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ORIGINAL ARTICLE

Surgery Improves Pain and Quality of Life in Multiple Myeloma Patients with Symptomatic Osteolytic Spinal Lesions

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ABSTRACT

Purpose: A prospective study that aims to present the functional outcome and the survival of 21 consecutive selected Multiple Myeloma (MM) patients who underwent 25 surgeries for symptomatic vertebral body osteolysis.

Methods: 25 wide spectrum surgeries including percutaneous augmentation, hybrid fixation and circumferential decompression were performed for symptomatic vertebral body osteolysis in 21 selected patients with MM. Tomita osteolysis classification, Karnofsky disability scale, ASIA neurological impairment scale and VAS pain scale were used. Survival analysis was performed.

Results: All patients were followed for a minimum of 6 months postoperatively. Karnofsky Index improved from 66%±20% preoperatively to 81.3%±15%, onemonth and 83%±10% one year postoperatively. VAS score significantly reduced in all patients from 7.08±2 preoperatively to 3.35±1.5 at the latest evaluation. One patient with ASIA grades D and 2 with ASIA grades C improved postoperatively to ASIA E. The one-year survival from index diagnosis was 85.2% (95% CI, 60.6% - 96.0%), while it dropped to 55.4% (29.4% - 75.1%) five-year postoperatively. The one-year survival rate from index surgery was 65.9% (95% CI, 38.8% - 83.2%), and dropped to 33.5% (95% CI, 11.1% - 58.0%) five-years postoperatively.

Conclusions: There are several modalities of surgery for symptomatic osteolytic vertebral body lesions in MM patients. Surgery was proved a safe procedure with few complications it reduced pain and improved quality of life. Together with hematological and radiation therapy it may increase the survival of MM patients.

KEY WORDS: multiple myeloma; spinal lesions; kyphoplasty; tumor

Introduction

Multiple myeloma (MM) is a systemic neoplasm of plasma cells that affects 1-4 per 100,000 people per year and is commonly associated with bone pain, usually due to spinal and rib osteolyses, in 70% of this kind of patients [1-4]. Skeletal osteolyses are the most frequent cause of morbidity and mortality in patients affected by this pathology [5].

Spinal involvement can be the initial clinical

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presentation of the disease in 34-64% of the MM patients, leading often to intractable pain and/or neurological complications due to spinal cord or cauda compression [6], [7]. In the one third of the patients, MM is diagnosed after a pathological spinal fracture has occurred[8], moreover new vertebral body fractures occur in approximately 15-30% of patients with MM annually [5].

Recent advances in therapeutic approaches, such as autologous stem cell transplantation, radiotherapy and chemotherapy, bracing and surgery in certain cases, helps towards lessening the occurrence and severity of adverse effects of this disease, as well as managing associated complications [7], [9-14]. Although medical treatments & radiation help towards slowing down the natural history of MM [5], they do not correct any structural vertebral destruction that may have already been occurred, either as osteolysis or as a fracture and wedge deformity in up to 70% of all patients with MM [15-17]. In vertebral body osteolyses and/orvertebral body fractures, the main goal of surgical intervention is pain relief, reduction of angular deformity for prevention of potential neural element compression and spinal canal decompression. In the last few years, percutaneous Minimal Invasive Surgery (MIS), vertebral augmentation techniques such as Vertebroplasty (VP), Balloon Kyphoplasty (BK) and KIVA [18], are well tolerated and drastically decrease pain while simultaneously improve patient's quality of life [15], [16], [17], [19]. Radiofrequency-targeted vertebral augmentation was recently developed to address potential adverse issues reported with VP and BK [2], [20], [21], [22]. However, in patients with vertebral body osteolyses with involvement of the posterior vertebral body wall some authors have raised concerns regarding the high leakage rates associated with low viscosity polymethylmethacrylate (PMMA) bone cement [23], [24], [25], [26].

Survival after MM is highly variable; however, recent studies of various drug therapies have led to promising outcomes and reported survival beyond 10 years [12-13].

The aim of this prospective study is to present the functional outcome and survival rates following surgical treatment in 21 consecutive selected MM patients, who underwent a total of 25 surgeries, by a single senior orthopedic spine surgeon, in one tertiary institution and to review the relative literature.

Materials and methods

Twenty-one consecutive selected patients (7 women, 14 men) suffering from MM with established spinal involvement and associated intractable pain, who were surgically treated between 2004 and 2012 in the authors' Orthopaedic institution by a single spine surgeon (Table 1), were prospectively evaluated. The average±SD age of the patients at the index surgery was 70±21, range 49-90 years. The Tomita classification [31] was used to grade the extension of vertebral bodyosteolytic lesions, (Table1). VAS (0-10 scale) [28] and ASIA neurological classification [29] were used for evaluation of patients' pain level and neurological function. The quality of life was evaluated with the Karnofsky Index [30]. The inclusion criteria and indications for surgical intervention were MM or solitary spinal plasmocytoma with symptomatic spinal involvement (painful osteolysis±spinal fracture, neurological impairment or potential or progressive neurological impairment due to vertebral body fracture), intractable spinal pain resistant to conservative treatment (pain killers, brace, etc). Our surgical strategy was as follows: Patients neurologically intact and osteolysis in≥1 non-contiguous vertebral body (-ies) were treated with vertebral augmentation solely; in patients with multilevel contiguous cervical spine involvement vertebrectomy, mesh cage plus posterior fixation was made; patients with neurologic impairment were treated with posterior MIS reduction, pedicle screw stabilization plus vertebral body augmentation; patients with posterior cord/cauda compression (posterior spinal elements involvement) were treated via wide laminectomy and posterior pedicle screw fixation. Patient survival, using all-cause mortality as event of interest, was estimated with the Kaplan-Meier method [32]. Survivals from: a) index MM diagnosis and

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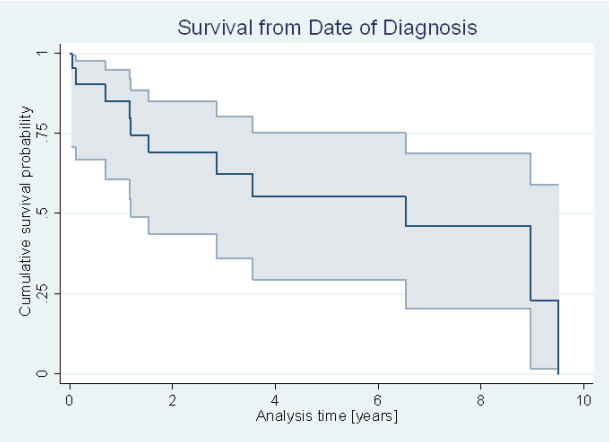

Fig. 1: *SURVIVORSHIP. The one-year survival from the index diagnosis was 85.2% (95% CI, 60.6% - 96.0%), while the 5 year survival dropped to 55.4% (95% CI, 29.4% - 75.1%), see Figure 1.*

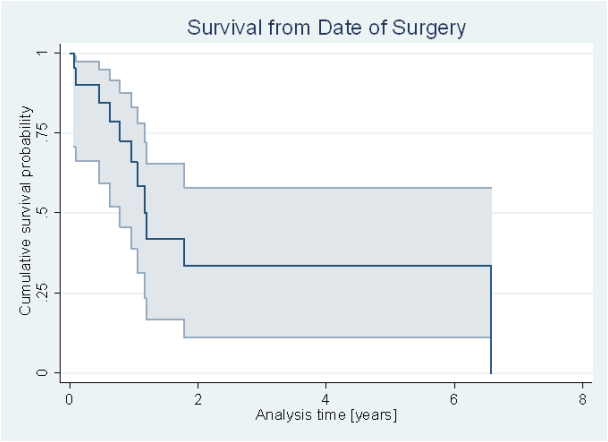

Fig. 2: *The one-year survival from the index surgery, was 65.9% (95% CI, 38.8% - 83.2%), while the five year survival dropped to 33.5% (11.1% - 58.0%), see Figure 2.*

b) index surgery were calculated.

Results

The most common spinal location of vertebral body osteolysis was the thoracolumbar junction (16/25 cases), and the less common was the cervical spine with only1 case (4%). Multilevel spinal localization was observed in 9/25 cases (Table 1).

Percutaneous augmentation was performed in the majority of the cases: 13/25 (52%); followed by hybrid MIS in 7/25 cases (28%); and posterior pedicle screw fixation in 4/25 cases (16%). Combined open anterior decompression corpectomy and mesh cage implantation supplemented by posterior lateral mass stabilization for multi-level cervical osteolytic lesions and associated kyphotic deformity was performed in one female patient (4%) for cervical kyphosis and potential for cervical spinal cord compression (Table 1).

Four from the 21 patients, were re-operated at different spinal levels for new symptomatic vertebral bodyosteolyses and/or associated fractures (Table 1). One patient (cases No. 6.1 & 6.2, Table 1), with previous augmentation of T11-vertebra was re-operated 6 months later because of pain in two adjacent vertebrae (T9 and T10), (Table 1). In one additional patient (cases No. 12.1 & 12.2,Table1), a cephalad extension of an already existed posterior pedicle screw construct was made for new T2 vertebral body osteolysis, 24.5 months following primary decompression and posterior stabilization for severe osteolytic lesion in a lower level (Table 1).

Five patients (cases 2, 9, 15, 18.1 & 19) were treated with MIS with or without simultaneous vertebral augmentation (Table 1).

The time lapsed from the index diagnosis to index surgery, for the 17/25 (68%) cases for which the diagnosis was already preoperatively known was 40±6.15 months (range 0.25-105).

Functional results

Daily performance (Karnofsky Index) was significantly improved from 66%±20% before surgery to 81.3%±15% one month following surgery and 83%±10%, one year after surgery in survived patients, (Table 2).

VAS score was reduced from 7.08±2 preoperatively to 3.35±1.5 at the time of last postoperative evaluation.

No neurological deterioration was observed postoperatively in 18/19 patients with preoperative ASIA grades E and D. One patient (case 5, Table 2) with preoperative ASIA grade D and 2 patients, cases 12.1 & 21.2, with ASIA C grades improved postoperatively to ASIA E, Table 2.

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TABLE 1.

Table 1: Cumulative data on 21 MM patients who underwent 25 surgeries for painful vertebral osteolyses. Four patients underwent two subsequent surgeries for other level osteolyses. Patients no 6, 12, 18 & 21 were operated twice. (F=female & M=male)

Cases NO	AGE AT SURGERY	GENDER	TOMITA OSTEOLYSIS GRADE	NEUROLOGICAL IMPAIRMENT ON ADMISSION	LOCATION OF OSTEOLYSES (Fractures are indicated)	SURGICAL TREATMENT	SURVIVAL FROM DIAGNOSIS (days)	SURVIVAL FROM SURGERY (days)
1	65	F	TYPE 6	NO	C3, C5, C6	COMBINED STAGED 360O (POST. C2-C6 & ANTERIOR DECOMPRESSION C3, C5, C6 WITH MESH CAGE)	2386	2401
2	83	F	TYPE 6	PARAPARESIS INCOMPLETE	L3, L4, L5	MIS POST. STABL3-L5	559	650
3	73	M	TYPE 7	NO	FRACTURES in T5, T8, T9, T10, T11	AUGMENTATION: T5, T8, T9, T10, T11	2566	2570
4	73	M	TYPE 7	NO	FRACTURES in T7, T12, L1, L2	AUGMENTATION: T7, T12, L1, L2	432	385
5	53	M	TYPE 7	PARAPARESIS INCOMPLETE	FRACTURES in T8, T10, L1, L2, L3	HYBRID FIXATION AUGMENTATION: L1, L2, L3, DECOMPRESSION & POST. STAB. T7-L3	508	498
6.1	68	F	TYPE 1	NO	T11	AUGMENTATION: T11	2990	414
6.2	69	F	TYPE 6	NO	T9, T10, T11	AUGMENTATION: T9, T10	2990	217
7	73	F	TYPE 6	NO	FRACTURES in L2, L3, L4	AUGMENTATION: L2, L3, L4	3486	339
8	63	M	TYPE 6	NO	L2-L5	AUGMENTATION: L2, L3, L4, L5	1299	226
9	78	F	TYPE 7	PARAPARESIS INCOMPLETE	FRACTURES inT11, L1	HYBRID FIXATION AUGMENTATION: T11, O1 MIS POST. STAB. T12-L2	38	31
10	81	M	TYPE 7	NO	FRACTURES in T11, T12, L4, L5	HYBRID FIXATION AUGMENTATION: T11, T12, L4, L5 DECOMPRESSION & POST. STAB. T10-L2	422	349
11	70	M	TYPE 6	NO	L1, L2, L3, L4	AUGMENTATION: L1, L2, L3, L4	1222	553

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12.1	49	M	TYPE 4	PARAPARESIS INCOMPLETE	FRACTURE in T6 WITH EPIDURAL METASTASIS	DECOMPRESSION & POST. STAB. T3-T8	1043	897
12.2	51	M	TYPE 6	NO	FRACTURE in T2	EXTENSION OF POST. STAB. TO T1	1043	165
13	65	M	TYPE 7	NO	FRACTURES in T11, T12, L2, L3, L4	AUGMENTATION: L2, L3, T11, T12, L4	1293	617
14	83	F	TYPE 7	PARAPARESIS INCOMPLETE	FRACTURES in T12, L1, L4, L5	AUGMENTATION: T12, L1, L4, L5	3276	425
15	77	M	TYPE 3	NO	FRACTURE in L3	HYBRID FIXATION AUGMENTATION: L3 MIS POST. STAB. L2-L4	3471	435
16	78	F	TYPE 6	NO	FRACTURES in T12, L1	AUGMENTATION: T12, L1	414	420
17	75	M	TYPE 7	NO	FRACTURES in L1, L2 OSTEOLYSES in T10, T11, T12, L3	HYBRID FIXATION AUGMENTATION: L1, L2 POST. STAB. T8-L5	968	687
18.1	64	M	TYPE 3	NO	FRACTURE in L3	HYBRID FIXATION AUGMENTATION: L3 MIS POST. STAB. L2-L4	3236	3250
18.2	69	M	TYPE 6	PARAPARESIS INCOMPLETE	FRACTURE in L5, OSTEOLYSES in S1, S2	AUGMENTATION: L5, S1, S2	3236	1295
19	78	M	TYPE 7	PARAPARESIS INCOMPLETE	FRACTURES in L2, L3, T7, T8, WITH EPIDURAL EXTENSION	HYBRID FIXATION AUGMENTATION: L2, L3, T7, T8 MIS POST. STAB. T12-L4	14	21
20	90	M	TYPE 6	NO	FRACTURES in L2, L3	AUGMENTATION: L2, L3	249	286
21.1	63	M	TYPE 7	NO	T2, T7, T8	AUGMENTATION: T7	1732	1760
21.2	64	M	TYPE 7	PARAPARESIS INCOMPLETE	FRACTURES in C7, T2, T3, T6, T7, T10, T11, L1	POST. STAB. C5-T4	1732	1534

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Survivorship

The one-year survival from the index diagnosis was 85.2% (95% CI, 60.6% - 96.0%), while the 5 year survival dropped to 55.4% (95% CI, 29.4% - 75.1%), see Figure 1.

Discussion

The reported median survival time from the index diagnosis has increased from an average of 2.5 to 4.5 years[21], [33]. The one-year survival in our patients from index diagnosis was 85.2% (95% CI, 60.6% - 96.0%), while the five-year survival dropped to 55.4% (29.4% - 75.1%).

Expansible vertebral body osteolyses and fractures with associated wedge deformity and spinal instability are quite often present (75%) in MM patients [34] and may result in compression of spinal cord or cauda leading to neurological impairment. In our study population, neurological impairment was present on admission in 6/21 (28.9%) MM patients, slightly higher than those previously reported (22% to 25%) [11], [13]. All 6 patients with preoperative neurologic impairment improved at least one ASIA grade while no patient deteriorated postoperatively.

The high benefit of surgery in symptomatic MM patients with spinal involvement seems to be the lower surgical complication rate (8%) [43] than the one observed in patients with metastatic spinal disease (19%) [44].

A recent study [43] on the treatment of MM patients suffering from osteolytic vertebral body fractures treated with combined BK and radiofrequency showed a significant reduction of VAS score from 8.1 to 2.5, with an average reduction of preoperative VAS of 5.6 points in 75% of the operated patients. In our series, pain relief was achieved in all 23 cases that survived for more than 30 days postoperatively. VAS was reduced from 7.08±2 preoperatively to 3.35±1.5 at the time of postoperative evaluation.

Choeet al [41] reported on a 4.6% incidence of pulmonary embolism in patients with MM after VP or BK with a high correlation between PMMA in the lungs and paravertebral PMMA leak, independent of treatment type (VP or BK). In no patient in our series lung embolism was clinically evident. However, in our series, complications of lower severity occurred in 3/25 surgeries (12%) -3/21 patients- and included acute renal insufficiency and transient lower limb muscle weakness. Our complication rate is significantly lower to those previously published of approximately 37.5% in [38].

During vertebral body augmentation, surgeons are often facing pulmonary and neurologic complications related to PMMA extravasation. In MM patients, PMMA extravasation rates following VP ranges from 1% to 48%, while it is less common in BK (<2%) [15], [16], [39], [40]. Recently, Julka et al reported cement extravasation in 12/32 (37.5%) patients, all without clinical sequelae [38]. In 52 VPs in 37 MM patients, vertebral augmentation reported in 3/37 (8%) patients with transient nerve root paresis because of cement leakage, while 1/37 (2.7%) patient required nerve root decompression with PMMA removal [42]. In our series, there was only one case with cement leakage into the foramina, in a patient (case 15) with severe (Tomita 3) vertebral body bone erosion that caused temporary nerve root irritation and resolved one month later.

The one-year survival rate from the date of surgery was 65.9% (95% CI, 38.8% - 83.2%), while the five-year survival rate dropped to 33.5% (95% CI, 11.1% - 58.0%). The most common cause of death following palliative surgery was multiple organ failure because of the MM in final stage.

Formal laminectomy alone is usually not recommended for decompression and osteolysis treatment in metastatic or MM patients, because a wide posterior decompression further destabilizes the spine. Laminectomy combined with stabilization was reserved in four patients with posterior spinal canal encroachment due to posterior elements involvement and dural compression. Consistent with previous studies [45], [46], [37], spinal instability due to vertebral body osteolyses, associated with intractable pain and potential for neurologic impairment were the indications for surgery in our patients. Surgery performed in our MM patients, was patient-specific and

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TABLE 2.

Karnofsky Index pre-operatively, 1 month and 1 year post-operatively, ASIA Impairment Scale and VAS Axial Pain Scale pre-operatively and post-operatively & postoperative complications & complications outcome

Cases NO	KARNOFSKY PREOP	KARNOFSKY 1 MONTH POP	KARNOFSKY 1YEAR POP	ASIA PREOP	ASIA POP	PAIN PREOP VAS	PAIN POP VAS	POSTOP COMPLICATIONS	COMPLICATIONS OUTCOME
1	70	80	80	E	E	6	3	Ø	Ø
2	70	80	80	D	D	7	3	Ø	Ø
3	70	80	80	E	E	8	3	Ø	Ø
4	70	80	80	E	E	6	3	Ø	Ø
5	50	70	80	D	E	9	4	ACUTE RENAL INSUFFICIENCY EARLY POSTOPERATIVELY	RENAL RECOVERY WITH MEDICATION
6.1	70	80	Ø	E	E	7	4	Ø	Ø
6.2	70	80	Ø	E	E	8	5	Ø	Ø
7	70	90	Ø	E	E	7	3	Ø	Ø
8	70	80	Ø	E	E	7	3	Ø	Ø
9	50	Ø	Ø	D	Ø	8	Ø	Ø	DIED 31 DAYS AFTER SURGERY (FINAL STAGE PATIENT)
10	70	80	Ø	E	E	7	4	Ø	Ø
11	90	100	90	E	E	5	2	Ø	Ø
12.1	50	80	90	C	E	5	2	Ø	Ø
12.2	70	90	Ø	E	E	6	2	Ø	Ø
13	80	90	90	E	E	7	2	Ø	Ø
14	70	80	70	E	E	7	4	Ø	Ø
15	60	70	80	E	E	8	5	RIGHT L4 MUSCLE WEAKNESS	NEUROLOGICALLY FULLY RECOVERED
16	70	90	Ø	E	E	7	3	Ø	Ø
17	60	70	80	E	E	8	4	Ø	Ø
18.1	70	90	90	E	E	7	3	Ø	Ø
18.2	60	70	90	E	E	8	4	Ø	Ø
19	50	Ø	Ø	C	Ø	8	Ø	ACUTE RENAL INSUFFICIENCY LEFT L2, L3 MUSCLE WEAKNESS	DIED 21 DAYS AFTER SURGERY-DEATH CAUSE: ACUTE RENAL FAILURE-MULTIPLE ORGAN FAILURE SYNDROME
20	60	80	Ø	E	E	8	3	Ø	Ø
21.1	70	80	Ø	E	E	8	4	Ø	Ø
21.2	60	80	80	D	E	5	4	Ø	Ø

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ranged from percutaneous augmentation with PMMA to MIS pedicle screw fixation combined with vertebral augmentation with PMMA, anterior open decompression and combined anterior decompression plus posterior pedicle screw fixation. In MM patients with neurologic impairment due to epidural compression by the MM lesion itself, without structural deficiency of the vertebral body, radiation is often able to diminish the local tumor lesion and the associated axial pain. However, radiation therapy alone cannot treat instability induced by vertebral body osteolysis and associated pathological fractures. Spinal instability resulted from vertebral body osteolysis requires mechanical stabilization to reduce axial pain and simultaneously to prevent potentially secondary neurological impairment due to spinal cord and cauda compression.

There are two strengths in our study. The first strength is the homogenous population with only pure MM patients. In the relative literature, most studies reported on mixed populations of MM and cancer patients [15], [47]. The second strength is that all patients were operated by one senior experienced orthopaedic spine surgeon.

Conflicts of Interest

The authors declare no conflict of interest.

The authors declare that no funding has been received for this research.

The authors declare that the research was performed according to the ethical standards as described by the Declaration of Helsinki and that an informing statement consent for participation in the study was obtained from all subjects.

The authors declare that the Hospital Ethics Committee approved this research.

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