HMPAO SPECT to Assess Neurologic Deficits during Balloon Test Occlusion

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The purpose of this study was to determine if one could objectively and preoperatively predict the safety of permanent occlusion of an internal carotid artery with ^{99m}Tc-HMPAO brain SPECT. **Methods:** Twenty-four patients underwent balloon test occlusion of the internal carotid arteries because of neck and skull base tumors. We assessed the uptake of both middle cerebral artery territories before and during balloon test occlusion with ^{99m}Tc-HMPAO brain SPECT using the semiquantitative analysis. The results were compared with other factors, including neurologic examination, arterial stump pressure and electroencephalogram. **Results:** Nineteen patients experienced no neurological deterioration or any problem during balloon test occlusion. The comparative uptake of their middle cerebral artery territories was 95%–101% of the pre-balloon test occlusion state. The remaining five patients showed severe neurologic symptoms, such as transient hemiplegia and unconsciousness. The comparative uptake of their middle cerebral artery territories was 77%–85% of the pre-balloon test occlusion state and was well matched with other factors. **Conclusion:** Technetium-99m-HMPAO brain SPECT before and during balloon test occlusion seems to be a simple and objective method for predicting permanent neurologic deficits when the comparative uptake of middle cerebral artery territories during balloon test occlusion is less than 85% of that before balloon test occlusion.

Key Words: cerebral angiography; SPECT; balloon test occlusion; technetium-99m-HMPAO

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The treatment of inoperable internal carotid artery aneurysms or extensive tumors involving the neck or skull base may require occlusion of the internal carotid artery. The circle of Willis provides collateral circulation for the territory of the occluded internal carotid artery but is completely intact in only 21% of patients (*1*). Permanent occlusion or surgical sacrifice of the internal carotid artery may cause subsequent stroke (*2*), which often involves large vascular territories and in some cases is lethal.

Balloon test occlusion of the internal cerebral artery with monitoring of clinical neurologic status has been used to identify patients who might develop ischemia and infarction with permanent occlusion (*3–5*). Five percent to 20% of patients with no clinical signs of ischemia during balloon test occlusion develop an infarction with permanent occlusion. A method using ^{99m}Tc-HMPAO to identify patients who clinically pass an internal carotid artery balloon test occlusion but who then may develop a cerebral infarction after permanent occlusion has been described (*2,6–8*).

In this study, we assessed the feasibility of using ^{99m}Tc-HMPAO brain SPECT to objectively and preoperatively predict neurologic deficits from the permanent occlusion of an internal carotid artery.

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METHODS

Patients

The study population consisted of 24 patients with various head and skull base tumors: 6 patients with pituitary tumor, 5 with thyroid carcinoma, 4 with mucoepidermoid carcinoma, 3 with angiofibroma, 3 with meningioma, 2 with massive jugulodigastric lymph node metastasis and one with osteogenic sarcoma of the maxilla. All patients had the possibility of accidental ligation of the internal carotid artery during operation because of close contact with the tumor mass.

We first performed cerebral angiography with contralateral carotid artery compression to evaluate the circle of Willis. The posterior communicating artery was assessed by carotid artery compression during vertebral angiography. Balloon occlusion of the internal carotid artery using a 5 French Swan-Ganz catheter through a 7 French Hemaquet introducer sheath was applied and the balloon was filled with contrast material. Occlusion was performed at the mid-cervical internal carotid artery level to avoid carotid body stimulation and petrosal segment of ICA injury by the catheter's stiff balloon segment. Ballooning was continued until its pulsatile motion from the cardiac cycle ceased. Neurologic examination of the patients was performed during the occlusion. Fifteen minutes after internal carotid artery balloon test occlusion, 20 mCi (740 MBq) of ^{99m}Tc-HMPAO were injected intravenously. The test occlusion was maintained for an additional 15 min (a total of 30 min), as long as patients remained without deficit on clinical neurologic examination. Patients were then transferred to the nuclear medicine department for cerebral SPECT images, which were obtained with the Siemens orbiter 7500 gamma camera. Sixty-four views were taken during 360° rotation about the long axis of the patients. A 64 × 64 matrix (pixel size 6.25 mm) was used; axial and coronal reconstruction was done by Microdelta computer. Occlusion study results were compared to those of the preocclusion study taken at least 3 days before the balloon occlusion test using the semiquantitative method. Semiquantitative analysis was performed using mirror technique, with regions of interest (ROIs) drawn on both middle cerebral artery (MCA) territories. Relative percent of ^{99m}Tc-HMPAO radioactivity was calculated as follows:

$$\frac{\dfrac{\text{Count of radioactivity on ROIs of affected side MCA territory from occlusion test}}{\text{Count of radioactivity on ROIs of opposite side MCA territory from occlusion test}}}{\dfrac{\text{Count of radioactivity on ROIs of affected side MCA territory from preocclusion test}}{\text{Count of radioactivity on ROIs of opposite side MCA territory from preocclusion test}}} \times 100.$$

TABLE 1
Stump Pressure Measurement and Relative Percent of MCA Territory on HMPAO-SPECT

Balloon occlusion result	Postocclusion mean stump pressure (mmHg)	Decrease in mean stump pressure (mmHg)	Relative percent of MCA territory on HMPAO-SPECT
Tolerated (n = 19)	55–85	10–45	95–101
Not tolerated (n = 5)	30–60*	30–70*	77–85

*Could not be performed on two patients because of sudden loss of consciousness.

Additional tests included neurological examination to classify patients into clinically tolerated and clinically not tolerated groups, electroencephalography, intracarotid stump pressure monitoring and cerebral angiography with contralateral carotid artery compression, which were compared to the brain SPECT findings.

RESULTS

Clinical neurologic examination during the 30 min of internal carotid artery balloon test occlusion showed 19 patients with no evidence of ischemia and 5 with abnormalities. In the clinically not tolerated group 4 patients developed motor weakness, 3 sudden loss of consciousness, 3 sensory changes and 3 abnormal EEG changes.

The clinically tolerated group and the clinically not tolerated group had postocclusion mean stump pressures of 55 to 85 mmHg and 30 to 60 mmHg, respectively; mean stump pressure decreases of 10 to 45 mmHg and 30 to 70 mmHg, respectively; and relative percentage of MCA territory of ^{99m}Tc-HMPAO SPECT was 95%–101% and 77%–85%, respectively (Table 1). Technetium-99m-HMPAO brain SPECT showed more perfusion deficits in the clinically not tolerated group than in the clinically tolerated group (Figs. 1, 2). Asymmetrical cerebral hypoperfusion on ^{99m}Tc-HMPAO SPECT with angiographic evidence of good cross-filling from the nonoccluded to the occluded side was demonstrated in two patients (Fig. 3).

DISCUSSION

Permanent occlusion of the internal carotid artery is a recognized treatment for certain intracranial aneurysms and extensive tumors involving neck and skull base when there is adequate collateral cerebral circulation (*9,10*). A previous report, however, demonstrated that occlusion of the common carotid artery or internal carotid artery carries about 30% risk of ischemia of the ipsilateral cerebral hemisphere (*9*). In 21% of the cases, onset of deficits is delayed for more than 48 hr after occlusion. It is thought that infarction after successful temporary and permanent carotid occlusion has two basic causes: (a) hypoperfusion and ischemia due to inadequate collaterals around the circle of Willis and (b) the cardiovascular status of the patient (*6,8*). The hypoperfusion problem is definitely more serious in the elderly, whose blood pressure and cardiac output are less stable, than in younger patients (*6*). The other major cause is embolism, from a clot developing in the occluded supraclinoid carotid artery stump and then becoming dislodged and entering the middle cerebral artery circulation (*6–8,11*).

To assess collateral circulation adequacy during the internal carotid artery occlusion test, various techniques have been recommended, including angiography (*12*), electroencephalography (EEG) (*13,14*), somatosensory evoked potentials (SEPs) (*15*), stump pressure (*16,17*), transcranial doppler (*18*), ^{133}Xe with external probes (*13,17*), stable xenon with CT (*3,19,20*) and PET (*21*). Stump pressure measurement correlates with intracranial blood flow, but the wide normal value range precludes its use as an absolute predictor of adequate cerebral blood flow and it is available only at a few institutions (*4,16*). A PET scan during the test occlusion period would be technically difficult (*21*). External probe measurement with ^{133}Xe is easy to perform in the angiography suite and offers reproducible quantitative measurements, but it does not provide regional perfusion information. Stable xenon CT cerebral blood flow imaging with balloon test occlusion may reveal focal areas of ischemia that are clinically indiscernible, but it requires special added features for the CT scanner (*6*).

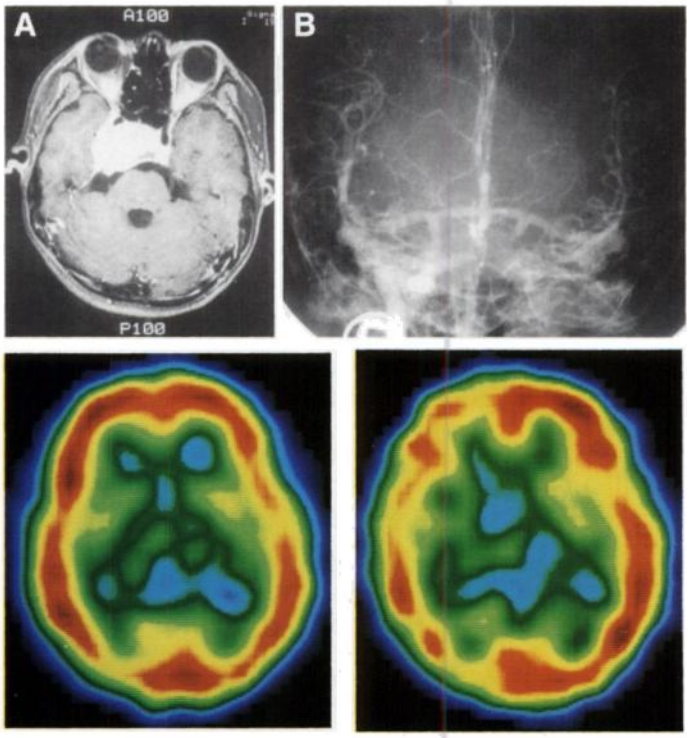

FIGURE 1. A 16-yr-old boy with pituitary adenoma. (A) Axial T1 weighted MR image shows pituitary tumor encircling the right internal carotid artery with extension to right parasellar area. (B) Carotid angiogram on AP projection shows good visualization of contralateral middle cerebral artery through the anterior communicating artery during left carotid compression. (C) Preocclusion brain SPECT shows no significant radioactivity difference between the cerebral hemispheres. (D) Postocclusion brain SPECT shows markedly decreased perfusion on the right cerebral hemisphere. Semiquantitative analysis revealed more than 15% perfusion deficits.

Matsuda et al. have used ^{99m}Tc-HMPAO SPECT to assess cerebral perfusion during test occlusion of the carotid artery (*22*). Technetium-99m-HMPAO is a lipophilic radiotracer with an extraction across the blood-brain barrier of about 0.75. Once inside the brain, it is rapidly converted into a hydrophilic form that is retained for hours. The contrast between normal and abnormal brain remains constant for 10 min to 2 hr. As ^{99m}Tc has a half-life of 6 hr, ^{99m}Tc-HMPAO SPECT studies may be repeated the next day to determine if a perfusion defect is reversible and related to the balloon test occlusion (*23,24*).

Results of a study by Monsein et al. suggest that patients who had no changes between baseline and test occlusion ^{99m}Tc-HMPAO SPECT studies should have adequate collateral circulation to sustain cerebral blood flow after occlusion of the internal carotid artery if no thromboembolic episodes occur (*7*). Similar reports on internal carotid occlusion with ^{99m}Tc-

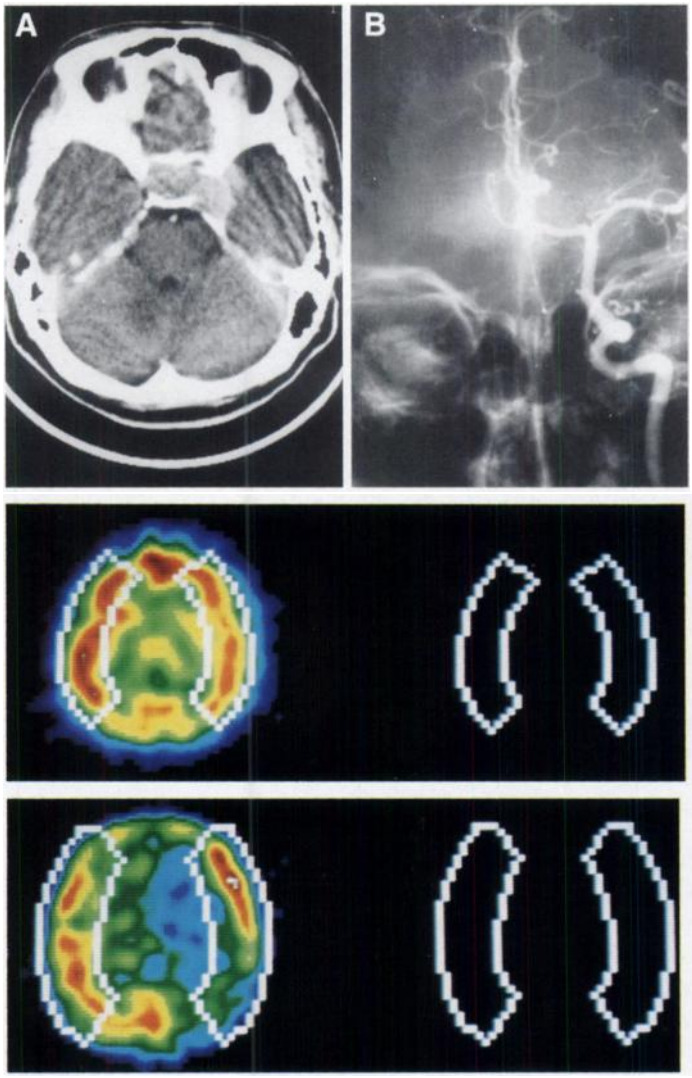

FIGURE 2. A 31-yr-old woman with pituitary adenoma. (A) Axial CT scan shows pituitary tumor encircling the left carotid artery. (B) Carotid angiogram on AP projection shows nonvisualization of the right middle cerebral artery during right carotid compression, probably from dysplastic change of right A1 portion. (C) Preocclusion brain SPECT shows no significant difference of radioactivity on semiquantitative analysis. (D) Postocclusion brain SPECT shows markedly decreased perfusion deficits in the left cerebral hemisphere. Loss of consciousness developed during left internal carotid artery occlusion.

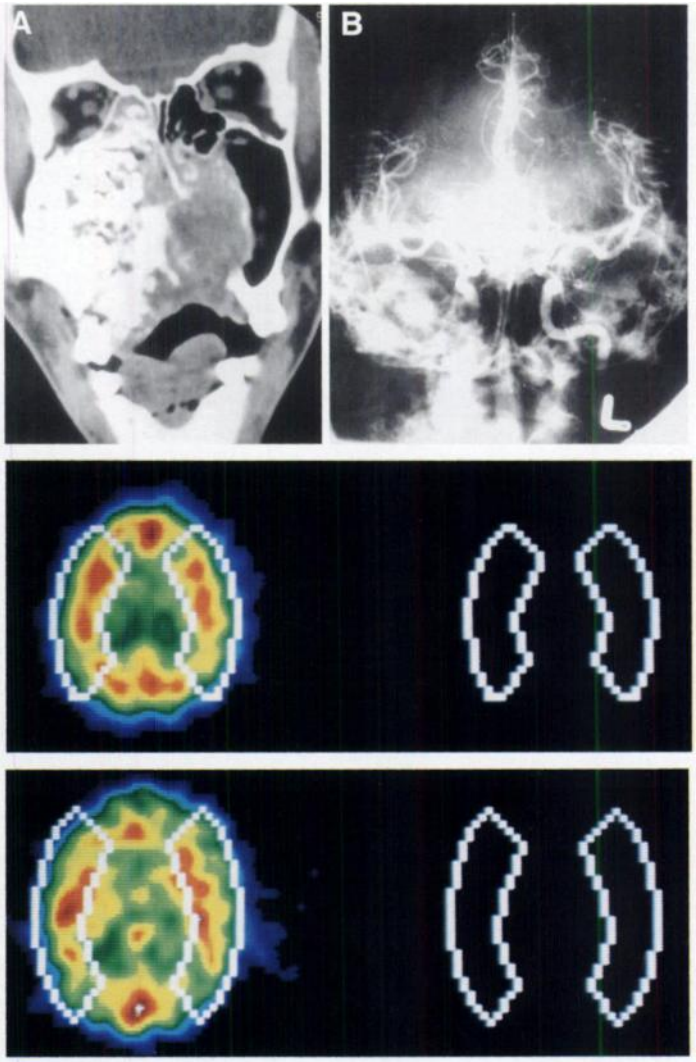

FIGURE 3. A 33-yr-old man with osteosarcoma on right maxilla. (A) Coronal CT scan shows bulky tumor mass on right maxilla. (B) Carotid angiogram on AP projection shows good cross-filling from left hemisphere to the right hemisphere on right internal carotid artery manual compression. (C) Preocclusion brain SPECT shows no significant difference of radioactivity between the cerebral hemisphere. (D) Postocclusion brain SPECT shows mildly decreased perfusion on anterior and posterior aspect of the right hemisphere.

HMPAO SPECT reveal that this procedure may be able to predict a good outcome after permanent carotid artery occlusion and to identify patients at greater risk for developing cerebral infarction after permanent occlusion (*2,6*).

To evaluate relative hypoperfusion according to balloon test occlusion, we used the semiquantitative method for measuring the relative percentage of middle cerebral artery territory. Accordingly, the relative percentage of middle cerebral artery territory on ^{99m}Tc-HMPAO SPECT in the clinically tolerated group ranged from 95%–101%, but only 77%–85% in the clinically nontolerated group. Two patients had angiographic evidence of good cross-filling from the nonoccluded to the occluded side of the internal carotid artery, but the anterior communicating artery showed asymmetric cerebral hypoperfusion on ^{99m}Tc-HMPAO SPECT during balloon test occlusion. Therefore, angiographic evidence of cross-filling is a poor predictor of a patient's ability to tolerate permanent occlusion.

As previously mentioned, there are several ways to predict which patients will not tolerate occlusion because of inadequate collateral circulation. Until recently, however, there had been no way to objectively predict which patients will not tolerate internal carotid occlusion because of thromboembolic complications.

CONCLUSION

Although the patient number was small and postoperative follow-up was scanty, our results suggest that ^{99m}Tc-HMPAO brain SPECT before and during balloon test occlusion is a simple and objective method for predicting permanent neurologic deficits when the comparative uptake of middle cerebral artery territories during balloon test occlusion is less than 85% of that before balloon test occlusion.

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Dopamine Transporters Decrease with Age

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Postmortem studies have documented degeneration of dopamine cells with age, but the changes that occur in healthy aging individuals is less clear. The purpose of this study was to evaluate the extent to which age-induced changes in dopamine transporters occur in subjects with no evidence of motor impairment. **Methods:** We evaluated 23 right-handed healthy volunteers (age range 20–74 yr) using PET and [^{11}C]*d-threo*-methylphenidate. The ratio of the distribution volume for [^{11}C]*d-threo*-methylphenidate in striatum to that in cerebellum was used as model parameter for dopamine transporter availability (Bmax/Kd + 1). **Results:** Dopamine transporter availability was significantly lower in subjects >40 yr of age than in those <40 yr. Estimates of dopamine transporter availability showed a significant negative correlation with age both for the putamen ($r = -0.72$, $p < 0.0001$) and the caudate ($r = -0.74$, $p < 0.0001$). Dopamine transporter availability was higher in the left than in the right putamen but did not differ between the left and right caudate. **Conclusion:** This study documents a 6.6% decrease per decade of life in striatal dopamine transporters of healthy volunteers.

Key Words: PET; dopamine transporters; degeneration

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According to projections by the U.S. Bureau of the Census, the number of individuals 65 yr and older will more than double by the middle of the next century to nearly 79 million. Whereas about 1 in 8 Americans were elderly in 1990, about 1 in 5 could be elderly in the year 2030 (*1*). This progressive increase in the elderly population places a sense of urgency on understanding the neurochemical changes accompanying normal aging. Aging is associated with changes in several neurotransmitters (*2*) as well as changes in specific motor, cognitive and emotional behaviors (*3*). The dopaminergic system appears to be among the most age-sensitive neurotransmitters (*4*). Of the behavioral changes associated with aging, the most conspicuous are those related to motoric function. For example, aging is associated with a higher frequency of dyskinesias (*5–6*) and of mild Parkinson-like motor changes such as rigidity (*7*). Some of these motoric changes may reflect an age related decline in nigrostriatal dopaminergic function (*8*).

Studies in animals as well as postmortem human brain studies, have in general documented a decline in brain dopamine activity with aging (*9,10*). Recently, imaging techniques such as PET and SPECT have enabled the measurement of changes in dopamine parameters as a function of age in living human subjects. Most of these studies have focused on dopamine receptors and have documented a decrease in D2 and D1 receptor density with aging (*11–18*). Changes in dopamine receptors, however, predominantly reflect changes in postsynaptic elements presumably GABAergic, muscarinic and glutamatergic neurons and not changes in dopaminergic neurons. Few studies have been conducted on age-related changes in dopamine neurons in living human subjects. Age changes in the dopamine neurons of living human subjects have been studied, using PET and SPECT tracers, to measure dopamine metabolism and dopamine transporter sites. Studies using [^{18}F]fluoro-DOPA to measure dopamine metabolism have been inconclusive documenting reduced uptake (*19*) as well as no changes (*20,21*). Preliminary studies using [^{11}C]nomifensine (*22*), [^{11}C]cocaine (*23*) and [^{123}I]β-CIT (*24*) as ligands for the

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