The intravertebral cleft in benign vertebral compression fracture: the diagnostic performance of non-enhanced MRI and fat-suppressed contrast-enhanced MRI

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ABSTRACT. We compared the diagnostic performance of non-enhanced MRI and fat-suppressed contrast-enhanced MRI (CEMRI) in diagnosing intravertebral clefts in benign vertebral compression fractures (VCFs). We retrospectively reviewed 99 consecutive patients who had undergone percutaneous vertebroplasty for VCFs. A cleft was defined as a signal void or hyperintense area on non-enhanced MRI (T_1 and T_2 weighted imaging) or as a hypointense area within a diffusely enhanced vertebra on CEMRI. A cleft was confirmed as a solid opacification on post-procedural radiographs. The interobserver reliability and MRI diagnostic performance were evaluated. The interobserver reliability of non-enhanced MRI was substantial ($k=0.698$) and the interobserver reliability of CEMRI was almost perfect ($k=0.836$). Post-procedural radiographs showed solid cleft opacification in 32 out of the 99 cases. The sensitivity and specificity of non-enhanced MRI were 0.72 and 0.82 (observer 1) and 0.63 and 0.87 (observer 2), respectively. The sensitivity and specificity of CEMRI were 0.94 and 0.63 (observer 1) and 0.85 and 0.60 (observer 2), respectively. The sensitivity of CEMRI was significantly higher than that of non-enhanced MRI, and the specificity of non-enhanced MRI was higher than that of CEMRI. CEMRI was highly reliable and sensitive, and non-enhanced MRI was specific for intravertebral clefts. Therefore, spine MRIs, including CEMRI, could provide useful information about intravertebral clefts before percutaneous vertebroplasty.

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Intravertebral clefts associated with vertebral compression fractures (VCFs) are radiographic signs representing cavities within fractured vertebrae and have long been considered pathognomonic for avascular necrosis of the spine (Kümmell's sign) [1–3]. However, several investigators have observed that intravertebral clefts are common in patients with osteoporotic compression fractures [4–6]. Currently, clefts are thought to represent corticocancellous disruption in mobile osteoporotic fractures, rather than avascular necrotic disease [4, 6].

Percutaneous vertebroplasty (PV) is an effective and minimally invasive procedure for the treatment of osteoporotic compression fractures [7, 8]. The advent of PV as the major treatment option for VCFs has prompted interest in intravertebral clefts occurring in benign VCFs. Recent studies have suggested that the clinical outcomes and complications associated with PV are influenced by the presence of clefts [4, 9–13]. Thus, radiological detection of clefts is indispensable for managing patients with VCFs.

Spine MRI is commonly used for the evaluation of acute VCFs. MRI is useful in distinguishing malignancy from acute osteoporotic VCFs [14, 15] and is effective in

demonstrating bone marrow oedema associated with acute compression fractures, which is one of the indications for performing PV [14, 16]. The MRI findings associated with intravertebral clefts have been well described [3–5]. However, there is controversy concerning the efficacy of MRI in diagnosing clefts. Specifically, the reliability and effectiveness of contrast-enhanced MRI (CEMRI), first assessed by Oka et al in 2005 [11], has not been properly evaluated. Such evaluation is important, given that CEMRI entails additional expense.

To evaluate the efficacy of the CEMRI for the prediction of intravertebral clefts, we assessed the interobserver reliability and diagnostic performance of non-enhanced T_1 weighted and T_2 weighted MRI (T_1 WI and T_2 WI) and CEMRI in the identification of intravertebral clefts in VCFs. We then compared the diagnostic performance of CEMRI with that of non-enhanced MRI.

Methods and materials

Subjects

We retrospectively reviewed the images of consecutive patients with VCFs who underwent pre-procedural spine MR examinations and PVs between September 2002 and January 2005. Indications for PV included

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intraosseous oedema, vertebral compression and clinical symptoms indicating an acute fracture. Patients with tumour-related fractures were excluded from this study, based on clinical history (previously diagnosed cancer or haematopoietic disease) and MR findings (convex posterior cortex, epidural mass, diffuse low-signal intensity of the body and pedicle on T1WI and inhomogeneous enhancement after gadolinium injection) [14].

This study consisted of 99 patients with 122 vertebral fractures. There were 19 men and 80 women, with a mean age of 72 years (range, 50–89 years). 77 patients had single-level VCFs and 22 patients had multiple-level VCFs. As statistical testing assumes independent observations, we randomly selected one fracture from a patient who had multiple fractures and included only one fracture per patient in the analysis to reduce bias. VCFs were principally located in the lumbar spine (58/99) and thoracic spine (41/99). Institutional review board approval was not required for this retrospective study of medical and radiological data that had already been collected.

Percutaneous vertebroplasty

PV procedures were performed using a previously reported technique [5, 9, 17]. PV was performed under stringent sterile conditions with C-arm fluoroscopy guidance. 13- and 11-gauge bone biopsy needles were used for the thoracic vertebrae and lumbar vertebrae, respectively. In each case, the needle tip was placed in the anterior part of the vertebral body close to the midline. Cement material was prepared by combining polymethylmethacrylate bone cement (Vertebroplastic; DePuy, AcroMed, Beeston, England) with sterilised barium sulphate powder (E-Z-EM, Lake Success, NY) to increase radio-opacity. The cement was carefully injected using a 2 ml Luer-lock syringe under fluoroscopic control until resistance was met, the cement reached the posterior quarter of the vertebral body or the mixture started to pass into the disc space or paravertebral space. Anteroposterior and lateral radiographs were obtained after the PV procedure was completed.

Imaging protocol

Pre-operative spine MRI (1.5-tesla system MRI, Signa Excite or Genesis Signa; GE Medical Systems, Milwaukee, WI) was performed using an eight-channel spine array coil. The imaging protocol included sagittal T_2 weighted fast spin-echo images (repetition time (TR) 4000 ms; echo time (TE) 120 ms; number of excitations (NEX) 4; echo train length (ETL), 2), sagittal T_1 weighted spin-echo images (TR, 550 ms; TE, 14 ms; NEX, 3; ETL, 3) and fat-suppressed contrast-enhanced sagittal T_1 weighted images (TR, 780 ms; TE, 8–14 ms; NEX, 2; ETL, 3). The field of view was 300 × 300 mm, with a matrix of 512 × 256, slice thickness of 4.5 mm and 0.5 mm gap for the routine sequences. Contrast material (15 ml of gadopentetate dimeglumine, Magnevist; Schering, Berlin, Germany) was injected intravenously before CEMRI scanning. In 29 patients, sagittal short-tau

inversion recovery (STIR) MRI (TR, 3333 ms; TE, 14 ms; NEX, 1; ETL, 2) was included in the spine MRI protocols.

Imaging analysis

Two experienced radiologists blinded to the post-procedural radiographs analysed the pre-procedural MR images independently. On T1WI and T2WI, intravertebral clefts were classified as fluid filled or gas filled, depending on the findings. A fluid-filled cleft was defined as a hyperintense linear band or ellipsoid area on T2WI [4]. A gas-filled cleft was defined as a signal void band on both sagittal T1WI and T2WI [3]. The hyperintensity of the cleft sign had to be equivalent to that of the cerebrospinal fluid. The signal void of the cleft sign on T1WI and T2WI had to be equivalent to that of the endplate of the vertebra. An ellipsoid or band-shaped area of hypointensity within a diffusely enhancing vertebra on CEMRI was regarded as a cleft (Figure 1). The STIR images of 29 patients were not included in the evaluation of the radiological imaging of the cleft because STIR was performed in only a small number of patients in this study, and the appearances of intravertebral clefts were similar to those seen on T2WI [18].

The interobserver reliability for identifying intravertebral clefts on MRI between the two observers was assessed using the pairwise kappa (κ) statistic. Interobserver reliability was graded according to a method proposed by Landis and Koch [19] (<0.2, slight; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, substantial; 0.81–1.0, almost perfect).

In order to determine the presence of intravertebral clefts, two radiologists analysed the cement distribution patterns on post-procedural radiographs by consensus. The cement filling the intravertebral cleft shows uniform opacity and sharp radiological margins, because the intravertebral cleft is a low-resistant, confluent reservoir for cement [4, 6, 11]. When the pattern of cement distribution was solid (the cement formed a mass with a sharp margin), we regarded the pattern as indicative of a VCF with a cleft. When the pattern was trabecular (cement spread along the fine bony trabeculae), we regarded the pattern as indicative of a VCF without a cleft. The MR images were correlated with the results of the post-operative radiograph analysis. The sensitivity, specificity, positive predictive value and negative predictive value of the different MRI techniques were determined in order to assess their diagnostic performance. The differences in sensitivity and specificity between non-enhanced MRI and CEMRI were assessed using an exact analogue of McNemar's test. A p -value of <0.05 was considered statistically significant.

Results

The results of the interobserver reliability analysis are shown in Table 1. Observer 1 noted that 35 out of 99 patients had vertebrae with findings suggestive of intravertebral clefts on non-enhanced MRI. Findings included 17 fluid-filled clefts, 14 gas-filled clefts and 4 clefts filled with both fluid and gas. Observer 2 found 29 clefts (fluid, 18; gas, 10; both fluid and gas, 1) on non-

Figure 1. Findings suggestive of intravertebral cleft on spine MRI. (a) In the first lumbar vertebra, an ellipsoid lesion with high signal intensity similar to cerebrospinal fluid is well depicted on T_2 weighted imaging (T2WI). We classified this as a fluid-filled cleft. (b) A linear signal void lesion is noted within the bone marrow of the first lumbar vertebral body on T_1 weighted imaging (T1WI) and T2WI (T1WI is not shown). We classified this as a gas-filled cleft. (c) A non-enhanced area is surrounded by well-enhanced bone marrow in the first lumbar vertebral body. We classified this as a cleft on contrast-enhanced MRI.

enhanced MRI. Positive cleft findings on CEMRI were seen in 55 cases by observer 1 and observer 2. Interobserver agreement for non-enhanced MRI was substantial ($\kappa=0.698$) and agreement for CEMRI was almost perfect ($\kappa=0.836$) (Figure 2).

A solid pattern of cement distribution was noted in 32 cases during analysis of the post-procedural radiographs. 10 patients exhibited solid cement distribution patterns in the thoracic spine (T8, 1; T12, 9) and 22 patients exhibited the same finding in the lumbar spine (L1, 10; L2, 10; L3, 1; L4, 1). A trabecular pattern of cement distribution was seen in 67 cases. In 32 VCFs with solid opacification of the cleft, a cleft was demonstrated in 23 cases (fluid, 11; gas, 8; both fluid and gas, 4) on non-enhanced MRI and 30 cases on CEMRI for observer 1. Clefts were demonstrated in 20 cases (fluid, 12; gas, 7; both fluid and gas, 1) on non-enhanced MRI and 28 cases on CEMRI for observer 2. The sensitivity of non-enhanced MRI was 0.72 for observer 1 and 0.63 for observer 2. The sensitivity of CEMRI was 0.94 for observer 1 and 0.85 for observer 2. The specificity of non-enhanced MRI was 0.82 for observer 1 and 0.87 for observer 2. The specificity of CEMRI was 0.63 for observer 1 and 0.60 for observer 2 (Table 2). An exact analogue of McNemar's test demonstrated that the sensitivity of CEMRI was higher than that of non-enhanced MRI (observer 1, $p=0.016$; observer 2, $p=0.008$)

(Table 3), and the specificity of non-enhanced MRI was significantly higher than that of CEMRI (observer 1, $p=0.002$; observer 2, $p<0.0001$).

Discussion

In this study, interobserver reliability in identifying clefts was better with CEMRI than with non-enhanced MRI. CEMRI had a higher sensitivity than non-enhanced MRI. However, non-enhanced MRI was more specific than CEMRI for the detection of clefts.

Some studies have underlined the importance of filling clefts with cement sufficiently to provide an optimal outcome [4, 7]. Lane et al [4] noted that four patients with insufficiently filled clefts did not achieve pain relief. Other studies have shown that treatment failure rate after PV is higher in patients with clefts than in patients without clefts [9, 20]. Although clefts are the targets of cement filling, this procedure may be associated with the risk of intradiscal cement leakage [5, 21], which may subsequently lead to serious complications, such as epidural leakage or repeated fractures of the adjacent vertebrae [13, 21, 22]. Intravertebral clefts are important factors influencing clinical outcomes and risk after PV. Hence, pre-procedural imaging of VCFs should provide

Table 1. The cleft findings of non-enhanced MR sequence (T1WI and T2WI) and fat-suppressed contrast-enhanced MRI (CEMRI)

Type of imaging	Observer	Positive finding of cleft (fluid/gas/both fluid and gas)	Interobserver agreement ^a
Non-enhanced MR Sequence (T1WI and T2WI)	1	35 (17/14/4)	$\kappa=0.698$
	2	29 (18/10/1)	
CEMRI	1	55	$\kappa=0.836$
	2	55	

T1WI, T_1 weighted imaging; T2WI, T_2 weighted imaging.

^aThe grading proposed by Landis and Koch (<0.2 , slight; 0.21–0.40, fair; 0.41–0.60, moderate; 0.61–0.80, substantial; 0.81–1.0, almost perfect)

Figure 2. A 69-year-old woman with a benign compression fracture of the first lumbar vertebra. (a, b) On T_1 weighted and T_2 weighted imaging, the signal of the upper half of the vertebral body appears as low signal intensity rather than as signal void. This led to a discrepancy between the two observers. (c) An area (arrows) with low signal intensity is clearly shown within diffusely enhancing bone marrow on CEMRI. The two observers defined this lesion as a cleft. (d) On a post-procedural radiograph, the injected cement is distributed within the cleft. There is a solid pattern with a smooth margin.

accurate information to the clinician about the presence of a cleft.

To date, there have been several reports on the diagnostic performance of spine MRI for the detection of intravertebral clefts within VCFs [4–6]. However, the previous studies reported variable results depending on the investigator. The low sensitivity (72% and 63% by two observers) of non-enhanced MRI in our series is in agreement with the results of some previous studies (Lane et al [4], 52.8%, Wiggins et al [20], 57%). In contrast to our results, another report noted that signs suggesting a fluid or gas cleft sign on non-enhanced MRI were highly sensitive for the vacuum clefts found on lateral radiographs (Peh et al [5], 100%). However, the intravertebral vacuum clefts seen on plain radiographs were insufficient for a reference standard [9] because clefts

that are filled with fluid or have collapsed and have no space cannot be demonstrated on plain radiographs.

In this study, the interobserver reliability of non-enhanced MRI was lower than that of CEMRI for identification of clefts in VCFs because there were discrepancies between the observers' findings in several VCFs with signs suggesting the presence of gas-filled clefts. Gas-filled clefts cannot be identified with confidence [11] because the signal void suggestive of gas-filled clefts does not significantly contrast with bone marrow oedema of low signal intensity. The question is 'Does the low signal intensity seen with clefts on non-enhanced MRI indicate only gas?'. In our experience, the areas of signal void on T1WI and T2WI did not closely match the areas of air density on lateral radiographs. Histological comparison has demonstrated that osteone-

Table 2. The diagnostic performance of MRI findings of the intravertebral cleft

MRI finding of the cleft	TP/FP/TN/FN	Sensitivity	Specificity	PPV	NPV
<i>Non-enhanced MRI (fluid- and/or gas-filled cleft)</i>					
OB1	23/12/55/9	0.72 (0.53–0.86)	0.82 (0.70–0.90)	0.66 (0.48–0.81)	0.86 (0.70–0.93)
OB2	20/9/58/12	0.63 (0.44–0.79)	0.87 (0.76–0.94)	0.69 (0.49–0.85)	0.83 (0.72–0.91)
<i>Fluid cleft sign^a</i>					
OB1	15/6/61/17	0.47 (0.29–0.65)	0.91 (0.82–0.97)	0.71 (0.48–0.89)	0.78 (0.67–0.87)
OB2	13/6/61/19	0.41 (0.24–0.59)	0.91 (0.82–0.97)	0.68 (0.43–0.87)	0.76 (0.65–0.85)
<i>Gas cleft sign^b</i>					
OB1	12/6/61/20	0.38 (0.21–0.56)	0.91 (0.82–0.97)	0.67 (0.41–0.87)	0.75 (0.65–0.84)
OB2	8/3/64/24	0.25 (0.11–0.43)	0.87 (0.76–0.94)	0.47 (0.23–0.72)	0.71 (0.60–0.80)
<i>Fat-suppressed CEMRI</i>					
OB1	30/25/42/2	0.94 (0.79–0.99)	0.63 (0.50–0.74)	0.55 (0.40–0.68)	0.95 (0.85–0.99)
OB2	28/27/40/4	0.85 (0.71–0.96)	0.60 (0.47–0.72)	0.51 (0.37–0.65)	0.91 (0.78–0.97)

The value in parentheses is 95% confidence interval. CEMRI, contrast-enhanced MRI; FN, false negative; FP, false positive; NPV, negative predictive value; OB, observer; PPV, positive predictive value; TN, true negative; TP, true positive

^aPositive findings are composed of only fluid sign and both fluid and gas sign (observer 1, 4 cases; observer 2, 1 case)

^bPositive findings are composed of only gas sign and both fluid and gas sign

Table 3. Comparisons of the sensitivity and specificity between non-enhanced MRI and CEMRI based on an exact analogue of McNemar's cleft

	Sensitivity comparison			Specificity comparison		
	Positive CEMRI	Negative CEMRI	Total	Positive CEMRI	Negative CEMRI	Total
Positive NEMRI	23 (20)	0 (0)	23 (20)	10 (8)	2 (1)	12 (9)
Negative NEMRI	7 (8)	2 (4)	9 (12)	15 (19)	40 (39)	55 (58)
Total	30 (28)	2 (4)	32 ^a	25 (27)	42 (40)	67 ^b

The value out of parenthesis is acquired from observer 1 and the value in parenthesis is from observer 2. Sensitivity comparison: observer 1, $p=0.016$; observer 2, $p=0.008$. Specificity comparison: observer 1, $p=0.002$; observer 2, $p=0.0001$. NEMRI, non-enhanced MRI; CEMRI, contrast-enhanced MRI

^aTotal number of cases with solid cement distribution on post-PV (percutaneous vertebroplasty) radiographs

^bTotal number of cases with trabecular cement distribution on post-PV radiographs

crisis, pseudoarthrosis lined with fibrocartilaginous membrane and non-union were observed in VCFs with clefts, with the trabecular network completely broken in the cleft area [11, 23]. It seems likely that the signal void on T1WI and T2WI may be due to a sclerotic fracture margin or collapse of fractured trabeculations, as well as gas.

Contrast enhancement in spine MRI is potentially beneficial in that it provides increased confidence in the diagnosis of bone marrow abnormalities. In our study, gadolinium enhancement allowed clear visualisation of the boundary between the residual trabecular bone and oedema, and the intravertebral clefts were easily identified within the homogeneously enhancing bone marrow oedema.

Our study showed that CEMRI is not specific for intravertebral clefts. We assumed that the non-enhanced area within the diffusely enhancing vertebrae might represent not only true intravertebral clefts, but also ischaemic areas that are pathologically different from clefts. Vertebral collapse most commonly occurs as a consequence of a vascular insult to the anterior segment of the vertebral body, which is supplied by the anterior

metaphyseal and peripheral arteries [3]. Failure of the reparative process, with inadequate revascularisation of bone marrow and fracture healing, may predispose patients to ischaemic necrosis of the vertebral body and may also result in subsequent vertebral collapse, seen as non-enhancement on CEMRI. Based on our results, the focal non-enhanced areas within the diffuse marrow enhancement were divided into three groups according to the presence of the fluid/gas cleft sign and the distribution of the cement. One group consisted of lesions with both the cleft sign and solid cement distribution, findings that probably represent mature osteonecrosis. The second group consisted of lesions without cleft signs, but with solid cement distribution, which would occur due to a trabecular fracture with a collapsed potential space that did not hold any other component, gas or fluid. The third group consisted of lesions without cleft signs and with trabecular cement distribution (a false-positive finding of CEMRI), probably representing a precursor of avascular necrosis or a minor insult of the vertebral vasculature without trabecular collapse. Although the specificity of CEMRI is low for clefts, its high sensitivity and reliability make it

Figure 3. A 69-year-old woman with a benign compression fracture of the second lumbar vertebra. (a) A fluid-filled cleft (arrow) is clearly demonstrated within the superior subendplate portion of the first lumbar vertebra on T_2 weighted imaging. (b) The vertebral body shows diffuse enhancement. A focal non-enhanced area is located in the superior subendplate marrow, as seen on contrast-enhanced MRI. (c) On a post-procedural radiograph, the cement (arrowheads) is localised within the central portion of the vertebral body and is distributed in a trabecular pattern. This case represents false identification of vertebral compression fracture without clefting on a post-procedural radiograph.

an effective pre-procedural imaging modality for PV. The enhancing pattern of a fractured vertebra may be predictive in the evaluation of blood supply in bone contusions. Therefore, we suggest that spine CEMRI performed prior to PV would provide beneficial information about vertebral injury. In order to overcome the low specificity for clefts, the analysis of the CEMRI should be performed in combination with another modality, such as non-enhanced MRI, high-resolution CT or lateral radiographs in flexion, which have high specificity.

There were some limitations to this study. First, cement filling might not be the "gold standard" for determining the presence of a cleft. We noted that two patients had intravertebral clefts on pre-operative MRI images but did not have solid opacification on post-procedural radiographs (Figure 3). This could have been due to an insufficient volume of cement reaching the subendplate cleft seen on MRI. MRI may be more accurate than post-PV radiographs in detecting clefts in cases in which the cleft does not fill with cement. Secondly, we could not confirm the pathology of the focal non-enhanced area within diffusely enhancing vertebrae. Not all instances of focal non-enhancement represented solid cement distribution on post-procedural radiographs, and this led to the relatively low specificity of CEMRI. We hypothesised above that non-enhanced areas within diffusely enhancing vertebrae represent not only osteonecrosis, but also the compromise of blood supply within the vertebral body without trabecular destruction. However, we could not provide any experimental evidence or literature supporting this hypothesis. Thus, further pathological evaluation of the non-enhanced areas within diffusely enhancing VCFs should be undertaken in the future by means of animal or *in vitro* study.

Conclusions

Our results indicate that non-enhanced MRI is specific and that CEMRI is a very sensitive and reliable MR imaging tool for identifying intravertebral clefts. Therefore, spine CEMRI, together with non-enhanced MRIs, seems to provide useful information about intravertebral clefts before PV is undertaken. Although the focal non-enhanced area within the diffusely enhancing vertebra is not specific for the intravertebral cleft, it is an interesting radiological finding that represents post-traumatic hypovascular lesion within the vertebral body.

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