Neurosurgical Forum LETTERS TO THE EDITOR

Reduced incidence of CSF leak following complete calvarial reconstruction of craniectomies

TO THE EDITOR: We read with keen interest the article by Eseonu et al.² (Eseonu CI, Goodwin CR, Zhou X, et al: Reduced CSF leak in complete calvarial reconstructions of microvascular decompression craniectomies using calcium phosphate cement. *J Neurosurg* 123:1476–1479, December 2015) regarding the reduced incidence of CSF leaks following complete calvarial reconstruction of craniectomies done for microvascular decompression (MVD) using calcium phosphate cement.

MVD is a very fruitful surgery and provides symptomatic relief in up to 95% of patients with trigeminal neuralgia.^{4,5} CSF leakage following MVD can be devastating. We commend the innovative idea of the authors in their efforts to reduce the incidence of CSF leaks following retrosigmoid craniectomy for MVD. The authors report on 221 patients who underwent retrosigmoid craniectomy for MVD to treat trigeminal neuralgia. Of 221 patients, 116 consecutive patients received polyethylene titanium mesh incomplete cranioplasty and the subsequent 105 patients received calcium phosphate for complete cranioplasty. They reported a statistically significant higher incidence of CSF leaks in the incomplete-cranioplasty group and no leaks in the calcium phosphate group. We would like to bring few important points in this article to the kind attention of the readers.

Dural closure was augmented with a collagen dural substitute, which was sutured to the dura and reinforced with collagen matrix and fibrin sealant. However, the article did not mention the number of patients in whom dural substitute was required for dural closure (in patients in whom primary dural closure was not possible) in each group, and this could be a cause of bias.³ Other causes of poor wound healing like diabetes, steroid use, and malnutrition were not evaluated and can be a very important cause of bias and need to be accounted for. Moreover, the rate of CSF leak reported in one of the largest series of MVD was 1.5%.¹ There might be some other factors responsible for a high CSF leakage rate in the patients who received polyethylene titanium mesh-augmented incomplete cranioplasty (CSF leakage rate 4.5%). Hence, a ran-

domized study to remove the confounding factors would be ideal to determine the superiority of one method of cranioplasty over other.

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Disclosures

The authors report no conflict of interest.

Response

No response was received from the authors of the original article.

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Endoscopic endonasal approach for clip ligation of cerebral aneurysms

TO THE EDITOR: We read with interest the article by Szentirmai et al.⁹ (Szentirmai O, Hong Y, Mascarenhas L, et al: Endoscopic endonasal clip ligation of cerebral aneurysms: an anatomical feasibility study and future directions. *J Neurosurg* 124:463–468, February 2016). The authors performed a cadaveric study on 9 specimens to study the vascular anatomy through the endoscopic endonasal approach. They also aimed to assess the possible maneuverability of anterior and posterior circulation vessels through the endoscopic approach to simulate the surgical treatment of aneurysms through the nose. They calculated the “maximal surgical corridor” areas and assessed the visibility of adjacent vessels and perforator anatomy. We would like to congratulate the authors for the selection of this interesting topic and performing this study and add several comments.

The authors calculated the maximal surgical corridor to approach different anatomical regions. It is not clear how they define the maximal surgical corridor. Although the anterior circulation vessels can be exposed through the transtubarcular approach,^{2,5,10} we believe the area of exposure needs to be defined specifically for different surgical targets (i.e., aneurysm locations). Such definition should include clear anatomical landmarks as boundaries. Therefore, considering internal carotid artery (ICA) and anterior communicating artery (ACoA) aneurysms in a single surgical area seems an oversimplification. Exposure of the clinoidal segment of the ICA and the ophthalmic artery complex requires a different trajectory from that of the ACoA complex.^{4,8} This is exceptionally important in endoscopic endonasal approaches (EEAs), where the area of exposure needs to be as large as necessary and as small as possible to minimize the risks of a CSF leak while providing optimal results.

In the *Results* section, the authors state that “...anterosuperiorly projecting aneurysm dome would offer the most favorable access...best visualization of the aneurysm neck...perforators...and minimal risk of sac rupture.” We agree with the authors that anterosuperiorly projecting aneurysms of the ACoA complex would be good candidates for clip ligation through an EEA. An EEA provides ample midline exposure along the tuberculum sellae and does allow control of adjacent structures like the optic chiasm. Also, there may be no need to resect the gyrus rectus to expose the aneurysm, as there may be in open surgery.¹² However, we cannot see the link between the methods and results of the study and such an interpretation of the results. The effect of expected anatomical variations, such as the pre-fixed optic chiasm and midline position of the anterior bend of the ICA (known as kissing carotids), may be decisive in defining the capabilities of the EEA in treating aneurysms. We believe that these anatomical features need to be included when assessing the role of the EEA in cerebrovascular surgery. It is important to note that in a cadaveric study, one cannot assess the risk of the sac rupture because there isn't a method to provide such evidence yet.

We believe that the exposure of an artery does not

necessarily mean ample exposure of the aneurysm. For example, the authors mention that for ophthalmic artery aneurysms, an ophthalmic artery with medial origin can be exposed through an endoscopic endonasal corridor. However, one cannot be certain that an aneurysm is safely exposed through this route. While we agree with the authors that “patient series are needed to clarify the safety of endoscopic endonasal corridor” for aneurysm surgery, we think that multiple cadaveric studies are needed to define the advantages and disadvantages of this approach for every possible aneurysm location. Such studies need to compare the classic transcranial approach(es) used for each specific aneurysm with the tailored alternative EEA in terms of instrument maneuverability, perforator exposure, extent of proximal and distal vessel control, and possible risks to the neural structures. Without these investigations, it seems too unsafe to proceed with case series in which the EEA is used for aneurysm clipping, because there is little scientific evidence to base the indications for the use of the EEA for each particular aneurysm. Such studies have been performed to compare different transcranial approaches^{3,6,11} and are also in evolution for the comparison of the EEA with transcranial approaches to address specific pathologies in specific locations. There are also several studies that evaluate the role of EEAs in cerebrovascular surgery.^{2,7,8,10} We think that more work still needs to be done to further delineate this role, especially as compared to the classic transcranial routes.

The authors stated that the EEA exposures gave them sufficient space to deploy 2–3 clips in different vascular areas. We agree that the ability to place a clip (temporary or permanent) is very important in aneurysm surgery, especially when it is done through an endoscopic endonasal route, but we strongly believe that the fact that the surgeon is able to apply a clip does not mean that exposure is satisfactory for aneurysm clipping. The distance of the vessel “exposed” needs to be compared to the distance between the proximal and distal locations of the clips that can be safely applied to evaluate the surgeon's ability to maneuver through that specific corridor. In our opinion the safety of clip application (i.e., one with adequate visualization of the target vessel, surrounding perforators, and clip tongs during placement) is as important as the ability to apply it. An EEA offers good visibility; however, we still do not know how much we can exactly do through that approach for different targets. In addition, the implicit limitation of the cadaveric model does not allow the placement of clips simulating a real-life scenario, as the absence of the aneurysm leads to overestimation of the results. In our opinion, targeted cadaveric studies on each aneurysm location and feature are required before reaching conclusions on the feasibility or role of the EEA in cerebrovascular surgery.

The authors propose that angled endoscopes provide “a special opportunity for visualizing perforating arteries.” We agree completely with this statement. However, regarding the endonasal approaches, it needs to be clarified that better visualization does not always equal better maneuverability. Although angled endoscopes allow the surgeon to see through steep corridors and corners, the current endoscopic instrumentation is limited in terms of maneuverability around the corners of the surgical corridor.¹

The authors state that they were able to place multiple instruments through the nostrils, which implies good maneuverability. We strongly agree that enhanced maneuverability is an essential part of aneurysm surgery, especially while targeting aneurysms through the deep and narrow corridor of an EEA. However, the number of instruments passed through the corridor cannot, per se, define the maneuverability. Measurement of surgical freedom or some similar variable would in fact assess the maneuverability. This emphasizes the importance of performing cadaveric studies to define the optimal aneurysm projection, instruments to be used, and corridor for each aneurysm location or, simply, the “indications” for EEA exploitation for specific aneurysms.

The authors emphasize the importance of temporary circulatory arrest with adenosine at the time of dural opening to prevent catastrophes in cases in which an aneurysm dome pushes towards the dura. Certainly, adenosine-aided circulatory arrest is a pearl in this field. Nevertheless, we think it should also be stressed that using last-resource options should not be considered as the standard when defining a new approach. Surgical research should be carried out first to design a dural opening technique that prevents the risk of dome perforation before concluding that the endonasal corridor is a safe and effective option for clipping large aneurysm protruding to the clivus. As we do not know the risks and benefits of a tailored EEA for each specific aneurysm location, we cannot solely rely on adenosine arrest or other “bail-out” measures to reach general conclusions on the indications of the EEA in aneurysm surgery.

Finally, the authors suggest that if, upon inspection, the EEA does not provide a satisfactory working channel, the surgery needs to be aborted and a classic transcranial route should be chosen. Unfortunately, we would disagree with this statement. We think the preoperative planning, based on scientific evidence, should enable the surgeon to determine if the EEA can be a favorable route to treat a specific aneurysm. This is the major need for defining indications for different surgical approaches and different pathologies. We agree that, despite taking all the precautions and measures, the chosen approach may ultimately prove unsatisfactory and warrant abortion. However, without clear indications and delineation of risks and benefits, the selection of an approach that may lead to an unsatisfactory exposure is not justified while the current transcranial and endovascular techniques offer a secure, well-tested alternative.

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Disclosures

The authors report no conflict of interest.

Response

Drs. Tayebi Meybodi and Benet provide a thoughtful review of our article and we appreciate the feedback. They raise several interesting points that we shall address. The first point they raise is that specific surgical approaches should be defined for each of the targets, namely each aneurysm location. The specificity of the approach will limit the opening and decrease the risk of a CSF leak. While this sounds appealing, our experience is that larger bone openings are generally needed for safe endonasal surgery and the closure must be suitable for the required opening. Particularly in aneurysm surgery where control of the feeding arteries is so important, namely “proximal control,” a large opening is required that is tailored not just to the location of the aneurysm but to all the feeding vessels.

The authors call for multiple cadaver studies to define the safety of the endonasal approach for every conceivable aneurysm location. Yet, at the same time, they admit that each case is different, presenting unique and specific anatomy that often cannot be fully appreciated in a cadaver situation. This is the difficulty of cadaver studies. Not only is every patient's anatomy slightly different, but every pathological situation is slightly different as well. Hence, cadaver studies will always fall short of reproducing the actual surgical scenario. For this reason, we opted to explore the endonasal approaches that have been described and determine in which aneurysm scenarios they might be applicable. These approaches are already well illustrated and need not be completely repeated to suit the needs of the vascular surgeons. The maximal extent of these approaches is well described, and only certain vessels can be reached with these approaches.

The authors feel that endonasal aneurysm surgery should be performed until each and every approach for every aneurysm location is determined, as they claim has been done for transcranial surgery. However, surgeons were attempting to clip aneurysms through a craniotomy in many different locations well before the cadaver studies had been done. Often, the human attempts are the inspiration for the cadaver studies and not vice versa. Moreover, many of the transcranial approaches used for skull base tumors were first defined for tumor and then applied to aneurysm surgery. The same scenario is at play with the endonasal approaches. The work has been done describing the approaches and the closures, and the next step is to try to apply these approaches to aneurysms to discover which scenarios can be successfully achieved. New approaches are not required specifically for vascular work but rather the opposite logic is at play—namely, which of the defined endonasal approaches will be suitable for which aneurysm situations.

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Sildenafil for cerebral vasospasm: is the proof of the pudding in the eating?

TO THE EDITOR: We have read with great interest the paper by Washington and colleagues⁴ (Washington CW, Derdeyn CP, Dhar R, et al: A Phase I proof-of-concept and safety trial of sildenafil to treat cerebral vasospasm following subarachnoid hemorrhage. *J Neurosurg* 124:318–327, February 2016).

Use of sildenafil to treat cerebral vasospasm (CVS) following subarachnoid hemorrhage (SAH) has been proposed in various animal experimental trials. We published

the first human trial of sildenafil in reversal of refractory CVS in surgically treated patients with spontaneous aneurysmal SAH.² Washington et al. cited this study.⁴ We observed sustained reversal of CVS in 11.1% (8/72) and transient reversal in 5.5% (4/72) of patients. We did not analyze the clinical outcome and angiographic evaluation of vasospasm; our study was a safety, efficacy, and feasibility study of sildenafil in humans with post-SAH vasospasm.²

Proof-of-principle or proof-of-concept (PoC) studies are defined as tools to detect a signal that the drug in development is active on a pathophysiologically relevant mechanism, as well as preliminary evidence of efficacy in a clinically relevant end point. Such studies may include tolerability and safety. PoC studies are small, brief, and scientifically rather than regulatory-driven designs.³ A PoC is a realization of a certain method or idea to demonstrate its feasibility, or a demonstration in principle, whose purpose is to verify that some concept or theory has the potential of being used.¹ The definition of PoC entails that a rigorous methodology need not be used. There are no standard guidelines on how to perform a PoC study and how extensive or limited a PoC exploration has to be.³ The “rigorous” methodology by Washington et al. only serves to confirm the existing PoC and does not in itself become a concept.⁴

We congratulate the team for evaluating the role and safety of intravenous sildenafil in patients with SAH-induced CVS. We agree that transcranial Doppler flow velocities are a subjective parameter. In its comparison, angiographic evaluation before and after administration of sildenafil provides an objective assessment. Administration of sildenafil resulted in an average percentage increase in vessel diameter of 62% (range 0%–200%), which is definitely a significant advantage in comparison to intraarterial injection of nimodipine and papaverine.⁴ One main methodological concern in performing this kind of work is related to the neurological outcome in the short and long term. Because both of the studies lack in assessment of neurological outcome, further studies are warranted.^{2,4}

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Disclosures

The authors report no conflict of interest.

Response

We sincerely appreciate the interest shown in the comments provided by Dr. Mukherjee and colleagues in regards to our recently published paper. Also, we commend them on their published work, which provided the first evidence that sildenafil improves CVS in human patients with SAH.² The results from these 2 studies provide convincing evidence that sildenafil has a positive impact on CVS following SAH. Additionally, we have recently demonstrated that sildenafil may also be acting to improve dysfunctional cerebrovascular autoregulation observed in patients with SAH-related CVS.¹

Based on the results above and the abundance of pre-clinical evidence, we believe that sildenafil holds great promise to be an effective treatment for delayed cerebral ischemia following aneurysmal SAH. These PoC studies are important in understanding the effects of sildenafil on the pathophysiology of delayed cerebral ischemia. Yet, they in themselves are in no way definitive proof of effectiveness, but rather serve as evidence guiding and directing future studies. Therefore, we absolutely agree that further studies that rigorously analyze the effects of sildenafil on rates of delayed cerebral ischemia and neurological outcome are warranted, and we are actively working to implement such trials in the near future.

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Diagnosis and prediction of surgical outcome in normal pressure hydrocephalus

TO THE EDITOR: I read with interest the article by Pomeraniec et al.² (Pomeraniec IJ, Bond AE, Lopes MB, et al: Concurrent Alzheimer's pathology in patients with clinical normal pressure hydrocephalus: correlation of high-volume lumbar puncture results, cortical brain biopsies, and outcomes. *J Neurosurg* 124:382–388, February 2016). The authors highlighted the diagnostic and manage-

ment dilemma in cases of normal pressure hydrocephalus (NPH) and in those of NPH with concurrent Alzheimer's disease, and they studied the value of preoperative high-volume lumbar puncture (HVLP) and intraoperative cortical biopsies. They concluded that HVLP has no value in predicting the outcome after shunt surgery and that cortical biopsies showing Alzheimer's disease may have a good correlation with outcome after shunting. But even then, in 13% of patients with negative cortical biopsies, Alzheimer's disease was shown on repeat biopsy because of the progressive nature of the disease. Hence, it would appear that neither HVLP nor cortical biopsy is reliable in surgical decision making and predicting outcome in NPH.

In this context, I would like to highlight the usefulness of measuring cerebrospinal fluid outflow resistance (R_{out}) using a simple, improvised, bedside bolus lumbar injection method (MIN method).^{3–5} This MIN method is a simplified form of the bolus injection method of Marmarou and colleagues.¹ We have been using this method routinely for diagnosis and surgical decision making in patients with NPH. We have found that, in patients with clinical and radiological features of NPH, an R_{out} greater than 18 mm Hg/ml/min correlated with very good outcome after shunt placement. R_{out} measurement is also useful when one faces a diagnostic dilemma as to whether a patient's condition is Alzheimer's disease or NPH.

This article by Pomeraniec and colleagues is to be commended for objectively evaluating the other methods, namely HVLP and cortical biopsies, for prediction of outcome after shunt surgery in patients with NPH.

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Disclosures

The author reports no conflict of interest.

Response

We thank Dr. Ramesh for his comments on our study in which we reviewed the cases of patients who underwent cerebrospinal fluid (CSF) shunting and brain biopsies for

presumed concurrent NPH and Alzheimer's disease. Dr. Ramesh and colleagues recently illustrated the utility of a modified lumbar injection method to measure CSF outflow resistance.⁴⁻⁶ They have shown bolus lumbar infusion to be useful in predicting positive shunt responsiveness in 87.5% of 8 patients in whom shunts were placed for NPH, with a follow-up ranging between 6 months and 1 year.⁵ Bottan and colleagues¹ previously studied constant-flow, constant-pressure, and bolus infusion methods for measuring CSF outflow resistance and highlighted the importance of viscoelastic parameters on bolus infusion in accurately determining the CSF outflow resistance. A lack of generally accepted threshold values for outflow resistance and a standardized technique for measurement have prevented infusion testing from becoming more ubiquitous in the clinical setting.¹ In our series, CSF outflow resistance was not measured and therefore a correlation to HVLP, brain biopsies, and outcomes was not evaluated.

Chief motivations for our review were the persistent diagnostic and management challenges of NPH, the high incidence of Alzheimer's disease in this patient population, and its resultant effects on the utility of shunting as a management strategy. The predictive power for improved outcome with shunt treatment in patients with suspected NPH falls dramatically when treatment decisions are based on current clinical and imaging features alone. The identification of NPH patients most likely to benefit from shunt procedures remains difficult.^{2,7,8} Marmarou and colleagues found that HVLP carried with it a higher degree of certainty for favorable response to shunt placement than clinical examination alone.³ The sensitivity of predicting successful outcomes based on clinical and imaging findings alone can be as low as 46%. Marmarou and colleagues found that the addition of HVLP yielded a sensitivity of 26%–61%. CSF outflow resistance studies via infusion tests had sensitivities of 57%–100% and a similar positive predictive value (PPV) of 75%–92%. Prolonged external lumbar drainage in excess of 300 ml yielded high sensitivity (50%–100%) and high PPV (80%–100%).³

Our study indicates that a significant percentage of patients with clinical NPH had histopathological findings consistent with Alzheimer's disease. As Dr. Ramesh points out, the PPV of HVLP is not ideal. HVLP in addition to biopsy and CERAD classification (Consortium to Establish a Registry for Alzheimer's Disease) provided a better predictor of clinical outcome as increasing plaque density appears to be inversely related to shunt effectiveness. HVLP in patients with NPH versus those with Alzheimer's pathology had a PPV of 45% versus 18% ($p = 0.0136$); however, a PPV of 45% does not reach clinical significance for decision making, and, in practice, biopsy results are not available preoperatively. Certainly, there is significant prognostic information to be gained from a concurrent biopsy at the time of shunt placement, supporting the notion that in some patients intervention may serve as both a diagnostic and a therapeutic purpose.

Dr. Ramesh highlights that 13% of patients who underwent repeat biopsy during shunt interrogation had findings consistent with Alzheimer's pathology, underscoring the progressive nature of Alzheimer's disease and the imperfect relationship of biopsy to outcome. Of the 5 patients in whom Alzheimer's disease was seen on repeat biopsy, 4

patients (80%) showed initial improvement in symptoms following the initial ventriculoperitoneal shunt procedure and 1 patient (20%) showed no improvement following surgery. All of the 4 patients with initial improvement eventually experienced recurrence and worsening of symptoms. There is certainly opportunity to improve diagnostic measures to identify these patients with higher sensitivity earlier.

A prevailing standard for the prognostic evaluation of patients with NPH with or without concurrent neurodegenerative changes is lacking. Supplemental tests have been shown to increase predictive accuracy, sometimes greater than 90%.³ Our data provide insight into why some patients have failed outcomes despite positive lumbar puncture results, but the data do not improve our ability to screen patients on initial presentation. We have found that biopsy results are helpful for discussions with families regarding future shunt interrogations when patients experience cognitive decline.

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Vascular tumor versus vascular malformation of the internal auditory canal

TO THE EDITOR: We read with great interest the article by Zhu and colleagues⁵ (Zhu WD, Huang Q, Li XY, et al: Diagnosis and treatment of cavernous hemangioma of the internal auditory canal. *J Neurosurg* 124:639–646, March 2016), and we believe the term “cavernous hemangioma” is worth discussing.

The term “cavernous hemangioma” has been widely used in the clinic, but a consensus regarding the nomenclature of hemangioma has not been established among different clinical departments.^{2,3} In some cases, mistreatment occurs due to this lack of a consensus regarding the name of the disease. In fact, “cavernous hemangioma” is characterized by congenital angiodysplasia, rather than a tumor.^{1–3}

According to the updated ISSVA (International Society for the Study of Vascular Anomalies) classification, cavernous hemangioma manifests as a venous malformation, a subtype of vascular malformation. However, vascular tumors are known as tumor types such as infantile hemangioma, congenital hemangioma (rapidly involuting congenital hemangioma and noninvoluting congenital hemangioma), tufted angioma, kaposiform hemangioendothelioma, spindle cell hemangioendothelioma, dermatological-acquired vascular tumors, and other rare hemangioendotheliomas.¹

Notably, cavernous hemangioma is characterized by a dilated vessel lumen and endothelium-lined vascular sinusoids. The size of the sinusoids varies, and they have the appearance of sponge-like structures. Sinusoids are enriched in venous blood and are interconnected. The biological properties of the vascular malformation differ from those of hemangioma. Upon vascular malformation, the endothelial cells may be at a resting stage for a long time.¹ In contrast, proliferative endothelial cells can be detected in hemangioma. Research has indicated that, compared to that in malformed vessels, the vascular endothelial growth factor level is significantly higher in hemangioma.^{1,3} In addition, Zhou et al. showed that the mRNA (messenger RNA) expression of Tie2 in vascular malformations was similar to that in soft-tissue vascular malformations, but obviously lower than in infant hemangiomas.⁴

The management of hemangioma and vascular malformation should be based on the natural course and biological characteristics of the disease. The benefits and potential risks should be carefully balanced before therapeutic decisions are made. Perhaps a more appropriate and specific nomenclature for cavernous hemangioma is required in order to understand the nature of this disease and improve the therapeutic strategy.

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Disclosures

The authors report no conflict of interest.

Response

No response was received from the authors of the original article.

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Fat-suppressed T2-weighted sagittal images

TO THE EDITOR: We read with considerable interest the technical note by Nakai et al.² (Nakai E, Takemura M, Nonaka M, et al: Use of fat-suppressed T2-weighted sagittal images after infusion of excess saline into the subarachnoid space as a new diagnostic modality for cerebrospinal fluid hypovolemia: technical note. *J Neurosurg* 124:580–583, February 2016).

In this report the authors describe 3 patients in whom a technique of performing MRI after infusion of saline into the lumbar subarachnoid space was presumed to be of diagnostic value and led to successful treatment. While this is an interesting technique with a logical conceptual basis, we had reservations regarding this publication of the authors' results. The images that accompany Case 1 may not demonstrate a real source of the CSF leak since the finding indicated in Fig. 2 looks remarkably like that shown in Fig. 1 from the paper titled “False localizing sign of C1–2 cerebrospinal fluid leak in spontaneous intracranial hypotension,” which also appeared in the *Journal of Neurosurgery*.³

In addition, the high signal indicated by the arrow in Fig. 6 is only in the subcutaneous fat, without any abnormal signal in the paraspinal soft tissues. The scanning technique used to create this image involves chemical fat suppression, which is frequently degraded by inhomogeneity of the magnetic field. As a result, high signal is frequently evident in the fat secondary to incomplete fat sup-

pression, and this is a well-described artifact on this pulse sequence.¹ This MR imaging pitfall most likely explains the high signal in subcutaneous fat that is evident in both the posterior and anterior neck subcutaneous fat on the provided image. This artifact is much less likely to occur on STIR sequences, and the authors might consider adding that imaging sequence in future examinations.

While we cannot comment about the contribution of this procedure with regard to the resolution of the patient's symptoms, the imaging determination of the site of leak in 2 of the 3 cases may have been misleading.

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Disclosures

The authors report no conflict of interest.

Response

We thank Drs. Mamourian and Nabavizadeh for their comments on our paper.

The most important point is that these 3 cases were catalysts for new ideas. The main point is that the images show a change before and after the injection. In the future, we will consider better imaging sequences, such as STIR sequences.

We consider the false localizing sign as follows. The CSF that leaked without pressure collected in the portion of the epidural space where it could easily accumulate. The CSF forced out by the pressure soaked into the connective tissue near the leakage site. We hypothesize that the changes on imaging occurred in the vicinity of the leakage site.

With the cooperation of other physicians, we will investigate more cases in the future. The results will be reported in a subsequent paper.

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