Prospective Registry of Carotid Artery Stenting in Japan—Investigation on Device and Antiplatelet for Carotid Artery Stenting

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Background: Carotid artery stenting (CAS) is minimally invasive but may cause perioperative cerebral infarction associated with distal embolization. We conducted a multicenter prospective observational study on the onset of vascular events after CAS to find out the efficacy and safety of CAS in Japan and to investigate the effects of antiplatelet drugs administered before and after CAS on efficacy and safety of CAS. *Methods:* A total of 949 patients with cervical carotid artery stenosis were enrolled at 43 institutions in Japan; 934 who had undergone CAS with antiplatelet drugs and followed for 1 year were analyzed. Primary end point was the incidence of the first event of death, ischemic stroke, hemorrhagic stroke, transient ischemic attack, myocardial infarction, or serious hemorrhage within 1 year after enrollment. Comparison of the incidences of events according to antiplatelet drugs was also conducted. *Results:* The primary end point was observed in 69 patients (7.4%) within 30 days of enrollment and in 40 patients (4.3%) between 31 days and 1 year after enrollment. The incidence of the first event for aspirin + cilostazol was significantly lower than that for aspirin + clopidogrel ($P = .01$), aspirin + clopidogrel + cilostazol ($P = .01$), and antiplatelet monotherapy ($P < .01$). Patient age ($P = .01$), presence of ischemic cerebrovascular disease ($P = .02$), presence of antidiabetic drugs ($P < .01$), femoral artery puncture ($P = .02$), guiding catheter used ($P = .02$), and Angioguard XP used ($P = .01$) were also correlated with the primary end point. *Conclusion:* Incidences of the primary end point within 30 days and 1 year of enrollment were comparable with previous reports, suggesting that CAS is a useful alternative for carotid endarterectomy in carotid stenosis patients with high risk for carotid endarterec-

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tomy. Further randomized controlled studies are needed to determine whether differences in mechanism of action of antiplatelet drugs might have contributed to the results of the present study. **Key Words:** Carotid artery stenosis—stenting—antiplatelet—adverse event.

Introduction

Carotid stenosis is a major cause of ischemic cerebrovascular disease. Carotid endarterectomy (CEA) has been established as a useful therapy more effective than pharmacologic treatment in prevention of ischemic cerebrovascular diseases.[1] Carotid artery stenting (CAS) has recently become widely performed as a less invasive treatment and has been reported to be as effective as CEA in prevention of cerebral infarction in patients at high risk for perioperative complications for CEA.[2] Based on such clinical evidence, relevant guidelines in Japan and the US recommend CAS in patients with high risk for cerebrovascular diseases.[3,4]

In Japan, stent placement has been conducted in full scale for treatment of carotid stenosis since the 1990s. Precise (Johnson & Johnson K.K., Tokyo, Japan), a carotid artery stent, and Angioguard XP (Johnson & Johnson K.K.), a distal embolic protection filer, have been approved since September 2007 and have been subject to Japanese National Health Insurance coverage since April 2008. CEA is more difficult to perform in Japanese population compared with Western population because the carotid artery bifurcation is located higher in the Japanese.[5] Thus, its usefulness anticipated, CAS was performed in 5755 cases and CEA in 3440 cases in 2010.[6] However, some reports suggest that CAS is inferior to CEA,[7,8] and others fail to prove the noninferiority of CAS to CEA,[9] warranting further investigation of usefulness of CAS in various populations.

CAS is minimally invasive but may cause perioperative cerebral infarction associated with distal embolization, by displacing atherosclerotic lesions and expanding the intravascular lumen. Also, inserting a foreign material into an artery may cause subacute thrombosis or postoperative thromboembolism. To prevent these perioperative complications, at least 2 antiplatelet drugs, with aspirin as a basic drug, are often used before and after CAS. However, there are no reports regarding the efficacy or safety of antiplatelet drugs with CAS, and which antiplatelet drugs are useful remains unclear.

We conducted a multicenter prospective observation study on the onset of vascular events after CAS, the Investigation on Device and Anti-platelet for Carotid Artery Stenting, to find out the efficacy and safety of CAS in Japan and to investigate the effects of antiplatelet drugs administered before and after CAS on efficacy and safety of CAS.

Materials and Methods

This study was a multicenter, prospective observational study to investigate the current status and safety of CAS in combination with antiplatelet drugs in 43 institutions in Japan highly experienced with CAS (Appendix). Patients were enrolled between June 2008 and June 2010 and followed with observation for 1 year after enrollment. Inclusion criteria were as follows: (1) CAS was scheduled to be performed for carotid arteriosclerosis or restenosis within 7 days of enrollment; (2) with symptomatic carotid stenosis (≥50%) or asymptomatic carotid stenosis (≥80%) defined by ultrasonography or angiography; (3) meeting the definition of CEA high risks; (4) oral antiplatelet drugs could be used; (5) life prognosis expected to be 1 year or longer; (6) modified Rankin scale grade 0, 1, 2, or 3, and (7) written consent to participate in this study was obtained. Carotid stenosis rate was measured using the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method when defined by angiography, or when defined by ultrasonography, peak systolic velocity (PSV) at a stenotic site surpassing 150 cm/s and 230 cm/s were diagnosed as the carotid stenosis exceeding 50% and 80%, respectively. Exclusion criteria were as follows: (1) incidence of ischemic stroke within 48 hours before enrollment; (2) incidence of hemorrhagic stroke within 90 days before enrollment; (3) intraluminal thrombus was observed in the target artery; (4) target artery completely occluded; (5) likely to be difficult to place a guiding catheter because of stenosis in the origin of common carotid artery on the treatment side or the brachiocephalic artery; (6) surgery or intravascular treatment scheduled to be performed for intracranial disease within 30 days of enrollment; (7) another invasive treatment was scheduled to be performed within 30 days of enrollment; and (8) the principal investigator or subinvestigator considered that participation in this study was not reasonable for other reasons.

The following patient characteristics were checked before CAS: age, sex, body height, body weight, blood pressure (supine position), electrocardiogram, modified Rankin scale, laboratory tests (C-reactive protein, fasting blood glucose level, total cholesterol, triglyceride, high-density lipoprotein cholesterol, creatinine, aspartate aminotransferase, alanine aminotransferase, white blood cell count, red blood cell count, hemoglobin, and platelet count), history of diabetes, dyslipidemia, hypertension,