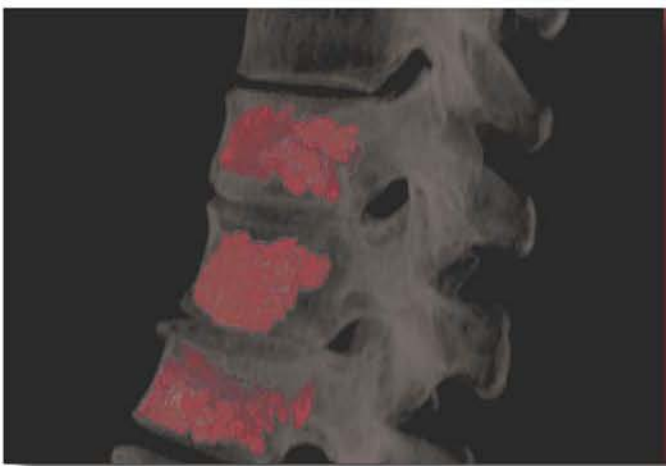
Chapter



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The Amount of Bone Marrow Edema Does Not Predict the Outcome in Single Level Percutaneous Vertebroplasty For Painful Osteoporotic Compression Fractures

Submitted

Abstract

In this study the influence of the pre-procedural intravertebral Bone Marrow Edema (BME) on post-operative pain relief in patients treated with single level Percutaneous VertebroPlasty (PVP) for non-acute osteoporotic vertebral compression fractures (OVCF) is investigated. Twenty-five patients with single level, BME containing OVCFs were included. BME volume and the percentage of the vertebral body filled with BME was volumetrically analyzed.

The mean BME volume was 11.4 mL (SD 8.2, range 2.6 – 29.3), which corresponded to a mean percentage of vertebral body volume of 46.0% (SD 19.5, range 10.0 – 71.4). During a 1-year follow-up, pain intensity was documented before PVP and 1, 4, 12 and 52 weeks after PVP.

A good clinical response to the PVP procedure was seen in all patients: pain decreased from 7.6 (SD 1.3) points before PVP to 5.3 (SD 2.6), 5.3 (SD 2.6), 3.7 (SD 2.3) and 2.9 (SD 2.2) points at 1, 4, 12 and 52 weeks follow-up. No association between the pain score and the percentage, ranging from 10%-70% BME, was found. The percentage of the vertebral body filled with BME on pre-procedural MRI does not predict the magnitude of pain reduction when performing PVP in single level non-acute OVCF.

Introduction

Percutaneous vertebroplasty, a procedure in which liquid bone cement is percutaneously injected into painful osteoporotic compressed vertebral bodies, is thought to relieve pain due to the stabilizing effect of the cured bone cement after polymerization. The precise mechanism (mechanical, or chemical) is still not completely known, but it has been shown that the bone cement halts movement within the fractured vertebral body and thus prevents further collapse.[1] Although recently some debate exists on the effect of this procedure, analysis of factors determining the clinical entity of Osteoporotic Vertebral Compression Fractures (OVCF) is of importance to evaluate the effectiveness of PVP.[2,3]

Subacute (>2 month old) and chronic (>6 month old) OVCFs are fractures which do not respond to at least 8 weeks of conservative treatment using analgesics, a short period of bed rest and a corset. Therefore, the indication triad for PVP in our institution consists of I) incapacitating pain at the fractured level,unresponsive to conservative treatment[4]; II) focal point tenderness, which increases when pressure is applied to the spinous process of the fractured vertebra[5,6]; and III) Bone Marrow Edema (BME) in the fractured vertebral body diagnosed at MR Imaging.[7-9]

In literature, it is stated that, intravertebral BME on MR Imaging is one of the indication criteria for treating painful OVCFs with PVP. A MR Imaging sequence with fat suppression, usually T2 Short Tau Inversion-Recovery (STIR) or Spectral Presaturation with Inversion Recovery (SPIR), leads to images in which structures with a high water content show a high signal and thereby visualize BME.

Intravertebral BME is seen in OVCFs that have not fully been healed. In these vertebra it is thought that persistent pain is caused by movement in unconsolidated (micro)fractures. The cause of persistent BME in chronic fractures might be explained by the altered healing cascade in these fractures compared to fractures in longbones.[10]

So far a small number of papers concerning BME in PVP have been published, however due to heterogeneous groups (acute vs chronic and multiple level vs single level), no conclusions regarding the influence of the volume of BME in chronic OVCFs can be made.[11-13] Furthermore there is no consensus about the percentage of the vertebral body that has to be filled with BME in order to be an indication for PVP nor on the relation to the clinical results after PVP.

The goal of our present study was to assess the influence of the pre-procedural intravertebral BME on the clinical outcome on pain in patients treated with PVP for single level non-acute OVCFs.

Patients and Methods

Patients were included from a consecutive series of 217 patients treated with PVP for painful OVCFs at our institution between August 2002 en January 2010. Inclusion criteria for PVP were: (I) An osteoporotic vertebral compression fracture including those with a severe compression deformity, (II) local mid-line back pain refractory to conservative treatment for at least 8 weeks, (III) back pain related to the site of the fracture on MR Imaging, (IV) the presence of intravertebral BME in the collapsed vertebral body on MR Imaging T2- weighted Short Tau Inversion Recovery (STIR) sequences, and (V) age over 40 years.

Exclusion criteria were (I) multiple OVCFs with intravertebral BME, (II) spinal cord compression or vertebral canal stenosis of >30% of the local canal diameter, (III) neurologic deficits, (IV) bleeding disorders, (V) infections related to the vertebral column, (VI) inability of the patient to lie in prone position for 2 hours, (VII) an American Society of Anesthesiologists-score ≥ 4 and (VIII) vertebral cleft fractures.

In this study, twenty-five patients (4 male, 21 female, mean age of 72.0 (SD 7.7) years) with a single level, intravertebral BME containing, OVCF with a mean time between onset of symptoms and PVP of 5.7 months (SD 2.6), were included for a prospective study.

All patients underwent a pre-operative radiograph of the spine (AP and lateral), a MR Imaging scan using a sequence with fat suppression, T2 Short Tau Inversion-Recovery (STIR) of the complete spine to visualize intravertebral BME with sagittal reconstructions using 5-millimeter slice thickness.

The levels of the treated chronically painful OVCFs were Th5(1), Th6(1), Th7(2), Th8(1), Th9(1), Th11(1), Th12(4), L1(1), L2(6), L3(3), L4(4). A mean of 2.5 (SD 2.5) old fractures without signs of intravertebral BME were present, mean spinal deformity index was 6.2 (SD 4.9).[14]

The volume of the intravertebral BME was measured by 2 independent observers (SPJM, LB) using a visual threshold (**Figure 1**). Excellent inter-observer agreement was found for measurement of the intravertebral BME volume (ICC 0.98, 95%CI: 0.96 – 0.99, $p < 0.001$). For calculation of the vertebral volume and intra-vertebral BME a DICOM viewer (Osirix 3.3, 64 bit, Kagi, Berkeley, California) was used.

The PVP procedure was performed as a uni-or bi-pedicular method using PMMA bone cement as described earlier, and during the PVP procedure in all cases a bone biopsy was performed, to rule out other causes than osteoporosis.[15,16]

During a 1- year follow-up all patients recorded a Pain Intensity Numerical Rating Scale (PI-NRS) before PVP and at 1, 4, 12 and 52 weeks after PVP. Patients underwent routine spinal radiographs at 6 and 52 weeks and at indication.

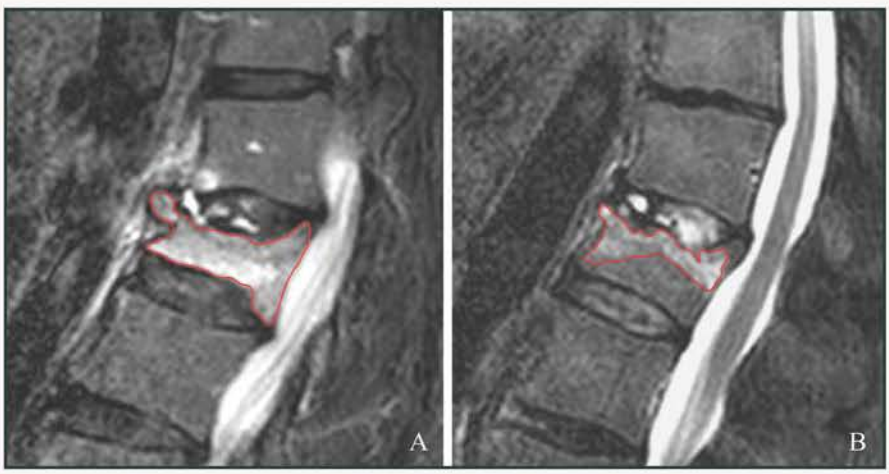

Figure 1. Measurement of intravertebral BME on T2 weighted STIR images (thickness 5 mm). Examples of BME containing vertebra of two patients. A: 64% and B: 27% of the total intravertebral volume is filled with BME. The border of the BME (high signal) is depicted by the red line.

Statistical analysis

The inter-observer agreement of the volume of intravertebral BME was assessed by calculation of the Intraclass Correlation Coefficient (ICC) (two-way mixed).

Measured values are reported as mean with Standard Deviation (SD) and range, estimates are reported as mean and 95% Confidence Interval (CI).

Patient-reported pain scores were analyzed using a linear mixed-model analysis, which takes the correlation between the repeated measurements within patients into account. Additional covariates in the analysis were patient age and gender, time since onset of symptoms, spinal deformity index and the occurrence of new OVCFs during follow-up.[17]

In all analyses, the model assumptions were assessed. A p-value of less than 0.05 was considered significant (SPSS statistical software 16.0, SPSS Inc, Chicago, IL).

Results

The mean pre-procedural PI-NRS score for back pain was 7.6 (SD 1.3) points, which decreased to 5.3 (SD 2.6), 5.3 (SD 2.6), 3.7 (SD 2.3) and 2.9 (SD 2.2) points after respectively one, four, 12 and 52 weeks post-procedurally ($p < 0.001$)(**Figure 2**). Six new OVCFs were noted in 5 patients after a mean of 8.0 months (SD 5.7). Three of these were adjacent fractures, which occurred after 1.3, 1.6 and 11.4 months. Two were symptomatic and one of these was treated with a second PVP procedure.

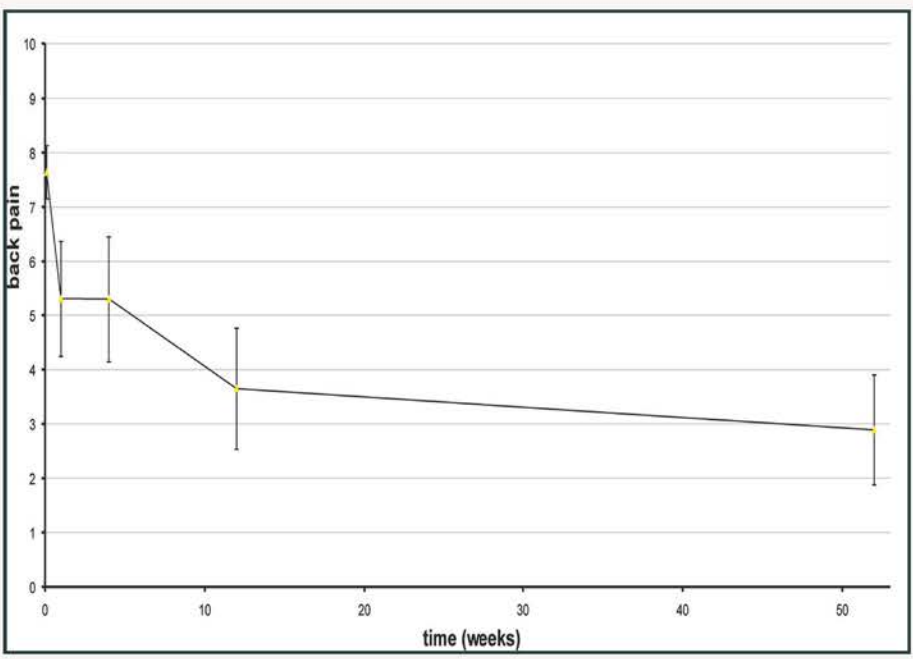

Figure 2. Mean back pain measured in pain intensity numeric rating scale score after one, four, 12 and 52 weeks post-operatively.

The mean intravertebral edema volume was 11.4 mL (SD 8.2, range 2.6 – 29.3), which corresponded to a mean percentage of vertebral body volume of 46.0% (SD 19.5, range 10.0 – 71.4)(**Figure 3**).

In multivariate repeated measures analysis, no association was found between the volume percentage of BME (in the range of 10% – 70%) and post-procedural back pain (0.04 per 10% vertebral body volume, 95%CI: -0.18 – 0.26, $p = 0.711$).

If the volume of BME was dichotomized in < 50% and ≥ 50%, intravertebral volume of BME (mean difference 0.27, 95%CI: -0.74 – 1.28, $p = 0.581$) or in <33% and ≥ 33% volume of intravertebral BME, no significant effect could be identified (mean difference 0.27, 95%CI: -0.74 – 1.28, $p = 0.581$ and 0.33, 95%CI: -0.61 – 1.28, $p = 0.466$).

Besides the positive effect of the PVP procedure itself, occurrence of a new OVCF during follow-up was consistently the only significant factor associated with the post-procedural outcome in terms of pain score (PI-NRS): occurrence of a new OVCF during follow-up was associated with a higher post-procedural pain score (mean increase 1.92, 95%CI: 0.86 – 2.92, $p = 0.001$).

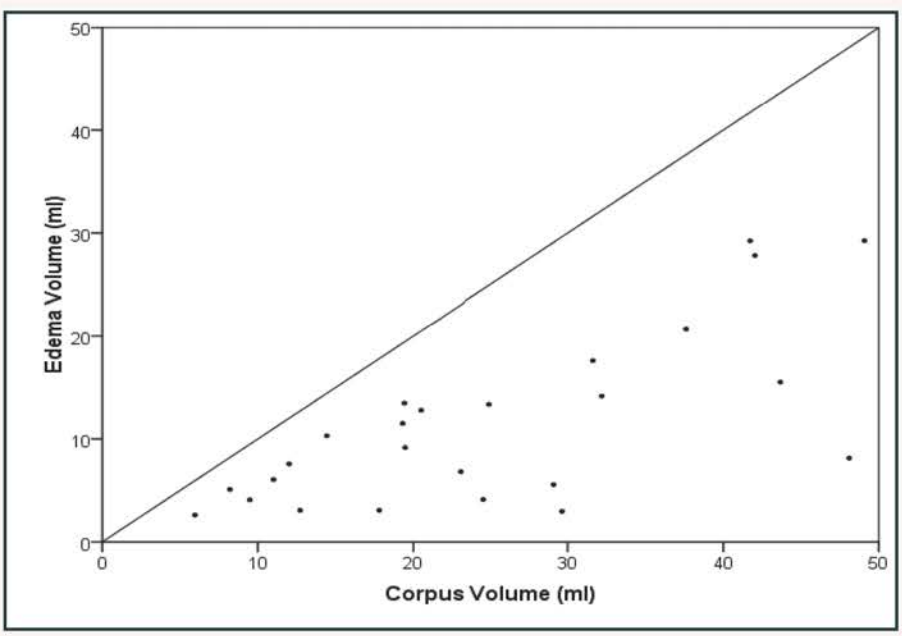

Figure 3. Shows the intravertebral BME volume (mL, y-axis) vs the intravertebral volume of the fractured vertebral body (mL, x-axis). The diagonal line depicts 100% filling with BME.

Discussion

Bone Marrow Edema (BME) due to unhealed (micro) fractures is seen in painful chronic osteoporotic vertebral compression fractures (OVCFs). Intravertebral BME persists in subacute and chronic painful OVCFs due to the altered healing cascade of the compression fracture caused by osteoporosis. The healing cascade of an OVCF is different compared to the well-organized healing cascade of a fractured long bone. The normal healing cascade in fractures of long bones consists of four stages. Resorption of necrotic bone is followed by matrix synthesis, bone formation and finally bone remodeling. In OVCFs with intravertebral BME on MR Imaging, these stages of bone healing are not seen as separate stages but show overlap.[10] The overlapping stages of the healing cascade seen in vertebral bodies containing BME may possibly be due to micro fractures due to slowly continuing collapse of the osteoporotic vertebral body.

In most clinics, intravertebral BME is one of the criteria for performing a PVP procedure. However, no guidelines on percentages of intravertebral BME in OVCF exists to be indicative as a threshold value for PVP. Moreover, the effect of BME in OVCF has not been quantitatively evaluated and studies are usually heterogeneous (multilevel versus single level OVCF). As such, the influence of the degree of intravertebral BME on the outcome of PVP remains unclear. In contrast to this lack of evidence, physicians often feel that a totally white vertebral body (100% vertebral body volume of intravertebral BME) at MR Imaging will have an excellent clinical outcome after PVP.

A review of the literature on intravertebral BME as (part of) the indication for PVP shows conflicting evidence. In 2005, Brown et al. showed no correlation between the outcome of PVP in chronic OVCFs and the presence of intravertebral BME at MR Imaging. However, they analysed BME in a dichotomous way (no BME (0%) vs. presence of any BME), patients had 1 to 5 OVCFs, and no pain score was used.[11] Contrary to this, 50-100% of intravertebral BME in OVCFs showed good pain reduction with PVP, compared to patients with less then 50% or no intravertebral BME.[8,13,18] All studies used either a dichotomy between no or presence of BME or between < 50% or more then 50% BME, while none of these studies used a volumetric analysis of the amount of BME on preoperative MR Imaging as was performed in the current study.

Debate exists on the use of a gadolinium enhanced T1 weighted MR I maging scan.[18,19] The current study shows no statistical difference in pain relief after PVP between patients with small or large percentages of intravertebral

BME. In order to prevent bias in the assessment of PVP, a strict inclusion protocol was used in the current study, these confounders are: first, pain generated by acute fractures (of which up to than 85% will resolve spontaneously within 8-12 weeks due to natural history).[20,21] Secondly, confounding due to pain from multiple fractures, and third exclusion of patients with intravertebral clefts, since these patients are a different entity and are merely a pseudo-arthrosis of the vertebral body due to necrosis.[22,23] Furthermore, these vertebral cleft fractures contain only a small area of very high signal on MR Imaging.[24]

Some limitations exist in the current study. First, the small size of the study cohort (25 patients), since only single level long-standing OVCFs were included and patients with vertebral cleft fractures were excluded. However, since repeated measurements during the first post-procedural year were obtained in all patients, the variability is highly reduced. Secondly, no control group - OVCF without intravertebral BME treated with PVP - was present. The latter, since presence of intravertebral BME was a prerequisite for treatment with PVP in our institution. Since data from literature is heterogeneous and includes multilevel and cleft fractures, no clear cut outcome scores etcetera were used and a control group from literature could not be used.

In conclusion, the amount of volumetric BME in long-standing single-level OVCF is not related to the post-procedural pain relief in the first year after PVP.

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