

**Manuscript Number: WJO-Manuscript NO: 76079**  
**Managements of osteoporotic vertebral compression fractures: a narrative review**  
**World Journal of Orthopaedics**

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Dear Founder and CEO Mr. Ma,

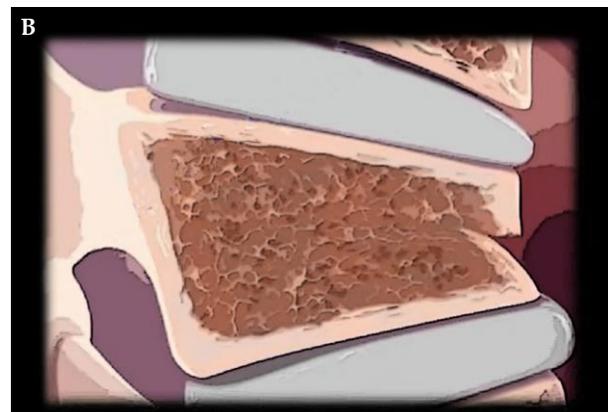
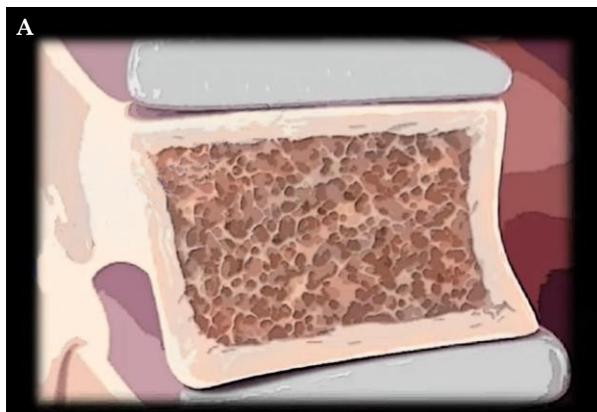
Thank you for providing us the opportunity to review the manuscript “WJO-Manuscript NO: 76079 Managements of osteoporotic vertebral compression fractures: a narrative review” for the *World Journal of Orthopaedics*. We appreciate the time you and the reviewers took to provide feedback on our manuscript as well as the valuable suggestions that will greatly improve our paper. We have incorporated the suggestions put forth by the reviewers. Please see below for specific responses to the reviewer’s comments.

**Reviewer #1:**

**Comment 1**

The subject of this review seems very interesting and medically important. However, the following points should be considered by the authors: 1. It is better for authors to add some figures to make their topics clearer, especially in Introduction and Diagnosis and Manifestation sections.

**Author Response:** We agree with the reviewer’s comment and included illustrative figures depicting osteoporotic vertebra and a vertebral compression fracture, see Page 5, Figure 1, shown below.



**Figure 1.** Osteoporotic vertebra before (A) and after (B) a compression fracture. Note the wedge shape of the vertebral body which can cause kyphotic deformity.

### Comment 2

I think this review would be more comprehensive if the authors could study the effects of laser and physiotherapy treatments on the managements of osteoporotic vertebral compression fractures.

**Author Response:** We agree with the reviewer and included information about these treatments, see Page 8 and the below text.

“If patients chose to exercise, programs should be implemented with the focus on improving flexibility, muscle strength, and core and gait stability<sup>[30]</sup>. It is important to note that exercise regimens should be tapered as pain improves<sup>[11]</sup>. Another potential treatment method for fracture repair is low-level laser therapy (LLLT). Although the exact mechanisms of LLLT are unknown, it is hypothesized to increase angiogenesis and bone formation while decreasing inflammation, as tested in animal studies<sup>[31,32]</sup>. By enhancing callus formation, LLLT could accelerate fracture healing and thus improve patient outcomes, but there is limited evidence for its use in patients with bone fractures<sup>[33]</sup>. Further research into the mechanisms of LLLT and the appropriate parameters for therapeutic use and minimal side effects need to be studied before clinical application.”

### Comment 3

I suggest authors add a list of abbreviations at the end of the paper.

**Author Response:** We thank the reviewer for bringing this to our attention. A table of the abbreviations has been added at the end of the manuscript, see Page 23, Table 1. The table is as shown below.

**Table 1. List of Abbreviations**

Abbreviation	Definition
OVCF	Osteoporotic vertebral compression fractures
VCF	Vertebral compression fractures
NSAID	Non-steroidal anti-inflammatory drug
HRQOL	Health-related quality of life
QALY	Quality-adjusted life years
AAOS	American Academy of Orthopedic Surgeons
MRI	Magnetic resonance imaging
CT	Computed tomography
DEXA	Dual-energy X-ray absorptiometry
BMD	Bone mineral density
SD	Standard deviation
AAN	American Academy of Neurology

PMMA	Polymethylmethacrylate
RANKL	Receptor activator of nuclear factor-kappa beta ligand
LLLT	Low-level laser therapy
TH	Thyroid hormone
SERM	Selective estrogen receptor modulators
PTH	Parathyroid hormone
mg	Milligrams
IU	International unit
PO	Orally
IV	Intravenous
SQ	Subcutaneous
IN	Intranasal
RR	Relative risk

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**Reviewer #2:**

**Comment 1**

Including PKP and PVP, various technical options are available, such as augmented screw fixation or CBT screws. In the presence of a neurological deficit, posterior fixation with decompression or o anterior reconstruction maybe required. The author should tell us about the indications for each of these techniques and what are the technical challenges and complications.

**Author Response:** We agree with the reviewer about the addition of other techniques, see Page 10.

“Other surgical interventions include decompression then screw implantation and vertebral fixation. Decompression is indicated if the patient has neurological deficits due to neural compression. Additionally, screw augmentation can be used to increase the pull-out strength and may be combined with cement injection if fenestrated screws are used<sup>[53]</sup>. Vertebral fixation, specifically posterior vertebral fixation, has limited indications, including burst fractures, multiple VCFs causing kyphotic deformity, and malunion<sup>[53]</sup>. Both of these interventions can be combined with cement injection, so they can result in similar complications as vertebroplasty and kyphoplasty, such as cement extravasation.”

**Comment 2**

Medications for Treatment of Vertebral Compression Fractures are complicated. The authors can create a table to summarize the mechanism, indication, adverse effects, dosage...

**Author Response:** A table of the pharmaceutical treatments was included on Pages 24-25, Table 2. The table is shown below.

**Table 2. Pharmaceutical Management of Osteoporosis and Efficacy**

Drug	Dosing	Efficacy	Adverse Effects
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## BISPHOSPHONATES

Alendronate	<ul style="list-style-type: none"><li>• 10 mg daily, PO</li><li>• 70 mg weekly, PO</li></ul>	<ul style="list-style-type: none"><li>• RR of 0.55 in postmenopausal women compared to placebo</li></ul>	<ul style="list-style-type: none"><li>• Esophageal irritation</li><li>• Dyspepsia</li><li>• Acute phase reaction</li></ul>
Ibandronate	<ul style="list-style-type: none"><li>• 2.5 mg daily, PO</li><li>• 150 mg monthly, PO</li><li>• 3 mg every 3 months, IV</li></ul>	<ul style="list-style-type: none"><li>• RR between 0.50 and 0.62 in postmenopausal women compared to placebo</li></ul>	<ul style="list-style-type: none"><li>• Atrial fibrillation</li><li>• Musculoskeletal pain*</li><li>• Renal toxicity*</li><li>• Atypical fracture*</li></ul>
Risedronate	<ul style="list-style-type: none"><li>• 5 mg daily, PO</li><li>• 35 mg weekly, PO</li><li>• 150 mg monthly, PO</li></ul>	<ul style="list-style-type: none"><li>• RR of 0.64 in postmenopausal women compared to placebo</li></ul>	<ul style="list-style-type: none"><li>• Osteonecrosis of the jaw*</li></ul>
Zoledronate	<ul style="list-style-type: none"><li>• 5 mg annually, IV</li></ul>	<ul style="list-style-type: none"><li>• 7% increase in spine BMD</li><li>• RR of 0.23 in postmenopausal women compared to placebo</li></ul>	

## RANKL INHIBITORS

Denosumab	<ul style="list-style-type: none"><li>• 60 mg every 6 months, SQ</li></ul>	<ul style="list-style-type: none"><li>• 68% decrease in incidence of radiographic vertebral fractures</li><li>• 9.2% increase in lumbar spine BMD</li></ul>	<ul style="list-style-type: none"><li>• Fatigue</li><li>• Weakness</li><li>• Diarrhea</li><li>• Hypophosphatemia</li></ul>
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## HORMONES

Raloxifene (SERM)	<ul style="list-style-type: none"><li>• 60 mg daily, PO</li><li>• 120 mg daily, PO</li></ul>	<ul style="list-style-type: none"><li>• RR of 0.65 in postmenopausal women compared to placebo (60 mg)</li><li>• RR of 0.54 in postmenopausal women compared to placebo (120 mg)</li><li>• 2.6% increase in lumbar spine BMD (60 mg)</li></ul>	<ul style="list-style-type: none"><li>• Flu syndrome</li><li>• Vasodilation</li><li>• Endometrial cavity fluid</li><li>• Peripheral edema</li></ul>
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		<ul style="list-style-type: none"> <li>• 2.5% in lumbar spine BMD (120 mg)</li> </ul>	
Teriparatide (PTH)	<ul style="list-style-type: none"> <li>• 20 microg daily, SQ</li> <li>• 40 microg daily, SQ</li> </ul>	<ul style="list-style-type: none"> <li>• 65% decrease in fracture risk (20 microg)</li> <li>• 69% decrease in fracture risk (40 microg)</li> <li>• 9% increase in lumbar spine BMD (20 microg)</li> <li>• 13% increase in lumbar spine BMD (40 microg)</li> </ul>	<ul style="list-style-type: none"> <li>• Nausea</li> <li>• Headache</li> <li>• Dizziness</li> <li>• Leg cramps</li> </ul>
Calcitonin (TH)	<ul style="list-style-type: none"> <li>• 200 mg daily, IN</li> </ul>	<ul style="list-style-type: none"> <li>• 33% decrease in fracture risk</li> <li>• 1-1.5% increase in lumbar spine BMD</li> </ul>	<ul style="list-style-type: none"> <li>• Epistaxis</li> <li>• Rhinitis</li> <li>• Ulceration of nasal mucosa</li> <li>• Hypocalcemia</li> </ul>
<b>SUPPLEMENTATIONS</b>			
Vitamin D	<ul style="list-style-type: none"> <li>• 400 IU daily, PO</li> </ul>	<ul style="list-style-type: none"> <li>• 15% decrease in fracture risk</li> </ul>	
Calcium	<ul style="list-style-type: none"> <li>• 1,500 mg daily, PO</li> </ul>		-

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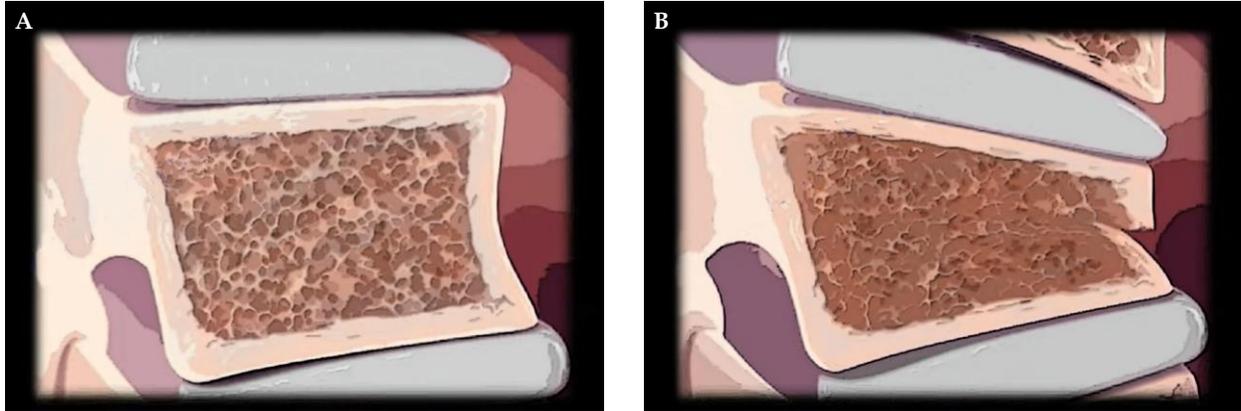
### Science Editor's Comments

It is best to add some figures or tables to make the topic clearer and more understandable. In addition, acronyms appearing for the first time should be marked with meaning, or a list of acronyms should be added to the manuscript.

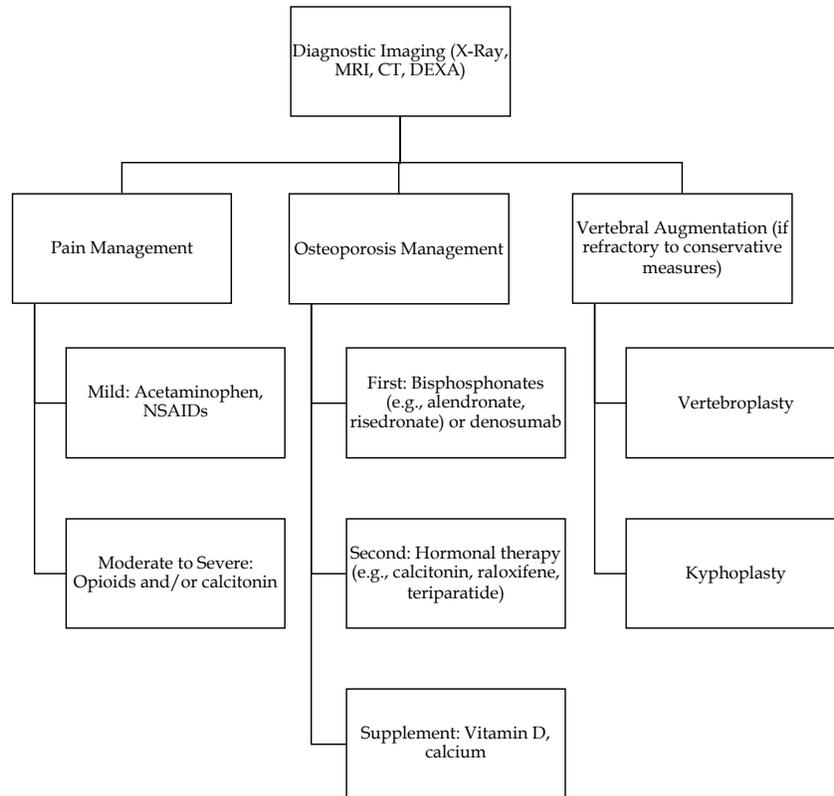
Language Quality: Grade C (A great deal of language polishing)

Scientific Quality: Grade C (Good)

**Author Response:** Thank you for these suggestions. We have included a figure of osteoporotic vertebra and a compression fracture were included on Page 5, Figure 1. A flowchart for diagnosis and treatment was included on Page 7, Figure 2. A table of abbreviations is included on Page 23, Table 1.



**Figure 1.** Osteoporotic vertebra before (A) and after (B) a compression fracture. Note the wedge shape of the vertebral body which can cause kyphotic deformity.



**Figure 2.** Treatment steps for osteoporotic vertebral compression fractures

**Table 1. List of Abbreviations**

Abbreviation	Definition
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QALY	Quality-adjusted life years

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CT	Computed tomography
DEXA	Dual-energy X-ray absorptiometry
BMD	Bone mineral density
SD	Standard deviation
AAN	American Academy of Neurology
PMMA	Polymethylmethacrylate
RANKL	Receptor activator of nuclear factor-kappa beta ligand
LLLT	Low-level laser therapy
TH	Thyroid hormone
SERM	Selective estrogen receptor modulators
PTH	Parathyroid hormone
mg	Milligrams
IU	International unit
PO	Orally
IV	Intravenous
SQ	Subcutaneous
IN	Intranasal
RR	Relative risk

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### **Company Editor-in-Chief's Comments**

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Orthopedics, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Please be sure to use Reference Citation Analysis (RCA) when revising the manuscript. RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. For details on the RCA, please visit the following web site:

<https://www.referencecitationanalysis.com/>. Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

**Author Response:** We thank the editor-in-chief for reviewing our manuscript and providing this insight.