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REVIEW

# Osteoporotic vertebral fractures: predictive factors for conservative treatment failure. A systematic review

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**Abstract**
*Purpose* To analyze clinical, radiographic and magnetic resonance findings that might predict risk of complications and conservative treatment failure of osteoporotic vertebral fractures.
*Methods* The authors conducted a systematic review of observational studies, collecting data on osteoporotic vertebral fracture and complications like vertebral collapse, kyphosis, pseudoarthrosis, and neurologic deficit. MeSH items such as 'spinal fracture/radiology,' 'spinal fracture/complications,' 'spinal fracture/diagnosis' were used. PRISMA statement criteria were applied, and the risk of bias was classified as low, medium, high, following the Newcastle–Ottawa Quality Assessment Scale (NOS).
*Results* Eleven cohort studies, either retrospective or prospective, met the eligibility criteria and were included in the review. Major risk factors that were statistically predictive of the following complications were as follows; (1) vertebral collapse: presence of intravertebral cleft, MR T1-WI 'total type fractures' and T2-WI 'hypointense-wide-type'. (2) Pseudoarthrosis (nonunion): middle-column damage, thoracolumbar vertebrae involvement, MR T2-WI confined high-intensity pattern and diffuse low intensity pattern. (3) Kyphotic deformity: thoracolumbar fracture and superior endplate fracture. (4) Neurologic impairment: a retropulsed bony fragment occupying more than 42% of the sagittal diameter of the spinal canal and a change of more than 15° in vertebral wedge angle on lateral dynamic radiography.
*Conclusions* Shape and level of the fracture were risk factors associated with the progression of collapse, pseudoarthrosis, kyphotic deformity and neurologic impairment. MRI findings were often related to the failure of conservative treatment. If prognosis can be predicted at the early fracture stage, more aggressive treatment options, rather than conservative ones, might be considered.

**Keywords** Osteoporotic vertebral compression fractures · Risk factors · Vertebral collapse · Pseudoarthrosis · Kyphotic deformity · Neurologic impairment

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## Introduction

Most osteoporotic vertebral fractures are treated conservatively with a bed rest period, pain control with analgesics, bracing, early rehabilitation and osteoporosis treatment with bisphosphonates [1]. This treatment usually leads to good results and the majority of vertebral fractures heal with excellent functional recovery, with few residual deformities and without pain. However, in some patients, the fracture healing is impaired with the onset of major complications such as pseudoarthrosis, final vertebral collapse, spinal deformity and spinal cord compression. Although these complications are rare, they are strongly related to poor prognosis, prolonged back pain, strong impairment of

daily living activities and reduced quality of life [2]. Moreover, very few epidemiologic data are available about their incidence.

Over the last years, the importance of investigating risk factors in association with these conditions has been emphasized. Thanks to technological progress, new imaging techniques and the increasing knowledge of pathologic mechanisms, authors were able to perform clinical studies with the aim of investigating radiographic or magnetic resonance findings that might be associated with and predict high risk of complications and conservative treatment failure.

Indeed, if prognosis can be predicted at the early fracture stage, more aggressive treatment options, rather than conservative one, might be considered aiming at avoiding complications and patients' sufferance.

The objective of this systematic review was to evaluate clinical and imaging findings that might suggest high risk of complications after the treatment of osteoporotic vertebral fractures and to quantify their ability to predict failure of the conservative treatment.

## Methods

### Criteria for the selection of studies

Retrospective and prospective observational studies were included in this review. Selected patients were adults (mean age > 65 years) with osteoporotic vertebral fractures, confirmed by clinical and radiologic diagnosis and exclusively treated conservatively.

Primary outcomes analyzed were complications of osteoporotic vertebral fractures: (1) vertebral collapse and its progression; (2) pseudoarthrosis (nonunion); (3) kyphotic deformity and (4) neurologic deficits. The onset of one or more of these complications was considered sufficient to determine failure of the conservative treatment.

### Database search

Literature research was performed, in accordance with the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) checklist and algorithm [3, 4] from 2003 to 2016 on PubMed, Cochrane database, Google Web search engine and Google Scholar. The keywords used in the research were 'vertebral compression fractures,' 'osteoporotic vertebral fracture,' 'vertebral collapse,' 'intravertebral cleft,' 'nonunion,' 'pseudoarthrosis,' 'vertebral collapse,' 'neurologic deficit'. MeSH items such as 'spinal fractures/epidemiology,' 'spinal fracture/radiology,' 'spinal fracture/complications,' 'spinal fracture/diagnosis' were also used. The search included publications in English language only. The authors limited the research to observational studies as they best evaluate associations between diseases and risk factors, while randomized controlled trials are not always indicated or ethical to conduct. All the articles considered significant were collected and their bibliography further scanned, in order to retrieve additional material for the review.

### Eligibility criteria and study selection

Studies included in the analysis had to meet the following inclusion criteria: (1) participants had to be patients with osteoporotic vertebral fracture(s); (2) patients must have received conservative treatment only; (3) studies had to analyze at least one of the primary outcomes.

Studies that included patients with other pathological fractures, such as those due to chronic steroid administration, infective disease, metastasis or myeloma, were excluded. Other exclusion criteria were: patients suffering from spinal stenosis, previous surgery at the vertebral body and complications subsequent to vertebroplasty or kyphoplasty.

The authors performed an initial search of all databases, finding citations that could be included in the review. Firstly, titles and abstracts were screened and checked. If screening titles and abstracts was not enough to decide whether to accept or reject the study, the full text of the citation was retrieved for further evaluation. Afterward, the full texts of potential eligible articles were assessed for inclusion.

### Data collection

Data were collected following a pilot tested data extraction form including title, authors, year of publication, size of the sample, gender ratio, number of vertebrae involved, duration of the follow-up and possible financial interests. As for the outcomes studied, pseudoarthrosis was defined by a recognizable intravertebral cleft on plain radiograph images or change of vertebral height between standing and supine positions on lateral views on a radiograph obtained after 6 months. Vertebral collapse and vertebral collapse progression were calculated using different criteria across the various studies. For a better understanding, the criteria used by each study are mentioned in the Result section. Kyphotic deformity was measured from superior to inferior endplate of the affected vertebra on lateral radiograph, using Cobb's angle method. Kyphosis progression was obtained by subtracting the angles calculated on initial examination from the ones calculated during the follow-up examination. Neurologic deficits were legs hyperreflexia/hyporeflexia, sensory deficit and sphincter dysfunction. If no data were available in the article's text or tables, graphs were consulted.

### Risk of bias assessment

The methodological quality of the studies which met the inclusion criteria was evaluated according to the Newcastle–Ottawa Quality Assessment Scale (NOS), as recommended by the Cochrane Collaboration for assessing the quality of non-randomized studies [5]. The NOS is a system based on a score (maximum 9 points) set in three different categories: selection of study groups, comparability of cases, controls and their ascertainment of the outcome/exposure on cases and controls. Studies were classified as high risk of bias (1–3 points), medium risk of bias (4–5 points), or low risk of bias (6–9 points).

## Results

### Studies characteristics

The initial research identified 319 potentially eligible results in the used database, plus 3 records among the bibliography of the found publications. Among these, 59 records were eliminated as they were duplicates. Through the examination of titles and abstracts, 248 articles were excluded because they did not meet the inclusion criteria, while one of them was excluded because written in Korean language. After the screening phase, a total of 14 potentially suitable studies were selected. Among these 14 publications, three articles identified as clinical reports were excluded [6–8]. Therefore, a total of 11 [9–19] studies met the setting criteria and were finally included in the systematic review (Fig. 1).

All studies were published in English language and had a cohort design: six of them were retrospective cohort studies, while four were prospective ones. Table 1 describes the

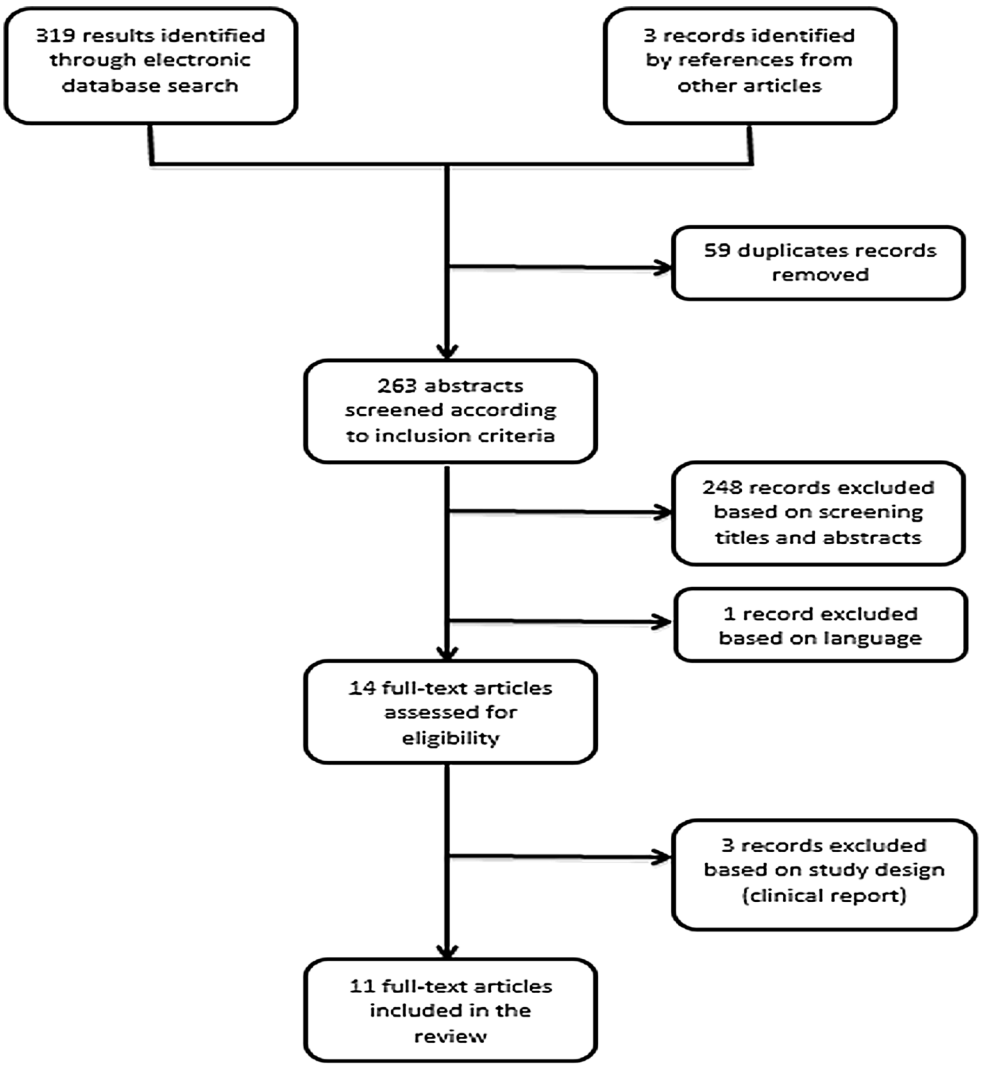


**Fig. 1** The PRISMA Flowchart of study selection process

**Table 1** Characteristics of the included studies

| References | Country | Age, mean ($\mu$) | Sample size | F–M | Fractured Vertebrae | Follow-up | Newcastle–Ottawa Scale Score | Outcome(s) |
|---|---|---|---|---|---|---|---|---|
| Sugita et al. [9] | Kyoto, Japan | $\mu$ :75.0 years (range 61–91 years) | 73 | 58 F–15 M | 84 | 12–62 months ($\mu$: 23.4 months) | 6 | Vertebral Collapse, pseudoarthrosis |
| Yu et al. [10] | Taiwan, China | $\mu$: 73.5 years (range 50–90 years) | 112 | 82 F–30 M | 121 | 12 months | 7 | Vertebral Collapse |
| Kanchiku et al. [11] | Ube, Japan | $\mu$: 79 years (range 68–93 years) | 14 | 11 F–3 M | 15 | 3–7 months ($\mu$: 5 months) | 6 | Vertebral Collapse Progression |
| Omi et al. [12] | Akita, Japan | $\mu$: 77.5 years (range 60–92 years) | 56 | 48 F–8 M | 63 | 6 months | 7 | Pseudoarthrosis, Vertebral collapse |
| Ha et Kim [13] | Seoul, South Corea | Group Ih $\mu$: 73.2 ± 6.4<br>Group IIh $\mu$: 69.1 ± 8.9<br>Group Ik $\mu$: 73.4 ± 6.4<br>Group IIk $\mu$: 69.1 ± 86<br>Group Ii $\mu$: 71.3 ± 5.8<br>Group IIi $\mu$: 69.8 ± 9.0 | 75 | 57 F–18 M | 75 | 6 months | 8 | Vertebral Collapse progression |
| Kanchiku et al. [14] | Yamaguchi, Japan | $\mu$: 79 years | 109 | 88 F–21 M | 129 | 6 months | 7 | Vertebral Collapse, Pseudoarthrosis |
| Wu et al. [15] | Taiwan, China | $\mu$: 70.2 years | 152 | 139 F–13 M | 256 | 1–6 months ($\mu$: 2.7 months) | 7 | Pseudoarthrosis |
| Tsujio et al. [16] | Osaka, Japan | $\mu$: 75.9 years | 350 | 296 F–54 M | 363 | 6 months | 9 | Pseudoarthrosis |
| Patil et Nene [17] | Mumbai, India | $\mu$: 64 years (range 45–85 years) | 64 | 33 F–31 M | 64 | 6–66 months ($\mu$: 27.5 months) | 7 | Kyphotic deformity |
| Hoshino et al. [18] | Osaka, Japan | $\mu$: 74 years (range 56–87 years). | 45 | 35 F–10 M | 45 | 2–36 months ($\mu$: 6.9 months) | 6 | Neurologic Impairment |
| Goldstein et al. [19] | Zerifin, Israel | $\mu$: 68.9 years (range 50–93 years) | 153 | 102 F–5 1 M | 153 | 3–93 months ($\mu$: 15 months) | 7 | Vertebral height kyphotic angle |

characteristics of the included studies. Two were performed in China, six in Japan and only one, respectively, in India, South Korea and Israel. No studies from USA or Europe were found. As for the primary outcomes, two studies analyzed only pseudoarthrosis, one investigated vertebral collapse, other three of them focused on the progression of vertebral collapse, one dealt with vertebral kyphosis, another one concentrated only on neurologic impairment. Moreover, three articles analyzed both vertebral collapse and pseudoarthrosis. Collectively, the studies included 1203 participants: 949 women and 254 men, with F:M ratio of 3.73:1 and 1368 fractured vertebrae, for multiple vertebral fractures in a single patient were frequent. Sample sizes ranged from 14 to 350 participants.

## Specific outcomes results

### *Vertebral collapse*

Seven studies (592 patients and 640 fractured vertebrae) managed to analyze the predictors of late vertebral collapse in osteoporotic vertebral fracture or its progression during the follow-up.

Sugita et al. [9] introduced a new radiologic classification of early osteoporotic vertebral fracture, according to which fractures are classified in five different types, as shown in Fig. 2. In this study, vertebral collapse was defined by an anterior or central height loss of more than 50% of the posterior height of the vertebra at the follow-up examination. Incidence of vertebral collapse was evaluated in every fracture type resulting in a good prognosis group, including concave and dented type, and a poor prognosis group, including swelled-front, bow-shaped and projecting type.

Yu et al. [10] studied a cohort of patients with vertebral osteonecrosis, defined as a non-enhanced area on MR enhanced T1-weighted images with collections of intravertebral fluid, air or both. The height of the fractured vertebrae affected by osteonecrosis was measured at the maximum point of collapse, then compared with the average height of normal vertebrae in the same spinal region (thoracic or lumbar) and the height loss was expressed as a percentage. The authors found that loss of more than 50% of vertebral height was more frequent in patients with intravertebral air only or mixed with fluid, rather than those with intravertebral fluid only. Moreover, it was possible to observe that vertebral compression fractures adjacent to the affected vertebrae were more common in affected vertebrae with intravertebral air only, rather than with intravertebral fluid only.

Kanchiku et al. [11] performed a study to investigate the bone marrow blood perfusion in fractured vertebrae using dynamic magnetic resonance imaging. The vertebral collapse was obtained by subtracting the height of the fractured vertebra at the point of maximum collapse from the average vertebral height of the vertebrae above and below the injured one and dividing the value by the average height of normal vertebrae. The progression of vertebral collapse was calculated by subtracting the collapse on initial examination from the follow-up examination one and expressed as a percentage. The authors underlined the statistically significant association between the percentage of MR non-contrast area—obtained dividing the non-contrast area by the total area of the vertebra—and the degree of vertebral collapse progression. Furthermore, the authors demonstrated that fractures with posterior wall involved showed higher non-contrast area percentage and vertebral collapse progression, compared to those with endplate or anterior wall damage.

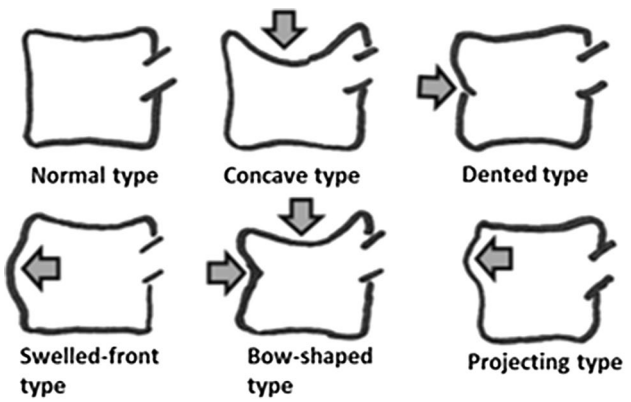


**Fig. 2** Sugita et al. [9] new radiologic classification of early osteoporotic vertebral fracture, where fractures are classified in five different types: (1) Concave type: endplate is falling in and the anterior wall is intact. (2) Dented type: center of the anterior wall of the vertebral body is dented. (3) Swelled-front type: the majority of the anterior wall of the vertebral body is swollen. (4) Bow-shaped type: anterior wall is pinched in and endplate is falling in, resembling the bow of a ship. (5) Projecting type: < 50% of the anterior wall of the vertebral body is projecting and a small bulging is present

Omi et al. [12] assessed the usefulness of short time inversion-recovery (STIR) in MRI to predict the progression of vertebral collapse in osteoporotic vertebral fractures. The vertebral collapse was calculated by dividing the anterior height by the average vertebral height of the vertebrae above and below the injured vertebrae. The vertebral collapse progression was calculated by subtracting the collapse on initial examination from the follow-up examination one, dividing it by the collapse at on initial examination and expressing it as a percentage. They found a significant difference in affected vertebrae with linear black signal area—which was a linear black signal occupying more than half the length of the vertebral body—that showed higher vertebral collapse progression, when compared to those with nonlinear black signal area.

Ha and Kim [13] proposed three criteria to define progressive vertebral collapse, which were height loss > 15%, kyphotic angle > 10°, and presence of intravertebral cleft sign during the follow-up. The vertebral collapse was obtained by subtracting the height of the fractured vertebra at the point of maximum collapse from the average vertebral height of the vertebrae above and below the injured one and dividing the value by the average height of normal vertebrae. The authors noticed that thoracolumbar fracture, mid-column damage and posterior wall damage were important risk factors for progressive collapse.

In their study, Kanchiku et al. [14] recently proposed a new magnetic resonance imaging-based classification, categorizing fractures into six types, according to T1-weighted image pattern, shown in Fig. 3. In this study, the vertebral collapse was obtained by dividing the height at the point of maximum compression by the average vertebral height of the vertebrae above and below the injured vertebrae. Following these principles, fractures defined as total type showed higher vertebral collapse, compared to other fracture types. The authors also applied the T2-weighted MR images classification proposed by Tsujio et al. [16], which is based on signal intensity changes: confined high intensity (or hyperintense limited type), diffuse high intensity (or hyperintense wide type), confined low intensity (or hypointense limited type), diffuse low

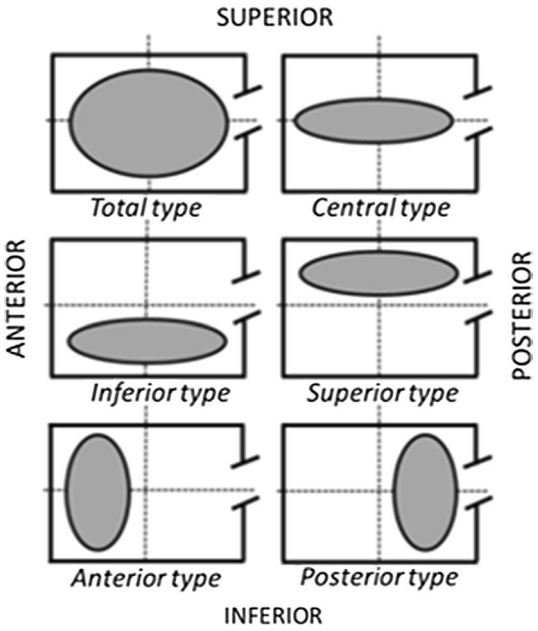


**Fig. 3** Kanchiku et al. [14] magnetic resonance imaging-based classification: fractures are categorized into six types, according to T1-weighted image pattern. The vertebral body is divided in four sections. Total vertebral body type is defined when the signal occupies more than half the area of each section in 3 of the 4 sections. Central type is defined by observing the signal variation limited to the center and not exceeding more than half the area. Inferior/superior types are defined by the signal occupying more than half of the two inferior or two superior sections, respectively. Similarly, anterior/posterior types are defined by the signal occupying more than half of the two anterior or two posterior sections, respectively

intensity (or hypointense wide type) and normal intensity. According to their findings, the frequency of vertebral collapse was greater for hypointense wide-type fractures than for hyperintense wide-type. Moreover, the authors subclassified total type fractures—which belongs to the T1-weighted classification—according to T2-weighted classification, observing a significant lower incidence of vertebral collapse in total hyperintense-wide-type fractures (Table 2).

Goldstein et al. [19] based their work on the AO classification. They found a correlation between type A4 vertebral fracture and the tendency to collapse given by the kyphotic angles difference and the by final height loss. Intravertebral cleft (IVC) was significantly correlated to collapse of more than 50% (IVC was significantly more common in A2- and A4-type fractures than in A1- and A3-type fractures). They reported a significant correlation also between initial height loss and final height loss. While they showed a significant correlation between patient age and final height loss, they sustained that the pathophysiological process of fractured vertebra collapse is not related to the patient sex.

*Pseudoarthrosis (nonunion)*

Five studies (740 patients with 895 vertebral fractures) investigated pseudoarthrosis as a complication of conservative treatment of osteoporotic vertebral fracture.

Wu et al. [15] noticed that fractures involving anterior column—formed by the body and the anterior wall of the vertebra—and middle column—formed by the posterior longitudinal ligament, the posterior wall of vertebral body and the intervertebral disk—had greater risk of pseudoarthrosis occurrence, than fractures involving only anterior column.

In their study, Sugita et al. [9] found also that vacuum cleft, which suggests nonunion, was more likely to appear in thoracolumbar fractures and in swelled-front, bow-shaped and projecting types.

Tsujio et al. [16] analyzed a cohort of patients and found that thoracolumbar fracture, middle-column damage and confined high intensity and diffuse low intensity area in the fractured vertebrae on T2-weighted MR images were significant risk factors for nonunion of OVFs with high ORs.

Omi et al. [12] demonstrated also that non-homogenous high signal change was a strong risk factor for nonunion, compared to homogenous high signal change obtained by STIR in MRI. Significant increase in nonunion prevalence was also found in those fractured vertebrae showing a linear black signal area, compared to those which showed a nonlinear one.

Moreover, applying the T2-weighted MR images classification proposed by Tsujio et al. [16], Kanchiku et al. [14] observed that total type showed higher incidence of pseudoarthrosis, when compared to other fracture types. Hypointense-wide-type, total hyperintense-limited and total hypointense-wide-type fractures were strongly associated with pseudoarthrosis (Table 3).

*Kyphotic deformity*

Two of the selected studies (217 patients and 217 fractured vertebrae) examined the predictors of segmental kyphotic deformity of the spine in osteoporotic vertebral fractures (Table 4). Patil et al. [17] found that thoracolumbar junction and end-plate fractures were statistically significant risk factors for the onset of segmental kyphotic deformity > 30° at final follow-up ($\mu$: 27.5 months), measured by Cobb angle method. No difference between the two groups was found considering anterior cortical wall fracture and associated adjacent level fracture.

Goldstein et al. [19] found a strong correlation between initial kyphotic angle e final kyphotic angles. Final kyphotic angle was also correlated with height loss difference (immediately after fracture and after treatment) and level of the fracture.

**Table 2** Predictors of vertebral collapse

| Predictors of vertebral collapse | Study | Diagnostic technique | Association with outcome | Effect in measure |
|---|---|---|---|---|
| Swelled-front, bow-shaped and projecting type fracture | Sugita et al. [9] | Rx | Significant incidence of collapse | ($P < 0.05$) |
| Osteonecrosis: Intravertebral air Osteonecrosis: Intravertebral air with fluid | Yu et al. [10] | MR | More frequent compared to intravertebral fluid only<br>More frequent compared to intravertebral fluid only | 89.6 vs 27.7%, ($P < 0.05$)<br>73.0 vs 27.7%, ($P < 0.05$) |
| Collapses in adjacent vertebrae | | | Frequent in affected vertebrae with intravertebral air only | 25.0 vs 8.5%, ($P < 0.05$) |
| Non-contrast area rate | Kanchiku et al. [11] | Dynamic MR | Correlation with progression of vertebral collapse exists | Spearman $r$ 0.97, ($P < 0.001$) |
| Posterior wall damage | | Rx, MR | Higher collapse compared to endplate/anterior wall fracture | ($P < 0.01$) |
| Linear black signal | Omi et al. [12] | MR (STIR) | Higher collapse progression than nonlinear black signal area | ($35 \pm 22$ vs $23 \pm 22\%$) ($P = 0.003$) |
| Posterior wall damage | Ha et Kim [13] | Rx, Mr | Increase in height loss $\geq 15\%$<br>Increase in kyphotic angle $\geq 10°$ | OR 62.9; 95% CI 7.4–536.1; ($P < 0.001$)<br>OR 9.4; 95% CI 5.1–35.9; ($P < 0.001$) |
| Middle-column damage | | | Increase in height loss $\geq 15\%$ | OR 16.3; 95% CI 1.1–225.4; ($P < 0.05$) |
| Thoracolumbar fracture | | | Presence of intravertebral cleft | OR 3.2; 95% CI 0.6–17.6; ($P < 0.005$) |
| T1WI Total type fracture | Kanchiku et al. [14] | MR | Higher collapse rate compared to other fracture types | $45 \pm 21$ vs $31 \pm 13\%$ ($P < 0.01$) |
| T2WI Hypointense-wide-type | | | Significant difference compared to hyperintense-wide-type fractures | $63 \pm 14$ vs $31 \pm 12\%$ ($P < 0.01$) |
| Hypointense limited, wide and hyperintense limited total type | | | Greater collapse than hyperintense-wide-type | $51 \pm 15\%$; $63 \pm 14\%$; $72 \pm 10$ vs $29 \pm 12\%$ ($P < 0.01$) |
| Type of fracture according to the AO classification.<br>Age | Goldstein et al. [19] | Rx, CT | Height loss difference and kyphotic angle difference were significantly according to the type of fracture<br>Significant correlation between patient age and final height loss | Height loss difference was 18.1% in A1, 27.1% in A2, 24.2% in A3, 25.7% in A4<br>vertebral collapse difference > 50%: 17.9% for A1, 62% for A2, 51.9% for A3, 88.6% for A4. $P < 0.05$ |
| IVC | | | IVC more common in A2 and A4 fractures type compared to A1 e A3<br>IVC significantly correlated to collapse of more than 50% | Percentage of IVC per type: A1 12.5%, A2 25%, A3 9.3%, A4 37.1% ($P = 0.004$)<br>IVC: in 28.4% of fractures with final collapse > 50% and in 7.6% of fractures with final collapse < 50% ($P = 0.001$) |

AO classification for vertebral fracture: A1 A2 A3 A4 type fracture

*Rx* radiography, *MR* magnetic resonance, *STIR* short time inversion-recovery, *CT* computerized tomography, *IVC* intravertebral cleft

**Table 3** Predictors of pseudoarthrosis

| Predictors of pseudoarthrosis | Study | Diagnostic technique | Association with outcome | Effect in measure |
|---|---|---|---|---|
| Anterior and middle-column damage | Wu et al. [15] | Rx | Higher incidence of nonunion than fracture with only anterior wall damage | ($P < 0.05$) |
| Swelled-front, bow-shaped and projecting type fracture | Sugita et al. [9] | Rx | Significant incidence of nonunion if compared to good prognosis fracture group | ($P < 0.05$) |
| Thoracolumbar fracture | Tsujio et al. [16] | Rx | Nonunion risk moderately increased | OR 5.1, 95% CI = 1.4–18.1, ($P < 0.01$) |
| Middle-column damage | | MR | Nonunion risk moderately increased | OR 3.5; 95% CI 1.4–8.4, ($P < 0.006$) |
| Confined high-intensity MR pattern | | MR | Nonunion risk strongly increased | OR 31.7, 95% CI 12.4–81.1, ($P < 0.001$) |
| Diffuse low intensity MR pattern | | MR | Nonunion risk significantly increased | OR 9.7, 95% CI 4.2–22.2, ($P < 0.001$) |
| Linear black signal<br>Non-homogenous high signal change | Omi et al. [12] | MR (STIR) | Higher nonunion incidence compared to nonlinear black signal area<br>Higher nonunion incidence compared to homogenous high signal change | (42 vs 10%) ($P = 0.005$)<br>(30 vs 0%) ($P = 0.009$) |
| T1WI Total type fracture | Kanchiku et al. [14] | MR | Higher pseudoarthrosis conversion rate than other fracture types | (27 vs 0%) ($P < 0.01$) |
| T2WI Hypointense-wide-type | | | Significant difference in nonunion incidence than other MR patterns | (43.8 vs 14.2%) ($P < 0.01$) |
| Hypointense-wide total type | | | Higher nonunion incidence than other types | (68.8 vs 32.10%) ($P < 0.01$) |
| Hyperintense-limited total type | | | Higher nonunion incidence than other types | (75 vs 30.1%) ($P < 0.01$) |

*Rx* radiography, *MR* magnetic resonance, *STIR* short time inversion-recovery

**Table 4** Predictors of spinal deformities

| Predictors of spinal deformities | Study | Diagnostic technique | Association with outcome | Effect in measure |
|---|---|---|---|---|
| Thoracolumbar fracture | Patil e Nene [17] | Rx | High incidence of kyphotic deformity (> 30°) compared to lumbar and thoracic fractures | (82.5 vs 77.7% Thoracic) (82.5 vs 33.3% Lumbar) ($P < 0.002$) |
| Superior endplate fracture | | | High incidence of kyphotic deformity (> 30°) compared to those without superior endplate fracture | (75.92 vs 24.08%) ($P = 0.00$) |
| AO type A2 and A4 | Goldstein et al. [19] | Rx, CT | High incidence of kyphotic deformity compared to A1 and A3 type | Kyphotic angle difference: 6.59° in A1, 9.88° in A2, 10.19° in A3, 11.43° in A4 |

AO classification for vertebral fracture: A1 A2 A3 A4 type fracture

*Rx* radiography, *CT* computerized tomography, *IVC* intravertebral cleft

*Neurologic impairment*

One study [18] (45 patients and 45 fractured vertebrae) analyzed factors affecting the onset and the severity of neurologic deficits. The authors retrospectively reviewed a cohort of patients with insufficient bone union following osteoporotic vertebral fracture. They found that occupation by a bony fragment of more than 42% of sagittal diameter of the spinal canal on mid-sagittal MR images and a change of more than 15° in vertebral wedge angle on lateral dynamic radiography

were factors that significantly contributed to the degree of neurologic deficit (Table 5).

## Discussion

Osteoporosis has been defined as a systemic syndrome involving primarily the skeleton, characterized by low bone mass and microarchitectural degeneration of bone tissue, leading to bone fragility and increasing fracture risk [20]. Vertebral fractures are the most common fractures in osteoporotic patients, but epidemiology is poorly established, since an important quota of these fractures is not detected in standard clinical practice. In the USA and Europe, the incidence of vertebral fractures in people aged 75–79 years is twice as high in women than in men (29.3 vs 13.6/1000 person/year) [21, 22]. Osteoporotic fractures are strongly related to disability, quality of life decrease and higher risk of mortality due to cardiopulmonary complications [23, 24]. This surely represents a heavy social and medical care burden, since cost for hospitalization, consequent rehabilitation and domiciliary assistance cost must be taken into account.

As Lee et al. [24] stated, osteoporotic fractures will probably remain prevalent and the only solution to the problem is to prevent the excessive occurrence and avoid complications. If avoiding complications is important, a key point is to determine the prognosis of every fracture and evaluate the risk factors that may lead to conservative treatment failure. Therefore, this systematic review of observational studies focused on the major complications that might arise after the conservative treatment of osteoporotic vertebral fracture and the relative risk factors that may have facilitated their occurrence.

According to Denis et al. [25] three column theory, middle column is formed by posterior longitudinal ligament, posterior wall of vertebral body and intervertebral disk. These structures are the key of spinal stability: if damaged, in addition to anterior or posterior column fractures, a greater risk of pseudoarthrosis and progression of vertebral collapse may arise. Indeed, Sugita's swelled-front type, bow-shaped and projecting type fractures collapsed easily, since these types may not only stand for a damage to anterior column, but also to middle one. Besides, projecting and swelled-front types might represent also a vascular ischemic damage to arteries that feed the vertebral body, thus leading to necrosis and edema which form the bulging area present on the anterior wall [9].

The thoracolumbar junction is the site which bears the greatest dynamic load in the entire spine [21], therefore, is much more prone to fracture nonunion [26]. Several studies [9, 27] proved that thoracolumbar fractures are related to the presence of intravertebral vacuum cleft (IVC), which represents a radiographic sign of avascular necrosis of the vertebral body (also known as Kümmell's sign) and a relevant clinical sign predictive for dynamic fracture mobility [28]. Both the presence of IVC and dynamic instability are clinically important, as these elements lead to dynamic stress and cumulative damage, which cause more vascular compromise and bone necrosis. In time, the progression of the damage could ease the onset of pseudoarthrosis and simultaneously lead to vertebral collapse [29, 30]. Vertebral osteonecrosis might also occur with a fluid sign hypointense on T1-weighted images and hyperintense on T2-weighted images [31, 32]. Yu et al. [10] observed that patients with intravertebral fluid developed intravertebral air during follow-up, while patients with intravertebral air did not show any intravertebral fluid. The authors speculated that fluid sign might represent an early stage, while the presence of air represents the evolution of the disease: indeed, vertebral collapse was significantly severe when air was noticed.

A solid diagnostic pillar in osteoporotic vertebral fractures is represented by MR imaging, which allows to detect bleeding, edema and medulla compression by retropulsed bony fragment. MRI may also detect fractures which are not evident on standard radiography and CT scan [33, 34]. Several studies attempted to clarify whether MRI pattern could estimate the prognosis of osteoporotic vertebral fractures: Kanchiku et al. [14] demonstrated with their new classification [35] that T1WI 'total type' fracture is related both to high incidence of vertebral collapse and pseudoarthrosis,

**Table 5** Predictors of neurologic impairment

| Predictors of neurologic impairment | Study | Diagnostic technique | Association with outcome | Effect in measure |
|---|---|---|---|---|
| Spinal canal occupation by bony fragments | Hoshino et al. [18] | Rx, MR | Significant risk if more than 42% of sagittal diameter is occupied | OR 9.23, 95% CI 1.15–74.1, ($P = 0.037$) |
| Angular instability (assessed by dynamic radiography) | | | Significant risk if vertebral wedge angle change is more than 15° | OR 9.24, 95% CI 1.49–57.2, ($P = 0.017$) |

*Rx* radiography, *MR* magnetic resonance

since the damage involved the vertebral body widely, resulting in an important instability. Moreover, it is thought that T2WI hyperintense-wide-type fractures represent an inflammatory edematous reaction with restrained trabecular destruction, while hypointense-wide-type and hyperintense-limited-type fractures are related to hematoma, fluid accumulation and spread damage, leading to a poor prognosis [36].

STIR MR sequences are often used in routine medical practice [37] and might be a useful tool to predict vertebral fracture prognosis in an early stage. Homogenous high signal change is thought to be related to less trabecular damage and bone edema, while non-homogenous high signal change suggests a widespread damage, easing the onset of fracture nonunion. As well, linear black area underlines an extensive trabecular damage with compressed cancellous bone, followed by early osteonecrosis.

As for kyphotic deformity, we found involvement of thoracolumbar junction to be a strong risk factor, since these vertebrae bears a great static and dynamic load in form of compressive forces, which weight mainly on the anterior part of the vertebral body, leading to progressive vertebral collapse. Superior endplate is often involved in osteoporotic vertebral fracture, due to the unique structure and different distribution of trabecular bone across the vertebral body [38, 39]. In addition to bending forces, disk-vertebral junction instability is responsible for kyphotic deformity increase.

As for neurologic deficits, both nonunion [40, 41] and presence of IVC [42] were reported to be risk factors, whose manifested few months after the fracture. Baba et al. [7] concluded in their report that the dynamic instability, with subsequent hypermobility at the fractured level, leads to gradual retropulsion of bony fragments into the spinal canal, which causes neurologic impairment. Hoshino et al. [18] confirmed this hypothesis in their study, since was found that angular instability and occupation of spinal canal were also related to the grade of severity of neurologic deficits.

This systematic review has limitation. First, the population in the studies were not always equivalent, as Kanchiku et al. [11] for example included a small number of patients with osteoporotic vertebral fractures which showed vertebral osteonecrosis, while the others included only patients with osteoporotic vertebral fractures. However, the majority of the studies included more than 50 patients and 50 fractured vertebrae with similar characteristics; therefore, we think that the population across the different studies can be compared in order to reach meaningful conclusion. Second, most of the studies gathered in the review had a 6-month follow-up period. We think that 6 months represent the minimum follow-up to achieve in the studies performed on the complications of osteoporotic vertebral fractures, as shorter period may not be sufficient to notice the onset of some complications such as pseudoarthrosis. On the other hand, the risk factors of failure in the studies with short follow-up (6 months) did not vary from those studies with longer follow-up (> 6 months). Consequently, studies with follow-up period equal or longer than 6 months are recommended to avoid biases and identify complications with late onset. The main limitation of this review was that some studies used different criteria to define vertebral collapse and the progression of vertebral collapse. This fact might make the comparison between the results of the various studies more difficult. Therefore, we suggest the authors to apply the same criteria or definition of vertebral collapse and vertebral collapse progression in the future studies methods, in order to make easier the comparison across the studies. Moreover, in this review, the effect of the pharmacological therapy has not discussed. For instance, Teriparatide use has been recently suggested for the treatment of severe osteoporosis due to its stimulation of bone formation and potential fracture healing and several authors reported positive effects on vertebral fracture [43–45].

To the best of our knowledge, this is the first systematic review that investigates the predictive factors associated with onset of major complications in the osteoporotic vertebral fractures. The clinical impact of this study is that the assessment of the presence of these factors may lead to different strategies: for example, kyphoplasty or vertebroplasty—rather than conservative treatment—might represent the alternative early treatments in the poor prognosis osteoporotic vertebral fracture.

The vertebroplasty and the kyphoplasty represent minimally invasive treatment for vertebral fractures, as they need only a local anesthesia, very short time of hospitalization and they are performed with a percutaneous access. Complications are rare and include temporary increase of pain, infection, cement leakage and pulmonary embolism. On the other hand, delaying the minimally invasive interventions may lead to the worsening of the vertebral fracture with thoracolumbar hyperkyphosis, persistent pain and neurologic impairment. This situation might not be solved by minimally invasive treatment and may require the invasive surgical treatment of spinal stabilization with longer period of hospitalization and greater complications, such as infection, hemorrhage and persistent pain.

## Conclusions

This review evidenced as the shape, the damage of middle column, the involvement of thoracolumbar junction and specific MRI and STIR findings can be predictors both of vertebral collapse and pseudoarthrosis. Posterior wall damage, presence of intravertebral air and dynamic MRI findings are additional risk factors for vertebral collapse. The site and the shape of the fracture are associated with segmental kyphosis,

while the onset of neurologic impairment is mostly related to retropulsion of bony fragments. Non-conservative treatment must be taken in consideration in the presence of one or more the discussed factors.

**Compliance with ethical standards**

**Conflict of interest** The work has not been published before in any language, is not being considered for publication elsewhere, and has been read and approved by all authors. Each author contributed significantly to one or more aspects of the study. No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article. There are no conflicts of interest around this study. The authors have full control of all primary data and agree to allow the journal to review their data if requested.

## References


1. Longo UG, Loppini M, Denaro L, Maffulli N, Denaro V (2012) Osteoporotic vertebral fractures: current concepts of conservative care. Br Med Bull 102:171–189
2. Ettinger B, Black DM, Nevitt MC et al (1992) Contribution of vertebral deformities to chronic back pain and disability. The Study of Osteoporotic Fractures Research Group. J Bone Miner Res 7(4):449–456
3. Liberati A, Altman DG, Tetzlaff J et al (2009) The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ 339:b2700
4. Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group (2009) Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med 151(4):264–269
5. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M et al. (2009) The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. http://www.ohri.ca/programs/clinical_epidemiology/oxford.html. Accessed 21 Apr 2016
6. Ito Y, Hasegawa Y, Toda K, Nakahara S (2002) Pathogenesis and diagnosis of delayed vertebral collapse resulting from osteoporotic spinal fracture. Spine J 2(2):101–106
7. Baba H, Maezawa Y, Kamitani K et al (1995) Osteoporotic vertebral collapse with late neurological complications. Paraplegia 33(5):281–289
8. Picazo DR, Villaescusa JR, Martínez EP, Pérez FD (2014) Late collapse osteoporotic vertebral fracture in an elderly patient with neurological compromise. Eur Spine J 23(12):2696–2702
9. Sugita M, Watanabe N, Mikami Y, Hase H, Kubo T (2005) Classification of vertebral compression fractures in the osteoporotic spine. J Spinal Disord Tech 18(4):376–381
10. Yu CW, Hsu CY, Shih TT, Chen BB, Fu CJ (2007) Vertebral osteonecrosis: MR imaging findings and related changes on adjacent levels. AJNR Am J Neuroradiol 28(1):42–47
11. Kanchiku T, Taguchi T, Toyoda K, Fujii K, Kawai S (2003) Dynamic contrast-enhanced magnetic resonance imaging of osteoporotic vertebral fracture. Spine (Phila Pa 1976) 28(22):2522–2526
12. Omi H, Yokoyama T, Ono A, Numasawa T, Wada K, Fujisawa Y (2014) Can MRI predict subsequent pseudarthrosis resulting from osteoporotic thoracolumbar vertebral fractures? Eur Spine J 23(12):2705–2710
13. Ha KY, Kim YH (2013) Risk factors affecting progressive collapse of acute osteoporotic spinal fractures. Osteoporos Int 24(4):1207–1213
14. Kanchiku T, Imajo Y, Suzuki H, Yoshida Y, Taguchi T (2014) Usefulness of an early MRI-based classification system for predicting vertebral collapse and pseudoarthrosis after osteoporotic vertebral fractures. J Spinal Disord Tech 27(2):E61–E65
15. Wu CT, Lee SC, Lee ST, Chen JF (2006) Classification of symptomatic osteoporotic compression fractures of the thoracic and lumbar Spine. J Clin Neurosci 13(1):31–38
16. Tsujio T, Nakamura H, Terai H, Hosino M et al (2011) Characteristic radiographic or magnetic resonance images of fresh osteoporotic vertebral fractures predicting potential risk for nonunion: a prospective multicenter study. Spine (Phila Pa 1976) 36(15):1229–1235
17. Patil S, Nene AM (2014) Predictors of kyphotic deformity in osteoporotic vertebral compression fractures: a radiological study. Eur Spine J 23(12):2737–2742
18. Hoshino M, Nakamura H, Terai H et al (2009) Factors affecting neurological deficits and intractable back pain in patients with insufficient bone union following osteoporotic vertebral fracture. Eur Spine J 18(9):1279–1286
19. Goldstein S, Smorgick Y, Mirovsky Y et al (2016) Clinical and radiological factors affecting progressive collapse of acute osteoporotic compression spinal fractures. J Clin Neurosci 31:122–126
20. No authors listed (1991) Consensus development conference: prophylaxis and treatment of osteoporosis. Am J Med 90(1):107–110
21. Cooper C, Atkinson EJ, O'Fallon WM, Melton LJ 3rd (1992) Incidence of clinically diagnosed vertebral fractures: a population-based study in Rochester, Minnesota, 1985–1989. J Bone Miner Res 7(2):221–227
22. European Prospective Osteoporosis Study (EPOS) Group, Felsenberg D, Silman AJ, Lunt M et al (2002) Incidence of vertebral fracture in Europe: results from the European Prospective Osteoporosis Study (EPOS). J Bone Miner Res 17(4):716–724
23. Kado DM, Browner WS, Palermo L et al (1999) Vertebral fractures and mortality in older women: a prospective study. Study of Osteoporotic Fractures Research Group. Arch Intern Med 159(11):1215–1220
24. Lee YL, Yip KM (1996) The osteoporotic spine. Clin Orthop Relat Res 323:91–97
25. Denis F (1983) The three column spine and its significance in the classification of acute thoracolumbar spinal injuries. Spine (Phila Pa 1976) 8(8):817–831
26. Ismail AA, Cooper C, Felsenberg D, Varlow J et al (1999) Number and type of vertebral deformities: epidemiological characteristics and relation to back pain and height loss. European Vertebral Osteoporosis Study Group. Osteoporos Int 9(3):206–213
27. Sohn JM, Kim KW, Ha KY et al (2009) Risk Factors for the progressive osteoporotic spinal fracture. J Korean Soc Spine Surg 16(3):153–159
28. McKiernan F, Jensen R, Faciszewski T (2003) The dynamic mobility of vertebral compression fractures. J Bone Miner Res 18(1):24–29
29. Kumpan W, Salonowitz E, Seidi G, Wittich GR (1986) The intravertebral vacuum phenomenon. Skeletal Radiol 15(6):444–447
30. Maldague BE, Noel HM, Malghem JJ (1978) The intravertebral vacuum cleft: a sign of ischemic vertebral collapse. Radiology 129(1):23–29
31. Naul LG, Peet GJ, Maupin WB (1989) Avascular necrosis of the vertebral body: MR imaging. Radiology 172(1):219–222
32. Baur A, Stäbler A, Arbogast S, Duerr HR, Barti R, Reiser M (2002) Acute osteoporotic and neoplastic vertebral compression fractures: fluid sign at MR imaging. Radiology 225(3):730–735

33. Ito Z, Harada A, Matsui Y et al (2006) Can you diagnose for vertebral fracture correctly by plain X-ray? Osteoporosis Int 17(11):1584–1591
34. Spiegl UJA, Beisse R, Hauck S et al (2009) Value of MRI imaging prior to a kyphoplasty for osteoporotic insufficiency fractures. Eur Spine J 18(9):1287–1292
35. Kanchiku T, Taguchi T, Kawai S (2003) Magnetic resonance imaging diagnosis and new classification of the osteoporotic vertebral fracture. J Orthop Sci 8(4):463–466
36. Cho T, Matsuda Sakurai M (1996) MRI findings on healing process of vertebral fracture in osteoporosis. J Orthop Sci 1(1):16–33
37. Yang HL, Wang GL, Niu GQ et al (2008) Using MRI to determine painful vertebrae to be treated by kyphoplasty in multiple-level vertebral compression fractures: a prospective study. J Int Med Res 36(5):1056–1063
38. Trout AT, Kallmes DF, Layton KF, Thielen KR, Hentz JG (2006) Vertebral endplate fractures: an indicator of the abnormal forces generated in the spine after vertebroplasty. J Bone Miner Res 21(11):1797–1802
39. Zhao FD, Pollintine P, Hole BD, Adams MA, Dolan P (2009) Vertebral fractures usually affect the cranial endplate because it is thinner and supported by less-dense trabecular bone. Bone 44(2):372–379
40. Kim DY, Lee SH, Jang JS, Chung SK, Lee HY (2004) Intravertebral vacuum phenomenon in osteoporotic compression fracture: report of 67 cases with quantitative evaluation of intravertebral instability. J Neurosurg 100(1 Suppl Spine):24–31
41. Peh WC, Gelbart MS, Gilula LA, Peck DD (2003) Percutaneous vertebroplasty: treatment of painful vertebral compression fractures with intraosseous vacuum phenomena. AJR Am J Roentgenol 180(5):1411–1417
42. Kaneda K, Asano S, Hashimoto T et al (1992) The treatment of osteoporotic-posttraumatic vertebral collapse using the Kaneda device and a bioactive ceramic vertebral prosthesis. Spine (Phila Pa 1976) 17(8 suppl):S295–S303
43. Iwata A, Kanayama M, Oha F, Hashimoto T, Iwasaki N (2017) Effect of teriparatide (rh-PTH 1-34) versus bisphosphonate on the healing of osteoporotic vertebral compression fracture: A retrospective comparative study. BMC Musculoskelet Disord 7–18(1):148
44. Seki S, Hirano N, Kawaguchi Y, Nakano M, Yasuda T, Suzuki K, Watanabe K, Makino H, Kanamori M, Kimura T (2017) Teriparatide versus low-dose bisphosphonates before and after surgery for adult spinal deformity in female Japanese patients with osteoporosis. Eur Spine J 26(8):2121–2127
45. Slavici A, Rauschmann M, Fleege C (2017) Conservative management of osteoporotic vertebral fractures: an update. Eur J Trauma Emerg Surg (Germany) 43(1):19–26