recurrent disease.[16–18] A single exception to this finding is the clinical trial from the National Cancer Institute that used Adriamycin, Cytoxan®, and methotrexate as adjuvant therapy for resected extremity sarcomas.[19] The retrospective data in this study did not show improved survival from chemotherapy when used as an adjuvant with total gross resection in those patients who had no distant metastases at the time of diagnosis; however, the data are subject to the same criticism as those related to adjuvant radiation. There is a role for anticancer chemotherapy in the management of some patients with soft tissue sarcomas, but purely adjuvant chemotherapy for patients who have had total gross resection still must be considered an unproven therapeutic approach. These nonrandomized data certainly cannot prove anything about adjuvant therapy either way, and prospective clinical trials with control groups not receiving chemotherapy should be continued to resolve this issue.

Patients who fail locally or systemically some time after the initial treatment program represent a group of particular concern because retreatment of most human cancers is rarely successful. For this reason, the higher than expected 5-year survival rates of sarcoma patients who had some form of secondary treatment in this survey were surprising. The success that was achieved, however, tended to be limited for the most part to patients with locoregional rather than distant failure. This should stimulate continued treatment efforts for patients who have development of local regrowth of their sarcomas, but it should not encourage inadequate initial treatment. Secondary treatment often results in greater disability than a more radical initial operation. Similarly, data reported from selected series of resection for pulmonary metastases are somewhat more encouraging than the data from this approach presented here.[10–12] Although uncontrolled, these findings regarding secondary treatment for both local failure and for pulmonary metastases from such a large pool of sarcoma patients may give surgeons a more realistic view regarding the overall results of treatment for recurrent or metastatic disease in the United States.

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