



MONOGRAPH COLUMN

**[Translated article] Truths and myths about
augmentation techniques in the treatment
of fragility fractures**

S. Santiago Maniega^a, J. Crespo Sanjuán^b, F. Ardura Aragón^a,
R. Hernández Ramajo^b, G.J. Labrador Hernández^b,
M. Bragado González^a, D.C. Noriega González^{a,*}

^a Unidad de Columna, Servicio de Cirugía Ortopédica y Traumatología, Hospital Clínico Universitario de Valladolid, Valladolid, Spain

^b Servicio de Cirugía Ortopédica y Traumatología, Hospital de Medina del Campo, Medina del Campo, Valladolid, Spain

Received 18 December 2023; accepted 18 April 2024

Available online 9 August 2024

KEYWORDS

Osteoporosis;
Kyphoplasty;
Vertebroplasty

Abstract The main event of osteoporosis is fragility fractures. Vertebral compression fractures are the most commonly fragility fracture related to osteoporosis.

Our goal is to review the available literature to confirm or deny concepts learned about spinal cementation and adapt our clinical practice according to scientific evidence.

In the complex world of spine surgery, constant innovations seek to improve the quality of life of patients. Among these, vertebral augmentation has emerged as an increasingly popular technique, but often shrouded in myths and misunderstandings. In this systematic review, we will thoroughly explore the truths behind vertebral augmentation, unravelling common myths and providing a clear insight into this technique. As specialists in the field, it is crucial to understand the reality surrounding these interventions to offer our patients the best possible information and make informed decisions.

© 2024 SECOT. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

PALABRAS CLAVE

Osteoporosis;
Cifoplastia;
Vertebroplastia

Verdades y mentiras de las técnicas de cementación en el tratamiento de las fracturas por fragilidad

Resumen La principal manifestación de la osteoporosis son las fracturas por fragilidad. Las fracturas vertebrales por compresión son las más comúnmente relacionadas con la osteoporosis.

DOI of original article: <https://doi.org/10.1016/j.recot.2024.04.007>

* Corresponding author.

E-mail address: dnoriega@saludcastillayleon.es (D.C. Noriega González).

<https://doi.org/10.1016/j.recot.2024.08.005>

1888-4415/© 2024 SECOT. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Nuestro objetivo es revisar la bibliografía disponible para ayudar a confirmar o desmentir conceptos aprendidos sobre la cementación vertebral y adaptar nuestra práctica clínica de acuerdo con la evidencia científica.

En el complejo mundo de la cirugía de columna vertebral, las innovaciones constantes buscan mejorar la calidad de vida de los pacientes. Entre estas, las cementoplastias han emergido como una técnica cada vez más popular, pero a menudo envuelta en mitos y malentendidos. En esta revisión sistemática exploraremos a fondo las verdades detrás de las cementoplastias, desentrañando mitos comunes y proporcionando una visión clara de esta técnica. Como especialistas en la materia, es crucial comprender la realidad que rodea a estas intervenciones para ofrecer a nuestros pacientes la mejor información posible y tomar decisiones informadas.

© 2024 SECOT. Publicado por Elsevier España, S.L.U. Este es un artículo Open Access bajo la CC BY-NC-ND licencia (<http://creativecommons.org/licencias/by-nc-nd/4.0/>).

Introduction

More than 50 million people in the United States¹ and almost 3 million people in Spain have osteoporosis and low bone mass. Fragility fractures are the main manifestations. Fractures of the hip, spine, and distal radius are the most frequent osteoporotic fractures. Approximately one in two women and one in five men will experience an osteoporotic fracture in their lifetime.² Vertebral compression fractures (VCF) are the most common fracture associated with osteoporosis, with an estimated worldwide incidence of 1.4 million new fractures each year,³ accounting for a quarter of all osteoporotic fractures.¹

Pain is the main manifestation of VCF, which usually lasts about 6–8 weeks.¹ Other complications of VCF include kyphotic deformity, weight loss, depression, reduced quality of life, and even death.⁴

Conservative treatment of this type of fracture involves analgesic management, limiting activities, bed rest, use of back braces, and physical therapy.¹

Opioid treatment and its adverse effects associated with sedation, nausea, and constipation further increases the risk for falls and delays recovery.¹ Bed rest is associated with increased incidence of pressure ulcers, pneumonia, urinary tract infection, and venous thrombosis.⁵

In patients with severe pain, spinal cementation (vertebroplasty and/or kyphoplasty) can help reduce pain and improve functional capacity.

Common indications for vertebroplasty (vertebral cementation) include osteoporotic vertebral fracture of more than 3–4 weeks refractory to medical treatment, Kummel's disease, painful symptomatic haemangioma, vertebra with extensive osteolysis, or invasion secondary to malignant tumour (metastasis, multiple myeloma, etc.).⁶

The most frequent indication for kyphoplasty is a recent traumatic vertebral fracture (less than 7–10 days) with a kyphotic angle greater than 15°, as well as all indications for vertebroplasty,⁶ the aim being to reduce the vertebral fracture and residual deformity.

Our aim is to conduct a review of the available literature to assist in understanding concepts learned about vertebral cementation and to adapt our clinical practice to the scientific evidence.

Cementation or conservative treatment

Alvarez et al.⁷ published one of the first prospective studies on the results of vertebroplasty and showed superior results in terms of pain control and quality of life, comparing vertebroplasty and conservative treatment in vertebral fractures.

The first randomised clinical trials comparing the results of vertebral cementation and conservative treatment began to be published from the 2000s onwards, and not all of them showed differences in favour of vertebroplasty.

The first prospective clinical trial comparing the results of vertebroplasty with conservative treatment of osteoporotic vertebral fractures (VERTOS)⁸ was published in 2007. Its inclusion criteria were age equal to or greater than 50 years, disabling pain, subacute and chronic fracture (6–24 weeks), and presence of bone oedema on MRI. Thirty-four patients participated ($n=18$ in vertebroplasty, $n=16$ in conservative treatment). At 24 h there was a significant improvement in VAS score after vertebroplasty (4.7 vs. 7.1; difference, 2.4; 95% CI, 3.7–1.0). At 2 weeks, the difference was no longer significant. The trial was terminated prematurely, due to the crossover of most patients from conservative treatment to vertebroplasty.

In 2009 Buchbinder et al.⁹ published their results of a multicentre, randomised, placebo-controlled clinical trial comparing the results of vertebroplasty in fractures of 12 months' duration or placebo treatment. They found no differences in pain, quality of life or perception of improvement at any point between one week and 6 months of follow-up. Also in 2009, and in a similar vein, the results of a clinical trial involving 131 patients undergoing vertebroplasty or a simulated procedure were published.¹⁰ No differences were found in terms of pain or function.

The Fracture Reduction Evaluation (FREE) trial, published in 2009, was the first prospective multicentre randomised clinical trial (RCT) comparing the results of kyphoplasty with conservative management. Three hundred patients ($n=149$ with acute or subacute fractures [<3 months], with presence of vertebral oedema on MRI) were included. Differences were found in the SF-36 questionnaire at the first month that were maintained up to 6 months. Its main limitations

Table 1 Summary of major clinical trials comparing conservative and surgical (vertebroplasty or kyphoplasty) treatment of vertebral compression fractures.

Study name	Year of publication	Number of patients	Follow-up period	Groups	Statistical significance
VERTOS	2007	34	2 weeks	Vertebroplasty vs. conservative	Pain only for 24 h
FREE	2009	300	12 months	Kyphoplasty vs. conservative	SF-36 up to six months
INVEST	2009	131	12 months	Vertebroplasty vs. placebo (anaesthesia)	Not assessable
VAPOUR	2016	120	6 months	Vertebroplasty vs. placebo (anaesthesia)	Pain up to 2 weeks
VERTOS IV	2018	180	12 months	Vertebroplasty vs. placebo (anaesthesia)	No differences

were the lack of masking and the inclusion of 4 patients with pathological fractures.

The Investigational Vertebroplasty Safety and Efficacy Trial (INVEST) compared kyphoplasty and placebo in 131 patients over the age of 50 years with fractures less than one year old (mean 16–20 weeks). No statistically significant differences were found at one month in values on the Roland-Morris Disability Questionnaire and the numerical pain scale. However, the trial's limitations were the inclusion of patients with old fractures, and fractures diagnosed by radiography alone.

Based on the results of early clinical trials, clinical guidelines initially did not recommend the use of vertebroplasty and kyphoplasty as an option for the management of painful osteoporotic VCF.

However, many more randomised controlled trials have since been published reporting the superiority of vertebral cementation over conservative treatment.¹¹

The Vertebroplasty for Acute Painful Osteoporotic Compression Fractures (VAPOUR) trial¹² was published in 2016. This prospective, double-blind RCT was specifically designed to address the role of vertebroplasty in patients with VCF. Pain reduction was significantly greater in patients who underwent vertebroplasty, and this difference was maintained up to 6 months. No differences were seen in the occurrence of new fractures.

Vertebroplasty vs. Sham Procedure for Painful Osteoporotic Vertebral Compression Fractures (VERTOS IV) was published in 2018. It was a randomised, double-blind RCT that enrolled 176 patients undergoing vertebroplasty or a sham procedure.

Both the VERTOS IV and VAPOUR trials demonstrated durable maintenance of vertebral body height in patients undergoing vertebroplasty, in contrast to those undergoing a sham procedure.

Table 1 summarises the main features of the above clinical trials comparing cementing techniques and conservative or sham treatment.

The accumulated evidence shows that kyphoplasty and vertebroplasty provide better results than non-surgical

treatment in RCTs and meta-analyses and an acceptable cost-benefit,^{11,13} confirming that the use of cement in the treatment of osteoporotic vertebral fracture does not increase the risk of adjacent fracture.

First, second, or third generation cementation

Vertebroplasty (first-generation cementation) involves percutaneous injection of bone cement (polymethylmethacrylate [PMMA]) directly into the vertebral body.

Kyphoplasty (second-generation cementation) involves an additional step in which a cavity is created, usually through a balloon, which is then removed, into which PMMA is injected. In addition to the advantages of reducing the fractured vertebral body, the creation of an intrasomatic cavity with less pressure and covered by impacted bone trabeculae and by the walls of the vertebral body, which is filled with cement, reduces the risk of its extravasation, thereby minimising the risk of complications due to cement extravasation.¹⁵ One of the drawbacks of kyphoplasty is the inability to maintain the restored height of the vertebral body after removing the balloon and before applying the cement, resulting in a loss of correction, especially of the vertebral endplate, and limiting its ability to reduce beyond the fractured vertebra.^{15,16}

Third-generation cementation involves expandable intravertebral devices using a transpedicular approach. Their expansion allows the fractured vertebral endplate to be reduced, restoring its height and integrity, and stabilising it with bone cement, theoretically maintaining the restored vertebral height long term, as they remain in the vertebral body while augmentation is performed.¹⁶

Although many RCTs have been published comparing vertebroplasty or kyphoplasty with medical management, there have been few prospective RCTs comparing the safety and efficacy of vertebroplasty with kyphoplasty. The largest RCT was Kyphoplasty and Vertebroplasty in the Augmentation and Restoration of Vertebral Body Compression Fractures

(KAVIAR),¹³ designed to detect a difference in subsequent radiographic fractures.

A total of 361 patients completed 1 month of follow-up (181 vertebroplasty, 180 kyphoplasty procedures). The mean procedure duration was longer with kyphoplasty, with no difference in clinical outcome or symptomatic complications.

A systematic review and meta-analysis comparing vertebroplasty and kyphoplasty included 2838 patients (1454 vertebroplasties and 1384 kyphoplasties) in 29 prospective RCTs.¹⁷ There was no difference in back pain or disability scores at any point between vertebroplasty and kyphoplasty. A meta-analysis of 845 patients¹⁸ did find short-term differences in favour of kyphoplasty in terms of short-term pain and disability, and kyphotic angle correction, volume of cement injected, and cement leakage.

Overall, in terms of restoring vertebral height and local kyphotic corrections, kyphoplasty is relatively better than vertebroplasty.⁴

A published clinical trial by Dohm et al.¹³ concludes that vertebroplasty has a shorter mean procedure time (kyphoplasty, 40.0 min; vertebroplasty, 31.8 min) and hospital stay (kyphoplasty, 22 h; vertebroplasty, 8 h). Both treatments provide similar sustained improvements in pain intensity, disability, and quality of life. Kyphoplasty has less cement extravasation and higher rates of kyphotic angle correction.

An analysis of the Medicare population concludes that patients treated with kyphoplasty have a statistically significantly higher survival rate (62.8% vs. 57.3% for vertebroplasty) and a 23% lower mortality rate than patients treated with vertebroplasty.⁶

Given an equivalent clinical outcome, the lower cost would make vertebroplasty preferable to kyphoplasty in economic terms. While several previously published studies have demonstrated lower inpatient and outpatient costs for vertebroplasty compared to kyphoplasty, long-term cost-effectiveness studies have suggested that kyphoplasty may in fact be more cost-effective.¹⁷ Ong et al.¹⁹ found that, despite the higher initial cost of kyphoplasty, vertebroplasty was less cost-effective due to the greater use of medical resources postoperatively over the 2 years after surgery.

The benefits of third-generation cementation are based on increased correction of the kyphotic angle and restoration of vertebral body and vertebral plate height.²⁰

A systematic review compared the efficacy and complications of balloon kyphoplasty with nonsurgical treatment, sham control, vertebroplasty and a third-generation technique. The authors concluded that, based on a small number of heterogeneous (and heavily biased) studies, there was no difference between kyphoplasty and other spinal augmentation procedures, and that further randomised studies were necessary to determine efficacy.²¹

The SAKOS study, a prospective, randomised, multicentre study (141 patients from 13 hospitals in five countries), demonstrated the noninferiority of SpineJack® devices after one year of follow-up in vertebral reductions in osteoporotic fractures vs. kyphoplasty and the superiority of kyphoplasty in reducing central vertebral height and the incidence of adjacent fractures.²⁰

In general, these implants require smaller volumes of cement,⁴ reducing the theoretical risk of cement leakage.

Fracture type

In addition to the treatment of AO type A1 VCF, kyphoplasty can be considered a therapeutic option even in treating incomplete osteoporotic burst fractures (AO type A3.1). Due to the involvement of the posterior wall, the risk of cement leakage is considered to be higher. Walter et al.²² performed a meta-analysis to evaluate the frequency and pattern of bone cement leakage in compression fractures, and concluded that kyphoplasty could be a safe method to treat burst fractures. In addition, the posterior longitudinal ligament and soft tissues around the vertebral body can potentially prevent bone cement leakage.

In a long-term study, Noriega et al.²³ demonstrated that treatment by kyphoplasty with expandable titanium implants is a safe and effective method in the treatment of AO type A3 fractures.

Fracture age

Patients can be included in trials by fracture age: acute (<6 weeks), subacute (6–12 weeks), and chronic (>12 weeks).¹

Although clinical guidelines call for cementation after a minimum of 6 weeks from the onset of pain, some groups have also included subacute fractures (between 3 and 6 weeks) when progressive collapse is detected.²⁴

MRI of the spine is useful to identify acute and sub-acute fractures, which generally respond well to percutaneous cementation. Acute fractures will demonstrate oedema as decreased T1 and increased T2 or STIR.¹¹ MRI can also help differentiate osteoporotic fractures from pathological fractures.

According to the Cardiovascular and Interventional Radiological Society of Europe (CIRSE) guidelines, any osteoporotic vertebral fracture older than 3 months is considered chronic; cementation in these fractures should only be proposed when accompanied by cavitation or bone oedema (findings compatible with osteonecrosis or incomplete healing).⁶

A retrospective study in patients with vertebral fractures of more than 12 weeks' duration with evidence of incomplete healing on MRI or bone scan found a 63% reduction immediately after the procedure and a 75–87% reduction compared to median baseline pain scores during the 1-year follow-up period.²⁵

The results of the VERTOS V trial²⁶ were published in 2023, which included 80 patients with fractures of more than 12 months' duration and compared the results between vertebroplasty and infiltration. They found better results in the vertebroplasty group in terms of pain, quality of life, and disability.

Unipedicular or bipedicular approach

The bipedicular approach is considered the standard in cementation techniques. However, considering aspects such as operating time, cement volume, and radiation dose, a unipedicular approach reduces operating time, limits X-ray exposure, and decreases the risk of cement leakage.⁴ In contrast, a higher rate of nerve injury appears to have been found with the unipedicular approach.⁴

A 2016 meta-analysis indicated that there was no significant difference in visual analogue score (VAS) or Oswestry disability index (ODI) between unilateral and bilateral vertebroplasty. Surgery time in unilateral vertebroplasty was shorter and required less cement. There was no difference in leak rate.

Safety

The main symptomatic complications of vertebroplasty are significant haemorrhage or vascular injury, symptomatic pulmonary embolism of cement, haemo- or pneumothorax, new fractures related to the procedure, neurological deficits, or death. These complications occur in less than 1% of cases. Infections have also been reported following cementing procedures, although their true prevalence is unknown.²⁷

Number of vertebrae to treat

There is currently no consensus on the maximum number of vertebrae that can be cemented in one session, although European and American guidelines suggest that no more than three levels should be treated in one session.²⁸

Some reviews consider it a relative contraindication to treat more than three vertebrae in one session.²⁹ Zoarski et al. state that treatment of up to five body levels is acceptable and that treatment of eight levels or more simultaneously is not accepted medical practice.

A report on vertebroplasties of more than three vertebral levels in one session reports an average amount of cement injected of 5.6 ml in the lumbar spine and 4.3 ml in the dorsal spine. The minimum number of injected levels was 4 and the maximum number of injected levels was 6.³⁰

Good results have been published in the treatment of six unilaterally cemented levels under local anaesthesia.³¹ This group does not recommend treatment of more than six levels or 25–30 ml of cement per session.

Mailli et al.³² found no statistical difference in pain relief or mobility when comparing vertebroplasty performed on up to three vertebrae with more than three levels per session.

From a practical point of view, it is more important to control the total cement volume than the number of vertebrae treated.

Volume of cement

Biomechanical and clinical studies suggest that too high a volume of bone cement and, consequently, high intradiscal pressure and high vertebral stiffness are a cause of complications and even failure of vertebroplasty. To avoid this, smaller cement volumes have been recommended; however, other studies have shown that very small volumes cannot restore the strength and stiffness of the vertebral fracture to a sufficient level resulting in failure of the procedure with persistent pain.³³

Some clinical studies have shown that cement volume has a positive correlation with cement leakage. A larger volume of injected cement is more likely to result in extravasation.³⁴

Some authors place the volume necessary to obtain therapeutic effect at 4.5³⁵–4.7 ml while others recommend injecting <3.5 ml of bone cement in the thoracic and <4 ml

in the lumbar spine to avoid leakage.³⁶ Another group recommends a maximum of 4–5 ml of cement in the lumbar vertebral bodies and 2–3 ml in the upper thoracic spine.²⁴

Clinical practice has confirmed that the volume of cement injected is not directly proportional to the analgesic effect, and therefore it is not necessary to fill the vertebra from endplate to endplate.³⁷ Injecting >4 ml of bone cement may produce pain relief, but a further increase in bone cement volume does not result in further improved efficacy.³⁶

Belkoff et al.³⁸ found that restoration of vertebral body stiffness in the thoracic and thoracolumbar segment requires doses of 4 ml of cement.

The volume of cement injected during the procedure in the literature ranges from 2.8 ml in the trial published by Buchbinder et al.⁹ to 7.5 ml in VAPOUR.¹²

The results of a cadaveric study indicate that 15% of the fractured vertebral body volume, corresponding to 4–6 ml of bone cement, is the amount of cement filler volume required to restore the biomechanics of the vertebral body.³³ In the case of third generation devices, cement equivalent to 10% of the vertebral volume is sufficient to stabilise the fractured vertebra.³⁹

Cement leakage

One of the main complications related to percutaneous cementation is cement leakage. Analysed by CT, cement leakage is present in 82% of cementations.^{4,40}

Although most leaks are clinically asymptomatic, serious complications may occur in 3.9–7.5% of patients.³⁴

Cement leakage usually occurs through the vertebral endplates into the disc,¹ quadrupling the risk of adjacent fracture.⁴¹

Leakage of cement into the spinal canal can lead to spinal canal stenosis and thermal injury to neural tissues. Cement may also leak into the neural foramen and cause nerve root compression. The respective frequency of these two complications is 0–.5% and 0–3.7%.⁴²

Leakage of cement into the perivertebral system and inferior vena cava can lead to serious complications such as cardiopulmonary failure, acute kidney injury, paradoxical embolism, or death.

During kyphoplasty, the peripheral bone is compacted through balloon inflation, allowing injection of cement at lower pressure and higher viscosity, reducing the rate of leakage.⁴³

Higher leakage rates are likely with cortical breakage, use of low viscosity cement, and injections of larger volumes.⁴³ Other associated factors include the degree of severity of vertebral fracture or early application of cement that has not reached its optimum viscosity.⁴

Although the presence of intravertebral cleft signal was identified as increasing the incidence of cement leakage, there is also a contrary view that cement leakage is less common.⁴³

Patients with higher bone density are also more likely to experience cement leakage. On the one hand, vertebrae with higher bone density generate greater resistance to bone cement injection, and therefore higher pressure is needed to inject the cement. And on the other hand, higher bone

density indicates a greater amount of trabecular bone per unit area and smaller spaces between the trabecular bone. Therefore, the same volume of cement requires more space to disperse, which increases the risk of leakage.⁴⁴

A systematic review and meta-analysis comparing vertebroplasty and kyphoplasty and including 2838 patients (1454 vertebroplasties and 1384 kyphoplasties)¹⁷ found no difference in the rate of symptomatic cement leakage, but kyphoplasty was associated with a lower rate of overall cement leakage and higher rates of kyphosis correction.

Cement viscosity may also influence the rate of cement leakage. Compared with traditional low-viscosity bone cement, which has a 3–5-min working time, high-viscosity bone cement can extend working time to more than 15 min. Theoretically, this can help the surgeon to control the bone cement injection process and to more accurately observe the dispersion of the bone cement in the vertebral body, in order to obtain better distribution of the bone cement and reduce the occurrence of leakage.³⁶ An injection of more than 6 ml of low viscosity cement significantly increases the leakage rate.

Regarding the volume of cement injected, Barriga et al.⁴⁵ conclude, through a prospective observational study, that the injection of small amounts of cement offers similar clinical results to those achieved with larger amounts, reducing the number of cement leaks.

There are also certain circumstances that decrease the likelihood of cement leakage, as reflected by Tomé et al.⁴⁶ in their retrospective analysis of 272 vertebrae using CT scanning. They include Kummel's avascular necrosis as a protective factor against cement leakage.

Adjacent fractures

Some patients may suffer subsequent fractures in untreated vertebrae after cementation, which generally require additional treatment.⁴⁷

However, it should also be noted that the natural history of osteoporotic vertebral fractures suggests that the incidence of subsequent new vertebral fractures is 19.2%.⁴²

In the literature, the incidence of new VCF ranges widely, from around 2% to 23% in kyphoplasty and from 2.4% to 52% in vertebroplasty. However, there is no significant difference in the incidence of adjacent vertebral fractures between these two procedures.⁴⁸ Most adjacent fractures occur mainly between 1 and 2 months after cementation.⁴⁸

There is debate as to whether the increased risk of vertebral fractures is caused by previous vertebroplasties, changed local biomechanics, natural susceptibility of the thoracolumbar junction to fractures, natural progression of the underlying disease, or a combination of all these factors.³

Overall, 1 in 5 patients develop a new vertebral fracture within 12 months of the initial vertebral fracture; the risk is higher in patients with multiple fractures.⁴⁹

From the cohort of patients in the clinical trial comparing vertebroplasty and placebo treatment, published by Buchbinder et al.⁹ in 2009, the results at 24-month follow-up were published in 2015,⁵⁰ where the differences with regard to occurrence of adjacent fractures were analysed. No differences were found between the two groups.

Three meta-analyses of published prospective trials found no difference in subsequent risk of VCF between the conservative management and vertebroplasty cohorts.^{14,51,52}

One meta-analysis suggests that low bone mineral density is more consistently associated with an increased subsequent risk of VCF.⁴⁷ Likewise, patients with corticosteroid-induced osteoporosis may have a higher incidence of new fractures after vertebroplasty than patients with primary osteoporosis. Female sex and fractures at the thoracolumbar junction may also be a risk factor for new adjacent fractures.⁴⁸ Procedure-related factors, such as kyphosis correction, showed no evidence of a significant relationship with increased vertebral fractures.

Biomechanical studies indicate that the stiffness of augmented vertebrae can be 36 times greater than that of normal cancellous bone.

Increased pressure and weight-bearing changes in multiple vertebrae may add additional pressure on untreated vertebral bodies and thus cause subsequent VCF. In addition, patients with symptomatic multiple fractures often have more severe osteoporosis compared to patients with single vertebral fractures, and this may also explain why these patients are more likely to develop new VCF after vertebroplasty.⁴⁷

Intradiscal cement leakage has also been suggested as a factor that may increase the incidence of new vertebral fractures.⁵³ The average time between vertebroplasty and new fracture is 48 days in patients with disc cement leakage and 98 days in patients without disc cement leakage.⁴¹ The significance between new fractures and increased cement volume or cement contact with the vertebral body is unclear.

Many authors have tried to find an effective method to reduce the risk of new fracture. Some suggested that prophylactically cementing the adjacent vertebrae could theoretically prevent refracture.⁵⁴ An in vitro biomechanical experiment supports this.³ However, clinical research results are inconsistent, and a meta-analysis suggests that prophylactic cementation is not adequate for the reduction of adjacent fractures.⁵⁴

Some authors have even suggested that cementation has a protective effect and may reduce the rate of adjacent fractures through restoring or maintaining sagittal balance, and preserving the physiological mechanical loading of the vertebral endplates.²⁰

Sandwich vertebra

In patients requiring cementation of multiple vertebral fractures we may encounter a sandwich vertebra, an intact vertebra sandwiched between two cemented vertebrae. A retrospective study of patients undergoing vertebroplasty/kyphoplasty analysed 127 patients with 128 fractures meeting sandwich vertebra criteria. Of the sandwich vertebra patients, 21.3% developed a compression fracture, half of them during the first year of follow-up.⁵ Another study found similar incidences of fracture in sandwich vertebrae (23.4%).⁵³

Prophylactic cementation of sandwich vertebra is a technique recommended by some authors, while others conclude that this procedure does not reduce the risk of recurrence.

It may therefore be appropriate to assess the individual risk of each patient.

Mortality

There is a significant increase in the mortality rate in patients with conservatively treated vertebral fractures compared to age-matched peers in the literature.⁵⁵ The excess mortality risk after VCF ranges from 2% to 42% at 12 months.¹

In an analysis of the US Medicare population (97,142 patients with VCF, 428,956 controls), mortality for patients with VCF was twice that of matched controls.

The 3- and 5-year mortality rates for patients with VCF were 46% and 69%, respectively, compared to 22% and 36% for matched controls.⁵⁶ Some studies suggest that the risk of mortality appears to be higher in men than in women.⁵⁶ Age is also an important risk factor. The relative risk of death is higher in younger individuals and decreases in both sexes with age.

Vertebral augmentation reduces in-hospital and long-term mortality after VCF compared to conservative treatment. The observed reduction may be associated with improved lung function in these patients.²⁷

In an analysis of 5766 hospital admissions for non-neoplastic VCF, kyphoplasty halved the in-hospital mortality rate (OR: .52, $p = .003$).⁵⁷ In another analysis of 1,038,956 vertebral fractures, 75,364 patients treated with vertebroplasty and 141,343 treated with kyphoplasty were identified.²⁷ In the subgroup with osteoporotic VCF treated conservatively, the risk of mortality was significantly higher compared to kyphoplasty and vertebroplasty; kyphoplasty had a 17% survival benefit compared to vertebroplasty.

The results at 4 years show that patients with VCF in the Medicare population treated with kyphoplasty and vertebroplasty experienced lower mortality than patients with VCF who received conservative treatment.²⁷

Mortality in relation to cement insertion has been reported in the orthopaedic literature in cases of arthroplasty, and one case after vertebroplasty, and four cases of pulmonary embolism, one fatal, have also been reported after the procedure.²⁴

A review of the Food and Drug Administration Manufacturer and User Facility Device Experience (MAUDE) has revealed five deaths attributed to PMMA allergy in more than 200,000 procedures.⁵⁸

Conclusions

Based on the latest scientific evidence regarding the treatment of osteoporotic vertebral fractures we can conclude:

1. The most common indication for vertebral cementation for VCF includes osteoporotic vertebral fracture of more than 3–4 weeks refractory to medical treatment and Kummel's disease.
2. If the goal is reduction of the vertebral body and its full restoration, similar to other joint fractures, early treatment is highly recommended.

3. Kyphoplasty and vertebroplasty provide better results than non-surgical treatment in terms of pain intensity and disability.
4. There are no differences in back pain or disability scores between vertebroplasty and kyphoplasty. Differences in favour of kyphoplasty are found with regard to correction of the kyphotic angle, volume of cement injected, and cement leakage.
5. Despite a higher initial cost of kyphoplasty, vertebroplasty is less cost-effective due to higher use of medical resources in the postoperative period in the 2 years after surgery.
6. Kyphoplasty can be considered a therapeutic option in the treatment of AO type 1 and type A3 fractures.
7. Clinical guidelines suggest cementation after a minimum of 6 weeks from the onset of pain, or between 3 and 6 weeks when progressive collapse is detected. Any VCF greater than 3 months is considered chronic, and cementation should only be proposed when accompanied by cavitation or bone oedema.
8. Considering aspects such as operative time, cement volume, and radiation dose, a unipedicular approach reduces operating time, limits exposure to X-rays, and reduces the risk of cement leakage.
9. There is no consensus on the maximum number of vertebrae that can be cemented in one session, although guidelines suggest treating no more than three levels. Treatment of more than six levels or 25–30 ml of cement per session is not recommended.
10. Cement volume has a positive correlation with cement leakage. From 4 ml to 6 ml of bone cement is the amount needed to restore the biomechanics of the vertebral body.
11. The rate of cement leakage is 82% of cementations. Most are clinically asymptomatic, but serious complications can occur in 3.9–7.5% of patients.
12. Higher incidences of cement leakage may be observed with cortical breakage, use of low viscosity cement, larger volume injections, increased severity of vertebral fracture, or early application of cement that has not reached its optimum viscosity.
13. The natural history of osteoporotic vertebral fractures suggests that the incidence of subsequent new vertebral fractures is 19.2%. No differences have been found between conservative management and vertebroplasty cohorts. Intradiscal cement leakage increases the incidence of new vertebral fractures.
14. Compression fractures occur in 21.3% of patients with sandwich vertebra, half of them during the first year of follow-up. Prophylactic cementation of sandwich vertebra is a technique recommended by some authors, while others conclude that this procedure does not reduce the risk of recurrence.
15. Spinal augmentation reduces in-hospital and long-term mortality after VCF compared to conservative treatment.

Level of evidence

Level of evidence I.

Ethical considerations

1. Did your work involve animal testing? No
2. Did your work involve patients or human subjects? No
3. Did your work involve a clinical trial? No
4. Are all the data shown in the figures and tables included in the manuscript given in the results and conclusions?
Yes

Funding

No specific support from public sector agencies, commercial sector, or not-for-profit organisations was received for this research study.

Conflict of interest

The authors have no conflict of interest to declare.

References

1. Chandra RV, Maingard J, Asadi H, Slater L-A, Mazwi T-L, Marcia S, et al. Vertebroplasty and kyphoplasty for osteoporotic vertebral fractures: what are the latest data? *Am J Neuroradiol*. 2018;39:798–806, <http://dx.doi.org/10.3174/ajnr.a5458>.
2. Amans MR, Carter NS, Chandra RV, Shah V, Hirsch JA. Vertebral augmentation. In: *Handbook of clinical neurology*. Elsevier B.V.; 2021. p. 379–94.
3. Aquarius R, Homminga J, Hosman AJF, Verdonchot N, Tanck E. Prophylactic vertebroplasty can decrease the fracture risk of adjacent vertebrae: an in vitro cadaveric study. *Med Eng Phys*. 2014;36:944–8, <http://dx.doi.org/10.1016/j.medengphys.2014.03.009>.
4. Long Y, Yi W, Yang D. Advances in vertebral augmentation systems for osteoporotic vertebral compression fractures. *Pain Res Manag*. 2020;2020:1–9, <http://dx.doi.org/10.1155/2020/3947368>.
5. Chiu PY, Kao FC, Hsieh MK, Tsai TT, Chen WJ, Niu CC, et al. A retrospective analysis in 1347 patients undergoing cement augmentation for osteoporotic vertebral compression fracture: Is the sandwich vertebra at a higher risk of further fracture? *Neurosurgery*. 2021;88:342–8.
6. Filippiadis DK, Marcia S, Masala S, Deschamps F, Kelekis A. Percutaneous vertebroplasty and kyphoplasty: current status, new developments and old controversies. *Cardiovasc Radiol*. 2017;40:1815–23.
7. Alvarez L, Alcaraz M, Pérez-Higueras A, Granizo JJ, de Miguel I, Rossi RE, et al. Percutaneous vertebroplasty: functional improvement in patients with osteoporotic compression fractures. *Spine (Phila Pa 1976)*. 2006;31:1113–8.
8. Voormolen MHJ, Mali WPTM, Lohle PNM, Fransen H, Lampmann LEH, van der Graaf Y, et al. Percutaneous vertebroplasty compared with optimal pain medication treatment: short-term clinical outcome of patients with subacute or chronic painful osteoporotic vertebral compression fractures. The VER-TOS study. *Am J Neuroradiol*. 2007;28:555.
9. Buchbinder R, Osborne RH, Ebeling PR, Wark JD, Mitchell P, Wriedt C, et al. A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures. *N Engl J Med*. 2009;361:557–68.
10. Kallmes DF, Comstock BA, Heagerty PJ, Turner JA, Wilson DJ, Diamond TH, et al. A randomized trial of vertebroplasty for osteoporotic spinal fractures. *N Engl J Med*. 2009;361:569–79.
11. Espahbodinea S, Ku JC, Alves Junr AC, Singh RJ, Deshmukh AS, Chavda V, et al. Percutaneous vertebral augmentation—pearls and pitfalls. *J Spine Surg*. 2023;9:13–6.
12. Clark W, Bird P, Gonski P, Diamond TH, Smerdely P, McNeil HP, et al. Safety and efficacy of vertebroplasty for acute painful osteoporotic fractures (VAPOUR): a multicentre, randomised, double-blind, placebo-controlled trial. *Lancet*. 2016;388:1408.
13. Dohm M, Black CM, Dacre A, Tillman JB, Fueredi G. A randomized trial comparing balloon kyphoplasty and vertebroplasty for vertebral compression fractures due to osteoporosis. *Am J Neuroradiol*. 2014;35:2227–36, <http://dx.doi.org/10.3174/ajnr>.
14. Anderson PA, Froysheter AB, Tontz WL Jr. Meta-analysis of vertebral augmentation compared with conservative treatment for osteoporotic spinal fractures. *J Bone Miner Res*. 2013;28:372–82, <http://dx.doi.org/10.1002/jbmr.1762>.
15. Moura DL, Gabriel JP. Expandable intravertebral implants: a narrative review on the concept, biomechanics, and outcomes in traumatology. *Cureus*. 2021;13:E17795, <http://dx.doi.org/10.7759/cureus.17795>.
16. Vanni D, Galzio R, Kazakova A, Pantalone A, Grillea G, Bartolo M, et al. Third-generation percutaneous vertebral augmentation systems. *J Spine Surg*. 2016;2:13–20, <http://dx.doi.org/10.21037/jss.2016.02.01>.
17. Gu CN, Brinjikji W, Evans AJ, Murad MH, Kallmes DF. Outcomes of vertebroplasty compared with kyphoplasty: a systematic review and meta-analysis. *J Neurointerv Surg*. 2016;8:636–42, <http://dx.doi.org/10.1136/neurintsurg-2015-011714>.
18. Zheng Z. Comparison of percutaneous vertebroplasty and balloon kyphoplasty for the treatment of single level vertebral compression fractures: a meta-analysis of the literature. *Pain Physician*. 2015;18:209–22, <http://dx.doi.org/10.36076/ppj/2015.18.209>.
19. Ong KL, Lau E, Kemner JE, Kurtz SM. Two-year cost comparison of vertebroplasty and kyphoplasty for the treatment of vertebral compression fractures: are initial surgical costs misleading? *Osteoporos Int*. 2013;24:1437–45, <http://dx.doi.org/10.1007/s00198-012-2100-0>.
20. Noriega D, Marcia S, Theumann N, Blondel B, Simon A, Hassel F, et al. A prospective, international, randomized, noninferiority study comparing an implantable titanium vertebral augmentation device versus balloon kyphoplasty in the reduction of vertebral compression fractures (SAKOS study). *Spine J*. 2019;19:1782–95, <http://dx.doi.org/10.1016/j.spinee.2019.07.009>.
21. Rodriguez AJ, Fink HA, Mirigian L, Guañabens N, Eastell R, Akesson K, et al. Pain, quality of life, and safety outcomes of kyphoplasty for vertebral compression fractures: report of a task force of the American Society for Bone and Mineral Research. *J Bone Miner Res*. 2017;32:1935–44, <http://dx.doi.org/10.1002/jbmr.3170>.
22. Walter J, Hacıyakupoglu E, Waschke A, Kalff R, Ewald C. Cement leakage as a possible complication of balloon kyphoplasty—is there a difference between osteoporotic compression fractures (AO type A1) and incomplete burst fractures (AO type A3.1)? *Acta Neurochir (Wien)*. 2012;154:313–9, <http://dx.doi.org/10.1007/s00701-011-1239-3>.
23. Noriega DC, Crespo-Sanjuán J, Olan WJ, Hernández-Ramajo R, Bell DP. Treatment of thoracolumbar type a3 fractures using a percutaneous intravertebral expandable titanium implant: long-term follow-up results of a pilot single center study. *Pain Physician*. 2021;24:E631–8.
24. Bhatnagar MK, Mathur SK, Cruz-Oliver E, Cáceres E. Vertebroplastia percutánea para el tratamiento de las fracturas vertebrales por compresión de origen osteoporótico. *Rev Ortop Traumatol*. 2004;48:186–94.
25. Gautam S, Gopal VG, Khuba S, Agarwal A, Muralidharan, Kumar S. Evaluation of the role of vertebral augmentation in chronic vertebral compression fractures: a

- retrospective study. *Intervent Pain Med.* 2023;2:100242, <http://dx.doi.org/10.1016/j.inpm.2023.100242>.
26. Carli D, Venmans A, Lodder P, Donga E, van Oudheusden T, Boukrab I, et al. Vertebroplasty versus active control intervention for chronic osteoporotic vertebral compression fractures: the VERTOS V randomized controlled trial. *Radiology.* 2023;308:e222535, <http://dx.doi.org/10.1148/radiol.222535>.
27. Edidin AA, Ong KL, Lau E, Kurtz SM. Morbidity and mortality after vertebral fractures: comparison of vertebral augmentation and nonoperative management in the Medicare population. *Spine (Phila Pa 1976).* 2015;40:1228–41, <http://dx.doi.org/10.1097/brs>.
28. Lavanga A, Guarnieri G, Muto M. Medical therapy and multilevel vertebroplasty in osteoporosis: when and why. *Neuroradiol J.* 2010;23:244–8, <http://dx.doi.org/10.1177/197140091002300215>.
29. Hochmuth K, Proschek D, Schwarz W, Mack M, Kurth AA, Vogl TJ. Percutaneous vertebroplasty in the therapy of osteoporotic vertebral compression fractures: a critical review. *Eur Radiol.* 2006;16:998–1004, <http://dx.doi.org/10.1007/s00330-005-0067-3>.
30. Zidan I, Fayed AA, Elwany A. Multilevel percutaneous vertebroplasty (more than three levels) in the management of osteoporotic fractures. *J Korean Neurosurg Soc.* 2018;61:700–6, <http://dx.doi.org/10.3340/jkns.2017.0253>.
31. Heini PF, Orler R. Vertebroplastik bei hochgradiger Osteoporose. *Orthopade.* 2004;33:22–30, <http://dx.doi.org/10.1007/s00132-003-0574-3>.
32. Mailli L, Filippiadis DK, Brountzos EN, Alexopoulou E, Kelekis N, Kelekis A. Clinical outcome and safety of multilevel vertebroplasty: clinical experience and results. *Cardiovasc Radiol.* 2013;36:183–91, <http://dx.doi.org/10.1007/s00270-012-0379-z>.
33. Martinčič D, Brojan M, Kosel F, Štern D, Vrtovec T, Antolič V, et al. Minimum cement volume for vertebroplasty. *Int Orthop.* 2015;39:727–33.
34. Chen W, Xie W, Xiao Z, Chen H, Jin D, Ding J. Incidence of cement leakage between unilateral and bilateral percutaneous vertebral augmentation for osteoporotic vertebral compression fractures: a meta-analysis of randomized controlled trials. *World Neurosurg.* 2019;122:342–8, <http://dx.doi.org/10.1016/j.wneu.2018.10>.
35. Röder C, Boszczyk B, Perler G, Aghayev E, Külling F, Maestretti G. Cement volume is the most important modifiable predictor for pain relief in BKP: results from SWISSspine, a nationwide registry. *Eur Spine J.* 2013;22:2241–8, <http://dx.doi.org/10.1007/s00586-013-2869-3>.
36. Wang M, Zhang L, Fu Z, Wang H, Wu Y. Selections of bone cement viscosity and volume in percutaneous vertebroplasty: a retrospective cohort study. *World Neurosurg.* 2021;150:e218–e227, <http://dx.doi.org/10.1016/j.wneu.2021.02>.
37. Chen X-S, Jiang J-M, Sun P-D, Zhang Z-F, Ren H-L. How the clinical dosage of bone cement biomechanically affects adjacent vertebrae. *J Orthop Surg Res.* 2020;15:370, <http://dx.doi.org/10.1186/s13018-020-01906-0>.
38. Belkoff SM, Mathis JM, Jasper LE, Deramond H. The biomechanics of vertebroplasty: the effect of cement volume on mechanical behavior. *Spine (Phila Pa 1976).* 2001;26:1537–41, <http://dx.doi.org/10.1097/00007632-200107150-00007>.
39. Rotter R, Schmitt L, Gierer P, Schmitz K-P, Noriega D, Mittlmeier T, et al. Minimum cement volume required in vertebral body augmentation—a biomechanical study comparing the permanent SpineJack device and balloon kyphoplasty in traumatic fracture. *Clin Biomech (Bristol, Avon).* 2015;30:720–5, <http://dx.doi.org/10.1016/j.clinbiomech.2015.04.015>.
40. Martin DJ, Rad AE, Kallmes DF. Prevalence of extravertebral cement leakage after vertebroplasty: procedural documentation versus CT detection. *Acta Radiol.* 2012;53:569–72, <http://dx.doi.org/10.1258/ar.2012.120222>.
41. Lin EP, Ekholm S, Hiwatashi A, Westesson PL. Vertebroplasty: cement leakage into the disc increases the risk of new fracture of adjacent vertebral body. *Am J Neuroradiol.* 2004;25:175–80 <https://pubmed.ncbi.nlm.nih.gov/14970015/>
42. Frankel BM, Monroe T, Wang C. Percutaneous vertebral augmentation: an elevation in adjacent-level fracture risk in kyphoplasty as compared with vertebroplasty. *Spine J.* 2007;7:575–82, <http://dx.doi.org/10.1016/j.spinee.2006.10.020>.
43. Zhan Y, Jiang J, Liao H, Tan H, Yang K. Risk factors for cement leakage after vertebroplasty or kyphoplasty: a meta-analysis of published evidence. *World Neurosurg.* 2017;101:633–42, <http://dx.doi.org/10.1016/j.wneu.2017.01.124>.
44. Xie W, Jin D, Ma H, Ding J, Xu J, Zhang S, et al. Cement leakage in percutaneous vertebral augmentation for osteoporotic vertebral compression fractures: analysis of risk factors. *Clin Spine Surg.* 2016;29:E171–6, <http://dx.doi.org/10.1097/bsd.0000000000000229>.
45. Barriga-Martín A, Romero-Muñoz LM, Peral-Alarma M, Florensa-Vila J, Guimbard-Pérez JH. Relación entre el volumen de cemento inyectado y el volumen vertebral en el resultado clínico y en la aparición de fugas tras vertebroplastia percutánea. *Rev Esp Cir Ortop Traumatol.* 2023;67:181–7, <http://dx.doi.org/10.1016/j.recot.2022.10.021>.
46. Tomé-Bermejo F, Piñera AR, Duran-Álvarez C, Román BL-S, Mahillo I, Alvarez L, et al. Identification of risk factors for the occurrence of cement leakage during percutaneous vertebroplasty for painful osteoporotic or malignant vertebral fracture. *Spine (Phila Pa 1976).* 2014;39:E693–700, <http://dx.doi.org/10.1097/brs.0000000000000294>.
47. Cao J, Kong L, Meng F, Zhang Y, Shen Y. Risk factors for new vertebral compression fractures after vertebroplasty: a meta-analysis. *ANZ J Surg.* 2016;86:549–54, <http://dx.doi.org/10.1111/ans.13428>.
48. Zhang T, Wang Y, Zhang P, Xue F, Zhang D, Jiang B. What are the risk factors for adjacent vertebral fracture after vertebral augmentation? A meta-analysis of published studies. *Global Spine J.* 2022;12:130–41, <http://dx.doi.org/10.1177/2192568220978223>.
49. Lindsay R. Risk of new vertebral fracture in the year following a fracture. *JAMA.* 2001;285:320, <http://dx.doi.org/10.1001/jama.285.3.320>.
50. Staples MP, Howe BM, Ringler MD, Mitchell P, Wriedt CHR, Wark JD, et al. New vertebral fractures after vertebroplasty: 2-year results from a randomised controlled trial. *Arch Osteoporos.* 2015;10:229, <http://dx.doi.org/10.1007/s11657-015-0229-0>.
51. Shi M-M, Cai X-Z, Lin T, Wang W, Yan S-G. Is there really no benefit of vertebroplasty for osteoporotic vertebral fractures? A meta-analysis. *Clin Orthop Relat Res.* 2012;470:2785–99, <http://dx.doi.org/10.1007/s11999-012-2404-6>.
52. Zhang H, Xu C, Zhang T, Gao Z, Zhang T. Does percutaneous vertebroplasty or balloon kyphoplasty for osteoporotic vertebral compression fractures increase the incidence of new vertebral fractures? A meta-analysis. *Pain Physician.* 2017;20:E13–28.
53. Han S, Jang I-T. Analysis of adjacent fractures after two-level percutaneous vertebroplasty: is the intervening vertebral body prone to re-fracture? *Asian Spine J.* 2018;12:524–32, <http://dx.doi.org/10.4184/asj.2018.12.3.524>.
54. Chen Z, Song C, Lin H, Sun J, Liu W. Does prophylactic vertebral augmentation reduce the refracture rate in osteoporotic vertebral fracture patients: a meta-analysis. *Eur Spine J.* 2021;30:2691–7, <http://dx.doi.org/10.1007/s00586-021-06899-w>.

55. Brigham and womens.org. Available from: <https://www.brighamandwomens.org/assets/bwh/patients-and-families/rehabilitation-services/pdfs/t-spine-vertebral-augmentation.pdf> [consulted 3.4.24].
56. Kanis JA, Oden A, Johnell O, de Laet C, Jonsson B. Excess mortality after hospitalisation for vertebral fracture. *Osteoporos Int*. 2004;15:108–12, <http://dx.doi.org/10.1007/s00198-003-1516-y>.
57. Zampini JM, White AP, McGuire KJ. Comparison of 5766 vertebral compression fractures treated with or without kyphoplasty. *Clin Orthop Relat Res*. 2010;468:1773–80, <http://dx.doi.org/10.1007/s11999-010-1279-7>.
58. Madassery S. Vertebral compression fractures: evaluation and management. *Semin Intervent Radiol*. 2020;37:214–9, <http://dx.doi.org/10.1055/s-0040-1709208>.