The perioperative enhancing factors that might help the postmenopausal women tolerate the spinal implants

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Abstract

Background Data: Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration, with a consequent increase in bone fragility. Moreover, it is a condition that is both preventable and treatable if caught in time.

Purpose: Evaluation the different perioperative enhancing factors available that might increase spinal fixation success rate in low bone density postmenopausal women.

Study Design: retrospective analysis of a case series.

Patients and Methods: Between May 2011 and May 2013, twenty four low bone density post-menopausal women were included in this retrospective study. All of them were admitted at KSMH-Hospital-Tabouk. During that period, they had either thoracic or lumbar implants for two major indications, osteoporotic vertebral compression fractures and osteodegenerative spondylolisthesis. Different techniques and precautions were followed to maximize the outcome. Pre-and postoperative bone densitometry, radiograph, pain and functional outcome assessment were documented. All patients were followed up for at least 12 months.

Results: The mean age of the ladies was fifty eight years. 62.5% of the patients were classified as osteoporotic, with a further 37.5%, being osteopenia. Ten surgical fractures and fourteen cases of spondylolisthesis had implants. In densitometry, little postoperative change happened in the fracture series. However, Remarkable improvement was obvious in the spondylolisthesis series. Based on postoperative radiograph control and follow up, no reported cases of implant failures, loosening, pull-out screws or pseudoarthrosis necessitated re-surgery in one hundred twenty inserted screws. Three cases of severely osteoporotic spondylolisthesis were supported with rhBMP-2 that showed adequate fusion before expected. Out
of twenty two cement injected screws in four spondylolisthesis cases, one screw showed silent extra vertebral leakage and failure of injection in another one. In the fracture series: The Beck’s index mean pre- and postoperative was (0.44 versus 0.67, \(P=0.013\)). The kyphotic angle mean pre- and postoperative was (13\(^{\circ}\) versus 8\(^{\circ}\), \(P=0.007\)). In the spondylolisthesis series: The total pre-and postoperative score of disc height narrowing was (77 versus73, \(P=0.95\)). No change in the osteophyte score pre-and postoperatively. Vacuum Sign was positive in 40% of fracture series and 57% of spondylolisthesis series. It did not show any change in the former. However, the latter showed an improvement in 37.5% cases completely and 25% partially. The lumbar lordosis angle mean pre- and postoperative was (25\(^{\circ}\) versus 29\(^{\circ}\), \(P=0.01\)). 40% in the fracture series with marked paraparesis and 7% in the spondylolisthesis regained the full power by the end of the year. Pre- and postoperative mean of low back pain rating scale were (115 versus 23, \(P=0.001\)), pre- and postoperative mean of walking distance in meters were (22 versus 448, \(P=0.001\)). 83.3% of the patients quit morphine in three months.

**Conclusion:** Treating the osteoporotic spine involves multidisciplinary approach with involvement of endocrinologist, rheumatologist, physical therapist and orthotic personnel. Preoperative planning is important as the spine surgeon should be aware of potential complications that can occur and various medical precautions and surgical techniques to minimize these complications. Local operative measures significantly improve the bony status at the operative site. However, Long term bone health is important even with complete fusion to avoid adjacent level deterioration.

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**Keywords:** Postmenopause, Osteoporosis, Implants

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**Introduction**

Osteoporosis has been recognized as an established and well-defined disease that affects more than 75 million People in the United States, Europe and Japan. As defined by the World Health Organization, osteoporosis is a generalized skeletal disorder of low bone mass (thinning of the bone) and deterioration in its architecture, causing susceptibility to fracture. Type I osteoporosis (postmenopausal osteoporosis) generally develops in women between the ages of 50 and 70. Type II osteoporosis (senile osteoporosis) typically happens after the age of 70 and affects women twice as frequently as men.

The gold standard for diagnosis of osteoporosis is dual energy X-ray absorption scan (DXA scan). It measures an individual’s bone density (BMD) and compares it to the densities of other people. The values generated by the DXA test can then be compared to both: Young adult population: called a “T score,” this test measures the variance between the patient and the young adult baseline. A score above -1 is considered normal; a score between -1 and -2.5 is considered osteopenia; and a score below -2.5 is considered osteoporosis. Age and gender matched control groups: a “Z score” measures the variance between the patients’ and control groups’ amount of bone. The control group consists of other people in the patient’s age group of the same size and gender.

There is direct relationship between the lack of estrogen after menopause and low bone mass. Therefore, there is also concern that successful use of hardware in spine stabilization procedure will be compromised in patients with low bone mass. One of the biggest challenges in the postmenopausal women is the loss of bone stock that can lead to real osteoporosis. This critical situation is responsible for a high risk of implant failures during spine surgery.

Osteoporotic vertebral compression fracture is the leading cause of disability and morbidity in elderly people. This condition is associated with severe and prolonged pain that can markedly alter the individual’s participation in daily life activities. Treatment of this condition remains a challenge. Over 30% of patients affected by vertebral...
osteoporosis fractures need surgical treatment and 12% present complications requiring an invasive surgical approach.\textsuperscript{34}

The vertebral body is formed by cancellous bone tissue biomechanically characterized by a high bone turnover (80%) and a lower calcified volume (20%). Therefore, this tissue withstands to dynamic stresses, deforming itself without breaking. Degenerative disc disease and senile neuromotor and neurosensory decay, are associated with a progression in spinal kyphosis. In the case of osteoporosis, the trabecular thinning results in a reduction of vertebral body strength and initiating secondary osteodegenerative changes. Therefore, Aging spine has been associated to various sagittal changes such as a loss of lumbar lordosis, an increased thoracic kyphosis, and eventually compensatory mechanisms such as pelvic retroversion and knee flexion in order to keep the head over the pelvis.\textsuperscript{52}

Degenerative spondylolisthesis has been reported to be 4-5 times more common in women than in men,\textsuperscript{45} although a recent report states that the presence in men might be underestimated.\textsuperscript{1} Bone mineral density has been shown to be independently associated with degenerative disc disease.\textsuperscript{16}

Oral administration of bisphosphonate or intermittent injection of parathyroid hormone treatment increases bone mass and reduce the risk of osteoporotic vertebral fractures. Moreover, accelerates the tolerability of osteoporotic spine towards the implants.\textsuperscript{46}

Percutaneous vertebroplasty can provide effective pain relief for patients with osteoporotic vertebral compression fracture. This technique stabilizes the fracture through the use of cement for mechanical augmentation.\textsuperscript{46} When performed with an expandable balloon, percutaneous balloon kyphoplasty is more effective in restoring vertebral height and correcting (partially) sagittal alignment.\textsuperscript{11} In order to improve safety in implant anchorage and better clinical outcomes, various systems have been developed for osteoporotic bone such as expandable screws and partially or fully cannulated fenestrated screws.\textsuperscript{13,36}

Bone morphogenetic proteins stimulated bone growth naturally in the human body. These proteins that exist in the body can be produced concentrated and placed in the area of the spine for a spinal fusion to take place. More importantly, they can create fusion without the need for any use of the patient’s own bone.\textsuperscript{32}

This study evaluated the different perioperative enhancing factors available that might increase spinal fixation success rate in low bone density postmenopausal women.

**Patients and Methods**

**Study Design:**
Between May 2011 and May 2013, twenty four post-menopausal women were included in this retrospective study. All of them were admitted at King Salman Military Hospital-Tabouk. During that period, they had spinal implants for two major indications, vertebral compression fractures with different grades of low bone density and osteodegenerative spondylolisthesis with different grades of spinal stenosis. Each patient included was indicated for surgical intervention in the thoracic or lumbar spine region. The indications reported in this study were intractable back pain due to acute or chronic vertebral compression fracture, pain refractory to nonsurgical treatment for more than 6 months or presented to the ER with neurological deficit. Also, Patients with persistent low back and leg pain with progressive decrease in walking distance and physical activity diagnosed as osteodegenerative spondylolisthesis. The inclusion criteria were patients five years or more after menopause had spinal implants. Those patients were diagnosed with different grades of low bone density either osteopenia or osteoporosis. Preoperative osteodensitometry T-score between -1 and -2.5 is considered osteopenia and below -2.5 is considered osteoporosis. The exclusion criteria were postmenopausal women with normal osteodensitometry or low bone density secondary to tumoral or inflammatory disease.

**Bone Densitometry:**
Bone densitometry of the lumbar spine was performed 1 year after the fusion surgery at the end of the follow-up period. bone mineral content (BMC, g) and Bone Mineral density (BMD, g/cm\textsuperscript{2}) were measured by dual energy X-ray absorptiometry (DXA) using a Hologic QDR-2000 densitometer (Hologic Inc., USA). Lumbar spine BMC and BMD were assessed using a standard anteroposterior L1– L4 scanning. T- and Z-scores were calculated using the scanner software and reference values. Postoperative Values after 12 months were calculated for each vertebra.
(L1 to L4) and compared to the preoperative values. We also correlate the difference in the preoperative and postoperative values with the radiological and functional outcomes.

**Radiographs:**
The lateral spine radiographs and the multislice reformatted midsagittal computed tomography were used for measurements. Five measurements were performed: vertebral wedging and kyphotic angle for the fracture series. Disc height, osteophyte score, and lumbar lordosis for the osteodegenerative spondylolisthesis. We used AUTOCAD software to measure the kyphotic angle in the fractures series and the lumbar lordotic angle in spondylolisthesis series. Vertebral wedging was measured on multislice reformatted midsagittal computed tomography by Beck’s index (Figure 1) as the anterior vertebral height relative to the posterior vertebral height; thus the lower a value below 1 the more the vertebra has collapsed anteriorly. The kyphotic angle was measured on multislice reformatted midsagittal computed tomography by Modified Cobb method that required either the superior or inferior endplates of the collapsed vertebral body (Figure 2). Postoperatively, Beck’s index and Kyphotic angle were followed up to document the deformity correction results.

Disc height was measured on the lateral spine radiographs using the Frobin method (Figure 3). The degree of disc height narrowing was scored in comparison with the L1/2 disc as 0 (0-20% reduction in disc height), 1 (20-50% reduction), or 2 (more than a 50% reduction), and the total score from the L2/3 to the L5/S1 disc was defined as the disc score. Osteophyte formation was assessed as a total number from L1/2 to L5/S1 (Osteophyte score) of more than 6 was defined as osteophyte (+). Lumbar lordosis was measured on the lateral spine radiographs, as suggested by Cobb method (Cobb L1-L5). The angle between a line drawn across the top of the body of the first lumbar vertebra and one drawn across the bottom of the body of the fifth lumbar vertebra for spondylolisthesis series (Figure 4).

**Figure 1:** Vertebral wedging was measured on multislice reformatted midsagittal computed tomography by Beck’s index as the anterior vertebral height relative to the posterior vertebral height. Beck’s index = A/B

**Figure 2:** The kyphotic angle was measured on multislice reformatted midsagittal computed tomography by Modified Cobb method that required either the superior or inferior endplates of the collapsed vertebral body (AUTOCAD SOFTWARE).
Surgical Procedure:
The surgical procedure was standardized and performed by the first author. In every case of fracture, open or percutaneous short-segment fixation of the fracture was carried out with or without decompressive laminectomy according to the neurological status and the MRI findings. Pedicle screws were systematically inserted under anteroposterior and lateral fluoroscopic guidance. Screws diameter was 5 or 6 mm, depending on the level of the fracture, and length was determined based on the preoperative CT scan. Finally, two pre-contoured rods were added directly in open surgery or inserted percutaneously to restore vertebral body height and traumatic kyphosis. Three cases needed an anterior support of the vertebral body was performed using a balloon kyphoplasty on the fractured level according to the standard balloon kyphoplasty procedure (Figure 5). Two of the emergency cases needed autologous vertebroplasty by using bone chips were packed meticulously into the void space of the collapsed vertebral body through the pedicle tract into the posterior side of the vertebral body. After decortication of the facet side and proximal part of the transverse process, bilateral osteoconductive allograft was placed on each side of the spine in open surgery. In every case of osteodegenerative spondylolisthesis, open surgical decompressive laminectomy with bilateral forminotomy at all compromised levels for adequate neurolysis. Right sided autologous graft and left sided osteoconductive allograft wrapped by surgicel were placed on each side after decortication. We used partially cannulated fenestrated screws that allow injection of the cement in the anterior half of the vertebral body.

For severely osteoporotic cases, approximately 1.5mL of Polymethyl methacrylate (PMMA) on each screw was then injected into the vertebral bodies through the pedicular screws under fluoroscopic control to prevent cement leakage (Kypho, Medtronic). The cemented screws help a better control maneuver to keep the implants in and restore the lumbar lordosis if possible. We locally used the Infuse Bone Graft (rhBMP-2) with osteoconductive allograft in three cases of severely osteoporotic spondylolisthesis (Infuse, Medtronic). The Infuse Bone Graft (rhBMP-2) consists of two parts: a solution containing rhBMP-2 (recombinant

Figure 3: Measurement of the intervertebral disc height according to the Frobin method. The four corners of the vertebra were identified in the lateral radiographs (1, 2, 3, and 4). The medial points, medial planes (midline) and the respective bisector were marked. Disc height was determined by the perpendicular distance between points 1 and 3 (dorsal height) and points 2 and 4 (ventral height). Disc height = (H1 + H2 + h1 + h2)/2.

Figure 4: Lumbar lordosis angle was measured on the lateral spine radiograph, as suggested by Cobb method (Cobb L1-L5) as the angle between a line drawn across the top of the body of the first lumbar vertebra and one drawn across the bottom of the body of the fifth lumbar vertebra (AUTOCAD SOFTWARE).
human bone morphogenetic protein 2) and the ACS (absorbable collagen sponge). The protein is a genetically engineered version of a natural protein normally found in small quantities in the body. The purpose of the protein is to stimulate bone formation (Figure 6).

**Bracing and Rehabilitation:**
We preferred to keep our patients bed ridden with prophylaxis Clexan 40 u OD subcutaneous for 6 weeks, then starting mobilization by the physiotherapist within rigid Thoraco-Lumbo-Sacral-Orthosis (TLSO) for another 6 weeks (Home care program), then independent walking within semi-rigid TLSO for 12 weeks. Moreover, Physical exercise continued for the rest of the year when full assessment of the implants, kyphotic correction, bony fusion, bone densitometry and functional outcome was achieved.

**Clinical Evaluation and Follow-up:**
Clinical outcomes were evaluated using demographic data, length of stay, pre- and postoperative pain medications, walking distance and potential complications for at least 12 months, corresponding to the expected natural delay of bone consolidation, was obtained in all cases.

**Perioperative Pharmacological Support:**
Three smoker ladies were instructed to quit except one that reduced. Improving bone dietary by: Calcium intake > 1gm/day, Protein intake 100 grams and Vitamin D >600 IU Based on 2200 calorie/day diet. All patients were supported by daily oral administration 5 mg of risedronate (bisphosphonate) for 12 months. Six patients, three in each series had daily subcutaneous injection of 20 mcg of teriparatide (Forteo) for six months.

**Pain and disability Assessment:**
Pain was assessed using the pain assessment index from the Low Back Pain Rating Scale (LBPRS). It is measured using 11-box numerical rating scales ranging from 0 representing no pain to 10 representing worst possible pain. It comprises three scales for back and leg pain separately (pain now, worst, and average pain last 14 days). Each response scale is added giving a scale ranging from 0 to 60. A high score indicates a high influence of back pain on the daily life of the patient and thus a poor function. The three different components were weighted: 60 points for pain scoring, 30 points for disability and 40 points for physical impairment. Therefore, combining them, the final LBPRS score ranges from 0 (in patient without back problems) to 130 (in disabled patient). The questionnaire can be filled out in about 10 min and scored in about 5 min at the end of the year.43

**Statistical Analysis:**
The statistical analysis to evaluate preoperative to postoperative changes based on radiographic
measurements and clinical outcomes variables was done at biostatistics unit of community medicine department at Zagazig University. For each test, the level of significance was set at 5%; that is, P values lower than 0.05 were considered as statistically significant.

Results

**Population Data:**
It was depicted in details in (Table 1) & (Table 2). Ten surgical fractures occurred in L1 in 2 cases, T12 in 2 cases, T9 and T10 in 4 cases and T8 and T11 in 2 cases. Therefore, six lumbar vertebrae were included in postoperative bone densitometry. Four (L1) and two (L2) were involved in fixation. However, two (L1) and one (L2) vertebrae had open surgery and bony graft. The main cause of fracture was fall down at the bathroom. Among 14 cases of osteodegenerative spondylolisthesis, 8 cases were in L5-S1, 5 cases were L4-L5 and one case at L3-L4 level. Twelve cases were fused at three levels L4-L5-S1. Two cases at two levels, one because of sacralised L5 and one case had L3-L4 fusion. Therefore, 14 (L4) and 1 (L3) lumbar vertebrae with bone graft were included in postoperative bone densitometry. Bone status was associated with pain history as 88% (8/9) of the osteoporotic patients had a preoperative pain history of more than two years compared to 60% (3/5) of the osteopenic patients.

**Table 1.** Bone Densitometry and Radiopaque Outcome (Vertebral Compression Fractures) – 10 Cases

| Bone Status:  | PREOPERATIVE | POSTOPERATIVE | P-value |
|--------------|--------------|---------------|---------|
|              | RANGE  | MEAN  | SD   | RANGE  | MEAN  | SD   |         |
| Normal       | 0      |       |      | 3      |       |      | (P=0.13)NS |
| Osteopenia   | 4      |       |      | 4      |       |      |         |
| Osteoporosis | 6      |       |      | 3      |       |      |         |
| Beck's Index (BI) | (0.18-0.68) | 0.44  | 0.11 | (0.37-0.84) | 0.67  | 0.13 | (P=0.013)S |
| Kyphotic Angle | (7°-19°) | 13°   | 4.2  | (5°-13°) | 8°   | 3.2  | (P=0.007)HS |
| BMC (g)      |        |       |      |        |       |      |         |
| L1           | (8.27-11.10) | 9.28  | 3.52 | (8.87-14.10) | 11.28 | 3.22 | (P=0.20)NS |
| L2           | (7.94-10.54) | 9.33  | 2.59 | (8.94-12.54) | 10.03 | 2.52 | (P=0.56)NS |
| L3           | (9.14-11.76) | 10.28 | 3.12 | (9.84-12.76) | 10.88 | 3.62 | (P=0.69)NS |
| L4           | (9.67-14.33) | 12.26 | 4.21 | (9.67-13.33) | 11.66 | 4.01 | (P=0.74)NS |
| BMD (g/cm²)  |        |       |      |        |       |      |         |
| L1           | (0.850-0.970) | 0.996 | 0.146 | (0.950-1.170) | 1.096 | 0.144 | (P=0.14)NS |
| L2           | (0.799-1.098) | 0.800 | 0.167 | (0.899-1.198) | 0.819 | 0.137 | (P=0.80)NS |
| L3           | (0.873-0.953) | 0.909 | 0.205 | (0.773-0.959) | 0.811 | 0.215 | (P=0.35)NS |
| L4           | (0.751-0.882) | 0.809 | 0.161 | (0.771-0.888) | 0.191 | 0.191 | (P=0.96)NS |
| T-SCORE      |        |       |      |        |       |      |         |
| L1           | (-0.6 to -2.8) | -1.9  | 1.33 | (-0.4 to -2.2) | -1.5  | 1.13  | (P=0.43)NS |
| L2           | (-1.8 to -3.2) | -2.4  | 1.07 | (-1.5 to -2.8) | -2.1  | 1.09  | (P=0.54)NS |
| L3           | (-1.2 to -2.8) | -2.1  | 1.58 | (-1.4 to -2.9) | -2.4  | 1.08  | (P=0.49)NS |
| L4           | (-2.6 to -3.5) | -2.9  | 1.69 | (-2.2 to -3.1) | -2.6  | 1.59  | (P=0.40)NS |
| Z-SCORE      |        |       |      |        |       |      |         |
| L1           | (-1.2 to -0.4) | -1.4  | 0.3  | (-1.6 to -0.6) | -1.2  | 0.2   | (P=0.09)NS |
| L2           | (-2.4 to -0.8) | -1.9  | 0.7  | (-2.1 to -0.9) | -1.6  | 0.4   | (P=0.25)NS |
| L3           | (-2.1 to -0.3) | -2.1  | 0.6  | (-1.1 to -0.6) | -2.1  | 0.5   | (P=0.99)NS |
| L4           | (-2.2 to -1.5) | -2.7  | 0.5  | (-1.8 to -1.1) | -2.2  | 0.3   | (P=0.12)NS |
Bone Densitometry outcomes:

In fracture series, the preoperative bone status was 4 cases osteopenia and 6 cases osteoporosis. Postoperative little change happened as 3 cases normal, 4 cases osteopenia and 3 cases remained osteoporotic \((P=0.13)\) insignificant. Most of the bone densitometry parameters increased to insignificant level (Table 1). However in spondylolisthesis series, the preoperative bone status was 5 cases osteopenia and 9 cases osteoporosis. Remarkable improvement happened postoperative 9 cases were reported normal, 2 cases osteopenia and 3 cases remained osteoporotic \((P=0.013)\) significant [Figures 7: 1-2]. All the bone densitometry parameters involved in surgery (especially L4 that involved in all surgeries) increased to significant level (Table 2).

### Table 2: Bone Densitometry and Functional Outcome (Degenerative Spondylolisthesis) – 14 Cases

|                      | PREOPERATIVE | POSTOPERATIVE | P-value |
|----------------------|--------------|---------------|---------|
|                      | RANGE | MEAN | SD     | RANGE | MEAN | SD     |         |
| Bone Status:         |       |      |        |       |      |        |         |
| Normal               | 0     | 5    | 9      | 9     | 2    | 3      | \((P=0.13)\)S |
| Osteopenia           |        |      |        |       |      |        |         |
| Osteoporosis         |        |      |        |       |      |        |         |
| Pain Scale           | 101-126| 115  | 8      | 104-44| 23   | 5      | \((P=0.001)\)HS |
| Walking Distance     | 16-34M | 22M  | 5      | 402-512M | 448M | 13     | \((P=0.001)\) HS |
| Angle of lordosis    | (18°-31°)| 25°  | 3.4    | (23°-34°)| 29°  | 4.2    | \((P=0.01)\)S |
| BMC (g)              |        |      |        |        |      |        |         |
| L1                   | (7.27-12.10) | 9.23 | 3.82   | (7.82-12.80) | 9.51 | 3.84   | \((P=0.84)\)NS |
| L2                   | (7.47-10.51)| 8.83 | 2.89   | (7.72-11.21)| 8.86 | 2.94   | \((P=0.97)\)NS |
| L3                   | (9.40-12.76)| 10.68| 3.62   | (10.82-14.82)| 12.72| 3.43   | \((P=0.13)\)NS |
| L4                   | (8.67-16.33)| 13.26| 5.21   | (51.79-63.72)| 56.65| 8.76   | \((P=0.00001)\)NS |
| BMD (g/cm²)          |        |      |        |        |      |        |         |
| L1                   | (0.740-0.940)| 0.886| 0.176  | (0.760-0.920)| 0.896| 0.179  | \((P=0.88)\)NS |
| L2                   | (0.789-0.898)| 0.864| 0.207  | (0.792-0.902)| 0.867| 0.209  | \((P=0.96)\)NS |
| L3                   | (0.773-0.893)| 0.899| 0.215  | (0.796-1.068)| 0.908| 0.222  | \((P=0.91)\)NS |
| L4                   | (0.651-0.782)| 0.709| 0.181  | (2.417-2.881)| 2.670| 0.367  | \((P=0.0001)\)NS |
| T-SCORE              |        |      |        |        |      |        |         |
| L1                   | (-0.4 to -2.7)| -1.8 | 1.73   | (-0.5 to -2.4)| -1.9 | 1.43   | \((P=0.85)\)NS |
| L2                   | (-1.2 to -3.2)| -2.2 | 1.03   | (-1.2 to -3.2)| -2.2 | 1.02   | \((P=0.40)\)NS |
| L3                   | (-1.2 to -3.8)| -2.6 | 1.52   | (-0.3 to -2.8)| -1.7 | 1.69   | \((P=0.30)\)NS |
| L4                   | (-2.4 to -3.7)| -2.9 | 1.89   | (12.3-16.5)| 14.12| 2.07   | \((P=0.0001)\)NS |
| Z-SCORE              |        |      |        |        |      |        |         |
| L1                   | (-1.3 to -0.6)| -0.9 | 0.4    | (-1.2 to -0.6)| -0.93| 0.4    | \((P=0.84)\)NS |
| L2                   | (-2.1 to +0.4)| -0.4 | 0.6    | (-2.1 to +0.4)| -0.5 | 0.7    | \((P=0.40)\)NS |
| L3                   | (-2.2 to +0.6)| -1.3 | 0.4    | (-2.1 to +0.4)| -1.1 | 0.6    | \((P=0.30)\)NS |
| L4                   | (-2.0 to -1.1)| -1.5 | 0.7    | (-2.4 to +0.7)| 15.2 | 2.1    | \((P=0.0001)\)HS |
Radiological Outcomes:
Based on postoperative CT scan, and on a total of 120 screws inserted, one case of silent extrapedicular screw was noted at T7 passing between the right side of the spine and the head of the adjacent rib. No implant failure, loosening or pull-out screws were reported at the immediate postoperative CT control and the last follow-up. All cases showed complete bony fusion over stable implants at the end of the follow-up period except one heavy smoker lady who could not quit showed some delay. In the fracture series: The Beck’s index mean pre- and postoperative was 0.44 (0.18-0.68, SD 0.11) and 0.67 (ranging from 0.37 to 0.84, SD 0.13), respectively. This difference was statistically significant (0.44 versus 0.67, \( P=0.013 \)). The kyphotic angle mean pre- and postoperative was 13° (7-19°, SD 4.2) and 8° (5-13°, SD 3.2). The difference was statistically highly significant (13° versus 8°, \( P=0.007 \)). In the spondylolisthesis series: The pre-and postoperative degree of disc height narrowing was scored as 0 in 8/56 discs, 1 in 19/56 discs and 2 in 29/56 discs, the total score was 77 and 0 in 8/56 discs, 1 in 23/56 discs and 2 in 25/56 discs, the total score was 73. This difference was statistically non-significant (77 versus 73, \( P=0.95 \)). 21/24 (87.5%) of the ladies were osteophyte (+) this did not change postoperatively. Vacuum Sign was positive in 4/10(40%) of fracture series and in 8/14(57%) of spondylolisthesis series. It did not show any change in the former. However, the latter showed an improvement in 3/8 (37.5%) cases completely and 2/8(25%) partially (Figure 8: 1-2). The lumbar lordosis angle mean pre- and postoperative was 25° (18-31°, SD 3.4) and 29 (23-34°, SD 4.2).The difference was statistically significant (25° versus 29°, \( P=0.01 \)).

Surgical Outcomes:
The instrumentation was on average performed on 2 levels short-segment fixation in fracture series and 3 levels in spondylolisthesis series. The screw diameter was 6 mm except in the 2 cases of T8 and T9 fracture in which 5 mm screws were used. During screws and rods insertion, no implant failure or pull-out was noted. 4 cases of fracture were operated on emergency basis because of significant neurological deficit. Two of them were supported with autologous vertebroplasty. Decompressive laminectomies were performed for 6 cases of fractures and all cases of spondylolisthesis with adequate forminotomies for the latter series. A balloon kyphoplasty was performed.
performed in 3 cases neurologically intact with persistent back pain more than 6 months. One of them showed middle rather than anterior third injection. In spondylolisthesis series, no significant difference in the bony healing between the both sides with average 147 days. However, 3 cases supported with Infuse Bone Graft (rhBMP-2) showed adequate healing before the expected time with complete back pain free with average 138 days. Among 22 cement injected screws in four spondylolisthesis cases, One screw showed silent extra vertebral leakage (Figure 9) and failure of injection in another one (Figure 10). No cases of implants failure or pseudoarthrosis in both groups that necessitated re-surgery. All except one was convinced to quit smoking. During immediate postoperative period, one patient with long time preoperative recumbency had a pulmonary embolism irrelevant to cement leakage. She was treated with medical therapy. No other complications occurred such as infection or neurologic impairment.

**Clinical Outcomes:**
Mean length of stay was 8.4 days (7-15 days, SD 1.2) in the fracture series with marked paraparesis and 1/14 (7%) in the spondylolisthesis with right sided foot drop showed substantial improvement after 5 months of intense course of physiotherapy and regained the full power by the end of the year. Mean pre- and postoperative LBPRS were 115 (101-126, SD 8) and 23 (10-44, SD 5), respectively. This difference was statistically highly significant (115 versus 23, \( P=0.001 \)). Mean pre- and postoperative walking distance in meters were 22 (16-34, SD 5) and 448 (402-512, SD 13), respectively. This difference was statistically highly significant (22 versus 448, \( P=0.001 \)). 20/24 (83.3%) of the patients used to get grade III analgesics before the surgical procedure. They quit morphine in three months.
Discussion

Although the skeletal system appears to be a static structure macroscopically, the bone is a collection of dynamic tissues microscopically. Remodeling, including bone absorption and formation in the microcracks of bone occurs continuously. Bone remodeling is performed by basic multi-cellular unit within the bone remodeling cavity, and this unit is composed of osteoclasts, osteoblasts, bone lining cells and osteocytes. Complete regeneration of adult skeleton through remodeling takes 10 years and remodeling serves to repair damage and prevent aging and fracture. Remodeling with positive balance occurs in the growing skeleton, and negative remodeling causes reduced bone mineral density and osteoporosis.49

Osteoporosis is a disease caused principally by the significant loss of bone mineral density. Early in life, more bone is laid down than is removed, and an individual’s peak bone mass is typically achieved by around age 30. After peak bone mass is reached, the remodeling process (the process of laying down new bone and removing old bone) takes away more bone than is replaced. Hence making the bones more prone to osteoporosis.3

Among several etiologies of osteoporosis, menopause is the most common cause. Bone loss in both women and men begins in the 40s and rapid bone loss in women occurs during the first 5-10 years after menopause. In addition, women accumulate less bone mass than men during the developmental period. Therefore, the incidence of fracture is higher in women than in men.14

Estrogen plays an important part in maintaining bone strength because it helps keep bone remodeling rates low. There are two lines of cells for bone remodeling, the bone-eating cells (osteoclasts) and the bone-forming cells (osteoblasts). Without estrogen, the osteoclasts are favored and more bone is resorbed than laid down, resulting in thinning of the bone.25

Therefore, when women reach menopause and their estrogen levels decrease, the rate of bone loss increases to about 2% to 3% per year. After 8 to 10 years, the rate of bone loss returns to the previous rate of 1% and 0.5% per year, respectively. This loss of bone density, particularly after women reach menopause, is one of the primary causes of osteoporosis in women.14 Oestrogens probably have anabolic effects on the muscles and ligaments of the spine. Oestrogen deficiency may induce lower

Figure 9: Reconstructed CT-3D of severely osteoporotic L5-S1 spondylolisthesis (Grade II) showing intravertebral PMMA injection at L4 and silent external leak at L5.

Figure 10: Axial CT showed intravertebral injection in the right screw and failure of injection in the left because of PMMA hardening.
mechanical resistance in spinal ligaments which may play a role in muscle strength.\textsuperscript{25}

Although DXA- Bone Densitometry (two-dimensional X-ray-based technology) dependent on bone size and does not discriminate trabecular bone from the cortical bone, DXA-based vertebral fracture assessment measures vertebral height, at the anterior, middle and posterior aspects and provides information which is used to classify the severity and type of vertebral deformity. The imaging technology of peripheral quantitative computed tomography provides volumetric measures of trabecular and cortical bone properties separately at appendicular sites in the skeleton at a low radiation dose. Further study is needed to assess other measurement properties of DXA-based vertebral height measures and to identify methods for assessing more proximal vertebral levels.\textsuperscript{15}

In our pre and postoperative bone densitometry outcome: Bone mineral density (BMD) of the single vertebrae has been shown to vary within the lumbar spine, but with a decline from L5 to L1 being the most remarkable phenomenon. In fracture series, the preoperative bone status was 4 cases osteopenia and 6 cases osteoporosis. Postoperative little change happened as 3 cases normal, 4 cases osteopenia and 3 cases remained osteoporotic. This difference was insignificant. In fact, 3 cases moved from the lower category up so that, the number of osteopenic group (the middle category) remained constant. Most of BMD parameters increased to insignificant level may be the pharmacological effect. However in spondylolisthesis series, the preoperative bone status was 5 cases osteopenia and 9 cases osteoporosis. Remarkable improvement happened postoperatively, 9 cases were reported normal, 2 cases osteopenia and 3 cases remained osteoporotic. This difference was significant.

All bone densitometry parameters involved in surgery (especially L4 that involved in all spondylolisthesis surgeries) increased to significant level. Therefore, BMD of L4 completely converted T- and Z-score from the negative to the positive side. These results of the bony status reflected the condition of the bone at the operative site only where bone graft was added. They did not reflect the bony status of the body or even the non-operated vertebrae of the lumbar spine that remained unchanged or a little increased by the pharmacological effect comparable to that happened in the fracture series. So, we believe that this result can prove how much the local operative measures were sufficient enough to increase the bone density by adding graft and how much DXA-study is bone size dependent technique. However, it was false for the rest of the non-operated spine and the whole bone status. Really, this fact was also supported by DXA-hip results for each patient.

Gaber et al,\textsuperscript{19} failed to demonstrate any correlation between BMD and pain or disability, as assessed with the Oswestry Disability Questionnaire. Likewise, Nicholson et al,\textsuperscript{43} could not demonstrate any association between history of back pain and BMD or Z-score. In our series, Bone status was associated with pain history as 88% of the osteoporotic patients had a preoperative pain history of more than two years compared to 60% of the osteopenic patients. One explanation to our finding could be a higher degree of physical inactinity in the patients with more severe pain, leading to a larger bone loss and diagnosed as osteoporosis preoperatively especially in spondylolisthesis series.

Up to 10% of women over 60 years may be affected by degenerative spondylolisthesis. One study has shown different amounts of matrix metalloproteinases in ligamentum flavum, suggesting a biochemical pathway for increased collagen laxity, which subsequently could lead to the slip.\textsuperscript{45}

Bone mineral density has been shown to be independently associated with degenerative disc disease and spondylolisthesis. This could explain two cases out of four postoperative laminectomy spondylolisthesis were having intact facets that started to slip progressively after the menopause. Moreover, In elderly ladies, iatrogenic cause of instability following spinal surgery may occur because of pre-existing degenerative changes in the facet joints and intervertebral disc.\textsuperscript{16}

Several studies have investigated the morphology of the facet joints as a possible cause of the degenerative slip and found that the angulation was associated with slip and changed through the decades of life, thus explaining the fact that the degenerative slip first occurs in the later part of life. Studies suggested that the sagittally oriented facet joints is a prerequisite for development of degenerative spondylolisthesis, but that development only occurs
in patients with low BMD, perhaps because they are unable to generate a remodeling response that will cause the formation of osteophytes which subsequently will stabilize theolisthesis and prevent it developing into a clinical significant slip.\textsuperscript{33,54} On the other hand, Cubuk et al,\textsuperscript{15} investigated the relation between BMD, both spinal and hip, and facet joint orientation and found no difference in facet joint orientation between osteoporotic, osteopenic, and normal patients. Most of the facets in our series were in severe osteoarthritis rather than the hypothesis of angulation or sagittal orientation.

There exist reports on the outcome of lumbar arthrodesis following instrumentation in patients over 60 years of age, which indicated the prevalence of delayed and collapsed fusion in elderly patients to be higher than that in younger patients. The fusion rates of elderly patients reported were over 90%. In other words, old age and osteoporosis are not contraindication in spinal arthrodesis. The number of elderly patients who needs spinal surgery will increase and the prevalence of osteoporosis in elderly patients is high.\textsuperscript{39}

Spine surgeons are more and more concerned by aging spine and they have to deal with trauma, degenerative or tumoral cases in patients with an important loss of bone stock. Performing an osteosynthesis in these patients can be difficult due to the osteoporosis and comorbidities that increase complications rates. Furthermore in elderly, mechanical failures of implants and rates of pseudarthrosis are higher. There are numerous pre-operative, intra-operative, and post-operative strategies available to increase spinal fixation success rate in osteoporotic patients. Moreover, fixation complications in the elderly can be anticipated, avoided, and appropriately treated.\textsuperscript{54}

These strategies depend on three major items: improving bone condition, improving implants fixation and improving bone fusion:

\textbf{1) Improving Bone Condition:}

Once diagnosis of primary osteoporosis has been made, treatment is warranted. Smoking has been associated with low BMD and postoperative pseudoarthrosis.\textsuperscript{44} All our smokers quit except one who reduced. Most of our patients followed the dietary formula as mentioned before.

Land-based exercise studies have demonstrated that exercise programs of varying length and design improve balance, increase muscle strength and reduce the incidence of falls over a one to 10 year follow-up in older women with osteoporosis compared with control groups.\textsuperscript{5} We preferred to follow very gradual physiotherapy program after complete subsidence of the back pain.

In order to obtain good fusion rate in osteoporotic patients, we should be aware of the antiresorptive and anabolic agents.\textsuperscript{46} In the study of anti-resorptive agents over a two-year period, there was a comparison of placebo, estrogen, calcitonin and alendronate. Increases in bone density were noted with all agents, as follows: Estrogen 5%, Alendronate 8% and Calcitonin 2%. There was no residual protection from bone loss after stopping the estrogen and calcitonin, however, after stopping the Alendronate a positive bone balance was noted.\textsuperscript{42} In our series, all patients were supported by daily oral administration 5 mg of risedronate (bisphosphonate) for 12 months. The pharmacological effect of Alendronate improved the bony status. The BMD of non-fused lumbar vertebrae and the hip really reflect this pharmacological effect. However, this positive change did not reach the significant level.

Bisphophonates are typical anti-resorptive agents that include alendronate, ibandronate, etidronate and pamidronate. The mechanism of bisphosphonate is to promote apoptosis of mature osteoclasts and result in slow rate of bone remodeling. Many animal studies presented the effects of bisphosphonates on the skeletal system. In animal studies that investigated fracture healing and pull-out strength of implants, bisphosphonates did not adversely affect the skeletal system However, according to recent studies, bisphosphonates inhibit or delay spinal fusion through reduced incorporation between grafted bone and host bone.\textsuperscript{47}

Only one drug acts as anabolic agent to osteoporosis, recombinant human PTH, Teriparatide. Although high levels of PTH cause decreased BMD through increased bone resorption, low and intermittent PTH elevation increases bone formation secondary to its anti-apoptotic effect on osteoblasts.\textsuperscript{20} All our patients were supported by daily oral administration 5 mg of risedronate (bisphosphonate) for 12 months and six patients, three in each series had daily subcutaneous injection of 20 mcg of teriparatide (Forteo) for six months. If PTH treatment is not followed by antiresorptive
therapy, the increased BMD would be lost. However, the experience of PTH use is so far limited in the United States and Europe to 2 years and 18 months, respectively. Therefore, it needs to develop additional anabolic agents that can be continuously used in osteoporotic patients. The results of animal studies suggested that PTH enhanced the healing of bone fracture, BMD, mechanical strength and arthrodesis of the spine.\textsuperscript{46}

2) Improving Implants Fixation:

Cancellous bone is more affected by osteoporosis than cortical bone, therefore lower BMD has been a major factor in poor screw fixation, screw loosening and fixation failure, loss of correction, lower fusion rates and increased adjacent level degeneration/fractures.\textsuperscript{26} Therefore, many techniques have been employed to enhance the pullout strength of the pedicle screw in osteoporotic ladies.

We followed the minitapping technique as minimization of tapping hole can affect the pullout strength in osteoporotic bone. Zindrick et al,\textsuperscript{56} stated that Tapping decreases stability Moreover, Carmouche et al,\textsuperscript{9} recommended no tapping or undertaping.

We used bigger and longer screws as it may provide good solution for fragile bones. Each screw must be implanted in a pedicle that can accept a minimum 5.5mm diameter screw and the length of the screw must be sufficient to reach the first anterior third of the vertebral body. On the other hand, Brantley et al,\textsuperscript{8} suggested that screw diameter and length had little or no effect on fixation stiffness in osteoporotic bone.

Convergent insertion angle has two advantages, enhancing pedicle screw pullout and reducing risk of cement leakage. Moreover, cortical bone trajectory increases pullout by 30%.\textsuperscript{50} We preferred the cortical trajectory and close cortical path inside the cancellous body to be parallel and close to the end plate as possible. We believe that this path is having relatively dense bone and screw tolerability.

Screw augmentation with Polymethyl methacrylate (PMMA) has yielded favorable outcomes. The amount of cement to be injected and its distribution into the vertebral body are also important to adapt to each case.\textsuperscript{51} A sufficient amount of cement must be injected in order to achieve a strong anchorage of the screw, but an injection of too much cement will increase the risk of leakage.\textsuperscript{11} A maximal injection of 2mL by screw is recommended to achieve these goals and even less above T6.\textsuperscript{39} We injected maximum 1.5 mL for all levels.

We had 9 % failure rate among 22 cement injected screws in four spondylolisthesis cases. One screw failed because of cement hardening (delayed injection) and another one showed silent leakage because of lack of convergent path and premature injection of too liquid cement. Another screw was not long enough and the injection was in the middle rather than the anterior third. The cemented screws help a better control maneuver to keep the implants in and restore the lumbar lordosis

While between 5 and 39% of cement leakage are reported in the literature, the convergent approach into the vertebral body and the partially fenestrated screws were carrying the lowest risk of cement leakage.\textsuperscript{51}

Percutaneous osteosynthesis can be a valuable option as it leads to a decrease of surgical time, blood loss, and infectious complications. These techniques minimize muscle trauma and help to a quicker postoperative recovery. Another interest in percutaneous approach under fluoroscopic guidance is the very low rate of extrapedicular screw compared to conventional techniques. Using this intraoperative control, it is therefore possible to implant the screws according to the vertebral morphology in terms of length and diameter.\textsuperscript{53}

However, when used alone, a percutaneous osteosynthesis can lead to a pseudarthrosis followed by screws pull-out and a recurrence of the traumatic kyphosis. In order to avoid these risks, some authors have advocated the use of long constructs. That is not convenient to the old and osteoporotic patients.\textsuperscript{38} Therefore, performing an anterior support of the fractured level can therefore be necessary, using a balloon kyphoplasty during the same surgical session at the fractured level. We preferred to start the kyphoplasty after posterior fixation in order to decrease the pressure needed to inflate the balloon and to inject the cement with low pressure to avoid leakage. Recent studies reported satisfactory results using the combination of these cement-augmented screws with a percutaneous approach.\textsuperscript{35}

In cadaveric study of Becker and his coworkers to examine the effect of PMMA augmentation technique on screw pull out by using 4 different
techniques: First group: standard solid screw, second group: perforated screw with vertebroplasty, third group: solid screw with vertebroplasty and last group: solid screw with kyphoplasty They found that Vertebroplasty techniques better than control and kyphoplasty On the other hand, kyphoplasty is more effective in restoring vertebral height and correcting (partially) sagittal alignment. However, both techniques lack osseointegration and has limited biocompatibility, which may result in the collapse of adjacent vertebra and associated complications that require revision surgery.

The use of intracorporeal devices in addition to bone grafting for internal support to maintain body height and support cancellous bone regeneration has been reported and provides a new option for treating vertebral compression fractures. The biological augmentation of intravertebral expandable pillars is used to reconstruct the vertebra through internal mechanical support and also by encouraging bony fusion. In addition to being enveloped by bone chips, the expandable pillars are made of titanium alloy, which is known for its excellent biocompatibility. These pillars can be filled up with bone chips, which expand after settling. However, they were implanted through the posterior approach and without corporectomy. Omitting corporectomy could diminish the surgical risk of neurovascular damage and blood loss. Furthermore, preservation of the end plates prevents subsidence of these pillars into the adjacent segments.

Wu and his colleagues suggested that use of multiaxial expandable pedicle screw can improve fixation strength in poor quality bone. They added that the addition of an expandable pedicle screw design adds a valuable tool to the growing spine instrumentation in low bone density spine. Recently, Hoffman et al, compared the complications of associated with use of rhBMP2 for posterolateral spine fusion in younger vs. older patients. While older patients had a longer hospital stay; other complications were similar.

Lee and colleagues compared fusion rates and time to fusion in patients receiving iliac crest bone graft (ICBG) versus rhBMP in 195 posterolateral lumbar fusions. They came up with that in the no risk factor group, fusion rates were higher in the rhBMP group while the fusion rate was higher with ICBG in the high risk group. The authors concluded that “When compared with patients with fusion-related risk factors, the use of rhBMP-2 was comparable with autograft but was not sufficient to overcome

3) Improving Bone Fusion:

Non-decortication of the transverse process did not result in arthrodesis and primary vascular supply to the fusion mass originated from decorticated bone, not from the adjacent muscle.

Three factors are vital for bone formation as osteoconductive scaffold, osteogenic cell and osteoinductive materials. Therefore, the characteristics of host bed such as vascularity and quality of bone marrow, the distance of fusion site and the quality of bone graft should be assessed by the surgeon prior to surgery.

Recombinant bone morphogenetic protein (rhBMP-2) was first identified in 1965 by Marshall Urist and colleagues at UCLA. As part of the transforming growth factor-β (TGF-beta) superfamily of proteins, rhBMPs bind to cell-surface receptors where they initiate signals that control cell growth, differentiation, and migration. These effects can powerful induce bone formation. It took 30 years of careful work with rhBMP dosing and carriers before rhBMP-2 was FDA approved for use in fusion surgery. In 2008, it received FDA approval for use in posterolateral spine fusion surgery to repair pseudarthrosis in osteoporotic patients.

In our series, we used rhBMP-2 in combination with osteoconductive allograft in three cases after decortication the facet area and adjacent transverse process in severely osteoporotic patients who were compromised with multiple co-morbidities that showed bony fusion earlier than expected with this bone status and complete subsidence of their back pain in three months. No reported compilations in this little number.

Glassman and his colleagues reported that rhBMP-2 was an iliac crest bone graft substitute “viable ICBG replacement” when they compared 52 patients over the age of 60 undergoing posterolateral lumbar fusion with ICBG with 50 patients undergoing surgery with rhBMP. In this series, 16 ICBG and 10 rhBMP patients required revision procedures for persistent symptoms. Recently, Hoffman et al, compared the complications of associated with use of rhBMP2 for posterolateral spine fusion in younger vs. older patients. While older patients had a longer hospital stay; other complications were similar.

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all aspects of the weakened osteoinductive capacity encountered in patients with these risk factors.\textsuperscript{31}

Osteoporosis results in fragile bone through negative bone remodeling. As such, prior to performing spinal fusion on osteoporosis patients, surgeons should consider multidisciplinary strategies, including the use of the antiresorptive and anabolic agents and proper instrumentations. Moreover, surgeons must consider bone graft quality, proper osteoinductive materials (for example, bone morphogenetic proteins (BMPs), increasing the ability of osteoblasts [for example, with intermittent administration of parathyroid hormone (PTH)] and preventing factors that may hinder fusion, including long-term use of non-steroidal anti-inflammatory agents and smoking, before performing spinal fusion on elderly postmenopausal osteoporotic ladies.

**Conclusion**

Treating the osteoporotic spine involves multidisciplinary approach with involvement of endocrinologist, rheumatologist, physical therapist and orthotic personnel. Preoperative planning is important as the spine surgeon should be aware of potential complications that can occur and various medical precautions and surgical techniques to minimize these complications. Local operative measures significantly improve the bony status at the operative site. However, Long term bone health is important even with complete fusion to avoid adjacent level deterioration.

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