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Vertebroplasty and Kyphoplasty: A Systematic Review of 69 Clinical Studies

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Study Design. Systematic literature review.

Objective. To evaluate the safety and efficacy of vertebroplasty and kyphoplasty using the data presented in published clinical studies, with respect to patient pain relief, restoration of mobility and vertebral body height, complication rate, and incidence of new adjacent vertebral fractures.

Summary of Background Data. Vertebroplasty and kyphoplasty have been gaining popularity for treating vertebral fractures. Current reviews provide an overview of the procedures but are not comprehensive and tend to rely heavily on personal experience. This article aimed to compile all available data and evaluate the clinical outcome of the 2 procedures.

Methods. This is a systematic review of all the available data presented in peer-reviewed published clinical trials. The methodological quality of included studies was evaluated, and data were collected targeting specific standard measurements. Where possible, a quantitative aggregation of the data was performed.

Results. A large proportion of subjects had some pain relief, including 87% with vertebroplasty and 92% with kyphoplasty. Vertebral height restoration was possible using kyphoplasty (average 6.6°) and for a subset of patients using vertebroplasty (average 6.6°). Cement leaks occurred for 41% and 9% of treated vertebrae for vertebroplasty and kyphoplasty, respectively. New fractures of adjacent vertebrae occurred for both procedures at rates that are higher than the general osteoporotic population but approximately equivalent to the general osteoporotic population that had a previous vertebral fracture.

Conclusions. The problem with stating definitely that vertebroplasty and kyphoplasty are safe and effective procedures is the lack of comparative, blinded, randomized clinical trials. Standardized evaluative methods should be adopted.

Key words: osteoporotic, vertebral fracture, vertebroplasty, kyphoplasty. **Spine 2006;31:1983–2001**

Osteoporosis is estimated to afflict 200 million women worldwide.[1] A total of 1.5 million new fractures, nearly half of which are vertebral (700,000), are reported in the United States each year, outnumbering fractures of the hip and ankle combined.[2–5] Vertebral fracture may result in pain about the fracture site, loss of height caused by vertebral collapse, spinal instability, and, in many cases, kyphotic deformity.[6] Although some patients respond to the conservative treatment of medications, bracing, and bed rest, many do not. Chronic pain and kyphotic deformity may lead to depression, decreased appetite (leading to poor nutrition), decreased pulmonary function, impaired mobility, and a reduction in the quality of life, the ultimate result being a significant increase in morbidity.[7–11] To relieve chronic pain, bed rest is often the only solution. However, this solution can result in a vicious cycle of increased bone loss caused by inactivity and, correspondingly, increased vertebral fracture risk.[8] Thus, interest has been fostered in percutaneous cement injection methods for fracture stabilization that reduce or eliminate pain, allowing a return to normal activity in a short period of time.

Galibert *et al*[12] first reported vertebroplasty in 1987 for the minimally invasive treatment of hemangiomas, which, since then, has been adapted for use in the treatment of intractable, focal, intense pain localized to a vertebral fracture. Kyphoplasty was introduced in 1998 to restore vertebral body height and help realign the spine, using an inflatable balloon to reduce the fracture before the injection of cement.[8,13] Currently, vertebroplasty and kyphoplasty have been gaining popularity to stabilize vertebral fractures mainly caused by osteoporosis but also including malignant involvement of the spinal column, hemangioma, and vertebral osteonecrosis.[14] There is a need for critical evaluation of the supporting evidence to provide, where possible, a quantitative aggregation of the safety and efficacy of the procedures. A number of reviews of the 2 procedures currently exist.[3,13,15–21] Although they provide an excellent overview of the procedures, they are not comprehensive and tend to rely heavily on personal experience rather than objective assessment. This article will compile the available data presented in peer-reviewed published clinical studies to address the following questions:

1. Does vertebroplasty/kyphoplasty reduce patient pain? How does this compare to conservative treatment? Is pain reduction durable over the long-term?
2. Does vertebroplasty/kyphoplasty restore patient function?
3. Does vertebroplasty/kyphoplasty restore the normal spinal alignment?

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4. What are the complications associated with the procedures?
5. Does the incidence of augmented or adjacent vertebral fracture increase after vertebroplasty/kyphoplasty?
6. Does kyphoplasty offer a significant improvement in terms of restoration of spinal alignment, pain management, and reduction in cement leakage over traditional vertebroplasty?

■ Materials and Methods

To our knowledge, there are no published reports of randomized clinical trials for either vertebroplasty or kyphoplasty, therefore, the search was extended to include nonrandomized clinical trials.[22] No restrictions were placed on the age or gender of the subjects, or the duration, localization, and type of symptoms experienced.

Search Strategy. MEDLINE, Cochrane Library, and ISI Current Contents were searched. No restrictions were placed on language, publication date, or publication type for the initial searches within these databases. Searches were performed in June and November 2004 and repeated in June 2005. For the initial search, the terms "vertebroplasty" and "kyphoplasty" were used because they have been established terms from the inception of the techniques. Specific key words were used to focus the search results on clinical studies, further refined by manual inspection of the abstracts. Articles were excluded from further analysis for reporting no clinical outcomes (*i.e.*, article was a review, editorial, technical, or animal study), involving techniques other than vertebroplasty/kyphoplasty, or if the study was published in a language other than English, German, French, or Spanish. To reduce potential confounding factors, included studies were limited to subject populations that had more than 80% primary or secondary osteoporotic vertebral compression fractures and procedures that used polymethyl methacrylate cement. We tested our search strategy by ensuring that our search results included all the studies identified by previous reviews.[3,13,20,23]

Methodological Evaluation. To date, a standardized method for the evaluation of nonrandomized studies has not been formalized. We used a modified version of the methodological quality assessment proposed by Downs and Black[24] and later modified by MacLehose *et al*,[25] and included recommendations of other investigators (Table 1).[26,31] It contains all the elements recommended by the Agency for Healthcare Research and Quality, Cochrane Collaboration Back Review Group, NSW Department of Health, NHS R&D Health Technology Assessment Programme, and the Ottawa Health Research Institute.[28,30–32] Questions were grouped into the categories: reporting; external validity; internal validity, including bias and confounding; and power (Table 1). Internal validity refers to systematic errors of biases or confounding factors inherent in the study design. External validity refers to how the results provide a correct basis for generalization to other circumstances.[33] At least 2 reviewers reviewed articles. Reviewers gave each element a score of 1 (yes) or 0 (no, unclear). We aimed for consensus, but if necessary, a third reviewer was consulted.

Data Collection. Data were collected for each study under the headings "general information," "participants," "intervention," "outcomes," "complications," and "follow-up." General information included the type of intervention, pathology, and type of study. Participant information was comprised of the age and gender of the subjects, description of symptoms, and drop out during follow-up. Cement type, injected amounts, approach, number of sessions, number of vertebra per session, levels augmented, usage of fluoroscopy, computerized tomography (CT), and venography were all noted under the heading "intervention." Outcome data were collected detailing pain relief, general health, functional improvements, satisfaction with treatment, and reduction in kyphosis. Complications included cement leakage (asymptomatic and symptomatic), neurologic deficits, cardiovascular, pulmonary, and any other clinically relevant complication. Long-term follow-up information was comprised of all the items recorded under the heading "outcome," with the addition of new fracture details. It is noteworthy that studies that did not explicitly state whether cement leakage, complications, or new fractures did or did not occur were not included in totals used to calculate the proportion of subjects/vertebrae that were affected.

Statistics. Statistics were kept to a descriptive level. Comparative data (*i.e.*, differences in VAS) are reported as the difference between the means ±95% confidence level calculated from the standard error of the difference between 2 sample means. Binomial proportional data are expressed as the proportion ± 95% confidence level calculated from the standard error using the normal approximation. The combined mean across multiple studies was weighted according to the number of subjects and is expressed as the combined mean ± the combined 95% confidence level (calculated from the within study variance).

■ Results

Methodological Analysis

The majority of articles reviewed were retrospective in nature, including 37 retrospective, 25 prospective, and 7 study design not reported. The evaluated articles were of varying methodological quality. Mean quality score was 17.6 ± 3.7 standard deviation (SD) (range 9–23.5) of a maximum of 29. The summary of the methodological score for each question is provided in Figure 1. Although descriptive parameters were often reported (question Nos. 1–4, and 9), no study was randomized, and only a few studies had an aspect of the study that was blinded (question Nos. 16 and 26).[34–39] While not specifically targeted in the methodological quality assessment, it was noted that very few studies included a control group.[40,41] Items that were not consistently reported were confounding factors, bias and limitations (question Nos. 5, 7, 24, and 27).

On the whole, the main findings were not clearly described (question No. 4), and results were presented without information on their variability (question No. 8). Follow-up times were assessed with respect to the aim of the study. Remarkably, those studies whose aims were to assess the pain relief and occurrence of new fractures after vertebroplasty and kyphoplasty often had short or no follow-up times (question No. 19). No studies were excluded on the basis of methodological quality because removing articles that scored in the bottom 50% had little effect on outcomes.

Table 1. Methodological Quality Assessment Questions

Question No.	Type	Methodological Question	References
1	R	Is the aim clearly stated and answered by the conclusion?	24–28
2	R	Are the main outcomes to be measured clearly described in the introduction or methods section?	24,25
3	R	Are the characteristics of the patients included in the study clearly described?	24,28
4	R	Are the interventions of interest clearly described in the introduction or methods section?	24,25,28,29
5	R	Are the distributions of principal confounders in each group of subjects to be compared clearly described?	24,28
6	R	Are the main findings of the study clearly described?	24,25,28
7	R	Are the conclusions supported by results with biases and limitations taken into consideration?	28
8	R	Does the study provide estimates of the random variability in the data for the main outcomes?	24,25,28
9	R	Have all important adverse events that may be a consequence of the intervention been reported?	24,25
10	R	Have the characteristics of patients lost to follow-up been described?	24,25,28
11	R	Have actual probability values been reported (*e.g.*, 0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	24,25
12	E	Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	24,30
13	E	Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	24
14	E	Were the staff, places, and facilities where the patients were treated, representative of the treatment the majority of patients receive?	24,25
15	I (bias)	Does the study consist of consecutive patients?	26,28,29
16	I (bias)	Was an attempt made to blind either the subjects to the intervention or blind those measuring the main outcomes of the intervention?	25
17	I (bias)	If any of the results of the study were based on "data dredging," was this made clear?	24–26
18	I (bias)	Are follow-up times the same for all subjects? If not, is this reported or corrected for?	24,25,28
19	I (bias)	Was the follow-up appropriate for the aim of the study?	26,28–30
20	I (bias)	Were the statistical tests used to assess the main outcomes appropriate?	24,25,28,29
21	I (bias)	Were the main outcome measures used accurate (valid and reliable)?	24,25,28
22	I (bias)	Was the funding or sponsorship independent of the intervention procedure?	28
23	I (con)	Were the patients in different intervention groups (trials and cohort studies), or were the cases and controls (case-control studies) recruited from the same population?	24
24	I (con)	Were all the patients at a common point in the course of the disease to which the intervention was to be applied?	29
25	I (con)	Were study subjects in different intervention groups (trials and cohort studies), or were the cases and controls (case-control studies) recruited over the same period of time?	24,25
26	I (con)	Were study subjects randomized to intervention groups?	24,25
27	I (con)	Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	24,28
28	I (con)	Were losses of patients to follow-up taken into account?	24
29	P	Did the study have sufficient power to detect a clinically important effect where the probability value for a difference being due to chance is less than 5%?	24,26,28

There were 2 questions regarding patient characteristics and randomization (question Nos. 3 and 26) subdivided because it was thought that a simple yes/no did not allow enough flexibility, and 1 question, regarding the description of the main finding (question No. 6), was given a score between 0 and 2 because of its perceived importance.[25]
E indicates external validity; I (bias), internal bias; I (con), internal confounding; P, power; R, reporting.

Clinical Details

Studies providing the data for this review are referenced in Table 2. Vertebroplasty studies (12 prospective, 29 retrospective, and 6 unreported) showed the results of 2958 subjects (n = 47 studies), including 1959 females, 676 males, and 323 unreported with a mean age of 72 years (mean range 59–79, n = 45 studies), who underwent 4456 procedures. Kyphoplasty studies (13 prospective, 8 retrospective, and 1 unreported) showed the results of 1288 subjects (n = 22 studies), including 829 females, 403 males, and 56 unreported with a mean age of 72 years (mean range 67.5–75, n = 20 studies), who underwent 1624 procedures. Of vertebroplasty and kyphoplasty procedures, 50% and 60%, respectively, were performed within the thoracolumbar region of the spine (T11–L2 inclusive).

Pain

As shown in Figure 2, a large proportion of subjects had some pain relief independent of the type of procedure: vertebroplasty 87% (n = 1552, 32 studies, 95% confidence interval [CI] 78% to 95%); and kyphoplasty 92% (n = 447, 7 studies, 95% CI 86% to 98%). Visual analog pain scores (VAS) (normalized to 10-point scale) were reduced from an average of 8.2 (n = 666, 12 studies, 95% CI 7.8–8.6) and 7.15 (n = 183, 4 studies, 95% CI 6.6–7.7) to 3.0 (95% CI 2.4–3.6) and 3.4 (95% CI 2.7–4.1) for vertebroplasty and kyphoplasty, respectively (Figure 3). There were 2 studies that showed SF-36 scores for kyphoplasty.[8,97] Body pain scores increased between 22.4 and 47.1 points, while the physical function scores decreased between 17.2 and 29.3 points. The only items that did not have any statistically significant improvement were general health, role emotional, and mental health.

Physical Function

A 16% to 47% full-scale improvement in physical function was reported after vertebroplasty for 7 studies using different variants of a 5-point mobility scale.[10,36,61–64,91] Between 49% and 90% of subjects reported ambulation

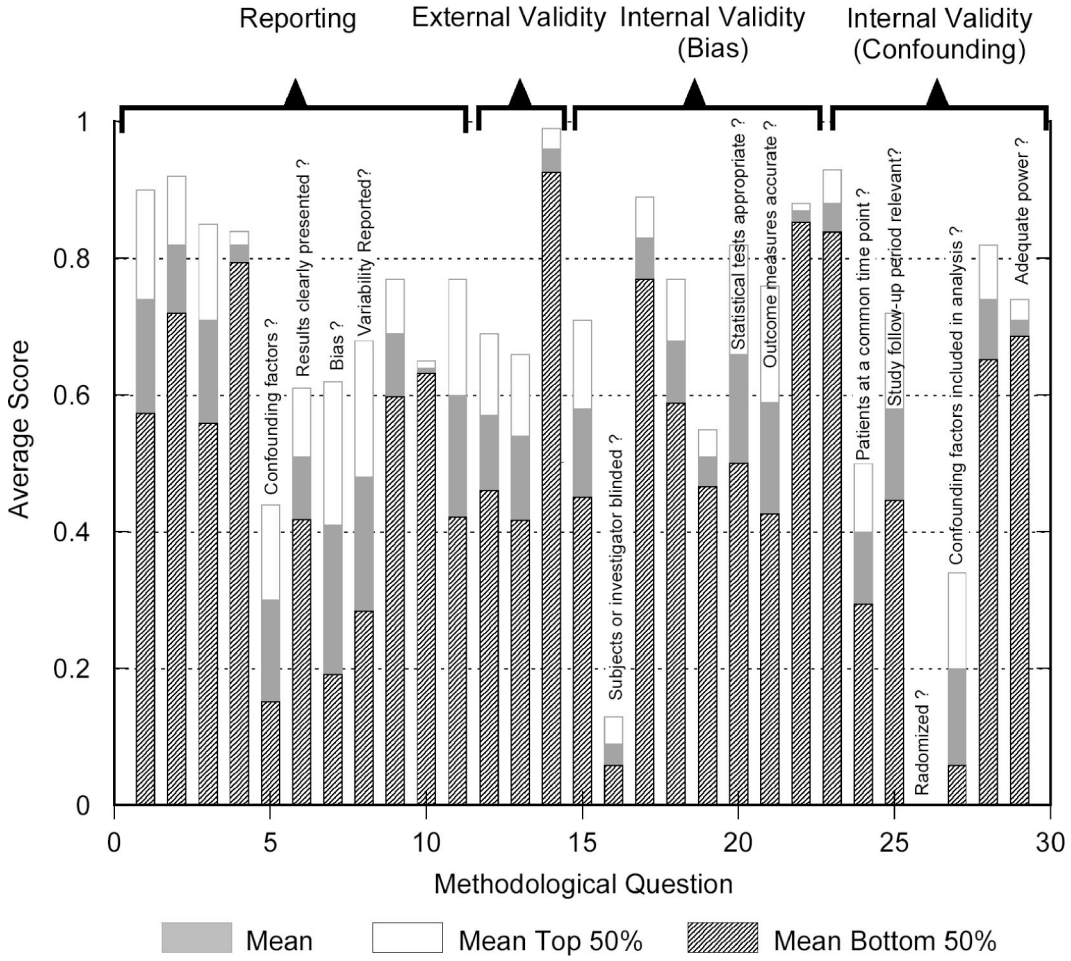

Figure 1. Methodological quality assessment score. Randomized trials were not available, and blinded trials were infrequent. The bars represent the average score for all kyphoplasty and vertebroplasty articles reviewed.

improvements in 4 studies assessed by qualitative patient response.[14,34,35,65] There were 3 studies that showed improvements in physical function using a validated health-related outcome instrument: Nottingham Health Profile[42,43] and Oswestry Disability Index (ODI) (preoperative 61%, postoperative 46%, n = 23 subjects).[44] Two kyphoplasty studies showed improvements in disability (mean ODI preoperative 60%, postopera-

Table 2. References for Clinical Details

Clinical Details	Vertebroplasty Studies Referenced	Kyphoplasty Studies Referenced
Study design		
Prospective	4,14,39,40,42–50	8,41,44,51–60
Retrospective	10,17,34–38,61–82	83–90
Not Reported	91–96	97
Pain relief		
Subjects with some pain relief (%)	17,34–37,42,43,46,47,49,50,61,62,65,66,68–70,72,73,75–81,91,92,94,95,98	8,41,44,51,52,55–60,83,84,87–89,97,99
Pain relief VAS	4,10,36,40,42–44,46–49,61–64,66,70,75,79,80,91,100	8,44,51–53,55,58,83,88,89,99
Mobility	10,14,34–36,43,44,48,50,61–65,73,91,101	44,51
Height restoration		
Height	39,44,45,66,67,76,82,93,96	41,44,51,53,56,59,83,84,88,89,97
Correction of kyphosis	39,44,45,66,67,76,82,92,93	41,44,51–55,83,84,87
Subjects with no increase in height or reduction in kyphosis angle (%)	39,44,45,66,67,82,92,93,96	41,44,51–53,89,97,99
Complications		
Leakage	4,17,34,36,37,39,42–50,66–70,72,74–78,80,91,92,95,101,102	8,41,44,51,52,54–60,83,84,87–89,97,
Leakage location	4,14,17,34,36,37,39,42–50,66,68–70,72,74–78,80,91,92,95,101,102,	8,51,52,55,56,58,60,83,97,99
Procedural *versus* cement complications	4,10,14,17,34,36,37,40,42,49,50,63,68,69,70,74,75,101	8,41,51,54–57,87,88,97,
Serious complications reported	4,10,14,17,34,36,37,39,40,42–45,47–50,61,63,65–70,74–78,80,92,95,101	8,41,51,52,54–57,59,83,84,87–89,97,
New fractures	4,34,40,42,44,46–49,65,68–71,75,95,101	41,51,52,54,56–58,83–86,88

VAS indicates visual analog pain scores.

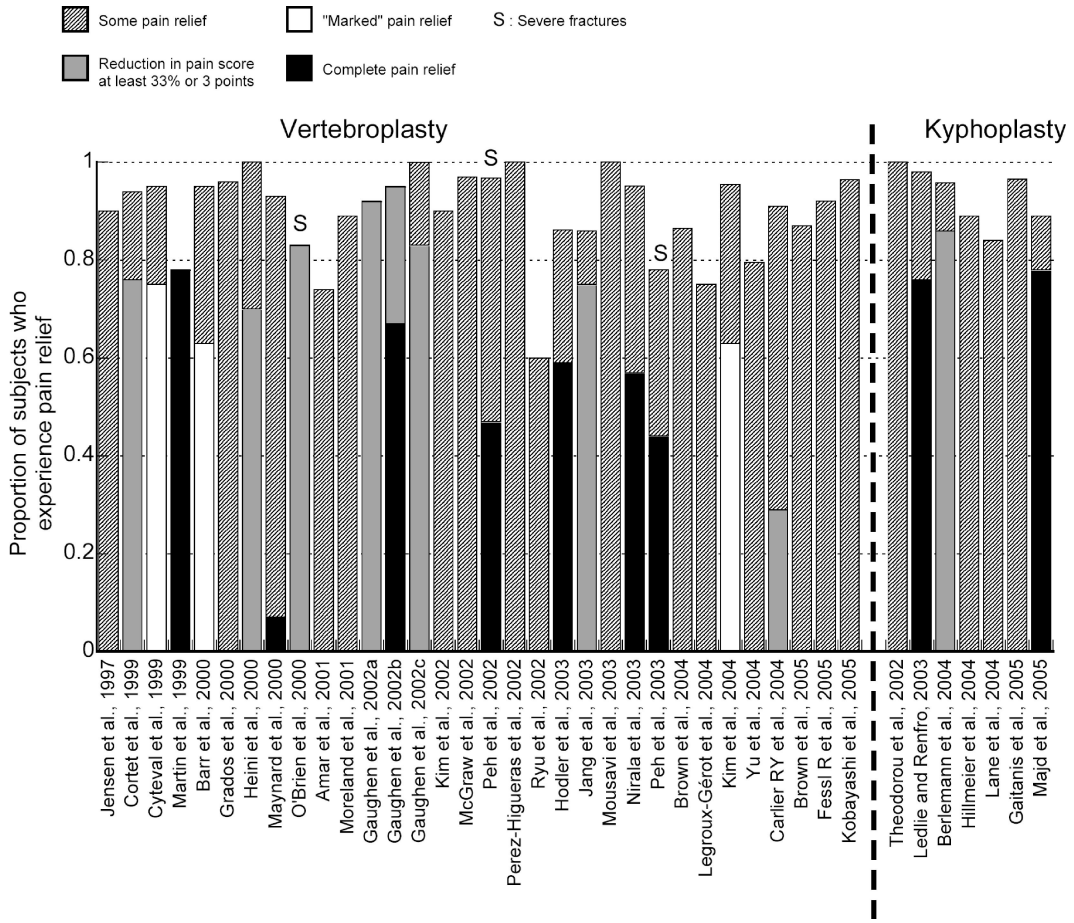

Figure 2. Proportion of subjects who undergo vertebroplasty and kyphoplasty, and have pain relief. Pain relief is illustrated for 4 different methods in which it was reported. "Some pain relief" includes all patients who had a reduction in pain, regardless of the magnitude. Studies that used the descriptor "Marked Pain Relief" did not indicate the magnitude of pain relief experienced. The other 2 methods are self explanatory. Severe fracture is defined as a loss of vertebral height more than 67% of its original height.

tive 32%, n = 77 subjects).[44,51] Reporting improvements in physical function appears to be of secondary importance to the investigators, therefore, measurement scales used are inconsistent, thus scores cannot be pooled.

Kyphosis/Vertebral Height Correction

A qualitative examination of the data presented in Tables 3 and 4 appears to indicate that vertebral height restoration is similar for either procedure, provided a mobile fracture or intravertebral cleft is present. However, few studies considered measurement precision or corrected for magnification error between radiographs (Tables 3, 4). Interstudy comparisons are further complicated by the use of different methods for percentage height restoration and reduction of kyphosis angle calculation.[45] Mean kyphotic angle restoration was 6.6° (n = 335, 4 studies, range 5.0°–8.4°)[66,67,92,93] and 6.6° (n = 505, 9 studies, range 3.4°–9.9°)[51,52–55,83,84,103] for vertebroplasty and kyphoplasty, respectively. Not all subjects had a reduction in kyphotic angle or restoration of height (less than 5° change in kyphotic angle or an increase in height as defined by the investigator). A mean of 34% (n = 404, 9 studies, 95% CI 22% to 46%) and 39% (n = 512, 8 studies, 95% CI 28% to 50%) of kyphoplasty and vertebroplasty interventions, respectively, did not result in an appreciable restoration of height or kyphotic angle.

Complications

Immediate complications associated with vertebroplasty and kyphoplasty can be separated into 2 categories, procedural and cement leakage (ratio 5:14 kyphoplasty, 25:49 vertebroplasty). Reported procedural complications include infection,[63,68,69] fractures of the transverse process, pedicle, sternum and ribs,[10,14,37,40,63,94,97] and respiratory distress caused by the anesthetic.[34,98] Cement leakage occurred in 41% (n = 2283 vertebrae, 27 studies, 95% CI 32% to 50%) of vertebrae during vertebroplasty and 9% (n = 1486 vertebrae, 18 studies, 95% CI 2.6% to 15.8%) of vertebrae during kyphoplasty (Figure 4).

It is noteworthy that mean leakage rate was calculated independent of the measurement method used and patient inclusion criteria. The distribution of leaks was 32% and 11% epidural, 32.5% and 48% paraspinal and 30.5% and 38% intradiscal, 1.7% and 1.5 pulmonary and 3.3% and 1.5 foraminal for vertebroplasty (1081 leakage locations reported, 30 studies) and kyphoplasty

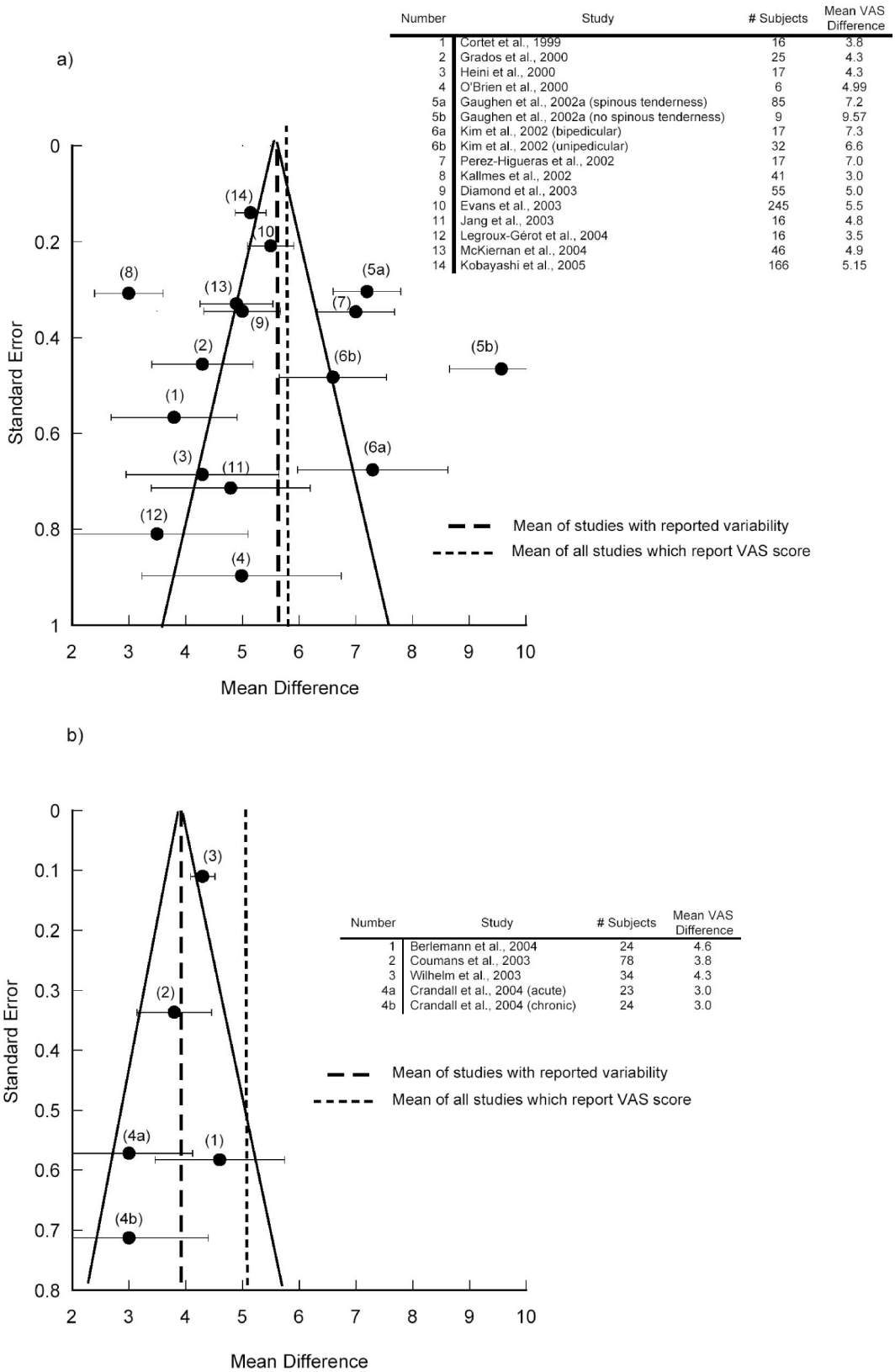

Figure 3. Funnel plots for vertebroplasty (**A**) and kyphoplasty (**B**) VAS difference scores between preoperative and postoperative values. Variability was not provided for all studies. Therefore, 2 means were constructed, one for studies in which variability was reported and another for all studies. The solid line indicates the region in which one would expect 95% of the data to lie within. The kyphoplasty plot shows a symmetrical inverted funnel, indicating a probable lack of publication bias. The same is not true for the vertebroplasty plot. Asymmetry could be caused by publication bias, inadequate methodological quality, or interstudy differences in subject inclusion criteria. VCF indicates vertebral compression fracture.

Table 3. Kyphoplasty–Restoration of Height, Reduction in Kyphosis

Investigator (y), Reported No./ Total No. Subjects	Symptom Duration (range)	Inclusion Criteria (description)	Accuracy (description) Standardization of Radiographic Assessment (description)	Vertebrae With no Height Restoration (H) or Kyphosis Correction (K) (%)	Height Restoration				Kyphosis Reduction		
					Preop Vertebral Height Lost (mm/% of reference)	Postop Vertebral Height Restored (mm)	% Height Restored Relative to Reference (method 4)	% Height Restored (methods 2 and 3)	Preop Angle (°)	Angle Reduction (°)	Reduction (%)
Lieberman *et al*[97] (2001), 49/70	5.9 mos (0.5–24)	Marrow signal changes (MRI)	Repeatability ± 1.1 mm	33 (H) (Δheight < 1.1 mm)	M/8.7 ± 4.3 M/33% ± 16	M 2.9 ± 2.7 M 4.1*	M 11.2	M 35 (3) M 46.8* (3)	—	—	—
Theodorou *et al*[84] (2002), 24/24	3.27 mos (0.5–11)	Acute fracture (MRI)	None	—	A 7†/25% M 7†/28% P 3†/10%	A 3.7 M 4.7 P 1.5	A 13† M 19† P 5†	A 17.6† (2) M 26.1† (2) P 5.8† (2) A 52 ± 33.2 (3) M 65.7 ± 36 (3) P 53.4 ± 49 (3)	25.5 ± 10	9.9	38.8†
Darius *et al*[87] (2003), 8/8	—	—	None	—	—	—		—	8.3 †	4.14	50†
Ledlie and Renfro[88] (2003), 36/133	2.4 mos (0–14)	Acute fracture (MRI, CT, bone scan)	None	—	A 33% M 35%	—	A 23 M 25	—	—	—	—
Phillips *et al*[54] (2003), 52/52	3.8 mos (0.9–12.3)	Edema (MRI)	None	42.3 (K)	—	—	—	—	17.5‡ 29.5*	8.8‡ 14.2*	50.2‡ 48.2*
Wilhelm *et al*[55] (2003), 56/56	2.26 mos (0.4–72)	—	None	—	—	—	—	—	11.5‡	5‡	43.5‡
Berlemann *et al*[52] (2004), 27/27	1 d (2–180)	Mostly acute VCF	None	22.2 (K)	—	—	—	—	17 ± 6.6	8 ± 4.7	47.7
Crandall *et al*[53] (2004),									Combined preop standing and preop supine radiographs		
i) 40/40 ii) 46/46	i) <2.5 mos ii) >4 mos	Incomplete fracture healing (MRI)	Intraobserver variability ± 1 mm, ±2°	i) 8 (H) ii) 20 (H) (<10% lost height restored)	43% Height measured at the most compressed point	—	i) 28 ii) 23	i) 66.7 (3) ii) 52 (3)	i) 15 ii) 15	i) 7 ii) 5	i) 47 ii) 33
Hillmeier *et al*[56] (2004), 138/138	—	—	None	—	M 38%	—	M 10†	—	—	—	—
Lane *et al*[59] (2004), 37/37	—	—	None	—	—	—	—	A 51.2 ± 29 (3) M 60.3 ± 29 (3)	—	—	—
Rhyne *et al*[83] (2004), 82/82	1 mos (0.2–27.7)	Edema (MRI)	None	—	—	A 4.6 (0–22) M 3.9 (0–25) P 0.3 (0–21)	—	23 (2) 23 (2) 1 (2)	22.5‡	3.4‡	15.1‡
Gaitanis *et al*[51] (2005), 49/49	4.6 mos	—	None	10 (K) author defined	A 8.4/28% M 9.1/29%	A 4.3 M 4.9	A 14 M 15.7	A 19 (2) M 22 (2) A 51 (3) M 54 (3)	15.8‡	7.9‡	50‡

(*Table continues*)

Table 3. ***Continued***

Investigator (y), Reported No./ Total No. Subjects	Symptom Duration (range)	Inclusion Criteria (description)	Accuracy (description) Standardization of Radiographic Assessment (description)	Vertebrae With no Height Restoration (H) or Kyphosis Correction (K) (%)	Height Restoration				Kyphosis Reduction		
					Preop Vertebral Height Lost (mm/% of reference)	Postop Vertebral Height Restored (mm)	% Height Restored Relative to Reference (method 4)	% Height Restored (methods 2 and 3)	Preop Angle (°)	Angle Reduction (°)	Reduction (%)
Kasperk *et al*[41] (2005), 72/72	>12 mos	—	None	100 (K)	M 41%	—	M 6	M 10 (2) (at 6 mos)	8.7	0	0
Grohs *et al*[44] (2005), 35/35	5 mos	No dynamic mobility	None	46 (K)	20%	—	5.8	—	13	6	46
Feltes *et al*[89] (2005), 20/20	(1–2.5 mos)	—	None	100 (H)	M 34%†	0	0	0	—	—	—
Majd *et al*[57] (2005), 229/360	—	Incomplete fracture healing (MRI)	None	A 37 (H)	A 24%	—	A 7	A 30 (3)	22*	15*	32*
				M 31 (H) <20% restoration of lost height	M 25%		M 10	M 40 (3)		125 of 222 subjects	

All values are expressed as the mean ± SD.
Preoperative (preop) vertebral height loss (%) is defined as the reference vertebral height − fractured vertebral height/reference vertebral height.
No change in kyphosis defined as correction less than 5° between the preoperative and postoperative (postop) angle, or as defined by the specific author(s).
Method 2: Percent height restoration relative to initial fracture height.[45]
Method 3: Percent height restoration relative to lost vertebral height.[45]
Method 4: Percent height restoration relative to reference vertebral height.[45]
*Data reported for those vertebrae in which augmentation resulted in a restoration of vertebral height.
†Value(s) calculated or estimated from the available data.
‡Cobb angle measurement includes a disc, therefore, slight changes in the patient's posture at the time of the lateral radiograph may affect results.
A indicates anterior; M, middle; MRI, magnetic resonance imaging; P, posterior; VCF, vertebral compression fracture.

Table 4. Vertebroplasty–Restoration of Height, Reduction in Kyphosis

Investigator (y), Reported No./Total No. Subjects	Symptom Duration (range)	% IVC, DM	Accuracy (description) Standardization of Radiographic Assessment (description)	% Vertebrae With no Height Restoration (H) or Kyphosis Correction (K)	Height Restoration				Kyphosis Reduction		
					Preop Vertebral Height Lost (mm/% of reference)	Postop Vertebral Height Restored (mm)	% Height Restored Relative to Reference (method 4)	% Height Restored (methods 2 and 3)	Preop Angle (°)	Angle Reduction (°)	Reduction (%)
Jang *et al*[66] (2003), 16/16	10.6 mos (1–36)	100 IVC 100 DM (MRI)	None	31 (K) 0 (H)	—	A 7	—	A 37.3 (2)	13.4 ± 11	8.4 ± 6.8	62.45
Teng *et al*[93] (2003), 73/73	90% <6 mos	53 IVC (x-ray)	Intraobserver and Interobserver Reproducibility, ‡mag	45 (K)	A/51.5% M/52.2% P/20.5%	A 5.1* M 4.5* P 2.1* based on average height of T12	A 16.7 ± 16.7 A 23.9 ± 16.7† M 14.5 ± 13 M 19 ± 14.3† P 7.2 ± 11 P 9.2 ± 11.4†	A 28.9 ± 31.2 (3) A 40.2 ± 24.1† (3) M 26.7 ± 23.7 (3) M 30.6 ± 26† (3)	16 ± 7.3	7.4 ± 6.7	44.1 ± 33.8 55.3 ± 29.9†
Hiwatashi *et al*[96] (2003), 85/85	—	—	Accuracy 1 mm	A 35.3 (H) M 30.6 (H) P 52.3 (H) (defined by author)	A 6 25% M 9 41% P 4 16%	A 2.5 M 2.7 P 1.4	A 10.4 M 12.3 P 5.6	A 13.9 (2) M 20.8 (2) P 6.7 (2) A 41.7 (3) M 30 (3) P 35 (3)	—	—	—
McKiernan *et al*[39,45] (2003), 65/65	3.9 mos	35 IVC 35 DM (MRI)	A 0.4 mm SD M 0.5 mm SD Ka 15.6% ‡mag	64.6 (H) (restoration only observed in 23 DM VCF)	A 12.7/58%§	A 3.1* A 8.4§ M 3.1* M 8.7§ P 1.2* P 3.4§	A 28.6§ M 30.8§ P 9.5§	A 106.3 (2)§ M 97.6 (2)§ P 13.8 (2)§ A 51.7 (3)§ M 58.8 (3)§ P 34.7 (3)§	17.8§	2.54* 7.18§	40§
					Note: reported only results for 23 DM vertebrae. Nonmobile fractures no height gain				Note: reported only results for 23 DM vertebrae. Nonmobile fracture no reduction in kyphosis angle		
Kim *et al*[76] (2004), 70/70	10.6 ± 9.8 mos	100 IVC 47 instability (39 edema, MRI)	None	—	15.1/53%	4	14*	30 (2) 26.6 (3)	9.9*,‖	—	—
					Anterior height used for wedge and flat VCF and middle for concave						
Lee and Chen[67] (2004), 200/200	5.4 mos (2–12)	34.5 IVC 39 DM (x-ray)	None ‡mag	29.5 (K) (author defined)	A 42% ± 21.2% M 44% ± 20%	—	A 19* M 20.2*` P 4.2*	A 46 ± 29.5 (3) M 46.7 ± 25.4 (3) P 35 ± 32.4 (3)	15.4 ± 7.2	8.8 ± 6.7	43.1 ± 30
Carlier *et al*[92] (2004), 46/46	>3 mos	20 IVC 31 D M (MRI, CT)	Ka 2.72° SD	45.6 (K)	—	—	—	—	18 ± 7.7	5 ± 3.5	27.8

(*Table continues*)

Table 4. ***Continued***

Investigator (y), Reported No./Total No. Subjects	Symptom Duration (range)	% IVC, DM	Accuracy (description) Standardization of Radiographic Assessment (description)	% Vertebrae With no Height Restoration (H) or Kyphosis Correction (K)	Height Restoration				Kyphosis Reduction		
					Preop Vertebral Height Lost (mm/% of reference)	Postop Vertebral Height Restored (mm)	% Height Restored Relative to Reference (method 4)	% Height Restored (methods 2 and 3)	Preop Angle (°)	Angle Reduction (°)	Reduction (%)
Grohs *et al*[44] (2005), 29/29	3 mos	0DM	None	100 (K)	17%	—	0	—	13	0	0
Dublin *et al*[82] (2005), 40/40	(1–5 mos)	—	None ‡mag	15 (H) (defined by author)	—	—	—	M 47.6 (3)	—	3.5	—

All values are expressed as the mean ± SD.
Preoperative (Preop) vertebral height loss (%) is defined as the reference vertebral height − fractured vertebral height/reference vertebral height.
No change in kyphosis defined as correction less than 5° between the preoperative and postoperative (Postop) angle, or as defined by the specific author(s).
Method 2: Percent height restoration relative to initial fracture height.[45]
Method 3: Percent height restoration relative to lost vertebral height.[45]
Method 4: Percent height restoration relative to reference vertebral height.[45]
*Value(s) calculated or estimated from the available data.
†Gas present in the vertebral body (intravertebral cleft).
‡mag: Height expressed as percentage of the normal vertebral body (adjacent).
§Data reported for those vertebrae in which augmentation resulted in a restoration of vertebral height.
‖Cobb angle measurement includes a disc, therefore, slight changes in the patient's posture at the time of the lateral radiograph may affect results.
A indicates anterior; DM, dynamic mobility; IVC, intravertebral cleft; Ka, kyphosis angle; M, middle; MRI, magnetic resonance imaging; P, posterior.

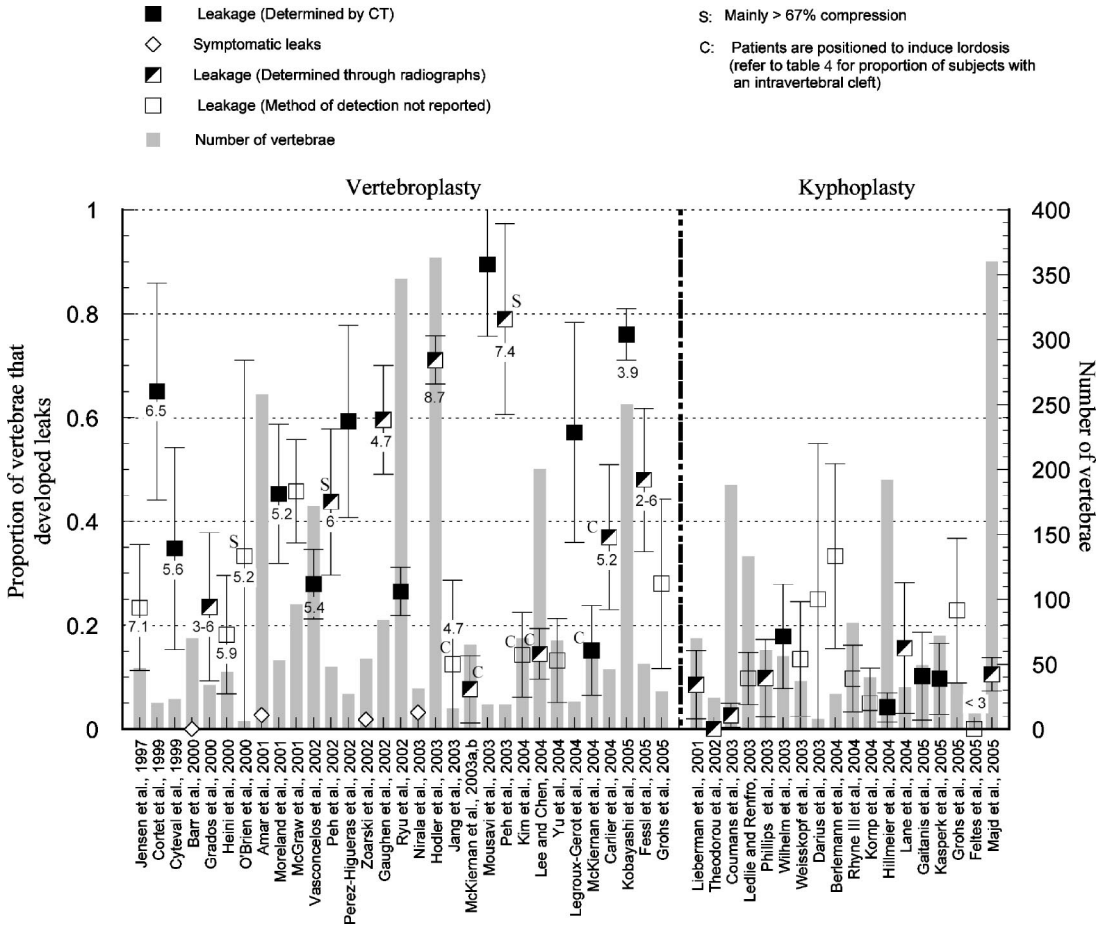

Figure 4. Proportion of vertebrae in which leaks developed during vertebroplasty and kyphoplasty. The body of evidence to date suggests a high degree of variability in leakage rates for vertebroplasty and kyphoplasty. Differing results may be caused by the amount of cement injected or percentage of the vertebra filled, level augmented, severity of the fracture, viscosity of the cement, injection pressure, leakage detection method used, and whether only clinically relevant leaks were reported. Leakage data are presented as the mean ±95% CI. Numbers given below the data points are the mean injected cement volumes (mL).

(65 leakage locations reported, 10 studies), respectively. Most leaks were clinically asymptomatic. Clinical complications occurred for 2.6% and 1.3% of augmented vertebrae and 3.9% and 2.2% of subjects for vertebroplasty (n = 2080 subjects, 3120 vertebrae, 31 studies) and kyphoplasty (n = 844 subjects, 1451 vertebrae, 17 studies), respectively. Because pulmonary emboli can cause serious ramifications, asymptomatic emboli were counted as a clinical complication. Pulmonary emboli occurred in 0.6% and 0.01% of augmented vertebrae for vertebroplasty and kyphoplasty, respectively, while neurologic complications occurred in 0.6% and 0.03% of vertebrae.

New Fracture Rate After Vertebroplasty or Kyphoplasty

There were 17 vertebroplasty (n = 933 subjects) and 12 kyphoplasty (n = 766 subjects) clinical trials that reported new fractures (Figure 5). Of new vertebral fractures using vertebroplasty (n = 120 fractures, 12 studies[40,42,44,46–49,69–71,94,95]) and kyphoplasty (n = 115 fracture, 9 studies[41,44,52,54,56,57,83,85,86]), 60% and 66%, respectively, were adjacent to the augmented vertebra. Unfortunately, follow-up times were not consistent among studies, and normalization of new fracture rates by assuming a linear trend is invalid, therefore, making direct comparisons among studies of differing time lengths impossible.[85] It was noted that both Hillmeier[56] and Kornp[58] *et al* commented on the presence of new fractures after kyphoplasty, but actual values were unavailable.

■ Discussion

Our review of literature has identified 69 mainly noncontrolled single-group cohort studies. The lack of controls, methodological flaws, and lack of information concerning patient inclusion criteria and fracture definition preclude definitive conclusions. Despite these limitations, we have addressed each question outlined in the introduction and provided a critical evaluation of the current study methodology with future recommendations.

Limitations of This Study

This review does have limitations. Publication bias may exist by limiting our search to peer-reviewed literature. The inclusion of low-quality studies may be considered a limitation of our study methodology. However, the effect

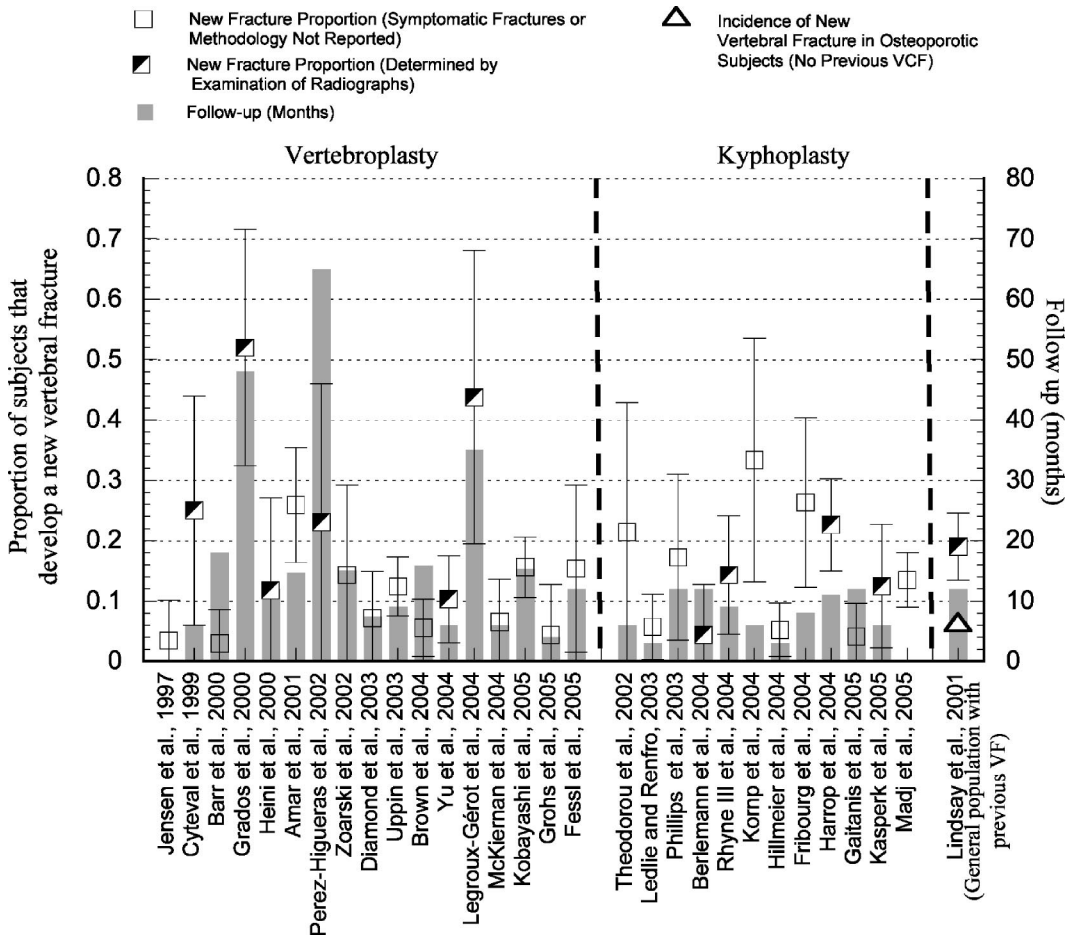

Figure 5. New fracture rate for vertebral augmentations using vertebroplasty and kyphoplasty. The raw reported number of new fractures for the 2 procedures is qualitatively similar. Data from the study by Lindsay *et al*[104] has been included, which denotes the incidence rate of a new vertebral fracture during the first year following a vertebral fracture within a general osteoporotic population. New fracture data are presented as the mean ±95% CI, while follow-up is presented as the mean.

of methodological quality was assessed, and no significant changes in outcomes were found by removing articles that scored in the bottom 50%. At this juncture, it was thought that confounding factors, patient descriptions, inclusion, and counter-indications were lacking from too many studies to perform a more detailed analysis. Summary means are a reflection of all studies and, as such, can be influenced by study or procedural inclusion criteria. Finally, an article of this scope may be considered premature, that until randomized, blinded clinical trials are performed, the use of summarizing results is questionable. To the contrary, we believe that it is only by assessing what has been performed and evaluating the trends that we can determine the need for future research.

Does Vertebroplasty/Kyphoplasty Reduce Patient Pain? How Does This Compare to Conservative Treatment? Is Pain Reduction Durable Over the Long-term?

The pain relief experienced by patients appears to be promising for both kyphoplasty and vertebroplasty in the short-term (<1 year). The majority of patients have "some pain relief" (Figure 2). Only 2 nonrandomized prospective studies assessed pain relief obtained after the procedure compared with conservative treatment.[40,41] Augmenting acute painful vertebral fractures, using vertebroplasty, resulted in an immediate (24 hours) decrease in pain scores (53%) after surgery. After 6 weeks, both the operated and control groups had a similar clinical outcome (pain score and physical function). In contrast, when assessing the outcome of chronic painful vertebral fractures at 6 months, only the surgical treatment (kyphoplasty) resulted in pain relief compared with controls. It is not known what determines whether a subject will have pain relief. Pain relief is often almost immediate, but in some patients, especially those who have been bedridden for longer periods of time, improvements may be delayed.[17,72,105] Long-term follow-up results were not as frequently reported. However, it appears that pain relief is durable; little change was noted between postoperative scores and long-term results.[4]

A standard definition of a clinically relevant improvement in pain relief would enhance the comparability, validity, and applicability of the studies (Figure 2). Success should be assessed by the procedure's ability to provide clinically meaningful pain relief for the patient. The effectiveness of the treatment is better reflected in a change in pain grouping (mild pain [1–4], moderate pain

[5–6], and severe pain [7–10]) than a straight reduction in pain score.[106,107] It is recommended that a reduction of 33% of the initial preoperative pain score be adopted as clinically relevant,[73,107,108] which will eliminate bias associated with pretreatment pain level and ensure consistent, relevant reporting. Furthermore, well-designed studies should be performed to identify patients for whom vertebroplasty or kyphoplasty presents a clear benefit, weighed against the risks associated with the procedure and potential drawbacks of conservative treatment (*e.g.*, loss of BMD, physical condition).[8]

What Are the Complications Associated With the Procedure?

Leakage of the polymethyl methacrylate is the most common complication and may pose significant physical danger, even in small quantities.[17,67,109] Leakage of unreacted monomer, or less likely polymethyl methacrylate or venography dye, may produce systemic effects resulting in toxic reaction or allergic effects leading to acute arterial hypotension or fever.[34,50,74,75,110] Although there is considerable leakage reported during both procedures (Figure 4), the actual leakage rate might have been underreported because of reporting bias or the detection method used.[48,111,112] Schmidt *et al*[112] reported low leakage detection rates and only showed fair interobserver reliability using radiographs. Thus, comparing studies in which leaks were determined by either intraoperative fluoroscopy or postoperative radiograph could be confounded by interobserver effects. It is our opinion that until asymptomatic cement leakage can be disregarded as irrelevant, the best method to monitor cement leakage, CT, should be used to report all leaks, not just those deemed clinically relevant.[111,112] The information gained through the use of postoperative CT must be balanced against increased patient exposure to radiation and cost.

The majority of clinical complications stem directly from cement leakage (66% vertebroplasty and 73% kyphoplasty). The vast majority of cement leakage is asymptomatic (96% vertebroplasty and 89% kyphoplasty). However, in cases in which cement leakage is immediately clinically asymptomatic, the long-term effect of these "benign" leaks is unknown. Relatively common intradiscal leaks may affect the mechanical loading of either the intravertebral disc or adjacent vertebra. Lin *et al*[113] reported that 58% of vertebral bodies adjacent to an intradiscal leak fractured during follow-up compared with only 12% of vertebral bodies adjacent to augmented vertebrae in which no intradiscal leakage occurred.

Although they are rare, symptomatic leaks may have dramatic consequences, such as paraplegia and death.[114–119] Cement leakage into the neural foramen is often symptomatic, resulting in neurologic complications.[34] Neurologic complications were reported in 7 vertebroplasty[10,36,49,68,74,75,102] and 4 kyphoplasty studies[41,55,56,67] described as radiculopathy, a worsening of pain or spinal compression or injury. Case reports have documented further major neurologic complications, including paraparesis, spinal claudication, and paraplegia, as a result of vertebroplasty.[120,121]

Cement extravasation into the paravertebral veins may lead to pulmonary embolism or cardiovascular distress. There were 7 vertebroplasty[4,17,34,37,42,74,75] and 5 kyphoplasty studies[8,54,87,88,97] that showed pulmonary embolism or cardiac complications. Pulmonary emboli may be a result of cement extravasation or bone marrow and fat particles that are forced out of the vertebra into the circulation.[122,123] Other instances of pulmonary embolisms, some serious, have been noted in case studies.[124,125] More pulmonary emboli cases may actually occur than reported because it is not common practice to perform chest radiographs on asymptomatic patients. Chest pain felt after vertebroplasty is often attributed to the procedure but may be caused by embolism. Chest radiographs taken after the procedure may help in the early diagnosis of dyspnea.[124,125]

Higher leakage rates have been reported for single-group cohort vertebroplasty studies compared to kyphoplasty studies (Figure 4). The only study that compared kyphoplasty and vertebroplasty using matched groups found little difference in leakage rates (28% and 23% of vertebra had cement leaks for vertebroplasty and kyphoplasty, respectively).[44] It is noteworthy that although kyphoplasty leaks were all intradiscal, 4 vertebroplasty leaks were into the more critical epidural and segmental vessels regions, although none were symptomatic.[44] It has been hypothesized that higher injection pressures and lower cement viscosity associated with vertebroplasty may create an environment in which leaks are more likely to occur.[52,109]

However, in a recent study, no significant difference in intravertebral pressure was found between vertebroplasty and kyphoplasty.[126] It has been postulated that the creation of a cavity may decrease leakage risk. It is interesting to note that those vertebroplasty studies that reduced kyphosis through patient positioning, and often had associated intravertebral clefts, had lower cement extravasation rates than the mean (Figure 4). Kim *et al*[76] noted that during cement filling of vertebrae, which had intravertebral clefts, using vertebroplasty, the IVC was filled before the surrounding trabecular bone in a similar manner to that which occurs during kyphoplasty. Thus, if cement filling is terminated once the cavity is filled, there may be less chance of cement extravasation.[66]

Berlemann *et al*[52] noted that attempting to fill the vertebra rather than just the cavity produced during kyphoplasty resulted in higher leakage rates (33%), more similar to leakage rates observed during vertebroplasty. In contrast, Rhyne *et al*[83] only filled the cavity produced during kyphoplasty and reported a lower leakage rate (10%). Finally, patient inclusion criteria (fracture severity definition, vertebra location, and BMD[77,78]), methodology (leaks determined by CT, radiograph, intraoperatively[111,112]), cement parameters (type, percent fill of vertebra[52,77]), and operator experience must be similar to compare the safety of the 2 procedures, otherwise one

runs the risk of determining the effect of the confounding factors rather than the procedures themselves.

Does Vertebroplasty/Kyphoplasty Restore Patient Function?

Numerous clinically developed but invalidated scales were used to measure physical function. A standardized method would make comparison among studies possible. However, some conclusions can be inferred from the studies reviewed. The relief from pain does seem to allow a large majority of patients to increase their physical function levels. The majority of those patients who had impairments in function before surgery are able to ambulate without assistance after surgery. Improvements in physical function should only be reported for the subset of patients who have preoperative impairments. Inclusion of patients who are normal before surgery will not accurately reflect the efficacy of the intervention to improve physical function because the ratio of impaired and normal subjects will influence the sensitivity.

Does Vertebroplasty/Kyphoplasty Restore Normal Spinal Alignment?

Both kyphoplasty and vertebroplasty have the ability to reduce the kyphotic angle and restore vertebral height associated with vertebral fractures (Tables 3, 4). Studies assessing the ability of vertebroplasty to restore height identified preoperative dynamic mobility as a good indicator of the potential to restore vertebral height.[39,92,93] McKiernan *et al*[39] showed that osteoporotic mobile fractures can achieve some height restoration following vertebroplasty, while nonmobile fractures cannot. Carlier *et al*[92] reported that the postoperative reduction in kyphosis angle using vertebroplasty can be predicted from the preoperative dynamic mobility, something that remains to be shown for kyphoplasty. Vertebroplasty has no mechanical methods to restore vertebral height and relies on patient positioning or the insertion of bolsters to induce lordosis, to increase the height of the vertebra and reduce the kyphotic angle.[45,66,67,76,92,93]

A majority of the kyphoplasty studies that showed height restoration were performed on vertebrae with acute fractures, which had edema present, or were incompletely healed fractures (Table 3). The presence of these observations increases the probability that the fracture is mobile. Therefore, kyphoplasty may only be successful in restoring height if the fracture is mobile; its ability to restore vertebral height must be assessed relative to the spontaneous correction of the patient's kyphosis through positioning alone.[127,128] Mobility is mainly associated with the presence of an intravertebral cleft but has been observed in cases in which they are not present.[92,129] Carlier *et al*[92] reported significant differences in height restoration between those subjects in whom an intravertebral cleft was visible and those in whom it was not. Thus, studies that show vertebral height restoration must control for the occurrence of dynamic fracture mobility and intravertebral cleft, the presence of which was only documented for some vertebroplasty studies (Table 4).

Of concern is the high percentage of subjects who do not have any restoration of height following either procedure. One hypothesis is that height restoration is dependent on the age of the fracture. Berlemann *et al*[52] reported that fracture age was one of the predictors of fracture correction, a sentiment that was echoed by Lieberman *et al*.[97] However, Phillips *et al*[54] found no correlation between the age of fracture and amount of deformity correction. Age of the fracture may not be as critical as its mobility in determining whether a fractured vertebra has the potential to regain height or reduce kyphosis.

Publishing and interpreting increased vertebral height must consider confounding factors (the age, severity, and mobility of the fracture), reporting methodology, and also the accuracy of the measurement method chosen. Study results were presented as a percentage reduction of kyphotic angle or the percentage of height restored, which may favor severe or mild fractures, depending on the calculation method chosen.[45] The method of reporting restoration of height should be standardized in accordance with the recommendations of McKiernan[45] and Teng[93] *et al* to allow direct interstudy comparisons. Likewise, reporting only the percentage reduction in kyphotic angle is highly sensitive to the initial kyphotic angle. The accuracy of the measurement method must be reported to ensure height restoration exceeds the error. To be 95% confident that a measured difference in kyphotic wedge angle represents a true change, the required difference has been between 3° and 11°.[92,127,130,131] Intraobserver height measurement SD has been between 0.4 and 1.1 mm.[129,132]

Attention to precision is important in determining the number of subjects for whom the treatment is effective. As is evident from Tables 3 and 4, few studies showed the precision of their methods, and in most, it was not evident if precision was then used in the analysis of the data. Patients whose measured results fall below the determine precision of the measurement method should be considered as nonresponsive. It was only evident in 3 studies if any correction for magnification error was performed (Tables 3, 4). Each radiograph must contain a reference object that allows the vertebral fracture heights to be corrected for, or, alternately, the fracture height can be expressed as a percentage of a reference height (visualized in each radiograph) to negate magnification error.[45,93] Finally, studies must show both height and kyphosis reduction. As reported by Kasperk *et al*,[41] it is entirely possible to have an increase in height and no reduction in kyphosis angle. Likewise, if only middle height is reported, it is possible to have no increase in height but a reduction of kyphosis angle (increase in anterior height only).

The whole objective of vertebral height restoration is to reduce spinal deformity and improve spinal alignment. Kyphotic angle is the angle between the superior and inferior endplates of the fractured vertebra. Unlike

Cobb angles, which include at least a disc between the measured endplates, this angle is not influenced by body position.[67,93] As shown in Tables 3 and 4, at least 5 studies used Cobb angle to determine kyphosis angle reduction. However, it would be useful to have a repeatable and sensitive measurement technique that allowed the overall spinal deformity to be determined.

Does the Incidence of Augmented or Adjacent Vertebral Fracture Increase After Vertebroplasty/Kyphoplasty?

It is difficult to determine if the incidence rate of new fractures increases after vertebroplasty/kyphoplasty because there is only 1 study[41] of limited statistical power and short follow-up that compares the new vertebral fracture rate within patients after the procedure compared with a conservative treatment group. Kasperk *et al*[41] determined that there was no significant difference between new fracture rates of patients who underwent kyphoplasty compared to controls (conservative treatment) over a 6-month period. Grohs *et al*[44] reported a higher incidence of new vertebral fractures for kyphoplasty than vertebroplasty. There were 6 (n = 35 augmented vertebrae) and 1 (n = 29 augmented vertebrae) new fracture(s) that occurred within 4 months for kyphoplasty and vertebroplasty, respectively. Unfortunately, the low study statistical power, lack of fracture definition, short follow-up, and reporting of only symptomatic fractures (rather than radiologically determined new fractures) preclude drawing emphatic conclusions. Additional factors that may confound the results of this study and others include degree of osteoporosis or spinal malalignment, patient physical function level, the quantity of cement injected, and intervertebral disc health.

The occurrence of new fractures after the procedure appears to be nonlinear, with the majority of new fractures occurring within 30 days.[71,85] Thus, the linear extrapolation of normalized annual fracture incidence rates will result in a faulty estimation. The vertebral fracture incidence rate appears to be higher after the procedure than within the general osteoporotic population that has not had a vertebral fracture develop (cumulative incidence rate of subjects with a mean age of 74 years is 6.6%), even among those studies that did not attain an average 1-year follow-up (Figure 5).[49,104] However, whether there is any difference between fracture rates after the procedure and those within a general osteoporotic population that has had a previous vertebral fracture (19%[104]) cannot be conclusively ascertained from the data. The presence of a preexisting fracture has been reported to increase one's risk of having a subsequent vertebral fracture develop by 12.6-fold.[133] It is noteworthy that two thirds of new fractures reported in studies included in this review were located adjacent to the augmented vertebra.

Grados[75] and Legroux-Gérot[42] *et al* calculated the odds ratio of vertebral fracture in the vicinity of a cemented vertebra to be 2.27 (95% CI 1.11–4.56) and 3.18 (95% CI 0.51–19.64), compared with 1.44 (95% CI 0.82–2.55) and 2.14 (95% CI 0.17–26.31) for a vertebral fracture in the vicinity of an uncemented fractured vertebra, respectively. Although this finding may suggest that the risk of fracture is increased adjacent to an augmented vertebra, it may also be caused by the natural progression of osteoporosis. A high incidence rate during the first few months after augmentation, as noted by a few investigators, may be a result of increased patient activity levels after the procedure or possible altered loading, resulting from changes in vertebral geometry or material behavior.[71,85,134,135] The postoperative care received by the patients was rarely mentioned in the reviewed articles but may play an import role in the new fracture rate.[85] Patients not instructed in proper body mechanics may be more likely to have a new vertebral fracture.

The incidence rate of new fractures after vertebroplasty/kyphoplasty may be even higher than that reported, depending on the method used to define a new vertebral fracture. New fractures may result in a poor outcome after the procedure but not to the extent that clinical action is required, thereby escaping detection.[34] Because it is estimated that only 23% of vertebral fractures are clinical events, long-term follow-up must include new radiologic analysis and not rely on patients returning for reevaluation because of recurrent pain.[7,104] To ensure that new fractures are properly identified, a standard definition, such as that proposed by Genant, must be used.[136] Furthermore, fractures that do not require clinical action can have significant long-term consequences.[128]

Does Kyphoplasty Offer a Significant Improvement in Terms of Restoration of Spinal Alignment, Pain Management, and Reduction in Cement Leakage Over Traditional Vertebroplasty?

At present, to compare kyphoplasty and vertebroplasty, it is necessary to use mainly the results of single group cohort studies, which is far from optimal. Similar results were noted for pain relief when comparing vertebroplasty and kyphoplasty studies. The only study[44] that compares kyphoplasty and vertebroplasty found that both procedures provided pain relief, but it was more pronounced for kyphoplasty after 2 years (73% and 41% reduction in VAS, respectively), the reason for which was not hypothesized. The body of evidence suggests a high degree of variability in the leakage rate for kyphoplasty and vertebroplasty. Whether the lower leakage rates are a result of patient inclusion criteria, creation of a void or trabecular dam (caused by inflation of the tamp during kyphoplasty), or higher cement viscosity needs to be clarified.[48] Height restoration is possible using kyphoplasty, although it is not effective for all patients.

However, it has also been noted that similar height restorations may be possible using vertebroplasty. Grohs *et al*[44] compared the height restoration of 2 matched

subject groups for kyphoplasty and vertebroplasty. They found some height restoration and kyphosis reduction for kyphoplasty, and none for vertebroplasty. However, there was no indication that an attempt was made to reduce the kyphosis for the vertebroplasty group through the use of patient positioning or bolsters, or if kyphosis reduction for patients who underwent kyphoplasty could be achieved by patient positioning alone. It is noteworthy that intravertebral pseudarthrosis was excluded from this investigation. Whether kyphoplasty offers a higher degree of kyphotic angle correction or allows a higher range of fractures to be treated compared with vertebroplasty needs to be ascertained. Long-term new fracture incidence rates appear to be similar for the 2 procedures, but this is based on qualitative examination of the presented data. The problem with stating conclusively that there is or is not a difference between kyphoplasty and vertebroplasty outcomes is the lack of comparative randomized clinical trials.

■ Recommendations for the Standardization of Methodology

Our methodological quality assessment revealed a need for standardized reporting and methodology, randomization, blinding of the patient or the investigator to the treatment received, reporting the variability of the data, and the use of a control group. Although it may be impractical to blind the patient to the procedure, effective study design can ensure that in prospective studies, the investigator is blinded to the patients' treatment allocation. Unblinded study designs may result in differential care bias affecting recorded scores.[25] Standardization would enhance the comparability, validity, and applicability of the studies. To assess reporting quality, we would encourage investigators to use the checklist presented in this article (Table 1).

We have outlined in each section methodological recommendations to ensure that reporting is relevant and accurate. The methods used to determine the safety and effectiveness of the procedures should include, as a minimum, the following:

- Results should be reported with respect to the fracture pathology.
- Radiologic assessment of fracture severity (using a method such as that proposed by Grigoryan[136] and Lenchik[137] *et al*) and an estimation of the age of the fracture should be included.
- Dynamic fracture mobility (supine lateral radiographs compared with standing radiographs)[39] and the presence of intravertebral clefts[129,100] must be noted if reporting height restoration. Height restoration that can be attributed to dynamic mobility must be corrected for if reporting a mechanical method of restoring vertebral height.
- Objective outcome measures should be used to assess a reduction in patient pain. VAS (raw values and the number of patients with clinically relevant reduction in pain) and a disease-specific functional outcome such as the ODI or the Osteoporosis Quality of Life Questionnaire should be included.[138]
- Physical function should be evaluated using 1 of the disease-specific function outcomes listed previously. The improvements should be related to those with preexisting impairments.
- Cement leakage, assessed by CT, should be documented.[112] Until small leaks can be definitively discounted as having no clinical consequence, all leaks should be reported.
- Kyphosis reduction and height restoration should be noted as per the recommendation of McKiernan *et al*.[45] In addition, height restoration relative to the initial height lost should be reported in accordance with the method of Teng *et al*.[93] Adjacent normal posterior border height should be replaced with the appropriate reference height on the adjacent vertebra (*i.e.*, anterior, middle, or posterior height). Precision of the radiographic measurement should be noted and accounted for during analysis. Magnification error should be corrected for by standardized radiograph techniques.[45,93] Vertebral wedge angle should be defined as the angle between the superior and inferior endplates of the fractured vertebra.[76]
- Radiographic assessment of new fractures at 3, 6, and 12 months for all patients should be performed using a fracture definition, such as that proposed by Grigoryan *et al*.[136]
- All clinical complications should be noted.

The majority of studies included in this review adds to our preliminary knowledge of the procedures, and offer insights into their potential benefits and complications. However, many questions still remain unanswered. They include but are not constrained to: Why does pain relief occur? How can cement leaks be avoided? Are asymptomatic leaks clinically relevant? How do clinical results of vertebroplasty differ from kyphoplasty? What inclusion criteria ensure that pain relief or kyphosis reduction is possible? Can new fractures be prevented (are they a result of the procedures or a natural progression of osteoporosis)? To facilitate the comparison of future studies, the adoption of a standardized reporting method would be highly beneficial. With the assistance of the recommendations proposed, it is now time to proceed to the next step with well-controlled clinical trials.

■ Key Points

- Some pain relief was reported for 92% and 87% of kyphoplasty and vertebroplasty procedures, respectively.
- Leakage rates were higher for vertebroplasty (41%) than kyphoplasty (9%).

- Height restoration is possible using kyphoplasty and for a subset of patients with mobile fractures using vertebroplasty. However, 34% and 39% of kyphoplasty and vertebroplasty (with mobile fracture) procedures, respectively, do not result in any height restoration.
- New fractures of adjacent vertebrae occurred after both procedures. Whether this is caused by altered loading, increased patient activity, or the natural progression of osteoporosis has yet to be determined.
- The adoption of standardized reporting and methodology, and an increase in methodological quality would enhance comparability, validity, and applicability of the studies.

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