Predictive Value of Angiographic Testing for Tolerance to Therapeutic Occlusion of the Carotid Artery

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BACKGROUND AND PURPOSE: **Controversy exists on how to assess a patient's tolerance before permanent carotid artery occlusion. We sought to determine the positive predictive value of synchronous opacification of hemispheric cortical veins at angiography of the contralateral carotid or vertebral artery as a predictor of tolerance to permanent carotid artery occlusion without development of ischemic injury.**

METHODS: **Seventy-six angiographic test occlusions were performed in 74 consecutive patients considered for therapeutic occlusion. Angiography of collateral cerebral vessels was performed during test occlusion. Synchronous filling (a < 0.5-second delay of opacification between the cortical veins of the occluded and collateral vascular territories) was considered a predictor for tolerance to permanent occlusion. To detect clinically silent ischemic defects, MR imaging was performed before and 6–12 weeks after permanent occlusion. Positive predictive value (95% confidence interval [CI]) of synchronous venous filling for absence of ischemic deficits after permanent occlusion was calculated.**

RESULTS: **No procedural complications of the test occlusion occurred. In 51 of 54 patients who passed the test, permanent occlusion was performed. Two patients, both in poor clinical condition after subarachnoid hemorrhage, died of diffuse vasospasm after permanent occlusion. Of the 49 surviving patients, one developed a transient discrete hemiparesis with small new hypoperfusion infarctions on MR images. All other patients remained neurologically unchanged with no new ischemic lesions on follow-up MR images. Positive predictive value of tolerance to carotid artery occlusion after passing the angiographic test was 98% (95% CI: 89–100%).**

CONCLUSION: **The angiographic test occlusion protocol reliably predicts tolerance to therapeutic carotid artery occlusion. It is safe and easy to perform.**

Endovascular balloon or coil occlusion of the internal carotid artery (ICA) is a simple and effective method to treat carotid artery aneurysms that are not suitable for direct occlusion (1–6). However, not all patients can tolerate abrupt occlusion of the carotid artery, and in these patients acute or delayed ischemic events will occur. Controversy exists on how to assess the patient's tolerance before permanent carotid artery occlusion. Although clinical test occlusion in the awake patient enables prompt detection of acute ischemia, absence of neurologic deficits during test occlusion does not preclude occurrence of delayed ischemia after definite occlusion. To our knowledge, no test protocol has been shown to accurately predict delayed cerebral hypoperfusion ischemia after permanent carotid occlusion (7–16).

The purpose of this study was to determine the positive predictive value of synchronous opacification of hemispheric cortical veins at angiography of the contralateral carotid or vertebral artery as a predictor of tolerance to permanent carotid artery occlusion without development of ischemic injury.

Methods

Patients

Between January 1996 and October 2003, occlusion of the ICA was considered in 74 patients (14 male and 60 female patients; mean age, 54.6 years; median, 54 years; range, 16–78 years). Twenty-five of these patients were included in a previous pilot study (6). Indication for carotid occlusion was determined in a multidisciplinary group consisting of neurologists,

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neurosurgeons, and interventional neuroradiologists (W.J.vR., M.S.). Indications for consideration of carotid occlusion were carotid aneurysm (n = 69), traumatic carotid cavernous fistula ([CCF] n = 2), high-grade petrous ICA stenosis symptomatic by transient ischemic attacks (n = 1), tentorial dural arteriovenous fistula with perimedullary venous drainage (n = 1), and anticipated carotid sacrifice in extensive skull base surgery (n = 1). The 69 carotid aneurysms were less suitable for coiling because of large size, partial thrombosis, wide neck, or fusiform shape and were located as follows: cervical segment (n = 2), petrosal segment (n = 1), cavernous sinus (n = 41), carotid ophthalmic (n = 6), carotid hypophyseal (n = 8), posterior communicating artery (n = 1), supraclinoid carotid artery (n = 9), and intracranial carotid bifurcation (n = 1). Forty-six aneurysms manifested with symptoms of mass effect, 12 with subarachnoid hemorrhage ([SAH] five in the acute phase), four with CCF, and one with epistaxis. Two aneurysms were incidental findings, and two were additional to another symptomatic aneurysm. There was one cervical dissection aneurysm symptomatic by transient ischemic attacks, and one patient had a pulsatile neck mass from a false aneurysm on the cervical carotid artery that developed after a retropharyngeal abscess. In some patients with carotid aneurysms or CCFs, treatment was intended to occlude the aneurysm or fistula, with preservation of the carotid artery. Test occlusion in these patients was performed at the beginning of the attempted treatment. If direct treatment failed, the carotid artery was occluded in those patients who had passed the test.

Patient data were prospectively collected. Within 1 month before test occlusion, all elective patients were investigated with MR imaging, which served as a baseline to detect possible clinically silent ischemic defects. MR imaging consisted of axial T2- and proton density-weighted spin-echo sequences (2337/90, 20 TR/TE) and a coronal T1-weighted spin-echo sequence (563/22 TR/TE). The five patients who were tested in the acute phase of SAH underwent CT before the test occlusion.

Carotid Test Occlusion

A 6F large-lumen guiding catheter was positioned in the ICA intended to be occluded. A second catheter was positioned in the contralateral ICA. A detachable latex balloon (Goldvalve no 16; Nycomed, Paris, France) or a nondetachable silicone balloon (Endeavor or Sentry; Boston Scientific, Freemont, CA) was positioned in the ICA, usually in the C4 segment or just proximal to the aneurysmal neck. The patient received heparin 5000 U, and the ICA was occluded by inflating the balloon. Occlusion of the carotid artery was verified by gentle hand injection of contrast material through the guiding catheter. Awake patients were neurologically monitored. This was done by a neurology resident who asked the patient simple questions and tested the motor function of the extremities at short intervals. The patient was instructed to report any change in sensory function, such as paresthesias. As soon as neurologic symptoms developed, the balloon was deflated and the patient had failed the test occlusion.

After this first global neurologic assessment, anteroposterior angiography was performed, at two frames per second, of the entire skull with injection of 10 ml of contrast material during 1.2 seconds in the contralateral ICA. This was followed by anteroposterior and lateral vertebral angiography if collateral circulation was through the posterior communicating artery. Opacification of the cortical veins in the territory of the occluded carotid artery had to be synchronous (< 0.5 second or one frame delay) with opacification of the cortical veins of the territory of the examined artery. Thus, if collateral filling was mainly through the anterior communicating artery, the venous phase of both cerebral hemispheres had to be synchronous on angiograms of the contralateral carotid artery. If collateral filling was mainly through the posterior communicating artery, the venous phase of the tested cerebral hemisphere had to be synchronous with filling of the cerebellar and temporo-occipital cerebral cortical veins on vertebral angiography. In some patients, collateral flow was through both the anterior and posterior communicating arteries. This generally caused dilution of opacified blood, with nonopacified blood leading to diminished density of the opacification of the veins in the vascular territory of the occluded carotid artery. In these situations, the filling of the veins could not be *symmetrical*, but if the veins filled *synchronously*, the patient was considered as having passed the test. If opacification of the cortical veins was not synchronous, the patient had failed the test occlusion and consequently no permanent carotid occlusion was performed.

In the beginning of our experience, clinical testing was maintained for 20–30 minutes after passing the angiographic test before permanent occlusion. Later on in our experience, permanent carotid artery occlusion was performed immediately after passing the angiographic test, as in all patients under general anesthesia. If the test occlusion was passed, the carotid artery was occluded with a detachable balloon and a second (safety) balloon was detached in the proximal ICA. In two patients with a CCF, the ICA was occluded with coils. In 10 patients, 12 test occlusions were performed with the patient under general anesthesia, and in these patients only angiographic testing could be performed.

After permanent carotid occlusion, the patients were transferred to the intensive care unit where fluid balance, neurologic status, and blood pressure were carefully monitored. Intravenous heparin (2–3 times baseline activated partial thromboplastin time) or subcutaneous heparin at therapeutic dosages was continued for 48 hours. MR imaging was performed before discharge and 6–12 weeks later. MR imaging consisted of axial T2- and proton density–weighted spin-echo sequences (2337/90, 20) and a coronal T1-weighted spin-echo sequence (563/22). Fluid-attenuated inversion-recovery (FLAIR) and diffusion-weighted imaging were not available. The MR images were interpreted and compared with baseline images by two of us in consensus (W.J.vR and M.S.). All patients who survived the initial period were followed up clinically for at least 3 months at the outpatient clinic. Neurologic follow-up examination was performed by either a neurologist or a neurosurgeon, usually the same physician who had referred the patient. Apart from evaluation of the clinical course of the presenting symptoms (mostly ophthalmoplegia or visual disturbances), attention was focused to new signs and symptoms of ischemic deficits that might have been attributed to the occlusion of a carotid artery, such as weakness of the extremities or sensory deficits.

The positive predictive value to carotid artery occlusion after passing the angiographic test was calculated as a proportion, with corresponding 95% confidence interval (CI). Since no permanent carotid occlusion was performed in patients who did not pass the test, the negative predictive value could not be assessed.

Results

Test Occlusions

In the 74 patients, 76 test occlusions were performed. There were no (0%) procedural complications (95% CI: 0–4.7%). One patient had three test occlusions: a 36-year-old woman had a ruptured posterior communicating artery aneurysm that was coiled on the second day after SAH. To treat an additional large wide-necked ophthalmic aneurysm in a later (postvasospasm) stage, angiographic test occlusion with the patient under general anesthesia was performed in the same session that showed synchronous venous filling. However, venous filling was not synchronous due to clinically silent general vasospasm on

the 17th day after SAH when a second test occlusion was performed after failed attempt to treat the large ophthalmic aneurysm by balloon-assisted coiling with the patient under general anesthesia. On day 34 after SAH, in the absence of vasospasm the venous filling was synchronous again on test occlusion after a second failed attempt at balloon-assisted coiling with general anesthesia, and the carotid artery was permanently occluded. The patient did well clinically, and follow-up MR imaging 8 weeks later did not show new ischemic lesions.

No Synchronous Venous Filling

In 20 patients, the ICA was not permanently occluded based on the findings during test occlusion: six patients developed neurologic deficits during test occlusion; in all six, angiographic testing showed nonsynchronous venous filling. Twelve patients passed the test clinically but not angiographically, and two patients did not pass the angiographic test performed with the patient under general anesthesia.

Synchronous Venous Filling

Fifty-four (73%) of the 74 patients had synchronous venous filling during test occlusion. The ICA was permanently occluded in 51 patients. Of these 51 patients, 45 were also observed clinically. Six patients underwent test and definite carotid occlusion under general anesthesia without clinical testing. The ICA was not permanently occluded in three patients who passed the angiographic test. In two of these three patients, both with a CCF, testing was performed with general anesthesia, but the CCFs could be occluded with preservation of the carotid artery. In the other patient, test occlusion was performed in the workup before extensive skull base surgery but the operation was accomplished without having to sacrifice the ICA.

Two patients with permanent carotid occlusion died shortly thereafter. The first patient was an 18-year-old woman with a 30-mm supraclinoid carotid aneurysm that had ruptured twice. At the time of carotid occlusion, she was in poor clinical condition (Hunt and Hess grade V). Six days later, she died of diffuse vasospasm and raised intracranial pressure. The second patient was a 53-year-old woman in poor clinical condition (Hunt and Hess grade V) after rupture of a large supraclinoid carotid aneurysm that was treated by carotid occlusion with the patient under general anesthesia. In the following days, she developed diffuse vasospasm leading to scattered infarctions in both cerebral hemispheres. Because of hydrocephalus, a ventricular shunt was placed. Three months later, she died of meningitis.

All 49 patients who survived the initial episode underwent at least one follow-up MR imaging examination 6–12 weeks after the carotid occlusion. One patient, a 65-year-old man with a ruptured cavernous sinus aneurysm causing CCF, developed a discrete hemiparesis 4 days after carotid occlusion, with small hypoperfusion infarcts in the watershed area of the occluded carotid artery territory on CT and MR images, not present on the baseline MR image, despite synchronous venous filling during test occlusion. His symptoms resolved within 2 weeks. All other patients were neurologically unchanged, and the follow-up MR images did not show new ischemic lesions.

The positive predictive value to uneventful carotid artery occlusion after passing the angiographic test was 98% (48 of 49 patients; 95% CI: 89–100%).

Discussion

In this large consecutive series of patients in whom carotid artery occlusion was considered, 73% had synchronous venous filling at angiography of collateral vessels during test occlusion, and in these patients the risk of ischemic deficits after permanent carotid artery occlusion proved to be very small. Only one patient had a transient mild hemiplegia with new ischemic lesions in the watershed area of the occluded carotid artery on T2-weighted MR images. However, since we did not perform diffusion-weighted or FLAIR imaging, some small, clinically silent ischemic injuries may have gone undetected. The angiographic test occlusion not only proved to be accurate in predicting tolerance to permanent carotid occlusion but also was easy to perform and safe, both in awake patients and in patients under general anesthesia.

The negative predictive value of the angiographic test could not be assessed since no permanent carotid occlusion was performed in patients who did not pass the test. In a review of reports in the English literature on therapeutic abrupt carotid artery occlusion, occlusion in 254 patients without any preoperative stroke risk assessment led to infarctions in 65 patients (26%); 30 (12%) were fatal (5). In 262 patients who had passed a clinical temporary occlusion test, carotid artery occlusion still led to immediate or delayed infarctions in 33 patients (13%); seven (3%) were fatal. Comparisons with the small risk of stroke in our study indicate that angiographic test occlusion enables accurate detection of a high proportion of patients who do not tolerate permanent occlusion.

Carotid artery occlusion in the acute phase of SAH is not recommended, since vasospasm may develop and ischemic events may be aggravated by diminished reserve capacity after occlusion of a carotid artery.

In the last decades, many other protocols have been developed to increase the sensitivity of the clinical test occlusion in an attempt to predict those patients at risk for *delayed* hypoperfusion ischemic deficits. Most of these protocols consist of additional tests that directly or indirectly estimate the effect of the test occlusion on cerebral blood flow: stable xenon-enhanced CT (7, 15), xenon-133 single photon emission CT (SPECT) (8), technetium-99m hexamethyl-propylene-amine oxide SPECT (9), (^{15}O)H_2O positron emission tomography (10), electroencephalography (11), transcranial Doppler ultrasonography (12), perfusion MR imaging (13) and hypotensive challenge (14). Many of these additional tests are cumbersome, complicated to perform, expensive, and not widely available. The main problem in (semi)-

quantitative tests is the definition of a threshold of tolerance, which has a direct consequence for the predictive value of the test. Each method has its advocates, but none, as yet, has been shown to accurately predict delayed cerebral ischemia after permanent carotid occlusion (15). Moreover, most studies have methodological weaknesses (16) or included a limited number of patients.

In our method, the threshold of a 0.5-second delay in opacification of the cortical veins in the compared vascular territories usually is easily appreciated. In doubtful cases, we find it helpful to view the angiograms in both forward and backward cine-loop while enhancing the contrast of the images.

Conclusion

In this series, the angiographic test occlusion protocol described was reliable in predicting the ability of a subject to tolerate carotid occlusion. In our experience, it is easy and safe to perform.

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