Neurosurgical forum


Response: I appreciate the concerns raised by Nandi and colleagues regarding our findings on the PPN in the context of PD. There is a great deal of controversy regarding the role of the PPN.

I offer our sincere apologies for the incorrect spelling of GP as GPi, which occurred during proofreading. Hypoactivity of the GP is connected to the STN in a rat model of PD. We apologize for the potential misinterpretation of my explanation regarding the role of the GABAergic output from the GPi and the SNr. The following correction (corrected spelling in bold type) has been made for the manuscript.

Namely, this result supports the hypothesis that excitatory glutamatergic projection from the STN affects the PPN neurons more than the inhibitory GABA-ergic projection from the endopontine region and the SNr. Alternatively, the hyperactivity of the STN in the parkinsonian state may not be solely due to hypointersynaptic activity of the GPi, but may be at least partially the result of hyperactivity of excitatory inputs originating either in the PPN or in a number of other putative afferents to the PPN. It has been proposed that these inputs might come from areas within the limbic system and the ascending reticular activation system as well as from the premotor and supplementary motor cortical areas, the SNpc and the caudate nucleus, putamen, superior colliculus, basal forebrain, and deep cerebellar nuclei.

In our paper did not differentiate between the distinct morphological parts of the PPN, namely the pars compacta and the pars dissipatus. In addition, although the paper made particular reference to single-cell recording studies, it did not discriminate between the known individual cell types of the PPN, namely the cholinergic, glutamatergic, dopaminergic, or adrenergic neurons. This paper was only concerned with the localization of a structure by using the histological location of the electrode tip after the iontophoresis of pontamine sky blue from the recording electrode (−18 μA for 20 minutes). Finally, as was mentioned, Crossman, et al., reported a marked increase in the synaptic terminal activity in the PPN of MPTP-exposed monkeys in their 2-DG studies. This is consistent with the marked increase in the descending GABAergic inhibition from the GPi and SNr.

Jin Woo Chang, M.D., Ph.D.
Yonsei University College of Medicine
Seoul, Korea

References


Angiography and Aneurysms

To The Editor: There are few doubts that four-vessel cerebral angiography is the most reliable diagnostic tool for vascular malformations in the brain. In their interesting retrospective study (Topcuoglu MA, Ogilvy CS, Carter BS, et al: Subarachnoid hemorrhage without evident cause on initial angiography studies: diagnostic yield of subsequent angiography and other neuroimaging tests. J Neurosurg 98:1235–1240, June, 2003) the authors demonstrated that this statement is true also for repeated angiography in patients with subarachnoid hemorrhage (SAH) and no vascular malformations revealed on the initial angiography study.

Abstract

Object. The aim of this study was to assess the diagnostic yield of imaging tests performed in patients in whom the cause of subarachnoid hemorrhage (SAH) had not been demonstrated on initial angiography.

Methods. By reviewing medical records of 806 patients with SAH who had been admitted during a 6.5-year period, the authors identified 86 in whom initial transfemoral catheter angiography failed to reveal the cause of SAH. Clinical and radiological data were analyzed to determine the diagnostic yield of subsequent catheter angiography, computerized tomography (CT) angiography, magnetic resonance (MR) angiography, and MR imaging of the brain and spine for various subtypes of SAH (bleeding not visualized on CT studies [CT-negative SAH], perimesencephalic SAH, and nonperimesencephalic SAH).

Of 41 patients with nonperimesencephalic SAH, 36, 32, and 21 underwent repeated catheter angiography, CT angiography, and MR angiography, respectively; brain MR imaging was performed in 23 patients (18 with Gd and 15 with susceptibility contrast sequences), and spine MR imaging in 17. Of 36 patients with perimesencephalic SAH, 31, 23, and 17 underwent repeated catheter angiography, CT angiography, and MR imaging of the brain and spine for various subtypes of SAH (bleeding not visualized on CT studies [CT-negative SAH], perimesencephalic SAH, and nonperimesencephalic SAH).

Of nine patients with perimesencephalic SAH, 7, 3, and 2 underwent repeated catheter angiography, CT angiography, and MR angiography, respectively; brain MR imaging was performed in eight patients (five with Gd and three with susceptibility contrast sequences), and spine MR imaging in seven. The cause of SAH could be determined in only four patients, all with nonperimesencephalic
SAH. The only test that yielded a diagnosis was catheter angiography (three aneurysms on the second and one on the third angiography, all surgically secured). Diffusion-weighted MR imaging demonstrated small, deep infarcts in five patients.

Conclusions. Repeated catheter angiography remains the most sensitive test to determine the cause of SAH that is not demonstrated on initial angiography, particularly in the subtype of nonperimesencephalic SAH. Newer, noninvasive imaging techniques provide little diagnostic yield.

In particular, surrogate investigations of CT scans, MR images, CT angiography, and MR angiography failed to reveal any vascular malformation not diagnosed on the first angiography. Reasons for negative first examinations included nonaneurysmal, perimesencephalic bleedings and unspecified reasons in the remaining patients. Reasons for positive second examinations were not analyzed by Topcuoglu and coworkers and probably mainly included temporarily thrombosed aneurysms.

From among the unavoidable biases due to the retrospective nature of the study, the timing of subsequent diagnostic tests may definitely influence the results. The second angiography was performed later than CT and MR angiography studies (11, 12, and 11 days; 1, 4, and 3 days; and 3, 6, and 23 days) in patients with CT-negative, perimesencephalic, and nonperimesencephalic SAH, respectively. The temporal dispersion of MR angiography in patients with nonperimesencephalic SAH (1–193 days) does not permit comparison with other groups, thus allowing considerably more time for temporarily thrombosed aneurysms to recanalize. Direct comparison between these different techniques remains difficult.

On the other hand, CT and MR angiography studies can be quickly performed, require skilled operators, but they are probably easier techniques than conventional cerebral angiography and are virtually free of risk and discomfort in the patients. Therefore, from a diagnostic point of view, a different scenario is possible. As a general rule, less sensitive but less invasive investigations should be performed as a first screening test and, if these are nondiagnostic or not detailed enough to indicate subsequent treatment, more sensitive and more invasive tests such as cerebral angiography are recommended. Once the most sensitive test yields negative results, it seems pointless to perform the less sensitive ones. As correctly stated by the authors, this does not mean that CT and MR studies are not useful in patients with SAH and negative angiograms; on the contrary, they may be extremely useful in studying brain parenchyma, which is the main target of tomographic investigations and invisible on cerebral angiography.

References


This paper confirms that repeated catheter angiography is the most sensitive test to determine the cause of SAH not demonstrated on initial angiography. Its value in the authors’ opinion is unquestionably greater than CT and MR angiography, neither of which alone can detect the cause of SAH.

Indeed, repeated catheter angiography is the final examination to be performed to exclude aneurysm as the cause of SAH. On the other hand, waiting 5 to 10 days (or longer) for a second examination is potentially dangerous because of the risk of repeated hemorrhage. Even worse, the risk of another hemorrhage is highest during this period. Therefore a less invasive imaging technique, such as three-dimension-al (3D) CT angiography, performed 2 to 3 days after SAH is a very valuable supplement following the first negative angiography.

In our experience, with 3D spiral CT angiography during the last 6 months, two aneurysms were recognized in two of seven patients after a first negative catheter angiography. Furthermore, in one case, CT angiography demonstrated a small bulge (diameter <2 mm, an aneurysm “in statu nascendi”) on the wall of the internal carotid artery, which had been invisible on catheter angiography.

In the other two cases CT angiography revealed multiple cerebral aneurysms, whereas only single aneurysms were visible on catheter angiography. In one of these, the aneurysm invisible on catheter angiography (located on the posteroinferior cerebellar artery) was the source of bleeding.

In the series by Topcuoglu, et al., repeated angiography was performed a mean of 11 ± 4 days after hemorrhage. In our department it is typically performed between 5 and 10 days after SAH in hopes that the clot resorption will demonstrate the aneurysm. Our experience indicates that CT angiography can show changes invisible on angiography as early as 2 to 3 days after SAH.

Less invasiveness and lower costs in comparison with catheter angiography as well as earlier diagnosis and treatment of ruptured aneurysms determine the importance of CT angiography in diagnosing the causes of SAH after a negative first angiography. Additionally, the usefulness of CT angiography increases in cases when the location of the revealed aneurysm is inappropriate to the distribution of blood on the initial CT scan and when the catheter angiography image is unclear.

On the contrary, in our experience, MR imaging is less useful than catheter angiography in determining the presence of aneurysms, but MR imaging with Gd in cases of nonperimesencephalic SAH seems to be essential for the exclusion of other causes of hemorrhage, such as tumors and angiographically occult aneurysms.

References
1. Hashimoto H, Iida JI, Hironaka Y: Use of spiral computerized to-


The recent advance of 3D CT angiography has allowed us precisely to diagnose cerebral aneurysms.1,5,7–10 The diagnostic accuracy of 3D CT angiography has been reported to be equal or superior to that of catheter angiography including digital subtraction (DS) angiography.5,6 Especially in surgical cases of cerebral aneurysms, 3D CT angiography provides useful and practical information for surgery. In some institutions, ruptured aneurysm surgery has been performed on the basis of 3D CT angiography findings alone.5,7

In our study of 60 patients with ruptured aneurysms evaluated prospectively both with 3D CT angiography and catheter angiography, we detected all the ruptured aneurysms with 3D CT angiography that we did with catheter angiography and demonstrated a 100% diagnostic accuracy on ruptured aneurysms. In the diagnosis of associated unruptured aneurysms, 3D CT angiography allowed us to visualize a 0.8-mm aneurysm of the anterior communicating artery, which was confirmed during the operation but catheter angiography had failed to demonstrate.6 Hashimoto, et al.,1 reported on six small (2–3 mm) ruptured aneurysms that were not revealed on DS angiography but were on 3D CT angiography.1 There have been several reports that 3D CT angiography detected aneurysms that catheter angiography did not.5,6,8,10 Furthermore, Villablanca, et al.,4 evaluated the diagnostic accuracy of 3D CT angiography in identifying 41 very small cerebral aneurysms (< 4 mm in diameter) and reported that the sensitivities of 3D CT angiography and DS angiography were from 98 to 100%, and 95%, respectively, and the specificity of 3D CT angiography and DS angiography was 100% in both. The 41 very small aneurysms consisted of 33 aneurysms that were 4 mm in maximal diameter, 13 aneurysms that were 3 mm, and 4 aneurysms that were 2 mm. The smallest aneurysm was 1.9 mm in diameter. A number of articles have proven that 3D CT angiography has a high and excellent diagnostic accuracy for small aneurysms. The authors reported, however, that repeated catheter angiography visualized four aneurysms that could not be detected on 3D CT angiography. The size of the aneurysms was 3 mm in two aneurysms, 2 mm in one, and 1 mm in one. According to previous reports, including ours,1,5,8,9 we believe that 3D CT angiography can consistently demonstrate aneurysms that are 2 mm in size.

The usefulness of 3D CT angiography for detecting aneurysms depends on technical differences. First, the high detectability of 3D CT angiography requires at least the following parameters: 1-mm slice thickness, 1-mm/second table speed, and 0.5-mm reconstruction pitch.5,8,9 The authors did not indicate the parameters for helical scanning. Second, neurosurgeons and radiologists who have extensive experience with 3D CT angiography also might improve the diagnostic accuracy. With greater experience and practice, the diagnostic sensitivity for smaller aneurysms can be improved. Third, the images we use are important. We have used the 3D images of the basic 11 projected 3D CT angiographies to avoid missing possible aneurysms sites, making it possible to check the artery from all directions.3 In the suspected aneurysm locations, the use of targeted 3D CT angiography facilitates the depiction. Unfortunately, the authors used maximum intensity projection (MIP) images in Fig. 2. An MIP image is basically a two-dimensional image that does not provide high detectability of small aneurysms. A small aneurysm is obscured by overlying its parent and surrounding vessels on the MIP image. The 3D CT angiography images might be able to demonstrate aneurysms that the authors could not diagnose on MIP images. Finally, the repeated angiography and 3D CT angiography studies were performed on different dates. If the 3D CT angiography was performed in a closer time frame to catheter angiography, the aneurysms might have been revealed. The authors conclude that the noninvasive imaging technique of 3D CT angiography provided little diagnostic yield. To address the conclusions, however, the authors should include more precise information.

Our strategy for evaluation of an SAH is that 3D CT angiography should be performed first. When 3D CT angiography does not reveal aneurysms, catheter angiography should then be undertaken to detect nonaneurysm lesions or aneurysms at special sites, such as the skull base. After this, the repeated neuroimaging modality should be 3D CT angiography. If an aneurysm is detected, the surgery can be performed using only 3D CT angiography without catheter angiography. We believe that catheter angiography should be omitted because of procedure-related complications such as rebleeding6 of the ruptured aneurysms or cerebral infarct.7

Finally, we wondered whether the authors performed the operation with 3D CT angiography alone. Do they still believe that catheter angiography is essential in any case? If the authors still need catheter angiography for aneurysm surgery, we believe that the repeated modality should be catheter angiography. If so, the authors must add catheter angiography even if a ruptured aneurysm was detected on 3D CT angiography.

The multidetector row CT scan by which volumetric data with superior resolution in the z axis can be obtained will eventually surpass, and may replace, catheter angiography as the gold standard imaging for cerebral aneurysms.4

MASATO MATSUMOTO, M.D.
KYOUICHI SUZUKI, M.D.
TATSUYA SASAKI, M.D.
NAMIO KODAMA, M.D.
Fukushima Medical University
Fukushima, Japan

References
3. Hsiang JN, Lanyu EY, Lani JMK, et al: The role of computerized tomographic angiography in the diagnosis of intracranial an-
   ment over single slice helical CTA for cerebral aneurysms. Acta 
   puterized tomography angiography-guided surgery of acutely rupt-
6. Takahatake Y, Uno E, Kawamatsu K, et al: [The three-dimension-
   al CT angiography findings of ruptured aneurysms hardly detect-
   able by repeated cerebral angiography.] No Shinkai Geka 28: 
7. Velthuis BK, Van Leeuwen MS, Witkamp TD, et al: Compu-
   terized tomography angiography in patients with subarachnoid 
   hemorrhage: from aneurysm detection to treatment without con-
   terization of very small cerebral aneurysms by using 2D and 3D heli-
   computerized tomography in the detection and characterization of 
   puterized tomographic angiography in detection of cerebral an-
   euryms in acute subarachnoid hemorrhage. Neurosurgery 41: 

To THE EDITOR: We have read with great interest the article published by Topcuoglu, et al. (Topcuoglu MA, Ogilvy 
   CS, Carter BS, et al: Subarachnoid hemorrhage without evident cause on initial angiography studies: diagnostic 
   classify their patients depending on the initial CT scan pattern of bleeding into three subgroups (for example, normal 
   CT scan, perimesencephalic bleeding, and nonperimesencephalic bleeding, as was originally done by Rinkel, et al.,
   and later on by van Calenberg, et al. This CT scan classification seems crucial as it is shown in this paper that patients 
   with either normal CT scans or a perimesencephalic pattern of bleeding into three subgroups (for example, normal 
   CT scan, perimesencephalic bleeding, and nonperimesencephalic pattern of bleeding, died because of rebreeding that 
   occurred before control angiography could be performed. Follow up during a median interval of 5.8 years reveals that 
   no patient has suffered further bleeding; thus, this algorithm seems appropriate to rule out possible lesions responsible 
   for repeated hemorrhage.

In our experience, the pattern of bleeding has also enabled us to separate patients according to the severity of the 
   illness and prognosis. Patients with the nonperimesencephalic pattern showed worse clinical grades at admission 
   and higher frequencies of both Fisher Grades 3 and 4 on initial CT scans in addition to symptomatic ischemia. In 
   addition, they presented with more complications during the hospital stay and needed longer admission times and 
   more frequent CSF shunt placement for symptomatic hydropcephalus.

Final prognosis of idiopathic SAH seems to be good in general, although several reports on prognosis following 
   perimesencephalic idiopathic SAH show that patients continue complaining of headaches and a substantial proportion 
   do not return to their previous jobs because of various neuropsychological problems. Our data show that although pa-
   tients with both normal CT scans and the perimesencephalic pattern of bleeding achieved a good outcome (more than 
   90% with GOS scores of 4 or 5), patients with the nonperimesencephalic pattern fared worse (percentages with GOS 
   scores of 4 and 5 decreasing to 80%) probably because of the more severe clinical status and the higher incidence of 
   systemic complications, cerebral ischemia, and hydrocephalus that occurred in this subgroup.

References
1. Alén JF, Lagares A, Lobato RD, et al: Comparison between peri- 

982 J. Neurosurg. / Volume 100 / May, 2004

Response: We agree with Drs. Bergui and Bradac that a temporarily thrombosed aneurysm might involve one of several factors (such as arterial vasospasm, aneurysm compression by adjacent hematoma, or technical factors) that might have resulted in false-negative initial catheter angiography in our patients, and that differences in the timing of subsequent imaging modalities might have influenced our results. We have discussed both of these issues at length in our article. We reemphasize that all of our patients proved to have tiny aneurysms, which are overwhelmingly missed on CT angiography and MR angiography compared with catheter angiography. Thus, it is unlikely that comparable timing of tests would have changed our results. Finally, although we agree with these authors that tests with lower sensitivity such as CT and MR angiography should be performed prior to catheter angiography for initial diagnostic evaluation, (mainly because of their lower risk profile), the results of our large study do not support the use of CT or MR angiography as subsequent diagnostic tests in cases in which a technically adequate initial catheter angiographic study is negative and factors such as vasospasm are absent.

We thank Lagares, et al., for their thoughtful comments concerning the treatment of patients with SAH without evident cause on initial catheter angiography. As in our study, these authors classified such patients into three groups based on CT scan findings and found that patients with nonperimesencephalic SAH are more likely to harbor aneurysms, have more severe clinical and radiological features on admission, and have worse long-term outcomes than patients with either perimesencephalic SAH or SAH and normal CT scans. Our combined experiences reaffirm the results of several previous studies that have demonstrated the use of this classification system in clinical decision-making and in assessing the prognosis of SAH in patients with negative initial catheter angiography. Lagares, et al., provide additional data showing higher rebleeding rates in patients with nonperimesencephalic SAH, which further emphasizes our stance that catheter angiography must be repeated particularly in patients with nonperimesencephalic SAH and nondiagnostic initial angiography. The purpose of our study was to assess the usefulness of subsequent diagnostic tests and not to assess rebleeding rates; therefore, we do not have comparable data on rebleeding rates. Nevertheless, in our study, rebleeding did not occur in any of the four patients with nonperimesencephalic SAH and negative initial catheter angiography who later proved to have aneurysms.

Lagares, et al., outline their approach in evaluating patients with SAH and negative initial catheter angiography. Our approach is similar: in general, angiography is repeated in all patients with nonperimesencephalic SAH and in all patients with SAH in whom the initial angiography is of poor quality, incomplete, or if factors such as vasospasm are present. Angiography is repeated as soon as possible to minimize the risk of rebleeding. In patients with vasospasm, angiography is repeated after serial transcranial Doppler studies show resolution of vasospasm. Given the similarities in our diagnostic approach, it is not surprising that we have similar data concerning the yield of subsequent angiography in patients with SAH and negative initial evaluations.

Kunert and colleagues share their positive experience with CT angiography and suggest using CT angiography as the preferred subsequent diagnostic test in patients with SAH and negative initial catheter angiography. They fail to state whether the catheter angiography study in their patients was technically adequate, and they do not indicate the size of the aneurysms detected on CT angiography. We reemphasize that the quality and interpretation of the initial catheter angiography study is extremely important, because a high false-negative rate on initial catheter angiography would increase the yield of any subsequent test. We believe that CT angiography, because it is less invasive, less expensive, and safer than catheter angiography, is justified as the initial diagnostic test in all patients with SAH; as indicated by the results of our larger study, however, it should be the subsequent diagnostic test only in select patients (for example, those with suboptimal initial catheter angiography). Indeed, the interval until the second test carries a small risk of rebleeding. It is debatable, however, whether this justifies earlier testing (5–10 days after SAH onset) as proposed by Kunert, et al. because the risk of vasospasm is highest during this period and it is well known that the diagnostic yield of the test is lower in the presence of vasospasm. Finally, Kunert, et al., state that Gd-enhanced MR imaging might be able to exclude other causes of SAH. We invite them systematically to review their own experience, because Gd-enhanced brain and spine MR imaging failed to reveal the cause of SAH in any patient with typical SAH symptoms in our study.

Matsumoto and colleagues claim that the sensitivity of CT angiography in detecting small (<3 mm) aneurysms is equal to or higher than that of catheter angiography. A systematic review by White, et al. however, shows that the sensitivity of CT angiography is only 61% (95% confidence interval 51–70%), which supports the results of our study in which CT angiography failed to detect small aneurysms that were identified on subsequent catheter angiography. We agree that technical factors and limited experience can account for lower sensitivity of CT angiography; however, the technical aspects of our CT angiography protocol are identical to those described by Matsumoto, et al., and
we believe our center has had extensive experience in performing and interpreting CT angiography in patients with SAH. Matsumoto, et al., question whether closer timing of the repeated catheter angiography and CT angiography might have changed our results. This issue has been discussed in detail in our article and in our response to Bergui and Bradac.

Matsumoto and colleagues describe their diagnostic strategy for evaluating patients with SAH. Although we agree that a positive CT angiography obviates the need for catheter angiography in most cases and that surgery can be performed on the basis of positive CT angiography results, we do not agree that “catheter angiography should be omitted because of procedure-related complications” and replaced by CT angiography alone. The results of our study do not support the use of CT angiography as the sole repeated imaging modality. Finally, Matsumoto and colleagues speculate that newer CT angiography techniques will one day replace catheter angiography as the gold standard in diagnosing the cause of SAH. Technology is advancing at a rapid pace and this might indeed prove true in the near future. At present, however, given the current limitations and capabilities of tests such as CT and MR angiography, we believe the results of our study are valid.

ANEESH B. SINGHAL, M.D.
MEHMET A. TOPCUOGLU, M.D.
CHRISTOPHER S. OGILVY, M.D.
Massachusetts General Hospital
Boston, Massachusetts

Reference