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● *Original Contribution*

OPTIMAL ULTRASOUND CRITERIA FOR DEFINING THE SEVERITY OF VERTEBRAL ARTERY IN-STENT RESTENOSIS

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Abstract—The aim of the study described here was to establish ultrasound criteria for defining the severity of vertebral artery in-stent restenosis. A total of 197 patients with vertebral artery stents were enrolled in this study. Color Doppler ultrasonography was performed after stenting. Peak systolic velocity and end-diastolic velocity within the stent (PSV_{stent}, EDV_{stent}) and at the intervertebral segments were recorded. The ratio of the PSV at the origin to that at the intervertebral segment was calculated. With digital subtraction angiography as the reference standard, the optimal cutoff values of hemodynamic parameters identifying 50%–69% and 70%–99% restenosis were determined by receiver operating characteristic analysis. The optimal cutoff values of hemodynamic parameters identifying 50%–69% restenosis were $PSV_{stent} \geq 170$ cm/s, $EDV_{stent} \geq 45$ cm/s and PSV ratio ≥2.7, and those for 70%–99% restenosis were $PSV_{stent} \geq 220$ cm/s, $EDV_{stent} \geq 55$ cm/s and PSV ratio ≥4.2. In conclusion, color Doppler ultrasonography is a reliable method for monitoring patients with avertebral artery stents. (E-mail: dryanghua99@163.com) © **2015 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Vertebral artery, Stenting, In-stent restenosis, Color Doppler ultrasonography, Diagnostic criteria.**

INTRODUCTION

It is well known that severe (70%–99%) stenosis at the origin of the vertebral artery (VA) is the major cause of posterior circulation ischemia (Kim et al. 2005). Stenting is a popular treatment strategy for severe stenosis at the VA origin. However, the long-term outcome of stenting is largely affected by restenosis. A systematic review reported that the incidence of restenosis after extracranial VA stenting was as high as 30% at a mean follow-up of 24 mo (Stayman et al. 2011). Therefore, these patients require intensive follow-up monitoring for recurrence.

As a non-invasive, accurate and cost-effective method, color Doppler ultrasonography (CDU) is an ideal follow-up tool for VA origin stenting (Kantarci et al. 2006). In a previous study, we established the threshold velocities indicative of different degrees of stenosis at the VA origin (Hua et al. 2009). However, because of the altered compliance of the stent–artery complex (Lal et al. 2004; Vernhet et al. 2003), the degree of stenosis in the stented artery is overestimated when velocity criteria for native arteries are used (AbuRahma et al. 2008; Cumbie et al. 2008; Lal et al. 2008; Zhou et al. 2008). Therefore, it is essential to establish the ultrasound criteria for in-stent restenosis after VA stenting.

In this study, with digital subtraction angiography (DSA) as the reference standard, we assessed the hemodynamic parameters used at CDU to determine the optimal thresholds for different degrees of in-stent restenosis after VA stenting.

METHODS

Patients

The study protocol was approved by our institutional review board. All patients were fully informed of the procedure and signed a consent form. The study was conducted in compliance with Health Insurance Portability and Accountability Act (HIPAA) regulations. Our hospital is a referral center for cerebrovascular disease receiving about 1,000 to 1,200 outpatients per day and performing 350 to 400 ultrasound examinations per day.

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The hospital is specialized in the endovascular treatment of cerebrovascular disease and receives patients from all over China. Between 2009 and 2012, a total of 2,548 patients were treated by stenting of cerebral arteries, the majority of which were carotid arteries, but subclavian, vertebral and intracranial arteries were also included.

We retrospectively selected 197 patients (164 males, 33 females), with a mean age of 64.2 ± 9.0 y (range: 40–84 y), from 450 consecutive patients who underwent VA stenting for atherosclerotic (70%–99%) stenosis at the VA origin at our institute from January 2009 to December 2012. In our institute, which follows the Chinese diagnosis and treatment guideline of interventional radioneurology (Chinese Neurosurgical Society, Chinese Congress of Neurologic Surgeons and China Neurologist Association 2005), the indication for VA origin stenting therapy is severe (70%–99%) proximal VA stenosis, with symptoms of posterior circulation ischemia, recurrent attacks of posterior circulation stroke (the infarction area located in the area supplying the stenotic vertebral artery as diagnosed by computed tomography or magnetic resonance imaging) and no improvement after standard medical therapy for 3–6 mo. To be included in this study, patients had to: (i) have unilateral severe (70%–99%) stenosis at the VA origin diagnosed by CDU and confirmed by DSA; (ii) have undergone CDU examinations within 1–2 wk before stenting and within 1 wk after stenting; and (iii) have undergone follow-up examinations of the VA with CDU at 3, 6 or 12 mo after the stenting procedure. Patients with suspected ≥50% restenosis evaluated by CDU underwent DSA, which confirmed the occurrence of restenosis. The exclusion criteria were as follows: (i) severe (70%–99%) stenosis, occlusion or dissection of the contralateral VA and subclavian artery (which may overestimate the velocity of the ipsilateral VA); (ii) severe (70%–99%) stenosis or occlusion of the intracranial VA or basilar artery; (iii) severe (70%–99%) stenosis or occlusion of carotid artery system and opening of the posterior communicating artery; (iv) residual stenosis (defined as ≥20% luminal narrowing on angiography after the procedure); (v) stent occlusion caused by acute thrombosis after the stenting procedure; and (vi) other conditions, such as cerebral hemorrhage, detected by computed tomography and severe heart disease with low cerebral blood flow.

DSA and stenting procedure

The DSA and stenting procedures were performed by experienced neurosurgeons in the operating room. During DSA, when necessary, super selective angiography, rotated DSA or 3-D-DSA was used to view the suspected vessels. All VA stenting procedures were performed using a Neurostar Plus/T.O.P double C-arm angiography system (Siemens, Munich, Germany) according to the protocol described previously (Wang et al. 2009). Briefly, a 100-cm 6F guiding catheter (Cordis Envoy, Cordis Endovascular System, Hialeah, FL, USA) was positioned in the targeted VA at the C3–4 level. A 0.014-in. microwire (PT Graphix or PT2, Boston Scientific, Natick, MA, USA) was passed through the lesion. The tip of the wire was located at the C2–3 level. A balloon-mounted stent was then delivered over the microwire and positioned across the lesion. According to the North American Symptomatic Carotid Endarterectomy Trial method (NASCET Collaborators 1991), degree of stenosis were stratified as <50%, 50%–69% and 70%–99% stenosis and occlusion.

Color Doppler ultrasonography

All CDU examinations were performed by experienced ultrasound physicians (with more than 5 y of experience) according to the vascular ultrasound protocol previously described by Bendick (2005). A Philips ultrasound system (IU-22, Philips, Amsterdam, The Netherlands) equipped with a 3.0- to 9.0-MHz linear array probe and a 2.0- to 5.0-MHz curvilinear array probe was used to examine the intervertebral segment and the VA origin. In general, we first obtained the blood flow image of the intervertebral artery segment, then followed the blood flow back toward its origin and adjusted the angle of the probe beam to obtain an adequate Doppler angle for velocity measurement. The ultrasound parameters measured before the stenting procedure included the diameter of the narrowest lumen and peak systolic velocity (PSV) and end-diastolic velocity (EDV) at the origin (os) and intervertebral (iv) segments of the VA (D_{os}, PSV_{os}, PSV_{iv}, EDV_{os}, EDV_{iv}). The ratio of PSV at the origin to PSV at the intervertebral segment was calculated. Degree of stenosis was evaluated according to the criteria for VA origin stenosis published previously (Hua et al. 2009). Within 1 wk and at 3, 6 and 12 mo after stenting, CDU were performed to identify the occurrence of residual stenosis and restenosis, respectively. During follow-up examinations, the length and diameter of the stent, as well as the PSV and EDV within the stent (PSV_{stent} and EDV_{stent}), were also recorded. Similar to most VA stenting follow-up studies (Antoniou et al. 2012), stenosis with ≥50% luminal narrowing, including an occlusion within the stent, was considered restenosis. During the follow-up period, patients suspected of having ≥50% restenosis on the basis of CDU underwent DSA, and the occurrence of restenosis was confirmed.

Statistical analysis

The Statistical Package for Social Sciences (SPSS Version 22.0, IBM, Armonk, NY, USA) software was used for statistical analyses. Numerical values are expressed as the mean ± standard deviation. The paired