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Effects of Polymethylmethacrylate Cement Viscosity and Bone Porosity on Cement Leakage and New Vertebral Fractures After Percutaneous Vertebroplasty: A Prospective Study

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Abstract

Study Design: A prospective randomized study.

Objectives: To evaluate the effect of bone cement viscosity as well as of bone porosity on cement leakage during vertebroplasty and to analyze the occurrence of new vertebral fractures after the procedure.

Methods: Between April 2012 and December 2013, 60 patients suffering from osteoporotic vertebral fractures underwent vertebroplasty. The patients were randomly assigned into 2 equal groups. High-viscosity cement was used in group A, while low-viscosity cement was used in group B. Patients were followed-up for a minimum of 2 years.

Results: Cement leakage occurred in 16 patients in group B (20 vertebral bodies) and in 6 patients in group A (9 vertebral bodies). The difference was statistically significant ($\chi^2 = 2.3$, $P = .01$). Lower *T*-scores were associated with significantly more cement leakage ($t = 3.338$, $P = .002$ in group A, and $t = 4.329$, $P = .000$ in group B). Patients with a *T*-score worse than -1.8 had a significantly higher risk of cement leakage if low-viscosity cement was used ($\chi^2 = 3.25$, $P = .05$). New vertebral fractures occurred in 14 (23%) patients, after a mean of 6.5 ± 5.5 months, 10 patients in group A and 4 in group B. The difference did not reach the statistical significance level ($\chi^2 = 3.354$, $P = .067$). Patients presenting with multiple fractures had a significantly more number of new vertebral fractures ($\chi^2 = 7.464$, $P = .006$).

Conclusions: The clinical outcome of vertebroplasty was not influenced by cement viscosity. However, lower cement viscosity and higher degree of osteoporosis were found to be significant risk factors for cement leakage. Furthermore, the number of vertebral body fractures on presentation was a predictor for the occurrence of new fractures postoperatively.

Keywords

vertebroplasty, viscosity, osteoporosis, fracture, compression, cement, leakage

Introduction

Percutaneous vertebroplasty is a widely used vertebral augmentation procedure for treating painful osteoporotic vertebral compression fractures when conventional therapies are not effective. Vertebroplasty consists of injecting cement into a collapsed vertebra in order to reinforce the fractured vertebra and gain pain relief. Polymethylmethacrylate (PMMA) is the most widely used cement type because of its good handling properties, strength, long time experience, and low costs.[1] One of the main characterizing parameters of PMMA bone cement is viscosity. This factor affects the spatial distribution of cement in the vertebral body, which, when inadequate, could alter the pattern of load transfer and might thereby induce new adjacent fractures.[1-3] Additionally, viscosity of bone cement is

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also an essential parameter regarding extra-vertebral bone cement leakage,[2,3] which occasionally lead to severe complications such as neurological deficits and pulmonary cement embolisms.[1-4]

Another important factor is the bone quality. This is not only the main cause of fracture in osteoporotic patients, but experimental study has shown that bone porosity should not be underestimated as a risk factor for bone cement leakage during vertebroplasty.[5] Furthermore, patients suffering from osteoporotic vertebral fractures have a high risk to develop another vertebral fracture.[6] In a constantly aging population, the term "new fracture after vertebroplasty" is gaining popularity among spine surgeons as well as in the literature dealing with percutaneous vertebroplasty.[6-11]

The purpose of this study was to evaluate the effect of bone cement viscosity as well as of bone quality on cement leakage during percutaneous vertebroplasty and to analyze the factors associated with the occurrence of new vertebral fractures after the procedure.

Materials and Methods

This study was designed as a single-center prospective randomized comparison between vertebroplasty using high-viscosity PMMA bone cement and vertebroplasty using low-viscosity PMMA bone cement for treating osteoporotic vertebral compression fractures in the thoracic and lumbar regions of the spine. Ethics approval was obtained from Institutional Review Board (Number 328-2012). Plain radiographs, magnetic resonance imaging (MRI), and dual-energy X-ray absorptiometry (DEXA) were evaluated before the surgery in each patient to determine the appropriateness of the procedure and plan the treated levels. The inclusion criteria were recent lumbar or thoracic vertebral compression fractures (proven by radiographs and MRI) with unsatisfactory pain relief (visual analogue scale [VAS] $\geq$5) after at least 4 weeks of conventional therapy, and a diagnosis of osteoporosis or osteopenia (proven by DEXA). Exclusion criteria included burst fractures with spinal canal stenosis, infection, radicular symptoms, presence of a previously treated osteoporotic fracture, and spinal metastasis.

The study included 60 patients treated between April 2012 and December 2013. The patients were randomly assigned into 2 groups. In group A, consisting of 30 patients, high-viscosity bone cement (Confidence Spinal Cement System, DePuy Spine Inc, Raynham, MA, USA) was used. Group B also consisted of 30 patients, who were treated using low-viscosity bone cement (Osteopal V, Heraeus Medical GmbH, Wehrheim, Germany). The operations were performed through 1 surgeon (M.A.). Randomization was performed according to the block randomization method. This method allows the randomization of the patients into groups that result in equal sample size in each group (in our study, 30 patients in each group). A detailed explanation of the method is described in the article by Suresh.[12] All patients had an informed consent that they will be involved in this study, but the patients remained blinded regarding the type of bone cement used. All the 60 patients were followed up for a minimum of 2 years. Written consent was obtained from each patient before enrollment.

Surgical Technique

The procedure of vertebroplasty has been well described previously.[5,13,14] We used a bipedicular approach in all patients and the Jamshidi needles were placed using 2 perpendicular X-ray devices with high-quality image control. The tip of the needle was placed in the anterior one-third of the vertebral body. Injected cement volume was recorded. During surgery, we considered adequate filling when in both anterior-posterior and lateral views 50% of the vertebral body is filled with cement, and as an endpoint we limited the injection volume to a maximum of 8 mL in the lumbar spine and 6 mL in the thoracic spine. These values are adopted after Nieuwenhuijse et al.[15] In their work, they recommended that the volume of the injected bone cement injection should be planned according to the level of the fractured vertebra. After the procedure, all patients remained for a minimum of 2 days in the hospital, and treatment with calcium, vitamin D supplements, and specific osteoporosis agents was started.

Outcome Assessment

Pain scores were recorded using visual analogue scale (VAS) before the procedure, at day 1, at 3 months, 1 year, and 2 years after the procedure. The Oswestry Disability Index (ODI) was used to measure patients' functional disability before the procedure, and at 3 months, 1 year, and 2 years after the procedure. Assessment of cement leakage was based on radiographs evaluated by an independent radiologist, supplemented by postoperative computed tomography scans in patients with suspected cement leakage in the radiographs. In addition, the location of leakage was classified as follows: (1) disc space, (2) epidural space, (3) paravertebral areas, and (4) peripheral veins.[16] The occurrence of a new vertebral body fracture during the follow-up was recorded and analyzed.

Statistical Analysis

Statistical tests used to analyse statistical significance included the Fisher exact and χ^2 tests as well as the Student's *t* test. The significance level was set to .05 throughout the study. The statistical analysis was performed using SPSS program (version 20) on IBM compatible computer.

Results

Preoperative Findings

In 50 patients, a single vertebral body was augmented while in 10 patients, multiple levels were augmented (2 to 3 levels). In group A, a total of 37 vertebral bodies was augmented (26 lumbar and 11 thoracic); while in group B, a total of 36 vertebral bodies were augmented (26 lumbar and 10 thoracic).

Table 1. Preoperative and Intraoperative Patients' Data.

Characteristic	Group A "High Viscosity"	Group B "Low Viscosity"	P
Age, years, mean ± SD	68.63 ± 6.9	71.53 ± 7	.18 (t test)
Gender, female/male, n	18/12	17/13	.21 (χ^2 test)
T-score, mean ± SD	−1.75 ± 0.38	−2.003 ± 0.43	.15 (t test)
VAS score, mean ± SD	7.5 ± 1.5	8 ± 1.4	.25 (t test)
ODI, mean ± SD	60% ± 18%	65% ± 12.5%	.14 (t test)
Levels operated, lumbar/thoracic, n	26/11	26/10	.16 (χ^2 test)

Abbreviations: ODI, Oswestry Disability Index; VAS< visual analogue scale.

Table 2. Types of Cement Leakage in Each Group.

Type of Leakage	Group A "High Viscosity"	Group B "Low Viscosity"	
Peripheral veins	3	13	$\chi^2 = 2.24$, $P = .004$
Disc space	4	9	$\chi^2 = 1.25$, $P = .105$
Epidural space	1	4	$\chi^2 = 3.16$, $P = .177$
Paravertebral areas	5	7	$\chi^2 = 2.51$, $P = .374$

The summary of patients' demographics is shown in Table 1. There were no statistically significant differences between the 2 groups in terms of age, gender, level operated, T-score, VAS score, and ODI score.

Intraoperative Findings

No intraoperative complications necessitating revision occurred in any of the 2 groups. The mean amount of cement injected in each vertebral body was 6.2 ± 1.4 mL. This was not significantly different in both groups ($t = 3.448$, $P = .656$). The operative time was significantly longer in group B (38.5 ± 10.6 minutes) than in group A (31.5 ± 7.6 minutes) ($t = 2.945$, $P = .005$). In group A, there were leakages in 6 patients in a total of 9 levels, 3 in a single level and 3 in double levels (9/37). In group B, there were leakages in 16 patients in a total of 20 levels, 12 in a single level and 4 in double levels (20/36). The difference between the 2 groups was statistically significant ($\chi^2 = 2.34$, $P = .01$). The types of cement leakage in each group are listed in Table 2.

The degree of osteoporosis represented by the T-score in the DEXA measurement was also found to be a significant factor affecting cement leakage. Patients with lower T-score values had significantly more cement leakage in both groups ($t = 3.338$, $P = .002$ in group A, and $t = 4.329$, $P = 0.000$ in group B; Figure 1). Further statistical analysis revealed that patients with a T-score value lower than or equal to −1.8 had a significantly higher cement leakage if low-viscosity cement was used instead of high-viscosity cement ($\chi^2 = 2.35$, $P = .05$).

Postoperative Findings

Both groups experienced significant pain relief and life quality improvement as shown in Table 3 and Figures 2 and 3. The patients who had cement leakage (22 patients) were compared with those who did not have leakage (38 patients) regarding the postoperative ODI and VAS. There was no statistically significant difference between the 2 groups (Student test $P = .12$ for VAS and $P = .08$ for ODI). Leaks had no negative clinical impact in both groups. Further statistical analysis showed that patients with multiple level fractures had lower mean improvement in ODI in comparison with the average mean improvement, but the difference was statistically insignificant (compared means using t test $P = .12$).

On the other hand, new vertebral fractures were reported in 14 (23%) patients during the period of follow-up (in 10 patients in the vertebra directly above or below the augmented vertebra, and in 4 patients in a distant vertebral body). These new fractures occurred within a time span of 3 to 14 months after the augmentation (mean follow-up of 6.5 ± 5.5 months). Among these 14 patients, 10 patients belonged to group A and 4 to group B. Although the difference was markedly in favor of the low-viscosity cement, this did not reach the statistical significance level ($\chi^2 = 3.354$, $P = .067$). Furthermore, factors such as age, gender, volume of injected cement, the occurrence of leakage, and T-score were not found to have a statistically significant effect on the occurrence of new vertebral fractures during the follow-up. On the other hand, patients presenting initially with multiple osteoporotic fractures have a significantly higher possibility to have a new vertebral fracture postoperatively ($\chi^2 = 7.464$, $P = .006$).

Discussion

Study Design

Over the past 2 decades, percutaneous vertebroplasty has become one of the most important techniques for the treatment of osteoporotic vertebral compression fractures.[1,17] However, this procedure must be done with caution, as the risk of extra-osseous cement leakage in various series ranged between 3% and 74%.[18,19] The cement viscosity issue is a crucial parameter that is associated with the risk of cement leakage.[20,21] Since the introduction of high-viscosity bone cement, several studies have evaluated its efficacy and safety.[1,5,13,14,16,17,22,23] Many investigators compared this type of bone cement with balloon kyphoplasty.[16,22,24] However, the results obtained are influenced not only by the different cement types used but also by

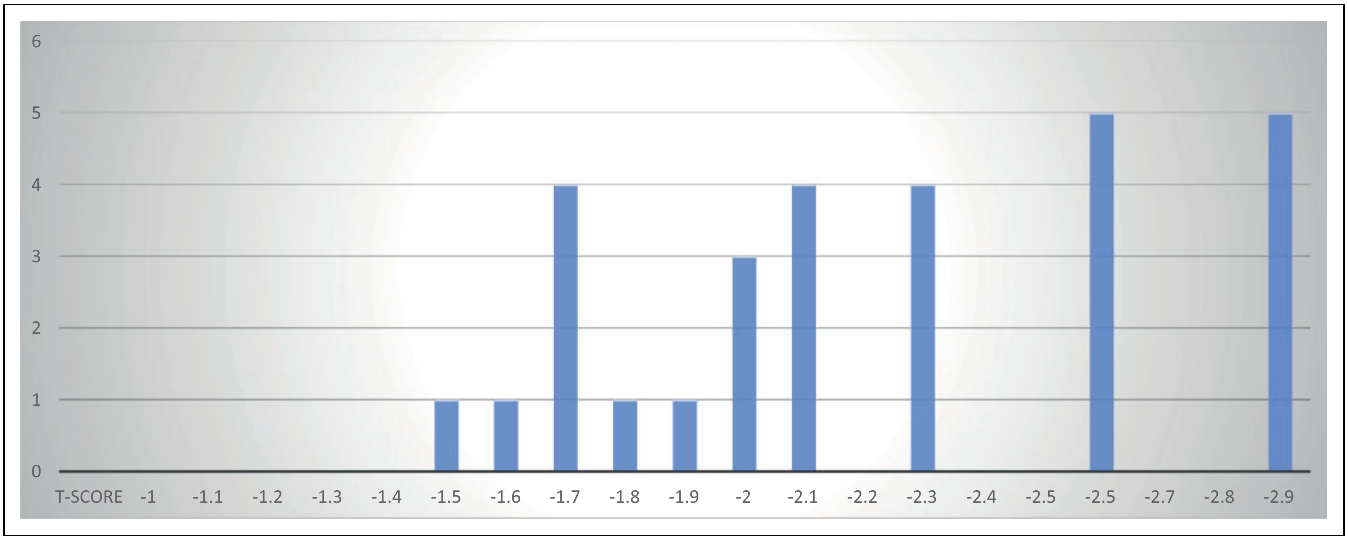

Figure 1. The number of levels with leaks.

Table 3. VAS Scores and ODI in Both Groups Before and After the Procedure.

	Group A "High Viscosity"	Group B "Low Viscosity"
Preoperative, mean ± SD		
VAS	7.5 ± 1.5	8 ± 1.4
ODI	60% ± 18%	65% ± 12.5%
Postoperative, mean ± SD		
VAS	1.5 ± 2	2.2 ± 1
ODI	15% ± 5%	12% ± 4.5%
P		
VAS	.01	.01
ODI	.001	.015

Abbreviations: ODI, Oswestry Disability Index; VAS< visual analogue scale.

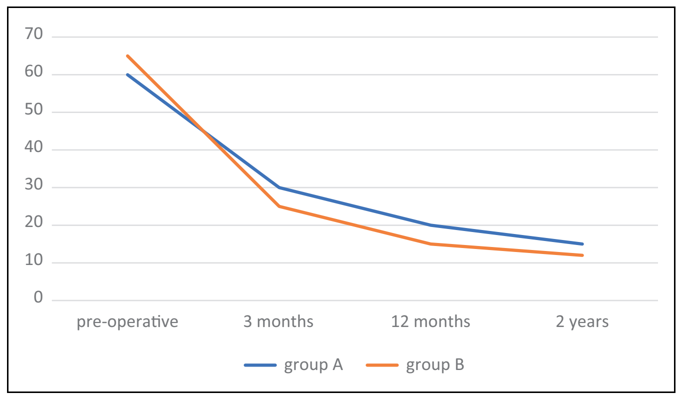

Figure 2. The changes of Oswestry Disability Index (ODI) during follow-up in both groups.

the technical differences between the 2 procedures. In order to eliminate the technical variable of the procedure, another group of authors compared the high-viscosity cement with the low-viscosity cement during percutaneous vertebroplasty. Zeng et al[23] performed the comparison retrospectively, while Nieuwenhuijse et al[1] published a prospective but nonrandomized study. In 2008, Anselmetti et al[13] performed a prospective randomized study comparing the 2 types of bone cement. However, the inclusion criteria in their work were not limited to osteoporotic fractures but extended to include pathological fractures and bone tumors.[13] In the current study, we performed the comparison in a prospective randomized manner according to level 1 of evidence. We aimed to minimize the number of variables by including only osteoporotic vertebral fractures and by applying the same operative technique in the 2 groups. The study included similar sample sizes between both groups and comparable patient types with no significant difference regarding age, gender, levels operated, *T*-score, VAS, or ODI.

Good clinical outcomes have been previously reported for vertebroplasty. In our study, as in other studies, both types of bone cement achieved satisfactory clinical outcomes, providing pain relief and improvement in the quality of life after surgery.[13,16,23,24]

Although spontaneous compression fractures are more common in the thoracic spine, more patients in this study were treated for lumbar fractures. This observation can be explained in this work based on the inclusion criteria, which were; Fractures that fail to improve clinically after 4 weeks of conservative treatment (patients who had VAS of more than 5 despite the conservative therapy), we noticed during the study that many patients with thoracic fractures responded well to the conservative therapy, which can be due to the less mechanical stresses in the thoracic region, and more mobility in the lumbar spine leading to longer healing time especially in older patients.

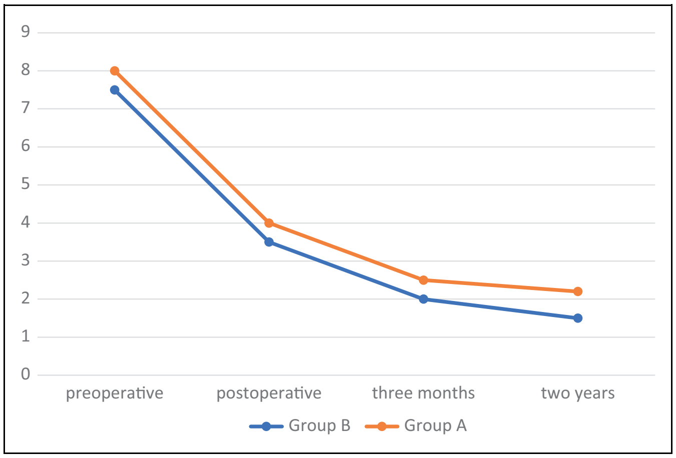

Figure 3. The changes of visual analogue scale (VAS) scores in both groups during the follow up.

Cement Leakage

Several techniques have been suggested to limit PMMA leakage during vertebroplasty. Bhatia et al[25] performed gelfoam embolization of the venous channels before cement injection and recommended using this technique to reduce cement extrusion. However; there was no control group in their study, and they reported an overall leakage rate of 26.2%. Recently, Hoppe et al[26] performed lavage prior to vertebral augmentation and reported an overall leakage rate of 37.9%. A total of 4 lavages was done for each vertebral body before cement injection.[26] In both studies, an additional procedure was performed before cement injection, which would prolong the operative time and influence the simplicity of the vertebroplasty procedure. The use of high-viscosity cement does not necessitate an additional step in the procedure. On the contrary, the operative time was significantly reduced in this study when applying high viscosity cement due to elimination of the waiting time for cement hardening. Moreover, the overall leakage rate was lower than in the series of Hoppe et al[26] and Bhatia et al,[25] reaching 20%. This value was significantly lower than in the low-viscosity cement group, in whom the leakage rate was 53.3%. This finding confirms prior clinical and experimental observations that highly viscous cements would increase the safety of vertebral augmentation compared with less viscous cements by significantly decreasing the leakage rate.[1,5,13,14,16,17,22,23]

Beside cement viscosity, bone density is also an important predictor for cement leakage. In an experimental study on an artificial vertebra model and human cadaveric spine, Loeffel et al[5] demonstrated that highly osteoporotic vertebrae augmented with thin PMMA are the most likely to produce irregular cement flow patterns and therefore exhibit a higher risk of cement leakage. They concluded that cement viscosity should be chosen proportionally to the degree of osteoporosis. These experimental findings have been strongly confirmed in our clinical study, which demonstrated that lower *T*-scores are associated with higher leakage rate in both groups. The recommendation of Loeffel et al[5] about the proportionality of cement viscosity and degree of osteoporosis led us to try to find a practical clinical application. Indeed, statistical analysis revealed that when the *T*-score is ≤ -1.8, the risk of cement leakage becomes significantly higher if low-viscosity PMMA is applied. Consequently, bone density measurement could help the surgeon in choosing the type of bone cement during vertebroplasty, with the *T*-score of -1.8 being the limit beyond which high-viscosity bone cement should be used to minimize cement leakage.

New Vertebral Fractures

New vertebral fractures are common in patients with osteoporosis who have undergone percutaneous vertebroplasty. The incidence of such new fractures is reportedly 5.5% to 52%.[6] In the current study, the incidence of new vertebral fractures in the follow-up period was 23%. Similar values have been reported by several authors as shown in Figure 4. Ren et al[6] demonstrated that the first year after the procedure is an important period for the occurrence of new fractures. Voormolen et al[10] reached the same conclusion, emphasizing that most of the fractures occur in the first 3 months, but in our study adjacent fractures occurred after a mean of 6.5 months. This difference is due to the relatively small number of patients enrolled in our study and indicates the need of further studies over longer period including more patients. Although more than half of these cases were reported in group A, cement viscosity was not found to be a significant risk factor of developing postoperative new vertebral fractures. Several investigators analyzed the risk factors that could be associated with this phenomenon. Komemushi et al[27] and Rho et al[28] reported that cement leakage into the disc is a significant predictor of new vertebral body fracture after vertebroplasty. Their explanation was that cement leakage into the disc space might cause a change in the stress distribution in the disc termed the "pillar effect" and decrease the buffering effect. In contradiction to this finding, Ren et al[6] reported leakage in the disc space unrelated to new fracture either at adjacent or nonadjacent levels. This finding is consistent with the results of the present work, indicating the irrelevance of new vertebral fractures to intradiscal leakage after vertebroplasty. A low *T*-score was a significant risk factor for subsequent vertebral compression fractures following vertebroplasty in the study of Rho et al[28] and Lu et al.[29] However, other studies have shown no significant correlation between the *T*-score and subsequent development of fractures,[6,30] consistent with the present study. Among the different variables in the current work, only the presence of multiple initial fractures preoperatively was found to be a significant predictor of new fractures postoperatively. This finding has been confirmed by most of the authors dealing with this special issue.[6,10,31,32]

Conclusion

Bone cement viscosity does not influence the clinical results after vertebroplasty. However, it plays a significant role as

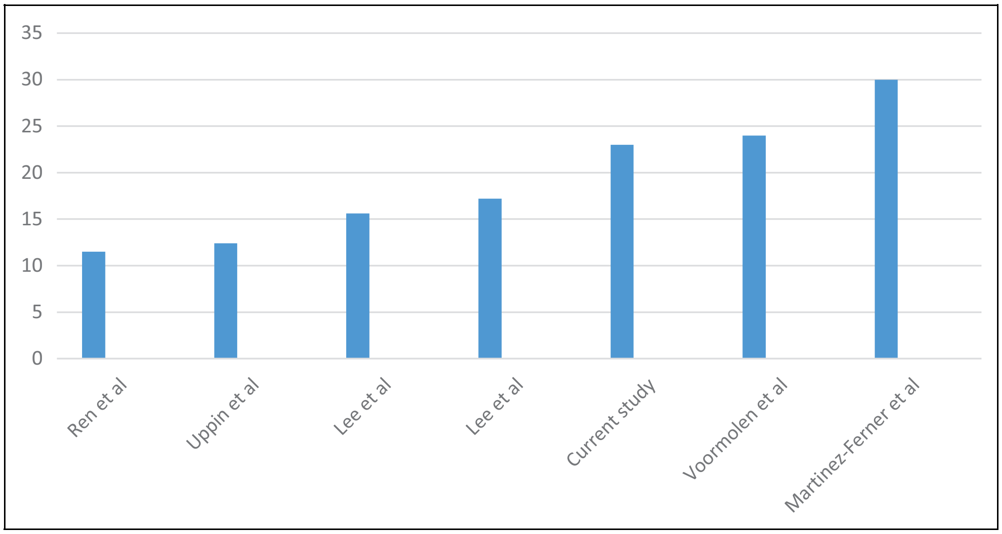

Figure 4. Incidence of new fractures after vertebroplasty.[7-11,13]

regards cement leakage. The 2 factors associated with increased occurrence of bone cement leakage are the use of low-viscosity cement and low *T*-score values. High-viscosity cement should be used, especially if the *T*-score is ≤ -1.8. The number of initial vertebral body fractures is an important predictor for the occurrence of new fractures postoperatively. Such a complication usually occurs in the first year after the procedure.

Declaration of Conflicting Interests

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