Stenting versus Endarterectomy and the Impact of Ultra-early Revascularization for Emergent Admissions of Carotid Artery Stenosis

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Background: The factors influencing outcomes after emergent admission for symptomatic carotid artery stenosis treated with revascularization by endarterectomy or stenting are yet to be fully elucidated. *Methods:* We analyzed revascularization of carotid artery stenosis for patients admitted emergently using the Nationwide Inpatient Sample (2008-2011). Admission characteristics, economic measures, in-hospital mortality, and iatrogenic stroke were compared between (1) endarterectomy and stenting, (2) patients with and without cerebral infarction, and (3) ultra-early (within 48 hours of admission) and deferred (up to 2 weeks) intervention. *Results:* 72,797 admissions meeting our inclusion criteria were identified. Factors associated with ultra-early revascularization were male patients, low comorbidity burden, stenosis without infarction, and stenting. Ultra-early intervention significantly decreased cost and length of stay, and stenting for patients without infarction decreased length of stay but increased cost. Patients without infarction treated within 48 hours had significantly lower mortality and iatrogenic stroke rate. Patients with infarction receiving ultra-early revascularization had increased odds of mortality and iatrogenic stroke in comparison with the deferred group. Patients with infarction receiving stenting experienced increased odds of mortality in comparison with those receiving endarterectomy, but there was no significant difference in iatrogenic stroke rate. Recombinant tissue plasminogen activator (rtPA) administration on the day of revascularization greatly increased the odds of iatrogenic stroke and mortality. *Conclusions:* Larger prospectively randomized trials evaluating the optimum timing of revascularization after emergent admission of carotid artery stenosis seem warranted. **Key Words:** Carotid artery stenosis—carotid endarterectomy—reperfusion—carotid stent—early medical intervention.

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Introduction

Carotid artery stenosis increases the risk of ischemic stroke. Revascularization reduces the risk of ischemic stroke in asymptomatic patients with carotid stenosis greater than 60% (Asymptomatic Carotid Artery Stenosis [ACAS] Trial) and symptomatic stenosis greater than 50% (North American Symptomatic Carotid Endarterectomy Trial [NASCET]).[1,2] Carotid endarterectomy (CEA) remains the gold standard treatment for carotid stenosis in these groups. Patients who are not candidates for CEA due to risk factors that increase surgical risk are considered for carotid artery stent (CAS) placement with angioplasty.

The factors influencing outcomes after emergent admission of patients with carotid artery stenosis that receive revascularization with CEA or CAS are yet to be fully elucidated. Randomized trials to compare CAS and CEA for the treatment of symptomatic carotid artery stenosis include the Endarterectomy versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis (EVA-3S) trial, the Stent-Protected Angioplasty versus Carotid Endarterectomy (SPACE) trial, the International Carotid Stenting Study (ICSS), and the Carotid Revascularization Endarterectomy versus Stenting trial (CREST).[3-6] EVA-3S was stopped prematurely because of excess mortality in patients receiving CAS.[3] The main criticism of this trial was operator experience, stent types, and that embolic protection devices were optional early in the trial.[7,8] SPACE was stopped after the second interim analysis due to recruitment and funding problems, failing to prove any difference between CAS and CEA.[4] CREST trial successfully enrolled 2502 patients and found that the overall effectiveness and safety of CAS and CEA were similar.[6] Although the full results of the ICSS trial are not yet available, an interim analysis revealed that at 120 days the stenting group had a significantly higher rate of any stroke and all cause death leading to the conclusion that CEA should remain the treatment of choice.[5]

In addition, there is conflicting opinion on the optimum time for intervention after an ischemic event. A study by Ois et al[9] documented the rate of recurrent stroke in symptomatic patients with greater than 50% stenosis was 20.9% in the first 72 hours, 6.7% between 72 hours and 7 days, and 3.7% between 7 and 14 days. Yet, the operative risks may outweigh the risk of recurrent stroke due to the risk of converting an ischemic cerebral infarction into a hemorrhagic one. Giordano et al[10] report significantly increased morbidity and mortality when intervening early and suggest an unstable situation immediately after stroke that contraindicates revascularization.

We extracted and analyzed data on the timing of, and treatment modality used for, nonelective symptomatic carotid revascularization using a national database. Our null hypothesis was that patients in both treatment groups would have similar clinical and economic outcomes independent of the timing of revascularization or presence of cerebral infarction at the time of revascularization.

Methods

Database Characteristics

We analyzed discharge data from the Nationwide Inpatient Sample (NIS), Healthcare Cost and Utilization Project, and Agency for Healthcare Research and Quality (Rockville, MD) from 2008 to 2011. This database represents approximately a 20% stratified sample of US nonfederal hospitals. Detailed information on the design of the NIS is available at http://www.hcup-us.ahrq.gov.

Inclusion/Exclusion Criteria

Patients were identified in the NIS database using a combination of International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnosis and procedure codes. Only patients with a nonelective admission were included. We required a primary diagnosis of carotid artery stenosis (with infarction: 433.11, without infarction: 433.10), along with CAS (00.63) or CEA (38.12). This eliminated approximately 60% of nonelective admissions with a primary diagnosis of carotid artery stenosis as they were discharged without a revascularization procedure. Only records that documented the day of the revascularization procedure were included. Cases were classified as "ultra-early" if the revascularization was performed within 48 hours of admission.[11] Cases performed on a subsequent day, up to the 14th day of admission, were termed "deferred". Patients treated beyond the 2-week period (n = 325) and patients who had multiple revascularization codes (n = 166) were excluded from this study to allow for homogeneity of the cohorts and better comparison between groups. Patients receiving mechanical thrombectomy (ICD-9-CM 39.74) on the day of the revascularization procedure were similarly excluded (n = 1825) as these patients represent a combined diagnosis of stenosis and thromboembolic occlusion, biasing the group treated with CAS toward a greater disease burden.

Patient and Hospital Characteristics

Patient factors included age, sex, primary payer, and day of admission. A modified Charlson Comorbidity Index was calculated for each patient using ICD-9-CM codes.[12] This index is a weighted-patient score designed to account for various comorbidities, including history of cancer, as well as cardiac, vascular, pulmonary, neurologic, endocrine, renal, hepatic, gastrointestinal, and immune disorders. Elixhauser measures, as provided in the NIS disease severity file, were used in place of similar Charlson measures and weighted accordingly, with the exception that mild liver disease was assigned 3 points.[13] Previous studies have demonstrated that slight modifications to the Charlson Index have minimal impact on the overall score.[14,15] Extracted hospital factors included teaching status and ownership.

Outcome Measures

The primary economic measures were hospital cost and length of stay. Hospital charges were converted to costs using the group weighted average cost-to-charge ratio. The costs were adjusted to 2013 levels using the inflation calculator provided by the Bureau of Labor Statistics