New Fractures after Vertebroplasty: Adjacent Fractures Occur Significantly Sooner

A.T. Trout, D.F. Kallmes and T.J. Kaufmann

AJNR Am J Neuroradiol 2006, 27 (1) 217-223
http://www.ajnr.org/content/27/1/217

ORIGINAL RESEARCH

A.T. Trout
D.F. Kallmes
T.J. Kaufmann

New Fractures after Vertebroplasty: Adjacent Fractures Occur Significantly Sooner

BACKGROUND AND PURPOSE: Whether vertebroplasty increases the risk of adjacent-level vertebral fractures remains uncertain. Biomechanical and clinical studies suggest an increased risk, but compelling data have not yet been put forth to settle this difficult issue. We believe that an analysis of the time interval between vertebroplasty and subsequent fractures may shed additional light on this debate. We specifically hypothesized that subsequent fractures would occur sooner and more frequently in the vertebrae adjacent to the treated level.

METHODS: We performed a retrospective analysis of the risk and timing of subsequent fractures in patients previously treated with vertebroplasty. Multiple linear regression was used to explore factors that influence the time to new fracture following vertebroplasty. Fractures were then divided on the basis of whether they occurred adjacent or nonadjacent to the treated level. Survival analysis was used to compare time to new fracture among the 2 groups, and the relative risk of both types of fracture was calculated.

RESULTS: In this study, 186 new vertebral fractures occurred in 86 (19.9%) of 432 patients. Seventy-seven (41.4%) fractures were of vertebrae adjacent to the level treated with vertebroplasty. Median times until diagnosis of new adjacent and nonadjacent level fractures were 55 days and 127 days, respectively. Time to fracture was significantly different between the 2 groups (logrank <0.0001). Distance of the new fracture from the treated level was also significantly associated with time to new fracture ($P < .0001$). Relative risk of adjacent level fracture was 4.62 times that for nonadjacent level fracture.

CONCLUSION: These data demonstrate an association between vertebroplasty and new vertebral fractures. Specifically, following vertebroplasty, patients are at increased risk of new-onset adjacent-level fractures and, when these fractures occur, they occur sooner than nonadjacent level fractures.

Percutaneous vertebroplasty (PVP) has been shown to provide benefit to patients with painful vertebral compression fractures in terms of both pain control and disability resolution.[1-3] Patients typically demonstrate rapid and durable pain relief and often regain lost function.[4,5] Despite the demonstrated benefit, there is a great deal of debate about whether vertebroplasty also increases fracture morbidity by either inducing or facilitating subsequent vertebral fractures.[6,7] Investigators have attempted to explore this issue through both clinical and biomechanical studies. Until now, much of the clinical data are anecdotal and either presented in case reports or as part of follow-up data in procedural efficacy studies.

To explore the issue of new-onset (incident) fractures, previous investigators have focused on fractures of adjacent level vertebrae. This focus is largely based on the assumption that the effects of vertebroplasty will be greatest at vertebral levels near the treated vertebral body. Therefore, if an increased rate of fracture of adjacent vertebrae can be demonstrated, a causative link may be possible. This connection is made more difficult, however, by the fact that clinical data to this point have been contradictory,[8-12] and it is possible that the natural history of vertebral compression fractures may include clustering at adjacent levels regardless of the presence of vertebroplasty.[13] Support for a connection between vertebroplasty and subsequent fractures, however, comes from biomechanical data which uniformly show significant changes in both vertebral loading and vertebral shape following vertebroplasty and thus point toward the likelihood of increased fracture risk in adjacent vertebrae.[14-17]

We believe that a study of the time course of occurrence of incident fractures in patients previously treated with vertebroplasty will shed further light on this debate. Specifically, if vertebroplasty is to be implicated as causative of new, adjacent-level fractures, we hypothesized that, following vertebroplasty, these fractures would occur with increased frequency and earlier than nonadjacent fractures, which may represent the natural history of the disease.

Methods

We performed a retrospective review of all patients treated with vertebroplasty at our institution between July 1999 and September 2004. During this interval, 432 patients were treated. Institutional review board approval was obtained for this study and all analyses of patient records were in accordance with HIPAA regulations. Patient records were reviewed to identify prevalent and incident fractures as well as vertebral levels treated. Fractures that were present on imaging before vertebroplasty either in acute or chronic form were designated as prevalent fractures. Incident fractures were defined as fractures that were newly diagnosed following vertebroplasty on the basis of MR imaging or bone scan. Time of diagnosis of incident fractures was determined based on the date of confirmatory imaging. Incident fractures were designated as either adjacent or nonadjacent to the vertebral level most recently treated with vertebroplasty. In the event that multiple levels were treated in a single session, adjacent/nonadjacent designations were made relative to the treated level that was nearest to the newly fractured vertebral body. If the incident fractures were subsequently treated and the patient developed additional fractures,

Received March 1, 2005; accepted after revision June 3.

From the Mayo Clinic College of Medicine (A.T.) and the Department of Radiology (D.K., T.J.K.), Mayo Clinic Rochester, Rochester, Minn.

Address correspondence to Andrew Trout, Mayo Clinic College of Medicine, Mayo Clinic Rochester, 200 First St SW, Rochester, MN 55905.

these were designated as either adjacent or nonadjacent to the most recently treated levels.

Of the 432 patients reviewed, 91 subsequently presented to our institution with painful incident vertebral compression fractures. Five of the 91 patients were treated for malignancy-associated vertebral compression fractures (multiple myeloma, 3; unknown myeloproliferative disease, 1; metastatic renal cell carcinoma, 1). These patients were excluded from the analysis. The remaining 86 patients were initially treated with vertebroplasty for osteoporotic fractures at a total of 137 vertebral levels.

Vertebroplasty Procedure

PV is typically offered to patients with refractory pain that is referable to an acute or subacute vertebral compression fracture of the thoracic or lumbar spine as evidenced on MR imaging or bone scan. Vertebroplasty is not offered when the following exclusion criteria are met: improvement with conservative management, technical contraindications, and noncorrelating pain.

Vertebroplasties were performed by staff radiologists according to the methods outlined elsewhere.[18] Specifically, patients were treated by using intravenous conscious sedation. Biplane fluoroscopy was used in all cases. Local anesthesia was administered over the skin, subcutaneous tissues, muscular tissues, and periosteum of the targeted pedicle. Transpediculate or parapedicular trajectories were used in all cases. Eleven-gauge needles were advanced into the central aspect of the vertebral bodies for unipediculate approaches, and placement of the needle was made into the midportion of the hemivertebra for bipediculate approaches.

Cement was prepared as described elsewhere.[18] In brief, the cement material was prepared by combining polymethylmethacrylate (PMMA) powder with sterile barium sulfate for opacification and gentamicin powder for infection control, followed by the addition of liquid monomer to make a thin, "cake-glaze" consistency material. The mixture was then injected with either an injector device (Cook Inc., Bloomington, Ind) or 1-mL syringes. Cement injection was considered complete when the cement reached the posterior one fourth of the vertebral body on the lateral projection. Injection was also immediately terminated in the event of epidural, venous, or transendplate extravasation. Following needle removal, patients were left on strict bed rest for 1 hour and then discharged. A maximum of 3 vertebral levels were treated in a single session based on clinician comfort levels.

Statistical Analysis

For the purpose of statistical analysis, each fracture was considered as a separate occurrence.

A Monte Carlo approximation for the Fisher exact test was used to compare the distribution along the spinal axis of prevalent and incident vertebral fractures as well as to compare the distribution of adjacent and nonadjcacent incident fractures.

Survival analysis by using the logrank statistic was used to compare time to diagnosis of incident vertebral fractures between 2 groups: patients with incident fractures adjacent to the treated levels and patients with nonadjacent incident fractures. The null hypothesis was that, following vertebroplasty, adjacent-level, incident fractures occur at similar time points as nonadjacent-level, incident fractures. The χ^2 test was used to compare the frequency of cephalad or caudad location of the incident adjacent-level fracture relative to the treated level. This test was based upon a null hypothesis that there would be equal frequency of fractures above and below the treated level.

Relative risk calculations were made on based on analysis of only the incident fractures that occurred after the initial vertebroplasty. For the purposes of this analysis alone, fractures following vertebroplasties of incident fractures were not included. Vertebrae between T2 and L5 were considered for analysis.

In addition, bivariate analysis and standard least squares multiple linear regression were performed to determine which factors might contribute to the length of time between vertebroplasty and incident compression fracture. Independent variables tested in the multivariable model were patient age, patient sex, distance of incident fracture from the most recent level treated by vertebroplasty (in number of vertebral levels), presence or absence of a cyst in the treated vertebra, and categorical zone of previous vertebroplasty(ies). Categorical zones of vertebroplasty were defined on the basis of the known bimodal frequency of compression fractures (peaks around T8 and T12–L1) that is also exhibited in our patient population.[19,20] The zones were as follows: zone 1, T2–T6; zone 2, T7–T10; zone 3, T11–L2; zone 4, L3–L5. Because some patients had been treated with vertebroplasty in 2 zones before occurrence of an incident fracture, the combined categories of zones 2 and 3 and of zones 3 and 4 were included as separate categorical variables. This gave a total of 9 degrees of freedom in the multiple linear regression model.

For the purposes of discussion, data from a study of adjacent-level fractures by Uppin et al[21] were reanalyzed by using survival analysis and the logrank statistic. Time to diagnosis of new adjacent- and nonadjacent-level fractures in that population was compared in an effort to relate those data to the results of the current study.

The statistical software used for all analyses was JMP version 5 (SAS Institute, Cary NC, 1989–2002) or SAS version 8.02 (SAS Institute, 1999–2001).

Results

One-hundred eighty-six incident vertebral fractures occurred in 86 patients (median number of incident fractures, 1.5; range, 1–10; Fig 1). The median age for these 86 patients was 72.5 years (range, 41–95 years), and 58 of the patients were women (67.4%). The median time to diagnosis of an incident fracture was 78 days (range, 2–1330 days). Seventy-seven (41.4%) of the 186 fractures occurred in vertebrae adjacent to the vertebral body most recently treated by vertebroplasty. Thirty-three (42.9%) of the adjacent-level fractures were caudad to the treated vertebra, whereas 39 (50.6%) were located cephalad. Five of the adjacent fractures had adjacent treated levels both above and below. This distribution was not significantly different from the null hypothesis of equal incident fracture frequency above and below the prevalent fracture ($P = .48$).

The distribution of incident fractures was significantly different ($P < .02$ for fractures following only the initial verterbroplasty in a given patient; $P < .001$ for fractures following all vertebroplasties) from that of prevalent fractures. Specifically, prevalent fractures occurred with greater frequency at the thoracolumbar junction (T11–L2) than did the incident fractures (Fig 1).

Among the incident fractures, the distribution of adjacent- and nonadjacent-level fractures was significantly different ($P = .009$). Adjacent-level fractures occurred with increased frequency at the thoracolumbar junction, whereas nonadjacent fractures were most common in the midthoracic region of the spine (Fig 2).

The median time to diagnosis of an incident adjacent-level

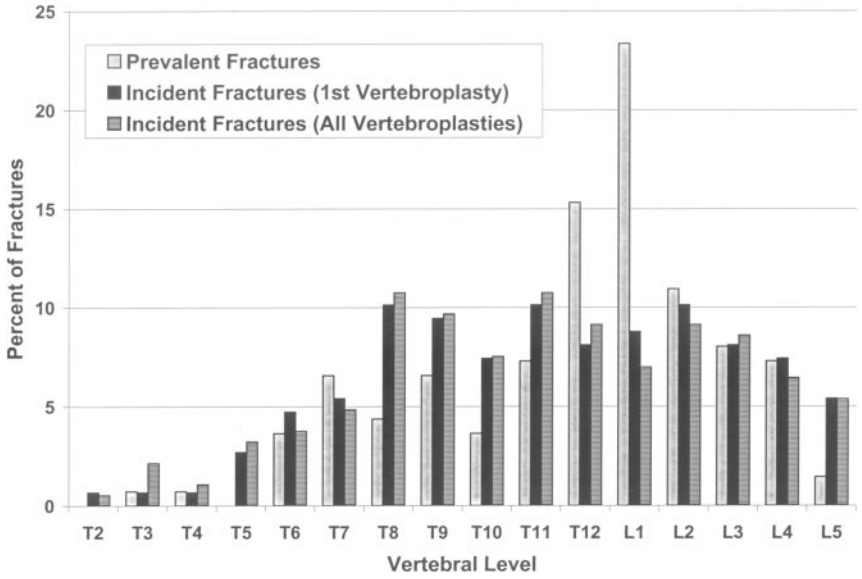

Fig 1. Location of prevalent and incident vertebral fractures. Two nonexclusive groups of incident fractures are shown—incident fractures following only the first vertebroplasty in a given patient and incident fractures following all vertebroplasties in a given patient. All data are shown as a percentage of that group of fractures. The distribution of prevalent fractures is bimodal with peaks around T8–T9 and T12–L1, with L1 as the most-common prevalent fracture location. The distributions of both groups of incident fractures were significantly different from the distribution of prevalent fractures with essentially a uniform distribution across the spine. There was no significant difference in the distributions of the 2 incident fracture groups.

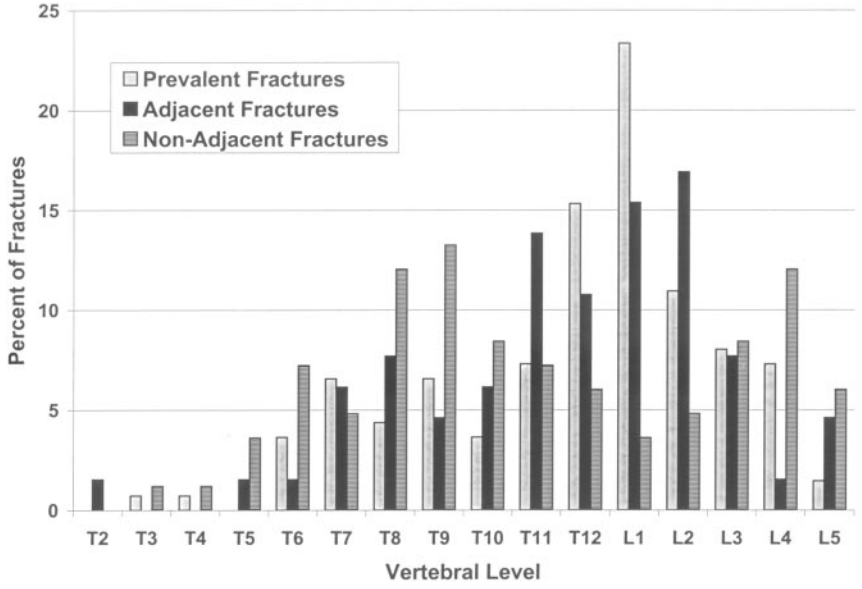

Fig 2. Distribution of prevalent and adjacent and nonadjacent incident fractures. The distribution of adjacent- and nonadjacent-level fractures is significantly different. Adjacent-level fractures predominate at the thoracolumbar junction (T11–L2), whereas nonadjacent-level fractures predominate in the midthoracic region of the spine (T7–T9).

fracture was 55.0 days (range, 2–1238 days), whereas the median time to diagnosis of an incident nonadjacent-level fracture was 127.0 days (range, 3–1330 days). Interquartile ranges were 78 days and 315.5 days for adjacent-level and nonadjacent-level fractures, respectively. Time to fracture was significantly different between the 2 groups (logrank <0.0001; Fig 3), and we therefore reject the null hypothesis that there was no difference in the time course of fractures between groups.

In multivariable analysis, the independent variable of distance of incident fracture from prior vertebroplasty was significantly associated with the dependent variable of time between vertebroplasty and incident fracture (F ratio, 17.9; $P < .0001$). That is, distance between the incident fracture and the treated level increases as time between vertebroplasty and incident fracture increases (Fig 4).

Zone of prior vertebroplasty was also significantly correlated with time between vertebroplasty and incident fracture in multivariable analysis (F ratio, 3.06; $P = .0113$). The zonal categories of 2 *and* 3, 3 *and* 4, and 4 had associated mean times between vertebroplasty and incident fracture that were less than the mean time between vertebroplasty and incident fracture for all zonal categories combined.

Relative Risk of Fracture

By including 16 vertebrae (T2–L5) in 86 patients, a total of 1376 vertebrae ($16 \times 86 = 1376$) are encompassed for analy-

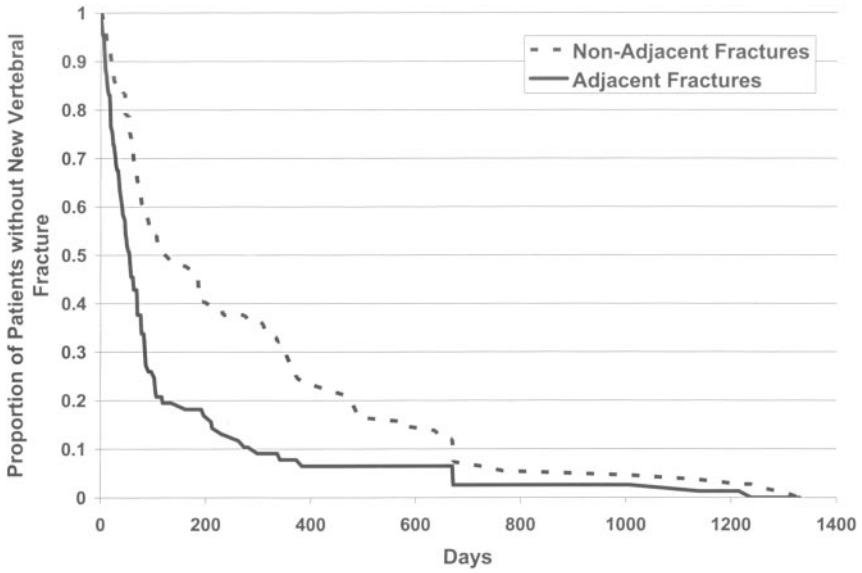

Fig 3. Survival curve depicting time incident of adjacent- and nonadjacent-level fractures in our patient population. Fractures adjacent to treated levels occur significantly sooner than fractures of nonadjacent vertebral bodies.

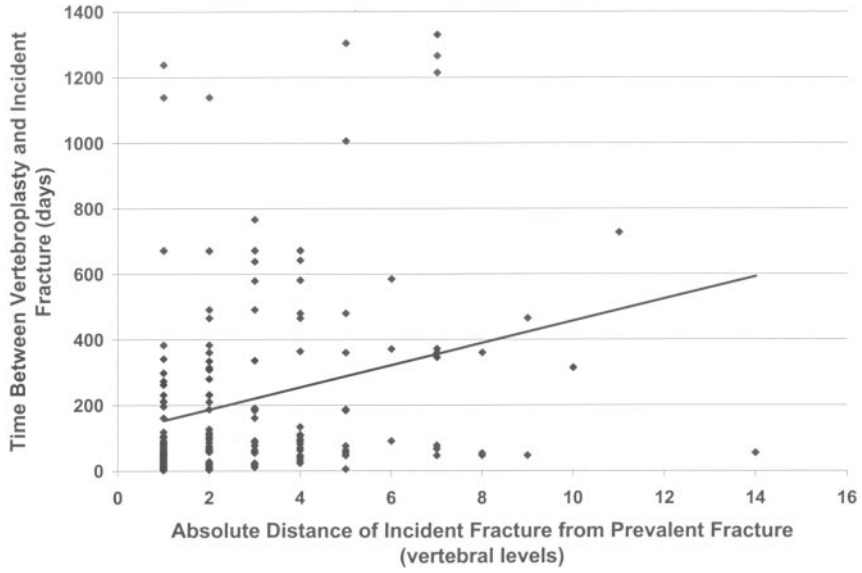

Fig 4. Time from PVP to new fracture versus distance from PVP to new fracture. The distance from prior PVP to a new, incident fracture decreases as time from PVP to the incident fracture decreases as indicated by the simple linear regression line (estimate, 33.8; SE, 8.9; $P = .0002$).

sis. Patients were treated at 137 of these vertebrae, yielding a total of 272 adjacent levels (2 patients were treated at L5, which is considered to have only a single adjacent vertebral level). Because of treatment at multiple levels and untreated chronic fractures, 117 adjacent vertebrae and 127 nonadjacent vertebrae were not at risk for fracture. Thus, 915 nonadjacent vertebrae and 155 adjacent vertebrae were considered at risk for subsequent fracture.

In the subpopulation considered for this analysis (incident fractures only after first vertebroplasty in a given patient), 148 incident fractures occurred in 86 patients. Sixty-five of these fractures were of adjacent vertebrae yielding a relative risk of 4.62 (confidence interval = 4.35–4.89; $P < .0001$) for fracture of adjacent versus nonadjacent vertebrae.

Reanalysis of Data of Uppin et al

Thirty-six new fractures occurred in the patient population described by Uppin et al.[21] Median time to new adjacent-level fractures was 21 days (range, 3–278 days), whereas the median time to new nonadjacent-level fractures was 31 days (range, 7–305 days). This difference trended toward, but did not reach, significance (logrank = 0.12; Fig 5).

Discussion

Vertebroplasty has been shown to significantly benefit patients with acute painful vertebral fractures in terms of pain relief, improved quality of life, and reduced medication requirements.[1-3] It is still unclear, however, whether the procedure in fact increases the risk of subsequent fractures. Al-

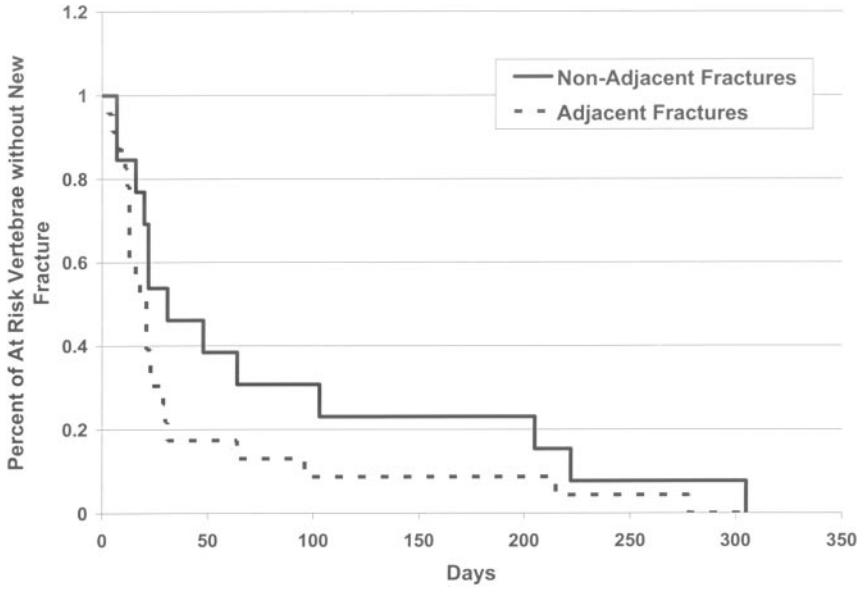

Fig 5. Survival curve depicting time to new fracture based on data from Uppin et al.[21] Although not statistically significant, fractures of vertebrae adjacent to treated levels trend toward occurring sooner than fractures of nonadjacent levels.

though we have not demonstrated a direct causal relationship between vertebroplasty and subsequent fractures, we consider the findings of the current study provocative. We observe a significant relationship between the time course of fractures occurring after vertebroplasty and the distance of those new fractures from the treated level. Fractures of vertebral bodies adjacent to those treated with vertebroplasty occurred significantly sooner than fractures not immediately adjacent to a treated level. This relationship is further supported by multivariable modeling that shows a relationship between the absolute distance of the incident fracture from the treated level and the timing of the incident fracture. In addition, we have shown a relative risk of 4.62 for fracture of vertebrae adjacent to treated levels versus fractures of vertebrae that are not adjacent to treated levels. Unfortunately, comparable risk data on individuals not treated with vertebroplasty are not available at this time. Although we cannot prove that treating a vertebral body with vertebroplasty induces the fracture of adjacent vertebrae, our data suggest vertebroplasty speeds, and possibly facilitates, the fracture of adjacent vertebrae.

One potential explanation for the early onset of new fractures following vertebroplasty is altered biomechanics in the treated area of the spine. This hypothesis is well supported by biomechanical data. Finite element models show that cement in an augmented vertebral body acts as a "pillar" that both reduces the normal inward bulge of the treated endplate and increases the stiffness of both the intervertebral joint and the whole motion segment.[14,15] In addition, the pressure in the adjacent intervertebral disk increases significantly, resulting in higher loading on the adjacent vertebral bodies as well as increased deflection of the adjacent endplate.[14,15,17] The combination of these effects leads to failure of adjacent vertebral bodies at significantly lower spinal loads.[16] More specifically, Berleman et al demonstrated in a finite element model that failure typically occurs in the nonaugmented vertebral body immediately caudad to the treated level while both adjacent caudad and cephalad vertebrae fracture in untreated controls.[16] We did not observe a significant difference in the cephalad versus caudad occurrence of new adjacent fractures after vertebroplasty.

One potential argument that would dispute the relevance of the findings reported herein is the argument of clustering. This argument has 2 main elements: temporal clustering and spatial clustering. The temporal clustering argument is based on data by Lindsay et al[12] that showed that patients with a baseline fracture are at increased risk of subsequent fracture within a year when compared with healthy controls. To date, the only prospective demonstration of temporal clustering of subsequent fractures was a very small series, comprising 8 patients, by Kaplan et al[13] that showed the clustered occurrence of new onset fractures within 8 months of an untreated "sentinel" fracture. Temporal clustering may explain the occurrence of subsequent fractures in our population, but it does not necessarily explain the fact that adjacent-level fractures occur on a different time course than nonadjacent-level fractures.

The spatial clustering argument centers on the known propensity for fractures to occur in the midthoracic (T7–T9) and thoracolumbar (T11–L1) regions of the spine.[19,20,22] The thrust of this argument is that treated fractures are more common in these regions and that nearby vertebrae are inherently at an increased risk for fracture even in the absence of a treated vertebra. Our data appear to contradict this argument. The distribution of incident fractures is significantly different from that of prevalent fractures, in that incident fractures are essentially uniformly distributed across the spine (Fig 1) with little predisposition for specific spinal zones. The distribution, however, of the subgroup of only adjacent-level fractures is significantly biased toward the thoracolumbar junction.

In the absence of a control group of untreated fractures, the issue of clustering is difficult to address because, if vertebroplasty actually increases the rate of subsequent fractures, one would expect spatial and temporal "clustering" of fractures under those conditions as well.

By using various methodologies, previous authors have addressed the issue of whether vertebroplasty causes new fractures. None of these previous studies can be considered conclusive, but many have raised suspicion that cement in the vertebral body or disk space may increase the risk of new onset fractures at adjacent levels. Grados et al described a significantly increased risk (odds ratio = 2.27) of vertebral fracture in the vicinity of cemented vertebral bodies when compared with the risk in the vicinity of uncemented vertebrae, but no control group of untreated patients was offered.[8] Lin et al cited a relationship between cement leakage into the disk space and subsequent fracture risk.[23] They showed that 58% of vertebrae adjacent to disks containing cement subsequently fractured versus only 12% of vertebrae adjacent to disks not containing cement that subsequently fractured.[23] Uppin et al described a series of 22 patients with 36 new vertebral fractures following vertebroplasty.[21] They noted that 24 (67%) of the new fractures were of adjacent vertebral bodies and that 24 (67%) of the new fractures occurred within 30 days of vertebroplasty; however, no statistical conclusions regarding the timing of new fractures were drawn. Our data are in general agreement with these previous studies and offer an additional statistical basis for exploring this complex issue.

Although the studies listed above point toward a relationship between vertebroplasty and subsequent fractures, other investigations provide conflicting results. Laredo and Hamze[24] anecdotally compared the results described by Uppin et al[21] and Grados et al[8] with the results of a study of the natural history of vertebral compression fractures[12] and concluded that there was no evidence of an overall increased incidence of new vertebral fractures after vertebroplasty. Despite mixed evidence about whether vertebroplasty increases the absolute incidence of new fractures, our data and those of other authors indicates that vertebroplasty may cause fractures to occur earlier than they otherwise would have, particularly in vertebral bodies that are adjacent to treated levels.

Kim et al and Fribourg et al both focused specifically on the time course of subsequent fractures,[10,25] as we have in the current study. Kim et al described 72 new fractures in a patient population of 212 treated vertebral levels. The authors demonstrated a 1-year fracture-free rate of 93.1% and a mean fracture-free interval of 32 months. They also noted a rapid decrease in the fracture-free rate in the first 2 months consistent with the data presented by Uppin et al.[21] Features that conferred an increased risk of subsequent fracture were location of an adjacent vertebral body in the thoracolumbar junction and location of a vertebral body immediately adjacent to a treated level (relative risk of 2.70 and 3.03, respectively). The latter finding is confirmed in the present study.

Fribourg et al focused more specifically on the time course of new vertebral fractures.[25] The authors undertook a retrospective review of 38 kyphoplasty patients who were treated at 47 vertebral levels. Within the mean follow-up of 8 months, 10 patients sustained 17 new vertebral fractures. Thirteen of these fractures were considered adjacent to treated levels and the authors demonstrated that these adjacent fractures occurred significantly sooner than the nonadjacent fractures. The median intervals until adjacent and nonadjacent fractures were 37 and 370 days, respectively. These results, though based on a much smaller sample set and based upon kyphoplasty patients, support the conclusion we have been able to make with a larger dataset of vertebroplasty patients and a more robust statistical analysis.

Although they did not focus on the timing of new vertebral fractures, a reanalysis of the data included in the article by Uppin et al further supports our findings.[21] The difference in time to new adjacent- or nonadjacent-level fractures in that population did not reach significance, but adjacent-level fractures did trend toward occurring sooner following vertebroplasty. The fact that these data do not show a statistically significant relationship may only be a reflection of the sample size (only 36 new fractures) and a keen observer notes the similarity between the survival curves based on these data and those generated in our study.

Although the sample sizes are small, the studies by Fribourg et al and Uppin et al support the findings demonstrated by our study. The present study shows, without a doubt, that fractures of vertebral bodies adjacent to levels treated by vertebroplasty occur sooner than fractures of nonadjacent vertebrae, and we consider these results provocative. The results of this study are particularly relevant because this is the largest dataset and most robust analysis of this issue to date. There are several limitations, however, to our study. First, new fractures were defined based upon clinical criteria and acute MR imaging findings[26-28] rather than morphologic criteria. There is a great deal of discussion in the literature regarding the appropriate definition of new vertebral fractures based on morphologic criteria.[29,30] Although this is an important academic issue, vertebral body changes that are demonstrable on MR imaging or bone scan and can be related to a patient's symptoms warrant treatment even if they do not meet the strict morphologic criteria described in the literature. Second, for the purpose of analysis each fracture was considered as a separate occurrence. There is a body of evidence that demonstrates the interrelationship of various spinal levels and these factors could be playing into the likelihood and timing of subsequent fractures.[20,31,32] Ultimately, to account for these interrelationships, complex models will need to be developed. At this time, however, it is not our intention to prove a causative relationship. Instead, we hope to illustrate one of the factors that is likely playing a role in subsequent fractures. Finally, this is a retrospective study and has all of the limitations inherent therein. This, however, does not diminish the importance of these results in terms of advancing the understanding of the effects of introducing cement into the spine.

If the role of vertebroplasty in subsequent fractures is ultimately defined, the natural progression of the disease and the location of subsequent fractures in untreated individuals needs to be understood.[6] Jensen et al commented on this and in a small cohort of patients demonstrated that patients with new fractures after vertebroplasty were not significantly more likely to have a fracture of an adjacent level than a control group of patients with multiple compression fractures.[9] In addition, Kallmes et al noted that in a cohort of patients with multiple osteoporotic fractures, 68% of the fractures were contiguous suggesting a "clustering effect" to the natural history of vertebral fractures in osteoporosis.[7] It is clear from these 2 small studies that both epidemiologic investigations and prospective controlled trials are warranted if we are to accurately define this relationship. Specifically to prove the

association between vertebroplasty and subsequent fractures observed in this study, a randomized, prospective trial comparing vertebroplasty patients to untreated controls is warranted.

Finally, although the current study suggests an association between vertebroplasty and subsequent vertebral fractures, the benefits of the procedure need to be taken into account. In view of the positive outcomes that have been repeatedly associated with vertebroplasty, the procedure should not necessarily be abandoned or withheld in light of the findings of the current study. Instead, these data should serve to create awareness of a very real potential that vertebroplasty may increase the risk of subsequent fracture, as compared with the natural history of osteoporosis.

Conclusion

Although we cannot prove a causative relationship between vertebroplasty and subsequent vertebral fractures, our data add valuable information to the continuing debate. Vertebral bodies adjacent to those treated with vertebroplasty have greater than 4 times the risk of fracture than vertebrae that are not adjacent to treated levels. In addition, it is clear that there is a temporal effect of introducing cement into a vertebral body with adjacent vertebrae fracturing significantly sooner than more distant vertebrae.

References

1. Evans AJ, Jensen ME, Kip KE, et al. **Vertebral compression fractures: pain reduction and improvement in functional mobility after percutaneous polymethylmethacrylate vertebroplasty retrospective report of 245 cases.** *Radiology* 2003;226:366–72
2. McGraw JK, Lippert JA, Minkus KD, et al. **Prospective evaluation of pain relief in 100 patients undergoing percutaneous vertebroplasty: results and follow-up.** *J Vasc Interv Radiol* 2002;13:883–86
3. Diamond TH, Champion B, Clark WA. **Management of acute osteoporotic vertebral fractures: a nonrandomized trial comparing percutaneous vertebroplasty with conservative therapy.** *Am J Med* 2003;114:257–65
4. Winking M, Stahl JP, Oertel M, et al. **Treatment of pain from osteoporotic vertebral collapse by percutaneous PMMA vertebroplasty.** *Acta Neurochir (Wien)* 2004;146:469–76
5. Zoarski GH, Snow P, Olan WJ, et al. **Percutaneous vertebroplasty for osteoporotic compression fractures: quantitative prospective evaluation of long-term outcomes.** *J Vasc Interv Radiol* 2002;13:139–48
6. Jensen ME, Kallmes DF. **Does filling the crack break more of the back?** *AJNR Am J Neuroradiol* 2004;25:166–67
7. Kallmes DF, Jensen ME. **Percutaneous vertebroplasty.** *Radiology* 2003;229:27–36
8. Grados F, Depriester C, Cayrolle G, et al. **Long-term observations of vertebral osteoporotic fractures treated by percutaneous vertebroplasty.** *Rheumatology (Oxford)* 2000;39:1410–14
9. Jensen ME, Dion JE. **Percutaneous vertebroplasty in the treatment of osteoporotic compression fractures.** *Neuroimaging Clin N Am* 2000;10:547–68
10. Kim SH, Kang HS, Choi JA, et al. **Risk factors of new compression fractures in adjacent vertebrae after percutaneous vertebroplasty.** *Acta Radiol* 2004;45:440–45
11. Davis JW, Grove JS, Wasnich RD, et al. **Spatial relationships between prevalent and incident spine fractures.** *Bone* 1999;24:261–64
12. Lindsay R, Silverman SL, Cooper C, et al. **Risk of new vertebral fracture in the year following a fracture.** *JAMA* 2001;285:320–23
13. Kaplan FS, Scherl JD, Wisneski R, et al. **The cluster phenomenon in patients who have multiple vertebral compression fractures.** *Clin Orthop* 1993;297:161–67
14. Baroud G, Heini P, Nemes J, et al. **Biomechanical explanation of adjacent fractures following vertebroplasty.** *Radiology* 2003;229:606–607; author reply 607–608
15. Baroud G, Nemes J, Heini P, et al. **Load shift of the intervertebral disc after a vertebroplasty: a finite-element study.** *Eur Spine J* 2003;12:421–26
16. Berlemann U, Ferguson SJ, Nolte LP, et al. **Adjacent vertebral failure after vertebroplasty: a biomechanical investigation.** *J Bone Joint Surg Br* 2002;84:748–52
17. Polikeit A, Nolte LP, Ferguson SJ. **The effect of cement augmentation on the load transfer in an osteoporotic functional spinal unit: finite-element analysis.** *Spine* 2003;28:991–96
18. Jensen ME, Evans AJ, Mathis JM, et al. **Percutaneous polymethylmethacrylate vertebroplasty in the treatment of osteoporotic vertebral body compression fractures: technical aspects.** *AJNR Am J Neuroradiol* 1997;18:1897–904
19. Wasnich RD. **Vertebral fracture epidemiology.** *Bone* 1996;18(suppl 3):179S–83S
20. Cooper C, Atkinson EJ, O'Fallon WM, et al. **Incidence of clinically diagnosed vertebral fractures: a population-based study in Rochester, Minnesota, 1985–1989.** *J Bone Miner Res* 1992;7:221–27
21. Uppin AA, Hirsch JA, Centenera LV, et al. **Occurrence of new vertebral body fracture after percutaneous vertebroplasty in patients with osteoporosis.** *Radiology* 2003;226:119–24
22. Lunt M, O'Neill TW, Felsenberg D, et al. **Characteristics of a prevalent vertebral deformity predict subsequent vertebral fracture: results from the European Prospective Osteoporosis Study (EPOS).** *Bone* 2003;33:505–13
23. Lin EP, Ekholm S, Hiwatashi A, et al. **Vertebroplasty: cement leakage into the disc increases the risk of new fracture of adjacent vertebral body.** *AJNR Am J Neuroradiol* 2004;25:175–80
24. Laredo JD, Hamze B. **Complications of percutaneous vertebroplasty and their prevention.** *Skeletal Radiol* 2004;33:493–505
25. Fribourg D, Tang C, Sra P, et al. **Incidence of subsequent vertebral fracture after kyphoplasty.** *Spine* 2004;29:2270–76; discussion 2277
26. Baur A, Stabler A, Arbogast S, et al. **Acute osteoporotic and neoplastic vertebral compression fractures: fluid sign at MR imaging.** *Radiology* 2002;225:730–35
27. Do HM. **Magnetic resonance imaging in the evaluation of patients for percutaneous vertebroplasty.** *Top Magn Reson Imaging* 2000;11:235–44
28. Uetani M, Hashmi R, Hayashi K. **Malignant and benign compression fractures: differentiation and diagnostic pitfalls on MRI.** *Clin Radiol* 2004;59:124–31
29. Black DM, Palermo L, Nevitt MC, et al. **Defining incident vertebral deformity: a prospective comparison of several approaches: the Study of Osteoporotic Fractures Research Group.** *J Bone Miner Res* 1999;14:90–101
30. Melton LJ, Egan KS, O'Fallon WM, et al. **Influence of fracture criteria on the outcome of a randomized trial of therapy.** *Osteoporos Int* 1998;8:184–91
31. Lunt M, Ismail AA, Felsenberg D, et al. **Defining incident vertebral deformities in population studies: a comparison of morphometric criteria.** *Osteoporos Int* 2002;13:809–15
32. Nevitt MC, Ross PD, Palermo L, et al. **Association of prevalent vertebral fractures, bone density, and alendronate treatment with incident vertebral fractures: effect of number and spinal location of fractures: the Fracture Intervention Trial Research Group.** *Bone* 1999;25:613–19