J Korean Neurosurg Soc 37 : 187-192, 2005

Clinical Article

The Role of Surgery in the Treatment of Spinal Myeloma

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Objective : Spinal myeloma has been treated with radiation therapy and chemotherapy. However, the role of surgery was not fully evaluated. This study is performed to evaluate the efficacy of surgery in the treatment of spinal myeloma.

Methods : 22 patients who were treated with surgery for spinal myeloma from August 1999 to April 2003 were analyzed. Radiological finding, surgical methods and result were reviewed in retrospective study. For compression fracture due to myeloma infiltration, percutaneous vertebroplasy(PVP) was done. Decompression surgery with or without fixation was performed for patients with neurologic deficit. The modalities of surgery consist of PVP (14 cases), corpectomy and fixation (7 cases), and laminectomy and epidural mass removal (3 cases). To evaluate clinical outcome, visual analogue pain score and Frankel neurological scale were used.

Results : In 14 cases of PVP, total 57 vertebral segments were treated including 21 thoracic vertebral bodies and 36 lumbar vertebral bodies. Pain relief was achieved in all cases. The pain score changed from 7.7 (preoperatively) to 2.5 (postoperatively). And pain relief effect was maintained over than one year. Frankel grade improved in decompression cases.

Conclusion : Surgical treatment can alleviate pain and improve neurologic deficit immediately in spinal myeloma patients.

KEY WORDS : Spinal Myeloma · Decompression · PVP(Percutaneous vertebroplasty).

Introduction

Multiple myeloma is a malignant proliferation of plasma cells that typically involves the bone marrow. A myeloma may be considered as neoplastic proliferation of a single line of the plasma cells producing a specific protein. The annual incidence rate in Korea is, according to Yang, 0.2 per 100,000 population[20]. Estimates of spine involvement at the presentation vary from 70% to 100% of the patients[5]. Because of the distribution of the hematopoietic cells, the skeletal system is involved by multiple myeoloma, and, particularly, the spine is most commonly affected site of multiple myeloma.

The most common presenting clinical symptom is the skeletal pain from the vertebral compression fracture or rib fracture. Vertebral compression fracture are presented in 55~70% of the patients with the multiple myeloma and are presented as the initial clinical sign in 34~64% of these patients[14]. According to many authors, as many as 70% of primary chief complaint during initial manifestation of the disease is lower back pain[7-10].

Main treatment modality for multiple myeloma is chemotherapy. In the case of symptomatic spinal myeloma, radiation therapy is recommended. The goal of treatment is to relieve pain and to prevent impending neurological compromise. Because the pain relieving effect of radiation therapy is usually delayed by 10 to 15 days, and its effect on bone recon-struction is partial and requires several weeks to develop fully[3,7,10]. Therefore In the case of severe intractable pain, neurological complications, or spinal instability, surgical approach can be considered.

The surgical strategy for multiple myeloma includes PVP and open decompressive surgery with or without stabilization. An appropriate surgical method was selected for each patient based on neurological impairment and cause of pain. The authors evaluated the efficacy of surgery in the treatment of spinal myeloma.

Materials and Methods

A total of 22 patients who underwent surgery for spinal myeloma between august 1999 to march 2003(Table 1), were evaluated retrospectively. They are 12 men and 10 women (mean age 56.5 years, ranging from 40 to 70 years).

• Received : May 25, 2004 • Accepted : October 28, 2004
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All patients underwent preoperative evaluation including radiography, computer tomography(CT), and magnetic resonance image(MRI). The pattern and extent of myelomatous involvement was analyzed on MR Image.

The marrow involvement pattern by myeloma was classified into diffuse type and variegated type. Diffuse type was defined as total replacement of fatty marrow of vertebral body on T1 weighted image with evidence of marrow enhancement on gadolinium enhancement [12] (Fig. 1A, B). A variegated type of involvement was considered to be present when multiple myeloma innumerable tiny foci of marrow replacement on background of uninvolved marrow were observed on T1 weighted images with subsequent enhancement of these foci on gadolinium enhancement (Fig. 1C, D). The surgical strategy consists of 14 cases of percutaneous vertebroplasty(PVP), 7 cases of corpectomy and fixation, and 3 cases of laminectomy and epidural mass removal.

The severity of pain was measured with visual analogue pain score(VAS) for both preoperation and 1,6,12 months after the treatment. Neurological status was measured with Frankel scale. The efficacy criterion was the change of the pain score(VAS) for PVP group and Frankel scale for open decompressive surgery group respectively.

In decompressive surgery group, anterior approach was done in two cases, posterior approach was done in five cases. For graft, iliac bone was used in two cases, bone cement in five cases. In remaining 3 cases, simple laminectomy and tumor removal was performed to relieve cord compression by epidural mass formation.

Results

Radiological findings-Marrow involvement on MRI

Marrow signal change in spinal myeloma shows low signal intensity on T1WI, high signal intensity on T2WI and homogenous or heteorgenous enhancement with gadolinium.

Table 1. Characteristics of 22 patients with multiple myeloma

Patient No.	Age at 1st intervention	Sex	Symptom	Location	Surgical treatment	Status	MRI	Pre	Post	Survival(Month)
1	48	F	Pain(axial)	T12,L2,4	PVP	Dead	Varigated	RT	CTx	2
2	58	M	Pain(axial)	T6,9,10,12,L1,2	PVP	Lost	Varigated	RT	CTx	27
3	62	F	Neck Pain (axial+radicular)	T1	OP	Dead	Diffuse	CTx	RT	5
4	62	M	Back Pain(axial)	L1,2,3	PVP	Lost		CTx	CTx+RT	1
5	60	M	Pain	T2,3,12	PVP					
			Pain	L1,3,4	PVP	Live	Varigated	CTx	CTx+RT	49
			Pain	L2,3	PVP					
6	56	M	Pain	L2	PVP	Lost	Diffuse	CTx+RT	CTx	40
7	53	F	Pain	T7,8,12,L1,3,4	PVP	Lost	Diffuse	CTx		21
8	67	M	Pain(radicular)	T6 epidural mass	OP	Lost	Post		RT	2
9	52	F	Pain(axial)	L5	PVP	Lost	Diffuse	CTx	CTx+RT	15
				T12,L1	PVP					
10	75	F	Pain(axial+radicular)	L2	OP	Live	Diffuse		CTx	43
11	53	M	Pain(axial+radicular)	T6, L3	PVP + OP	Lost	Diffuse	CTx+RT	CTx	10
12	59	F	Pain, Motor Impairment	T3, T10,12, L2,4,5	PVP + OP	Lost	Diffuse	CTx+RT	CTx	29
13	65	M	Pain(axial)	L3,4	PVP	Lost	Diffuse	CTx+RT		2
14	47	F	Pain, weakness	L1	OP	Live	Diffuse		RT	28
15	59	F	Pain(axial+radicular)	C5	OP	Live	Diffuse	CTx+RT	CTx	26
16	40	M	Pain(axial)	T12,L2,L1,3,4	PVP	Live			CTx	17
17	63	M	Paraplegia(axial)	T12	OP	Lost	Diffuse		CTx	8
18	40	M	Paraplegia	T3	OP	Lost			RT	4
19	57	M	Pain, Non Ambulation (axial+radicular)	T11,12,L1,2,3	OP	Live	Varigated		CTx	11
20	46	F	Non Ambulation(axial)	T12,L2,5	PVP	Live	Diffuse		CTx	12
21	53	M	Pain(axial)	T10,11,L1,T12,L2	PVP	Live	Varigated	CTx+RT	CTx	11
22	70	F	Pain, Non Ambulation (axial+radicular)	T12,L2,L3,4,5	PVP	Live	Varigated	CTx+RT	CTx	11

M : male, F : female, T : thoracic, L : lumbar, pvp : percutaneous vertebroplasty, OP : open decompressive surgery, Pre : pre-operation, Post : post-operation, MRI : magnatic resonace image, RT : radiation therapy, CTx : chemotherapy

On preoperative MRI, diffuse involvement was observed in 11 cases and variegated appearance was observed in 7 cases (Fig. 1). In remaining 4 patients, there were no previous MRI images before treatment.

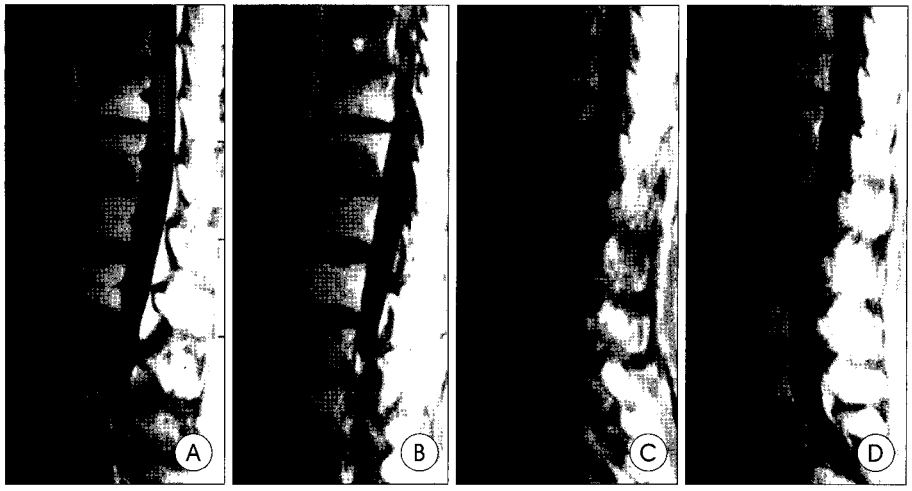

Fig. 1. Symptomatic myloma appearing as diffuse pattern of marrow involvement on T1 weighted sagittal magnetic resonance image of the lumbar spine (A). T1 weighted postcontrast image reveals diffuse enhancement of marrow (B). Symptomatic myeloma appearing as a variegated pattern of marrow involvement in lumbar spine (C). With gadolinium enhancement, it showing inhomogeneous enhancement throughout the lumbar spine (D).

Clinical outcome

PVP was done in 14 cases with painful compression fracture. Total 57 segments were treated, 21 of which were thoracic level and 36 of which were lumbar level. The most commonly involved spinal levels were T12, L1, and L2.

The postoperative pain relief was achieved in PVP cases. The change of pain score after PVP is shown in Table 2 and Figure 3. The average of pain score changed from 7.7(preoperatively) to 2.5(one month after PVP). On long term follow up, pain relieving effect was maintained. At 6 months after PVP, the mean pain score was 2.09 in 11 cases. At 12 months the score changed to 2.2 in five cases. At 36 months the mean score was 3.2 in three cases.

The progression of compression on augmented vertebral body was seen in three segments. But second trial of PVP was done in one case with clinical symptom.

Ten patients with neurological deficit or impending neurological deficit underwent open decompressive surgery. One patient (patient number 12 on table 1) had multi-level vertebroplasty and open de-compressive surgery due to progression of the disease. Seven patients (32%) presented with neurological symptom prior to surgery. After the surgery, all of the patient's Frankel grade improved. For those patients, who were presented with impending paralysis, recovered completely. Out of 4 paraplegic patients (who are Frankel grade C or below), 2 patients were improved to moderate sensory impairment with motor dysfunction. All 4 patients with sensory and partial motor impairment were improved postoperatively (Fig. 4).

The Kaplan-Meier survival curve for all patients enrolled into this study is presented in figure 5. Two patients died at first short assessment period, 9 patients remained alive to the last follow up, and 11 were lost to follow up. The follow up of the patients was from 2 to 49 months. The mean overall survival of the patients was 44 months (95%CI). Their 12-month survival rate was 95% and the 25-month survival rate was 83%.

Discussion

Radiological findings

Some authors have informed that most vertebral compression fractures in patients with multiple myeloma appeared to be

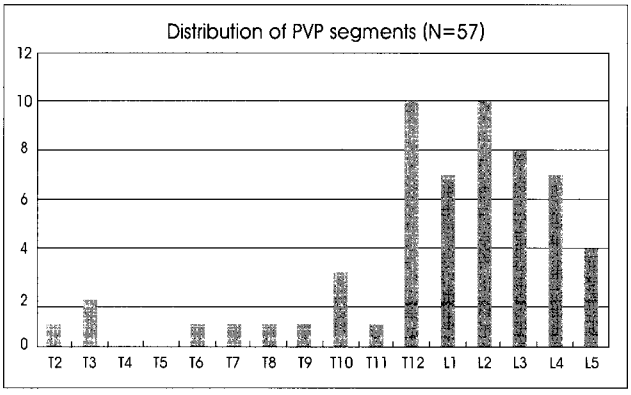

Fig. 2. Distribution of percutaneous vertebroplasty segments.

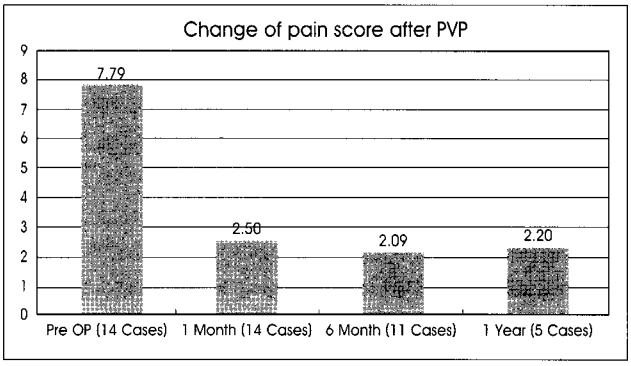

Fig. 3. Change of pain score after percutaneous vertebroplasty.

Table 2. Change of score after the surgical treatment

Patient	Pain score					Frankel neurological scale	
Number	Pre	Post	1months	6months	12months	Pre	Post
1	8	4	4			E	E
2	9	1	1	1	1	E	E
3						D	E
4	7	1	1			C	D
5	9	3	3	1	1	C	E
6	7	2	2	2	3	E	E
7	7	4	4	3	3	E	E
8						B	C
9	8	2	2	2	3	E	E
10						E	E
11	8	5	5	3		E	E
12	7	3	3	2		C	D
13	7	2	2			E	E
14						D	E
15						E	E
16	8	3	3	3		D	E
17						D	E
18						A	D
19						D	E
20	9	1	1	2		E	E
21	7	1	1	2		E	E
22	8	3	3	2		E	E

Pre : pre-operation, Post : post-operation

	Surgical outcome of open surgery				
Post (case) / Pre (case)	A	B	C	D	E
A	0	0	0	1	0
B	0	0	1	0	0
C	0	0	0	1	1
D	0	0	0	0	4
E	0	0	0	0	2

Fig. 4. A : complete motor and sensory paralysis below lesion; B: complete motor paralysis, but some residual sensory perception below lesion ; C: residual motor function, but of no practical use; D : useful but subnormal motor function below lesion ; E : normal Pre : Pre-operation, Post : post-operation, Arabic number : number of cases.

benign. In their report, as much as 70% of cases showed band of low signal intensity parallel to the fracture end plate[10,11], which is the manifestation of benign compression fracture. In our radiological study, most of the vertebral compression fractures appeared malignant on MRI image.

Typical malignant features are diffusely low signal intensity on T1 weighted images, high or heterogeneous signal intensity in T2 weighted images, and round irregular foci on marrow replacement[10,12,17]. Since plasma cell of multiple myeloma infiltrate both a nodular and interstitial fashion, MR image of our patients' revealed two patterns of myelomatous involvement. Our cases showed more diffuse type of marrow involvement than variegated types. In report of Moulopoulos et al on 29 cases of newly diagnosed multiple myeloma, authors reported that marrow involvement was seen in 69% of the patients with three MR imaging types of marrow involvement : focal, diffuse, and variegated patterns[14]. In our cases, focal type was not found. This result may be due to limited number of cases and severity of disease progression when they were discovered.

Operative findings and outcome

The spine is a frequent site of malignant osteolytic lesions in multiple myeloma patients. Initially, the lesion can be solitary (plasmacytoma), but with disease progression, it becomes multiple lytic lesion[9,19]. Multiple myeloma causes excessive bone resorption via increased osteoclastic activity, which causes diffuse osteopenia and focal osteolytic lesions leading to fractures, and epidural mass formation in multiple myeloma patients. The epidural mass may lead to cord compression leading to paralysis in 10% of the multiple myeloma[6,11]. The patients usually experience severe pain and disability.

In our study, 17 out of 22 patients (77%) showed vertebral compression fracture as an initial clinical sign of multiple myeloma. According to Lecouvet et al., vertebral compression fractures are present in 55~70% of patients with multiple myeloma and are the initial clinical sign in 34~64% of the patients[11]. The most frequently involved segments were T-L junction (T11-L2) (50%), This finding was similar to the study by Lecouvet et al, in which 50% of vertebral compression was reported to occur between T11 and L3. The distribution of vertebral compression fractures in patients with multiple myeloma was similar to that in patients with osteoporosis. In osteoporosis patients, as much as 92% of oseoporotic fractures were observed between the sixth thoracic vertebra and fourth lumbar vertebra[12]. This similarity in fracture distribution between osteoporosis and myeloma results from combined effects of diffuse bone weakening and biomechanical factors, such as muscle tone and spinal curvature[12].

Percutaneous vertebroplasty in 14 patients have achieved excellent pain relief and had no significant leakage. The pain relief effect was well maintained for up to 1 year in followed up patients. These results were similar to reported by other authors[3,4]. The PVP has been recently introduced to treat the compression fractures of both malignant and benign causes. Cement augmentation of the vertebral body has been used for relief of pain in the spine. Many authors have speculated that pain relief may be due to mechanical, vascular, chemical and thermal force produced by methylmethacrylate injection, and also due to the stabilization of micro fractures and reduction of

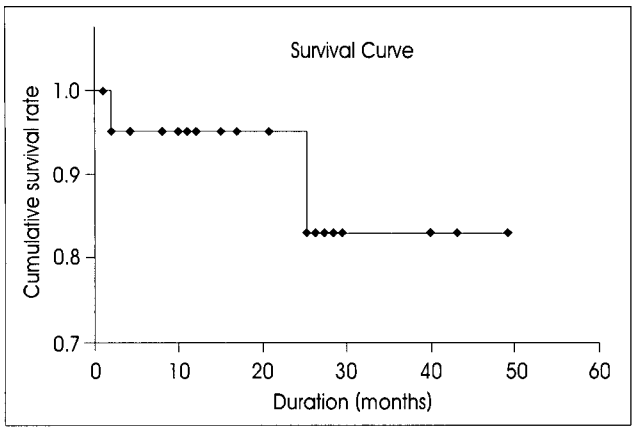

Fig. 5. Overall survival of all the patient enrolled by the Kaplan-Meier method. Mean overall survival is 44 months(95% CI). Two patients died during the follow-up period, 9 patients remained alive to last follow-up, and 11 were lost to follow-up.

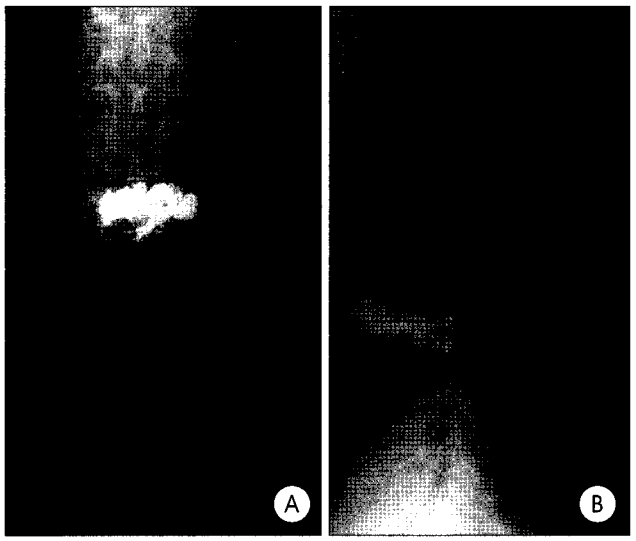

Fig. 6. Frontal(A) and lateral(B) plain x-ray taken after L3 vertebroplasty.

mechanical force[3,5]. During vertebroplasty, neurological complication due to epidural leakage of bone cement can be devastating. Also pulmonary embolism caused by bone cement has been reported by other authors[3,5,17]. But we didn't experience significant complications.

There are some characteristic operative findings in PVP of spinal myeloma. We could see frequently the myelomatous involvement of pedicle. So the needle anchorage was not easily performed under transpedicular approach. After insertion of needle in the vertebral body, near fluid consistency of tumor mass was felt. The aspiration of marrow content showed backflow of blood from the needle. Unilateral injection of bone cement was enough to fill the entire vertebral body. Epidural leakage of bone cement was rarely observed. Even in cases with posterior wall defect we can perform PVP (Fig. 6). We performed

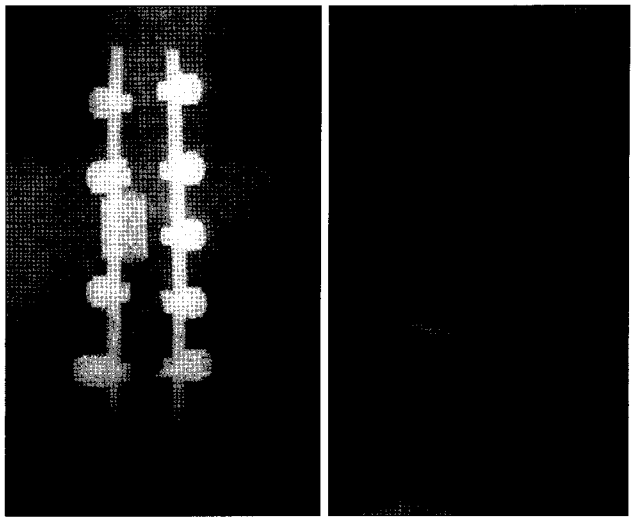

Fig. 7. Transpedicular device T10-L2 after laminectomy and cage insertion of T12 after corpectomy.

decompression operation in 10 cases. All the operated patients showed good result (Fig. 7). The tumor mass was soft, friable and of little blood. When performing fixation, we had a difficulty in instrumentation due to low bone density of adjacent vertebral body. This phenomenon was due to systemic osteoporosis. Some of researchers advocate open surgical decompression in combination with vertebroplasty[15].

Survival

Twenty of our patients are alive during follow up. The mean follow-up period was 20months. To our knowledge, only few articles mentioned the correlation between surgical treatment and the survival. According to report by Kim et al., the difference in duration of postoperative survival between postoperative ambulatory and non ambulatory group was statistically significant[10]. Therefore improvement of therapy and supportive care for myeloma probably increased overall survival rate.

Surgical indications

Several authors have suggested radiation instead of surgical intervention of metastatic spinal disease, but there were no specific indication for vertebral myeloma patients[2,13,15]. Therefore, we have modified and suggest following indication for surgical intervention of multiple myeloma. This helps to plan the type of surgical strategy applied[1,6,7,12,15,16,18].

1. Intractable pain unresponsive to nonoperative measures.
2. Existence of growing tumor that is recurring after radiation or medical therapy.
3. Patients who have reached spinal cord tolerance after prior radiation therapy.
4. Spinal instability manifested as pathological fracture,

progressive deformity, or neurological deficit.

5. Significant neurological deficit due to cord compression by epidural tumor.

With these indications, the hemato-oncologist, radiation-oncologist should be consulted for possible benefit for the patients before the surgical intervention.

Conclusion

We suggest those patients with painful malignant vertebral compression fracture or who have neurological impairments should consider surgical treatment. Percutaneous vertebroplasty provided pain relief effect in compression fracture, maintained stability, and allow early ambulation. Open decompressive surgery was effective in neurologically impaired patients. These surgical treatment allows rapid functional recovery in patients with spinal myeloma. But on long term follow up, the result didn't turn out to be superior to radiation therapy. And it is left to be confirmed whether surgical treatment can provide survival prolongation in the treatment of spinal myeloma.

References

1. Chataigner H, Onimus M, Polette A : Surgical treatment of myeloma localized in the spine. **Rev Chir Orthop Reparatrice Appar Mot 84** : 311-318, 1998
2. Cobb CA, Leavens ME, Eckles N : Indications for nonoperative treatment of spinal cord compression due to breast cancer. **J Neurosurg 47** : 653-658, 1977
3. Cortet B, Cotton A, Boutry N, Dewatre F, Flipo RM, Duouesnoy B, et al : Percutaneuos vertebroplasty in patients with osteolytic metastases or multiple myeloma. **Rev Rhum Engl Ed 64** : 177-183, 1997
4. Cotton A, Dewatre F, Cortet B, Assaker R, Leblond D, Duquesnoy B, et al : Percutaneous vertebroplasty for osteolytic metastases and myeloma : effects of the percentage of lesion filling and the leakage of methyl methacrylate at clinical follow-up. **Radiology 200** : 525-530, 1996
5. Dudeney S, Lieberman IH, Reinhardt MK, Hussein M : Kyphoplasty in the treatment of osteolytic vertebral compression fractures as a result of multiple myeloma. **J Clin Oncol 20** : 2382-2397, 2002
6. Durr HR, Wegener B, Krodel A, Muller PE, Jansson V, Refior HJ : Multiple myeloma : surgery of spine : retrospective analysis of 27 patients. **Spine 27** : 320-326, 2002
7. Formica C, Gavino D, Giudive V : Tumors of the spine. Indication for surgical treatment. **Chir Organi Mov 83** : 23-33, 1998
8. Jonsson B, Sjostrom L, Jonsson H, Karlstrom G : Surgery for multiple myeloma of the spine. a retrospective analysis of 12 patients. **Acta Orthop Scand 63** : 192-194, 1992
9. Kyle RA : Multiple myeloma : review of 869 cases. **Mayo clin Proc 50** : 29-40, 1975
10. Kim DY, Jung SK, Jo GT, Jung CK, Kim HJ : A survival analysis of surgically treated metastatic spine tumor. **J Korean Neurosurg Soc 33** : 247-251, 2003
11. Lecouvet F, Richard F, Vande Berg B, Malghem J, Maldague B, Jamart J, et al : Long term effects of localized spinal radiation therapy in vertebral fractures and focal lesions appearance in patients with multiple myeloma. **Br J Hematol 96** : 743-745, 1977
12. Lecouvet FE, Vandeberg BC, Maldague BE, Michaux L, Malghem J : Vertebral compression fractures in multiple myeloma. part I. distribution and appearance at MR imaging. **Radiology 204** : 195-199, 1997
13. Mclain RF, Weinstein JN : Solitary plasmacytomas of the spine : a review of 84 cases. **J Spinal Disord 2** : 69-74, 1989
14. Moulopoulos LA, Varma D, Dimopoulos MA, Leeds NE, Kim EE, Johnston DA, et al : Multiple myeloma : spinal MR imaging in patients with untreated newly diagnosed disease. **Radiology 185** : 833-840, 1992
15. Onimus M, Schraub S, Bertin D, Bosset JF, Guidet M : Surgical treatment of vertebral metastasis. **Spine 11** : 883-891, 1986
16. Park WM, Jang JS, Rhee CH, Gwak HS, Lee SH : Percutaneous vertebroplasty in spinal metastasis and myeloma. **J Korean Neurosurg Soc 29** : 1484-1490, 2000
17. Shin MJ, Oh SH, Yoon DH, Chin DK, Cho YE, Kim YS : Surgical treatment of spinal plasma cell tumors. **J Korean Neurosurg Soc 32** : 118-124, 2002
18. Stallmeye MJ, Zoarski GH, Obuchowski AM : Optimizing patient selection in percutaneous vertebroplasty. **J Vasc Interv Radiol 14** : 683-696, 2003
19. Weill A, Chiras J, Simon JM, Rose M, Sola-Martinez T, Enkaoua E : Spinal metastases : indications for and results of percutaneous injection of acrylic surgical cement. **Radiology 1996** : 241-247, 1996
20. Yang SH, Kim TY, Kim BK, Ko YU, Gwak DS, Kim NG, et al : The statistical research of multiple myeloma in Korean. **J Korean Hematol Soc 30** : 345-341, 1995