

Assessment of Hemodynamic Reserve in Candidates for EC-IC Bypass using SPECT and ^{123}I -IMP with Diamox^R Test

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Introduction

The role of extracranial-intracranial (EC-IC) bypass is to establish a new vascular channel of blood supply to the brain threatened by ischemia due to occlusion or stenosis of the main cerebral artery and insufficient collateral blood flow. However, the conclusion of the International Cooperative Study indicated that EC-IC bypass for medically eligible patients does not significantly reduce the risk of stroke²⁾³⁾. Nevertheless, a subgroup of patients who have clearly hemodynamic compromise might still benefit from this procedure, because medically eligible patients operated on inside the trial do not necessarily have distinctly hemodynamic impairments that can be recently predicted by means of positron emission tomography (PET)¹⁾ and single photon emission computed tomography with $^{133}\text{Xenon}$ -inhalation (Xenon-133 SPECT)¹⁴⁾.

The present study attempts to assess the hemodynamic reserve in candidates for EC-IC bypass, using SPECT and N-isopropyl-I-123-p-iodoamphetamine (IMP) for the evaluation of cerebral vasodilatory capacity by the acetazolamide (DIAMOX^R) test.

Material and Methods

This study included 79 patients who had suffered TIA, RIND or minor stroke, ranging in age from 5 to 83 years with a mean age of 58 years. Their occlusive lesions were demonstrated angiographically as follows: occlusion of the internal carotid artery (ICA) in 15 patients, occlusion of the middle cerebral artery (MCA) in 10, occlusion of the ICA and the MCA in 2, occlusion of the basilar artery (BA) in 5, occlusion of the vertebral artery (VA) in 4, stenosis of the ICA in 13, stenosis of the MCA in 11, stenosis of the BA in 6, stenosis of the VA in 6, and moyo- moyo disease in 7.

CT scan of these patients showed no demonstrable hypodensity area except for a small hypodensity area in the subcortical terminal zone in some patients.

^{123}I -IMP Study

SPECT images were obtained using the HEADTOME SET 031 (Shimazu Inc. Kyoto, Japan) whose detector array system consists of 64 NaI crystals in a 38cm diameter circle and provides three or six transverse slices

simultaneously. When the counting rate per slice was 1000 K counts with the use of high-resolution collimator, the spatial resolution in center of the plane was 9 mm, measured as full width at half maximum (FWHM). IMP acquisitions were made 2 different times after intravenous bolus injection of 222MBq IMP, one acquisition lasted 15 ~ 18 minutes. Early imaging which demonstrated a regional cerebral perfusion was begun 10 minutes after injection and delayed imaging which indicated a "redistribution activity" of IMP was performed 5 hours later in the resting condition.

Regional radio activity of IMP in the presumably affected area which was normal on CT scan was compared with the radio activity of IMP in the unaffected area on each image. Hypoperfusion area in the early image was classified into three categories such as mild, moderate, and severe hypoperfusion area. Redistribution activity to IMP in the delayed image was classified into three categories such as complete, mildly incomplete and moderately incomplete redistribution. Cerebral vasoreactivity was studied separately from the resting condition using another 222MBq IMP injection, 5 ~ 7 minutes following an intravenous bolus injection of 1 g of Diamox. Regional radio activity of IMP activated by Diamox was assessed with the same design as the resting condition.

Regional cerebral vasodilatory capacity in the affected area was graded in the resting and Diamox-activated IMP SPECT images as follows : Grade 0 indicated no

hypoperfusion area in the early images under both resting and Diamox-activated conditions ; Grade I demonstrated a mild or no hypoperfusion area on the resting early image and a mild hypoperfusion area on the Diamox-activated early image with complete redistribution on the both delayed images ; Grade II showed a mild hypoperfusion area on the resting early image with complete redistribution on the delayed image and a moderate hypoperfusion area on the Diamox-activated early image with a mildly incomplete redistribution on the delayed image ; Grade III indicated a moderate hypoperfusion area on the resting early image with a mildly incomplete redistribution on the delayed image and a more reduced perfusion on the early image under the Diamox-activated condition. (Table 1) These IMP SPECT studies were performed on all patients, and post-operative studies were performed 1 to 3 months later in patients who were selected for EC-IC bypass surgery.

Results

Regional cerebral vasodilatory capacity in all patients were assessed as follows : Grade 0 in 14 cases, Grade I in 31 cases, Grade II in 33 cases and Grade III in 1 cases (Table 2). Thus, a limitation of cerebral vasodilatory capacity in the affected area was noted in 64 patients (as total number of Grade I ~ III). Of these patients, 32 EC-IC bypass surgery was performed upon 7 cases of Grade I, 24 cases of Grade II and one case of

Table 1 Cerebral vasodilatory capacity graded in the resting and Diamox-activated IMP SPECT images.

Grade	Resting			DIAMOX ^R	
	early	delayed		early	delayed
Gr. 0	○	○	→	○	○
Gr. I	⊙ (⊙)	○	→	⊙	○
Gr. II	⊙	○	→	●	⊙ (⊙)
Gr. III	●	⊙	→	●	●

Activity (affected/unaffected) : ● < ⊙ < ○ < ○

Hypoperfusion (early) : severe moderate mild (normal)

Redistribution (delayed) : (defect) moderately mildly complete
incomplete incomplete

Table 2 Assessment of cerebral vasodilatory capacity by the Diamox test in 79 patients included 32 patients on whom EC-IC bypass was performed.

Grade	Case No	EC-IC Bypass	Postop. Grade*		
			Gr. 0	Gr. I	Gr. II
Gr. 0	14	0			
Gr. I	31	7	→ 2	5	0
Gr. II	33	24	→ 0	24	0
Gr. III	1	1	→ 0	0	1
Total	79	32	2	29	1

*1-3 months after surgery

Grade III. The patency of EC-IC bypass was demonstrated by cerebral angiography 1 - 2 weeks after the operation, a newly established collateral blood supply was satisfactory in all surgical patients. In addition to that, all surgical patients were stroke free during the postoperative course including when IMP SPECT studies were performed. In 7 patients of preoperative Grade I, cerebral vasodilatory capacity was evaluated postoperatively as Grade 0 in 2 cases and Grade I in 5 cases. All 24 patients of preoperative Grade II were judged postoperatively as Grade I, and one case of preoperative Grade III was evaluated postoperatively as Grade II. Therefore, it is clear that EC-IC bypass surgery improves cerebral vasodilatory capacity mainly in patients who were assessed preoperatively as Grade II and III. Pre- and postoperative IMP SPECT findings were represented in Fig. 1 and 2.

One case in figure 1 developed a left-sided hemiparesis (RIND). Cerebral angiography demonstrated occlusion of the right middle cerebral artery (MCA). In the preoperative IMP SPECT studies, a mild hypoperfusion area was shown in right MCA territory on the resting early image and a moderate hypoperfusion area was demonstrated in the same territory on the Diamox-activated early image with a mildly incomplete redistribution on the delayed image (Grade II). In the postoperative IMP SPECT study, a mild hypoperfusion area was indicated in right MCA territory on the both resting and Diamox-activated early images with complete redistribution on the delayed images (Grade I). The other case in figure 2 suffered a gait and standing difficulty (minor stroke). Cerebral angiography showed occlusion of the basilar artery and retrograde filling of bilateral posterior cerebral arteries (PCAs) and bilateral superior cerebellar

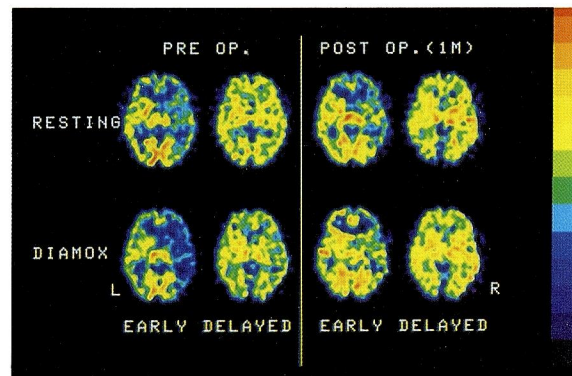


Fig. 1 IMP SPECT studies ; This 54-year old man developed a left-sided hemiparesis (RIND). Right STA-MCA anastomosis was performed on for occlusion of the right MCA. In the IMP SPECT studies, cerebral vasodilatory capacity in the right MCA territory was assessed as preoperative Grade II and postoperative Grade I.

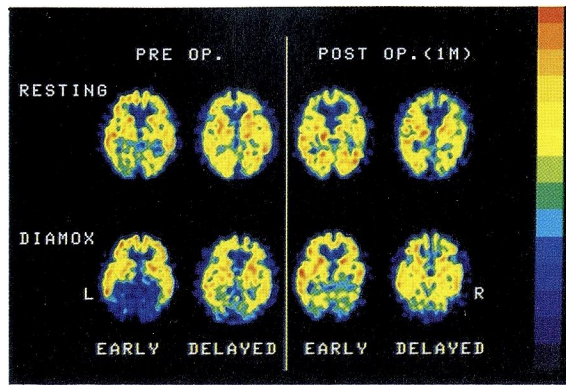


Fig. 2 IMP SPECT studies ; This 61-year old woman suffered a gait and standing difficulty (minor stroke). Right STA-SCA anastomosis was performed on for occlusion of the basilar artery. In the IMP SPECT studies, cerebral vasodilatory capacity in the bilateral PCAs and SCAs territories was evaluated as preoperative Grade II and postoperative Grade I.

arteries (SCAs). By means of resting and Diamox-activated IMP-SPECT studies, vasodilatory capacity in the bilateral PCA and SCA territories was assessed as preoperative Grade II and postoperative Grade I.

Discussion

It is generally accepted that measurement of cerebral blood flow (CBF) might be a useful tool for the evaluation of hemodynamic effects of EC-IC bypass for stroke patients. However, long-term evaluation of regional CBF after EC-IC bypass, using Xenon-133 inhalation technique, indicated failure of long-term augmentation of CBF on the side of operation¹⁵. Using Xenon-133 SPECT, Vorstrup found that 18 of 22 operated patients had no change in flow distribution 3 months after the bypass¹³. Therefore, the tomographic measurement of local cerebral metabolism or regional cerebral vasoreactivity may be a reliable method for identifying a subgroup of patients with impaired collateral reserve.

Powers et al. documented physiological responses to focal cerebral ischemia in humans using PET studies as follows ; cerebral oxygen metabolism was maintained in face of decreased blood flow by compensatory mechanisms which included vasodilation (increased cerebral blood volume (CBV)) and an increase of oxygen extrac-

tion fraction (OEF)¹¹. Baron et al. described reversal of focal misery perfusion syndrome (increased OEF) by EC-IC bypass¹. Leblanc et al. identified postoperative decrease in CBV and increase in CBF/CBV ratio, indicating improved hemodynamic function⁸. Gibbs et al. noted a prediction of reduced cerebral perfusion pressure (CPP) and hemodynamic reserve using CBF/CBV ratio, from an analysis of the relation between CBF/CBV and OEF⁴. Thus, a subgroup of patients with impaired hemodynamic reserve could be identified by PET studies.

On the other hand, cerebral vasoreactivity of patients who clearly responded to EC-IC bypass was estimated by measurement of rCBF and CO₂-reactivity with Xenon-133 inhalation technique. Norrving et al. observed a reduced CO₂ response in patients with compromised collateral channels¹⁰. Halsey et al. showed a failure of EC-IC bypass to augment resting flow level, but an improvement of CO₂ response in patients with severely impaired collateral channels⁵. In addition to those findings, Vorstrup et al. evaluated cerebral vasodilatory capacity by the acetazolamide (Diamox) test before EC-IC bypass surgery to identify hemodynamic cases^{13,14}. Rapid inhibition of carbonic anhydrase in the erythrocyte and the capillary endothelium throughout the cerebral tissue by an intravenous injection of 1 g of the drug resulted in an

increase of CBF by 55 and 70% after 3 and 20 minutes, respectively, in the normal brain tissue, while CMRO₂ is constant¹²⁾. An increase of CBF produced by Diamox is similar to the effect of breathing CO₂. Using Xenon-133 SPECT, Vorstrup et al. observed an increase in the regional vasodilatory capacity in the majority of patients after EC-IC bypass surgery¹⁴⁾. Therefore, cerebral vasodilatory capacity might be limited by compensatory mechanism with vasodilation due to reduced CPP. As mentioned above, a subgroup of patients with compromised hemodynamic reserve could be identified by SPECT and pharmacological activation.

N-isopropyl- (I-123) -p-iodoamphetamine, as another single photon emitter, has recently been introduced for tomographic measurement of CBF in humans^{6) 7) 9)}. After intravenous injection, IMP is nearly completely extracted on first pass through the brain, and early distribution is maintained for over 1 hour despite slow wash-out from the brain because IMP activity is slowly replenished by new IMP delivered from a pulmonary reservoir⁶⁾. But, the early image of IMP SPECT is thought to reveal the distribution of regional CBF as compared with microsphere technique and Xenon-133 SPECT⁷⁾. On the contrary, redistribution of IMP activity in the delayed image could reflect a balance between wash-in and wash-out of IMP. Morreti et al. indicated that the delayed image might show a metabolic activity of the brain or a different turnover of IMP in relation to the structure and tissue integrity⁹⁾. In our own studies (not published), it is thought that the less the wash-in of IMP, the more prolonged the wash-out of IMP, in addition to that, a moderate hypoperfusion area on the resting early image with incomplete redistribution on the delayed image correlates with symptomatic reversible ischemia. So, the resting delayed image might indicate tissue viability or reversibility of ischemic brain.

Early and delayed images of IMP SPECT with Diamox activation could evaluate regional cerebral vasodilatory capacity with higher spatial resolution and accuracy than using Xenon-133 SPECT. Therefore, assessment of hemodynamic reserve not only in the carotid system but in the vertebro-basilar (VB) system is available using IM-

P-SPECT. And, the side-to-side asymmetry or the carotid system-to-VB system dysproportion enhanced by Diamox activation is more prominent on the early image of IMP SPECT. From our results, EC-IC bypass seemed to be less suitable for patients with a mild impairment of hemodynamic reserve, but beneficial for patients with a moderate limitation of hemodynamic reserve (Grade II and III). Compromised hemodynamic reserve and reduced CPP implied by measurement of cerebral vasodilatory capacity can identify patients who will benefit from EC-IC bypass. Further studies with this subgroup of patients are needed to confirm the effectiveness of EC-IC bypass for preventing stroke.

Conclusions

It is assumed that a limitation of cerebral vasodilatory capacity by Diamox test indicates compensatory cerebral vasodilation for reduced cerebral perfusion pressure (CPP) due to insufficient collateral blood flow, because an improvement of the regional vasodilatory capacity was observed postoperatively in a subgroup of patients.

Assessment of hemodynamic reserve and reduced CPP using Diamox-activated IMP SPECT can help to identify patients who will benefit from EC-IC bypass surgery not only in the carotid system but also in the vertebro-basilar system.

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