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ORIGINAL ARTICLE

Effectiveness and safety of extracranial carotid stent placement: A nationwide self-controlled case-series study

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KEYWORDS
carotid atherosclerotic disease;
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Background: Carotid angioplasty and stent (CAS) placement has emerged as an attractive revascularization strategy for patients with internal carotid artery stenosis. However, the effectiveness and safety of CAS were not fully evaluated, mainly because of methodological difficulties in finding an appropriate comparison group.
Methods: Patients who underwent CAS were identified from Taiwan's National Health Insurance claims database between 2005 and 2008. The incidence rate of ischemic stroke after CAS was compared with that of the year prior to the procedure using a self-controlled case series analysis and a conditional Poisson regression model. Logistic regression was conducted to identify factors associated with poor outcome.
Results: A total of 1258 patients who had undergone CAS were included, and 73 cases (5.8%) of death or ischemic stroke occurred during the index hospitalization. Within 1 year after CAS, 74 patients died and 80 experienced an ischemic stroke. Of the 1184 patients who were followed for 360 days, the rate ratio for ischemic stroke decreased to 0.21 (95% CI: 0.08–0.51) between 31 and 180 days, and 0.10 (95% CI: 0.03–0.32) between 181 and 360 days. Statin therapy was associated with a reduced risk of death or ischemic stroke in the 1st month (odds ratio of 0.53; 95% CI: 0.32–0.90). Conversely, the use of nonsteroidal anti-inflammatory agents, possibly histamine-2 receptor blockers, and CAS performed by low-volume operators were associated with a twofold increased risk.

Conflicts of interest: All authors have no conflicts of interest to declare.

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Conclusion: CAS reduced the long-term risk for ischemic stroke. Self-controlled case series analysis might be an appropriate design for evaluating device safety and effectiveness.

Introduction

Extracranial internal carotid artery stenosis is an important cause of ischemic stroke. Carotid endarterectomy (CEA) and carotid stenting (CAS) are the two major treatment strategies for extracranial carotid revascularization. The results from the North American Symptomatic Carotid Endarterectomy Trial and the European Carotid Surgery Trial have demonstrated that, in symptomatic patients with high-grade (70—99%) internal carotid artery (ICA) stenosis, CEA is highly beneficial for patients with recent transient ischemic attacks (TIA) and nondisabling strokes; and the role of CEA is less certain in symptomatic patients with mild (<50%) to moderate (50—69%) stenosis, as well as asymptomatic patients.[1—3] CAS, however, has emerged as a potential alternative treatment for patients with carotid artery disease who are at high risk for CEA.[4] In the Study of Angioplasty with Protection in Patients at High Risk for Endarterectomy Trial, which included both symptomatic and asymptomatic patients (i.e., close to 70% asymptomatic) with ICA stenosis and a high risk for CEA, it was found that CAS with the use of an emboli-protection device was not inferior to CEA in patients with severe ICA stenosis and coexisting conditions.[5] Additionally, there were no significant differences in the 3-year outcome (i.e., stroke, myocardial infarction, or death) between the CEA and CAS groups.[6]

However, due to relatively limited evidence on the effectiveness and safety of CAS, the widespread use of CAS should not be uniformly justified in patients with various cerebrovascular risks.[7,8] Some reports demonstrate that CAS resulted in a higher risk of stroke, myocardial infarction, and death.[9] Also, little is known about whether or not CAS provides additional clinical benefits over optimal medical treatment. Although the current guidelines in Taiwan recommend that CAS is only considered for patients with symptomatic stenosis of >60% or asymptomatic stenosis of >80% with certain conditions (i.e., patients who are unable to receive CEA, who previously received radiotherapy, and who have tandem stenosis in the carotid artery),[10] in recent years, a rapidly increasing number of patients underwent CAS, and CEA has become a rare practice in Taiwan.[11—13]

The effectiveness and safety of CAS in the treatment of internal carotid artery stenosis in real clinical settings were not fully evaluated, mainly because of methodological difficulties. Patients undergoing CAS may differ substantially from those who did not in terms of the anatomic characteristics of the carotid artery (e.g., focal stenosis or long segment occlusion), clinical presentations, and functional status. Therefore, it is difficult to identify a suitable comparison group of untreated patients or a comparable group that received CEA with similar baseline risks. In this setting, a self-controlled case-series design may be appropriate to overcome the issue of no appropriate comparison group.[14] The objective of this study was to evaluate the efficacy, safety, and risk factors associated with poor outcome in patients with significant ICA stenosis receiving CAS, using a nationwide, self-controlled case-series analysis.

Materials and methods

Patients and participants

Taiwan's National Health Insurance (NHI) claims database includes complete outpatient visits, hospital admissions, prescriptions and procedures, disease, and vital status for 99% of the 23 million people in Taiwan. We determined the longitudinal medical history of each beneficiary by linking several computerized claims data sets and the National Death Registry using the civil identification number unique to each beneficiary and date of birth.

The patients who underwent CAS placement between 1 January 2005 and 31 December 2008 were identified via services or procedure claims in the inpatient data set. The date of hospitalization was defined as the index date. A total of nine different types of stents were approved for treating carotid artery stenosis in Taiwan during the study period (Table S1). For those who had received two or more CAS procedures, the date of the first hospitalization was defined as the index date. Exclusion criteria were as follows: (1) patients who underwent CAS in 2004; (2) had missing information on sex; (3) were previously admitted to a hospital or outpatient clinic under the diagnosis code of atrial fibrillation and flutter (i.e., International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM] code of 427.3) and cancer (code 140-239); or (4) did not have continuous insurance coverage 12 months before the index date. The protocol of this study was approved by the National Taiwan University Hospital Research Ethics Committee.

Outcome definition

The outcome of interest was death or major ischemic stroke leading to hospitalization, which was defined by the following criteria: (1) a hospital discharge diagnosis code of 433, 434, and 436 from the inpatient data set; (2) a record of receiving a computed tomography or magnetic resonance imaging of the brain; (3) hospitalization for 7 days or longer; (4) obtaining a certificate for stroke; and (5) a record of rehabilitation, consultation, or therapy during hospitalization. A previous validation study using a hospital chart review reported a high accuracy of 98% using this definition.[15]