Osteosarcoma of the spine: prognostic variables for local recurrence and overall survival, a multicenter ambispective study

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OBJECTIVE Primary spinal osteosarcomas are rare and aggressive neoplasms. Poor outcomes can occur, as obtaining marginal margins is technically demanding; further Enneking-appropriate en bloc resection can have significant morbidity. The goal of this study is to identify prognostic variables for local recurrence and mortality in surgically treated patients diagnosed with a primary osteosarcoma of the spine.

METHODS A multicenter ambispective database of surgically treated patients with primary spine osteosarcomas was developed by AOSpine Knowledge Forum Tumor. Patient demographic, diagnosis, treatment, perioperative morbidity, local recurrence, and cross-sectional survival data were collected. Tumors were classified in 2 cohorts: Enneking appropriate (EA) and Enneking inappropriate (EI), as defined by pathology margin matching Enneking-recommended surgical margins. Prognostic variables were analyzed in reference to local recurrence and survival.

RESULTS Between 1987 and 2012, 58 patients (32 female patients) underwent surgical treatment for primary spinal osteosarcoma. Patients were followed for a mean period of 3.5 ± 3.5 years (range 0.5 days to 14.3 years). The median survival for the entire cohort was 6.7 years postoperative. Twenty-four (41%) patients died, and 17 (30%) patients suffered a local recurrence, 10 (59%) of whom died. Twenty-nine (53%) patients underwent EA resection while 26 (47%) patients underwent EI resection with a postoperative median survival of 6.8 and 3.7 years, respectively ($p = 0.048$). EI patients had a higher rate of local recurrence than EA patients ($p = 0.001$). Patient age, previous surgery, biopsy type, tumor size, spine level, and chemotherapy timing did not significantly influence recurrence and survival.

CONCLUSIONS Osteosarcoma of the spine presents a significant challenge, and most patients die in spite of aggressive surgery. There is a significant decrease in recurrence and an increase in survival with en bloc resection (EA) when

ABBREVIATIONS EA = Enneking appropriate; EI = Enneking inappropriate.

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compared with intralesional resection (EI). The effect of adjuvant and neoadjuvant chemotherapeutics, as well as method of biopsy, requires further exploration.

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ALTHOUGH osteosarcoma is the most common primary malignant bone tumor, only 3%–5% of cases occur in the spine.^{1,21,32,52,55,59,62} Due to the low incidence, treatment paradigms have been based on small series and case reports^{1,51,52,57,58} and by extrapolating data from larger appendicular series.^{28,37,39,49,51,55} As originally outlined by Enneking et al., musculoskeletal sarcoma is best treated with wide resection and adjuvant therapies where histologically appropriate.³ Thus, it is currently believed that multimodality therapy, including adjuvant or neoadjuvant chemotherapy and surgery, is the most effective treatment for primary osteosarcoma of the spine.^{3,19,44,48,56} However, despite aggressive treatment, historically survival has been poor.^{44,51,55}

The primary goal of the surgical treatment of spinal sarcomas is curative resection with negative margins. Depending on the size and location of the tumor, achieving this oncological goal may result in significant patient morbidity. In multiple case reports and mixed histology studies, aggressive resection improves neurological and functional status and may extend survival.^{2,4,5,9,25,27,34,35,38,43,58} However, in the vast majority of these older studies, palliative intralesional resections were performed. In contrast, treating extraspinal sarcomas with en bloc resections and wide or marginal negative margins has improved local tumor control and long-term survival.^{8,17,20,24,30,31,33,41,47,50,53,54,63} Beginning with Tomita, advances in spinal surgery have enabled en bloc resection of spinal column tumors throughout the fixed and mobile spine.^{12–16,45,46,60,61,65}

Similar to extraspinal surgery, the terminology for surgical staging, extent of resection, and grading of margins can be applied. The Enneking classification was originally intended for appendicular tumors^{22,23} and predicts prognosis based on surgical margins. Although anatomical considerations in the spine make direct application difficult, it is possible to classify resections as Enneking appropriate (EA) or Enneking inappropriate (EI) based on the surgical margins. To account for the complexity of spine anatomy, the Weinstein-Boriani-Biagini classification system was developed.⁷ These systems have been validated and are considered feasible to apply to primary spine tumor surgery in order to optimize patient care and research reliability.^{6,10,26}

The aim of this study is to identify the prognostic variables for recurrence and survival in surgically treated patients suffering from primary osteosarcomas of the spine using ambispectively collected multiinstitutional data. Specifically, the impact of EA and EI resections using contemporary surgical techniques and the use of neoadjuvant chemotherapy are explored.

Methods

Design

An international, multicenter, retrospective review of prospectively collected data or ambispective design with cross-sectional follow-up was conducted. Ethics board approval was received by each participating spine center. Twelve spine oncology referral centers from 3 geographic regions contributed data. The patients included in this study had a diagnosis of primary osteosarcoma of the spine, underwent surgical intervention at one of the participating spine centers between March 1987 and April 2012, and received regular surgical follow-up. Patients were excluded if they were admitted for the treatment of a metastatic spinal tumor or if they were diagnosed with a primary spinal cord tumor.

Demographic data, tumor histology, final pathological resection margins, Enneking stage,²³ chemotherapy and radiation therapy timing, local recurrence, and survival data were collected from the clinical charts and institutional databases. Whenever necessary, governmental databases were accessed to retrieve data concerning survival. A secure Web-based application (REDCap, Vanderbilt University) was used to store and manage the aggregated data.

Patients were analyzed in 2 groups: EA or EI. For osteosarcomas, wide or marginal margins are recommended by the Enneking criteria. If this was achieved, surgery was EA, and if this was not achieved, surgery was EI. Of note, patients who underwent a previous surgery for their sarcoma and the resection was previously described as being intralesional were also considered to be EI.

Surgical Technique

A range of surgeon preferences and differences in tumor location, size, and aggressiveness of the tumors lead to different surgical techniques being carried out (Table 1). Some centers strictly followed the Enneking principles, while others did not. Sometimes the proximity of critical anatomy and extent of tumor prevented the recommended margins.

Pathological Results

The final results for the EA or EI margins and tumor grade were based on the pathological evaluation of the surgical specimen, which was performed by an experienced musculoskeletal pathologist. The Enneking classification distinguishes between wide and marginal resections, yet due to the complex anatomy of the mobile spine, these 2

TABLE 1. Summary of the treatment details

Variable	No. of Patients (%)
Preoperative embolization (n = 51)	
No	39 (76)
Yes	12 (24)
Surgical approach (n = 58)	
Posterior	19 (33)
Anterior/posterior	19 (33)
Posterior/anterior	7 (12)
Posterior/anterior/posterior	4 (7)
Other	9 (16)
Pathological results of surgical specimen (n = 54)	
Wide or marginal	34 (63)
Intralesional	20 (37)
Fixation used (n = 57)	
Posterior	37 (65)
Both	8 (14)
None	12 (21)
Reconstruction (n = 56)	
No	20 (36)
Yes*	36 (64)
Autograft	17 (33)
Allograft	9 (17)
Titanium cage	11 (21)
Carbon fiber cage	12 (23)
Vascular autograft	2 (4)
Cement	1 (2)
Enneking appropriateness (n = 55)	
EA	29 (53)
EI	26 (47)
Chemotherapy timing (n = 58)	
Preoperative	19 (33)
Postoperative	9 (16)
Both	19 (33)
None	11 (19)
Radiation therapy timing (n = 58)	
Preoperative	9 (16)
Postoperative	15 (26)
None	34 (59)

* The same patient can contribute to more than 1 category.

categories were combined into 1 category because sparing the dura from marginal resection is generally preferred over a wide resection (which includes the dura as a margin), except possibly in the setting of sacral amputation.

Treatment

In addition to surgical treatment, multidisciplinary teams, which included medical and radiation oncologists, consulted patients both pre- and postoperatively to determine the need for adjuvant and neoadjuvant chemotherapy and radiation therapy. Similar to the surgical techniques, treatment was center and patient dependent.

Statistical Analysis

Descriptive statistics, such as the mean, standard deviation, percentage, and frequency, were used to summarize the demographic data. For differences between groups, the chi-square tests (Pearson's and Fisher's exact tests, as appropriate) were used for categorical variables, and the Student t-test and Mann-Whitney test, as appropriate, for continuous variables. Univariate analysis, which used Kaplan-Meier survival curves and log-rank tests, was performed over a 10-year period postoperatively to identify factors that potentially influenced local recurrence and mortality. Statistical significance was decided when $p \leq 0.05$. All statistical analyses were performed using STATA (version 12.0).

Results

A total of 58 patients with a mean age of 36.0 years (range 11.3–76.4 years) received surgical treatment for a primary spinal osteosarcoma (Table 2). Thirty-two (55%) patients were female, and 26 (45%) patients were male. Pain was reported in 52 (95%) patients. Fifteen (26%) patients had a previous spine tumor operation, and 12 (21%) of these were reported as intralesional resections that resulted in an EI procedure. A histological diagnosis by CT-trocar biopsy was made in 30 (61%) patients. Most lesions were located in the mobile spine (n = 41; 71%). Almost every patient presented with a high-grade lesion (n = 53; 96%) and most spanned more than 1 vertebra (n = 48; 83%) (Table 3). The mean tumor size was known in 52 patients in 3 dimensions: anterior-posterior (7.9 ± 4.8 cm); left-right (7.4 ± 4.9 cm); and cephalad-caudad (7.1 ± 5.9 cm). Patients were followed for a mean period of 3.5 ± 3.5 years, spanning a maximum of 14.3 years. Data concerning the metastatic disease status were not collected.

Treatment

Fifty-one patients reported preoperative embolization, with 12 of these (24%) receiving treatment (Table 1). The 2 most common surgical approaches were posterior (n = 19; 33%) and anterior/posterior (n = 19; 33%). Fixation was used in 45 (79%) patients. Twenty (36%) patients did not receive spine reconstruction, most likely because neoplastic and iatrogenic effects were not mechanically significant. In addition to surgical treatment, 47 (81%) patients received chemotherapy and 24 (41%) patients received radiation therapy. Data about the Enneking appropriateness of surgery were available for 55 patients: 29 (53%) patients received an EA procedure and 26 (47%) received an EI procedure. The distribution of the study variables according to Enneking appropriateness is shown in Table 4. None of the EA-treated patients underwent a previous spine tumor surgery ($p < 0.001$). The type of biopsy differed between EA- and EI-treated patients ($p = 0.001$). The majority of patients who received an EA procedure (n = 20; 80%) also received CT-trocar biopsies, while only 8 (38%) EI-treated patients received CT-trocar biopsies. The tumor volume was larger in EA-treated patients compared with EI-treated patients ($p = 0.007$). In total, 24 of 29 (83%) EA-treated patients received neoadjuvant chemotherapy compared with 13 of 26 (50%) EI-treated patients

TABLE 2. Summary of the patient clinical characteristics*

Variable	Value
Mean age at surgery in yrs (n = 58)	36.0 ± 16.1
Sex (n = 58)	
Female	32 (55)
Male	26 (45)
Pain at diagnosis (n = 55)	
No	3 (5)
Yes	52 (95)
Pathological fracture at diagnosis (n = 56)	
No	44 (79)
Yes	12 (21)
Previous spine tumor operation (n = 58)	
No	43 (74)
Yes	15 (26)
Biopsy (n = 49)	
Open	11 (22)
CT-trocar	30 (61)
Intraoperative	8 (16)
Preoperative Frankel/ASIA grade (n = 52)	
A	1 (2)
B	1 (2)
C	6 (12)
D	14 (27)
E	30 (58)
Spine level (n = 58)	
Mobile	41 (71)
Fixed	17 (29)
Local recurrence (n = 57)	
No	40 (70)
Yes	17 (30)
Survival (n = 58)	
Alive	34 (59)
Dead	24 (41)

ASIA = American Spinal Injury Association.

* Data are presented as number of patients (%) or mean ± standard deviation.

($p = 0.035$). Statistical differences were not found between Enneking cohorts when comparing the other baseline characteristics such as age at surgery ($p = 0.749$), sex ($p = 0.875$), spine level ($p = 0.234$), number of vertebral levels spanned by the tumor ($p = 0.128$), timing of chemotherapy ($p = 0.062$), and timing of radiation therapy ($p = 0.740$).

Local Recurrence

During the study period, 17 (30%) patients developed a local recurrence, 10 of whom later died. Local recurrence information was unknown for 1 patient because the patient had already died. The median time to first local recurrence for all patients was not reached during the analysis. Considering only those patients for whom we have data available for Enneking appropriateness, 3 (10%) EA patients and 11 (44%) EI patients developed a local recurrence (Table 4). The Kaplan-Meier analysis conducted

TABLE 3. Summary of the osteosarcoma characteristics

Variable	Value*
Enneking stage (n = 55)	
Low grade (I)	2 (4)
Intracompartmental (Ia)	0 (0)
Extracompartmental (Ib)	2 (100)
High grade (II)	53 (96)
Intracompartmental (IIa)	1 (2)
Extracompartmental (IIb)	52 (98)
No. of vertebral levels spanned by the tumor (n = 58)	
1	10 (17)
2–3	30 (52)
≥4	18 (31)
Mean tumor size in cm (n = 52)	
Anterior-posterior	7.9 ± 4.8
Left-right	7.4 ± 4.9
Cephalad-caudad	7.1 ± 5.9
Mean tumor vol ellipsoid body in cm ³ (n = 51)†	473.1 ± 978.4

* Data are presented as number of patients (%) or mean ± standard deviation.

† Tumor volume ellipsoid body = $\pi/6 \times \text{height} \times \text{width} \times \text{depth}$.

over a 10-year period following surgical resection demonstrated a significant difference between the 2 Enneking procedures, and the EI procedure has a higher rate of local recurrence ($p = 0.001$; Fig. 1). There were no other statistical differences found on the univariate analysis when evaluating the rate of local recurrence, including the use of adjuvant or neoadjuvant chemotherapy (Table 5).

Survival

Twenty-four (41%) patients died during the study period. The median survival of all patients was 6.7 years post-operatively. Considering only those patients for whom we have data available for Enneking appropriateness, 9 (31%) EA patients and 13 (50%) EI patients died (Table 4). The Kaplan-Meier analysis conducted over a 10-year period following resection demonstrated a significant difference in favor of greater survival following EA treatment ($p = 0.048$) (Fig. 2). There were no other statistical differences found when evaluating patient survival on the univariate analysis (Table 5).

Discussion

Osteosarcoma of the spine is a rare but aggressive tumor with a poor prognosis. Recent advances in treatment, including aggressive en bloc resection and the use of adjuvant and neoadjuvant chemotherapeutics, trend toward longer survival times and less recurrence, although the data are limited. This study is the largest collection of spinal osteosarcomas studied to date, and the only ambispective and multicenter data set available.

Consistent with previous studies, these data continue to demonstrate that spinal osteosarcoma is a sinister diagnosis. In this study, 30% of patients suffered recurrence and 41% of patients died by the final follow-up. However, these numbers reflect an improvement over previous sur-

TABLE 4. Comparison of Enneking cohorts*

Variable	EA	EI	p Value
Mean age at surgery (yrs) (n = 55)	36.6 ± 15.5	35.2 ± 17.0	0.749†
Sex (n = 55)			0.875‡
Female	15 (52)	14 (54)	
Male	14 (48)	12 (46)	
Previous spine tumor operation (n = 55)			<0.001§
Yes	0 (0)	14 (54)	
No	29 (100)	12 (46)	
Biopsy (n = 46)			0.001§
Open	5 (20)	5 (24)	
CT-trocar	20 (80)	8 (38)	
Intraoperative	0 (0)	8 (38)	
Spine level (n = 55)			0.234‡
Mobile	18 (62)	20 (77)	
Fixed	11 (38)	6 (23)	
No. of vertebral levels spanned by the tumor (n = 55)			0.128§
1	4 (14)	5 (19)	
2–3	12 (41)	16 (62)	
≥4	13 (45)	5 (19)	
Tumor vol ellipsoid body (cm ³) (n = 50)**	IQR 58.3–675.2	IQR 16.8–175.9	0.007¶
Chemotherapy timing (n = 55)			0.062§
Preoperative	11 (38)	8 (31)	
Postoperative	2 (7)	6 (23)	
Both	13 (45)	5 (19)	
None	3 (10)	7 (27)	
Radiation therapy timing (n = 55)			0.740§
Preoperative	5 (17)	4 (15)	
Postoperative	5 (17)	7 (27)	
None	19 (66)	15 (58)	
Local recurrence (n = 54)			0.011§
No	26 (90)	14 (56)	
Yes	3 (10)	11 (44)	
Survival (n = 55)			0.152‡
Alive	20 (69)	13 (50)	
Dead	9 (31)	13 (50)	

IQR = interquartile range.

* Data are presented as number (%), mean ± standard deviation, or interquartile range (25–75th percentile).

† Determined using the Student t-test.

‡ Determined using the Pearson's chi-square test.

§ Determined using the Fisher's exact test.

¶ Determined using the Mann-Whitney test.

** Tumor volume ellipsoid body = $\pi/6 \times \text{height} \times \text{width} \times \text{depth}$.

vival rates.^{51,55} Likely, this reflects both the addition of aggressive resection and chemotherapeutics to the treatment armamentarium and parallels improvements in survival when these tools were applied to patients suffering from appendicular osteosarcomas.^{38,49,51,55} Additionally, as this cohort includes patients treated as far back as 1987, prior to the acceptance of en bloc resection and chemotherapeutics as the treatment of choice, this series likely underestimates current survival rates.

Local recurrence was significantly higher in the EI

cohort compared with the EA cohort. Contrary to other reports¹⁵ open versus needle biopsy did not have a statistically significant impact on local recurrence. Nevertheless, it is important to note that a significant difference in the type of biopsy performed between the EA and EI cohorts was found. As a result of the small sample size, the current study is underpowered to explore if the type of biopsy plays a significant role in patient outcome. Furthermore, of the patients with local recurrence, 59% died by the completion of the study. This concurs with previ-

FIG. 1. Kaplan-Meier analysis of time to first local recurrence following surgery in EA versus EI patients. The number at risk indicates the number of patients included in the analysis. The median time to first local recurrence for EI procedures is 2.3 years postoperation, while for EA procedures the median first time to local recurrence was not reached in this analysis.

ously published results, underscoring the importance of EA surgery and the high mortality associated with local recurrence. In a series of mixed sarcomas of the spine, positive resection margins resulted in a 5-fold increase in local recurrence, with a 92% mortality rate following local recurrence.⁵⁷ These findings underscore the impact of tumor capsular disruption on local recurrence and survival. Unfortunately, due to the extreme technical challenges of en bloc resection in the spine and the morphology of the tumor itself, capsular disruption is not always avoidable if neurological elements are preserved. Thus, minimizing

tumor spillage in planned capsular disruptions or sacrificing neurological anatomy may be necessary. While preoperative chemotherapy may help minimize the impact of controlled tumor transgression during surgery, this has not been formally studied.

Aggressive EA surgery points toward a significant survival advantage over EI surgery. In this study, median survival following EI resection was 3.7 years, while it was 6.8 years in the EA cohort. Historical data remain limited in spinal osteosarcoma cohorts. Schwab et al. published the largest case series of 17 patients with osteosarcoma of the

FIG. 2. Kaplan-Meier analysis of survival following surgery in EA versus EI patients. The number at risk indicates the number of patients included in the analysis. The median survival for EI procedures is 3.7 years postoperation, while for EA procedures the median survival is 6.8 years postoperatively.

TABLE 5. Univariate results derived from the log-rank test used to evaluate the survival and incidence of local recurrence over a 10-year period following resection

Variable	Local Recurrence*			Survival		
	No. of Patients	No. of Observed Events (recurrences)	p Value	No. of Patients	No. of Observed Events (deaths)	p Value
Age at surgery (yrs)			0.600			0.882
<25	18	7		18	7	
25–44	22	6		23	9	
≥45	16	3		17	8	
Previous spine tumor operation			0.486			0.872
Yes	15	5		15	6	
No	41	11		43	18	
Biopsy			0.118			0.584
Open	11	6		11	4	
CT-trocar	29	7		30	11	
Intraoperative	7	1		8	4	
Spine level			0.813			0.226
Mobile	41	13		41	17	
Fixed	15	3		17	7	
No. of vertebral levels spanned by the tumor			0.621			0.554
1	10	2		10	4	
2–3	30	10		30	16	
≥4	16	4		18	4	
Tumor vol ellipsoid body (cm ³)†			0.703			0.193
<100	24	8		25	9	
≥100	26	5		27	11	
Enneking appropriateness			0.001			0.048
EA	29	3		29	9	
EI	24	10		26	13	
Chemotherapy timing			0.233			0.063
Preoperative	19	5		19	8	
Postoperative	9	5		9	5	
Both	18	4		19	4	
None	10	2		11	7	

* Complete information is available for 56 of 58 patients.

† Tumor volume ellipsoid body = $\pi/6 \times \text{height} \times \text{width} \times \text{depth}$.

mobile spine and demonstrated a survival advantage of en bloc resection (median survival 77.3 months) versus intralesional resection (median survival 16.8 months)⁵⁰ that did not reach statistical significance. In a small series, the 5 patients with wide or marginal tumor resections had a statistically significant survival advantage over the 17 patients with intralesional or no surgery.⁴⁴ Aggressive surgery was also supported in the study by DeLaney et al. that explored the utility of proton beam adjuvant therapy; however, this study was based on tumor volume, not margins, and thus does not obviate the need for EA surgery.¹⁹ In a mixed histology series of sarcomas, Groves et al. found that en bloc resection offered a significant survival advantage over intralesional resection.²⁹ Although studies remain scant and limited due to small sample sizes, by using a systematic review format and consensus recommendations Sciubba et al. strongly recommend en bloc resection for local control

and possible overall survival despite very low evidence.⁵¹ Specifically, they recommended that a multidisciplinary panel determine the feasibility of en bloc resection and that an experienced team perform this procedure. It should be noted, however, that the feasibility of en bloc resections is tumor dependent, as technical challenges and proximity to critical structures may make EA resections unfeasible or require the patient to accept significant impairment. Surgeons must use good judgment and patient preference when determining the surgical approach.

Neoadjuvant chemotherapy has become accepted as the standard treatment for osteogenic sarcoma of the spine. While the value of chemotherapy for spinal osteosarcoma has not been specifically evaluated, its value has been clearly demonstrated in extremity osteosarcoma with a biological rationale that is expected to be independent of primary tumor location. The current study is under-

powered to detect an absolute benefit to chemotherapy, as 47 of 58 patients had chemotherapeutic treatment and the small comparison cohort makes analysis difficult. Nevertheless, it is important to note that significantly more EA-treated patients received neoadjuvant chemotherapy compared with EI-treated patients; thus, neoadjuvant chemotherapy may have a positive impact on overall outcome. Other spine studies, while also underpowered, have demonstrated a trend toward longer survival with neoadjuvant therapy.^{52,56} In one study in which patients were treated with high-dose methotrexate and Adriamycin, it was concluded that the preferred treatment for spinal osteosarcoma should include neoadjuvant therapy and at least a marginal resection to optimize outcome.⁴⁴ Similarly, a study of 26 patients treated with multimodality therapy, including en bloc resection and neoadjuvant therapy, demonstrated better survival than historical controls,⁴⁸ such as those that predate the modern chemotherapeutic era.^{1,52} Others have reported that patients undergoing neoadjuvant chemotherapy with contaminated surgical margins have avoided local and distant recurrences and theorized that this may be due to chemotherapeutic response.⁵⁰ Although data focusing on the spine are scant, it is notable that the addition of chemotherapy to wide surgical excision in appendicular osteosarcoma has greatly increased survival.^{36,37,39,40,42,49,51,55,64} Importantly, a large study by Link et al. demonstrated that patients undergoing surgery only had a 2-year relapse-free survival rate of 17% versus 66% in the adjuvant chemotherapy group among 36 randomized patients, which was further supported by similar results in 77 patients who refused randomization.³⁷ Gherlinzoni et al. further found that the incidence of local recurrence was related above all to adjuvant chemotherapy-induced tumor necrosis.²⁸ Thus, it is reasonable to extrapolate the gains of aggressive surgery and neoadjuvant chemotherapy to the spine. Based on a combination of evidence involving appendicular and axial osteosarcoma studies, Sciubba et al. strongly recommended neoadjuvant chemotherapy based on a moderate level of evidence in their systematic review of osteosarcoma treatment.⁵¹

The role of adjuvant radiotherapy in the local treatment of spinal osteosarcoma remains incompletely defined at this time. While not traditionally considered a radiosensitive tumor, advanced radiation techniques (e.g., stereotactic radiotherapy delivery and proton beam therapy) may be able to deliver tumoricidal doses while not exceeding local neurological or adjacent organ toxicity constraints.^{11,18} At present, adjuvant radiotherapy remains investigational as a primary or adjuvant local control modality for spinal osteosarcoma.

Although this study is the largest cohort of spine osteogenic sarcomas in the literature and the first multicenter study of its kind, there are limitations. Spinal osteosarcoma is rare, and despite a multicenter ambispective design, the sample size is still small, making it challenging to explore the influence of neoadjuvant and adjuvant chemotherapies. Both the local recurrence and survival findings are also limited by the relatively short follow-up time for a tumor study. This probably biases toward the null hypothesis; however, longer follow-up with this now-established cohort would strengthen validity. Furthermore, terminol-

ogy, pathological differentiators, and innovations in surgical and adjuvant therapy may not be reflected in this study based on its multicenter format and time frame for data collection. These limitations can only be reduced by a carefully designed, rigidly performed prospective study, which has been initiated by the AOSpine Knowledge Forum Tumor and involves several more centers. Research questions about EA and EI margins, planned transgressions, health-related quality of life, adjuvant and neoadjuvant treatment protocols, biopsy techniques, molecular and genetic phenotyping, and the prognosis of tumors, have been included.

Conclusions

Osteosarcoma is an aggressive tumor; however, EA surgical procedures significantly reduce local recurrence and increase survival. While these findings are significant, the differences in adjuvant chemotherapy, type of biopsy, and previous spine tumor operations between cohorts may bias these results. Therefore, further studies are needed to explore the effects of EA surgery and adjuvant and neoadjuvant chemotherapeutics, in addition to the type of biopsy performed, in spinal osteosarcoma patients.

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Disclosures

Dr. Rhines is a consultant for Stryker and Globus. Dr. Sciubba is a consultant for Medtronic and has a financial relationship with DePuy Synthes. Dr. Fisher is a consultant for Medtronic and NuVasive, and has a financial relationship with Medtronic. Dr. Rose is a consultant for K2M. Dr. Germscheid has financial relationships with AOSpine. Dr. Chou is a consultant for Medtronic, Globus, and Orthofix.

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Author Contributions

Conception and design: Dekutoski, Rose, Luzzati, Rhines, Varga, Fisher, Chou, Fehlings, Reynolds, Williams, Quraishi, Sciubba, Gokaslan, Boriani. Acquisition of data: Dekutoski, Luzzati, Rhines, Varga, Fisher, Chou, Fehlings, Reynolds, Williams, Quraishi, Sciubba, Gokaslan, Boriani. Analysis and interpretation of data: Clarke, Luzzati, Rhines, Fisher, Fehlings, Germscheid, Gokaslan, Boriani. Drafting the article: Clarke, Varga, Fisher, Germscheid, Sciubba, Boriani. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Clarke. Statistical analysis: Clarke, Germscheid. Administrative/technical/material support: Germscheid. Study supervision: Rhines, Varga, Fisher, Gokaslan, Boriani.

Supplemental Information

Previous Presentations

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