



Vertebral body osteonecrosis: proposal of a treatment-oriented classification system

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Received: 1 March 2018 / Accepted: 9 April 2018 / Published online: 16 April 2018
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Abstract

Purpose To present a classification system for vertebral body osteonecrosis (VBON) based on imaging findings and sagittal alignment and consequently to propose treatment guidelines.

Methods Chart review and classification of imaging and clinical findings. An analysis of literature about VBON has been evaluated to conceive the classification. The current data allows to correlate radiological findings with different stages of the pathophysiological process and consequently to propose a patient-tailored treatment plan.

Results The classification identifies 4 stages: stage 0 (theoretical phase), stage 1 (early phase), stage 2 (instability phase) and stage 3 (fixed deformity phase). Local (angular kyphosis expressed as anterior–posterior wall height ratio) and global (sagittal vertical axis and pelvic tilt) sagittal alignment are considered as complementary modifiers to tailor the most suitable treatment. Stage 1 is generally managed conservatively. Stage 2 and 3 often require different surgical approaches according to local and global sagittal alignment.

Conclusions The classification allows a systematic staging of this disease and can help establish a proper and patient-oriented treatment plan. Further researches are advocated to fully validate the proposed classification system.

Graphical abstract These slides can be retrieved under Electronic Supplementary Material.

Key points

Vertebral osteonecrosis; Vertebral non-union; Classification; Sagittal alignment; Adult deformity

1. Vertebral body osteonecrosis (VBON) is a clinical entity characterized by a pattern of cell death and a complex process of bone resorption and formation that can evolve in a mechanical insufficiency of vertebral body and finally in a vertebral collapse.
2. The lack of a proper identification of VBON as an independent clinical entity and the inability to systematically grade this pathological condition have produced a confusing report of treatment options.
3. The aim of this study is to present a classification system for VBON based on imaging findings and sagittal alignment and consequently to propose treatment guidelines.

Stage 0	Stage 1	Stage 2	Stage 3
"Theoretical phase"	"Early phase"	"Instability phase"	"Fixed deformity phase"
X-ray -	X-ray -	X-ray +	X-ray +
CT-scan -	CT-scan -	CT-scan +	CT-scan +
Bone-scan -	Bone-scan -	Bone-scan +	Bone-scan +
MR -	MR -	MR +	MR +

MODIFIERS

Angular Kyphosis	Sagittal Alignment
A Anterior/Posterior wall height ratio > 75%	1 SVA < 50 mm, PT < 10°
B Anterior/Posterior wall height ratio < 75%	2 SVA < 50 mm, PT > 10°
	3 SVA > 50 mm, PT > 10°

SV-A: Sagittal Vertical Axis; S: Spondylolisthesis; I: Instability; PT: posterior Pelvic Tilt; RPT: Theoretical Pelvic Tilt (RPT = $-7 + 0.379 \times \text{height}$, according to Valler's Formula)

GENERAL RULE:
Stage + Angular Kyphosis Modifier + Sagittal Alignment Modifier = Classification
(i.e. S2A2, I2A3)

Take Home Messages

1. The classification system combines imaging findings and sagittal considerations in order to propose the most tailored and less invasive treatment for each patient.
2. In Stage 2, vertebral instability can be managed with vertebral augmentation techniques (kyphoplasty/cranio-caudal expandable devices) as useful mini-invasive options for anterior support reconstruction.
3. In Stage 3, fixed vertebral deformity can be managed with corpectomy or vertebral osteotomies according to local and global sagittal profile.

Keywords Vertebral osteonecrosis · Vertebral non-union · Classification · Sagittal alignment · Adult deformity

Electronic supplementary material The online version of this article (<https://doi.org/10.1007/s00586-018-5600-6>) contains supplementary material, which is available to authorized users.

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Introduction

Vertebral body osteonecrosis (VBON) is a clinical entity characterised by a pattern of cell death and a complex process of bone resorption and formation that can evolve in a mechanical insufficiency of vertebral body and finally in a vertebral collapse [1, 2]. Clinically, patients complain of pain, disability, deformity and sometime neurological

deficits. The consequent regional deformity can involve sagittal and/or coronal plane [3, 4].

The pathophysiology of VBON can be idiopathic or secondary to cytotoxicity, genetic factors and decreased intraosseous blood flow. The post-traumatic genesis is one of the most common secondary mechanisms; this clinical entity is known in literature as “Kümmell’s disease”. The possible pathogenesis is based on the interruption or reduction of blood supply consequent to fracture and inadequate revascularization of bone marrow [3–6].

Vertebral biopsy is the gold standard for diagnosis of osteonecrosis. The intravertebral vacuum sign is considered the pathognomonic sign of vertebral osteonecrosis on X-rays and computed tomography (CT) scan. On magnetic resonance imaging (MRI) air, fluid or double-line sign are considered highly suggestive for VBON [3–5]. Early reports in literature were centred on conservative treatments such as bracing and bed rest [3]. New adjuvant therapeutic tools such as bisphosphonates, teriparatide and capacitive coupling electrical stimulation have also been proposed [7, 8]. Vertebral augmentation (VA) techniques are reported in literature with discordant results [9–11]. Several authors proposed major surgical approaches to correct the deformity such as vertebral osteotomies (non-3-column-osteotomies (non-3CO) and 3-column-osteotomies (3CO)) [12–14].

The lack of a proper identification of VBON as an independent clinical entity and the inability to systematically grade this pathological condition have produced a confusing report of treatment options between acute traumatic vertebral fractures, osteoporotic vertebral fractures, non-union and post-traumatic spinal deformities. In this paper, a new classification system is presented with the primary aim of grading VBON based on imaging findings and sagittal alignment of the spine and consequently to propose treatment guidelines.

Methods

Rationale for a classification

This classification system has been proposed to grade VBON and consequently to establish the most appropriate treatment. The goals of the classification are to provide the rationale regarding:

- Indication of less invasive patient’s oriented treatment to reduce surgical risk, morbidity and mortality.
- Principles to restore anterior column support solving the situation of vertebral instability and preventing possible catastrophic neurological involvement.
- Selection of appropriate methods to obtain correction of sagittal and/or coronal consequent deformity.

Study design

Chart review and classification of radiographic and clinical findings.

Classification principles

The VBON classification is based on two criteria: radiological findings related to the pathophysiological process and sagittal alignment (Fig. 1).

The most substantial available evidence regarding osteonecrosis refers to the femoral head and a similar pathological pathway is presumed for spine. The current literature allows to correlate radiological findings with different stages of the pathophysiological process.

The classification is mainly based on standing full spine frontal and lateral radiographs, MRI and CT scan. Another useful tool, mainly in early diagnosis can be the bone scan; limitations are poor spatial resolution and low specificity. Additional imaging tools can be required in some patients for differential diagnosis.

As in femoral head osteonecrosis, MRI has been proved to be a highly accurate method for early diagnosis. The necrotic zone is visible on MRI: a low intensity area on T1-weighted images and a high intensity zone on T2-weighted images and on short-tau inversion recovery (STIR) sequence images [3–5]. A differential diagnosis with acute traumatic or osteoporotic vertebral fracture must be performed. In VBON, CT scan and X-rays are negative for fracture. In bone scan, the necrotic region of bone does not take up the technetium-99 isotope and therefore appears “cold”. A surrounding rim of reactive bone remodeling can appear “hot” on the scan [15].

Later, the predominance of bone resorption creates a mechanical insufficiency primarily of cancellous bone, and subsequently of cortical bone with anterior columns instability. Nakamae et al. demonstrated that this situation of vertebral instability is the major cause of pain and disability and directly correlate with neurological involvement [16]. The evolution of this mechanical insufficiency can be a vertebral collapse and a possible sagittal and/or coronal deformity. In this stage, “intravertebral vacuum cleft” (IVC) can occur on X-rays and CT scan. The cleft can be detected on radiographs as horizontal accumulation of gas and appears as a transverse, linear or semi-lunar radiolucent shadow. Sometimes, IVC appears in extension stress and disappears in flexion on X-ray analysis, confirming the hypothesis of vertebral body instability [3–5, 16]. Libicher et al. [17] demonstrated that IVC indicates local bone ischemia associated with a non-healing vertebral collapse and pseudoarthrosis. In bone scan, the viable areas

Stage 0	Stage 1	Stage 2	Stage 3
“Theoretical phase”	“Early phase”	“Instability phase”	“Fixed Deformity phase”
X-ray -	X-ray -	X-ray +	X-ray +
CT-scan -	CT-scan -	CT-scan +	CT-scan +
Bone-scan -	Bone-scan +	Bone-scan +	Bone-scan -
MRI -	MRI +	MRI +	MRI -

MODIFIERS

Angular Kyphosis	Sagittal Alignment
A Anterior/Posterior wall height ratio > 75%	1 SVA < 50 mm; PT ≤ thPT
B Anterior/Posterior wall height ratio < 75%	2 SVA < 50 mm; PT > thPT
	3 SVA > 50 mm; PT > thPT

SVA: Sacral Vertical Axis; **1:** balance; **2:** hidden imbalance; **3:** imbalance; **PT:** patient Pelvic Tilt; **thPT:** theoretical Pelvic Tilt (thPT = $-7 + 0.37 \times \text{Pelvic Incidence}$; according Vialle’s Formula)

GENERAL RULE:

Stage + Angular Kyphosis Modifier + Sagittal Alignment Modifier = Classification
(i.e. STAGE 2,B,2)

Fig. 1 Proposal of novel VBON classification according to relevant imaging findings and sagittal biomechanical parameters. *CT scan* computed tomography scan, *MRI* magnetic resonance imaging

of bone surrounding the necrotic region are engaged and often show a hot lesion that obscures the original cold area [15]. In MRI, IVC appears as an area of hypointensity on T1 and T2 weighted images. Several authors described also a collection of intravertebral fluid that appears as a well-defined area of low signal intensity on T1 weighted images and a high intensity signal on T2 weighted images. This finding is defined as “fluid sign” [3–5, 12]. Yu et al. [18] reported that the coexistence of both air and fluid in the same affected body was not rare (21.5%). As in femoral head osteonecrosis, another MRI finding has been described in spine as highly indicative of osteonecrosis: the “double-line sign”, a low signal intensity outer rim and a high signal intensity inner rim on T2-weighted images [3–5, 12].

Finally, the resolution of vertebral instability evolved in a fixed morphologic alteration of vertebral body clearly detectable on X-rays and CT scan. On MRI, no evidence of “air sign”, “fluid sign” and “double-sign” are present.

Sagittal deformity has higher prevalence and more significant clinical implications than coronal misalignment. In elderly osteoporotic patients, sagittal misalignment can also produces new vertebral body fractures due to a mechanically unfavourable effect known as “domino effect” [19].

Two modifiers are present in the classification system to better analyse local and global sagittal alignment.

Local sagittal profile is evaluated as angular kyphosis expressed as anterior–posterior wall height ratio. Modifier A is assigned to a ratio more than 75%, a ratio less than 75% is considered as Modifier B.

Global sagittal alignment is evaluated considering sagittal vertical axis (SVA) and pelvic tilt (PT). Compensatory mechanisms can be adopted defining a situation of compensated imbalance (“hidden sagittal imbalance”) or of uncompensated sagittal imbalance [20]. Modifier 1 indicates sagittal balanced patients (SVA < 50 mm and PT ≤ thPT); Modifier 2 expresses compensated sagittal imbalance (SVA < 50 mm and PT > thPT) and Modifier 3 states for a sagittal imbalanced (SVA > 50 mm and PT > thPT) subjects. Theoretical pelvic tilt (thPT) is calculated according to Vialle’s formula (thPT = Pelvic incidence (PI) × 0.37 – 7°) [20].

Results

Stage 0 a theoretical grade. All imaging studies are negative.

Stage 1 no evidence of vertebral body collapse on X-rays and CT scan. On MRI, the necrotic area has a low intensity signal on T1 images and high intensity signal on T2 and STIR images. On bone scan, a cold area can be surrounded by a hot rim. A conservative treatment should be considered. The Jewett brace is indicated to give support to the spine. Adjuvant therapeutic tools such as bisphosphonates, teriparatide and capacitive coupling electrical stimulation can be adopted [7, 8]. The persistence of pain and imaging findings after four months can implicate a surgical solution [21, 22]. VA can be adopted. A biopsy can be performed to confirm the diagnosis. Modifiers are not applicable in this stage.

Stage 2 a vertebral body collapse is observed on X-rays and CT scan. IVC as instability sign can be detected on X-rays and CT scan. On MRI, “air sign”, “fluid sign” and/or “double-line sign” are present. In this phase, angular kyphosis and sagittal balance modifiers has to be considered. The aim of surgical treatment is to avoid complete vertebral body collapse and consequent deformity, to prevent neurological involvement, to restore anterior column and to improve pain and disability. Due to the vertebral instability, the deformity correction can be assimilated as an acute vertebral fracture and managed through different posterior-only surgical techniques (VA and/or instrumentation \pm osteotomies).

Stage 2, A, 1 (Anterior–posterior wall height ratio more than 75% with a balanced spine): even if the spine is balanced, a situation of vertebral body instability is present. VA is indicated to solve pain and restore anterior support.

Stage 2, A, 2–3 (Anterior–posterior wall height ratio more than 75% with a compensated or not sagittal imbalance): sagittal imbalance might be pre-existing or the result of combination of VBON and bone/soft tissue degeneration (spondyloarthritic changes, previous vertebral body fractures, degenerative disc disease, muscles degeneration). VA at level of VBON and/or posterior instrumentation in association with 3-CO or multiple non-3CO are the treatments of choice.

Stage 2, B, 1 (Anterior–posterior wall height ratio less than 75% with a balanced spine): a good spinal alignment is still present (rare condition, mainly in the thoracic spine) probably due to compensation of adjacent discs and muscle activity. A reduction of the kyphotic vertebra with expandable device or kyphoplasty is advised and supplementary non-3CO can be

performed to restore an adequate regional sagittal profile. In this phase, a simple vertebroplasty cannot allow an adequate vertebral body height restoration (Fig. 2). *Stage 2, B, 2–3* (Anterior–posterior wall height ratio less than 75% with a compensated or not sagittal imbalance): the vertebral body collapse is present in association with sagittal imbalance. An anterior column reconstruction is advised. The anterior support can be traditionally obtained with corpectomy and expandable cages. An alternative to anterior surgery can be VA with kyphoplasty or cranio-caudal expandable device followed by posterior instrumentation. If the anterior column reconstruction does not achieve the desired correction, posterior osteotomies (3CO and multiple non-3CO) can be considered.

Stage 3 vertebral instability is solved and evolved in a permanent morphologic alteration of vertebral body easily detected on X-rays and CT scan. Usually, a kyphotic vertebral body is present. The surgical treatment aims to restore sagittal and/or coronal alignment and to improve pain and disability.

- *Stage 3, A, 1* (Anterior–posterior wall height ratio more than 75% with a balanced spine): on X-rays and CT scan, a “vertebra plana” is detected. Since the spine is balanced, no therapeutic procedures are required.
- *Stage 3, A, 2–3* (Anterior–posterior wall height ratio more than 75% and sagittal imbalance): sagittal imbalance can be probably pre-existing or the result of combination of VBON and bone/soft tissue degeneration. On X-rays and CT scan, a “vertebra plana” is detected. Vertebrectomy with posterior fusion, combination of multiple non-3CO or 3CO with posterior fusion are useful solutions.
- *Stage 3, B, 1* (Anterior–posterior wall height ratio less than 75% with a balanced spine): a good spinal alignment is present (very rare condition, mainly in high thoracic area) probably due to compensation of adjacent discs and muscle activity. A progression to sagittal misalignment can arise due to bone and/or soft tissue degeneration. In this stage, no surgical treatments are needed.
- *Stage 3, B, 2–3* (Anterior–posterior wall height ratio less than 75% with an imbalanced spine compensated or not): local and global deformity correction is needed. Different surgical strategies can be adopted due to surgeon’s experience and clinical status and comorbidities of the patient. Vertebrectomy with pos-



Fig. 2 Sample case of a 2,B,1 patient treated with cranio-caudal expandable devices, multiple Ponte/Smith-Petersen osteotomies and posterior fusion. **a** Preoperative full spine lateral x-ray; **b** postopera-

tive full spine lateral x-ray; **c** Axial CT scan of T12 VBON; **d** Sagittal CT scan view of the thoracolumbar spine

terior fusion, combination of multiple non-3CO with posterior fusion or a pedicle subtraction osteotomy (PSO) at the level of deformity with posterior fusion are useful solutions (Fig. 3).

Discussion

The treatment of VBON can be adjusted according to the level of pain and disability, neurological status, patients' comorbidities and surgical risk related to the planned technique. In case of neurological involvement, decompression of neural elements is the priority. According to the clinical status, the surgeon can decide to treat only the instability phase without considering the sagittal deformity correction for pain-relief purpose only.

This classification system divides sagittal imbalanced patients as compensated or not according to clinical and radiological parameters. Nevertheless, both conditions are pathological and the same treatment has to be performed [20].

Difference between vertebral non-union and VBON is debated and not still cleared. Clinical and imaging features of VBON and vertebral non-union are overlapping [3–5, 9–18, 23]. In particular, vertebral non-union is comparable to the second stage of the proposed classification. We believe that these two clinical entities could be included in a common classification and treated in a similar way.

Some evidences suggest that a complete histological healing of a vertebral fracture occurs in four months [21]. According to these data, we consider non-union a fracture that still remains symptomatic with positive imaging findings after 4 months of adequate treatment [21, 22].

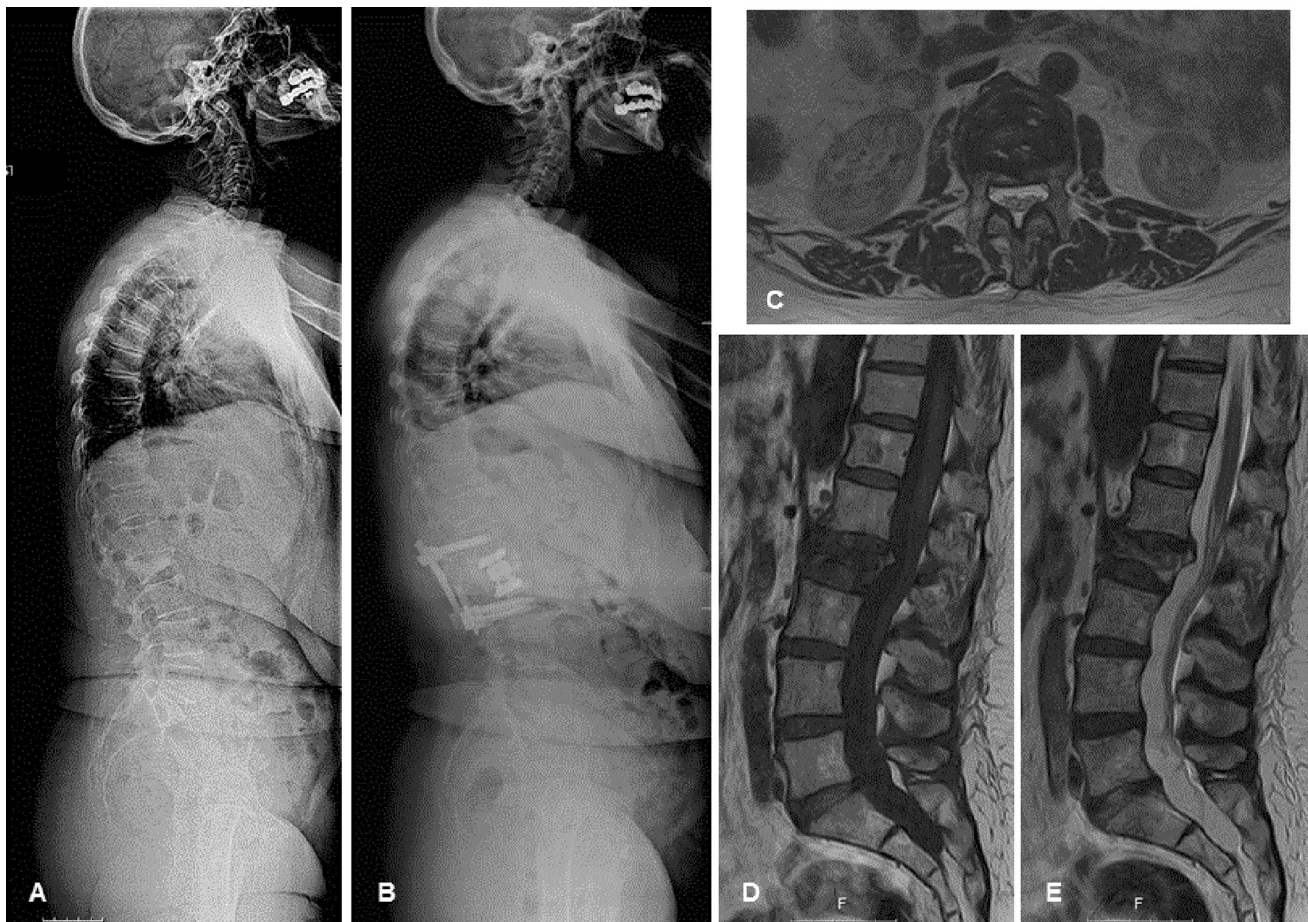


Fig. 3 Sample case of 3,B,2 patient treated with L2 corpectomy and posterior fusion. **a** Preoperative full spine lateral x-ray; **b** postoperative full spine lateral x-ray; **c** axial MRI of L2 VBON; **d** T1-weighted MRI of the lumbar spine; **e** T2-weighted MRI of the lumbar spine

The classification system combines imaging findings and sagittal considerations to propose the most tailored and less invasive treatment for each patient (Fig. 4).

Anterior approaches to spine and 3CO are high demanding procedures characterised by conspicuous complications rate and should be saved only for selected cases [24].

In stage 2, vertebral instability can be managed with VA such as in acute traumatic or osteoporotic vertebral fracture. Kyphoplasty and cranio-caudal expandable devices appear as adequate solution to restore vertebral body geometry. The cranio-caudal expandable devices particularly demonstrated the best potentiality to restore vertebral shape and to align in parallel the end plates [10, 25].

In stage 3, PSO can be performed at the deformed level to transform a kyphotic vertebral body in vertebra plana restoring the adequate local sagittal profile.

The choice of fusion levels must be carefully planned mainly in thoracic area and thoracolumbar junction to avoid risk of junctional disease and hardware failure [20].

A limitation of this classification is the need of standing full spine frontal and lateral radiographs to evaluate sagittal profile of the patient. In stage 2, this evaluation can be difficult due to the pain related to vertebral instability. Patients usually use braces to support spine and to control pain and disability. The choice of sagittal parameters as modifiers is due to the more significant correlation of these variables with pain and disability [20].

To the best of our knowledge, the presented classification is the first attempt to grade vertebral body osteonecrosis and to structure a patient-oriented treatment algorithm.

Undoubtedly, this proposal needs to be supported and validated by outcomes and complications evaluation of proper number of cases. We advise further high quality studies for classification endorsement. This will be our priority for future investigations.

Funding There is no funding source for this article.

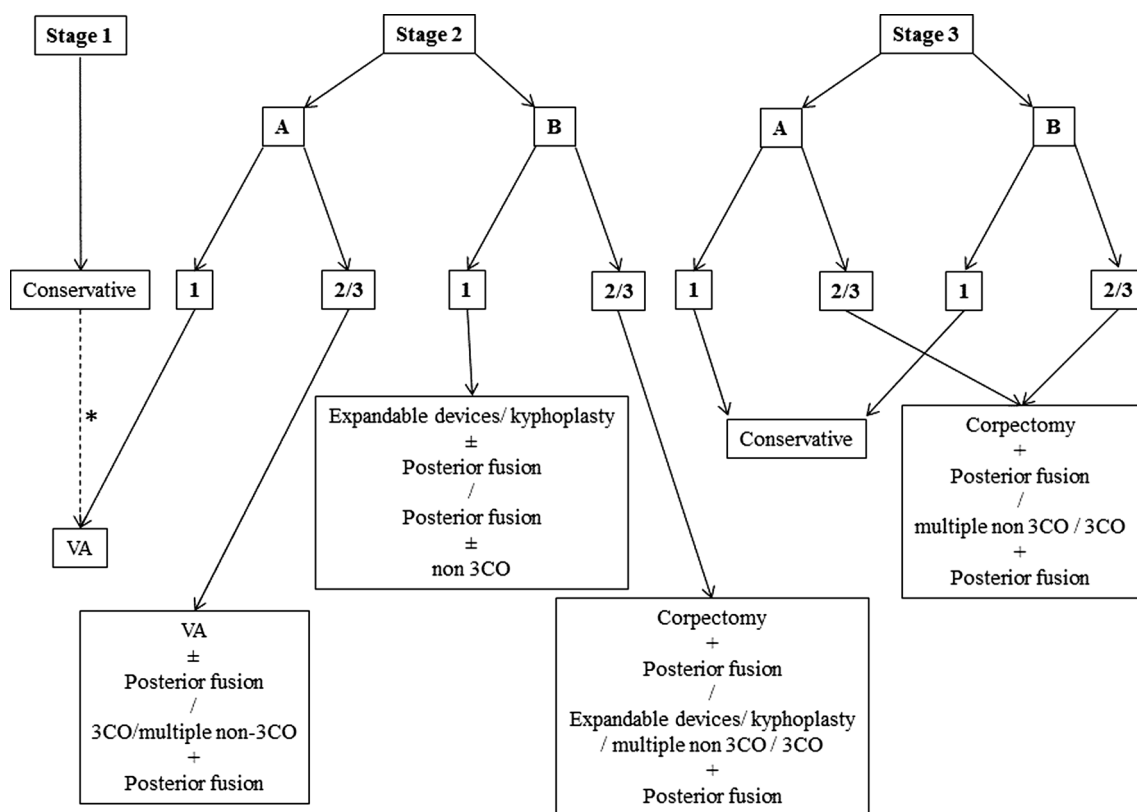


Fig. 4 Treatment algorithm according to the proposed classification. VA vertebral augmentation, 3CO three-column-osteotomy, non-3CO non -three-column-osteotomy, or, + and, ± with or without. *Positive

clinical and imaging findings after 4 months of conservative treatment can implicate a surgical solution

Compliance with ethical standards

Conflict of interest Pedro Berjano received honorarium for surgeons' education activities from Nuvasive, Medacta, DepuySynthes and his department received unrestricted research grants from Nuvasive, Medacta, DepuySynthes and K2 M. Claudio Lamartina received honorarium for surgeons' education activities from Nuvasive, Medacta, DepuySynthes and K2 M and his department received unrestricted research grants from Nuvasive, Medacta, DepuySynthes and K2 M. No other disclosures by the rest of authors.

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