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Defining the Incidence and Clinical Significance of Lymph Node Metastasis in Soft Tissue Sarcoma

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Abstract

Introduction—The incidence and clinical significance of lymph node metastasis (LNM, N1) in soft tissue sarcoma (STS) is unclear. Recent studies have focused on extremity/trunk STS (ETSTS). We sought to define the subgroup of patients with LNM at sarcoma diagnosis across all disease sites and histologies.

Methods—We identified and categorized 89,870 STS patients from the National Cancer Data Base (1998–2012) by nodal stage. Pathologically confirmed LNM (pN1) were identified in 1404 patients; 1750 had clinically suspicious but not pathologically confirmed LNM (cN1). Survival analyses were performed by Kaplan-Meier method.

Results—Of 3154 patients (3.5%) with pN1 or cN1 LNM at presentation, 1310 had synchronous distant metastasis (M1). LNM affected a small proportion of patients (5.8% head/neck, 5.3% intrathoracic, 5.1% intra-abdominal, 2.0% ETSTS). Angiosarcoma (6%), epithelioid (13%), clear cell (16%), and small cell sarcoma (19%) had the highest incidence of LNM, although liposarcoma, fibrous histiocytoma, and leiomyosarcoma accounted for the greatest number of LNM patients. For pN1M0 disease, median overall survival (OS) was 28.2 months, varying by histology. Among patients with pN1M0 STS, angiosarcoma, clear cell sarcoma, leiomyosarcoma, and fibrous histiocytoma were associated with worse median OS (19.4, 23.8, 27.1, and 29.3 months) compared to epithelioid sarcoma and liposarcoma (49.6 and 56.0 months, $p<0.001$).

Conclusion—Despite clinical suspicion, pathologic LN evaluation in STS is inconsistently performed. LNM occurs across anatomic disease sites and is unevenly distributed across histologies. Although M1 disease portends poor prognosis regardless of LN status, LNM predicts worse OS in a histology-dependent manner in M0 disease.

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Introduction

Lymph node (LN) metastases (N1) in patients with soft tissue sarcomas (STS) are uncommon, although the true incidence at the time of diagnosis across histologic subtypes and disease location is unclear. The reported incidence of LN metastasis in the literature varies widely, with rates typically reported in the range of 1.6–12%.[1–8] LN metastasis in STS is a negative prognostic factor for disease-specific survival (DSS) and overall survival (OS) with prior studies reporting 5-year survival rates ranging 10–33%[3,4,6,9,10] among patients with N1 disease. However, whether the clinical impact of N1 disease approximates that of distant metastatic disease (M1) is unknown as many prior studies examining LN metastasis in STS were often small single institution retrospective series and included patients with N1 disease at both initial disease presentation and at recurrence, those who underwent a variety of multimodality systemic and loco-regional treatments (including chemotherapy, regional therapy, radiation therapy, and lymphadenectomy), and also patients with synchronous M1 disease.[3,7–10]

The limited literature examining the incidence and clinical implication of LN metastasis in STS has predominantly focused on STS of the trunk and extremity disease sites[8,9,11,12] and a subset of histologic subtypes, including synovial sarcoma, rhabdomyosarcoma, clear cell sarcoma, epithelioid sarcoma, and angiosarcoma.[2–7,13,14] Although it has been thought that patients with these tumors are at the highest risk of LN metastasis, the data are sparse and not without major limitations. The aim of this study was to define the subgroup of STS patients with LN metastasis at diagnosis across all disease sites and histologies using a large prospectively maintained, hospital-based national cancer registry, the National Cancer Database (NCDB).

Materials and Methods

Data source

The NCDB is a prospective, hospital-based cancer registry sponsored by the American College of Surgeons and the American Cancer Society. The NCDB captures approximately 70% of all new cases of cancer in the United States and includes clinicopathologic, treatment, and outcome variables. The data are de-identified and thus this study was considered exempt by The University of Texas MD Anderson Cancer Center Institutional Review Board.

Inclusion and exclusion criteria

The NCDB Sarcoma Participant Use File (1998–2012) contained 99,876 patients, which was narrowed to 89,870 patients as follows. Within the NCDB, sarcomas are classified using the International Classification of Diseases for Oncology third edition (ICD-O-3). ICD-O consists of two axes that describe the tumor: 1) the topographical code describes the anatomical site (or organ system) of origin of the tumor and 2) the morphological code describes the cell type (or histology) of the tumor. Topographical codes C480, C490, C491, C492, C493, C494, C495, and C496 were included and histologic diagnoses were individually reviewed to exclude those that were non-sarcomatous or mixed as previously

described (Supplemental Table 1).[15] Additional subgroups were also excluded: pediatric patients, central nervous system and bone sarcomas, patients not treated at the reporting hospital, and patients with incomplete information.

Definition of lymph node involvement

Patients were categorized by nodal and distant metastatic stage according to the seventh edition of the American Joint Committee on Cancer (AJCC) sarcoma staging guidelines.[16] Nodal stage status was further categorized as pN1 for patients who had pathologically confirmed nodal disease and cN1 for patients who had clinically suspicious but not pathologically confirmed nodal involvement. Pathologically confirmed nodal disease (pN1) was identified using the PUF data item "REGIONAL_NODES_POSITIVE" rather than the data item "TNM_PATH_N" as the former is based on pathology information only while the latter is completed by registry staff, although there was overall excellent concordance between these two data items. Patients were thus classified as pN1 if they were documented as having regional lymph nodes involved by "REGIONAL_NODES_POSITIVE" regardless of "TNM_PATH_N" status. Clinically suspicious but not pathologically confirmed nodal involvement (cN1) was defined using the PUF data items "REGIONAL_NODES_POSITIVE" and "TNM_CLIN_N." "TNM_CLIN_N" is defined by the American Joint Committee on Cancer (AJCC) Staging Manual version 7 in the NCDB. Patients were classified as cN1 if "REGIONAL_NODES_POSITIVE" was documented as "no nodes examined" or "unknown whether nodes are positive, not applicable, or not stated in patient record" but for whom "TNM_CLIN_N" was positive for lymph node involvement. A small number of patients (n=136) were excluded as "REGIONAL_NODES_POSITIVE" and "TNM_CLIN_N" were discordant such that they were documented in the NCDB as having regional lymph nodes negative for tumor involvement on pathologic review but clinically node positive.

Of note, for patients who had regional lymph nodes pathologically evaluated, there was insufficient data available within the NCDB to determine if 1) lymph node sampling had been deliberate and the patient underwent either fine needle aspirate, core needle biopsy, or sentinel lymph node biopsy, 2) lymph node evaluation had been deliberate and the patient underwent regional lymphadenectomy), or 3) lymph node sampling had been unintentional with regional lymph node included in surgical resection specimen. Additionally, for patients who were documented as having clinical lymph node involvement under the data item "TNM_CLIN_N," information regarding how clinical lymph node staging was performed (whether on physical exam and/or imaging) is not available in the NCDB.

Statistical analysis

Survival data was available for the years 1998–2011 in the NCDB (n=82,675). The Kaplan-Meier estimator was used to calculate unadjusted OS curves and the results were compared using the log-rank test. $P < 0.05$ was considered statistically significant. SAS version 9.4 was used to conduct all analyses.

Results

Pathologic evaluation of lymph node status is inconsistently performed

We identified 89,870 patients from the NCDB (1998–2012) with STS. Overall, LN metastasis affected a small proportion of patients (n=3154, 3.5%). Pathologic evaluation of LN status in patients with STS in the NCDB was inconsistently performed. Of 3154 (3.5%) patients with LN metastasis at presentation, 44.5% (n=1404) had pathologically confirmed LN metastasis (pN1) and 55.5% (n=1750) had clinically suspicious but not pathologically confirmed LN involvement (cN1). Of patients with LN metastasis at diagnosis, 58.5% of patients (n=1844) had LN metastasis without distant metastatic disease (cN1M0 or pN1M0) while 41.5% (n=1310) had synchronous distant metastases (cN1M1 or pN1M1) (Table 1). LN involvement was pathologically confirmed more often in patients without distant metastatic disease [58.7%, (pN1M0)/(pN1M0+cN1M0)] than in those with distant metastatic disease [24.6%, (pN1M1)/(pN1M1+cN1M1) (Table 1).

Lymph node metastasis in STS occurs across disease sites

LN metastasis affected those with STS of the head/neck (5.8%, n=328 of 5,667 patients), intrathoracic (5.3%, n=392 of 7,340 patients), and intraabdominal/retroperitoneal (5.1%, n=1,457 of 28,661 patients) sites more frequently than those with STS of the trunk or extremities (2%, n=977 of 48,202 patients) ($p<0.001$). Among those without distant metastatic disease (M0) at presentation, LN metastasis also affected those with STS of the trunk or extremities less frequently compared to STS of other disease sites (head neck 4.5%, intrathoracic 3.1%, intraabdominal/retroperitoneal 4.5%, trunk/extremity 1.1%) ($p<0.001$) (Table 1).

Lymph node metastasis does not impact upon OS in the presence of synchronous M1 disease but is associated with worse OS in the absence of M1 disease

Distant metastatic disease (M1) at STS presentation is associated with worse OS (median 0.8 years, 5-year OS 10 %) (Figure 1). N stage had no impact on OS among patients with synchronous M1 disease, with similar OS between N0M1, pN1M1, and cN1M1 subgroups of patients (median OS 0.8, 1.0, 0.5 years, respectively; 5-year OS 10.1, 14.2, 7.2 %, respectively) (Figure 1).

Patients with LN metastasis in the absence of distant metastatic disease had intermediate OS compared to those with N0M0 and M1 disease (median OS in years: N0M0=8.5, pN1M0=2.4, cN1M0=1.1, M1=0.8; 5-year OS: N0M0=61.1%, pN1M0=34.1%, cN1M0=21.9%, M1=10%).

Incidence of lymph node metastasis at presentation is unevenly distributed across histologies

The incidence of LN metastasis differed across STS histologies with small cell sarcoma (19.1%), clear cell sarcoma (15.9%), epithelioid sarcoma (13.1%), and angiosarcoma (6.1%) having the highest percent of patients presenting with LN involvement (Table 2, Figure 2a). Patients with these histologies who had LN metastasis frequently had synchronous distant metastatic disease at presentation as well (Figure 2b). Additionally, as small cell sarcoma,

clear cell sarcoma, and epithelioid sarcoma are less common STS histologies overall (accounting for 0.7%, 0.6%, 1.3%, and 3.6% of the overall study cohort, respectively), the more prevalent histologies of liposarcoma (22.7% of the cohort), fibrous histiocytoma (14.6% of the cohort), and leiomyosarcoma (17.5% of the cohort) accounted for the greatest number of LN metastasis patients in this cohort (n = 478, 371, and 331, respectively, Table 2).

Lymph node metastasis in STS is associated with worse OS across all histologies, with greatest negative impact in histologies with better overall prognosis

Across all STS histologies, LN metastasis in the absence of distant metastatic disease negatively impacts OS and confers an intermediate OS compared to patients with N0M0 and M1 disease. However, degree of impact of LN metastasis on OS may differ between histologic subtypes. Among patients with pN1M0 STS, angiosarcoma, clear cell sarcoma, leiomyosarcoma, and fibrous histiocytoma were associated with worse median OS (19.4, 23.8, 27.1, and 29.3 months) compared to epithelioid sarcoma and liposarcoma (49.6 and 56.0 months, $p<0.001$). Survival curves of patients with N1M0 disease more closely approximates those of M1 patients than N0M0 patients for histologies such as leiomyosarcoma, clear cell sarcoma and angiosarcoma compared to epithelioid sarcoma, for example (Figure 3).

Discussion

In this study, we defined the subgroup of patients with LN metastasis at presentation of soft tissue sarcoma using the NCDB, a national cancer registry. We found that although pathologic evaluation of LN status in STS is inconsistently performed, the overall incidence of LN metastasis at presentation across STS histologies and disease locations is low (3.5%). Additionally, the incidence of LN metastasis is lowest (2%) in the trunk and extremity locations, which are the disease sites that have been the subject of much of the recent literature on LN metastasis in STS. We also report that the impact of LN metastasis at presentation in STS on OS appears to be a prognostic factor only in the absence of synchronous distant metastatic disease (2.1% of patients) (Table 1). For patients with M0 disease, the risk of LN metastasis at presentation is highest for select STS histologies, including small cell sarcoma (6.2%), clear cell sarcoma (11.1%), epithelioid sarcoma (8.7%), and angiosarcoma (4.0%) (Figure 2b, Supplemental Table 2).

We report an overall low incidence of LN metastasis in STS at presentation, which is consistent with rates reported by others including an early study by Fong (2.6%)[6] and more recent studies by Daigeler (1.8%)[4] and Behranwala (3.4%).[3] Higher rates of LN metastasis have been reported by Mazaron (5.9%),[7] Ecker (5.9%),[5] and Sherman (15%),[11] although these studies examined selected patient cohorts at increased risk of LN metastasis. Unlike others, we found that LN metastasis at presentation in patients with STS of the trunk and extremity occurred not only infrequently (2% of cases overall), but in the absence of synchronous distant metastatic disease only affected ~1% of patients. This is contrary to exceedingly high rates of LN metastasis in STS of the trunk and extremity reported by Fong and Behranwala of 62.6% and 70%[3,6] in single institution, retrospective studies but similar

to the reported incidence of 0.9% in a SEER database study by Johannesmeyer et al.[8] Indeed, in this study, head/neck/face, intrathoracic and intraabdominal/visceral sites all had higher rates of pathologically confirmed lymph node metastasis (pN1M0 3%, 1.7% and 1.5%, respectively) and higher rates of clinically suspicious but not pathologically confirmed lymph node metastasis (cN1M0 1.5%, 1.4%, and 1.4%, respectively) compared to extremity/truncal sarcomas (pN1M0 0.7% and cN1M0 0.4%) (Table 1). It is difficult to determine the reason for these differences using the NCDB given the limitations of this registry. However, there are multiple potential hypotheses that warrant evaluation in future studies. First, it is possible, depending on sarcoma disease site, that there may be systematic differences in how the treating clinicians examine, image, and stage patients. Additionally, it is possible that inadvertent lymph node removal with the primary sarcoma specimen at the time of surgery is more likely to occur for the head/neck/face, intrathoracic, and intraabdominal locations than for extremity or truncal locations. Another possible contributing factor may be that sarcoma histologies in this study were unevenly distributed across disease sites (Supplemental Table 2).

Our results support the assertion that the risk of LN metastasis at presentation is higher in select STS histologies, including small sarcoma (19.1%), clear cell sarcoma (15.9%), epithelioid sarcoma (13.1%), and angiosarcoma (6.1%) (Figure 2a, Table 2, Supplemental Table 2). Excluding patients with synchronous distant metastatic disease at presentation, the rates of LN metastasis at presentation across these histologies in this cohort were 6.2%, 11.3%, 8.7% and 4%, respectively (Figure 2b). Increased risk of LN metastasis in these histologic subtypes have previously been reported, although rates have varied widely (clear cell sarcoma 10.8–38%, epithelioid sarcoma 9.8–30%, angiosarcoma 3.2–20%).[3–8,10] Unlike some of these studies, however, we did not find significant rates of LN metastasis in other previously reported histologies, such as synovial sarcoma 3.3%.[3,5–8,10] Such studies have been limited by small patient numbers, mixture of synchronous and metachronous LN metastasis presentation, and likely variation in practices with respect to LN evaluation and staging by imaging, radiographically guided or surgical biopsy or excision. The prognostic impact of LN metastasis, and thus the potential benefit of any nodal staging and treatment in these high-risk STS histologies, appears to be restricted to the subset of patients with isolated N1 disease in the absence of M0 disease (Figure 2, Figure 3, Supplemental Table 2).

It is intriguing that cN1M0 disease is associated with worse OS compared to pN1M0 disease both across histologies (Figure 1) and within histologies (Figure 3). Although this finding cannot be fully explained given the inherent limitations of the NCDB, it is hypothesis-generating and would be of interest to investigate in future studies. It is possible that patients with cN1M0 disease had higher burden of metastatic disease compared to those with pN1M0 disease such that lymph node enlargement was detectable on physical exam or imaging. Patients with cN1M0 vs pN1M0 disease within a given histology may have also received different treatment approaches and regimens affecting their disease outcomes.

The utility of LN staging in STS, whether pursued in a disease site or histology specific approach remains unclear and multi-institutional prospective data are needed to better address this question. Within the NCDB for sarcoma for the study period, we cannot distinguish between lymph node sampling/evaluation performed intentionally by biopsy (i.e.

fine needle aspiration, FNA; core needle biopsy, CNB; or sentinel lymph node biopsy, SLNB), regional lymphadenectomy, or unintentional en bloc inclusion/resection of lymph nodes with the primary tumor at the time of surgical resection. Some have advocated considering routine evaluation and staging for LN involvement at time of STS presentation, particular for histologies considered to have significant risk of regional LN involvement.[2,13] Although the data are limited, multiple groups have reported the feasibility of SLNB in STS of the trunk and extremities.[13,14,17–19] There has been no prospective data that definitively demonstrates that SLNB or regional lymphadenectomy improves patient outcome in STS, however. Overall, the data regarding the utility, positive and negative predictive values, and applicability of LN evaluation by either imaging or tissue evaluation remains limited and inadequate to guide management of high-risk STS patients.

The impact of radical lymphadenectomy of regional nodal basins in patients with LN metastasis at time of diagnosis or which develop metachronously has been investigated in several small, retrospective studies and is currently recommended a part of a multidisciplinary treatment plan for patients with stage III extremity/truncal and head/neck STS in the National Comprehensive Cancer Network (NCCN) guidelines.[6,9,10,12,20] Fong et al reported longer median survival in patients with LN metastasis who underwent lymphadenectomy compared to patients not treated with resection (16.3 versus 5.9 months, p=0.003), although this study included patients with metachronous LN metastasis as well as bone sarcomas in addition to STS.[6] Al-Refaie et al examined the role of lymphadenectomy for isolated LN metastasis in extremity STS in 35 patients, with 20 of these patients diagnosed with LN metastasis at time of primary sarcoma diagnosis.[9] In these patients who underwent lymphadenectomy, 5-year OS was 52% compared to 66% for those with metachronous LN metastasis, although the difference did not reach statistical significance (p=0.35). These survival data are significantly better and inconsistent with what has previously been reported in the literature for patients with N1M0 disease (Behranwala 23.9%, Daigeler 12.8%)[3,4] and with our findings for this NCDB cohort. The authors report a positive effect of lymphadenectomy on survival outcome in patients with LN metastasis. However, the study is limited by small case numbers and confounded by patients having received multimodality treatments including external-beam radiation, systemic chemotherapy, and isolated limb perfusion. More recently, Sawamura identified 49 patients with LN metastases among 871 (6%) with STS with 45% of these LN metastases presenting at initial diagnosis.[10] Five-year OS was 27% in this group, however those who underwent “lymph node excision” were observed to have improved survival at 1.5 years follow-up, although this difference disappeared at 5-years follow-up.

Our study is not without limitations, including those inherent to any NCDB analysis. First, the data from the NCDB is acquired from hospitals across the US and thus there may be variability in management of STS and possible inconsistencies in pathologic diagnoses across institutions. Secondly, data regarding disease-free survival and disease-specific survival are not included in the NCDB. Lastly, prior to 2016, it was not possible to determine the means by which pathologic evaluation of N stage was performed. These might have included radiographically guided biopsy, such as fine needle aspiration; surgical lymph node excision, either by SLNB, lymphadenectomy of a regional nodal basin; or incidental removal of peri-tumoral lymph nodes during resection of the primary sarcoma. Nevertheless,

the NCDB remains a powerful resource to interrogate rare events such as LN metastasis occurring in STS, a spectrum of rare tumors.

In conclusion, LN metastasis from STS are rare, although pathologic lymph node evaluation is inconsistently performed and the true incidence of LN metastasis is challenging to establish. LN metastasis occurs across anatomic disease sites, least commonly affecting STS of the trunk and extremities and more commonly associated with small cell sarcoma, clear cell sarcoma, epithelioid sarcoma, and angiosarcoma histologies. Although patients with distant metastatic disease have poor prognosis regardless of LN metastasis status, in those without distant metastases at presentation LN metastasis is a negative predictor of OS in a histology-dependent manner. The utility and best approach to LN evaluation and staging as well as management of LN metastasis remains unclear and warrants multi-institutional prospective examination.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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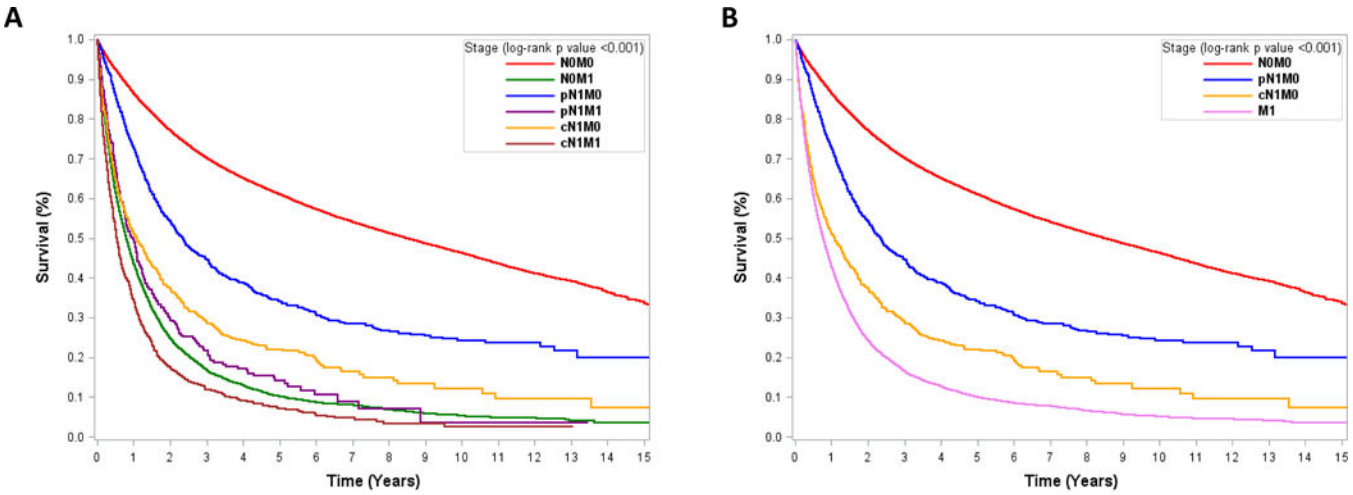

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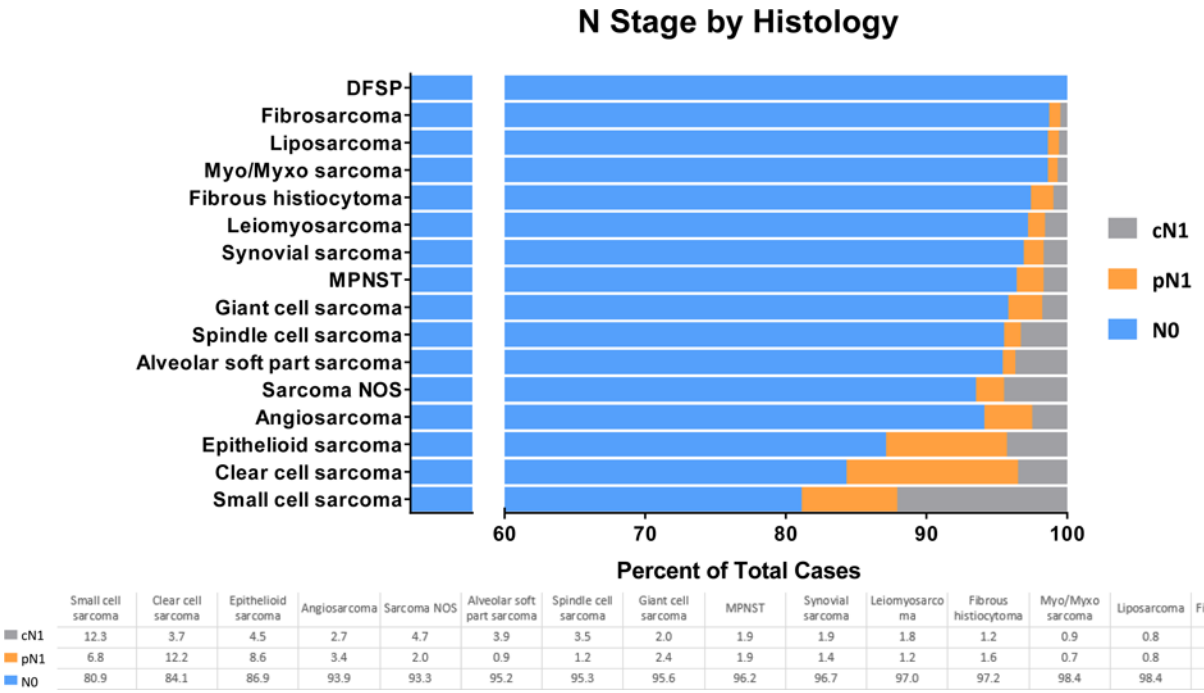
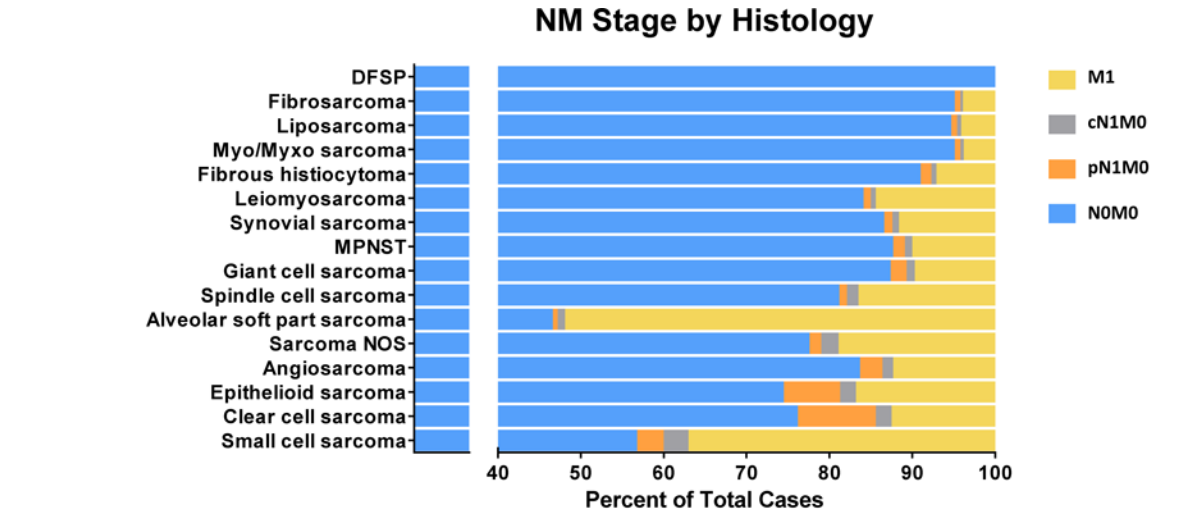
Stage	N	%	Median survival time (years)	5-year survival (%)
N0M0	72,474	87.7	8.47	61.1
pN1M0	992	1.2	2.35	34.1
cN1M0	684	0.8	1.10	21.9
M1	8525	10.3	0.77	10.0
N0M1	7360	8.9	0.80	10.1
pN1M1	299	0.4	0.98	14.2
cN1M1	866	1.1	0.54	7.1

Figure 1.

Overall survival by sarcoma stage (1998–2011). (A) Survival curves by N and M stage; (B) Survival curves by N stage in patients without distant metastatic disease compared to those with metastatic disease of any N stage; (C) Median and 5-year overall survival by N and M stage



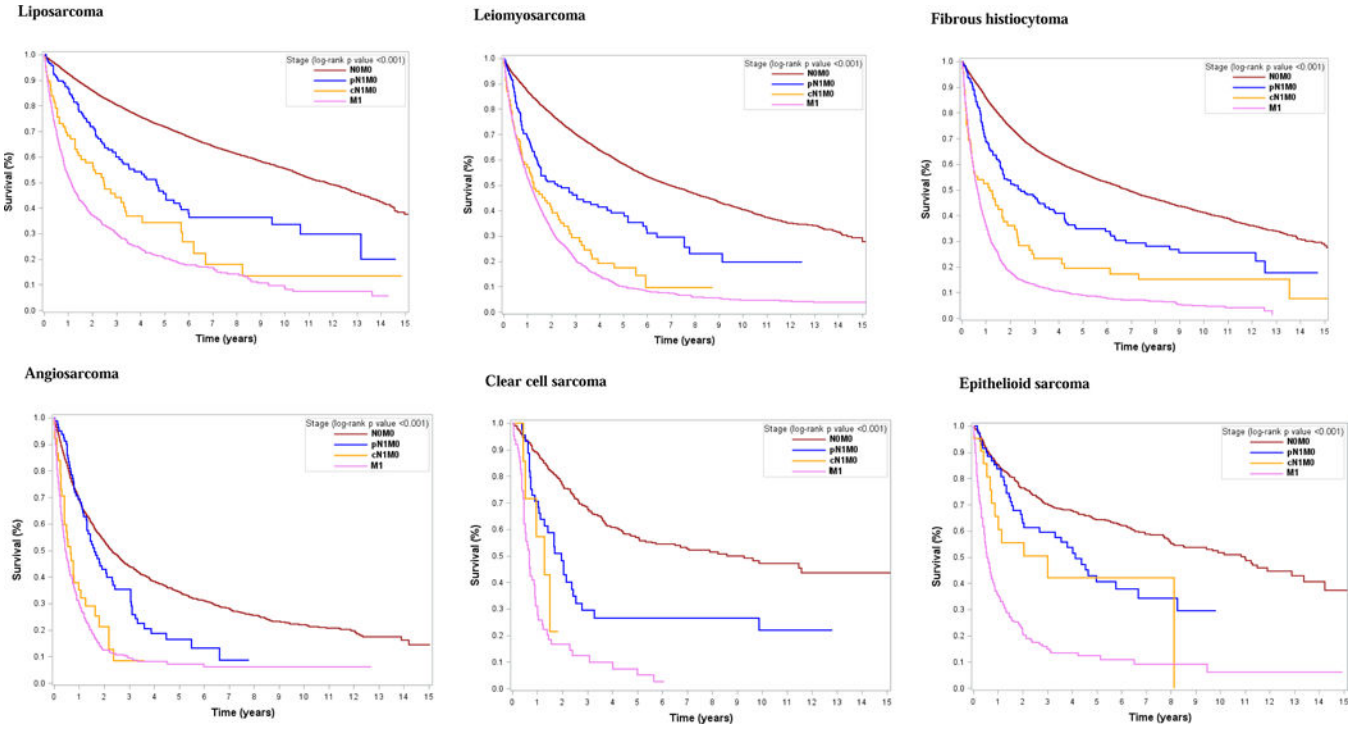
	Small cell sarcoma	Clear cell sarcoma	Epithelioid sarcoma	Angiosarcoma	Sarcoma NOS	Alveolar soft part sarcoma	Spindle cell sarcoma	Giant cell sarcoma	MPNST	Synovial sarcoma	Leiomyosarcoma	Fibrous histiocytoma	Myo/Myxo sarcoma	Liposarcoma	Fibrosarcoma	DFSP
cN1	12.3	3.7	4.5	2.7	4.7	3.9	3.5	2.0	1.9	1.9	1.8	1.2	0.9	0.8	0.7	0.2
pN1	6.8	12.2	8.6	3.4	2.0	0.9	1.2	2.4	1.9	1.4	1.2	1.6	0.7	0.8	0.8	0.0
N0	80.9	84.1	86.9	93.9	93.3	95.2	95.3	95.6	96.2	96.7	97.0	97.2	98.4	98.4	98.5	99.8



	Small cell sarcoma	Clear cell sarcoma	Epithelioid sarcoma	Angiosarcoma	Sarcoma NOS	Alveolar soft part sarcoma	Spindle cell sarcoma	Giant cell sarcoma	MPNST	Synovial sarcoma	Leiomyosarcoma	Fibrous histiocytoma	Myo/Myxo sarcoma	Liposarcoma	Fibrosarcoma	DFSP
M1	37.2	12.8	17.0	12.5	19.2	52.2	16.8	10.0	10.3	11.9	14.7	7.4	4.1	4.4	4.3	0.1
cN1M0	3.0	1.9	1.9	1.3	2.1	0.9	1.4	1.0	0.9	0.8	0.6	0.6	0.4	0.5	0.3	0.1
pN1M0	3.2	9.4	6.8	2.7	1.4	0.6	0.9	1.9	1.4	1.0	0.9	1.3	0.7	0.7	0.7	0.0
N0M0	56.5	75.9	74.2	83.4	77.3	46.3	80.9	87.1	87.4	86.3	83.8	90.7	94.8	94.4	94.8	99.7

Figure 2.

Distribution of N and NM stage by histology. (a) N stage by histology; (b) NM stage by histology



Stage	5-year survival (%)					
	Liposarcoma	Leiomyosarcoma	Fibrous histiocytoma	Angiosarcoma	Clear cell sarcoma	Epithelioid sarcoma
N0M0	71.9	58.4	56.4	34.3	57	64.4
pN1M0	45.5	39	34.7	16.6	26.5	40.6
cN1M0	34.4	17.4	19.4	-	-	42
M1	20.3	10	8.9	8.1	7.5	12.3
N0M1	20.4	10.2	9.5	5.7	13.4	8.5
pN1M1	34.3	18.9	11.1	19.6	0	34.7
cN1M1	14.5	4.8	1.5	11.1	0	22.9

Figure 3.

Histology-specific overall survival by NM stage. (A) Survival curves by N and M stage; (B) 5-year overall survival by N and M stage

Table 1

Soft tissue sarcoma stage by disease site

	N0M0 Number (row %)	pN1M0 Number (row %)	cN1M0 Number (row)	M1 Number (row %)
All sites (n=89,870)	78,665 (87.5 %)	1,082 (1.2 %)	762 (0.9 %)	9,361 (10.4 %) pN1M1: 322 cN1M1: 988
Head/Neck/Face (n=5,667)	5,055 (89.2 %)	169 (3.0 %)	82 (1.5 %)	361 (6.4 %)
Intrathoracic (n=7,340)	6,205 (84.5 %)	123 (1.7 %)	102 (1.4 %)	910 (12.4 %)
Intraabdominal/Visceral (n=28,661)	23,395 (81.6 %)	436 (1.5 %)	388 (1.4 %)	4,442 (15.5 %)
Extremity/Truncal (n=48,202)	44,010 (91.3 %)	354 (0.7 %)	190 (0.4 %)	3,648 (7.6 %)

cN1: clinically suspicious but not pathologically confirmed lymph node metastasis

M0: no distant metastatic disease

M1: distant metastatic disease

pN1: pathologically confirmed lymph node metastasis

Table 2

Soft tissue sarcoma patients with lymph node metastasis (pN1M0, pN1M1, cN1M0, or cN1M1 disease) by tumor histology and disease site

Histology	% (Number) of Patients with Lymph Node Metastasis Among All Patients with the Indicated Sarcoma Histology and Disease Location				
	All Sites	**Head/Neck/Face**	**Intrathoracic**	**Intraabdominal/Visceral**	**Extremity/Truncal**
Small cell sarcoma	**19.1** % (126)	11.1% (2)	5.6 % (1)	26.5 % (112)	6.9 % (12)
Clear cell sarcoma	**15.9** % (86)	18.7 % (3)	18.2 % (4)	23.4 % (11)	15.0 % (68)
Epithelioid sarcoma	**13.1** % (148)	21.3 % (10)	15.3 % (13)	15.6 % (48)	11.2 % (77)
Angiosarcoma	**6.1** % (200)	7.1 % (78)	4.5 % (29)	9.6 % (46)	4.9 % (47)
Sarcoma NOS	6.7 % (663)	9.9 % (63)	10.2 % (113)	9.2 % (314)	3.7 % (173)
Alveolar soft part sarcoma	4.8 % (16)	0 % (0)	8 % (2)	8.1 % (5)	3.7 % (9)
Spindle cell sarcoma	4.7 % (215)	5.5 % (19)	6.2 % (37)	6.8 % (37)	2.8 % (60)
Giant cell sarcoma	4.4 % (212)	10.8 % (27)	7.3 % (31)	6.5 % (62)	2.9 % (92)
MPNST	3.8 % (61)	4.6 % (7)	8.3 % (17)	4.0 % (16)	2.5 % (21)
Synovial sarcoma	3.3 % (135)	5.6 % (13)	6.6 % (27)	4.1 % (22)	2.5 % (73)
Leiomyosarcoma	3.0 % (**478**)	3.9 % (28)	4.3 % (37)	4.2 % (347)	1.1 % (66)
Fibrous histiocytoma	2.8 % (**371**)	4.9 % (53)	4.5 % (46)	5.8 % (107)	1.8 % (165)
Myo/Myxo sarcoma	1.6 % (11)	0 % (0)	0 % (0)	3.3 % (4)	1.4 % (7)
Liposarcoma	1.6 % (**331**)	2.5 % (11)	2.2 % (10)	2.8 % (240)	0.7 % (70)
Fibrosarcoma	1.5 % (87)	4.3 % (15)	2.9 % (15)	2.6 % (23)	0.9 % (34)
DFSP	0.2 % (6)	0.4 % (1)	0.3 % (1)	0.2 % (1)	0.2 % (3)

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