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REVIEW ARTICLE

Does Vertebroplasty Cause Incident Vertebral Fractures? A Review of Available Data

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SUMMARY: Vertebroplasty has been in practice in the United States for approximately 10 years and has been described as providing significant benefit to patients with painful vertebral compression fractures. Although the procedure appears to provide dramatic pain relief, it is not without complications. The primary point of discussion in this paper is whether vertebroplasty predisposes patients to the development of additional vertebral fractures, at a rate higher than that seen in the absence of vertebroplasty. To date there remains no definitive answer to this question. There is, however, a significant body of data available in the literature that relates to this issue. This review explores and attempts to synthesize the data both supporting and refuting a relationship between vertebroplasty and the development of subsequent fractures.

Vertebroplasty is widely used as a treatment for painful osteoporotic compression fractures. Whereas it has generally been safe, occasional complications are associated with the procedure, including the development of additional vertebral fractures. Additional fractures are frequently reported after vertebroplasty but the *causal* relationship between the procedure and new-onset (incident) vertebral fractures remains unproved. Such a causal relationship is difficult to prove because of the propensity for patients with osteoporosis and vertebral compression fractures to develop additional fractures simply as a result of their underlying disease. This issue has been debated extensively in the literature with little consensus to date. Investigators have frequently reported rates of incident fracture after vertebroplasty,[1-14] but an increased rate of fracture above that of the natural history of the disease has not been definitively demonstrated. Definitively demonstrating or excluding a causative relationship will require well-designed, randomized, controlled trials comparing vertebroplasty with conservative therapy. Unfortunately, there are many barriers to performing these trials, a discussion of which is beyond the scope of this article. Thus, in the absence of definitive data, we set out to explore this issue through a comprehensive summary and discussion of the available data.

Defining the relationship between vertebroplasty and incident fractures is important for several reasons. If it can be established that vertebroplasty increases the rate of incident fractures above the natural history expected in patients with osteoporosis, this risk will need to be discussed with the patient during the consent procedure. In addition, if a significant association is observed, prophylactic vertebroplasty of at-risk vertebrae might be appropriate. Finally, if such a relationship can be established, it should prompt exploration and advancement of procedures, techniques, and cement design to minimize this risk.

As investigators have discussed the rate of incident fracture after vertebroplasty, several hypotheses have been proposed to explain why an increased rate of subsequent vertebral compression fracture might be observed. The most basic explanation is that existing (prevalent) fractures are an indicator of poor bone quality and structure beyond that reflected by bone mineral attenuation (BMD).[15,16] From a biomechanical perspective, it has been suggested that strengthening the treated level with cement infusion leads to increased mechanical forces on the adjacent vertebrae, thereby predisposing to fracture.[17] In addition, because their symptoms have improved, patients may become more physically active after the procedure.[12,18] Increased activity, creating more opportunities for the patient to fall and sustain trauma to the spine, increases the risk of incident fracture.[12,18] Finally, it has been postulated that bone loss may occur at an accelerated rate in vertebrae adjacent to the prevalent fracture.[15]

We will systematically review the arguments and available data supporting and refuting a causal relationship between vertebroplasty and incident vertebral compression fractures.

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Data Supporting a Causal Relationship

Biomechanical Data

There is a growing body of data, both bench-top and clinical, suggesting that vertebroplasty is associated with increased rates and an altered distribution of incident fractures. Multiple authors have shown that vertebroplasty increases the stiffness and ultimate failure load, or strength, of the treated vertebra.[19] Although the treated vertebra itself has increased strength, the local spinal segment surrounding the treated vertebra may actually be weakened. Using a functional spinal unit (FSU) composed of 2 cadaveric vertebral bodies and the intervening disk, Berlemann et al[20] showed that the failure load for FSUs containing a treated level was significantly (19%) lower than that for untreated FSUs. They hypothesize that weakening of the spinal unit could be explained by a "stress riser" effect in which the increased stiffness of the treated vertebra alters the load transfer to the noncemented adjacent level.

Other investigators have focused on the impact of intravertebral cement on the adjacent endplates and disk spaces, and these findings offer potential mechanistic explanations for the weakened FSU noted by Berlemann et al,[20] above. In normal vertebrae, axial cushioning is achieved by a combination of outward bowing of the annulus fibrosis as well as by substantial inward bowing of the vertebral endplates. Using a finite element model, Baroud et al[21,22] demonstrated that cement in the treated vertebral body "acts like a pillar" that reduces by 93% the physiologic inward bulge of the endplates of the

treated level. Because the endplate of the treated vertebra is resistant to inward bowing, pressure is increased in the disk and enhanced bowing and inward deflection is seen in the endplate on the opposite side of the disk. Augmented inward bowing of the adjacent vertebral endplate would place this vertebra at risk for fracture. Indeed, in the simulations reported by Baroud et al, the untreated, adjacent vertebra showed a 17% decrease in failure load compared with untreated spinal segments, concordant with the weakened FSU findings noted above.[21,22] Polikeit et al[23] confirmed the effect of vertebroplasty on adjacent vertebrae with a finite element model similar to that of Baroud et al. These latter authors demonstrated increased pressure in the adjacent nucleus pulposus both above and below the treated vertebra, which translated into a 20% increased inward deflection of the endplate of the adjacent vertebral body.[21,22]

Clinical Data

Numerous authors have published studies that include data on rates and patterns of incident fractures after vertebroplasty. A summary of these reports is shown in Table 1. The ideal dataset to define the risk of incident fracture would include cohorts of patients treated either with vertebroplasty or with conservative management in which other treatments, including antiresorptive, systemic osteoporosis treatments, are optimized and standardized. Furthermore, the number and severity of pre-existing (prevalent) fractures, which have been shown to have substantial impact on risk of incident fracture,[24-27] would be similar between groups. Unfortunately, this ideal dataset does not exist.

In the absence of randomized, controlled trials of patients treated with and without vertebroplasty, surrogate markers of increased fracture risk have been studied. Multiple authors have hypothesized that if vertebroplasty causes incident fractures that would not have occurred otherwise, the timing and pattern of these fractures would be altered by the procedure. In particular, early-onset fractures or fractures near the treated levels might suggest causation. Fractures clustering to the endplate nearest the cement might also suggest causation, especially in light of the biomechanical data. Of course, without a valid control group to help understand the risk of fracture in this at-risk, osteoporotic patient population, none of these surrogate markers can be considered definitive evidence of incident fracture risk.

Overall Rate of Incident Vertebral Fracture in Patients with Osteoporosis

Table 1 shows that, on average, approximately 20% of patients treated with vertebroplasty will return with incident fracture within 1 year. By definition, however, osteopenic patients presenting with vertebral fractures are at high risk for subsequent fracture even in the absence of vertebroplasty. This risk, which probably represents the natural history of the disease, has been defined primarily through drug trials for new osteoporosis medications. As noted above in the study by Lindsay et al,[24] patients not treated with antiresorptive medication or other systemic osteoporotic therapy who suffer an initial fracture will suffer an additional fracture at a rate of 20% of patients at 1 year.[24,28,29] Treatment with antiresorptive medication typically decreases this risk by almost half.[28,30-32]

In addition to the status of treatment with osteoporosis medications, multiple other factors influence the risk of incident fracture. The number and severity of prevalent fractures have each been well demonstrated to profoundly influence the risk of incident fracture.[24-27] The presence of a single prevalent fracture increases the risk of incident fracture up to 5-fold[24,25,33,34] compared with patients with no previous fracture. This risk seems to increase directly with the number of prevalent fractures (1 fracture risk ratio [RR] = 3.2; 2 fractures RR = 5.4; 3+ fractures RR = 10.6),[33] and some authors have shown risk increases for the development of incident fractures in the presence of multiple prevalent fractures as high as 7- to 9-fold.[25] Prevalent fracture severity has been shown by one study[26] to be the best independent predictor of future fracture risk, with 10%, 24%, and 38% of patients with mild, moderate, and severe prevalent fractures, respectively, sustaining a subsequent fracture. The relative importance of each of these factors, however, is still being explored; a recent prospective trial showed that the only characteristic that differed between vertebroplasty patients who developed incident fractures and those who did not was the number of prevalent fractures.[35] The authors found no significant differences in age, sex, presence of secondary osteoporosis, BMD, fracture morphology, fracture severity, type of cement, cement volume, or presence of cement leakage.

Few of the potential confounding issues discussed in the preceding paragraph have been addressed in the vertebroplasty literature regarding new fracture risk. In an effort to differentiate the effect of untreated prevalent fractures from the effect of vertebroplasty, we compared the rates of incident fracture adjacent with treated and untreated prevalent fractures in our patient population (A.T.T. and D.F.K., unpublished data). In these patients, there was a significantly increased risk of fracture adjacent to the treated levels (18% adjacent to untreated, 37% adjacent to treated; RR = 2.06; $P < .001$), indicating that the effect of vertebroplasty may be greater than that of a prevalent fracture alone.

Fracture location may also be critically important to this debate. The natural history of osteoporotic vertebral compression fractures involves the bulk of fractures occurring in the midthoracic (T7–T9) and thoracolumbar (T11–L1) regions of the spine.[15,36,37] This spatial clustering is thought to be due to the biomechanical forces peculiar to those regions. In particular, the midthoracic region is the location of greatest thoracic kyphosis and the thoracolumbar junction represents the articulation between the relatively rigid thoracic spine and the relatively mobile lumbar segments.[37] This zonal predisposition complicates the association between vertebroplasty and incident fractures. Given that fracture rates are highest in these spinal zones, the bulk of vertebroplasty patients are treated for fractures in these zones. Thus, without comparison to untreated controls, it becomes difficult to prove that incident adjacent fractures that also largely occur in this zone are due to the effect of the vertebroplasty rather than to the known predilection for fracture in those spinal regions.[15] This is the major thrust of the "clustering" argument that is frequently raised as an explanation for incident fractures. Proponents of this argument typically cite the findings of Kallmes and Jensen,[6] who observed that in a cohort of patients with multiple prevalent fractures, 68% of the fractures were contiguous. In addi-

Table 1: Summary of incident fractures reported in the vertebroplasty literature

Study	No. of Patients/ Fractures Treated	No. of Incident Fractures/Patients with Incident Fractures (% of Treated Patients)	Adjacent? (%)	Follow-up	Notes
Alvarez et al[52]	260/423	15 patients (6%)			
Amar et al[53]	97/258	21 patients (22%)		14.7 mo	Osteoporosis and malignancy-induced fractures
Barr et al[17]	38/70	1/1 (3%)	Yes (100)	18 mo	Prophylactic treatment of T9, T10, L1, L2
Chen et al[54]	27 patients	2 patients (7%)	Yes (—*)	1 y	Patients with intraosseus clefts; scheduled imaging follow-up; only reported adjacent fractures
Cortet et al[45]	16/20	0/0 (0%)		6 mo	Prospective study, no control
Cyteval et al[55]	20/20	5/5 pts (25%)	1 (20)	6 mo	Study design not indicated
Diamond et al[46]	55/71	3 patients (5%)	No (0)	215 d	Prospective study, controlled, nonrandomized
Diamond et al[1]	126 patients (88 VP)	40 (29 VP)/30 (21 VP–27%)	Yes (43)	629 d	Extension of Diamond et al[46]; 21 patients died, 7 lost to follow-up (% based on patients with maximal follow-up)
Do et al[2]	167/264	29 patients (17%)	Yes (62)	6–36 mo	Prospective study, no control; no significant difference in likelihood of incident fracture occurring above or below treated level
Grados et al[3]	25/34	34/13 (52%)		48 mo	
Grohs et al[56]	23/29	1/1 (4%)	Yes (—*)	2 y	Prospective, nonrandomized comparison of kyphoplasty and vertebroplasty; only reported adjacent fractures
Heini et al[4]	17/45	2/2 (12%)	2 (100)	1 y	Prospective, no control; scheduled imaging follow-up
Jensen and Dion[5]	109/174	27/19 (17%)			
Kallmes and Jensen[6]		58 patients	Yes (50)		
Kim et al[18]	106/212	72 fractures	Some RR of fracture at adjacent level = 3.03	36 mo	Only looked at the 5 vertebrae immediately above and below the treated level; scheduled imaging follow-up
Kobayashi et al[7]	175/250	36/31 (18%)	21 (58)	15.3 mo	Prospective study, no control
Legroux-Gerot et al[8]	16/21	12/7 (44%)	3 nonadjacent; 3 (25%) adjacent to untreated fxs; 6 (50%) adjacent to treated fxs	35 mo	Prospective study, no control
Lin et al[40]	38/96	22/14 (37%)	11 (50%)†: 8 (73%) were fractures of the endplate immediately abutting the cement leakage	12 mo	Study of relationship between cement leakage and incident fractures
McKiernan et al[57]	44/66	4/3 (8%)	2 (50)	6 mo	Prospective study, no control; 5 patients died within 6 mo
Perez-Higueras et al[9]	13/27	4/3 (23%)	2 (50)	5 y	Prospective study, no control; scheduled imaging follow-up
Syed et al[10]	253/511	121/55 (11%)	60 (49.6)	1 y	"Many patients experienced incident fractures after 1 yr", but these were excluded
Syed et al[41]	308 patients	78 fractures	41 (52.5%)	36.5 wk	Study of the relationship between cement leakage and incident fracture; osteoporosis and malignancy-induced fractures
Tanigawa et al[11]	76/206	56/28 (37%)	38 (67.8)	11.5 mo	Prospective study, no control; scheduled imaging follow-up
Uppin et al[12]	177 patients	36/22 (12%)	24 (67)		
Voormolen et al[35]	66/102	26/16 (24%)	14 (53.8)	1 y	Prospective study, no control; scheduled imaging follow-up
Yu et al[13]	68/68	7 patients (10%)	Yes (—*)	13 mo	Study design not indicated; only reported adjacent fractures
Zoarski et al[14]	30/54	3 patients (13%)		15–18 mo	Study design not indicated; only 23 respondents at long-term follow-up

Note:—VP indicates vertebroplasty; fxs, fractures. These data were gathered from the data given in the published manuscripts. Unless otherwise indicated, all studies were retrospective in design.

* Percentage not calculated because only adjacent fractures reported.

† Eleven fractures clearly indicated as adjacent and associated with cement leakage. Data presented are not clear regarding the location of fractures not associated with cement leakage (may be additional adjacent fractures).

tion, Kim et al[18] showed that in patients treated with vertebroplasty, the risk of adjacent fracture was 2.7 times greater in the thoracolumbar junction than elsewhere in the spine. That being said, in our population, incident fractures show a distribution that is significantly different from prevalent fractures and skewed toward the midthoracic levels.[38] In addition, other au-

thors, including Voormolen et al,[35] have found "no one specific initially treated level [to be] associated more often with new vertebral compression fractures or with adjacent new fractures."

The temporal clustering of incident fractures has also been described. In a small cohort of patients ($n = 8$), most of whom were treated with glucocorticoids, Kaplan et al[39] observed the clustering of incident fractures within 8 months of diagnosis of a prevalent fracture. If this phenomenon is well defined as part of the natural history of the disease, it may be that incident fractures rapidly follow prevalent fractures even in the absence of vertebroplasty.

Although all of the described variables affect the rate of incident fracture, osteoporosis treatment regimen, number and severity of prevalent fractures, and clustering effects are rarely, if ever, documented in vertebroplasty series. Therefore, direct comparison between the osteoporosis literature and vertebroplasty literature regarding incident fracture risk is difficult or impossible.

Surrogate Markers of Increased Rate of Fracture

In the absence of data from prospective, controlled studies that would allow direct proof of an increased risk of vertebral fracture after vertebroplasty, we look to surrogate markers as indicators of this risk. Features of incident fractures that might imply a causal relationship include location of the fractured vertebra, specific location of the fracture within the vertebra, timing of the incident fracture, and high rates of fracture in specific situations.

Adjacent Vertebral Body Fracture Risk. Multiple authors have proposed that analysis of the rate of incident fracture occurring adjacent to the treated level might shed light on whether vertebroplasty causes incident fractures. Based upon the biomechanical data described above, it stands to reason that increased rates of incident fracture would be most likely to manifest as fracture of the vertebrae immediately adjacent to the treated level. Unfortunately, the bulk of the osteoporosis literature detailing the risk of incident fracture in the absence of vertebroplasty does not include data about specific, relative locations between prevalent and incident fractures. Thus, this literature cannot be used to determine patterns of incident and prevalent fractures inherent in the natural history of the disease.

Across most published vertebroplasty studies, somewhere between 50% and 67% of incident fractures occur adjacent to the treated vertebra (Table 1).[6,12] This represents a significantly increased risk of fracture of adjacent vertebrae, an effect that was confirmed by Grados et al[3] who found the risk for incident fracture to be 2.27 versus 1.44 for vertebrae adjacent to treated and untreated levels, respectively (P value not given). Kim et al also confirmed this finding and showed a 3.03-fold increased risk for fracture adjacent to a treated level.[18] The effect has not always been as strong as in these studies. Legroux-Gerot et al[8] performed an analysis similar to that of Grados et al and found a slightly, but not significantly, increased risk for fracture in the vicinity of a treated vertebral body (OR 3.18, 95% CI = 0.51–19.64 versus OR 2.14, 95% CI = 0.17–26.31, P value not given).[8] As the authors admit, however, the sample size in this study was quite small ($n = 16$), which contributes to the large confidence intervals and may relate to the lack of significance.

We addressed this issue by performing a comparison that we believe is potentially more relevant than prior studies.[38] Assuming that vertebroplasty has no effect on the location/distribution of incident fractures, one might make the assumption that each nonfractured vertebra is at equal risk for incident fracture. With this in mind, there are many more nonadjacent vertebrae than adjacent vertebrae, a factor that must be taken into account in the analysis. In addition, many of the patients who are presenting for therapy have pre-existing fractures along the spinal axis, which may preclude those vertebral levels from subsequently fracturing. Thus, these previously fractured vertebrae might reasonably be removed from the analysis. If these 2 arguments are accepted, then rates of adjacent incident fracture that are equivalent to rates of nonadjacent fracture actually represent a disproportionate number of fractures of the adjacent vertebrae. To account for these factors, we undertook a relative risk calculation based upon the assumptions that each treated level, except L5, has 2 adjacent vertebrae and multiple nonadjacent vertebrae that are at risk for fracture, unless other factors preclude those levels from fracture. Using this analysis it is clear that in patients treated with vertebroplasty, the risk of fracture of an adjacent level is significantly greater than the risk of nonadjacent fracture (RR = 4.62, 95% CI = 4.35 to 4.89; $P < .0001$).[38]

Although we believe that this analysis is superior to a side-by-side frequency comparison, we recognize that our assumption that all vertebrae are equally at risk for incident fracture is simplistic in that it does not account for the "clustering effects" and zonal predisposition discussed above. Ideally, all of these factors would be accounted for but this would probably require a complex model that has yet to be developed.

Unique Situations: Adjacent Vertebral Body Fracture Risk in Association with Cement Leakage and Intraosseus Clefts. Because of the lack of the ideal dataset, exploration of the relationship between vertebroplasty and incident fractures has also been conducted through the analysis of unique situations. Lin et al[40] performed a retrospective analysis of patients treated with vertebroplasty who developed incident fractures and showed a significant association between disk-space cement leakage and incident fractures. In particular, the authors demonstrated a significantly increased risk of incident fracture adjacent to those disks that contained extravasated cement (Table 1).[40] These findings fit well with the known biomechanical effects of vertebroplasty and lend credence to the theory that incident fractures of adjacent vertebrae may be related to the implanted cement. It is noteworthy that a recent study[41] with more patients than that of Lin et al[40] failed to confirm this finding. There was, however, an increased rate of incident fractures in patients with disk space leakage that the authors did not acknowledge (26 fractures in 81 patients with leakage; 52 fractures in 227 patients without leakage).

We explored a similar situation in the treatment of vertebral fractures that contained intraosseus clefts.[42] These are interesting cases in that they may represent extreme manifestations of the biomechanical effects of vertebroplasty because the treated clefts become focal cement masses after vertebroplasty. Based upon this hypothesis and the findings of Lin et al,[40] we expected significantly increased rates of fracture associated with treatment of

cleft-bearing vertebrae. In our population, 63 patients were treated for intraosseus clefts. Twenty-one (33%) of these patients developed incident fractures, whereas 52 (20.8%) of the patients treated for simple fractures developed incident fractures. This translates to an increased risk of incident fracture of nearly 2-fold (OR, 1.9; 95% CI, 1.04 to 3.49; $P = .037$) in patients treated for intraosseus clefts. In addition, the relative risk for fracture adjacent to a treated cleft was 2.02 (95% CI, 1.46 to 2.58; $P = .013$) compared with a treated simple fracture. These findings are both congruent with the biomechanical data and are indications that there is a clear effect of implanting cement in the spine.

Incident Fracture Timing. The time course for the development of incident fractures is another variable that has been used to help define the relationship between vertebroplasty and incident fractures. If it can be demonstrated that fractures of vertebrae adjacent to the treated level occur sooner than those of nonadjacent levels, this may suggest a link between vertebroplasty and incident fractures.

The first analysis of this issue was performed by Uppin et al,[12] who showed that 67% of incident fractures in their population occurred within 30 days of the initial vertebroplasty.These findings have been confirmed prospectively by Tanigawa et al,[11] who observed 43% of incident fractures occurring within 30 days of the vertebroplasty procedure.

We undertook a detailed analysis of this phenomenon in our patients and found that fractures of adjacent vertebrae occur significantly sooner than those of nonadjacent vertebrae.[38] Among all patients who developed incident fractures ($n = 86$), the median time to fracture was 78 days. Incident fractures of adjacent vertebrae, however, developed significantly sooner than fractures of nonadjacent levels (median, 55 and 127 days, respectively; logrank <0.0001). This finding was confirmed by multivariate analysis which showed that the absolute distance between the incident fracture and the treated level was independently associated with the time to incident fracture ($P < .0001$).

Although these findings are provocative, in that they both confirm prior data and strengthen the evidence for an association between vertebroplasty and incident fractures, they were based on symptom-driven, rather than scheduled, follow-up imaging.

Intravertebral Fracture Pattern. Each of the previously discussed surrogate markers point to an association between vertebroplasty and incident fractures, but it remains possible that these findings can be explained by spatial and temporal clustering effects, respectively. To address incident fractures after vertebroplasty while avoiding the potentially confounding effects of clustering, we undertook a focused analysis of the intravertebral fracture pattern, rather than the distribution of fractures along the spinal axis, after vertebroplasty.[43] In particular, we attempted to define the typical (natural history) localization of vertebral endplate fractures (superior versus inferior endplate) in the absence of vertebroplasty and compare that pattern with the localization of endplate fractures after vertebroplasty.

Among patients who developed incident fractures ($n = 86$), we defined the baseline fracture localization by looking at the fracture pattern of the prevalent fractures ($n = 313$) in prevertebroplasty imaging. We then looked at the endplate localization for 3 subgroups of incident fractures: nonadjacent incident fractures, adjacent incident fractures below the treated level, and adjacent incident fractures above the treated level. In the absence of vertebroplasty, 57% of prevalent fractures occur along the superior endplate. Eleven percent occurred along the inferior endplate, and 32% were holovertebral ($P < .0001$). This result is congruent with the finding of a previous study by Palmer et al[44] and indicates that superior endplate fractures are the norm. After vertebroplasty, nonadjacent fractures and adjacent fractures below the treated level show a similar distribution to prevalent fractures (Table 2), with superior endplate fractures predominating. This is expected given that nonadjacent fractures should not be subject to abnormal biomechanical forces after vertebroplasty, and adjacent fractures below the treated level will have increased forces along the superior endplate but this will be masked by the baseline superior endplate predominance.

Table 2: Localization of endplate fractures

	Superior Endplate (%)	Inferior Endplate (%)	Holovertebral (%)
Prevalent fractures	57	11	32
Incident fractures			
Nonadjacent	69	25	6
Adjacent above treated level	84	12	4
Adjacent below treated level	30	57	13

Note:—Among prevalent fractures, superior endplate fractures predominate. Following vertebroplasty, however, in fractures immediately above the treated level (adjacent above), inferior endplate fractures predominate.[42]

Adjacent fractures immediately above the level treated with vertebroplasty, however, show a disproportionate number of inferior endplate fractures ($P < .0001$). This is a significant finding because this localization is contrary to what we have defined as the natural history for endplate fractures adjacent to noncemented vertebrae and may be indicative of abnormal biomechanical effects exerted by the cemented vertebra. It is noteworthy that these findings are consistent with the biomechanical data of Polikeit et al[23] noted above as well as the findings by Lin et al,[40] in which 8 of the 11 fractures adjacent to cement leakage were of the immediately abutting endplate.

Data Refuting a Causal Relationship

Biomechanical Data

Contrary to the multiple studies described above that indicate that vertebroplasty sets up abnormal biomechanics in the spine, a recent biomechanical analysis indicates that the procedure may instead restore normal load bearing in the spine.[45] Vertebral fractures decrease spinal segment stiffness and decompress the intravertebral disk.[45] These effects, combined with kyphotic changes, transfer load to the posterior spinal elements to the point that, in elderly spines, 90% of the load is shifted to the neural arch. Using cadaveric spinal motion segments similar to the FSUs described above but with intact spinal ligaments, Farooq et al[45] demonstrated that vertebroplasty restores segment stiffness and intradiskal pressure to prefracture levels; the result is a more normal pattern of load bearing in the spine.

Clinical Data

Several clinical trials show little association between vertebroplasty and incident fractures. Two prospective trials of vertebroplasty found no evidence for high rates of incident fractures after the procedure. Cortet et al[46] reported no incident fractures at 6 months in a cohort of 16 patients treated at 20 vertebrae. In a nonrandomized comparison of vertebroplasty and conservative therapy ($n = 79$, 55 vertebroplasty patients), Diamond et al[47] reported incident fractures (none of which were adjacent to treated vertebrae) in only 3 of the vertebroplasty patients during 215 days of follow-up. In a subsequent update, the authors demonstrated no increased risk of incident fracture between the control group and the group treated with vertebroplasty (hazard ratio, 1.13; 95% CI, 0.52 to 2.46; $P = .76$) and specifically no increased rate of incident fracture of adjacent levels in the vertebroplasty patients ($\chi^2 = 0.41$, $P = .52$). The latter finding is supported by the data of Do et al,[2] who noted, in their prospectively monitored vertebroplasty population, that the rate of adjacent-level incident fracture (62%) was similar to the frequency of contiguous prevalent fractures (62%) in the patients who had been treated for multiple baseline fractures.

Population comparisons have also been used in an attempt to show that there is no increased risk of incident fractures after vertebroplasty. A retrospective review by Jensen and Dion found that of 109 treated patients, those who returned with incident fractures ($n = 19$, 27 fractures) were not significantly more likely to have a fracture of an adjacent level than a matched, historical group of patients with multiple painful fractures at baseline ($n = 21$, 43 fractures).[5]

Perhaps the most frequently quoted data regarding the risk of new fracture in the absence of vertebroplasty is that of Lindsay et al.[24] The authors analyzed the risk of fracture among the placebo groups enrolled in 4 large-scale randomized trials of the antiresorptive agent risedronate. Among these patients, those who suffered a fracture during the trial had a 19.2% incidence of additional fracture within 12 months of the initial fracture. Several authors have used this rate of incident fracture as a comparison to fracture rates among vertebroplasty patients. Syed et al[41] compared the incident fracture rate (55 incident fractures among 253 treatments, or 21.7%) in their population to that reported by Lindsay et al[24] and concluded that there was no evidence for an increased incidence of fractures after vertebroplasty. Laredo and Hamze[48] had previously reached this conclusion by comparing the rates of incident fracture reported by Uppin et al[12] and Grados et al[3] (12.4% and 52%, respectively) with that reported by Lindsay. It is noteworthy that Laredo and Hamze recently revisited their conclusion and stated that although "there is no evidence that the overall incidence of new vertebral fractures is increased after vertebroplasty," the incidence of new vertebral fractures in adjacent vertebrae may be increased.[49]

Conclusion

Unfortunately, in the absence of the ideal dataset, it is difficult to make strong conclusions about the causal relationship between vertebroplasty and incident fractures. Ideally randomized, controlled, prospective trials comparing vertebroplasty with comparative management would be performed to explore many of the issues addressed in this article. That being said, some authors argue that the procedure represents a patient's only option for pain relief after conservative therapy has failed; thus, it may be unethical to withhold the procedure even for the purpose of advancing scientific understanding.[50] We disagree with this position, however, and hope that clinical trials studying vertebroplasty and its effects can be completed in the future.

Notwithstanding our imperfect understanding of how vertebroplasty affects the risk of future fractures, 2 issues are particularly important to patient care. First, all osteopenic patients with spontaneous spinal fracture are at high risk of new fracture, with or without vertebroplasty. These patients should receive optimal medical management of their osteopenia or osteoporosis, because proper medical therapy can decrease risk of new fracture by half. Second, the potential risk for new fracture should be discussed before vertebroplasty with all patients.

Beyond counseling and providing care for current patients, future clinical investigation of vertebroplasty ideally would analyze new fracture risk and develop methods to mitigate such risk. We strongly recommend that detailed reporting and analysis of incident fracture risk, complete with information about concomitant use of systemic osteoporotic therapy and number and severity of prevalent fractures, be incorporated when possible in future clinical studies of vertebroplasty. In addition, to provide an important benchmark, it is critical that the natural history of osteoporotic vertebral compression fractures is clearly and completely defined,[51] including definitive demonstration of clustering phenomena (for which the current evidence is very weak) as well as biomechanical modeling of the whole spine, both in vitro and in vivo. Techniques aimed at diminishing the risk of new fracture, including prophylactic vertebroplasty, low volume vertebroplasty,[19] and development of alternative cements, are also of substantial interest.

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