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Body Wall and Visceral Nonrhabdomyosarcoma Soft Tissue Sarcomas in Children and Adolescents

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Abstract

Background—Predictors of outcome have not been established for pediatric visceral and body wall non-rhabdomyosarcoma soft tissue sarcomas (NRSTS).

Methods—Retrospective review of clinical features and outcome of 61 patients with visceral and body wall NRSTS evaluated at our institution between March 1962 and December 1999.

Results—Median age at diagnosis was 9.9 years (range, birth–17.4 years). Tumors were >5 cm in 43 (70%), high grade in 33 (54%), invasive in 25 (41%) and metastatic at presentation in 14 (23%) patients. Visceral tumors (n=27) were more likely than body wall tumors (n=34) to be >5 cm (93% versus 53%, $p<0.001$) and invasive (70% versus 18%, $p<0.001$), and were less likely to be resected at diagnosis (44% versus 85%, $p=0.001$). Estimated 10-year event-free survival (EFS) and overall survival (OS) for the entire cohort were $45.5\pm6.9\%$ and $56.8\pm6.7\%$, respectively. The 10-year EFS and OS were better for patients with body wall sites than for those with visceral sites ($61.8\pm8.5\%$ and $67.5\pm8.2\%$ versus $24.2\pm9.4\%$ and $43.0\pm10.3\%$, $p=0.004$ and $p=0.004$). The 10-year estimated cumulative incidence (CI) of local recurrence was higher for patients with visceral sites than for those with body wall sites ($64.3\pm9.8\%$ versus $26.5\pm7.7\%$, $p=0.004$), whereas CI of distant recurrence was similar for the two sites ($15.2\pm7.2\%$ versus $23.5\pm7.4\%$, $p=0.39$).

Conclusions—Pediatric patients with visceral NRSTS are more likely to have invasive, large, and unresectable tumors compared to those with body wall tumors. More than two-thirds of visceral NRSTS recur locally and fewer than half of patients with visceral tumors survive.

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Keywords

non-rhabdomyosarcoma soft tissue sarcoma; pediatric; trunk; body wall; visceral

Introduction

Nonrhabdomyosarcoma soft tissue sarcomas (NRSTS) are a heterogeneous group of histologically and biologically distinct tumors of mesenchymal origin that comprise approximately 3-4% of all pediatric malignancies [1]. In children and adolescents, the most common histologies include synovial sarcoma, malignant peripheral nerve sheath tumor, malignant fibrous histiocytoma and fibrosarcoma [1-5]. Tumor size, grade, invasiveness, resectability, and extent (presence or absence of metastases) contribute to overall outcome [2,6-8]. Complete surgical resection offers the best chance of cure [4,9]. Radiotherapy plays an important part in local control of microscopic residual disease after surgery and may facilitate delayed resection of initially unresectable tumors. The role of chemotherapy remains controversial, though its use is most clearly indicated in a neoadjuvant setting, with or without radiotherapy, to facilitate resection of tumors that are unresectable at initial presentation.

NRSTS can occur anywhere in the body, but most often originate in the extremity and less often in the trunk and head and neck regions [2,7]. As in adults, non-extremity sites overall seem to have a worse outcome than extremity tumors [2,10,11]. Studies in adults suggest that the factors that influence outcome in patients with trunk wall and extremity tumors (tumor grade, size, extent of resection) are similar and thus these patients are often treated together on clinical trials.[12,13] Adults with retroperitoneal tumors have a worse overall prognosis, which is predicted mainly by tumor grade and extent of resection. In this study, we retrospectively reviewed the clinico-pathologic features and outcomes of patients with body wall and visceral NRSTS to better understand the features that predict outcome in pediatric patients. Better understanding the nature of tumors at these anatomic sites may provide insights into a better approach to treatment.

Patients and Methods

Patients

Between March 1962 and December 1999, 234 patients younger than 21 years of age with NRSTS were evaluated at St. Jude Children's Research Hospital. One-hundred and twenty-three had primary tumors arising in the extremity and 44 in the head and neck. The remaining 67 patients had tumors arising in the trunk wall and viscera. Patients with tumors of the shoulder girdle, axilla, and buttock were considered to have extremity tumors and thus were not included in this study. Six patients were excluded from this analysis because records of their treatment before arrival at our institution were incomplete (n=1), because of previous treatment for another malignancy (n=3), or because they were seen for consultation only (n=2). The records of the remaining 61 patients were reviewed for this study, which was approved by the St. Jude Institutional Review Board.

Demographic data collected for this group of 61 patients included sex, race, age at the time of diagnosis, and duration of follow-up. The histologic subtype of NRSTS was determined from the pathology report for the initial tumor biopsy or resection. Histologic grade was assessed using the Pediatric Oncology Group grading system [14], which takes into account patient age and the histology, cellularity, necrosis, mitotic activity, and nuclear features of the tumor. Tumors were categorized as being either low (grade 1 or 2) or high (grade 3) grade. Patients were divided into two categories, body wall or visceral, based on the site of origin of the tumor. Body wall tumors were defined as those tumors of the trunk arising outside of the pleural and

peritoneal cavities, and outside of the retroperitoneum. Visceral tumors arose within the boundaries of the pleural and peritoneal cavities, or within the retroperitoneum. Additional tumor characteristics that were identified included the size (≤ 5 cm or > 5 cm in maximal diameter), local invasiveness (yes or no), regional lymph node status (positive or negative), and metastatic involvement (present or absent). The stage of disease was determined according to the American Joint Committee on Cancer (AJCC) guidelines for soft tissue sarcomas [15].

The treatment administered to each patient, including surgery, chemotherapy, and radiotherapy, was noted. Response to therapy was categorized as complete response (CR) [no evidence of tumor], partial response (PR) [$\geq 50\%$ decrease in the sum of the products of the maximum perpendicular diameters of the tumor(s)], stable disease (SD) [$< 50\%$ decrease or $< 25\%$ increase in the sum of the products of the maximum perpendicular diameters of the tumor(s)], or progressive disease (PD) [$\geq 25\%$ increase in the sum of the products of the maximum perpendicular diameters of the tumor(s) or the development of disease at new sites]. The sites of tumor recurrence, therapy administered after recurrence, and response to this therapy, were also recorded. For patients who died, the cause of death was identified if possible. In patients who received radiation therapy an analysis of sites of failure relative to their treated volume and dose was completed. This analysis was limited to a subset of 16 patients irradiated after 1980 in the era of CT and subsequently MR imaging to allow correlation of the site of failure with the treatment fields.

Statistical Methods

Associations between categorical variables were examined using Fisher's exact test or the Kruskal-Wallis test (for ordered factors such as AJCC stage). The Wilcoxon rank sum test was used to compare age at diagnosis by site of tumor. Due to small sample sizes, exact tests were used.

Overall survival (OS) was defined as the time interval from diagnosis to death from any cause or to last follow-up. Event-free survival (EFS) was defined as the time interval from date of diagnosis to date of tumor recurrence/progressive disease, second malignancy, or death from any cause or to last follow-up. OS and EFS were estimated using the method of Kaplan and Meier; standard errors were calculated using the method of Peto and Pike. [16] OS and EFS estimates are presented as probabilities ± 1 standard error. The exact log rank test was used to test for differences in survival and event-free survival distributions among patient groups. Cox proportional hazards models were used to examine the impact of site (body wall vs. visceral) on outcome, adjusted for known prognostic factors (e.g., tumor size, invasiveness, presence of metastatic disease).

Local failure was defined as the time interval from diagnosis to local disease recurrence. Competing risks included distant recurrence or death prior to local relapse. Distant failure was defined as the time interval from diagnosis to distant disease recurrence. Competing risks included local recurrence or death prior to relapse. Patients having both local and distant recurrence simultaneously were considered as having local relapse for the analysis of local failure and as having distant relapse for the analysis of distant failure. Cumulative incidence of local (and distant) failure was estimated using the methods of Kalbfleisch and Prentice [17]. Gray's test [18] was used to compare the cumulative incidence of local failure (and distant failure) among patient groups.

Results

Patient Characteristics

The characteristics of the 61 patients and their tumors are shown in Table 1. The median age at the time of diagnosis of NRSTS was 9.9 years (range, birth – 17.4 years), 51% of the patients were male, and 89% were white. The most common histologic subtypes were malignant peripheral nerve sheath tumor (MPNST) (n=10), synovial sarcoma (n=8), and leiomyosarcoma (n=7). Just over half of the tumors (54%) were high grade, and more than two-thirds (70%) were > 5 cm in maximal diameter. Only 8% of patients had nodal involvement by tumor, and 23% had distant metastatic disease.

Thirty-four patients had tumors of the body wall and 27 had tumors in visceral locations. The most common body wall sites were the back (n=11), chest wall (n=9), groin (n=6), and abdominal wall (n=5). The most common visceral sites were the retroperitoneum (n=9), abdomen (n=5), mediastinum (n=4), intestine (n=3) and pelvis (n=3). There was no evidence of differences in distributions of age at diagnosis, gender or race by tumor location (Table 1). Among the three most common tumor types, MPNST and synovial sarcoma were seen more commonly at body wall sites, whereas leiomyosarcoma was exclusively seen at visceral sites. Patients with visceral tumors had a significantly higher proportion of tumors that were > 5 cm (93% vs. 53%, $p<0.001$) and invasive (70% vs. 18%, $p<0.001$) compared to those with body wall tumors. The percentage of patients with high histologic grade ($p=0.61$), nodal involvement ($p=1$) and distant metastatic disease ($p=0.126$) was similar in patients with body wall and visceral tumors.

Associations among Factors

There were significant associations observed among tumor characteristics. For example, size and invasiveness were highly correlated ($p<0.001$). Of 43 patients with large tumors, 25 were invasive (58%), compared to no invasive tumors among the 18 patients with small tumors (0%). Invasiveness was also associated with metastatic involvement ($p<0.001$); 12 of 25 patients (48%) with invasive tumors presented with metastatic disease, compared to only 2 of 36 patients (6%) with non-invasive tumors. Histologic grade was significantly associated with size ($p=0.011$), invasiveness ($p=0.036$), and metastatic involvement ($p=0.065$). High-grade tumors tended to be larger, invasive, and more often metastatic at the time of initial presentation.

Treatment

Over the span of 37 years, patients received a variety of treatments that are summarized in Table 2. Visceral tumors were less likely to be amenable to resection (either wide local or marginal) than body wall tumors ($p=0.001$). Almost 90% of patients with body wall tumors underwent either a wide local or marginal excision of tumor compared to 48% of patients with visceral tumors. Chemotherapy was given to 30 patients (49% of the population). Twenty of these patients received a regimen that included vincristine, cyclophosphamide and dactinomycin and/or doxorubicin. Eight patients received a treatment regimen that included ifosfamide and doxorubicin (n=7) and/or ifosfamide and etoposide (n=4). Treatment for 7 patients included dacarbazine. Twenty-three patients (38%) received external beam radiotherapy (EBRT), 16 of them after 1980. Median dose was 51.4 Gy (range, 30-64.8 Gy) for all patients and 54 Gy (range, 30-64.8 Gy) for the 15 patients treated after 1980. One additional patient treated after 1980 terminated radiotherapy after 12 Gy of a planned 44 Gy because of family preference. Two patients with body wall tumors also received low dose rate brachytherapy to doses of 25 Gy and 25.6 Gy in addition to EBRT. Patients with visceral and body wall sites of involvement had similar doses of EBRT delivered ($p=0.72$), receiving median doses of 54 Gy (range, 35.4-64.8 Gy) and 50.4 Gy (range, 30-60.5 Gy), respectively.

Outcome

Thirty-one (51%) of the 61 patients were alive at the time of this analysis, with a median follow-up of 15.1 years (range, 1.6 – 36.8 years). Twenty-one of the 31 (68%) survivors had been seen or contacted within the past 2 years. Thirty-three patients have experienced relapse/progression (21 local, 7 distant, 5 both). The ten-year estimated cumulative incidences of local/regional failure and distant failure are $43.0 \pm 6.5\%$ and $19.8 \pm 5.2\%$, respectively. Thirty patients have died. The cause of death was progressive disease in all but 8 patients. Four patients' deaths were related to treatment-related toxicity, 1 to an unknown cause, 1 to a motor vehicle accident and 2 to second malignancy (1 osteosarcoma and 1 MPNST, both in the radiation field). Estimated 10-year event-free survival (EFS) and overall survival (OS) for the entire cohort are $45.5\% \pm 6.9\%$ and $56.8\% \pm 6.7\%$, respectively.

The 10-year EFS and OS were significantly better for patients with body wall sites than for those with visceral sites ($61.8\% \pm 8.5\%$ and $67.5\% \pm 8.2\%$ versus $24.2\% \pm 9.4\%$ and $43.0\% \pm 10.3\%$, $p = 0.004$ and $p = 0.004$, respectively) (Fig. 1). The 10-year estimated cumulative incidence (CI) of local disease recurrence was significantly higher for patients with visceral sites than for those with body wall sites ($64.3\% \pm 9.8\%$ versus $26.5\% \pm 7.7\%$, $p = 0.004$), whereas CI of distant recurrence was similar for the two sites ($15.2\% \pm 7.2\%$ versus $23.5\% \pm 7.4\%$, $p = 0.39$).

Because patients in this study were treated over a 37 year period, we wondered if patients treated in more recent years (after 1980) fared better due to advances in sarcoma therapy and supportive care. There were no statistically significant differences in the clinical features and tumor characteristics of patients in the early ($n = 17$) and late ($n = 44$) eras. Analysis of patient outcomes based on treatment era, before 1980 versus after 1980, showed no significant difference in 10-year EFS and OS ($41.2\% \pm 11.2\%$ versus $47.3\% \pm 8.3\%$, $p = 0.92$ and $47.1\% \pm 11.4\%$ versus $60.7\% \pm 7.9\%$, $p = 0.71$, respectively).

Thirty-four of 44 patients treated after 1980 underwent a wide local or marginal excision as a component of therapy, ten of whom received adjuvant radiation therapy. Patients who underwent a wide local or marginal excision had better local tumor control than those who did not (10-year estimates of the CI of local recurrence: $32.8\% \pm 8.3\%$ versus $70.0\% \pm 16.5\%$, $p=0.025$). Local recurrence occurred in 11 of 34 patients who underwent wide or marginal excision (2 of whom also received RT) and in 7 of 10 patients who did not undergo gross tumor resection. The local recurrence rate for patients managed with resection and adjuvant radiation therapy was not significantly different than that of patients managed with surgery alone (10-year CI of local failure: $20.0\% \pm 13.5\%$ versus $38.1\% \pm 10.3\%$, $p=0.27$).

Prognostic Factor Analysis

We investigated several tumor and treatment characteristics as predictors of survival and EFS, including site (body wall vs. visceral), histologic grade (1/2 vs. 3), tumor size (≥ 5 cm vs. > 5 cm), invasiveness (non-invasive vs. invasive), and metastatic involvement (yes vs. no) (Table 3). We also examined the extent of surgery (wide local/marginal excision vs. gross residual disease) as a predictor of survival and EFS. Tumor size, invasiveness, and the presence or absence of metastatic disease were significant predictors of both EFS and OS. Patients with small or non-invasive tumors had improved outcome, as did patients without metastatic disease. Patients with metastatic involvement at diagnosis had dismal outcomes (10-year EFS estimate, $7.1 \pm 4.9\%$). There was evidence that patients with low-grade tumors had improved survival compared to patients with high-grade tumors (10-year estimates: $74.2\% \pm 8.9\%$ vs. $42.4\% \pm 8.6\%$) ($p=0.025$), but there was not a statistically significant difference in EFS by histologic grade ($p=0.124$). Not surprisingly, patients able to have wide local/marginal resection had improved outcome. There was evidence of significant differences in both survival and EFS

between patients with wide local excision and those with marginal excision ($p=0.045$ for OS, $p=0.037$ for EFS).

Multiple regression analysis was restricted due to the small numbers of events (30 events for OS, 34 events for EFS) and due to significant associations between factors. Because of these limitations, Cox proportional hazards models were used that included only 2 factors each: site group (body wall vs. visceral) since this is of primary interest, and each of the known prognostic factors (tumor size, invasiveness, presence of metastatic disease, histologic grade, and having a wide local/marginal resection). There was evidence that site is likely not an independent predictor of outcome. When adjusted for tumor size, site was no longer a significant prognostic factor for survival or EFS. Similarly, when adjusted for invasiveness, the presence of metastatic disease and the extent of resection, site was no longer a significant prognostic factor of survival or EFS. When adjusted for histologic grade, site remained a significant independent predictor of both survival and EFS; patients with visceral tumors had worse outcome.

Discussion

This report describes a single institution experience with centrally located NRSTS of the body wall and viscera in children over a 37 year period. These tumors represented 29% of all NRSTS treated at our institution. Within this subset of patients, the proportion of patients with visceral and body wall sites was similar; however, there were notable differences in terms of pathologic features, treatment, and outcome. Histologic subtypes in body wall sites were consistent with those observed in pediatric NRSTS as a whole [19]. However, in visceral sites, leiomyosarcoma and liposarcoma were among the most common histologies, as in adults with retroperitoneal sarcomas [20-23]. Tumors located in the viscera were larger, more likely to be invasive, and less amenable to surgical resection than those tumors located in the body wall. These characteristics have been reported as prognostic of a poor outcome at any site in children [2, 4,5,7], and inadequate surgery contributes to an inferior outcome in adults with retroperitoneal soft tissue sarcomas [20,22,23]. Tumor grade, which is a strong predictor of outcome in both pediatric [2,3,5] and adult [24,25] soft tissue sarcomas, was also correlated with survival in patients with truncal tumors.

The pattern of treatment failure also differed between body wall and visceral sites. Visceral tumors were more likely to recur locally, whereas the incidence of distant recurrence was similar among patients with body wall and visceral tumors. Most patients with visceral sites did not undergo wide local or marginal excision, an important component of local therapy. A higher incidence of local recurrence and difficulty in achieving a complete surgical resection have been described for retroperitoneal soft tissue sarcomas in adults [21-23]. Inability to achieve a complete surgical resection has been attributed to the large size of these tumors at diagnosis and proximity to vital structures and organs in the retroperitoneum.

The effectiveness of chemotherapy is difficult to assess in this case series where a variety of different histologic subtypes were included and many different chemotherapy regimens were used over a 37 year period. Similarly, the indications for delivery of radiation therapy and the doses delivered were not standardized in this series and limit the ability to infer whether local control rates are influenced by its use. Despite these limitations and the small number of patients receiving each modality, the local failure rate for patients managed with resection and adjuvant radiation therapy was not significantly different than those managed with surgery alone, further highlighting the importance of surgical resection in the management of these patients.

As a group, non-extremity sites of NRSTS are reported to have a worse outcome compared to extremity sites [2,5,26]. To our knowledge, there are no reports in pediatric NRSTS directly comparing clinical features and outcome between extremity and trunk tumors as defined in our

report. We performed an exploratory analysis using 123 patients with extremity NRSTS diagnosed at our institution during the same timeframe and the cohort of patients with trunk tumors presented here. We found that patients with extremity NRSTS had improved survival compared those with trunk NRSTS (10-year estimates: $72.8\% \pm 4.8\%$ versus $56.8 \pm 6.7\%$, $p=0.028$). When trunk sites were further categorized as body wall or visceral, survival was similar between extremity and body wall sites ($72.8\% \pm 4.8\%$ versus $67.5\% \pm 8.2\%$, $p = 0.98$), but a significant difference was noted between extremity and visceral sites ($72.8\% \pm 4.8\%$ versus $43.0\% \pm 10.3\%$, $p<0.001$). However, just as we observed when comparing body wall and visceral sites, site (extremity vs. visceral) was no longer prognostic after adjusting for tumor size, invasiveness, and the presence or absence of metastatic disease (data not shown). These findings suggest that as long as treatment assignment is based on the factors that influence survival, future clinical trials for pediatric NRSTS should include patients with tumors arising at all anatomic sites.

Limited progress in the treatment of trunk NRSTS is suggested by our finding that patients diagnosed after 1980 fared no better than those diagnosed previously. Although the overall therapeutic approach to soft tissue sarcomas has changed little over the last several decades, it appears that advances that have been made in imaging, surgical techniques, radiotherapy planning and delivery, and chemotherapy have had little impact on the outcome of these patients. Management of these tumors presents specific challenges to our traditional therapeutic modalities of surgery, chemotherapy and radiation. The location or extent of the tumor often limits the delivery of adequate local therapy and current chemotherapeutic agents are relatively ineffective at eliminating the primary tumor or improving its resectability. Improvements in surgical techniques and advances in radiation therapy technology such as proton beam therapy may improve our ability to completely remove the tumor and safely deliver an effective radiation dose. However, probably of greater importance given the limited efficacy and significant toxicity of today's therapy, is to explore surgical therapy alone for low-risk patients and to better characterize the biology of these rare tumors to identify novel interventions for higher-risk patients. This approach is currently underway in the ongoing Children's Oncology Group therapeutic and biology studies and may provide direction for future therapeutic trials.

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Figure 1.
Overall survival (A) and event-free survival (B) by site.

Table 1
Clinical and Tumor Characteristics of 61 Pediatric Patients with Visceral and Body Wall NRSTS

	All Patients (n=61)	Body Wall (n=34)	Visceral (n=27)	P-value
Age (years)				
Range	Birth - 17.4	0.1 – 17.4	Birth – 17.2	0.38
Median	9.9	10.2	6.4	
Sex				
Male	31 (51%)	19	12	0.44
Female	30 (49%)	15	15	
Race				
White	54 (89%)	29	25	0.45
Black	7 (11%)	5	2	
Histology				
MPNST	10 (16%)	7	3	ND
Synovial sarcoma	8 (13%)	7	1	
Leiomyosarcoma	7 (11%)	0	7	
Sarcoma NOS	5 (8%)	1	4	
Alveolar soft part sarcoma	4 (7%)	4	0	
Fibrosarcoma	4 (7%)	3	1	
Liposarcoma	4 (7%)	1	3	
Other*	19 (31%)	11	8	
Grade				
1 or 2	28 (46%)	17	11	0.61
3	33 (54%)	17	16	
Size				
≤ 5 cm	18 (30%)	16	2	<0.001
> 5 cm	43 (70%)	18	25	
Invasiveness				
Non-invasive	36 (59%)	28	8	<0.001
Invasive	25 (41%)	6	19	
Nodal Involvement				
No	56 (92%)	31	25	1.0
Yes	5 (8%)	3	2	
Metastatic Involvement				
No	47 (77%)	29	18	0.126
Yes	14 (23%)	5	9	
AJCC Stage				
IA	12 (20%)	10	2	0.082 [^]
IIA	13 (21%)	5	8	
IIB	4 (6%)	4	0	
III	18 (30%)	10	8	
IV	14 (23%)	5	9	

Abbreviations: MPNST, malignant peripheral nerve sheath tumor; ND, not done.

* Angiomatoid malignant fibrous histiocytoma (n=3), malignant fibrous histiocytoma (n=2), mesenchymoma (n=2), epithelioid sarcoma (n=2), clear cell sarcoma (n=2), infantile fibrosarcoma (n=2), dermatofibrosarcoma protuberans (n=2), hemangiopericytoma (n=1), infantile hemangiopericytoma (n=1), Triton tumor (n=1), angiosarcoma (n=1)

[^] Result was a comparison of stages IA/IIA/IIB vs. stage III vs. stage IV (comparison of stage I vs II vs III vs IV, p=0.036)

Table 2
Treatment and Response of 61 Pediatric Patients with Visceral and Body Wall NRSTS

	All Patients (n=61)	Body Wall (n=34)	Visceral (n=27)	P-value
Initial Surgical Treatment^a				
Wide Local Excision (WLE)	26 (43%)	19 (56%)	7 (26%)	0.002 ^b
Marginal excision	15 (25%)	10 (29%)	5 (19%)	
Intralesional excision or biopsy	20 (33%)	5 (15%)	15 (56%)	0.001 ^c
Ability to achieve WLE/marginal excision at any time				
Yes	43 (70%)	30 (88%)	13 (48%)	0.001
No	18 (30%)	4 (12%)	14 (52%)	
Treatment				
Surgery + EBRT+ Chemotherapy	5 (8%)	2 (6%)	3 (11%)	ND
Surgery + EBRT	5 (8%)	3 (9%)	2 (7%)	
Surgery + Chemotherapy	9 (15%)	9 (26%)	0 (0%)	
Surgery only	24 (39%)	16 (47%)	8 (30%)	
EBRT + Chemotherapy	11 (18%)	2 (6%)	9 (33%)	
EBRT only	2 (3%)	0 (0%)	2 (7%)	
Chemotherapy only	5 (8%)	2 (6%)	3 (11%)	
Best Response				
CR	42 (69%)	27 (79%)	15 (56%)	0.043
PR	9 (15%)	4 (12%)	5 (19%)	
SD	1 (2%)	0 (0%)	1 (4%)	
PD	9 (15%)	3 (9%)	6 (22%)	
Tumor Recurrence				
Local/regional	21 (34%)	5 (15%)	16 (59%)	0.004 ^d
Distant	7 (11%)	4 (12%)	3 (11%)	0.392 ^e
Both	5 (8%)	4 (12%)	1 (4%)	

EBRT, external beam radiotherapy; WLE, wide local excision

^a Initial surgeries were considered those that occurred within 3 months of the diagnosis date.

^b Comparison of WLE, marginal excision and intralesional excision/biopsy

^c Comparison of WLE/marginal excision and intralesional excision/biopsy

^d Comparison of cumulative incidence of local/regional failure

^e Comparison of cumulative incidence of distant failure

Table 3
Results of Prognostic Factor Analyses for Patients with Truncal NRSTS

Factor	N	10-year EFS % (SE)	P-value [^]	10-year Survival % (SE)	P-value [^]
Site Group					
Body wall	34	61.8 (8.5)	0.004	67.5 (8.2)	0.004
Visceral	27	24.2 (9.4)		43.0 (10.3)	
Grade					
1 or 2	28	56.4 (10.3)	0.124	74.2 (8.9)	0.025
3	33	36.4 (8.4)		42.4 (8.6)	
Size					
≤5 cm	18	83.0 (9.5)	<0.001	88.9 (7.9)	<0.001
>5 cm	43	30.2 (67.3)		44.2 (7.8)	
Invasiveness					
Non-invasive	36	60.7 (9.0)	0.002	74.5 (7.8)	<0.001
Invasive	25	24.0 (7.9)		32.0 (8.8)	
Metastatic Involvement					
No	47	57.1 (7.8)	<0.001	69.9 (7.1)	<0.001
Yes	14	7.1 (4.9)		14.3 (7.6)	
Extent of Initial Surgical Resection					
Wide local excision (WLE)	26	69.0 (9.9)	0.004 ^a	80.6 (8.4)	<0.001 ^a
Marginal excision	15	40.0 (12.6)	0.008 ^b	60.0 (12.6)	<0.001 ^b
None	20	20.0 (8.0)	0.037 ^c	25.0 (8.8)	0.045 ^c

[^] P-values were obtained from exact log rank tests

SE: standard error

^a Comparison of WLE vs. marginal excision vs. none

^b Comparison of WLE/marginal vs. none

^c Comparison of WLE vs. marginal