Vertebroplasty and balloon kyphoplasty in osteoporosis: friends or foes?

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Summary

Osteoporotic vertebral fractures are a common cause of pain and disability and increased mortality in western countries. We have analyzed three studies about Vertebroplasty and Balloon Kyphoplasty that have been recently published. We discuss potential complications, results of each technique, and whether the long-term outcome is similar in patients treated with Vertebroplasty and Balloon Kyphoplasty and non-surgical treatment, to decide the correct use of these minimally invasive techniques and for such patients.

KEY WORDS: balloon kyphoplasty, vertebroplasty, vertebral compression fractures, osteoporosis, mobility osteoporosis, functional outcomes.

Introduction

Osteoporotic vertebral fractures are a common cause of pain and disability and increased mortality (1). Approximately 750,000 new vertebral fractures occur in the United States each year (2) and among adults over the age of 50, up to a quarter of them will have at least one vertebral fracture in their lifetime (3). Every year about 1.4 million vertebral compression fractures come to clinical attention worldwide (4). The pain generally subsides in weeks to months as a fracture heals (5). Sometimes, despite non-surgical management, including analgesia, bed rest, physiotherapy, and back bracing, pain resolves slowly, and can persist (6) and increase in intensity or can become chronic (5) and some require hospitalization, long-term care, or both (7). The resulting vertebral deformity can cause height loss, kyphosis, reduced pulmonary function, and mobility impairment (6, 8). Vertebral fracture is associated with an increased risk of future fractures (9). Therefore, interventions that effectively manage pain and shorten recovery time would be of great benefit (10). Surgical intervention is generally not considered because the potential surgical risks are further exacerbated by the increased age of the individual and the likelihood of comorbidities (11); it is usually reserved for fractures that cause neurological impairment (10). Vertebroplasty (VP) and Balloon Kyphoplasty (BKP) are minimally invasive techniques to stabilize the vertebral body. Both methods allow for the introduction of bone cement into the fracture site (12).

VP and BKP have been advocated as a treatment for painful osteoporotic vertebral fractures (10, 13, 14) and have become routine therapy for osteoporotic vertebral fractures.

Observational studies about VP suggest that there is an immediate and sustained reduction in pain after this procedure (13). Numerous case series and several small, unblinded, nonrandomized, controlled studies have suggested the effectiveness of VP in relieving pain from osteoporotic fractures (15, 16), but data about VP from high-quality randomized, controlled trials are lacking (17). A randomized, open trial (34 patients) (18) and two quasi-experimental, open, controlled, before-after studies suggest the efficacy of VP comparing VP with conservative treatment (19, 20). Each study showed an early benefit of VP, but the lack of a true sham control and the lack of blinding raise concern that the observed benefits reflected a placebo response, an effect that may be magnified with an invasive procedure (21). There are also several uncontrolled studies suggesting that VP may increase the risk of subsequent vertebral fractures, particularly in vertebrae adjacent to treated levels, sometimes after cement has leaked into the adjacent disk (22). Controlled studies have shown conflicting results (19, 20), therefore currently, there are insufficient data to value the true risk of subsequent vertebral fracture after VP (22). BKP is a minimally invasive procedure that is able to reduce pain, vertebral deformity, and disability (10). Balloon inflation compacts the cancellous bone and pushes the endplates apart, which might partly restore height and correct angular deformity (23). Once the balloons have been removed, the resulting void is filled with viscous bone cement to stabilise the vertebral body (10). The procedure can be done under general anaesthesia or conscious sedation, either as a day case, or with an overnight stay, dependent on medical need (10). Although studies have reported improved function and reduced pain after BKP treatment, (24-26) there are no data from randomised trials valuating its efficacy and safety (10). We have analyzed three studies about VP and BKP that have been recently published:

1) "A Randomized Trial of Vertebroplasty for Painful Osteoporotic Vertebral Fractures. Rachelle Buchbinder, Ph.D., Richard H. Osborne, et al. (NEJM august 6, 2009 Vol 361. No. 6)". A multicenter, randomized, double-blind, placebo-controlled trial in which participants with one or two painful osteoporotic vertebral fractures that were of less than 12 months' duration and unhealed, were randomly assigned to undergo VP or a sham procedure.
2) "A Randomized Trial of Vertebroplasty for Osteoporotic Spinal Fractures. David F. Kallmes, M.D., et al. (NEJM 361;6 nejm.org august 6, 2009)": A randomized, controlled trial, called the Investigational Vertebroplasty Safety and Efficacy Trial (INVEST), they evaluated the efficacy of PMMA infusion in VP for patients with painful osteoporotic compression fractures at 1 month, as compared with a simulated procedure without PMMA.
3) "Efficacy and safety of Balloon kyphoplasty compared with

non-surgical care for vertebral compression fracture (FREE): a randomised controlled trial. Douglas Wardlaw, et al. (www.thelancet.com Vol 373 March 21, 2009)". They compared the efficacy and safety of BKP with non-surgical management for the treatment of acute vertebral compression fractures, to test the hypothesis that BKP would result in increased improvement in quality of life.

Technique of vertebroplasty

The procedure was performed using single-plane fluoroscopy or biplane monitoring, CT fluoroscopy, a combination of CT and single-plane fluoroscopy decreases procedure time and allows an accurate visualization of the needle position and cement distribution (27). VP can be performed under local anaesthesia in almost all patients, therefore, patients affected by cardiopulmonary diseases or suffering from other risk factors non-compatible with general anaesthesia can be treated (28). General anaesthesia is necessary only in patients undergoing multiple-level VP or unable to stay still during the treatment under local anaesthesia (28, 29). VP is performed with the patient in a prone position with bolsters under the sternum and pelvis to reduce kyphosis at the fractured vertebra (30). Prepared polymethylmethacrylate (PMMA) (approximately 3 ml) is slowly injected into the vertebral body, and satisfactory infiltration of the vertebral body is confirmed radiographically (17). An extrapedicular or a transpedicular approach can be used to enter the vertebral body (31). The access path depends on the level to be treated. For lumbar vertebrae and lower thoracic spine treatment is preferred transpedicular approach, while in the mid and upper thoracic spine an extrapedicular, intercostovertebral access is suggested (32, 33). VP can be performed by unipedicular or bipedicular approaches. There are evidences that a unipedicular access when the needle tip is positioned in the anterior third of the vertebra across the midline is sufficient for a homogeneous cement distribution within the central part of the vertebra (34-36).
An angiographic analysis of the vertebral venous system before cement introduction has been suggested to identify potential routes of venous cement extravasation (28, 37). However, some authors recommend venography only for hypervascularized lesions (28, 37). The cement flow changes over the time and it should be used during its tooth-paste like phase to reduce the possible extravasation in the surrounding tissue (38). Effectively, viscosity of the cement seems to be the key factor for reducing the risk of PMMA cement leakage and it should be adapted to the degree of osteoporosis encountered in each patient (38). It is extremely important to inject the barium-impregnated cement under live fluoroscopy or while using multiple single-frame fluoroscopic views (38). If it occurs, the extravasation of the cement from the vertebral body, particularly in the posterior part of the vertebral body next to the spinal canal, the procedure must be immediately halted and the situation assessed (38). A certain degree of cement extrusion from the vertebra can be tolerated without any deleterious effects for the patient, but there have been reported cases in which cement extrusion has caused neurological damage (39). The cement injection can be stopped when the anterior two third of the vertebral body are filled and the cement is homogenously distributed between both endplates (40, 31). No data are reported on the cement volume that is necessary for good results about stiffness and reduction of complaints. However, it has been shown that 2,5-4 ml of cement provides good filling of the vertebra and it is sufficient for consolidation and pain relief (41). The introduced cement reaches its definitive strength after about two hours from the intervention (32). Neurological and pulmonary function should be monitored and an increase of pain or other acute changes should be immediately evaluated to prevent complications or extravasations of the cement into spinal canal (32). The administration of anti-inflammatory drugs for 2-4 days can be useful to reduce possible inflammatory status due to the heat during PMMA polymerization (40). The antibiotic administration is indicated similar to open bone surgery that requires PMMA implant, particularly in patients with immune disease (40).

Technique of kyphoplasty

BKP uses inflatable bone tamps to restore the vertebrae structure (42, 43). BKP begins with prone positioning on a radiolucent table with bolsters and by using biplanar fluoroscopy guide (anteroposterior and laterolateral projection) to execute a safe procedure and to introduce the cannula through a minimal skin incision into vertebral pedicle and body (42, 43). The entry into the vertebral body is performed using an extrapedicular or transpedicular approach (44). Unlike VP, however, after the cannula is appropriately placed in the vertebral body, a hand drill is placed through the cannula with the goal to create a channel through which the balloons can be inserted into medullary space (44). Always with fluoroscopic guide the manual drill is used to penetrate the vertebral body and the penetration is stopped at a distance of 2-5 mm from the anterior vertebral wall (45), the manual drill is then removed and the inflatable balloons are inserted into the cannula and then connected to the contrast pre-filled syringe (45). The balloons are placed in the cavity and inflated using a manometer with a digital pressure gauge (45). The balloons contain saline solution with barium in order it may be visualized under fluoroscopy as it is inflated (45). It is recommended to inflate the balloons under live fluoroscopy to ensure that they correctly reduce the fracture and don't damage the vertebral end plate (45). After the tip of the balloons are fluoroscopically checked, they are slowly inflated in 20-50 PSI steps under radiological guide until the normal height of the vertebral body is restored or the maximal inflation volume of the balloons is reached (45). After a correct inflation the balloon(s) are removed and PMMA pre-filled cannulas are inserted into the working cannulas (45). When two balloons are to be used, most surgeons first place them both and then inflate them at the same time or alternatively ("back-and-forth") to prevent "herniation" of the first balloon to the controlateral side, thus preventing ideal placement of the second balloon (45). The consistency of the cement used for BKP is different than that for VP. For VP, the cement must be in a more liquefied state to permeate and spread into the vertebral cancellous bone, whereas for BKP, it can be in a more viscous or "doughy" state because it is deposited in a cavity created by the balloon (45). When a cement leak (out of the intended cavity) is detected, the deposition should be stopped immediately and the cement allowed hardening for 1 to 2 minutes before slowly depositing it again under live fluoroscopic guidance (45).

Trials

1) The New England Journal of Medicine published a study of a randomized trial of vertebroplasty for painful osteoporotic vertebral fractures in august 2009 (17). The authors Rachelle Buchbinder et al. performed a multicenter, randomized, double-blind, placebo-controlled trial in which participants with one or two painful osteoporotic vertebral fractures were randomly assigned to undergo VP or a sham procedure (17). Inclusion criteria were the presence of back pain of no more than 12 months' duration and the presence of one or two recent vertebral fractures, defined as vertebral collapse of grade 1 or high-

er according to the grading system of Genant et al. (46) and edema, a fracture line, or both within the vertebral body on magnetic resonance imaging (MRI) (47). The presence of bone marrow edema indicates an acute fracture (48).

The objective of this study was to determine the short-term efficacy and safety of VP for reducing pain and improving function and mobility (17). A 2-year follow-up period was planned and outcomes were assessed at 1 week and at 1, 3, and 6 months, the primary outcome was overall pain at 3 months (17). A total of 71 participants (91%) (35 of 38 in the VP group and 36 of 40 in the placebo group) completed the 6-month follow-up (17). The baseline characteristics of the participants were similar in the two groups (17).

In the VP group, the mean (±SD) volume of cement injected in the vertebrae was 2.8 ± 1.2 ml, and minimal leakage was recorded in the case of 14 participants (37%) (17).

The primary outcome was the score for overall pain (over the course of the previous week) as measured on a scale of 0 to 10 at 3 months (49, 50) (Table I). Secondary outcomes included quality of life, measured with the use of the Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO), a 41-item vertebral- fracture–specific and osteoporosis-specific questionnaire (51); the Assessment of Quality of Life (AQoL) questionnaire, (52), and the European Quality of Life-5 Dimensions (EQ-5D) scale (53). Other secondary outcomes included the scores for pain at rest and pain in bed at night and the score on a modified (49)-item version of the Roland-Morris Disability Questionnaire (54). Perceived recovery with respect to pain, fatigue, and overall health was measured on 7-point ordinal scales ranging from “a great deal worse” to “a great deal better.” Adverse events, including incident clinical fractures, were assessed at each time point with the use of open-ended questions (17).

There were significant reductions in overall pain (pain at night and at rest) and similar improvements in physical functioning, quality of life, and perceived improvement in both study groups, therefore VP did not resulted in significant advantage in any measured outcomes at any time point (17). There is only exception for the total QUALEFFO score at 1 week, which favoured the placebo group (17). Use of opioids decreased during follow-up, without significant differences between two groups (17).

Three participants (one in the VP group and two in the placebo group) reported new rib fractures at 1 week (17). Seven incident vertebral fractures (three in the VP group and four in the placebo group) occurred during the 6-month follow-up period (17).

Table I - Outcome Measure 1 Week 1 Month.

Outcome Measure	1 Week			.* 1 Month		
	Change in Vertebroplasty Group	Change in Placebo Group	Adjusted Between-Group Mean Difference (95% CI)	Change in Vertebroplasty Group	Change in Placebo Group	Adjusted Between-Group Mean Difference (95% CI)
Pain score						
Overal	1.5 ± 2.5	2.1 ± 2.8	–0.7 (–1.8 to 0.4)	2.3 ± 2.6	1.7 ± 3.3	0.5 (–0.8 to 1.7)
At rest	0.8 ± 3.0	1.3 ± 3.9	–0.2 (–1.5 to 1.1)	1.4 ± 2.9	1.2 ± 4.0	0.5 (–0.9 to 1.8)
In bed at night	0.9 ± 2.7					
QUALEFFO total score§	–0.5 ± 7.4					
AQoL score	0.0 ± 0.2					
RDQ score‖	1.8 ± 5.0					
EQ–5D score	0.1 ± 0.3					
	Change in Vertebroplasty Group	Change in Placebo Group	Relative Risk (95% CI)	Change in Vertebroplasty Group	Change in Placebo Group	Relative Risk (95% CI)
Perceived pain — no. (%)						
Better	6 (16)	13 (35)	0.5 (0.2 to 1.1)	12 (34)	9 (24)	1.5 (0.7 to 3.0)
No change	26 (70)	23 (62)		21 (60)	20 (53)	
Worse	5 (14)	1 (3)		2 (6)	9 (24)	

Plus–minus values are means ± SD. Values were calculated on the basis of 37 participants in each group at 1 week; 35 in the Vertebroplasty group and 38 in the placebo group at 1 month; 36 and 37 in the two groups, respectively, at 3 months; and 35 and 36 in the two groups, respectively, at 6 months. CI denotes confidence interval.

Pain score: was assessed on a scale of 0 to 10, with higher numbers indicating more pain and with 1.5 as the minimal clinically important difference.

Scores on the Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO) range from 0 to 100, with higher scores indicating worse quality of life.

Scores on the Assessment of Quality of Life (AQoL) questionnaire range from –0.04 to 1.0, with 1 indicating perfect health and 0.06 representing the minimal clinically important difference.

Scores on the Roland-Morris Disability Questionnaire (RDQ) range from 0 to 23, with higher scores indicating worse physical functioning and 2 to 3 points representing the minimal clinically important difference. The values were calculated on the basis of 30 participants in the vertebroplasty group and 29 in the placebo group at each time point.

Scores on the European Quality of Life-5 Dimensions (EQ-5D) questionnaire range from 0 to 1, with 1 indicating perfect health and 0.074 representing the minimal clinically important difference. The values were calculated on the basis of 30 participants in the Vertebroplasty group and 29 in the placebo group at each time point.

The relative risk is for the comparison of ”better” with “no change” or “worse” (with “better” defined a priori as being a successful outcome).

Pain was classified as “better” if the participant indicated that the pain was moderately or a great deal bette.

This study, in contrast to previous studies, was a randomized trial that included a control group undergoing a sham procedure and participants, investigators (other than the interventional radiologists), and outcome assessors were unaware of the intervention assignment and in which no crossover was permitted (17). Moreover, the participants were similar to those enrolled in previous controlled studies (18-20, 54). All participants were required to have bone edema in the affected vertebrae on MRI, a finding that is reported to predict a beneficial response to treatment (48).
In conclusion, this trial showed no significant benefit of VP over a sham procedure during 6 months of follow-up among patients with recent osteoporotic vertebral fractures (17).

2) Recently New England of medicine published an other study about Vertebroplasty for osteoportic spinal fractures. In this multicenter randomized, controlled trial, called the Investigational Vertebroplasty Safety and Efficacy Trial (INVEST), the authors evaluated the efficacy of PMMA infusion in VP for patients with painful osteoporotic compression fractures, as compared with a simulated procedure without PMMA (55). They hypothesized that patients who had undergone VP would report less pain and back pain-related disability at 1 month (the primary outcomes) than those in the control group (55). 131 patients, who had one to three painful osteoporotic vertebral compression fractures, have been randomly assigned to undergo either VP or a simulated procedure without cement (control group). Fractures needed to be less than 1 year old, as indicated by the duration of pain, or by the presence of marrow edema on magnetic resonance imaging or increased vertebral-body uptake on bone scanning, because the fracture duration of up to 1 year is associated with a good response to VP (56).
The primary outcomes, measuring back-pain intensity, were scores on the modified Roland-Morris Disability Questionnaire (RDQ) (on a scale of 0 to 23, with higher scores indicating greater disability) and patients' ratings of average pain intensity during the preceding 24 hours at 1 month (on a scale of 0 to 10, with higher scores indicating more severe pain) (Table II). Patients were allowed to cross over to the other study group after 1 month. Secondary outcomes included scores on the Pain Frequency Index and the Pain Bothersomeness Index (57), the Study of Osteoporotic Fractures-Activities of Daily Living (SOF-ADL) scale (58) and the European Quality of Life-5 Dimensions (EQ-5D) scale28 (a generic health-status measure, reflecting mobility, self-care, activity limitations, pain, and psychological distress); the use of opioid medications; and scores on the Physical Component Summary (PCS) and Mental Component Summary (MCS) subscales of the self-administered Medical Outcomes Study 36-Item Short- Form General Health Survey (SF-36), version 2.29. The PCS valuates limitations in self-care and social, physical, and role activities, pain, and perceived health. The MCS assesses psychological distress and social and role disability.
Sixty-eight patients underwent to vertebroplasties and 63 to simulated procedures. The baseline characteristics were similar in the two groups. Both groups had immediate improvement in disability and pain scores after the intervention and at 1 month there was no significant difference between the VP group and the control group in either the RDQ score (difference, 0.7; 95% confidence interval [CI], −1.3 to 2.8; P = 0.49) or the pain rating (difference, 0.7; 95% CI, −0.3 to 1.7; P = 0.19). At 3 months, there was a higher crossover rate in the control group than in the VP group (43% vs. 12%, P<0.001). Any serious adverse event was found in each group, except that one patient in the VP group had an injury to the theca sac during the procedure, with resultant hospitalization and an other patient in the control group was hospitalized overnight after the procedure with tachycardia and rigors of unknown cause.
Therefore improvements in pain and pain-related disability associated with osteoporotic compression fractures in patients treated with VP were similar to the improvements in a control group.
The limitations of this study are that they allowed crossover at 1 month because both physicians and patients were reluctant to accept a longer period, complicating the interpretation differences in outcomes after 1 month in the two groups. However, there is evidence that nearly all the benefits of vertebral augmentation occur within the first month (59), and in addition, since the half-life of bupivacaine is only 3 hours, any benefit from this drug would have disappeared at 1 month. Second, they did not consider other medical treatments that they received that might have affected their outcomes. Third, the per-

Table II - Primary Outcomes.

	Vertebroplasty Group	Control Group	Treatment Effect (95% CI)	P Value
Measure				
RDQ				
At baseline	16.6 ± 3.8	17.5 ± 4.1		
At 3 days	13.0 ± 5.2	12.5 ± 5.5	−0.9 (−2.7 to 0.8)	0.30
At 14 days	12.4 ± 5.8	12.3 ± 5.9	−0.6 (−2.4 to 1.2)	0.35
At 1 mo	12.0 ± 6.3	13.0 ± 6.4	0.7 (−1.3 to 2.8)	0.49
Pain intensità				
At baseline	6.9 ± 2.0	7.2 ± 1.8		
At 3 days	4.2 ± 2.8	3.9 ± 2.9	−0.4 (−1.5 to 0.5)	0.37
At 14 days	4.3 ± 2.9	4.5 ± 2.8	0.1 (−0.8 to 1.1)	0.77
At 1 mo	3.9 ± 2.9	4.6 ± 3.0	0.7 (−0.3 to 1.7)	0.19

Plus-minus values are means ± SD.
Between-group comparisons, *confidence intervals*, and *P values* were calculated with the use of analysis-of-covariance models with adjustment for studygroup assignment, baseline value of the outcome measure, and study center. Negative treatment effects favor the control procedure, and positive treatment effects favor vertebroplasty.
Scores on the Roland-Morris Disability Questionnaire (RDQ) range from 0 to 23, with higher scores indicating more severe disability.
Scores on the pain-intensity scale range from 0 (no pain) to 10 (worst pain).

sistence of pain after VP or fracture healing may indicate causes of the pain other than fracture, a possibility that their baseline imaging excluded to a certain extent but not entirely. Fourth, their previous finding showed that the fracture age is not associated with the response to VP (56) but it remains possible that VP is effective only for fractures of a certain age (60).
In conclusion, at 1 month, it has been shown any significant differences on measures of back-pain intensity, quality of life and functional disability, between patients undergone either a VP or a control intervention (simulated VP without infusion of PMMA).

3) One of the last important studies about BKP was published on The Lancet, it was a randomised controlled trial to assess the efficacy and safety of the kyphoplasty. They enrolled patients with one to three acute vertebral fractures and randomly assigned them to receive BKP treatment (149) or non-surgical care (151). 138 participants in the BKP group and 128 controls completed follow-up at 1 month. The follow-up was obtained at discharge from hospital and at 1, 3, 6, 12 months after the treatment.
The primary endpoint was analyze the difference in change from baseline to 1 month in the short-form (SF)-36 physical component summary (PCS) score (scale 0-100), a validated global quality-of-life measure weighted, between the BKP and control groups (10) (Table III). Quality of life and other efficacy measurements and safety were assessed up to 12 months.
There was not difference on frequency of adverse events between groups. There were only two serious adverse events related to BKP, such as haematoma and urinary tract infection. Other serious adverse events, such as myocardial infarction and pulmonary embolism, were not related to procedure.
Compared with non-surgical management, BKP did not result in a significant increase in new radiographic vertebral fractures at 1 year. In their trial, the rate of subsequent fracture, although most patients used bisphosphonates or other osteoporosis treatments, was numerically higher in the BKP group but was not significantly different from that of controls (61, 62). A probable explanation for this high rate is that patients included in this study had symptomatic vertebral fractures, whereas in other reports, incident fractures were identified morphometrically at baseline (9). The high subsequent fracture rate confirms the importance of osteoporosis treatments, that reduce risk of future fractures in osteoporotic patients who qualify for BKP (10).
This randomised controlled trial evidenced that in patients with acute vertebral fractures, balloon BKP improved quality of life, mobility, function, and pain more rapidly than surgical management, with significant differences in improvement at 1 month (10).The differences of most outcome measures between BKP and control were diminished at 12 months because the non-surgical group improved over time, likely because fracture was healed (10).The limitation of this study was that the intervention was not blinded, which could have contributed to the greater improvements seen in the BKP group (10). On the other hand, other potential biases (e.g., the high frequency of new vertebral fractures similar in both groups) might have decreased the improvements in pain and disability after BKP treatment (10).
In conclusion their findings showed that balloon BKP is an effective and safe treatment for patients with acute painful vertebral fractures (10).

Table III - Adverse events in the Kyphoplasty and non-surgical care groups.

	Kyphoplasty (N=149)	Control (N=151)
Adverse events within 12 months	130	122
Withdrew because of adverse event	1	1
Serious adverse events* within 12 months	58	54
Anaemia	3	1
Back pain	10	10
Cardiovascular and vascular disorders		
Coronary heart disease	7	4
Arrhythmia	2	2
Pulmonary embolism	3	0
Stroke	1	1
Haematoma	1	0
Other	6	5
Infections		
Clostridium infection	1	1
Sepsis	1	2
Urinary tract infection	1	2
Neoplasms/cancer	6	6
Nervous system disorders	3	2
Psychiatric disorders	3	0
Respiratory disorders		
Pneumonia	6	5
Other	5	1
Serious adverse events that resulted in death		
Cardiovascular	5	13
Pneumonia	0	1
Cancer	2	1
Other	2	2

Conclusions

The finding of the lack of VP benefit observed on the study of Buchbinder R et al. agrees with most, but not all, earlier reports (17). In contrast to previous studies, this randomized trial included a control group assigned to a sham procedure, investigators and outcome assessors were unaware of the intervention assignment, whereas the participants were similar to those enrolled in previous controlled studies (18, 20, 54). The results of uncontrolled or poorly controlled studies tend to overestimate the treatment benefit because confuse the favourable natural history of the condition, the tendency for a regression to the mean, and the placebo response to treatment, with the real results of the VP (21, 63). A sample larger than that in their trial will be needed in order for the study to have adequate power to assess the effect of VP on this outcome.
The Investigational Vertebroplasty Safety and Efficacy Trial (INVEST), has shown that at 1 month, improvements in pain and pain-related disability associated with osteoporotic compression fractures were similar among those treated with PMMA infusion in VP and those treated with a simulated procedure without PMMA.
Finally, the study FREE suggests that BKP is an effective and safe procedure for patients with acute vertebral fracture, in fact compared with non-surgical management, balloon BKP resulted in improvements in quality of life, function, mobility, and pain at 1 month; however these differences in improvement diminished by 1 year (10).
These findings suggest that further studies would be necessary to determine whether the long-term outcome is similar in pa-

tients treated with VP and non-surgical treatment, and to decide the correct use of VP and for such patients.

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