LETTERS TO THE EDITOR

Focal cortical dysplasia type IIIa and isolated hippocampal sclerosis

TO THE EDITOR: We read with great interest the paper by Dührsen et al.7 (Dührsen L, Sauvigny T, House PM, et al: Impact of focal cortical dysplasia Type IIIa on seizure outcome following anterior mesial temporal lobe resection for the treatment of epilepsy. J Neurosurg [epub ahead of print July 28, 2017. DOI: 10.3171/2017.2.JNS161295]). The authors’ study is an effort to gain a deeper insight into the correlation between histopathological features and seizure outcome in temporal lobe epilepsy (TLE) treated using anterior mesial temporal lobe resection (AMTLR).

Recent neuropathological classifications of epileptogenic lesions such as hippocampal sclerosis (HS), granule cell pathology (GCP), and focal cortical dysplasia (FCD) achieved a more precise definition of histopathological features and subtypes, which in turn may allow more accurate clinicopathological correlations and prognostic assessment. The 2011 International League Against Epilepsy (ILAE) classification introduced a new class, FCD type III, evidencing that those cases in which cortical lamination abnormalities (typical of FCD type I) are adjacent to a principal lesion present clinical features and seizure outcome similar to those of the latter.

We absolutely agree with the hypothesis that FCD IIIa is a single epileptic unit and therefore an individual disease pattern, and that reelin, a glycoprotein responsible for neuronal migration and architecture in the hippocampus and cortical layers, may play an important role in a subset of FCD IIIa.13 However, Dührsen et al. report that patients with FCD IIIa (the combination of HS and FCD type I in the temporal pole) had a significantly better seizure outcome after AMTLR than patients with HS alone. These results challenge the original description of FCD IIIa, in which the principal lesion-determining seizure outcome is HS.

In our experience, patients with FCD IIIa who were submitted to AMTLR showed a seizure outcome similar to patients with isolated HS (84% vs 82% in Engel class I) and a better outcome than patients with isolated FCD type I (63% in Engel class I).10,12 A worse postsurgical outcome for isolated FCD type I was reported by many other authors.18,19 In 60%–70% of cases HS is associated with FCD in the temporopolar cortex.4,6,8,10,11,19 Dührsen et al. observed FCD IIIa in only 25.5% of patients, but the challenges in this field of neuropathology are well known.2,14 Furthermore, it has been hypothesized that atypical HS subtypes, i.e., HS ILAE types 2 and 3, are associated with less favorable outcome,2,10,11,16,20 which may also be related to the status of the dentate gyrus (namely the absence or presence of GCP),2,10,13 but in the series by Dührsen et al. these pathological findings have not been provided.

We agree with the authors that the presence of FCD type I is currently difficult to detect by MRI.10,18 In the face of clinical and imaging features of TLE related to HS, the only manner to decide the extension of temporal resection and consequently the surgical strategy (i.e., selective amygdalohippocampectomy [SAH] or AMTLR) is the use of noninvasive preoperative neurophysiological study (long-term video-electroencephalography monitoring), which only rarely highlights a strictly mesial epileptogenic zone. Temporal pole neocortex is frequently involved in the epileptogenic network either functionally or with a postsurgically documented pathological substrate (such as FCD type I).6,10,19 These data should imply a clear advantage of AMTLR in terms of seizure outcome. Instead, although we agree with the authors about considering AMTLR the optimal surgical strategy for TLE associated with HS, the superiority of this approach over SAH has not yet been determined.16

The authors report that 33.3% of the patients included in the study were undergoing a second procedure because of persistent seizures, which may suggest the presence of a more complex epileptogenic network, as in temporal plus epilepsy. The authors’ results of a worse seizure prognosis for isolated HS may therefore have some explanations, such as a possible role of histopathological subtypes of HS and granule cell status on seizure outcome.3,10,15,20 The extension of resection of mesial temporal structures,17 and the presence of temporal plus epilepsy.1,9

Marco Giulioni, MD
Gianfranco Vornetti, MD
IRCCS Foundation Neurological Institute “C. Besta,” Milan, Italy

Gianluca Marucci, MD, PhD
IRCCS Institute of Neurological Sciences, Bellaria Hospital, Bologna, Italy

References
Is there any relationship between estrogen receptor/progesterone receptor status and recurrence of meningioma?

TO THE EDITOR: We read with great interest the article by Hua and colleagues, who have reported the prognostic value of estrogen receptor (ER) expression in a total of 87 patients whose tumors were pathologically diagnosed as WHO grade III meningioma (Hua L, Zhu H, Li J, et al: Prognostic value of estrogen receptor in WHO Grade III meningioma: a long-term follow-up study from a single institution. J Neurosurg [pub ahead of print August 18, 2017. DOI: 10.3171/2017.2.JNS162566]). The authors concluded that patients treated for recurrent meningioma had worse progression-free survival than those treated for primary disease (p = 0.001) and that ER expression (p = 0.008) was an independent prognostic factor for progression-free survival of patients with WHO grade III meningioma. We commend the authors for performing such an interesting study. We noticed, however, that they did not analyze cases in which tumors demonstrated both ER/PR status and recurrence of meningioma.

A few studies have explored the relationship between ER/PR status and recurrence of meningioma and have demonstrated a relationship between ER/PR status and meningioma recurrence. If such a relationship exists, which ER/PR status can predict recurrence?

The authors report no conflict of interest.
I meningioma—one group made up of patients who experienced recurrence and the other made up of patients who had no recurrence. The authors found that PR negativity was strongly associated with meningioma recurrence (p < 0.0001). Such an association has also been found by others. Fewings et al. noted that PR-positive meningiomas were less likely to recur than PR-negative ones (p = 0.013) and proposed that PR negativity is associated with recurrence of meningiomas. Furthermore, Konstantinidou and colleagues found that ER expression was lost or reduced in atypical meningiomas and loss of PR expression was an indicator of early recurrence. In contrast, Rubinstein et al. observed that PR concentrations were significantly higher in recurrent meningiomas than in initially excised meningiomas.

However, some studies have shown that ER-positive/PR-positive status was not associated with recurrence of meningioma. Guevara et al. evaluated 42 patients with meningioma and compared the groups with and without disease recurrence after a 10-year follow-up period, demonstrating that tissue expression of ERs and PRs was not associated with tumor recurrence. Additionally, Abdelzaher et al. analyzed a total of 60 cases of meningioma and investigated several immunohistochemical variables, including ER and PR expression. They found that neither ER expression nor PR expression was an independent predictor of tumor recurrence on multivariate analysis (p > 0.05), which is consistent with the findings of Guevara et al. In comparing patients with and without recurrence of grade I meningioma, Mairi et al. found that PR status had a strong predictive value but ER status was not relevant.

In conclusion, the associations of PR/ER status and recurrence are complicated and controversial in meningioma, and further studies are warranted.

Fujun Liu, MD
Wei Chen, MD
Jing Chen, MD, PhD
West China Hospital, West China Medical School, Sichuan University, Chengdu, Sichuan, People’s Republic of China

References

Disclosures
The authors report no conflict of interest.

Response
On behalf of all the authors who contributed to our published study, we would like to thank Dr. Liu and his colleagues for their comments and would also like to take the opportunity to respond.

In our series, only 4 tumors (4.60%) were both ER and PR positive. We then combined ER and PR expression of positive and weak positive into one group, and the proportion increased to 10.34%, with 9 tumors being both ER and PR positive (Table 1), which was significantly lower than the proportions reported by Dr. Pravdenkova and colleagues. This result is possibly due to the low positive–PR immunostaining rate in WHO grade III meningiomas. In the study by Pravdenkova et al., 162 (98.2%) of the patients had lower-grade meningioma, whereas grade III meningioma only accounted for 1.8% of cases.

We further classified our 87 meningioma patients into 4 groups according to the ER/PR status of their tumors, namely ER+/PR+, ER+/PR−, ER−/PR+, and ER−/PR−. Through log-rank survival analysis, we found that there was a statistically significant difference in the overall survival (OS) of patients in the 4 groups (p = 0.005). Patients in the ER+/PR− group had the worst outcome with respect to OS. However, no significant difference was observed with respect to progression-free survival (PFS) (p = 0.174, Fig. 1). Cox proportional hazard analysis revealed that ER/PR status was not an independent factor for either OS (p = 0.135) or PFS (p = 0.213).

Our results further indicated that ER/PR status was not associated with tumor recurrence and was not an independent prognostic factor for either OS or PFS, which was similar to the findings reported by Guevara et al. However, ER/PR status was a prognos-

| TABLE 1. ER and PR expression in 87 WHO grade III meningiomas |
|-----------------|---------|---------|
|                 | PR Positive | PR Negative |
| ER positive     | 9        | 45       |
| ER negative     | 4        | 29       |
tic factor for OS. In our series, OS was worse in the ER+/ PR− group than in the other 3 groups.

Our study only included patients with WHO grade III meningioma. As we indicated, ER was an independent predictive factor for both OS and PFS, while PR did not show similar effects. When combining ER and PR expression together for analysis, we found that ER/PR status was associated with OS but not PFS, and ER/PR status was not an independent prognostic factor in grade III meningioma. The relationship between ER/PR status and prognosis in lower-grade meningioma is still controversial.

We thank Dr. Liu and his colleagues for their considered suggestions, as they highlight the need for further retrospective studies in the field of meningioma and ER/PR status. Studies with larger cohorts and longer follow-up are warranted.

Lingyang Hua, MD
Hongda Zhu, MD
Qing Xie, MD
Ye Gong, MD
Huashan Hospital, Shanghai Medical College, Fudan University, Shanghai, China

References

Direct versus indirect bypass for adult ischemic-type moyamoya disease

TO THE EDITOR: We read with interest the article by Deng et al.2 (Deng X, Gao F, Zhang D, et al: Direct versus indirect bypasses for adult ischemic-type moyamoya disease: a propensity score–matched analysis. *J Neurosurg* [epub ahead of print August 11, 2017. DOI: 10.3171/2017.2.JNS162405]) demonstrating that direct bypass (DB) is better than indirect bypass (IB) in preventing recurrent ischemic strokes in adults with ischemic-type moyamoya disease. A common shortcoming of some studies on moyamoya disease is the heterogeneity of the patient population (adult vs pediatric, ischemic-type vs hemorrhagic-type moyamoya disease). The authors should be commended for using a propensity score–matched analysis to create homogeneous groups of adult patients with ischemic-type moyamoya disease undergoing DB compared with IB surgery.

This study corroborates the findings of other studies that have demonstrated the superiority of DB over IB in adult patients with ischemic- or hemorrhagic-type moyamoya disease.3,5 Our group published a meta-analysis that demonstrated the superiority of DB over IB in preventing long-term hemorrhage (defined as any intracranial hemorrhage occurring after 30 days of revascularization) in adults with moyamoya disease. Furthermore, our pooled analyses showed that DB is significantly better than IB in preventing long-term ischemia.6

We are curious about the modality of follow-up imaging performed in surgically treated adult moyamoya patients in this study. PET studies in untreated moyamoya patients have demonstrated increased blood flow to the basal ganglia when compared with the middle cerebral artery (MCA) territories. Following DB, PET studies show a transition of blood flow from the basal ganglia to the MCA cortical areas.4 Similarly, follow-up digital subtraction angiography (DSA) studies show more robust angiogenesis in MCA territories and greater regression of moyamoya

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**FIG. 1.** Kaplan-Meier survival curves for PFS (**A**) and OS (**B**) by ER/PR status.
vessels in DB than in IB cases. PET and DSA studies confirm visual confirmation on clinical studies with data showing the superiority of DB over IB in adults with moyamoya disease. Additionally, imaging studies confirm the obvious fact that DB actively addresses the pathology of cerebral perfusion in patients with moyamoya disease, whereas IB works passively through the process of secondary angiogenesis.

Finally, we are curious to know how many surgeons operated on the patients included in the study. The choice of DB vs IB is often surgeon dependent. The variations in surgical technique may add unintended biases to the study. To create a propensity-matched cohort of direct and indirect bypass cases, more patients from the DB group were dropped than from the IB group (before propensity matching: DB, n = 143 patients; IB, n = 77 patients; after propensity matching: n = 70 patients in each group). This asymmetry in patient selection resulting from propensity matching could potentially lead to an underreporting of immediate and long-term complications in the DB group.

Rimal H. Dossani, MD
Hal Sun, MD, PhD
Louisiana State University Health Sciences Center, Shreveport, LA

References

Disclosures
The authors report no conflict of interest.

Response
We would like to thank Drs. Dossani and Sun for the interesting discussion regarding our article, and we greatly appreciate the opportunity to respond to their comments. The authors agree with us on the point that DB is better than IB in preventing recurrent ischemic strokes in adult ischemic-type moyamoya disease (MMD), and they agree that propensity score–matched analysis is a useful method to create homogeneous groups of patients undergoing DB compared with IB surgery.

In fact, although many studies support the superiority of DB over IB, there are also studies with different conclusions. We think that the superiority of one method over the other remains a matter of debate. As we stated in our paper, this controversy might be caused by the heterogeneity of the patient population. The key problem is a lack of any randomized controlled trials (RCTs). For several reasons, RCTs comparing the effects of different surgical modalities for MMD are not easy to conduct. Although we have used propensity score matching to counter the effects of heterogeneity and to reduce the influences of non-randomization, the study was still not an RCT, and this method has its own limitations. For example, as pointed out by Drs. Dossani and Sun, more patients from the DB group were dropped than from the IB group in our study, which may affect the conclusion. Therefore, well-designed multicenter RCTs are needed to compare the effects of different surgical modalities.

As to the modality of follow-up imaging in our institute, we do not use PET as a routine imaging tool. Rather, as a routine examination to evaluate brain perfusion, we employ CT perfusion (CTP) for its feasibility and accuracy, and in our study it was performed preoperatively, 3–7 days postoperatively, and during the follow-up period. We found that DB could improve brain perfusion within several days of surgery, even leading to hyperperfusion in some patients. IB, on the other hand, rarely had this immediate effect. We used DSA, MR angiography (MRA), or CT angiography (CTA) to evaluate the patency of the anastomosed artery and the extent of angiogenesis after surgery. For the majority of adult patients, DB can result in better angiogenesis than IB. For pediatric patients, it should be noted, IB can also lead to a very good result. However, IB may take several months to produce angiogenesis. In addition, we are also in favor of a combined bypass, which may have the advantages of both the direct and indirect procedures.

All the MMD patients in our study were from Stroke Center Ward 3, Department of Neurosurgery, Beijing Tiantan Hospital. The majority of the operations were performed by 3 senior surgeons (Drs. Dong Zhang, Rong Wang, and Yan Zhang). We admit variations in surgical techniques may have effects on clinical outcome. The different surgeons should be considered as a factor in propensity score matching, and then its potential bias could be excluded.

Currently supported by the National Science and Technology funding (“13th Five-Year Plan,” 2015BAI09B04), we are now performing a prospective multicenter study in China to compare the effects of different surgical modalities. This project is led by Beijing Tiantan Hospital, and a total of 24 institutes take part in it. Although it is still a nonrandomized study, we hope it will offer more convincing evidence.
The authors also mentioned that with ET sacrifice, the available maximum resection volume in the petroclival region via an endoscopic transnasal approach (EEA) was 1.5 cm³; however, they lacked a clinical correlation. Therefore, it is difficult to ascertain the clinical application for this data. It is very common to encounter tumors that cause bone destruction as well as compression and displacement of the surrounding soft tissues. During tumor resection, the space created by the tumor and subsequently its removal serves as the working corridor. By following the tumor pathways, the surgeon can resect a large volume of tumor. Therefore, in a cadaveric study, it is impossible to determine the maximum resection volume.

Finally, the authors mentioned that the resection of the cartilaginous ET and mobilization of the paraclival ICA expands a deep window “6 times.” It would be useful if the authors could clarify which primary measurement was used for the comparison (i.e., “6 times” the size of what corridor?).

We would like to congratulate the authors for a great study and echo their statement that tumors in the petroclival area are a challenge regardless of the chosen approach. These types of studies are important to identify safe and effective alternative approaches to the petroclival region.

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Disclosures
Dr. Carrau is a consultant for Medtronic Corp. Dr. Prevedello is a consultant for Medtronic, Stryker, and Codman. He also receives an honorarium from Leica Microsystems, royalties from KLS-Martin, and laboratory and fellowship support from Storz.

Response
We thank Dr. Muto and colleagues for their critique of our recently published article, “Expanding the endoscopic transnasal corridor to the petroclival region: anatomical study and volumetric comparative analysis.” In this day and age, limiting the surgical steps to strict necessity
is a fundamental concept. Necessity can be dictated by local anatomy, pathology, and the goals of treatment. Endoscopic techniques for surgery in the skull base now share the stage with well-established microsurgical strategies as a safe and less invasive route to select complex pathologies; however, the endoscopic experience is still growing, and the more anatomical facts we learn the more we excel in our enterprise.

The expansive maneuvers that added to the complexity of the transpterygoid approaches to the lateral skull base and their contribution to the creation of a surgical window to the petroclival and cerebellopontine angle (CPA) region are individually evaluated in our study. The lateral expansion of that window to the anterior CPA was analyzed as a volumetric comparison of petrous apex bone removal via the EEA before and after 2 maneuvers: 1) removal of the ET; and 2) mobilization of the paracaval ICA. Resection volumes went from 0.21 cm³ before the maneuvers to 1.3 cm³ afterward; i.e., 6 times larger. Muto et al. point out that the petrous apex can be reached endoscopically without ET sacrifice by using angled drills, as demonstrated in their recent cadaveric work comparing the anterior petrosectomy with the EEA to the petrous apex.1

Although we agree with the authors on the angled transclival approach option as a less invasive alternative to the more direct transpterygoid approach, one has to be aware of the risks and limitations there, in the absence of a soft extradural tumor such as chordoma or chondrosarcoma that leads the way to the petrous apex without much drilling and is easily resected with angled suction tips. That is, endoscopic drilling around the lacerum and petrous ICA is not without risks of vascular injury, which remains underreported beyond podium presentations. Our concern with angled drilling is the possibly higher risk of vascular injury—an issue that should be objectively ruled out. In the coronal plane, posterior and lateral to the paracaval and petrous ICA, the angled view does not grant surgical freedom with instrumentation and bimanual dissection in the CPA; this is an overcrowded region with critical neurovascular structures where functional preservation of cranial nerves is a challenge regardless of the surgical approach.

Therefore, we believe in the benefits offered by improved direct visualization and the use of slightly curved high-speed drills and straight surgical instruments in a wider surgical corridor.

Jacob Freeman, MD
A. Samy Youssef, MD, PhD
University of Colorado, Aurora, CO

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Prior ablative procedure: a prognostic factor for poor outcome of microvascular decompression?

TO THE EDITOR: We read with great interest the article published by Theodros and colleagues (Theodros D, Goodwin CR, Bender MT, et al: Efficacy of primary microvascular decompression versus subsequent microvascular decompression for trigeminal neuralgia. J Neurosurg 126:1691–1697, May 2017). The authors present a study comparing microvascular decompression (MVD) in 175 patients with trigeminal neuralgia (TN) who experienced failed ablative procedures with 306 patients who underwent MVD as their first surgical intervention. The authors concluded that patients who underwent other procedures prior to MVD had less pain relief and a higher incidence of facial numbness. This article has discussed an important issue: effects of prior ablative procedures on the efficacy of MVD in patients with TN.

Based on the hypothesis that vascular compression of the trigeminal nerve plays a major role in the etiology of TN, MVD is considered the gold standard surgical procedure for this disease, with a high rate of long-term success.2 Nevertheless, MVD is an invasive procedure and is not always accomplished without certain risks. Although MVD can often be performed safely, the risk of devastating complications is much greater than with less invasive procedures. Therefore, minimally invasive procedures, such as stereotactic radiosurgery, percutaneous procedures, and peripheral procedures, provide attractive alternatives for patients who are unwilling to accept the underlying risk of MVD, especially as an initial procedure. Nonetheless, the long-term results of these ablative procedures are usually disappointing, with reported success rates of 40%–50%.3 If ablative procedures fail, patients usually elect to undergo MVD. However, whether MVD is less effective or more dangerous in patients with prior ablative procedures is still controversial.

Similar to the findings of Theodros et al., another study by Barba and Alksne in 1984 with a limited sample size reported that patients undergoing MVD as a primary procedure were cured at a rate of 91% versus 43% in patients treated with destructive procedures prior to MVD, and Barba and Alksne concluded that prior destructive surgery was a prognostic factor for poor outcome in patients undergoing MVD.4 However, most studies have demonstrated that MVD can still be performed without reduced efficacy in patients with prior ablative procedures.5 We also found that the success rate of MVD in patients with prior Gamma Knife surgery (GKS) was similar to those with no history of GKS in our department.6 Furthermore, large prognostic studies had indicated that there was no relationship between prior ablative procedures and the effectiveness of pain relief after MVD.2 In our previous prospective cohort study evaluating the possible prognostic factors of long-term excellent outcome of MVD surgery by multivariate logistic regression analysis, we found that ablative procedures before MVD did not show any significant effect on long-term pain relief.7 Therefore, the prognostic value of prior ablative procedures remains contro-
versial. Notably, there is consensus among most scholars that a higher risk of facial numbness is present with MVD following ablative procedures than with MVD alone. We also found that the risk of facial numbness after MVD in patients with prior GKS was significantly higher than the risk in patients without GKS in our previous study.4 And we suspect that the trigeminal nerve is more susceptible to damage from surgical manipulation during MVD after prior ablative procedures. Hence, patients with prior ablative procedures should likely be advised of an increased risk of numbness following MVD.

In this study, there are many confounding factors that are probably related to differences in outcomes. First, there were significant differences between the two groups in mean age at surgery (49.98 ± 12.17 vs 55.22 ± 13.36 years) and TN symptom duration (4.448 ± 4.303 vs 7.224 ± 5.491 years). However, previous studies have clearly demonstrated that duration of symptoms is a reliable predictor of outcome, and a longer duration of TN symptoms tends to result in worse outcome.5 Furthermore, the authors did not give detailed information about other factors, such as nature of the pain, preoperative neuroimaging features, and types of vascular compression, which may also influence outcomes.

In summary, prospective studies are needed to assess the role of prior ablative procedures as a potential prognostic factor for poor outcome of MVD. Additionally, further studies investigating whether the type and number of prior ablative procedures affect the efficacy of MVD are also important.

Jian Cheng, MD
Ding Lei, MD
Heng Zhang, MD, PhD
West China Hospital, Sichuan University, Sichuan, China

References

Disclosures
The authors report no conflict of interest.

Response
The authors appreciate the insightful letter put forth by Cheng and colleagues. The efficacy of MVD for the treatment of TN is an area of active research. Of particular interest is the role of prior ablative therapies for the treatment of TN and how they may ultimately influence patient outcomes following MVD. The vascular compression hypothesis provides a rationale for MVD, which is considered the gold standard surgical procedure.1 Despite the high rates of long-term success and low complication rates, some patients are averse to the idea of open surgery and the associated risks.2–5 Thus, we sought to investigate the effect prior ablative therapies may have on the outcome of patients undergoing MVD at a single institution.

As noted, there are limitations to the study put forth, as well as limitations inherent to retrospective studies. Indeed, notable differences between the patient populations as noted by Cheng and colleagues could explain differences observed in the present study. The additional variables mentioned also may play a role in influencing outcomes. Furthermore, other unappreciated confounders may explain the differences in outcomes. Lastly, we agree that future prospective studies will elucidate the roles that prior therapies, and other variables, may play in affecting patient outcomes following MVD.2

Thus, we conclude, and are in agreement with Cheng et al., that future prospective studies will help provide clarity to an active area of research.

Debebe Theodros, BS
Michael Lim, MD
Johns Hopkins Hospital, Baltimore, MD

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Intraoperative aneurysm rupture during awake clipping of cerebral aneurysms

TO THE EDITOR: I read with avid interest the article by Abdulrauf et al.1 (Abdulrauf SI, Vuong P, Patel R, et al: “Awake” clipping of cerebral aneurysms: report of initial series. J Neurosurg 127:311–318, August 2017). The authors reveal the potential advantages of the awake aneurysm surgery for detecting those cases in which neurological deterioration develops during temporary clipping and in which a concomitant neurophysiological change is not found. The technique may have the potential to decrease the risk of ischemic injury. However, I have some concerns.

First, the important complication of intraoperative aneurysm rupture (IAR) needs to be addressed. Inadequate anesthesia is a risk factor for IAR as it may lead to perioperative hypertensive episodes during positioning of the patient, skull pin fixation, local anesthetic infiltration, skin incision, periosteal dissection, and dural opening. Such an event may lead to sudden fluctuations in transmural pressure gradient, making the patient more vulnerable to IAR.2

Moreover, in the setting of IAR, reducing the intracranial pressure by a short period of moderate to severe hyperventilation may be a reasonable rescue measure,3 but establishing a definitive airway during the surgical procedure may become challenging.

Second, because this was a retrospective study, one would be interested to know the details of the surgical technique that the authors employed for the awake clipping in different patients since the craniotomy areas and exposure vary between various craniotomies, namely supraorbital and pterional keyhole approaches4 or supraorbital keyhole and standard pterional approaches.5

Nitish Agarwal, MBBS
All India Institute of Medical Sciences, New Delhi, India

References

Disclosures
The author reports no conflict of interest.

Response
We would like to thank Dr. Agarwal for his interest in our study, and we would like to respond to the specific questions as follows.

First, the risk of IAR is clearly of significant concern during aneurysm clipping, whether the procedure is performed with general endotracheal anesthesia (GET) or conscious sedation (CS). Our series was composed of patients with unruptured intracranial aneurysms (UIAs), and we have not advocated the use of CS for ruptured aneurysms. The latter is mainly due to the fact that the benefit of the procedure under CS is based on full patient cooperation with awake testing, which would not be possible in cases of ruptured aneurysms. Regarding the risk of rupture, in our experience, which now totals over 100 cases in which UIAs were clipped in patients under CS, we have not found a higher risk of IAR. We had 2 cases in which an IAR occurred, and both cases were managed as if the surgery were performed with the patients under GET, but neither patient required GET during or after the procedure. In the personal opinion of the senior author (S.I.A.), the risk of IAR may be lower in the CS cases than in GET cases as there is less risk of significant blood pressure variations under CS. Regarding the use of hyperventilation, which clearly is not possible under CS, we do not use this categorically for any of our UIA clipping cases, and we did not use it even prior to the CS cases when we used to perform this procedure under GET.

Second, this series, UIA clipping under CS, was actually a prospective one. In the article, we used our historical retrospective data pertaining to UIA clipping in patients under GET to create a cohort for comparison with our prospective group of patients who underwent clipping while under CS. We are routinely performing the following various skull base craniotomies: cranio-orbitozygomatic, supraorbital and pterional keyhole approaches, supraorbital keyhole and standard pterional approaches.

Saleem I. Abdulrauf, MD
Jorge F. Urquiaga, MD
Maheen Q. Khan, MD
Saint Louis University, St. Louis, MO

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