Restenosis after Carotid Artery Stenting Using a Specific Designed Ultrasonographic Protocol

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Background: Nowadays, the number of patients undergoing carotid artery stenting (CAS) is increasing rapidly, and these patients require *follow-up* to monitor the patency of the device and the potential development of an in-stent restenosis (ISR). *Methods:* Patients undergoing CAS at our institution underwent duplex ultrasound (DUS) at 6 months, 12 months, and yearly thereafter, using a prespecified protocol. Restenosis was defined as a more than 50% diameter-reducing stenosis. Patients with DUS-diagnosed restenosis underwent carotid computerized tomography angiography (CTA) to confirm the presence of ISR. The frequency of restenosis was calculated by Kaplan–Meier survival estimates and was compared during a 2-year follow-up period. Interactions between restenosis and baseline variables were assessed using odds ratio. *Results:* Between August 2007 and March 2012 were performed 100 procedures in 96 patients, with a median age of 72.9 years. The mean duration of *follow-up* was 29.2 months (±8.4). Restenosis occurred in 6 carotid arteries. The Kaplan–Meier estimate for the frequency of restenosis in 2 years was 6.0% and for severe restenosis was 3.0%. There were no occlusions. Diabetic patients seem to have a higher risk of ISR (OR = 3.23, 95% CI .55-18.9). Carotid CTA was in agreement with the degree of stenosis estimated by DUS in all cases. *Conclusions:* Our results, using a DUS protocol and a specific peak systolic velocity threshold, showed that the frequency of restenosis at 2 years after CAS is 6.0% and so that CAS is probably a durable revascularization procedure. We emphasize the diagnostic agreement achieved between DUS and carotid CTA. **Key Words:** Carotid—Doppler—restenosis—stenting—ultrasonography.

Introduction

Stroke is one of the most common causes of death and the leading cause of disability in Western countries.[1] One in 10 strokes is caused by atherosclerotic stenosis of the internal carotid artery (ICA) and 1 in 4 patients with recently symptomatic carotid stenosis will suffer a stroke within 2-3 years under medical treatment alone.[2,3] In the last decade, carotid artery stenting (CAS) has emerged as an alternative to carotid endarterectomy (CEA) for revascularization of stenotic carotid arteries. CAS has potential advantages over CEA like avoiding local complications (such as cranial nerves injuries) or reducing general risks of surgery such as myocardial infarction; on the other hand, recent trials showed a higher short-term risk of nondisabling stroke after CAS compared with CEA, which remains the "gold standard" treatment for carotid stenosis. The relative merit of CAS versus CEA remains a matter of considerable debate.

CAS induces permanent alterations of the physiological flow behavior. As reported by Vernhet et al,[4]

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Received July 28, 2013; revision received November 4, 2013; accepted December 1, 2013.

The authors declare to have no conflict of interests.

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1052-3057/$ - see front matter

http://dx.doi.org/10.1016/j.jstrokecerebrovasdis.2013.12.002

"the compliance mismatch between the native carotid artery and the stented segment, the positive arterial remodeling (stent expansion)[5,6] and the enhanced stiffness of the stent-arterial wall complex can induce alterations in compliance and in carotid hemodynamics and modifications of Peterson's elastic modulus of the stented vessel[7]; changes in wall shear stress can bring endothelial dysfunction ultimately leading to intimal hyperplasia and restenosis (negative arterial remodeling)[8]". So, in-stent restenosis (ISR) is a possible complication of the procedure and will become increasingly prevalent because of the increase in the use of carotid stents. Doubts regarding duration of CAS had been expressed based on exaggerated neointimal hyperplasia with coronary[9] and intracranial stents.[10] The reported incidence of carotid ISR is very variable,[11-14] depending on its definition and the duration of *follow-up* and has been reported to vary between 1% and 50%.[11,15,16] The durability of the revascularization procedure is of main importance because a restenosis could reduce the benefit of CAS in preventing stroke.

The role of duplex ultrasound (DUS) in ISR diagnosis is a matter of debate.[17-19] The stent material is highly reflective but it does not produce any significant artifact and DUS can provide image details of the stent and the vessel wall. A high incidence (32%) of more than 50% carotid ISR was reported[20] when applying the standard carotid DUS velocity criteria for nonstented carotid arteries. Thus, it is now accepted that ultrasound velocity criteria designed for native carotid arteries could overestimate stenosis degree in the presence of a stent because the "reduced compliance of the vessel wall could increase the peak systolic velocity (PSV)."[21] Therefore, use of an appropriate velocity threshold is central in the correct diagnosis of restenosis after CAS, but at the present time DUS criteria have not been standardized for patients undergoing CAS.

Here, we report the 2-year anatomic durability of CAS using a specific designed ultrasonographic protocol, comparing the DUS restenosis diagnosis with carotid computerized tomography angiography (CTA). Other important goal was to identify possible baseline characteristics affecting the risk of ISR.

Methods

The indication for CAS included severe carotid stenosis (>70% reduction of the lumen diameter, measured by DUS and confirmed by carotid CTA) and associated recent (<90 days) transient ischemic attack (TIA), nondisabling ocular or cerebral ischemic events; all asymptomatic ICA stenosis had undergone CAS as part of an experimental, single-center, nonrandomized protocol for patients with more than 80% carotid stenosis (measured by DUS and confirmed by carotid CTA) and unstable angina, who needed urgent coronary artery bypass grafting (CABG; data partially published).[22] Cardiac surgery was performed immediately after CAS; aspirin and unfractioned heparin were administrated during CAS, and clopidogrel was started after CABG. Written informed consent was obtained from all participants.

CAS was undertaken with a self-expanding nitinol stent (PRECISE), and distal protection devices (ANGIOGUARD) were used in all patients. Procedural success was defined as successful stent deployment with a residual diameter stenosis less than 30%, as determined by postprocedural quantitative carotid angiography.

DUS was done at 6 months, 12 months, and yearly thereafter and was undertaken by 2 certified neurosonologists, using a prespecified protocol: 8 samples from each side, 6 at 1- to 2-cm intervals along the common and internal carotid arteries, including proximal, medial, and distal stent, 1 from the external carotid artery, and 1 from the vertebral artery. When the 2 neurosonologists disagreed, the case was solved by consensus. The main goal was to analyze the frequency of restenosis, defined as more than 50% diameter-reducing stenosis or occlusion occurring at the treated carotid artery, initially identified at the DUS and confirmed by carotid CTA. We also defined severe restenosis as more than 70% diameter-reducing stenosis. Assessment of restenosis was done when the PSV at any location within the treated ICA reached or exceeded 2.0 m/s. The threshold for the diagnosis of severe restenosis (>70%) was 3.0 m/s PSV. Occlusion was established on DUS when no flow signal was detected at any location within the treated internal or common carotid artery. Results were collected in a prospective registry. The frequency of TIA/stroke was also assessed in each DUS visit. Patients with PSV greater than 2.0 m/s underwent carotid CTA to confirm the presence of ISR. Carotid CTA was performed in the caudocranial direction using a 64-detector Siemens scanner. Data acquisition consisted of 64 × .65-mm reconstructed slices of .6 mm, pitch of 1.2, and rotation time of .33 seconds. Subsequently, 70-85 mL of nonionic contrast material was injected at a rate of 4.5 mL/s after a bolus-tracking technique. The reconstructed images were processed with the TeraRecon workstation. The degree of stenosis on carotid CTA was measured using North American Symptomatic Carotid Endarterectomy criteria.[2] The in-stent least luminal diameter was identified by reviewing all sections through the stent and comparing them with the distal nontapering portion of the ICA identified by analyzing all sections distal to the stent.[23] Patients who had at least 1 follow-up ultrasound within 24 months were included in this analysis.

The frequency of restenosis was calculated by Kaplan–Meier survival estimates and was compared during a 2-year follow-up period. Interactions between restenosis and baseline variables were assessed using odds ratio. Analyses were done with SPSS (version 21.0).