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MAGNETIC RESONANCE IMAGING FINDINGS OF SUBSEQUENT FRACTURES AFTER VERTEBROPLASTY

OBJECTIVE: The biomechanical effect of injected cement has been considered as the cause of adjacent vertebral fracture (AVF) after vertebroplasty, but the clinical evidence supporting this hypothesis is still insufficient.

METHODS: We retrospectively reviewed 33 patients with subsequent fractures among 278 patients who underwent percutaneous vertebroplasty at our hospital from January 2002 to December 2005. The bone marrow edema pattern of subsequent fractures on magnetic resonance imaging was analyzed in 33 patients. In addition, the relationship between the location and distribution pattern of inserted cement and site of subsequent fractures was investigated.

RESULTS: Among 33 subsequent fractures, we found 13 cranial AVFs, 7 caudal AVFs, and 13 remote fractures. The incidence rate of AVFs was 7.3% of 273 patients. Among 33 subsequent vertebral fractures, 13 were cranial AVFs (Group 1), 3 were superior, 7 were inferior, and 3 were overall (23.1%, 53.8%, and 23.1%, respectively). Of 7 caudal AVFs (Group 2), 7 were superior (100%). In 13 remote fractures (Group 3), 10 were superior, 1 was inferior, 2 were overall (76.9%, 7.7%, and 15.4%, respectively). In AVFs, bone marrow edema appeared mainly toward injected cement ($P = 0.005$). When injected cement made a solid mass rather than interdigitation, the occurrence rate of cranial AVFs was high ($P = 0.004$).

CONCLUSION: Bone marrow edema of AVFs appeared significantly toward the previous injected cement. This phenomenon supports the idea that the biomechanical effect of injected cement is one of the causative factors which affect the occurrence of AVF after percutaneous vertebroplasty. In particular, when injected cement forms a solid mass rather than interdigitation, the risk of cranial AVF may increase.

KEY WORDS: Adjacent vertebral fracture, Bone marrow edema pattern, Percutaneous vertebroplasty

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Since Galibert et al. (6) first reported vertebroplasty for minimally invasive treatment of hemangiomas in 1987, percutaneous vertebroplasty (PVP) using polymethylmethacrylate has been widely used for the treatment of painful osteoporotic vertebral compression fractures. However, subsequent fractures accompanying recurrent pain often occur after PVP, and more than half of subsequent fractures occur in adjacent vertebral bodies (12, 18–20). Therefore, the biomechanical effect of injected cement has been considered as the cause of adjacent vertebral fracture (AVF), but the clinical evidence supporting this hypothesis is still insufficient.

ABBREVIATIONS: AVF, adjacent vertebral fracture; **BME**, bone marrow edema; **MRI**, magnetic resonance imaging; **PVP**, percutaneous verebroplasty

In patients with multiple compression fractures, the treatment location is commonly determined by bone scintigraphy and magnetic resonance imaging (MRI). The loss of normal signal intensity on MRI indicates acute or subacute fractures and is used as the main indicator of treatment location. Especially, the hypointense signal of the vertebral bone marrow space on T1-weighted image represents bone marrow edema (BME), which occurs by disruption of normal marrow trabeculae with interstitial fluid leakage and hemorrhage. The pattern and extent of BME depend on insult mechanism and are usually seen in localized

areas by acute direct impaction force or chronic repeated microtrauma (3, 16).

In MRI findings of patients with subsequent fractures after PVP, the authors observed that the BME pattern in AVFs appears differently from that in primary fractures. The purpose of this study was to investigate the cement effect on AVFs by analyzing BME patterns on MRI findings of subsequent fractures as well as the influence of the location and distribution pattern of injected cement on the occurrence of AVFs.

PATIENTS AND METHODS

We retrospectively reviewed 273 consecutive patients who underwent PVP with polymethylmethacrylate for osteoporotic compression fractures at our hospital from January 2002 to December 2005. We excluded patients who underwent kyphoplasty, steroid-dependent patients, and oncology patients in this study. All patients were followed for a minimum of 2 years. In 33 of 233 patients, recurrent pain occurred during the follow-up period. Plain radiography, bone scintigraphy, and MRI were performed for 33 patients, and symptomatic subsequent vertebral fractures were diagnosed. The mean age of the patients was 72 years (age range, 52–86 years), and 28 were women. The 33 subsequent vertebral fractures were grouped into cranial AVFs (Group 1), caudal AVFs (Group 2), and remote fractures (Group 3), according to the relationship of the location with the treated vertebrae.

First, BME patterns of 394 primary fractures that occurred in 273 patients were analyzed to classify the general BME pattern of osteoporotic compression fractures on MRI. According to the location of BME (low signal intensity) on T1-weighted sagittal images, the BME pattern of fractured vertebral body was classified into 3 types: 1) superior, when BME appeared on the superior endplate of the vertebral body; 2) inferior, when BME appeared on the inferior endplate; and 3) overall, when BME appeared on the whole portion of the vertebral body (Fig. 1).

According to the deviation of injected cement in the vertebral body on lateral plain x-ray film, the location of cement was classified into 3 types: 1) superiorly located, when bone cement deviated in the upper portion of the vertebral body; 2) inferiorly located, when bone cement deviated in the lower portion of the vertebral body; and 3) middle located, when bone cement was located in the middle portion of the vertebral body or there was no deviation. According to the appearance of bone cement on lateral plain x-ray film, the distribution pattern of bone cement was classified into 2 types: 1) interdigitation, when bone cement was interspersed throughout the trabeculae, and 2) solid mass, when bone cement lumped without interspersion (Fig. 2).

Through these classifications, the difference of BME patterns in subsequent vertebral fractures (Groups 1, 2, and 3) was evaluated. In addition, under our hypothesis that bone cement could influence adjacent fractures, the relationship between the location and distribution pattern of injected cement and subsequent vertebral fractures was investigated. Statistical analysis was performed using the χ^2 test (SPSS, version 12.0; SPSS, Inc., Chicago, IL); a P value of less than 0.05 was considered statistically significant.

RESULTS

Incidence of Subsequent Fractures and Adjacent Vertebral Fractures

There were 33 subsequent vertebral fractures after PVP, and the incidence rate of subsequent vertebral fractures was 12.1%.

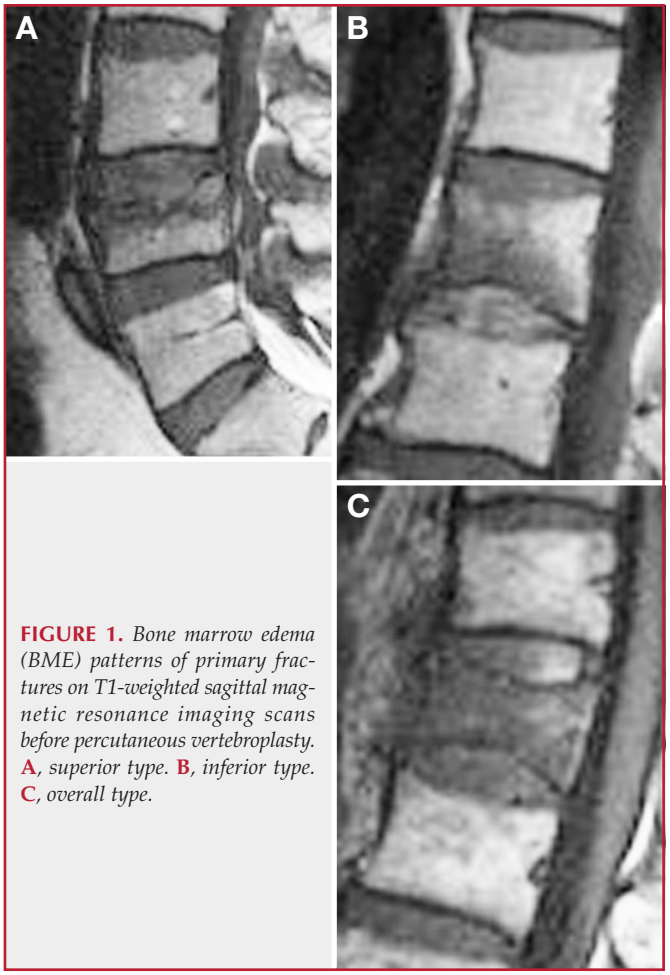

FIGURE 1. *Bone marrow edema (BME) patterns of primary fractures on T1-weighted sagittal magnetic resonance imaging scans before percutaneous vertebroplasty.* **A**, *superior type.* **B**, *inferior type.* **C**, *overall type.*

Among 33 subsequent fractures, 13 were cranial AVFs (Group 1, 39.4%), 7 were caudal AVFs (Group 2, 21.2%), and 13 were remote fractures (Group 3, 39.4%). Therefore, the incidence rate of AVFs was 7.3% of 273 patients and 60.6% of 33 patients with subsequent fractures. The median time to occurrence of adjacent fractures was 7.2 months, whereas the median time to occurrence of remote fractures was 14.8 months.

BME Pattern of Subsequent Fractures

Among 394 primary fractures, 229 were superior types of BME, 87 were inferior types, and 78 were overall types (58.1%, 22.1%, and 19.8%, respectively). Superior types of BME were the most common BME pattern of primary vertebral fractures.

Analyzing the BME pattern of 33 subsequent vertebral factures, 13 were cranial AVFs (Group 1), 3 were superior types, 7 were inferior types, and 3 were overall types (23.1%, 53.8%, and 23.1%, respectively). Of 7 caudal AVFs (Group 2), 7 were superior types (100%). In 13 remote fractures (Group 3), 10 were superior, 1 was inferior, and 2 were overall (76.9%, 7.7%, and15.4%, respectively). BME of cranial AVFs appeared mainly on the inferior endplate, unlike primary fractures or remote fractures in which

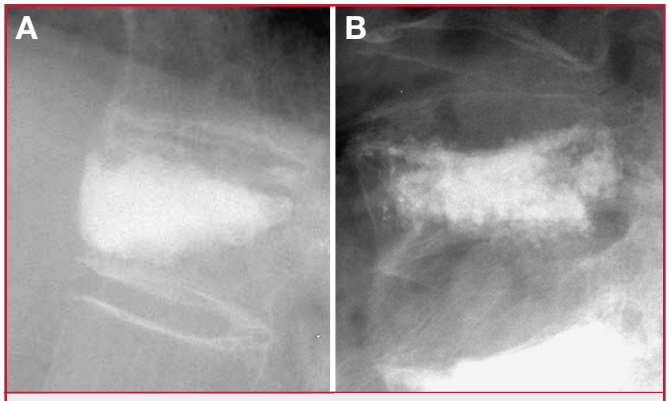

FIGURE 2. *The distribution patterns of bone cement in the vertebral body.* **A**, *solid mass type.* **B**, *interdigitation type.*

BME appeared mainly in the superior endplate. BME of caudal AVFs appeared mainly on the inferior endplate with higher rates than primary or remote fractures. Therefore, BME of AVF appeared mainly toward injected cement (Fig. 3). The difference between individual groups was statistically significant ($P = 0.005$) (Fig. 4).

Location and Distribution Pattern of Bone Cement and Its Relation with Subsequent Fractures

Analyzing the location of injected cement in 33 patients with subsequent vertebral fractures, 15 were superiorly located, 6 were inferiorly located, and 12 were middle located types. Among 15 patients with superiorly located cement, cranial AVFs were found in 7, caudal AVFs were found in 2, and remote fractures were found in 6 (46.7%, 13.3%, and 40.0%). Among 6 patients with inferiorly located cement, cranial AVF was found

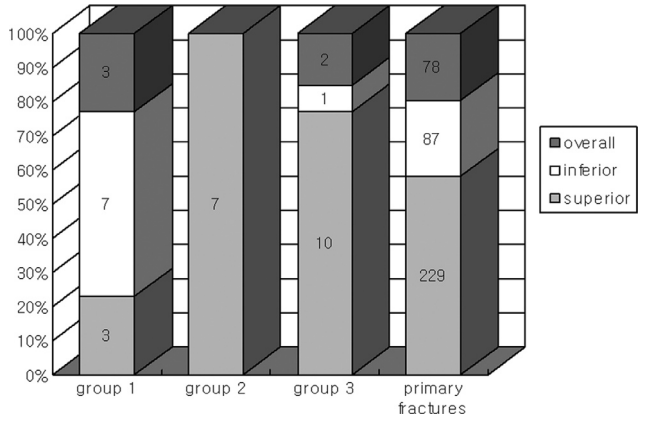

FIGURE 3. *Bar graph presenting the percentages of BME patterns in primary and subsequent fractures. In primary fractures and Group 3 (remote fractures), superior types of BME were dominant. Inferior types of BME were dominant in Group 1 (cranial adjacent vertebral fracture [AVF]) and superior types were highly dominant in Group 2 (caudal AVF).*

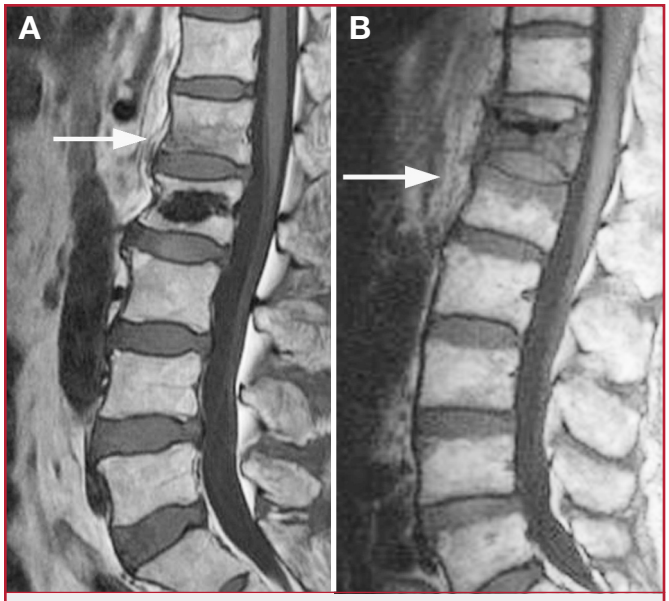

FIGURE 4. *BME pattern of adjacent vertebral fracture after percutaneous vertebroplasty. BME of the cranial adjacent vertebral fracture appears on the inferior endplate toward the injected cement (*A*) and BME of the caudal adjacent vertebral fracture appears on the superior endplate toward the injected cement (*B*) (white arrow, BME).*

in 1, caudal AVFs were found in 2, and remote fractures were found in 3 (16.7%, 33.3%, and 50%). Among 12 patients with middle located cement, cranial AVFs were found in 4, caudal AVFs were found in 3, and remote fractures were found in 5 (25%, 33.3%, and 41.7%). Therefore, when injected cement was located toward one side in the vertebral body, AVFs showed a tendency to occur in the direction where cement was deviated, but there was no statistical significance ($P = 0.848$).

Analyzing the distribution pattern of injected cement in 33 patients, 12 were solid mass types and 21 were interdigitation types. Among 12 patients with solid mass pattern, cranial AVFs were found in 9 and remote fractures were found in 3 (75.0% and 25.0%, respectively). Among 21 patients with an interdigitation pattern, cranial AVFs were found in 4, caudal AVFs were found in 7, and remote fractures were found in 10 (33.3%, 19.1%, and 47.6%). Therefore, when injected cement made a solid mass rather than interdigitation, the occurrence rate of cranial AVFs was high ($P = 0.004$).

DISCUSSION

The incidence of subsequent fractures after PVP is variable and ranges from 8% to 52% (1, 4, 7, 8, 10, 17). However, the occurrence rate of adjacent facture is relatively high and has been reported to be as high as 42% to 67% of subsequent vertebral fractures (12, 18–20). Therefore, the biomechanical effect of injected cement has been considered as a cause of AVF after PVP. Nevertheless, the clinical evidence supporting this hypothesis is insufficient and there is still controversy between

the cement effect and the natural process by preexisting osteoporosis as a cause of AVF. The authors observed that BME of subsequent vertebral fractures appeared differently according to fracture site, especially in AVFs. In our study, superior types of BME were dominant, occupying 58.1% of primary fractures and 76.9% of remote fractures. On the contrary, in cranial AVFs, inferior types of BME were dominant, occupying 53.8%, and in caudal AVFs, the frequency of superior BME was higher than in primary and remote fractures. These results mean that there is a tendency that BME of AVF appears toward previously injected cement. Moreover, if the cement effect on overall type of BME is considered, this tendency could be increased. This phenomenon supports the idea that the biomechanical effect of injected cement is one of the causative factors that affect the occurrence of AVFs after PVP. Baroud et al. (1) explained the occurrence of AVFs after PVP as a biomechanical model. They suggested that the cement in the augmented vertebra acts as an upright pillar that reduces the physiological inward bulging of the endplates of the augmented vertebra. Subsequently, adjacent vertebrae experience a higher loading in the same range and shift in adjacent loading act as the cause of adjacent fracture. Trout et al. (18, 19) supported the cement effect on AVF, reporting earlier occurrence of AVF than non-AVF and high occurrence of inferior endplate fracture immediately cephalad to the treated level.

As risk factors of AVF, cement leakage into disc space and large volumes of cement were reported as causative factors (2, 12, 14). Berlemann et al. (2) reported that maximum filling with bone cement provoked fracture in adjacent, non-augmented vertebrae through biomechanical study. However, the filling volume of bone cement is usually limited below 5 mL clinically to prevent cement leakage into disc or epidural space, and there is difficulty in investigating the relationship between the filling volume of bone cement and AVFs in vivo. Instead, based on our previous results, we investigated the distribution pattern and location of injected cement, which could be considered as a biomechanical factor of cement. In our study, there was no statistical significance between the occurrence of AVFs and the location of injected cement. In the cement distribution pattern, the occurrence rate of cranial AVFs was high when bone cement made a solid mass. From these results, we can deduce that when injected cement makes a solid mass, stiffness of bone cement increases and consequent higher loading shift causes AVF. As far as the authors know, there has been no mechanical study on the distribution pattern of bone cement and stiffness. However, Keller et al. (9) reported that adjacent segment stresses were increased as much as 45% after kyphoplasty, and in other literature, higher occurrence of subsequent fracture has been reported after kyphoplasty (4, 5, 7). Kyphoplasty, which technically produces a cavity in vertebral body by balloon expansion, has a tendency to show cement filling of solid mass. Therefore, the increased risk of adjacent fracture after kyphoplasty may correspond with our results. In addition, the intravertebral cleft can be considered as another factor of solid mass distribution. Generally, the intravertebral cleft has been considered pathognomic for avascular necrosis and a rare cause of compression fractures (13, 15). However, Lane et al. (11) reported that intravertebral clefts are more common than previously described, occupying 31.8% of 236 compression fractures. They identified intravertebral clefts through cleft pattern of opacification, that is, solid mass distribution, at the time of vertebroplasty. Therefore, we could predict the possibility of AVF after PVP by the existence of the intravertebral cleft on preoperative MRI.

In our study, there are some limitations. First, the definitions to categorize the location and distribution of bone cement were not strict and there could be some differences in interpretation. In particular, the location of cement was only interpreted through 2-dimentional plain lateral films. Second, the timing of subsequent fractures and trauma history were excluded from our study, and delayed fractures may be related to additional minor trauma and natural course by osteoporosis. Third, our study was a retrospective study. Because the number of subsequent fractures was not sufficient, nonparametric statistical testing was performed. Nevertheless, our study is meaningful because MRI findings of subsequent vertebral fractures were analyzed focusing on BME pattern and the effect of the location and distribution pattern on AVF were investigated. Finally, we recommend that additional biomechanical study should be done considering the location and distribution pattern of bone cement.

CONCLUSIONS

BME of AVFs appeared significantly toward previous injected cement. This phenomenon supports the idea that the biomechanical effect of injected cement is one of the causative factors that affect the occurrence of AVF after PVP. In particular, when injected cement forms a solid mass rather than interdigitation, the risk of cranial AVF may increase.

Disclosure

The authors have no personal financial or institutional interest in any of the drugs, materials, or devices described in this article.

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COMMENTS

Vertebral body augmentation has recently become a popular and widely used procedure. Although the current indications for its application are probably overbroad, the ability to manage patients with incapacitating, refractory pain can be viewed as a worthwhile addition to the spinal surgeon's armamentarium. However, as anyone who manages these patients can attest to, adjacent or proximate new fractures pose a vexing problem, and the question of whether the treatment has simply increased the likelihood of new fractures remains an unanswered question.

In this report by Han et al., efforts were made to elucidate what technical or radiographic factors may have been predictive of a new vertebral compression fracture (VCF). The authors' main conclusion, that solid aggregations of cement are more prone to cause new VCFs, is likely to be accurate, and they found that cement that interdigitates into the bone marrow is less likely to be problematic. However, since the surgeon frequently cannot control the distribution of polymethylmethacrylate, it may simply be that the more severely compromised skeletons were also more likely to cause solid cement distribution patterns.

Ultimately, better solutions to this problem will be needed in the future as we struggle to manage the growing population of elderly patients who are otherwise healthy for their age but are skeletally crippled. New biomaterials with a modulus of elasticity closer to osteoporotic bone, improved methods of bracing and surgical fixation, and more effective medical agents to treat the core disease will be necessary. The authors have performed fine work and achieved excellent clinical results.

Michael Y. Wang
Miami, Florida

Han et al. describe the patterns of subsequent VCFs after vertebroplasty. They found that the performance of vertebroplasty altered the pattern of VCFs in terms of the morphology of magnetic resonance imaging (MRI) findings. When subsequent VCFs occurred adjacent to the index procedure, the fracture tended to be close to the cement. It is unclear whether all patients underwent follow-up MRI examinations or just those with symptomatic new VCFs. The data presented do indicate that increasing the stiffness of one vertebral body may result in increased stress in the immediately adjacent vertebral body.

Daniel K. Resnick
Madison, Wisconsin

The authors have demonstrated MRI evidence for bone changes in segments adjacent to vertebroplasty in a sizable clinical population. Certainly, the observation that adjacent segment fractures are common is indisputable. This is well documented throughout the spine literature and is a risk that must be identified to any patient undergoing the procedure. Indeed, some practitioners recommend prophylactic injection of adjacent segments that are presumed to be at high risk. Although not entirely unreasonable, prophylactic injection is not currently being practiced in this institution.

Having said that, I am not entirely certain that the authors can extrapolate their conclusions from the data presented. First of all, the nature of fractures at adjacent segments is predominantly a biomechanical phenomenon. MRI, while extremely valuable in determining pathology, is not a biomechanical technique. Rather, determination of biomechanical data requires an experimental study measuring load deformation as well as internal stresses within bone. These have been previously published and are referenced by the authors.

As the current authors correctly note, there are no basic studies on the distribution pattern of bone cement and incidence of fracture. However, I suspect that it is more a phenomenon of the cement mass, rather than whether it is interdigitating or solid. This effort probably would be best accomplished through mathematical modeling using a validated lumbar spine model, since it would be very difficult to recreate the variables in the cadaver environment.

Although the authors have made an interesting observation, much of it is predictable on the basis of previous knowledge of stress fractures in bone. The authors have actually asked more than they have answered; the rest of the determination remains for the laboratory.

Dennis J. Maiman
Milwaukee, Wisconsin

The authors retrospectively reviewed 273 patients who underwent a percutaneous vertebroplasty procedure over a 3-year period and reported 33 symptomatic subsequent vertebral fractures. Of the 273 patients, 13 (4.8%) had adjacent fractures, and 7 (2.6%) had remote fractures. The fracture's bone marrow edema (BME) pattern on MRI as well as the relationship between the location and distribution pattern of inserted cement and subsequent fractures was analyzed. The authors reported that significant BME was visible toward the injected cement; in the rostral adjacent vertebral fracture (AVF), BME developed in the

inferior endplate, and in the caudal AVF, BME was found in the superior endplate. Additionally, they noted that injected cement in the form of a solid mass rather than an interdigitating mass seemed to increase the risk of developing a cranial AVF.

These authors present additional useful information in our attempt to elucidate the factors that cause further VCFs. They report an increased influence of cement positioning and dispersion in creating fractures. Unfortunately, this is most likely an oversimplification of a complex process. Although cement injected into the vertebral body does appear to influence the local biomechanical forces, its effects, globally, on the spinal biomechanics are poorly defined. The present study notes an increase in the AVF toward the polymethylmethacrylate augmentation; however, others have reported no subsequent increase in fracture rates after vertebral augmentation (2). Unfortunately, the natural history of VCFs is poorly understood. Lindsay et al. (3) reviewed more than 2500 postmenopausal women and reported that the incidence of a new vertebral fracture in the year after a VCF was 19.2% without any intervention.

The authors of this study should be commended that their subsequent VCF rate was only 4% (33 symptomatic patients), when based on the natural history study of Lindsay et al. (3), it should be 19.2% (157 patients). This illustrates the numerous influences on these patients and is most likely attributable to the fact that only one-third of VCFs are symptomatic. Furthermore, additional factors such as the use of osteoporosis medication, the patient's overall sagittal alignment, focal kyphosis, bone density, volume of cement, lower body mass index, intradiscal cement leakage, and injection techniques influence subsequent fracture rates. The use of MRI to infer biomechanical affects should be used with caution, because the correlation of MRI with vertebral augmentation has not been elucidated (1).

The authors note that the cement dispersion may influence future fracture rates. This raises the question of whether the cement was injected in this pattern or whether it followed the "path of least resistance." The cement most likely is influenced by the amount of cancellous bone trabeculae in the vertebral body: with minimal trabeculae, the cement would congeal in a single mass, but with increased trabeculae and resistance, the cement would be interdispersed. Therefore, the dispersed polymethylmethacrylate would have increased strength as a result of the inherent bone structure. Overall, this is an interesting and educating article that provides further insight into our understanding of human physiology, biomechanics, and surgical treatment options for VCFs.

James S. Harrop
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Percutaneous vertebroplasty is becoming a common treatment for osteoporotic vertebral fractures. The authors report 33 patients who had an AVF after undergoing percutaneous vertebroplasty. They found that the pattern of BME at the AVF was significantly related to the location of the previously injected cement. That is, the BME associated with a cranial AVF appeared most frequently on the inferior endplate toward the injected cement. Likewise, BME involving the caudal vertebral AVF tended to appear more frequently in the superior endplate toward the injected cement.

They also noticed that cement injected in a solid mass rather than in an interdigitated mass seemed to be associated with a higher risk of cranial AVF. This observation is interesting. However, it is unclear how symptomatic these 33 fractures were and how these 33 fractures were treated. Nevertheless, the observations made by the authors make sense, and it is nice to have these points documented so well.

Volker K.H. Sonntag
Phoenix, Arizona

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