Epidemiological, functional and oncologic outcome analysis of spinal sarcomas treated surgically at a single institution over ten years

Mari L. Groves, MD Patricia L. Zadnik, BA Paul Kaloostian, MD Jackson Sui, BS C. Rory Goodwin, MD PhD Jean-Paul Wolinsky, MD Timothy F. Witham, MD Ali Bydon, MD Ziya L. Gokaslan, MD Daniel M. Sciubba, MD

PII: S1529-9430(14)00674-3
DOI: 10.1016/j.spinee.2014.07.005
Reference: SPINEE 55935

To appear in: The Spine Journal

Received Date: 26 February 2014
Revised Date: 17 June 2014
Accepted Date: 9 July 2014


This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.
Epidemiological, functional and oncologic outcome analysis of spinal sarcomas treated surgically at a single institution over ten years

Mari L Groves MD, Patricia L Zadnik BA, Paul Kaloostian MD, Jackson Sui BS, C. Rory Goodwin MD PhD, Jean-Paul Wolinsky MD, Timothy F Witham MD, Ali Bydon MD, Ziya L Gokaslan MD, Daniel M Sciubba MD

The Johns Hopkins University School of Medicine, Baltimore MD

Corresponding Author
Daniel M Sciubba
610 North Wolfe Street
Baltimore, Maryland
dsciubba@jhmi.edu
410-955-4424
Abstract:

Background/Context: Spinal sarcomas are aggressive tumors that originate from cells of mesenchymal origin, specifically fat, cartilage, bone and muscle. They are high-grade lesions, and treatment of spinal sarcomas can involve chemotherapy, radiation therapy, and surgery. In the appendicular skeleton, sarcomas are often treated with amputation, however in the spinal column, surgical resection poses a unique set of challenges.

Purpose: Large-scale studies of spinal sarcoma are needed to better understand optimal treatment regimens and the impact of en bloc or intralesional resection on patient outcome.

Study design/setting: A cohort of 25 sarcoma patients treated at a single medical institution between 2002 and 2012 was reviewed.

Patient Sample and Outcome measures: Patients were classified by tumor type for subgroup analysis, including chondrosarcoma, osteosarcoma, and other malignant spinal sarcoma. Demographic data for review included patient age, tumor type, tumor location, surgery type, exposure to chemotherapy and radiation therapy.

Methods: Survival statistics and Kaplan-Meier curves were calculated using GraphPad Prism 5.0. The threshold for statistical significance was set at p < 0.05. Unpaired, two-tailed, equal variance t-tests were performed for statistical analyses in Microsoft Excel 2010. Portions of this work were supported by the AOSpine Primary Tumor Knowledge Forum. The authors report no potential conflicts of interest related to this manuscript.
**Results:** Twenty-five patients with spinal sarcomas were treated over the ten-year period. Diagnosis included chondrosarcoma (n=9), osteosarcoma (n=4) and other sarcoma (n=12). Mean age at the time of diagnosis was 42 years. Pain was present at the time of diagnosis in 92% of patients. Median survival after surgery was 59.5 months for chondrosarcoma, undefined for other sarcomas and 16.8 months for osteosarcoma. Median survival following en bloc resection was undefined. Median survival following intralesional resection was 17.8 months. The difference in median survival between en bloc and intralesional resection was statistically significant (p=0.049).

**Conclusion:** The authors report the largest cohort of patients with spinal sarcoma. Median survival in this cohort was longest for patients with sarcomas of varying pathology. Median survival was longer for chondrosarcoma. En bloc resection demonstrated a survival advantage over intralesional resection. Long term follow-up is needed for patients with spinal sarcoma to establish definitive survival data.

**Key Words:** Sarcoma; Osteosarcoma; Chondrosarcoma; Outcome
Introduction:

Spinal sarcomas are a rare group of spinal malignancies that are associated with high rates of morbidity and mortality. Epidemiological studies of spinal sarcomas, such as from the Surveillance Epidemiology and End Results (SEER) database cancer statistics review from 1975-2009, demonstrate that sarcomas represent less than 5% of all osseous neoplasms and less than 0.2% of all new cancers. Sarcomas can occur in a variety of osseous regions throughout the body. However, sarcomas of the spine and surrounding structures often elicit debilitating consequences due to severe focal pain and neurological morbidity.

Chondrosarcoma represents 25% of sarcomatous tumors and increases in likelihood in patients over the age of 50. Chondrosarcomas are part of a family of malignant tumors where the cells differentiate uncontrollably into cartilaginous tissue. It is further classified as central, peripheral, or periosteal, with mesenchymal and clear cell variants. Osteosarcoma tends to be more common, representing 35% of all sarcomas and 3 to 15% of all primary spine tumors. There exist a variety of subtypes including conventional osteosarcomas, telangiectatic, small-cell, giant-cell, epithelioid, and osteoblastoma-like osteosarcomas

Whereas previous studies have been confined by limited patient data or the size of their patient population, this database of spinal sarcomas is comprised of 25 spinal sarcoma patients who underwent surgical resection at a single institution from 2002 to 2012. We investigate the impact of en bloc resection on patient outcome through analyzing a single institutions surgical management of spinal sarcomas over the last decade. While the SEER database provided invaluable epidemiological data of 1378 sarcoma patients, it did not stratify outcomes based on surgical approach from each surgical institution separately. Thus, by looking only at patients from a single institution during a single decade, this study allows for a controlled standard of
care, which we hope may then be used by neurosurgical and orthopedic spinal surgeons to
determine functional and oncologic survival data for a variety of surgical techniques and
treatments.

Methods:

Study population

Demographic, treatment and outcome data was collected retrospectively from the
electronic medical record following protocols dictated by the Institutional Review Board (IRB
application NA_00066200). 25 consecutive patients with histology-confirmed spinal sarcomas
treated at a single institution from 2002-2012 were reviewed. Patient medical records, including
clinic notes, primary radiographs, computed tomography (CT) scans and magnetic resonance
imaging (MRI) were reviewed. Pathology reports were also reviewed.

Study criteria

All patients included in this study presented with histologically confirmed sarcoma of the
spine. Covariates identified were epidemiological data such as age, gender, length of
hospitalization, location of sarcoma, number of spinal levels involved, surgical approach, tumor
volume, pathology of sarcoma, extent of resection, pain at diagnosis, Frankel score, presence of
myelopathy and cauda equina, adjunctive treatment, local recurrence, and overall survival. The
diagnosis of other sarcoma included epithelioid sarcoma (n=3), pleomorphic undifferentiated
sarcoma (n=2), spindle cell sarcoma (n=2), alveolar soft part sarcoma (n=1), unusual low grade
sarcoma (n=1), postradiation sarcoma (n=1), fibromyxoid sarcoma (n=1) and Ewing sarcoma
(n=1).
Surgical approach was recorded from operative notes. Pain at diagnosis was self-reported by patients at any pre-operative clinic visit within 3 months of surgery. The number of spinal levels involved and the presence or absence of a pathologic fracture was determined from the radiology reports of preoperative CT and MRI scans.

Vital statistics were recorded from the Social Security Death Master File accessed online. All vital statistics reflect the status of patients as of July 31, 2012. Survival data for non-US citizens was recorded as unknown. Recurrence data is recorded for all patients at the last clinical follow up. Recurrence was determined from post-operative neurosurgery clinic notes reporting the neurosurgeon’s interpretation of radiographic recurrence at the time of last follow up.

Tumor size and volume was recorded from primary review of preoperative MRI or CT scans. Volume was calculated via the formula for the volume of an ellipsoid \((4\pi/3)r_1r_2r_3\). Radii were taken as one-half the cranial-caudal, anterior-posterior and lateral measurements of the tumor.Measured values were corroborated with radiology reports.

Following surgery, patients were seen at one month then at three, six, nine and twelve months. Patients were followed every six months in the second year, then yearly, or as clinical progression dictated their plan of care. MRI with and without contrast was used to evaluate tumor recurrence at the time of clinical follow-up. Early complications, defined as occurring within thirty days postoperatively, and late complications, defined as occurring after thirty days postoperatively were recorded.

Statistical Analysis

Survival statistics and Kaplan-Meier curves were calculated using GraphPad Prism 5.0 (GraphPad, La Jolla, CA). The threshold for statistical significance was set at \(p < 0.05\). Unpaired,
two-tailed, equal variance t-tests were performed for statistical analyses in Microsoft Excel 2010. 95% confidence intervals were determined using the Confidence Interval Calculator for Proportions (Online, McCallum-Layton; 2010).

Results:

Patient Population

Twenty-five patients with spinal sarcomas were treated over the ten-year period. Mean age at the time of diagnosis was 42 years (range 17-75 years) and the disease was found predominantly in women (56%). The mean age at presentation differed by tumor type. Chondrosarcoma (46.7 years ±10.4 years) and osteosarcoma (48.8 years ± 23.5 years) presented at an older mean age than other sarcomas (36.2 years ±18.0 years). Median length of stay after surgery was 16 days (range 4 – 52 days). Median follow up time was 11.8 months (range 0.1 – 71.6 months).

Clinical Presentation

Pain was present at the time of diagnosis of a majority of patients (92%). Pathological fractures were typically not present at the time of diagnosis (12%). Myelopathy was present in a majority of patients (68%), more so in cases involving chondrosarcoma (67%) and osteosarcoma (100%) than other sarcomas (58%). Cauda equina was absent in a majority of patients (16%). Ten patients (40 %) had undergone a previous spinal tumor resection. Pre-operative Frankel scores of the sarcoma patients were C (28%), D (36%), and E (36%).
Surgical Approach

Chondrosarcoma and osteosarcoma were found predominantly in the cervical, thoracic, or lumbar spine, while other sarcomas are more common in the sacral spine. The median number of vertebral levels involved was three (range 1-7). A posterior approach was used most commonly (56%) followed by surgeries involving both an anterior and posterior approach (40%). The most common procedure was a laminectomy or hemilaminectomy, which was performed in 15 cases (60%). The most common type of reconstruction used was an allograft (48%), followed by the use of a titanium cage (32%). Often times, chondrosarcoma patients underwent no form of reconstruction (60%).

Adjuvant Treatment

Adjuvant treatment was used in 15 cases (60%). Six patients received preoperative chemotherapy (24%), four received postoperative chemotherapy (16%), seven underwent pre-op radiation (28%), and ten underwent post-op radiation (40%). Local recurrence occurred in six cases (24%).

Complications

Complications noted earlier than thirty days postoperatively (early complications) and later than thirty days (late complications) were stratified by either en bloc resection or intrallesional resection. In the En bloc resection group, five patients (33.3%) required reoperation secondary to wound dehiscence, and three patients (20%) developed deep venous thrombosis less than thirty days postoperatively. Greater than thirty days postoperatively, four patients (26.7%) required reoperation for three cases of wound dehiscence and one case of
instrumentation failure that resulted in loss of correction of deformity. The other two cases of instrument failure did not have any loss of deformity correction and no operative intervention was pursued. In the Intralesional resection group, two patients (23.0%) required reoperation secondary to wound dehiscence and postoperative hematoma, and one patient (10%) developed deep venous thrombosis less than thirty days postoperatively. Greater than thirty days postop, there was one complication of esophageal erosion requiring revision surgery to remove the cervical plate in the intralesional group. (Table 1)

Patient Survival

Median survival following surgery for chondrosarcoma was 59.5 months (range 0.2-70.6 months), undefined for other sarcomas (range 0.2-26.5 months) and 16.8 months for osteosarcoma (range 0.5-28.5 months). (Figure 1) The difference in survival was not statistically significant on Mantel-Cox testing. (p=0.27) Median survival following en bloc resection was undefined. Median survival following intralesional resection was 17.8 months. (Figure 2) Survival following en bloc resection was significantly different than survival after intralesional resection on Gehan-Breslow-Wilcoxon test (p = 0.049). The survival difference was not statistically significant on Mantel-Cox testing (p=0.07).

Discussion:

This subset of malignant spinal tumors encompasses chondrosarcomas, osteosarcomas, as well as a variety of other sarcomatous tumors including Ewings sarcoma. Although previous studies have examined the broad epidemiologic outcomes of patients at multiple institutions, these studies did not investigate outcomes relative to the specifics of treatment.10,11,12 Our
review highlights the important aspects of surgical management, namely the benefit of en bloc resection for spinal sarcoma.

Surgical management of sarcomas is diverse, and is dependent on location of tumor burden. For example, the orthopedic literature recommends wide excision or amputation of extremity sarcoma when feasible, with use of adjuvant treatments such as phenol, radiation, and chemotherapy as needed. En bloc strategies available to patients include corpectomy, sacral amputations, and finally hemipelvectomy. However, surgical resection of spinal sarcomas cannot extend this concept of amputation at mobile spine levels due to the necessity of adjacent anatomical structures. The results of this study suggest that en bloc resection, when feasible, should be offered to patients with diverse sarcomatous pathologies in the spinal column in order to optimize patient survival.

Chondrosarcoma patients have shown to have a 5-year survival rate close to 70% and a median survival ranging from 70 to 160 months. Our data showed a median survival of 60 months. This variation can be accounted for in part by our small patient pool (10 chondrosarcoma patients) and with not all patients reaching five years of follow up (median follow up 11.8 months, range 0.1 – 71.6). Osteosarcoma patients are shown to have a median survival ranging from 7 to 23 months. Our data demonstrates that the osteosarcoma patients had a median survival of almost 17 months. This is in accordance with previously published data from Schwab et al. who noted increased survival of 60 months in their cohort of 17 patients over 2 decades.

Prior studies have shown that an en bloc resection of spinal sarcomas with adequate margins decreases recurrence rates. However, a number of other studies have shown the dangers of an en bloc resection in the spine, including the increased morbidity of the procedure
and the varying difficulty in different locations of the spine.\textsuperscript{24, 25, 26} Through our database, we have shown that en bloc resection of spinal sarcomas does increase patient survival as compared to purely intralesional resection ($p = 0.049$).

The authors acknowledge the limitations of this study. This study was limited by its small cohort size, which resulted in some of the trends observed not reaching statistical significance. Our findings add to the growing amount of sarcoma literature, with a focus on cancer varieties and surgical approaches. In the future, these studies can be utilized to provide a better quality of care to patients affected by the disease.

\textbf{Conclusion:}

Sarcomas of the spine are a unique group of highly aggressive and malignant spinal tumors that represent a surgical and management challenge for the surgeon and the entire health care team. Reports continue to demonstrate a high morbidity and mortality in this population. However, the results of this study suggest that en bloc resection of these tumors, when possible, may increase patient survival. Continued improvement in surgical and adjuvant treatment will undoubtedly continue to further alter the survival curve for this population of spinal tumors.
Figure Legends

Figure 1. Survival by pathology. Median survival following surgery for chondrosarcoma was 59.5 months (range 0.2-70.6 months), undefined for other sarcomas (range 0.2-26.5 months) and 16.8 months for osteosarcoma (range 0.5-28.5 months). The difference in survival was not statistically significant on Mantel-Cox testing, (p=0.27).

Figure 2. Survival by Resection. Median survival following en bloc resection was undefined. Median survival following intralesional resection was 17.8 months. Survival following en bloc resection was significantly different than survival after intralesional resection on Gehan-Breslow-Wilcoxon test (p = 0.049). The survival difference was not statistically significant on Mantel-Cox testing (p=0.07).

Tables

Table 1. Complications of En bloc vs Intralesional resection.
References


### Complications of En bloc vs Intralesional resection

<table>
<thead>
<tr>
<th></th>
<th>EnBloc  (n=15)</th>
<th>%</th>
<th>Intralesional (n=10)</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Early\nComplications</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reoperation</td>
<td>5</td>
<td>33.3%</td>
<td>2</td>
<td>20.0%</td>
</tr>
<tr>
<td>Wound dehiscence</td>
<td>5</td>
<td>33.3%</td>
<td>1</td>
<td>10.0%</td>
</tr>
<tr>
<td>DVT</td>
<td>3</td>
<td>20.0%</td>
<td>1</td>
<td>10.0%</td>
</tr>
<tr>
<td>Hematoma</td>
<td>0</td>
<td>0.0%</td>
<td>1</td>
<td>10.0%</td>
</tr>
<tr>
<td><strong>Late\nComplications</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reoperation</td>
<td>4</td>
<td>26.7%</td>
<td>1</td>
<td>10.0%</td>
</tr>
<tr>
<td>Instrument Failure</td>
<td>3</td>
<td>20.0%</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Wound dehiscence</td>
<td>3</td>
<td>20.0%</td>
<td>0</td>
<td>0.0%</td>
</tr>
<tr>
<td>Esophageal Erosion</td>
<td>0</td>
<td>0.0%</td>
<td>1</td>
<td>10.0%</td>
</tr>
</tbody>
</table>