

**REPORT****Cerebrospinal fluid leakage and headache after lumbar puncture: a prospective non-invasive imaging study****Yen-Feng Wang,<sup>1,2,3</sup> Jong-Ling Fuh,<sup>2,3</sup> Jiing-Feng Lirng,<sup>2,4</sup> Shih-Pin Chen,<sup>2,3</sup>  
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The spatial distribution and clinical correlation of cerebrospinal fluid leakage after lumbar puncture have not been determined. Adult in-patients receiving diagnostic lumbar punctures were recruited prospectively. Whole-spine heavily T<sub>2</sub>-weighted magnetic resonance myelography was carried out to characterize post-lumbar puncture spinal cerebrospinal fluid leakages. Maximum rostral migration was defined as the distance between the most rostral spinal segment with cerebrospinal fluid leakage and the level of lumbar puncture. Eighty patients (51 female/29 male, mean age 49.4 ± 13.3 years) completed the study, including 23 (28.8%) with post-dural puncture headache. Overall, 63.6% of periradicular leaks and 46.9% of epidural collections were within three vertebral segments of the level of lumbar puncture (T12–S1). Post-dural puncture headache was associated with more extensive and more rostral distributions of periradicular leaks (length 3.0 ± 2.5 versus 0.9 ± 1.9 segments, *P* = 0.001; maximum rostral migration 4.3 ± 4.7 versus 0.8 ± 1.7 segments, *P* = 0.002) and epidural collections (length 5.3 ± 6.1 versus 1.0 ± 2.1 segments, *P* = 0.003; maximum rostral migration 4.7 ± 6.7 versus 0.9 ± 2.4 segments, *P* = 0.015). In conclusion, post-dural puncture headache was associated with more extensive and more rostral distributions of periradicular leaks and epidural collections. Further, visualization of periradicular leaks was not restricted to the level of dural defect, although two-thirds remained within the neighbouring segments.

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**Keywords:** cerebrospinal fluid leakage; magnetic resonance myelography; post-dural puncture headache; spontaneous intracranial hypotension

**Abbreviations:** CTM = computed tomographic myelography; MRM = magnetic resonance myelography; PDPH = post-dural puncture headache

## Introduction

Post-dural puncture headache (PDPH) occurs in up to one-third of patients receiving lumbar punctures (Kuntz *et al.*, 1992; Strupp *et al.*, 2001; Bezov *et al.*, 2010a; van Oosterhout *et al.*, 2013), and typically presents as an orthostatic headache that occurs within 5 days after dural puncture (Headache Classification Committee of the International Headache Society, 2004; Bezov *et al.*, 2010a). CSF leakage has been considered the cause of PDPH as it is the most evident consequence of lumbar punctures. However, the association between PDPH and the amount or pattern of post-lumbar puncture CSF leakage has been inconclusive (Iqbal *et al.*, 1995; Sakurai *et al.*, 2012, 2013; Fakhraan *et al.*, 2014).

Findings of conventional T<sub>2</sub>-weighted spinal MRI in PDPH include spinal hygroma, and retrospinal focal fluid collection, and only occasionally, the spinal CSF leaks could be visualized directly (Iqbal *et al.*, 1995; Vakharia *et al.*, 1997; Yousry *et al.*, 2001; Burtis *et al.*, 2005). Heavily T<sub>2</sub>-weighted magnetic resonance myelography (MRM) is a non-invasive radiation-free imaging technique with excellent sensitivity for signals of water/CSF. It has been demonstrated to be comparable to computed tomographic myelography (CTM), the purported gold standard, in localizing spinal CSF leaks in spontaneous intracranial hypotension (Tsai *et al.*, 2007, 2008; Wang *et al.*, 2009). More importantly, acquisition of heavily T<sub>2</sub>-weighted MRM involves neither intravenous or intrathecal contrast administration nor radiation exposure. With the advent of heavily T<sub>2</sub>-weighted MRM, post-lumbar puncture CSF leakage could be localized and quantified systemically. Further, periradicular leaks, i.e. CSF leaks along the nerve roots, on heavily T<sub>2</sub>-weighted MRM or CTM have been used as targets for targeted epidural blood patches or even surgical intervention in the treatment of spontaneous intracranial hypotension (Schievink, 2008; Wang *et al.*, 2009). However, a substantial proportion of patients with spontaneous intracranial hypotension did not have dural defects with active CSF leakage at surgery at the location of spinal CSF leaks identified on CTM (Cohen-Gadol *et al.*, 2006). Whether the visualized periradicular leaks accurately co-localize with the actual dural defects is yet to be confirmed.

## Subjects and methods

### Study participants

This was a prospective study involving adult in-patients who received diagnostic lumbar punctures. Lumbar punctures were carried out using 22-gauge Quincke needles through the mid-line L3–4 interspace with a standard protocol (Ellenby *et al.*, 2006). The amount of CSF collected was ~5 cc, except for patients with suspected normal pressure hydrocephalus or increased intracranial pressure, whereby the amount of CSF

drainage was around 20–30 cc. After the procedure, the patients were instructed to remain recumbent for 6 h, and were observed for 5 days for the development of PDPH. Heavily T<sub>2</sub>-weighted MRM was carried out immediately when the MRI machine was available. The inclusion and exclusion criteria are provided in the Supplementary material. The study protocol was approved by the Institutional Review Board of Taipei Veterans General Hospital and all participants gave written informed consent before entering the study.

### Clinical assessment and management

The diagnosis of PDPH was made according to the ICHD-2 criteria (Headache Classification Committee of the International Headache Society, 2004). Lumbar epidural blood patches were performed when purely conservative measures failed (Bezov *et al.*, 2010b).

### Heavily T<sub>2</sub>-weighted magnetic resonance myelography

Whole-spine (C1–S5) axial heavily T<sub>2</sub>-weighted MRM was acquired after lumbar puncture on a 1.5 T superconducting system (Signa HDxt or Signa Excite, GE Medical Systems) as previously described (Wang *et al.*, 2009). Heavily T<sub>2</sub>-weighted MRMs were interpreted by a senior neuroradiologist (J.-F.L.) blinded to the clinical conditions. Post-lumbar puncture CSF leakages were assessed with three measures: periradicular leaks (i.e. CSF leaks along the nerve roots), epidural collections, and retrospinal collections (Wang *et al.*, 2009). Technical aspects of heavily T<sub>2</sub>-weighted MRM and further descriptions of the CSF leakages are provided in the Supplementary material. In addition to localization of the CSF leakages, the numbers of spinal segments with periradicular leaks and epidural collections visualized on heavily T<sub>2</sub>-weighted MRM were used as surrogates to semi-quantify post-lumbar puncture CSF leakage. Maximum rostral migration (R<sub>Max</sub>) was defined as the number of spinal segments between L3 and the most rostral segment with CSF leakage.

### Statistical analysis

When comparing patients with and without PDPH, categorical data were analysed with the  $\chi^2$  test, and the Student's *t*-test was used for continuous variables. ANOVA was used for comparisons among (i) patients without PDPH; (ii) patients with PDPH but without epidural blood patch; and (iii) patients with PDPH and epidural blood patch; and *post hoc* analysis was performed using the least significant difference (LSD) method. Multivariate logistic regression modelling using the forward (Wald) method was carried out to determine factors predictive of PDPH, and their odds ratios (ORs) and 95% confidence intervals (CIs). For the multivariate analysis, factors with a *P*-value of < 0.05 in the univariate analyses were included, and adjustment for age and gender was made. All statistical analyses were carried out using PASW Statistics 18 for Windows (SPSS). All calculated *P*-values were two-tailed, and statistical significance was defined as *P* < 0.05.

## Results

### Study participants

During the study period (October 2010 to September 2013), 109 patients who received diagnostic lumbar puncture were screened, and 29 were excluded: MRI not available before discharge in 22, ineligible age in six, and withdrawal of consent in one. Eighty patients (51 female/29 male, age  $49.4 \pm 13.3$  years, range 20–79) completed the study (Supplementary Table 1), and 23 (28.8%) developed PDPH. Six patients failed conservative treatment, and responded to single lumbar epidural blood patches.

### Post-lumbar puncture spinal CSF leakage on heavily T<sub>2</sub>-weighted MRM

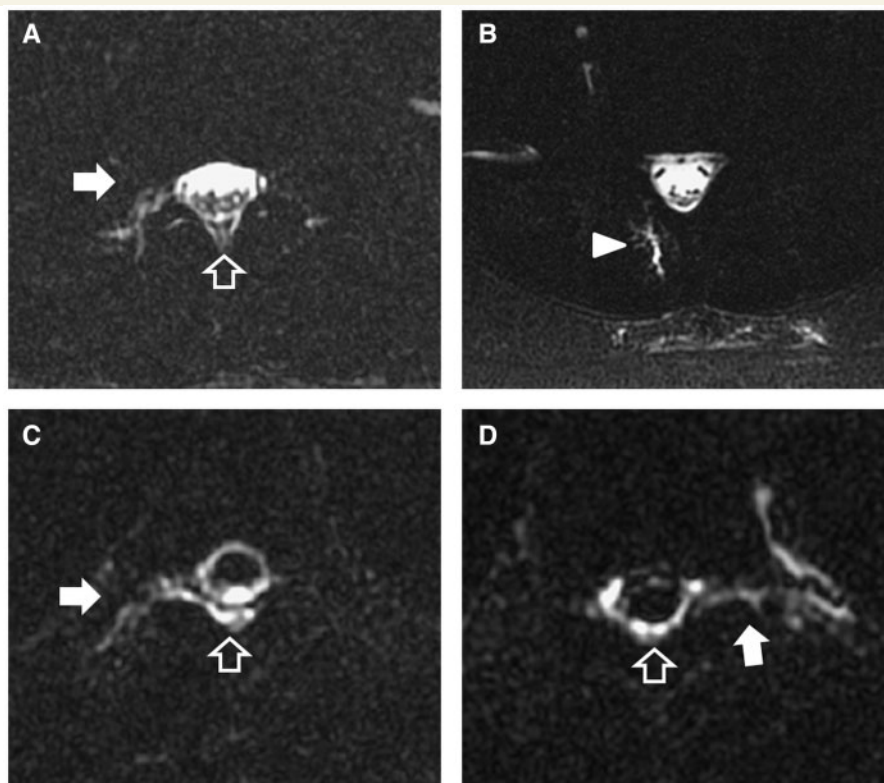
The mean interval between lumbar puncture and heavily T<sub>2</sub>-weighted MRM was  $2.4 \pm 2.1$  days (range 0–12), and the cumulative percentages of patients receiving heavily T<sub>2</sub>-weighted MRM within 2, 3, 4 and 5 days were 71.3%, 81.3%, 88.8% and 92.5%, respectively. Overall, 40 patients (50.0%) had periradicular leaks, 33 (41.3%) had epidural collections, and 30 (37.5%) had retrospinal collections (Fig. 1 and Table 1). Patients with periradicular leaks (age  $45.6 \pm 12.3$  versus  $53.1 \pm 13.4$  years,  $P = 0.011$ ) or epidural collections (age  $45.7 \pm 12.1$  versus  $52.0 \pm 13.7$

years,  $P = 0.037$ ) were younger than those without, whereas gender distribution, opening or closing pressure at lumbar puncture, body weight and BMI were comparable (data not shown).

In patients with periradicular leaks, 65% had more than one spinal vertebral segment involved, whereas 84.8% of patients with epidural collections had multiple segment involvement. On average, periradicular leaks were visualized at  $1.5 \pm 2.3$  segments, and the mean length of epidural collections were  $2.2 \pm 4.2$  segments. The distribution of periradicular leaks centred around the upper lumbar region (85.1% between T9 and S2) (Fig. 2A–C). Epidural collections were most commonly seen between the mid-thoracic to the upper lumbar regions (85.9% between T5 and S1). Retrospinal collections mostly accumulated in the lower lumbar region (92.9% between T12 and S1). In total, 52 patients (65.0%) had evidence of spinal CSF leakages beyond L3–4, and 63.6% of the periradicular leaks and 46.9% of the epidural collections were seen between T12 and S1, i.e. within three segments of the lumbar puncture level.

### Comparisons between patients with and without PDPH

Patients with PDPH were younger than those without (age  $44.2 \pm 12.8$  versus  $51.4 \pm 13.1$ ,  $P = 0.027$ ) (Table 1)



**Figure 1** Spinal CSF leakage in patients with post-dural puncture headache on heavily T<sub>2</sub>-weighted magnetic resonance myelography. Right periradicular leaks (filled arrows) and epidural collections (open arrow) at L2 (A) and L5 retrospinal collections (arrowhead; B) in a 43-year-old female patient. Right T5 periradicular leak (filled arrow; C) and left T10 periradicular leak (filled arrow; D) with epidural collections (open arrows) in a 40-year-old male patient (C and D).

**Table 1 Clinical characteristics and imaging findings in patients with and without PDPH**

	All patients	PDPH (n = 23)	No PDPH (n = 57)	P-value*
<b>Demographics</b>				
Age (years)	49.4 ± 13.3	44.2 ± 12.8	51.4 ± 13.1	0.027
Female patients (%)	63.8	69.6	61.4	0.492
Height (cm)	163.5 ± 8.9	164.5 ± 9.5	163.0 ± 8.7	0.552
Body weight (kg)	65.2 ± 13.4	63.2 ± 12.6	66.0 ± 13.8	0.404
Body-mass index	24.3 ± 4.4	23.2 ± 3.3	24.7 ± 4.8	0.167
<b>Indication for lumbar puncture</b>				
Suspected symptomatic headache	50%	52.2%	49.1%	0.805
<b>Pressure</b>				
Opening pressure (mmH <sub>2</sub> O)	160.3 ± 54.4	151.6 ± 40.0	162.9 ± 58.1	0.472
Closing pressure (mmH <sub>2</sub> O)	113.2 ± 42.0	112.3 ± 42.9	113.5 ± 42.1	0.923
<b>Any CSF leakage on HT2W MRM</b>				
Periradicular leaks	50%	95.7%	31.6%	<0.001
Length (seg)	1.5 ± 2.3	3.0 ± 2.5	0.9 ± 1.9	0.001
Cervical (%)	1.3%	4.3%	0%	0.113
Thoracic (%)	23.8%	52.2%	12.3%	<0.001
R <sub>Max</sub> (seg)	1.8 ± 3.3	4.3 ± 4.7	0.8 ± 1.7	0.002
Epidural collections	41.3%	69.6%	29.8%	0.001
Length (seg)	2.2 ± 4.2	5.3 ± 6.1	1.0 ± 2.1	0.003
Cervical (%)	2.5	8.7	0	0.024
Thoracic (%)	20	34.8	14.8	0.036
R <sub>Max</sub> (seg)	2.0 ± 4.4	4.7 ± 6.7	0.9 ± 2.4	0.015
Retrospondinal collections	37.5%	52.2%	31.6%	0.085

HT2W = heavily T<sub>2</sub>-weighted; seg = segments; R<sub>Max</sub> = maximum rostral migration. Data are expressed as mean ± standard deviation or percentage. \*Comparison between patients with and without PDPH.

and were more likely to have periradicular leaks (95.7% versus 31.6%,  $P < 0.001$ ), and epidural collections (69.6% versus 29.8%,  $P < 0.001$ ), but not retrospondinal collections (52.2% versus 31.6%,  $P = 0.085$ ). Compared to those without, patients with PDPH also had more extensive and more rostral distributions of periradicular leaks (length  $3.0 \pm 2.5$  versus  $0.9 \pm 1.9$  segments,  $P = 0.001$ ; R<sub>Max</sub>  $4.3 \pm 4.7$  versus  $0.8 \pm 1.7$  segments,  $P = 0.002$ ), and epidural collections (length  $5.3 \pm 6.1$  versus  $1.0 \pm 2.1$  segments,  $P = 0.003$ ; R<sub>Max</sub>  $4.7 \pm 6.7$  versus  $0.9 \pm 2.4$  segments,  $P = 0.015$ ) (Fig. 2D–F). Multivariate logistic regression analysis identified two factors associated with PDPH: the presence of periradicular leaks (OR 43.5, 95% CI 4.5–420.9,  $P = 0.001$ ) and the length of epidural collections (OR 1.3 per segment, 95% CI 1.1–1.5,  $P = 0.011$ ).

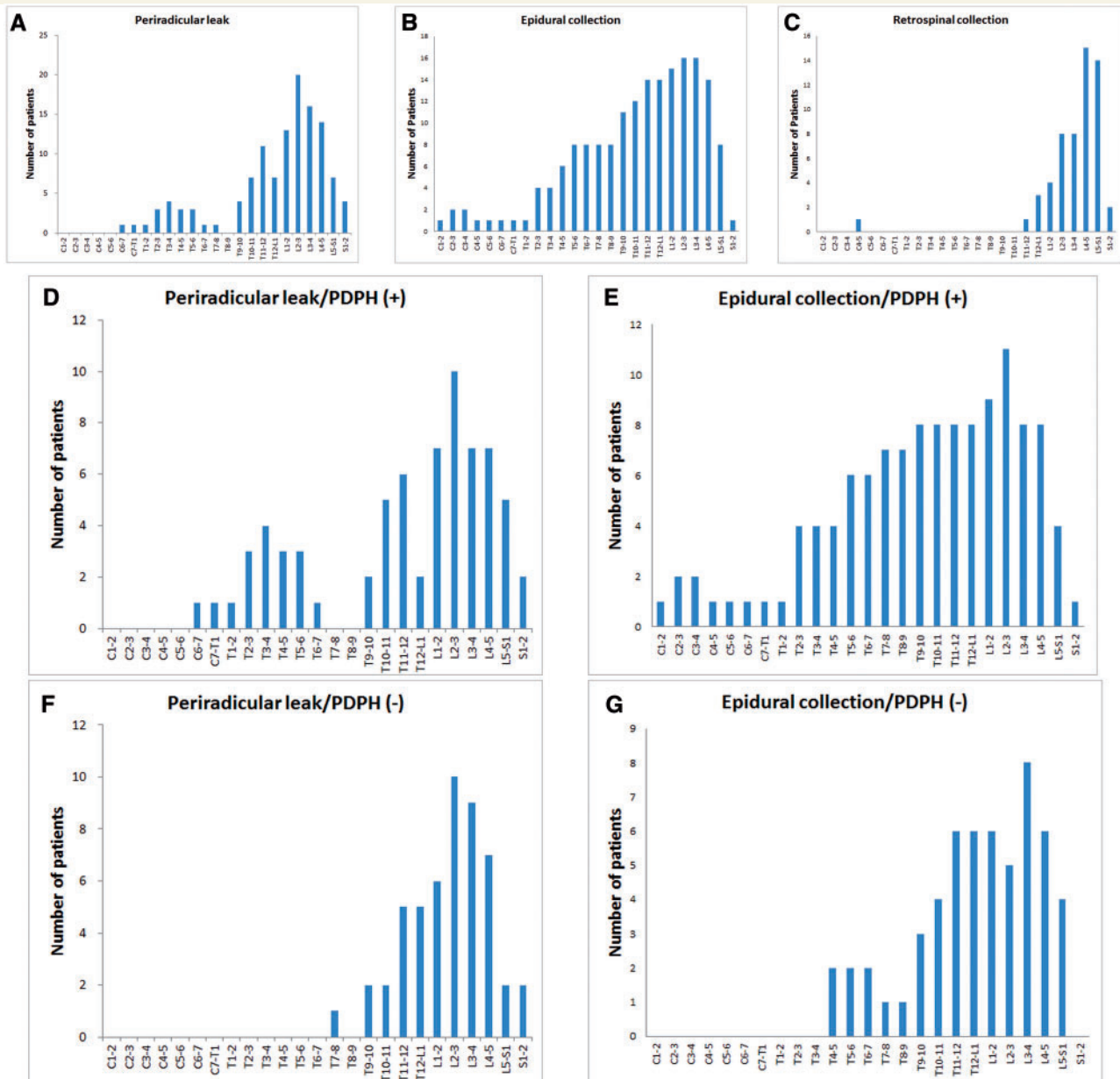
## Epidural blood patches in patients with PDPH

The need for epidural blood patch was associated with longer and more rostral distributions of epidural collections (length  $8.0 \pm 4.2$ ; R<sub>Max</sub>  $7.7 \pm 8.0$  segments), as compared to patients without PDPH (length  $1.0 \pm 2.1$ ,  $P < 0.001$ ; R<sub>Max</sub>  $0.9 \pm 2.4$  segments,  $P < 0.001$ ), and patients with PDPH responding to conservative measures (length  $4.4 \pm 5.8$ ,  $P = 0.037$ ; R<sub>Max</sub>  $3.6 \pm 6.1$  segments,  $P = 0.039$ ) (Table 2). Further, 91.1% of patients who responded to

conservative treatment did not have epidural collections above T9, whereas 95.8% of patients without epidural collections above T9 did not need epidural blood patches. By multivariate logistic regression analysis, only the length of epidural collections was predictive of epidural blood patch among all study participants (OR 1.2 per segment, 95% CI 1.1–1.4,  $P = 0.005$ ).

## Discussion

The findings suggest that the extent of CSF leakage on heavily T<sub>2</sub>-weighted MRM following diagnostic lumbar puncture parallels the risk of PDPH, as evidenced by higher detection rates and more extensive distributions of periradicular leaks and epidural collections. This is in line with Bier's hypothesis that continued CSF leakage through the lumbar puncture site could be an important contributing factor for PDPH (Raskin, 1990). In fact, the risk of PDPH increases with a larger needle size, which could lead to larger dural defects and thus more likely persistent leakage following the procedure (Carson and Serpell, 1996). Nevertheless, not all patients with periradicular leaks or epidural collections developed PDPH. Although the data showed that younger individuals were more likely to have periradicular leaks and epidural collections, other factors that could modify the susceptibility to PDPH remain to be determined. For example, the speed of CSF



**Figure 2** Distribution of spinal CSF leakages. In general, periradicular leaks were most commonly seen around the upper lumbar region (A), epidural collections were mainly distributed between middle thoracic to upper lumbar regions (B), and retrosinal collections were primarily seen in the lower lumbar region (C). When analysed separately, patients with post-dural puncture headache (D and E) had more rostral distributions of periradicular leaks (D and F) and epidural collections (E and G) than those without (F and G).

extravasation could possibly play a role, and this could better be assessed with dynamic imaging techniques, such as dynamic CTM (Luetmer and Mokri, 2003).

Heavily  $T_2$ -weighted MRM has a unique role in studying PDPH for its lack of radiation exposure, non-invasiveness and ability to delineate spinal CSF leakages. Ethical issues could arise for the use of invasive imaging techniques, such as CTM, radionuclide cisternography, or MRM with intrathecal gadolinium, i.e. gadolinium-enhanced magnetic resonance cisternography (Albayram *et al.*, 2008). Dural punctures involved in these techniques could

potentially aggravate CSF leakages and the associated symptoms, and would also lead to difficulty ascertaining the origin of the observed CSF leakages. In addition, the advantages of heavily  $T_2$ -weighted MRM over conventional  $T_2$ -weighted spinal MRIs were illustrated by its comparability to CTM in directly demonstrating spinal CSF leakages, especially periradicular leaks (Tsai *et al.*, 2007, 2008; Wang *et al.*, 2009). In contrast to the current findings, existing literature showed conflicting data regarding the correlation between the amount of CSF leakage and the risk of PDPH (Iqbal *et al.*, 1995; Bezov *et al.*, 2010a;

**Table 2 Comparisons among patients without PDPH, with PDPH but not epidural blood patch, and with PDPH and epidural blood patches**

	1: PDPH(–)	2: PDPH(+)/EBP(–)	3: PDPH(+)/EBP(+)	P-value
Periradicular leaks				
Length (seg)	0.9 ± 1.9	2.6 ± 1.8	4.2 ± 3.8	1 versus 2 <i>P</i> = 0.003 2 versus 3 <i>P</i> = 0.122
R <sub>Max</sub> (seg)	0.8 ± 1.7	3.8 ± 4.4	5.5 ± 5.9	1 versus 3 <i>P</i> < 0.001 1 versus 2 <i>P</i> < 0.001 2 versus 3 <i>P</i> = 0.228 1 versus 3 <i>P</i> < 0.001
Epidural collections				
Length (seg)	1.0 ± 2.1	4.4 ± 5.8	8.0 ± 4.2	1 versus 2 <i>P</i> = 0.001 2 versus 3 <i>P</i> = 0.037 1 versus 3 <i>P</i> < 0.001
R <sub>Max</sub> (seg)	0.9 ± 2.4	3.6 ± 6.1	7.7 ± 8.0	1 versus 2 <i>P</i> = 0.017 2 versus 3 <i>P</i> = 0.039 1 versus 3 <i>P</i> < 0.001

R<sub>Max</sub> = maximum rostral migration; EBP = epidural blood patch.

Sakurai *et al.*, 2013; Fakhraan *et al.*, 2014). Interestingly, the only large-scale study also identified epidural collections as a risk factor for PDPH in patients undergoing lumbar CTM (Fakhraan *et al.*, 2014), although the extent of epidural collections was not assessed. On the other hand, other studies were retrospective in design, had a small sample size, and more importantly, assessed only a limited proportion of the spinal regions (Iqbal *et al.*, 1995; Sakurai *et al.*, 2013). The whole-spine axial heavily T<sub>2</sub>-weighted MRM used in the present study provided a more comprehensive quantification of post-lumbar puncture spinal CSF leakages, and thus could be a more reliable measure.

Even though periradicular leaks on heavily T<sub>2</sub>-weighted MRM could be visualized beyond the level of lumbar puncture, 63.6% of the leaks were located within three segments. This could suggest that the majority of dural defects might be located in close proximity to the observed periradicular leaks. As the main bulk of epidural blood patches extends three to five segments from the injection sites (Beards *et al.*, 1993; Vakharia *et al.*, 1997), periradicular leaks on heavily T<sub>2</sub>-weighted MRM should be a reasonable guide for targeted epidural blood patches. On the other hand, as heavily T<sub>2</sub>-weighted MRM is radiographically comparable to CTM in localizing spinal CSF leaks (Wang *et al.*, 2009), it is possible that periradicular leaks on heavily T<sub>2</sub>-weighted MRM or CTM may not be accurate enough as a guide for surgical intervention. In fact, only a minority of CSF leaks identified on preoperative CTM corresponded to dural defects with active CSF leakage at surgery in patients with spontaneous intracranial hypotension, even in those with a ‘leaking diverticulum’ on CTM (Cohen-Gadol *et al.*, 2006). Moreover, it should be noted that a large proportion of ‘spinal CSF leaks’ detected by MRM with intrathecal gadolinium (Albayram *et al.*, 2008) could overlap with post-lumbar puncture periradicular leaks. Caution should be exercised in the interpretation of ‘spinal CSF leaks’ on MRM with intrathecal gadolinium, as such leaks could result from the lumbar punctures for

intrathecal gadolinium injection rather than from the spontaneous intracranial hypotension disease process.

Post-lumbar puncture epidural collections had a wider range of distribution than periradicular leaks. After extravasation from the dural rent resulting from lumbar puncture, CSF drainage could follow the direction of least resistance or gravity. The extravasated CSF could leave the spinal column via the neuroforamina immediately at the same level of dural defects or after traveling in the epidural space for a distance, which appears as periradicular leaks. On the other hand, following shrinkage of the thecal sac, accumulation of epidural collections (Fig. 2B) could reflect the anatomy of the spine, as the mid- to lower thoracic region is the dependent part when the patients lie supine. Although the clinical utility of epidural collections in localizing dural defects is limited, its distribution could be of some help in patient selection for epidural blood patches. Epidural blood patches have been the mainstay of treatment for PDPH, especially when conservative measures fail (Bezov *et al.*, 2010b). Based on our results, the vast majority (95.8%) of patients with epidural collections not extending above T9 responded to conservative measures, and therefore prophylactic epidural blood patches may not be suitable for such patients.

The limitations are addressed as follows. First, the study population consisted of a large proportion of headache patients and middle-aged females, and whether such selection bias could have an impact on our results was uncertain. However, it was recently reported that PDPH was not more common among migraineurs (van Oosterhout *et al.*, 2013), and suspected symptomatic headache was not a risk factor for PDPH in the present study. Second, lumbar puncture was carried out with 22-gauge Quincke needles. Whether the amount and distribution of spinal CSF leakage with other needle sizes or atraumatic needles could differ is yet to be determined. Third, there were variable intervals between lumbar puncture and heavily T<sub>2</sub>-weighted MRM, and it is not certain how this could alter the pattern of CSF

leakages. Nevertheless, the clinical and imaging findings should be temporally correlated, as all of the PDPH patients received heavily T<sub>2</sub>-weighted MRMs while they were symptomatic. Fourth, the lumbar punctures in the present study were performed under the guidance of bony landmarks rather than fluoroscopy, and it is possible that some of the lumbar punctures might be carried out at levels other than L3–4. Last, the findings are based on the consequences of dural defects introduced by lumbar puncture. It remains to be determined to what extent the findings may apply to dural defects that occur spontaneously as in the case of spontaneous intracranial hypotension.

In conclusion, this study suggests that PDPH is associated with more extensive and more rostral spinal CSF leakages, and the presence of periradicular leaks and the length of epidural collections on heavily T<sub>2</sub>-weighted MRM could serve as useful indicators for PDPH. Visualization of spinal CSF leakages beyond the level of lumbar puncture was common. However, a substantial proportion of the visualized periradicular leaks remained in close proximity to the spinal level of dural defects. On the other hand, epidural collections had a more extensive distribution.

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## Supplementary material

Supplementary material is available at *Brain* online.

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