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NEURO

The efficacy of fluoroscopy-guided epidural blood patch in the treatment of spontaneous and iatrogenic cerebrospinal fluid leakage

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Abstract

Objective To evaluate patient outcomes following fluoroscopy-guided epidural blood patch (FGEBP), factors affecting the outcome, and to identify the rate of fluoroscopy-guided lumbar punctures (FGLP) requiring FGEBP.

Methods All FGLPs and FGEBPs between January 2014 and May 2017 were retrospectively evaluated. Information regarding patient characteristics, details of previous dural puncture (DP), details of the FGEBP, and FGEBP outcome were recorded. The outcome was classified into three categories as "complete response", "partial response", and "no response". Patients with "complete response" were compared to the combined group of "no response" and "partial response", classified as "incomplete response". Two-sample/Fisher's exact (continued/categorical variables) tests were used ($p < 0.05$).

Results Sity-seven FGEBPs were performed in 63 patients (female/male, 36/27; mean age/BMI 38/28.2). Fifty-nine were referred following DP; 31 were performed by radiologists. The rate of FGLPs requiring FGEBP was 1.78% within 3.5 years. The mean DP-FGEBP interval was 4.8 days. "Complete response" was achieved in 56 (84.8%), "no response" was found following 4 (6%) procedures. Average applied blood volume was 16 cc (5–30 cc). No difference was found between "complete response" and "incomplete response" groups regarding age, sex, BMI, DP performer, DP level, DP fluoroscopy time, DP needle caliber/type, FGEBP level, FGEBP needle caliber/type, FGEBP fluoroscopy time, FGEBP performer, and applied blood volume ($p > 0.05$). Despite approaching significance, no statistically significant difference was found regarding the presence of previous DP ($p = 0.06$).

Conclusions The efficacy of FGEBP is high in a group of patients referred to radiology for treatment of CSF leakage with complete response in 84.8% of patients.

Key Points

- *Fluoroscopy-guided epidural blood patch completely resolved symptoms in 85% of post-dural puncture headaches.*
- *The success approaches 95% when including the patients with partial resolution of symptoms.*
- *Epidural blood patch rate is found 1.8% following 1703 fluoroscopy-guided lumbar punctures.*

Keywords Epidural blood patch · Fluoroscopy · Lumbar puncture · Post-dural puncture headache · Intracranial hypotension

Abbreviations

BMI	Body mass index
CSF-OP	CSF opening pressure
DP	Dural puncture
EBP	Epidural blood patch
FGEBP	Fluoroscopy-guided epidural blood patch
FGLP	Fluoroscopy-guided lumbar puncture
ICH	Intracranial hypotension
LP	Lumbar puncture
PDPH	Post-dural puncture headache
sICH	Spontaneous intracranial hypotension

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Introduction

One of the complications of lumbar puncture (LP) is intracranial hypotension (ICH) and post-dural puncture headache

(PDPH) due to CSF leakage through the dural defect [1, 2]. Over the years, we have observed an increase in the number of fluoroscopy-guided lumbar puncture (FGLP) performed by radiologists; thus, radiologists should be familiar with this complication.

ICH is a distinctive clinical entity that typically presents with a positional headache, worsening when upright. The most common source is an iatrogenic CSF leak following a spinal intervention such as LP, intrathecal catheter placement, or dural tear following spinal surgery [1]. Skull base trauma is another potential cause of leak [3]. Rarely, it may occur spontaneously due to dural weakness of the nerve root sleeves, dural tears secondary to adjacent intervertebral disc pathology, or fistulas between CSF and adjacent veins [4–6]. While most PDPHs resolve within hours with bedrest and conventional treatment, symptoms may persist with significant patient discomfort [7]. Absent a response to conventional noninvasive treatment, epidural blood patch (EBP) is a minimally invasive treatment option.

Studies related to efficacy of EBP are largely conducted by anesthesiologists or neurologists with non-image-guided EBP [8–11]. Published success rates of initial EBP varies between 37 and 84%. However, studies investigating the success of fluoroscopy-guided EBP (FGEBP) are few and consist of small case series and small patient groups [12–14].

The primary purpose of this study is to evaluate patient outcomes following FGEBP and factors affecting the outcome. Our second goal is to identify the rate of FGLPs requiring treatment with FGEBP in a large multisite academic radiology department.

Materials and methods

Patients: inclusion and exclusion criteria

This retrospective study was approved by the institutional review board. Searching with the aid of natural language processing software, *Vitrea Intelligence* (*Vital Images, Inc.*), all FGLPs (diagnostic, intrathecal drug administration, lumbar drain placement, myelograms, and cisternograms) and FGEBPs performed by radiologists in our department between January 2014 and May 2017 were collected. That yielded 1266 patients with 1770 procedures. Sixty-seven FGEBPs were applied to 63 patients within that data set. We then excluded a single repeat FGEBP from the data set.

Epidural blood patch procedure

All FGEBPs were performed using an *OEC 9900 mobile C-arm* (*GE Medical Systems Inc*). Patients were in the prone position. Initial needle trajectory was planned, and the needle entrance site was marked. After administration of local anesthetic, the spinal needle was advanced into the posterior epidural space via an interlaminar approach close to the midline. Using a loss of resistance technique, 1–5 cc of Isovue-M-200 was injected through tubing connected to a syringe into the posterior epidural space. Following confirmation of needle tip position with fluoroscopy, the patient's venous blood was collected from a peripheral intravenous access site and subsequently injected into the epidural space (Figs. 1 and 2). After the procedure, the patient is observed for 2 h while lying flat in bed. After this time period, as the procedure is typically performed in the outpatient setting, the patient is then discharged home with instructions to remain lying flat as much as possible for the remainder of the day.

Data analysis

Included procedures were saved in a PACS folder in randomized order. Information regarding the procedures was collected in a spreadsheet. The following information was obtained: patient age, sex, body mass index (BMI); patient type (inpatient vs outpatient); presence of previous dural puncture (DP) before FGEBP; the person performing the DP (non-radiologist vs radiologist, resident vs fellow vs staff vs nurse practitioner vs physician assistant); indication for DP; DP level, patient position, needle size, needle type (Quincke vs Sprotte vs Tuohy vs Lutz); CSF opening pressure (CSF-OP) if measured; DP-FGEBP time interval; indication for FGEBP; FGEBP level, needle size, needle type (Quincke vs Lutz), fluoroscopy time, applied amount of blood; FGEBP operator (resident vs fellow vs staff vs physician assistant); and the patient outcome following FGEBP. In addition, the laboratory parameters regarding the applied blood were recorded from the most recent laboratory tests, including the hemoglobin, hematocrit, white blood cell, platelet, INR, and aPTT levels. Patient outcome following the initial FGEBP was evaluated retrospectively from electronic medical records obtained within a month after the procedure. The outcome was classified into three categories. If the patient's symptoms completely resolved after the procedure, it was classified as "complete response". If no improvement was obtained, it was classified as "no response". If symptoms improved but did not completely resolve after 1 month, it was classified as "partial response". The efficacy of FGEBP was also evaluated in the subgroup of patients with suspected idiopathic intracranial hypertension, using a CSF-OP exceeding 25 cm H_2O as criteria for intracranial hypertension [15]. All data collection was performed by a neuroradiology fellow and two research fellows.

Statistical evaluation

Rates of each variable were calculated. In one patient, the initial FGEBP showed "no response", and FGEBP was repeated. Although the repeat EBP was successful, for data analysis,

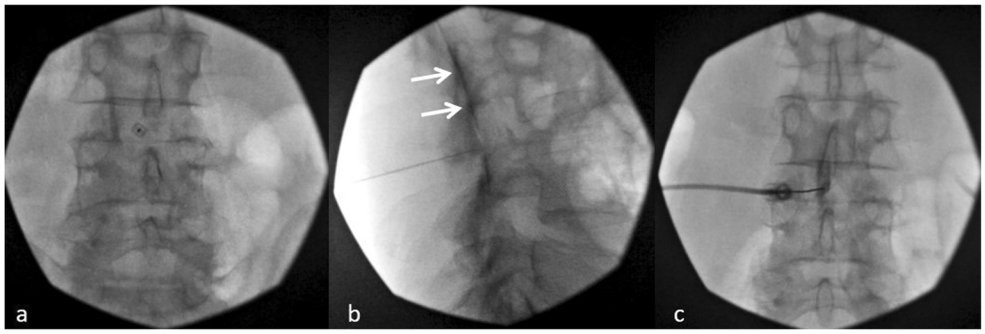

Fig. 1 A 63-year-old male with severe post-dural puncture headache 3 days after intrathecal chemotherapy. **a** A 22-G 3.5-in.-long Quincke needle was advanced to the posterior epidural space via a slight oblique right interlaminar approach at L3-4, the same level as the preceding LP. **b** Two cubic centimeters of contrast was injected in the contralateral oblique projection to confirm an epidural position of the needle. Note contrast layering along the spinolaminar line with the patient in the prone position (arrows). **c** On AP, the contrast confirmed an epidural position of the needle tip. Twenty cubic centimeters of the patient's own blood was injected into the epidural space. The patient's headache completely resolved at follow-up

the result of the second attempt was not included. The number of patients with outcome of "no response" was low. Therefore, for comparison analysis, the patients with "no response" and "partial response" were combined into an "incomplete response" category and compared to the "complete response" group. Two-sample *t* test (continuous variables) and Fisher's exact test (categorical variables) were used for analysis. The *p* value threshold for significance was set to $p < 0.05$.

Results

There were 63 patients (36 female, 27 male) with a total of 67 FGEBPs. With two of these procedures, there was inadvertent dural puncture and contrast observed in the thecal sac. In those two cases, the needle was pulled back and an epidural position of the needle was confirmed before administering the blood patch. In total, 100% technical success was ultimately achieved. Mean patient age was 38 (min 11, max 78). Mean BMI was 28.2 ± 8.1. Seventy-four percent of the procedures were performed in the outpatient setting.

FGEBP was performed on three different occasions in one patient and on two different occasions in another patient. In one patient, there were two EBPs, as the initial attempt did not alleviate symptoms and was thus categorized as "no response". Although the repeat procedure resulted in complete resolution of symptoms, that second procedure was excluded from our statistical analysis. Therefore, statistical analysis was performed for the 66 initial EBPs. Fifty-nine of those were referred to our clinic after a DP. Thirty-one of those DPs were performed by radiologists while 28 were performed by a clinician. In 7 procedures, there was no previous DP, and patients were referred for FGEBP due to a high suspicion of spontaneous intracranial hypotension (sICH) (Fig. 3).

Of the 59 procedures with history of previous DP, diagnostic LP was the most common reason with 39 cases (67.2%), followed by intrathecal chemotherapeutic administration, myelogram, lumbar drain placement, and inadvertent DP during attempted therapeutic epidural injection. L2-3 and L3-4 levels were the most frequent levels at which the DP occurred. Most of the DPs were performed using a 22-G needle (47; 85.5%), and the most commonly used needle was a Quincke needle (49; 90.7%), while Sprotte and Tuohy needles were rarely used. CSF-OP was documented only in 17 cases with a mean of 29.3 ± 12.5 cm H_2O (min 14, max 55).

There was "no response" to the FGEBP in 4 (6%) procedures. A repeat EBP was needed in a total of 2 cases yielding a repeat rate of 3%: one performed under fluoroscopy guidance with resolution of symptoms and the other performed intraoperatively by the surgeons after fixing the dural tear. "Complete response" was observed following 56 FGEBPs with a success rate of 84.8%.

For statistical analysis, the "incomplete response" group was compared to the "complete response" group (Table 1). No difference was found between groups regarding age, sex, BMI, and patient setting (inpatient vs outpatient) ($p > 0.05$). Despite approaching significance, there was no statistically significant difference between the groups regarding the presence of previous DP ($p = 0.064$). No statistically significant difference was found between groups regarding the DP performer, DP level, DP position, DP-FGEBP time interval, DP fluoroscopy time, DP needle caliber, DP needle type, FGEBP level, FGEBP needle caliber, FGEBP needle type, FGEBP fluoroscopy time, FGEBP performer, and volume of applied blood during FGEBP ($p > 0.05$).

The patients in the "complete response" group tended to have a higher CSF-OP (when recorded) during the LP that preceded the FGEBP with a mean CSF-OP of 30.3 ± 13 cm H_2O. By contrast, in the incomplete response group, patients tended to have a lower CSF-OP preceding the eventual FGEBP with a mean value of 21.5 ± 2.1 cm H_2O ($p = 0.03$). As we do not routinely measure CSF-OP unless requested or there is a compelling clinical reason to do so, only 17 patients had CSF-OP measurements available, all of whom were

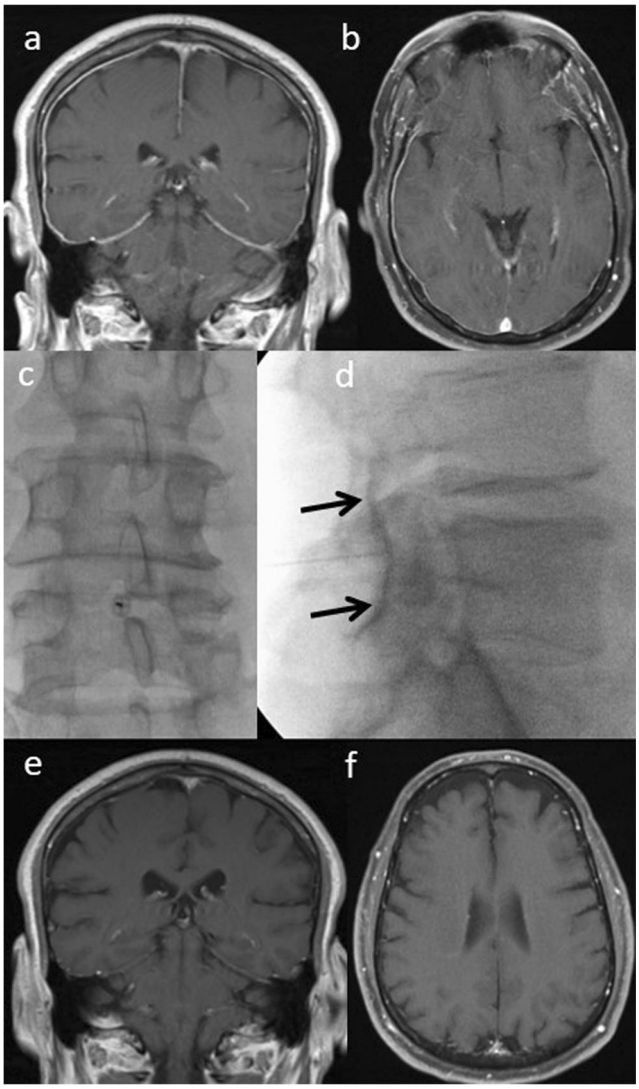

Fig. 2 A 59-year-old male presented to the emergency department with headache and double vision. **a** Post contrast MRI demonstrated diffuse dural thickening and enhancement. **b** In addition, the superior sagittal sinus exhibited a triangular contour with convex margins. To rule out intracranial hypotension from other causes of diffuse dural thickening, the patient underwent a lumbar puncture (LP). Opening pressure was low (< 5 cm H_2O). Laboratory tests on the patient's CSF were negative. Headache and double vision also worsened after the LP. **c**, **d** Thus, a fluoroscopy-guided epidural blood patch was applied at the same level as the LP via a right interlaminar approach. On lateral projection, both using loss of resistance technique and visualizing contrast spreading in the posterior epidural space, the needle tip position was confirmed. The patient's headache dramatically resolved, and double vision gradually resolved within a week. **e** Two months later, a follow-up brain MRI showed complete resolution of the previous dural enhancement. **f** Compared to (**b**), note how the margins of superior sagittal sinus have become concave

referred for suspected idiopathic intracranial hypertension. Of these 17 patients, 10 (59%) had intracranial hypertension. All 10 of those patients had a complete response following FGEBP. Of the 7 patients without intracranial hypertension (but with documented OP), 5 had a complete response following FGEBP and 2 had an incomplete response.

Of the 1703 FGLPs we performed over the 3.5-year time period, 31 of those patients underwent a FGEBP, corresponding to a FGEBP rate of 1.8%.

Discussion

EBP is a simple and minimally invasive treatment option in patients with ICH or PDPH which do not respond to conservative treatment [8, 16]. This can be performed blindly or under fluoroscopy guidance. In a blind EBP, it is possible to inadvertently inject the blood into the paraspinous soft tissues instead of the epidural space. There is also a possibility of DP during non-image-guided EBP. The advantage of FGEBP is definitive confirmation of the needle tip within the epidural space.

A disadvantage of a FGEBP compared to a blind EBP is radiation exposure. However, with a mean fluoroscopy time of 39 s for FGEBP, the rather low expected radiation dose for a one-time EBP arguably outweighs the risks inherent to that small exposure for the patient. Certainly, the radiation dose to the patient and to the proceduralist and technologist(s) can be minimized by minimizing fluoroscopy time while using pulsed and intermittent fluoroscopic imaging. Optimization of collimation and operator experience also impact exposure.

The largest studies in the literature regarding the efficacy of EBP are performed by anesthesiologists, especially involving a subset of postpartum female patients. Although there is a relatively low incidence of inadvertent DP and associated PDPH in patients who undergo spinal or epidural anesthesia, the number of patients who require EBP is relatively high [11]. In almost all of these studies, EBP was performed without imaging guidance and solely in postpartum female patients [8, 11, 17]. The published success rates of EBP without imaging guidance vary from 37 to 84% [8, 11, 16, 17]. In the largest study by Booth et al, EBP was performed without imaging guidance in 394 patients and symptoms resolved in 84% of the patients. Seventeen percent of the patients required two or more repeat EBPs to achieve complete resolution of headache [8].

Prior studies investigating the efficacy of FGEBP are comprised of small number of patients. These studies include patient groups ranging in size from 6 to 31 with success rates ranging from 67 to 100% [12, 13, 18]. In patients with sICH, targeted FGEBP in patients with a known location of CSF leak is superior to blind EBP when the location of the CSF leak was unknown (87% vs 52%) [12]. Alternatively, CT-guided EBP in patients with sICH due to ventral CSF leaks from disc herniations showed a 41% complete response rate, a 21% repeat rate, and ultimately 37% of the patients underwent surgery [5].

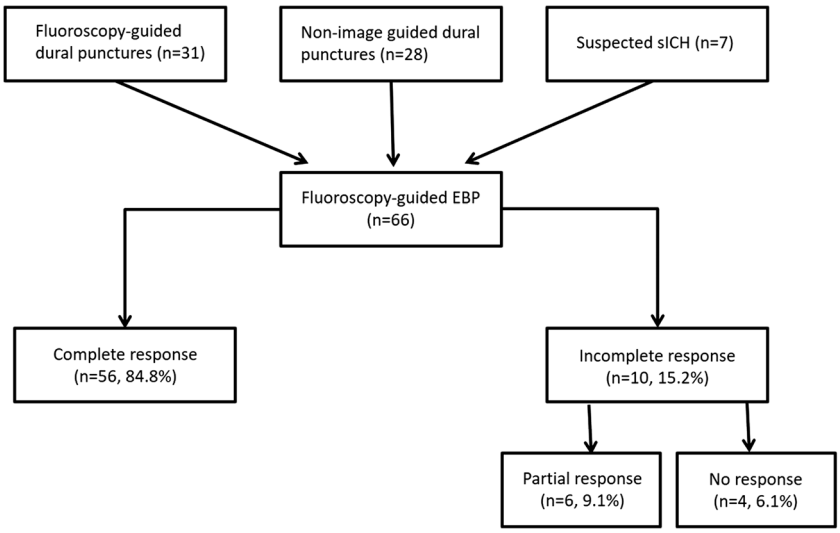

Fig. 3 Flow chart summarizing the results. sICH, spontaneous intracranial hypotension; EBP, epidural blood patch

To our knowledge, our patient group is the largest to date regarding the efficacy of FGEBP. We present results from a more heterogeneous group of male and female patients with a scope extending beyond postpartum patients. Most of our FGEBPs were performed due to CSF leakage following DP for diagnostic purposes, myelography, intrathecal chemotherapeutic administration, or lumbar drain placement. The percentage of procedures applied in the setting of suspected sICH was lower than what we had initially anticipated prior to beginning the study.

FGEBP is very effective at treating PDPH, with complete resolution of symptoms in 85% of patients following the initial FGEBP. Including the patients with partial response, the success rate of FGEBP approaches 95%. Our complete response rate in a more heterogeneous patient population is very similar to the results of Cho et al and Watanabe et al with smaller and less heterogeneous patient populations [12, 13]. Interestingly, our results are also similar to the largest non-image-guided EBP study conducted by Booth et al, comprised of solely postpartum female patients requiring EBP after epidural anesthesia [8]. However, our success rate is superior when compared with our combined complete + partial response group. In addition, our repeat rate of 3% is lower compared to other published rates.

For patients with previous DP, none of the following factors had a statistically significant impact on patient outcome: the proceduralist performing the procedure, DP level, patient position, DP needle type/size, and DP fluoroscopy time. In particular, by evaluating fluoroscopy time, we hoped to elucidate such risk factors as higher fluoroscopy times perhaps implying more difficult LPs requiring multiple punctures and hence a higher likelihood of CSF leak. Ultimately, we detected no such association. However, there was a significant difference between the two groups regarding the reason for prior DP. Patients undergoing lumbar drain placement were more likely to have an incomplete response following FGEBP. This difference is likely related to the larger dural defect occurring with the lumbar drain relative to the smaller defect with Quincke needle.

Interestingly, there was also a statistically significant difference between the two groups when accounting for the CSF-OP at the time of the DP. Patients in the "complete response" group tended to have a higher CSF-OP (when recorded). Furthermore, all the patients with documented intracranial hypertension who went on to FGEBP had a complete response, while patients with documented CSF-OP not meeting criteria for intracranial hypertension did not uniformly respond to FGEBP. As such, these findings might suggest that patients with idiopathic intracranial hypertension are more prone to develop PDPH but also respond relatively well to FGEBP. Perhaps, differences in dural elastance between the patient groups could account for this finding. Also, a larger volume of fluid is often drained in those patients with documented intracranial hypertension for therapeutic reasons, as compared to generally smaller volumes drained in patients without known intracranial hypertension. Nevertheless, our group of patients with documented CSF-OP is relatively small, limiting the degree of confidence regarding this observation. Therefore, the likelihood of developing PDPH after LP and the response to FGEBP in patients with idiopathic intracranial hypertension might serve as a focal point for further investigation in a larger patient population.

While not technically reaching statistical significance, there was a trend towards a difference between the "complete response" and "incomplete response" groups regarding the presence of previous DP ($p = 0.06$). Given the small number ($n = 7$) of patients without previous DP (presumed sICH), the lack of significant difference between the groups may be misleading, since the patients with sICH tend to be more resistant to EBP.

Variability in technical parameters, such as FGEBP level, needle caliber, needle type, fluoroscopy time, and operator

Table 1 Comparison between the complete response group and the incomplete response group

Variable	Stat/category	All FGEBP procedures $n = 66$	Symptom resolution		p
			Complete response $n = 56$ (84.84%)	Incomplete response (partial response + no response) $n = 10$ (6 + 4, 15.16%)	
History of previous DP	Yes	59 (89.39%)	52 (92.86%)	7 (5 + 2, 70.00%)	0.0646
	No	7 (10.61%)	4 (7.14%)	3 (1 + 2, 30.00%)	
Who performed the DP	Radiologist	31 (52.54%)	26 (50.00%)	5 (4 + 1, 71.43%)	0.4281
	Clinician	28 (47.46%)	26 (50.00%)	2 (1 + 1, 28.57%)	
Reason for DP	Unknown	1	1	0	*0.0387*
	Diagnostic lumbar puncture	39 (67.24%)	36 (70.59%)	3 (2 + 1, 42.86%)	
	Intrathecal chemotherapy	8 (13.79%)	8 (15.69%)	0	
	Lumbar drain placement	4 (6.90%)	3 (5.88%)	1 (0 + 1, 14.29%)	
	Myelogram	6 (10.34%)	3 (5.88%)	3 (3 + 0, 42.86%)	
	Inadvertent DP during epidural injection	1 (1.72%)	1 (1.96%)	0	
DP fluoroscopy time (sec)	n	30	27	3	0.4560
	Mean (SD)	30.01 (19.32)	29.06 (19.59)	38.50 (17.54)	
CSF opening pressure	n	17	15	2	*0.0323*
	Mean (SD)	29.30 (12.56)	30.34 (13.04)	21.50 (2.12)	
FGEBP reason	Unknown	1	0	1	*0.0186*
	CSF leak	3 (4.62%)	1 (1.79%)	2 (2 + 0, 22.22%)	
	Positional headache	2 (3.08%)	1 (1.79%)	1 (0 + 1, 11.11%)	
	Possible CSF leak	5 (7.69%)	4 (7.14%)	1 (0 + 1, 11.11%)	
	Post lumbar puncture headache	51 (78.46%)	47 (83.93%)	4 (4 + 0, 44.44%)	
	Post lumbar drain headache	4 (6.15%)	3 (5.36%)	1 (0 + 1, 11.11%)	
FGEBP level	L1-2	2 (3.03%)	2 (3.57%)	0	0.8065
	L2-3	27 (40.91%)	22 (39.29%)	5 (2 + 3, 50.00%)	
	L3-4	23 (34.85%)	20 (35.71%)	3 (2 + 1, 30.00%)	
	L4-5	10 (15.15%)	9 (16.07%)	1 (1 + 0, 10.00%)	
	L5-S1	1 (1.52%)	1 (1.79%)	0	
	Others	3 (4.55%)	2 (3.57%)	1 (1 + 0, 10.00%)	
FGEBP fluoroscopy time (sec)	n	57	50	7	0.2550
	Mean (SD)	39.66 (37.13)	34.53 (20.34)	76.34 (87.73)	
FGEBP blood volume (cc)	n	66	56	10	0.9297
	Mean (SD)	15.99 (4.96)	15.97 (5.16)	16.10 (3.90)	

Statistically significant p values are in italics

CSF cerebrospinal fluid, *DP* dural puncture, *FGEBP* fluoroscopy-guided epidural blood patch, *SD* standard deviation, *sec* second, *cc* cubic centimeter

experience, was not significantly different between the groups. In addition, there was no difference when evaluating the time interval between the DP and FGEBP and the level of FGEBP. We initially suspected that the amount of applied blood might contribute to the eventual outcome. However, it appears that both groups received a similar volume of blood during FGEBP without a significant effect on the outcome. Absent a correlation between the volume of administered blood and outcome, we typically administer 20 cc of blood, stopping short of this volume if the patient experiences significant discomfort. This is supported by a randomized clinical trial of obstetric patients where no difference was found between patient groups receiving 10 cc, 20 cc, or 30 cc of blood. However, several patients in that study could not tolerate the entire intended 30 cc blood volume due to pain with the authors concluding that 20 cc of blood was ideal [11]. These findings were also supported by the study of Booth et al, in which increasing the blood volume had no effect on the outcome [8].

Another goal of this study was to identify the rate of FGLPs which led to FGEBP for treatment of PDPH. While the underlying mechanism is unclear, it is postulated to occur secondary to a persistent dural defect and continued CSF leakage [2]. PDPH rates in non-fluoroscopy-guided LP studies vary between 5.5 and 32% [19]. A recent retrospective study by Rodriguez et al evaluated a large group of outpatients who had FGLP for either myelography or diagnostic purposes. In this study, all procedures were performed by a single proceduralist

using either a 22- or 25-G Quincke needle and followed by bedrest of 2–4 h with 0.8% of patients requiring later FGEBP [20]. Our rate of FGLPs requiring treatment with FGEBP of 1.8% in 1703 patients is low but notably higher than the study by Rodriguez et al. However, our patient population included inpatients and all procedures were performed by a heterogeneous group of radiology residents, fellows, and radiology staff. Also, while most FGLPs were generally performed by using a 22-G Quincke needle, a few patients had DP performed with a 20-G spinal needle. As a larger needle caliber is associated with a higher risk of PDPH [1, 21], this might contribute to our comparatively higher EBP rate. Furthermore, in our department, all patients routinely have 1 h of strict bedrest after the LP, which is shorter than the time in the study by Rodriguez et al [20].

There are a few limitations to this study. Since FGEBPs are not very common, our patient population, although robust, is still relatively small. Therefore, we did not have the sample size necessary to test the effect of these various clinical factors in the presence of one another in a multivariable logistic regression model. Furthermore, given the retrospective nature of this study, the information regarding the circumstances at the time of patient referral for FGEBP is incomplete. As such, we cannot reproduce the degree of confidence of suspected ICH immediately preceding the blood patch. This is a notable limitation of this study, as we rely on the clinical judgment of our referring colleagues to identify patients appropriately for a FGEBP. Although a measurement of CSF-OP immediately prior to FGEBP might better identify patients with ICH, this would also introduce the limitation of an additional DP that might predispose to headache or decreased effectiveness of the blood patch. Prospective long-term follow-up on patients after FGEBP was not investigated, which is another notable limitation.

Overall, the efficacy of FGEBP is high in a heterogeneous group of patients referred to a tertiary radiology department for treatment of PDPH and sICH, with complete resolution of symptoms in 84.8% of patients following FGEBP. The success rate approaches 95% when including the patients with partial resolution of symptoms. Secondly, the rate of FGLPs ultimately requiring a FGEBP is 1.8%.

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Compliance with ethical standards

Guarantor The scientific guarantor of this publication is Jeffrey B. Rykken.

Conflict of interest The authors declare that they have no conflict of interest.

Statistics and biometry Nathan Rubin, MS, from Biostatistics Core, Masonic Cancer Center, University of Minnesota, and Lei Zhang, MS, from Clinical and Translational Science Institute, University of Minnesota, Minneapolis, provided statistical advice for this manuscript.

Informed consent Written informed consent was waived by the Institutional Review Board.

Ethical approval Institutional Review Board approval was obtained.

Methodology
- retrospective
- cross sectional study
- performed at one institution

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