Clinical Article

Survival and Recurrence Rate after Treatment for Primary Spinal Sarcomas

Wonik Cho, M.D., Ung-Kyu Chang, M.D., Ph.D.

Department of Neurosurgery, Korea Cancer Center Hospital, Korea Institute of Radiological and Medical Science, Seoul, Korea

Objective : We have limited understanding on the presentation and survival of primary spinal sarcomas. The survival, recurrence rate, and related prognostic factors were investigated after treatment for primary sarcomas of the spine.

Methods : Retrospective analysis of medical records and radiological data was done for 29 patients in whom treatment was performed due to primary sarcoma of the spine from 2000 to 2010. As for treatment method, non-radical operation, radiation therapy, and chemotherapy were simultaneously or sequentially combined. Overall survival (OS), progression free survival (PFS), ambulatory function, and pain status were analyzed. In addition, factors affecting survival and recurrence were analyzed : age (≤42 or ≥43), gender, tumor histologic type, lesion location (mobile spine or rigid spine), weakness at diagnosis, pain at diagnosis, ambulation at diagnosis, initial treatment, radiation therapy, kind of irradiation, surgery, chemotherapy and distant metastasis.

Results : Median OS was 60 months, the recurrence rate was 79.3% and median PFS was 26 months. Patients with distant metastasis showed significantly shorter survival than those without metastasis. No factors were found to be significant relating to recurrence. Prognostic factor associated with walking ability was the presence of weakness at diagnosis.

Conclusion : Primary spinal sarcomas are difficult to cure and show high recurrence rate. However, the development of new treatment methods is improving survival.

Key Words : Primary spinal sarcoma · Survival · Recurrence · Prognosis.

INTRODUCTION

Sarcomas are a family of malignant tumors that arise from connective or mesenchymal tissue. Primary spinal sarcomas arise from the spine itself, usually from a structural component such as bone or cartilage[18]. Their incidence is very rare. According to the American Cancer Society, they account for less than 5% of all osseous neoplasms, and less than 0.2% of all cancers[24,25]. Dorfman and Czerniak[9] analyzed data on 2627 primary malignant tumors of bone including spine collected in the Surveillance, Epidemiology, and End Results (SEER) program. Their tumors were osteosarcoma (35.1%), followed by chondrosarcoma (25.8%), Ewing's sarcoma (16.0%), chondroma (8.4%), and malignant fibrous histiocytoma (MFH) (5.6%). These tumors can cause significant morbidity and mortality secondary to local invasion and destruction of adjacent structures including bone, nerves, and vascular structures, and they can metastasize to distant organs[19,24].

Tremendous advancement has been made in the surgical and medical therapy of malignant primary bone tumors[19,27,34], but their spinal involvement is still associated with poor prognosis[17,22]. The understanding of the epidemiology of primary spinal sarcomas has been limited to small case series and controlled trials in the treatment were impossible because of their rarity[23]. These facts resulted in non-uniform approach in the treatment of the spinal sarcomas[16,27]. And, a general understanding of the presentation and survival of primary spinal sarcomas is also lacking[39]. For this reason the establishment of a bone tumor registry provides a valuable source of information and facilitates reasonable treatment of these tumors[16,28]. It was known that primary sarcomas of the spine had low survival and high recurrence rate compared to sarcoma occurring in extremity[2,8,22,24,31,37,41]. The radical or wide excision is required in sarcoma treatment, but it is difficult to perform the radical excision

due to the risk of neural or vascular injuries[7,19]. In addition, high dose radiation cannot be delivered to residual mass, because it may produce radiation-induced spinal cord injury[3,5,16].

The purpose of this study is to investigate the survival and recurrence rate of primary spinal sarcoma patients who underwent non-radical surgery plus adjuvant therapy or nonoperative treatments. Also, prognostic factors affecting survival, recurrence, and ambulatory function were analyzed.

MATERIALS AND METHODS

Study cohort was the patients who were treated in our hospital due to primary spinal sarcomas from January 2000 to December 2010. The total number of patients was 29, and their medical records and radiologic images were analyzed retrospectively. The number of male patients was 19 and that of female patients 10. The average age of patients was 42.9 years old (range, 11 to 76 years). With regard to tumor histology, malig-

nant peripheral nerve sheath tumor (MPNST, 8 patients) was the most prevalent, and other tumors included chondrosarcoma (6 patients), osteosarcoma (5 patients), MFH (4 patients), Ewing sarcoma and synovial sarcoma (each 3 patients). Regarding lesion location, 21 patients had a tumor on mobile spine (8 lesion in cervical, 10 in thoracic and, 3 in lumbar spine), while 8 patients had a tumor on rigid spine (sacrum). With regard to the lesion multiplicity, 17 patients had a single lesion where the tumor was confined to one segment at diagnosis, and 12 patients had multiple level involvement. Ten patients showed distant metastasis during follow-up, and 3 patients had metastasis at diagnosis. The time for the development of distant metastasis was, on the average, 24 months. The site of distant metastasis was lung in 9 patients and brain in one patient. Demographic data in our study cohort were summarized in Table 1.

Twenty-seven patients complained of pain and 14 patients had motor weakness at the time of diagnosis. Twenty-six patients could walk at diagnosis, and 15 patients could walk also

Table 1. Demographic data in 29 patients of primary spinal sarcomas

Case No.	Age	Gender	Histology	Lesion site	Initial treatment	Radiation therapy	Chemo therapy	No. of operation	Distant metastasis
1	15	F	Ewing	C6, 7	Surgery	Conventional	Yes	1	No
2	32	M	MPNST	C3-5	Surgery	Both	No	2	Brain
3	23	M	Chondro	C7	Surgery	Both	Yes	2	No
4	47	F	MPNST	C3	Surgery	Both	No	1	No
5	62	F	Osteo	T10	Irradiation	Both	Yes	1	No
6	74	F	MFH	Sacrum	Chemo	Conventional	Yes	1	No
7	11	M	Ewing	Sacrum	Chemo	Both	Yes	0	No
8	68	F	Chondro	Sacrum	Surgery	Conventional	No	1	No
9	25	M	Osteo	Sacrum	Chemo	Conventional	Yes	0	Lung
10	28	M	MPNST	T5, 6	Surgery	Radiosurgery	No	1	No
11	71	M	MFH	T8	Surgery	None	No	1	No
12	51	F	MPNST	L1, 2	Surgery	Both	No	2	No
13	62	F	Chondro	Sacrum	Surgery	Radiosurgery	No	6	No
14	36	M	MPNST	C5, 6	Irradiation	Radiosurgery	No	0	No
15	37	M	Synovial	T12	Irradiation	Radiosurgery	Yes	0	Lung
16	59	M	MFH	T8	Surgery	Conventional	Yes	1	Lung
17	38	M	Osteo	L3	Chemo	Both	Yes	0	Lung
18	33	M	Chondro	T1, 2	Surgery	None	Yes	3	Lung
19	67	M	MPNST	T10, 11	Surgery	Conventional	No	3	Lung
20	72	M	Chondro	Sacrum	Surgery	Conventional	No	2	No
21	46	F	MPNST	C3	Surgery	Both	No	2	No
22	51	F	Osteo	T3	Surgery	Radiosurgery	Yes	1	No
23	76	M	MFH	T5, 6	Irradiation	Conventional	No	2	Lung
24	17	M	Synovial	Sacrum	Irradiation	Radiosurgery	Yes	4	No
25	18	M	Synovial	Sacrum	Surgery	Radiosurgery	Yes	1	No
26	23	M	Ewing	T5	Chemo	Both	Yes	2	Lung
27	34	M	Chondro	L3, 5	Chemo	Conventional	Yes	0	Lung
28	29	M	Osteo	C4, 5	Surgery	Conventional	Yes	1	No
29	41	F	MPNST	C7	Irradiation	Radiosurgery	Yes	3	No

No. : numbers, M : male, F : female, MPNST : malignant peripheral nerve sheathe tumor, MFH : malignant fibrous histiocytoma, Osteo : osteosarcoma, Chondro : chondrosarcoma, Ewing : Ewing sarcoma, Synovial : synovial sarcoma

Table 2. Histologic types of primary spinal sarcomas

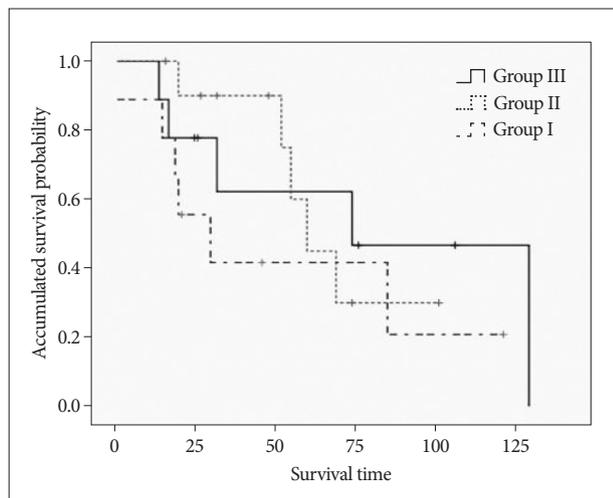| Group	Histologic type	Numbers	Total
Group I	Osteosarcoma	5	9
	Malignant fibrous histiocytoma	4	
Group II	Chondrosarcoma	6	9
	Ewing sarcoma	3	
Group III	Malignant peripheral nerve sheath tumor	8	11
	Synovial sarcoma	3	

Fig. 1. Kaplan-Meier estimated survival in patients with primary sarcoma of the spine according to histologic type. Median values of survival were 30 months (group I), 60 months (group II), and 74 months (group III). There was no statistical significance among three groups (p=0.427).

at the last follow-up. Among 14 patients who could not ambulate, 10 patients could not walk due to neurologic deficit and remaining 4 patients could not walk due to intractable pain. The period for which ambulatory function was maintained was average 46 months, 13 patients could walk longer than 46 months, whereas 16 patients shorter than 46 months.

In initial treatment, surgery was chosen in 17 patients, irradiation in 6 patients, and chemotherapy in 6 patients. A total of 23 patients received the surgical treatment during the follow-up. Operations were performed 44 times in a total of 23 patients and 12 patients received the surgery two or more times. As for surgical procedure, all the operations were subtotal or partial removal of tumors, not radical excision. Adjuvant treatments were conducted after subtotal removal. Complications related to surgery occurred in 7 cases. There were 4 cases of wound infection, one case of screw malposition, one case of hypoglossal nerve palsy, and one case of pulmonary complication. Every patient recovered from these complications without sequelae. As for radiation therapy, 27 patients received radiation therapy (RT) during the treatment period. Conventional RT was given to 10 patients, 8 patients received stereotactic radiosurgery, and 9 patients received both of them. Anticancer chemotherapy was performed in 17 patients.

Tumor was classified into 3 groups based on the histologic

types (Table 2). Osteosarcoma and MFH, being known to have similar clinical behavior, belonged to first group (group I). Ewing' sarcoma and chondrosarcoma which were reported to have long survival belonged to the second group (group II). The remaining MPNST and synovial sarcoma were included into the third group (group III).

In this study, we sought to determine overall survival (OS) and progression free survival (PFS) in primary sarcoma of spine, and to document pain level changes and ambulatory status during follow-up. Thirteen prognostic factors affecting survival, systemic recurrence and ambulatory function were analyzed : age (≤42 or ≥43), gender, tumor histologic type (osteosarcoma and MFH, or Chondrosarcoma and Ewing sarcoma, or MPNST and synovial sarcoma), lesion location (mobile spine or rigid spine), weakness at diagnosis, pain at diagnosis, ambulation at diagnosis, initial treatment method, radiation therapy, kind of irradiation, surgery, chemotherapy and distant metastasis.

Survival analysis was performed by using the log-rank test. Survival curves were created by using the Kaplan-Meier life-table analysis. Chi-square and Fisher exact tests were used for categorical variables and Student's t test were used for continuous and ordinal variables, as appropriate. A p value 0.05 (two-tailed) was considered significant. The data were compiled and analyzed with the software package SPSS, version 14.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Median of OS in the study cohort was 60 months [95% confidence interval (CI), 33.17-86.83 months]. The OS was different depending on the histologic type (Fig. 1). Osteocarcoma and MFH group showed the shortest survival of 30 months (95% CI, 5.59-54.40 months). In group II (MPNST and synovial sarcoma group) median survival was estimated to be 60 months. Ewing sarcoma and chondrosarcoma group, which was known to have the longest survival, showed median survival of 74 months (95% CI, 16.07-131.93 months). However, there was no statistical significance among three groups. Among total 29 patients, 13 patients were alive at the last follow-up and 16 patients died. Fourteen patients died of the disease progression and two patients the medical condition unrelated to tumor progression such as sepsis or acute renal failure. Statistically significant prognostic factors associated with survival were the presence of distant metastasis (Table 3). The patients with distant

Table 3. Prognostic factors relating to survival

Prognostic factors	Variables	p value
Age	Under 42 years vs. over 43 years	0.145
Gender	Male vs. female	0.178
Tumor group	Osteo, MFH vs. Chondro, Ewing vs. MPNST, Synovial	0.427
Lesion location	Mobile spine vs. rigid spine	0.458
Weakness at diagnosis	Weakness vs. normal motor power	0.441
Pain at diagnosis	Pain vs. no pain	0.662
Ambulation at diagnosis	Ambulatory vs. non-ambulatory	0.262
Initial treatment	Surgical treatment vs. non-surgical treatment	0.380
Radiation therapy	Irradiation vs. no irradiation	0.147
Kind of irradiation	Conventional radiation vs. radiosurgery vs. both	0.124
Surgery	Yes vs. no	0.829
Chemotherapy	Yes vs. no	0.290
Distant metastasis	Yes vs. no	0.002*

*Significant at $p<0.05$. MPNST : malignant peripheral nerve sheathe tumor, MFH : malignant fibrous histiocytoma, Osteo : osteosarcoma, Chondro : chondrosarcoma, Ewing : Ewing sarcoma, Synovial : synovial sarcoma

metastasis, whose median survival was 30 months (95% CI, 7.23-52.77 months) showed significantly shorter survival than the cases without metastasis whose median survival was 85 months (95% CI, 57.29-112.71 months; p=0.002) (Fig. 2).

Twenty-three out of 29 patients experienced the recurrence during the follow-up. The recurrence rate was 79.3% on follow-up. The recurrence implies not only the local recurrence at the tumor site but also the systemic recurrence including the distant metastasis. PFS of patients was 26 months (95% CI, 14.09-37.91 months). After 26 months, the recurrence or progression was shown in most patients. There were no statistically significant prognostic factors associated with recurrence (Table 4).

Among 27 patients who complained of pain at the time of diagnosis, pain improvement was achieved in 23 patients after the treatment. No change in pain score was seen in remaining four patients. Pain status was evaluated with visual analogue scale (VAS). Pain was determined to be controlled when post-treatment VAS decreased by more than two points or the amount of pain medication was reduced. At initial diagnosis, mean value of VAS was 8.44±1.25 points before treatment. Mean VAS fell to 4.56±2.10 points after the treatment with 3.89±2.08 point decrease (p=0.001). Pain score of patients who underwent the surgical treatment was measured upon the first follow-up after the surgery. Pain score of patients who received non-surgical treatments was measured within a month upon the completion of initial treatment. Likewise, pain was reduced after the initial treatment, but the pain increased again with recurrence after 27 months. There were no statistically significant prognostic factors associated with the pain control.

As a whole, median period during which ambulatory function was maintained was 54 months (95% CI, 43.33-104.67 months). Statistically significant prognostic factor associated with post-treatment ambulatory function was the presence of weakness at initial diagnosis (Table 5). Among patients who did not show motor weakness at initial diagnosis, patients who maintained the walking ability at the last follow-up were 86.7%,
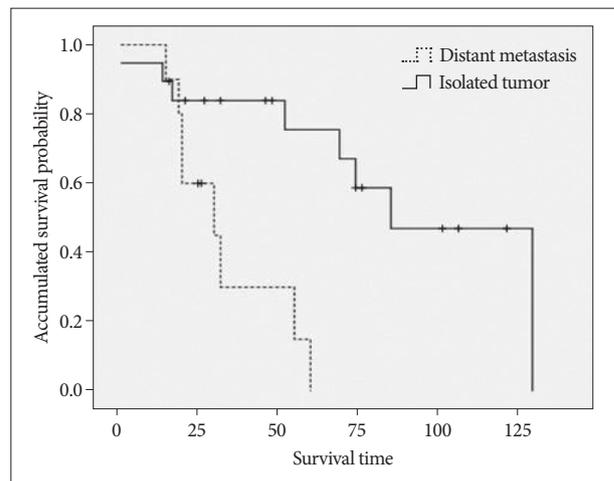

Fig. 2. The survival difference between group with distant metastasis and group without metastasis. Median values were 30 months (metastasis) and 85 months (no metastasis) (p=0.002).

which is twice as much as patients who had weakness at initial diagnosis (42.9%) (p=0.013) (Fig. 3).

DISCUSSION

Treatments for primary spinal sarcomas involve a multi-modality approach consisting of surgery, radiation therapy and chemotherapy[12,30]. The experience in the treatment of extremity sarcomas have been applied to cases of spinal sarcomas[3]. Although great advances have been achieved in the treatment, oncological outcome in spinal sarcomas is worse than that of soft tissue sarcomas in extremities[20,33,40]. In extremity sarcomas, many reports on survival and recurrence are available[2,31,36,37]. Vasileios et al.[37] reported that 5-year survival rate of MFH patients was 66% and the recurrence and the metastasis rates were 31%. Tural et al.[36] reported that the recurrence rate was 23% and 5-year survival rate was 72% through retrospective study of adult Ewing sarcoma patients. According to Stanelle et al.[31]'s

Table 4. Prognostic factors relating to recurrence

Prognostic factors	Variables	p value
Age	Under 42 years vs. over 43 years	0.832
Gender	Male vs. female	0.685
Tumor group	Osteo, MFH vs. Chondro, Ewing vs. MPNST, Synovial	0.713
Lesion location	Mobile spine vs. rigid spine	0.941
Weakness at diagnosis	Weakness vs. normal motor power	0.566
Pain at diagnosis	Pain vs. no pain	0.945
Ambulation at diagnosis	Ambulatory vs. non-ambulatory	0.753
Initial treatment	Surgical treatment vs. non-surgical treatment	0.241
Radiation therapy	Irradiation vs. no irradiation	0.222
Kind of irradiation	Conventional radiation vs. radiosurgery vs. both	0.449
Surgery	Yes vs. no	0.223
Chemotherapy	Yes vs. no	0.303
Distant metastasis	Yes vs. no	0.214

MPNST : malignant peripheral nerve sheathe tumor, MFH : malignant fibrous histiocytoma, Osteo : osteosarcoma, Chondro : chondrosarcoma, Ewing : Ewing sarcoma, Synovial : synovial sarcoma

Table 5. Prognostic factors relating to ambulatory function

Prognostic factors	Variables	p value
Age	Under 42 years vs. over 43 years	0.233
Gender	Male vs. female	0.713
Tumor group	OS, MFH vs. Chondro, Ewing vs. MPNST, Synovial	0.552
Lesion location	Mobile spine vs. rigid spine	0.124
Weakness at diagnosis	Weakness vs. normal motor power	0.013*
Pain at diagnosis	Pain vs. no pain	0.965
Ambulation at diagnosis	Ambulatory vs. non-ambulatory	0.090
Primary treatment	Surgical treatment vs. non-surgical treatment	0.427
Radiation therapy	Irradiation vs. no irradiation	0.183
Kind of irradiation	Conventional radiation vs. radiosurgery vs. both	0.123
Surgery	Yes vs. no	0.650
Chemotherapy	Yes vs. no	0.233
Distant metastasis	Yes vs. no	0.713

*Significant at $p<0.05$. MPNST : malignant peripheral nerve sheathe tumor, MFH : malignant fibrous histiocytoma, Osteo : osteosarcoma, Chondro : chondrosarcoma, Ewing : Ewing sarcoma, Synovial : synovial sarcoma

paper, it was reported that 73% of 5-year survival rate, 65% of 10-year survival rate in synovial sarcoma and 41% of recurrence rate of this disease. Arndt et al.[2] reported 65% of 5-year survival rate in osteosarcoma. In our study, 5-year survival rate was 41%, 61% and 45% in osteosarcoma/MFH group, chondrosarcoma/Ewing sarcoma group and MPNST/synovial sarcoma group, respectively. These data show the outcome is better in extremity sarcomas than in spinal sarcomas.

Since primary spinal sarcomas are very rare diseases[24,25], the standard treatment method has not been established[28,34,38,39]. However, treatment for osteosarcoma and chondrosarcoma is being conducted in uniform fashion. In cases of osteosarcoma, preoperative chemotherapy and radical surgery is usually performed[1,2,4,5]. Preoperative chemotherapy enables the tumor size to be reduced. Postoperative adjuvant chemotherapy is sometimes done when indicated. In chondrosarcoma, chemotherapy or radiation therapy is rarely indicated and the sole effective treatment is operative resection[14,15,21,32]. Improvement in surgical approach to the entire vertebral column has made it technically feasible to resect tumors involving the spine at all levels, and the development of new instrumentation systems has enabled surgeons to reconstruct entire vertebral segments after resection[27,34]. But, the proximity of the dural sac, aorta, vena cava, and esophagus makes it difficult to achieve adequate negative surgical margins[19]. The en bloc resection of a spinal segment is a relatively recent concept, which is different from a complete piecemeal corpectomy[7]. It is recognized that, with rare exceptions, the rate of local recurrence depends on the adequacy of the resection, even when adjuvant therapy is used[6,20,28,39].

The histological types of sarcomas were identified and confirmed by a pathologist at M.D. Anderson Cancer Center. Soft tissue sarcomas were further dichotomized as either high (G2) or low (G1) grade according to the classification of Enneking et al.[10] Low-grade tumors are well differentiated, have few mitoses, and moderate cytologic atypia. High grade lesions are characterized by poor differentiation, a high cell/matrix ratio, and a high

mitotic rate, necrosis, and microvascular invasion[1,2,34,41]. Tumor growth and progression are variable depending on the differences in the grade of differentiation. In addition, these histological differences produce the differences in the susceptibility to radiation and the reactivity to chemotherapy, and affect the selection of adjuvant treatment. Therefore, it is thought that survival rate is various depending on histologic type.

A number of studies have attempted to identify prognostic factors for survival in primary sarcomas of the spine[8,22,23]. Damron et al.[8] investigated the survival and epidemiologic data from the National Cancer database of the American College of Surgeons. Their data included both extremity and spinal sarcomas. They reported that 5-year survival rate was 53.9% for osteosarcoma, 75.2% for chondrosarcoma, and 50.6% for Ewing's sarcoma.

Mukherjee et al.[24] analyzed overall survival and prognostic factors affecting survival time in malignant primary osseous spinal tumors. They searched the SEER database to identify all registered cases of Ewing sarcoma, osteosarcoma and chondrosarcoma to assess histology specific survival during the period from 1973 to 2003. Total study patients were identified as 579 with chondrosarcomas, 430 with osteosarcoma, and 469 with Ewing sarcomas. Overall median survival was histology-specific (osteosarcoma, 11 months; Ewing sarcoma, 26 months; chondrosarcoma, 37 months) and significantly worse in patients with distant metastasis at presentation for all tumor types. Schoenfeld et al.[29] performed a retrospective review of cases of osteosarcoma involving the spine treated. The median overall survival for all patients was 29.5 months. Local recurrence developed in 27%, and metastasis occurred in 62%.

In our study, overall survival was 30 months in the osteosarcoma and MFH group and 72 months in the Ewing' sarcoma and chondrosarcoma group, which were quite different from those from Mukherjee et al's study. However, their study analyzed the data obtained from last 30 years, but our study analyzed the data from recent 10 years. Two-fold increase in survival is observed between previous 30 years and recent 10 years. The reasons for the increase in survival can be summarized as follows[6,11,13,19,27,33-35]; 1) early detection, 2) close follow-up, and 3) development of advanced treatment modalities - en bloc resection technique, effective chemotherapeutic agents, and sophisticated radiation delivery technique. The development of advanced diagnostic techniques leads to early detection of the disease, which implies that most of patients are diagnosed without distant metastasis[11,13,34]. This fact can be applied to recurrence detection. Close follow-up results in early detection of recurrence, leading to survival prolongation. Technical improvement in treatment modalities increased the survival. In surgical method, en-bloc spondylectomy enabled more extensive resection of the spinal lesions[27]. Rao et al.[27] compared survival rates in en-bloc spondylectomy and intralesional resection for patients with spinal sarcoma (including metastatic sarcoma). Patients undergoing en-bloc resection had a median survival of 26.2 months, and those with intralesional resection had a median survival of 18.6
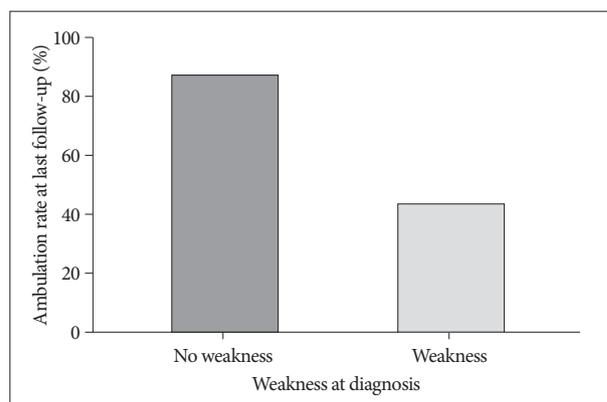

Fig. 3. The rate of patients who maintain ambulatory function at the last follow-up. In patients who did not have weakness at initial diagnosis, 86.7% of patients could walk at the last follow-up. However, in patients who had weakness at initial diagnosis, 42.9% could maintain ambulatory function at the last follow-up (p=0.013).

months. Teng et al.[35] conducted similar research targeting the patients with MFH of the spine. Compared to the 14 months median survival in debulking surgery group, that of the en-bloc resection group was 25 months. Both studies showed that en-bloc spondylectomy could improve tumor control and survival rate. In addition, the radiation therapy such as stereotactic radiosurgery and tomotherapy was developed and diversified, excellent local tumor control could be achieved without radiation injury to adjacent spinal cord[6,19,33].

It would be the best to compare the survival period based on each histologic type. However, it was impossible to compare individual histology, because the number of patients in each group was low. Thus, we grouped tumors with similar clinical characteristics and compared them. Although MFH is different from osteosarcoma in pathological finding (no tumor bone production), it is considered to be similar in clinical course and response to chemotherapy[26]. Therefore, These two tumors were included in the same group. Even if no significant difference was found in three groups, we assume that if more cases could be collected enough to compare individual histologic type, meaningful difference might be produced.

CONCLUSION

Primary spinal sarcomas are a mixed disease entity composed of several different histologic types. Treatment for them is challenging and not fully established. Present analysis showed that overall survival was 60 months, which is varying depending on histology and recurrence rate is so high. Close follow-up is required because recurrence could be within two or three years from initial diagnosis. The advancement in diagnostic and therapeutic techniques is gradually improving survival.

References
1. Allison DC, Carney SC, Ahlmann ER, Hendifar A, Chawla S, Fedenko A, et al. : A meta-analysis of osteosarcoma outcomes in the modern

medical era. **Sarcoma 2012** : 704872, 2012

2. Arndt CA, Rose PS, Folpe AL, Laack NN : Common musculoskeletal tumors of childhood and adolescence. **Mayo Clin Proc 87** : 475-487, 2012

3. Ballo MT, Zagars GK, Cormier JN, Hunt KK, Feig BW, Patel SR, et al. : Interval between surgery and radiotherapy : effect on local control of soft tissue sarcoma. **Int J Radiat Oncol Biol Phys 58** : 1461-1467, 2004

4. Bernthal NM, Federman N, Eilber FR, Nelson SD, Eckardt JJ, Eilber FC, et al. : Long-term results (>25 years) of a randomized, prospective clinical trial evaluating chemotherapy in patients with high-grade, operable osteosarcoma. **Cancer 118** : 5888-5893, 2012

5. Bölling T, Hardes J, Dirksen U : Management of bone tumours in paediatric oncology. **Clin Oncol (R Coll Radiol) 25** : 19-26, 2013

6. Castelli J, Thariat J, Benezery K, Courdi A, Chanalet S, Paquis P, et al. : [Spinals and paraspinals tumors treated by CyberKnife : feasibility and efficacy]. **Cancer Radiother 14** : 5-10, 2010

7. Chaichana KL, Parker SL, Mukherjee D, Cheng JS, Gokaslan ZL, McGirt MJ : Assessment of the extent of surgical resection as a predictor of survival in patients with primary osseous spinal neoplasms. **Clin Neurosurg 58** : 117-121, 2011

8. Damron TA, Ward WG, Stewart A : Osteosarcoma, chondrosarcoma, and Ewing's sarcoma : National Cancer Data Base Report. **Clin Orthop Relat Res 459** : 40-47, 2007

9. Dorfman HD, Czerniak B : Bone cancers. **Cancer 75 (1 Suppl)** : 203-210, 1995

10. Enneking WF, Spanier SS, Goodman MA : A system for the surgical staging of musculoskeletal sarcoma. 1980. **Clin Orthop Relat Res** : 4-18, 2003

11. Hillner BE, Siegel BA, Liu D, Shields AF, Gareen IF, Hanna L, et al. : Impact of positron emission tomography/computed tomography and positron emission tomography (PET) alone on expected management of patients with cancer : initial results from the National Oncologic PET Registry. **J Clin Oncol 26** : 2155-2161, 2008

12. Hsu W, Kosztowski TA, Zaidi HA, Dorsi M, Gokaslan ZL, Wolinsky JP : Multidisciplinary management of primary tumors of the vertebral column. **Curr Treat Options Oncol 10** : 107-125, 2009

13. Ilaslan H, Sundaram M, Unni KK, Shives TC : Primary vertebral osteosarcoma : imaging findings. **Radiology 230** : 697-702, 2004

14. Katonis P, Alpantaki K, Michail K, Lianoudakis S, Christoforakis Z, Tzanakakis G, et al. : Spinal chondrosarcoma : a review. **Sarcoma 2011** : 378957, 2011

15. Kawahara N, Tomita K, Murakami H, Demura S, Yoshioka K, Miyazaki T : Total excision of a recurrent chondrosarcoma of the thoracic spine : a case report of a seven-year-old boy with fifteen years follow-up. **Spine (Phila Pa 1976) 35** : E481-E487, 2010

16. Kelley SP, Ashford RU, Rao AS, Dickson RA : Primary bone tumours of the spine : a 42-year survey from the Leeds Regional Bone Tumour Registry. **Eur Spine J 16** : 405-409, 2007

17. Kim SH, Bak KH, Kim DW, Kang TH : Primary intramedullary spinal sarcoma : a case report and review of the current literatures. **J Korean Neurosurg Soc 48** : 448-451, 2010

18. Klimo P Jr, Codd PJ, Grier H, Goumnerova LC : Primary pediatric intraspinal sarcomas. Report of 3 cases. **J Neurosurg Pediatr 4** : 222-229, 2009

19. Levine AM, Coleman C, Horasek S : Stereotactic radiosurgery for the treatment of primary sarcomas and sarcoma metastases of the spine. **Neurosurgery 64 (2 Suppl)** : A54-A59, 2009

20. Lewis VO : What's new in musculoskeletal oncology. **J Bone Joint Surg Am 91** : 1546-1556, 2009

21. Lloret I, Server A, Bjerkehagen B : Primary spinal chondrosarcoma : radiologic findings with pathologic correlation. **Acta Radiol 47** : 77-84, 2006

22. McGirt MJ, Gokaslan ZL, Chaichana KL : Preoperative grading scale to predict survival in patients undergoing resection of malignant primary osseous spinal neoplasms. **Spine J 11** : 190-196, 2011

23. Mukherjee D, Chaichana KL, Adogwa O, Gokaslan Z, Aaronson O, Cheng JS, et al. : Association of extent of local tumor invasion and survival in patients with malignant primary osseous spinal neoplasms from the surveillance, epidemiology, and end results (SEER) database. **World Neurosurg 76** : 580-585, 2011

24. Mukherjee D, Chaichana KL, Gokaslan ZL, Aaronson O, Cheng JS, McGirt MJ : Survival of patients with malignant primary osseous spinal neoplasms : results from the Surveillance, Epidemiology, and End Results (SEER) database from 1973 to 2003. **J Neurosurg Spine 14** : 143-150, 2011

25. Pickle LW, Hao Y, Jemal A, Zou Z, Tiwari RC, Ward E, et al. : A new method of estimating United States and state-level cancer incidence counts for the current calendar year. **CA Cancer J Clin 57** : 30-42, 2007

26. Pobirci DD, Bogdan F, Pobirci O, Petcu CA, Roşca E : Study of malignant fibrous histiocytoma : clinical, statistic and histopatological interrelation. **Rom J Morphol Embryol 52 (1 Suppl)** : 385-388, 2011

27. Rao G, Suki D, Chakrabarti I, Feiz-Erfan I, Mody MG, McCutcheon IE, et al. : Surgical management of primary and metastatic sarcoma of the mobile spine. **J Neurosurg Spine 9** : 120-128, 2008

28. Schaser KD, Melcher I, Luzzati A, Disch AC : Bone sarcoma of the spine. **Recent Results Cancer Res 179** : 141-167, 2009

29. Schoenfeld AJ, Hornicek FJ, Pedlow FX, Kobayashi W, Garcia RT, DeLaney TF, et al. : Osteosarcoma of the spine : experience in 26 patients treated at the Massachusetts General Hospital. **Spine J 10** : 708-714, 2010

30. Sciubba DM, Okuno SH, Dekutoski MB, Gokaslan ZL : Ewing and osteogenic sarcoma : evidence for multidisciplinary management. **Spine (Phila Pa 1976) 34 (22 Suppl)** : S58-S68, 2009

31. Stanelle EJ, Christison-Lagay ER, Healey JH, Singer S, Meyers PA, La Quaglia MP : Pediatric and adolescent synovial sarcoma : multivariate analysis of prognostic factors and survival outcomes. **Ann Surg Oncol 20** : 73-79, 2013

32. Stuckey RM, Marco RA : Chondrosarcoma of the mobile spine and sacrum. **Sarcoma 2011** : 274281, 2011

33. Sundaresan N, Boriani S, Rothman A, Holtzman R : Tumors of the osseous spine. **J Neurooncol 69** : 273-290, 2004

34. Sundaresan N, Rosen G, Boriani S : Primary malignant tumors of the spine. **Orthop Clin North Am 40** : 21-36, 2009

35. Teng H, Xinghai Y, Wei H, Huang Q, Xiao J, Zhang C : Malignant fibrous histiocytoma of the spine : a series of 13 clinical case reports and review of 17 published cases. **Spine (Phila Pa 1976) 36** : E1453-E1462, 2011

36. Tural D, Molinas Mandel N, Dervisoglu S, Oner Dincbas F, Koca S, Colpan Oksuz D, et al. : Extraskeletal Ewing's sarcoma family of tumors in adults : prognostic factors and clinical outcome. **Jpn J Clin Oncol 42** : 420-426, 2012

37. Vasileios KA, Eward WC, Brigman BE : Surgical treatment and prognosis in patients with high-grade soft tissue malignant fibrous histiocytoma of the extremities. **Arch Orthop Trauma Surg 132** : 955-961, 2012

38. von Eisenhart-Rothe R, Toepfer A, Salzmann M, Schauwecker J, Gollwitzer H, Rechl H : [Primary malignant bone tumors]. **Orthopade 40** : 1121-1142, 2011

39. Wang VY, Potts M, Chou D : Sarcoma and the spinal column. **Neurosurg Clin N Am 19** : 71-80, 2008

40. Weber KL : What's new in musculoskeletal oncology. **J Bone Joint Surg Am 87** : 1400-1410, 2005

41. Wisanuyotin T, Radapat K, Sirichativapee W, Paholpak P, Kosuwon W, Sumnanoont C, et al. : Prognostic factors and clinical outcomes in synovial sarcoma of the extremities. **Asia Pac J Clin Oncol 9** : 80-85, 2013