Cerebral Blood Flow and Oxygen Metabolism Measurements Using Positron Emission Tomography on the First Day after Carotid Artery Stenting

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Background: The aim of the present study is the characterization of hemodynamics to predict hyperperfusion syndrome (HPS) after carotid artery stenting (CAS) with positron emission tomography (PET) obtained before and on the first day after the treatment. *Methods:* Cerebral perfusion and oxygen metabolism were evaluated by ^{15}O-gas PET in 18 patients with symptomatic internal carotid artery (ICA) stenosis before and on the first day after CAS. Regional cerebral blood flow (CBF), oxygen extraction fraction (OEF), cerebral metabolic rate of oxygen ($CMRO_2$), and cerebral blood volume (CBV) were measured in the ipsilateral and contralateral middle cerebral artery territories and compared between before and after CAS. *Results:* CBF increased in 16 of 18 patients on the first day after CAS and postoperative CBF was significantly higher than preoperative CBF bilaterally. OEF decreased in 15 of 18 patients on the first day after CAS and postoperative OEF was significantly lower than preoperative OEF in the ipsilateral hemisphere. $CMRO_2$ and CBV did not change significantly. None of the patients showed HPS after CAS. All patients who had preoperative OEF of 53% or more (misery perfusion) in the ipsilateral hemisphere showed 50% or more increase in CBF postoperatively. The preoperative OEF value significantly correlated with the rate of postoperative increase in CBF bilaterally. *Conclusions:* CAS increases cerebral perfusion and improves hemodynamic compromise in patients with symptomatic ICA stenosis. Although we could not clarify the usefulness of PET before and on the first day after CAS in predicting HPS, a high preoperative OEF is related to postoperative marked CBF increase and might be used as a predictor of HPS. Patients with greater hemodynamic compromise with a high preoperative OEF should be managed carefully to prevent HPS, but they have a greater chance of CBF increase after CAS. **Key Words:** Carotid artery stenting—cerebral blood flow—hyperperfusion syndrome—oxygen extraction fraction—positron emission tomography.
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Introduction

Internal carotid artery (ICA) stenosis, with thromboembolic and/or hemodynamic compromise causing cerebral infarction, can be successfully treated by carotid endarterectomy (CEA), which significantly reduces the risk of stroke in both symptomatic and asymptomatic patients, as compared with medical therapy alone.[1,2] Carotid artery stenting (CAS) is increasingly being used because of the development of safe and effective protection devices that significantly reduce the perioperative thromboembolitic complications and applied primarily as the minimally invasive alternative for patients considered high risk for CEA.[3] With increasing experience with dedicated CAS devices over the past decade, patients who are at standard risk for CEA are also increasingly treated with CAS. A recent large international randomized trial, Carotid Revasculization Endarterectomy versus Stenting Trial, demonstrated that CAS is not inferior to CEA in standard-risk symptomatic and asymptomatic patients.[4]

Hyperperfusion syndrome (HPS) is a rare but serious complication after CAS with a reported incidence of 1.1% in a large retrospective study.[5] Prediction and early detection of hyperperfusion are crucial to prevent the development of severe cerebral edema and intracerebral hemorrhage because the prognosis in patients with intracerebral hemorrhage after carotid revascularization is extremely poor.[6,7] Studies have reported that single-photon emission computed tomography (SPECT) is useful in predicting HPS and in detecting hyperperfusion state following CEA.[8,9] SPECT studies have demonstrated that impaired cerebral vasoreactivity (CVR) to acetazolamide is a useful predictive factor for HPS after CAS.[10] Increased oxygen extraction fraction (OEF) in positron emission tomography (PET) has been considered the most reliable indicator of hemodynamic compromise with reduced CVR in symptomatic patients with occlusive cerebrovascular disease.[11-13] However, there are few studies using PET to clarify the hemodynamic effect of carotid revascularization on cerebral perfusion.[14-16] No studies have been performed to determine whether PET can be useful in predicting HPS after CAS. Recently, Matsubara et al[16] examined cerebral perfusion and metabolism before and after CAS using PET and revealed acute increases in cerebral blood flow (CBF) and perfusion pressure 1-7 days after CAS. However, they did not thoroughly discuss the prediction of HPS after CAS with their PET data. HPS is reported to occur significantly earlier after CAS (1.5 ± 2.3 days) than after CEA (5.8 ± 2.3 days) and the onset peaked within 12 hours after CAS.[5] Therefore, an early PET study is essential to detect acute cerebral hemodynamic changes and predict HPS after CAS.

In the present study, we examined cerebral perfusion and oxygen metabolism using ^{15}O-gas PET obtained before and on the first day after CAS in patients with symptomatic ICA stenosis. This study was conducted to clarify whether measurement of cerebral perfusion and oxygen metabolism by PET on the first day after CAS can detect acute hemodynamic changes that may lead to HPS. Moreover, an elevated OEF is a reliable indicator of misery perfusion state in patients with chronic cerebral hypoperfusion.[17] Reperfusion therapy can be most effective and useful by increasing CBF in these patients. Therefore, we examined the hypothesis that the degree of cerebral hemodynamic compromise determined by elevated OEF is associated with the rate of increase in CBF after the treatment.

Materials and Methods

Patient Population

Between July 2009 and April 2012, 28 patients underwent carotid angioplasty and stent placement for symptomatic ICA stenosis at our institution. We retrospectively reviewed 18 patients who underwent cerebral perfusion and oxygen metabolism measurements with PET both within 1 month before and on the first day after CAS (Table 1). The remaining 10 patients, in whom CBF and oxygen metabolism 5-8 days after CAS were measured with PET or SPECT because of unavailability of PET on the first day after CAS, were excluded from this study population. Patients with coexisting conditions such as contralateral severe ICA stenosis and occlusion or ipsilateral middle cerebral artery (MCA) or distal ICA stenosis were also excluded. Sixteen of the 18 patients were men and 2 were women. Their mean age was 70.2 ± 5.2 ranging from 62 to 77 years (median: 72 years). In 8 subjects, carotid stenosis was associated with transient ischemic attack (TIA) and 10 had complete stroke. Nine stroke patients exhibited good functional recovery (modified Rankin Scale of 0-2) and 1 had moderate disability with a modified Rankin Scale of 4. All patients underwent complete 4-vessel cerebral angiography to confirm the presence of stenosis. The degree of ICA stenosis was 82.2 ± 12.4 ranging from 60% to 99% (median: 81%) according to the North American Symptomatic Carotid Endarterectomy Trial criteria.

CAS Protocol

At least 72 hours before the procedure, all patients were premedicated with 100 mg of aspirin and 75 mg of clopidogrel. A transfemoral approach was used in all cases. After diagnostic angiography, systemic anticoagulation with heparin (100 U/kg) was given intravenously to maintain an activated clotting time 2.3-3.0 times of the baseline value. After selective catheterization of the target artery, an 8F or 9F guide catheter (Brite Tip; Cordis Endovascular, Miami Lakes, FL) was placed proximal to the lesion. Distal protection was performed in all patients with Angioguard XP (Cordis Endovascular) in 4 patients, FilterWire EZ (Boston Scientific, Natick, MA) in 9 patients,

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