

# The role of advanced diagnostic technology in the selection of a patient with symptomatic but hemodynamically insignificant disease for carotid endarterectomy

Kristine Clodfelter Orion, MD, Jenna Ruppert, RDMS, RVT, Diana Call, RVT, Mahmoud Malas, MD, Kristen Piazza, PA-C, and Bruce A. Perler, MD, MBA, *Baltimore, Md*

**Current Level I evidence demonstrates no benefit for carotid endarterectomy in symptomatic patients with <50% carotid stenoses. However, unstable plaque morphology is increasingly recognized in the genesis of ischemic cerebral events. New advanced imaging technology, such as contrast-enhanced magnetic resonance angiography and ultrasound imaging, are emerging as important adjuncts in the evaluation of this patient population. We present a case where both modalities were beneficial in identifying plaque instability manifested by intraplaque hemorrhage and neovascularization in a patient with recurrent cerebral ischemic events and hemodynamically insignificant carotid disease. (J Vasc Surg Cases 2015;1:90-3.)**

Level I evidence derived from the North American Symptomatic Carotid Endarterectomy Trial<sup>1</sup> and the European Carotid Surgery Trial<sup>2</sup> established the role of carotid endarterectomy (CEA) for patients with symptomatic >50% internal carotid artery (ICA) stenoses. Conversely, these investigations demonstrated no benefit for CEA for symptomatic patients with <50% stenoses compared with medical management. We recently encountered a patient with a unilateral hemodynamically insignificant ICA stenosis who experienced recurrent cerebral ischemic events despite maximum medical therapy and without other potential causes. On the basis of magnetic resonance angiography (MRA) and contrast-enhanced duplex findings, we proceeded with CEA. This case illustrates that rarely one may encounter a patient with an unstable plaque in the absence of hemodynamic significance and who should be managed with CEA. The patient consented to publication of this report.

## CASE REPORT

A 72-year-old man was referred to vascular surgery by his neurologist after three separate cerebral vascular accidents. His

medical history was significant for coronary artery disease, hypertension, and hyperlipidemia. His first stroke was in 2007 and was manifested by right-sided weakness, slurred speech, and Wernicke aphasia. He received tissue plasminogen activator and he improved over the course of 3 months. He was found to have insignificant carotid disease. His second stroke occurred in January 2014 and was manifested by right-sided weakness and difficulty walking. Three months later in April, he experienced a third stroke with similar physical presentation. A carotid duplex examination at that time demonstrated bilateral <50% ICA stenoses.

The patient underwent a cardiology evaluation, with no obvious cardiac source found. He underwent conventional magnetic resonance imaging (MRI)/MRA evaluation, which revealed several strokes in the left middle cerebral artery (MCA) territory as well as in the left anterior communicating artery/MCA and MCA/posterior communicating artery watershed areas. Computed tomography angiography demonstrated calcified irregular plaque at both carotid bifurcations.

He then was referred for a repeat MRA using T1-weighted black blood images after gadolinium administration, which demonstrated a left carotid plaque with intraplaque hemorrhage (IPH), an enhancing fibrous cap, and an ulcer (Fig 1). This technique is designed specifically for the carotid to minimize the flow artifacts generated from recirculating flow in the bulb and uses a dedicated neck coil for carotid imaging.

He was referred for consideration of CEA. The patient's baseline neurologic examination consisted of mild dysarthria, 3/5 strength in his right arm, and 4/5 strength in his right leg. A repeat conventional duplex scan in our Intersocietal Accreditation Commission-accredited vascular laboratory revealed a <50% left ICA stenosis based on a peak systolic velocity of 104 cm/s, end-diastolic velocity of 13 cm/s, and an ICA/common carotid artery ratio of 1.0. Our diagnostic criteria for this nonsignificant ICA stenosis are: no spectral broadening with peak systolic velocity of <140 cm/s, end-diastolic velocity of <100 cm/s, and an ICA/common carotid artery ratio of <2.0. It also showed a suspicious primarily echolucent plaque with only the anterior surface being echogenic.

From the Division of Vascular Surgery and Endovascular Therapy, The Johns Hopkins Medical Institutions.

Author conflict of interest: none.

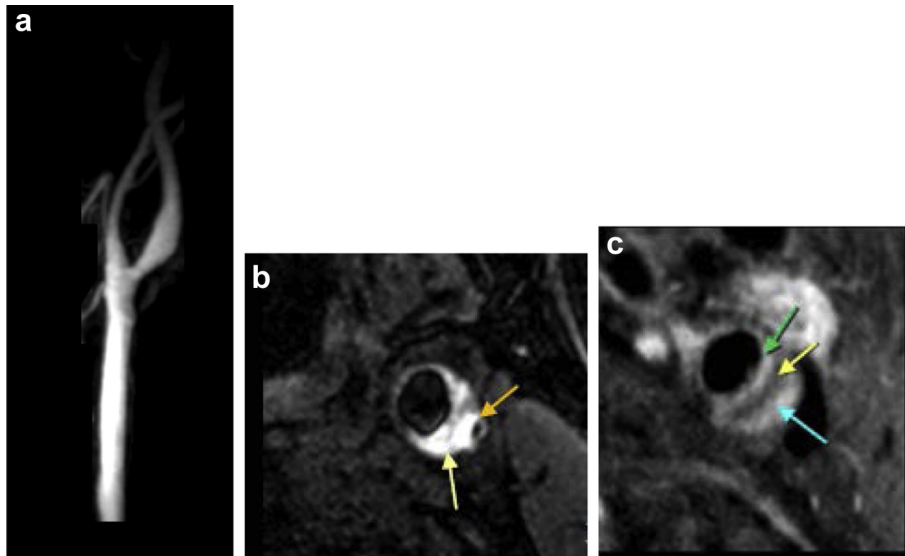
Reprint requests: Kristine Clodfelter Orion, MD, Division of Vascular Surgery and Endovascular Therapy, the Johns Hopkins Medical Institutions, Department of Surgery, The Johns Hopkins Hospital, 600 N Wolfe St, Halsted 668, Baltimore, MD 21287 (e-mail: [korion1@jhmi.edu](mailto:korion1@jhmi.edu)).

The editors and reviewers of this article have no relevant financial relationships to disclose per the Journal policy that requires reviewers to decline review of any manuscript for which they may have a conflict of interest.

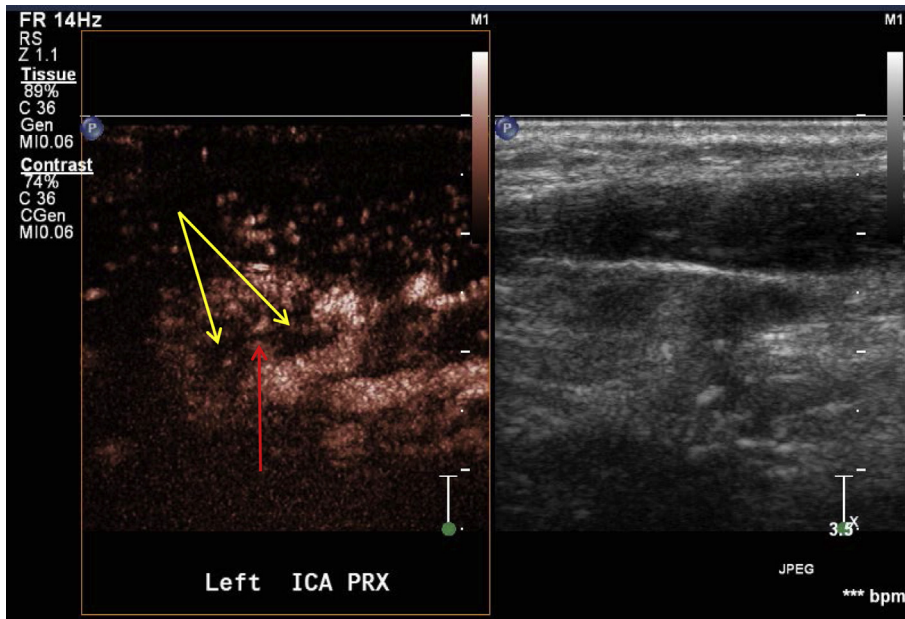
2352-667X

Copyright © 2015 The Authors. Published by Elsevier Inc. on behalf of the Society for Vascular Surgery. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

<http://dx.doi.org/10.1016/j.jvsc.2015.03.002>



**Fig 1.** Magnetic resonance imaging (MRI)/magnetic resonance angiography (MRA). **a**, Common, internal, and external carotid arteries. **b**, Axial reconstructions of three-dimensional high-resolution blood and calcium gradient-echo sequence. The *dark yellow arrow* indicates calcification, and the *light yellow arrow* indicates hemorrhagic plaque. **c**, Two-dimensional high-resolution cardiac-gated T1-weighted black blood MRI postcontrast. *Green* indicates fibrous cap, *light yellow* indicates the central lipid core, and *turquoise* indicates adventitial enhancement, a marker of neovascularization.

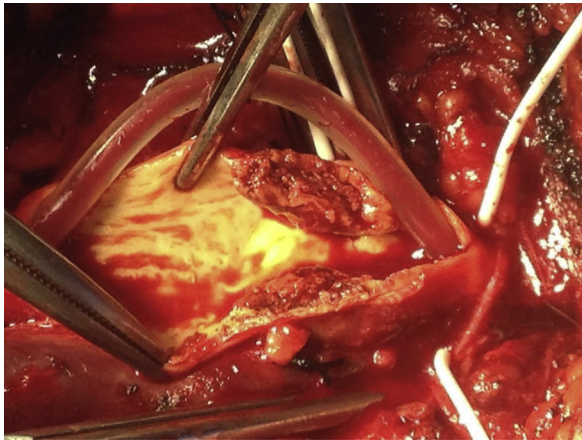


**Fig 2.** **Left**, Preoperative contrast-enhanced duplex scan of the internal carotid artery (ICA). The *yellow arrow* indicates echogenic plaque and lipid core, and the *red arrow* indicates the vasa vasorum and contrast-enhanced hemorrhage within the plaque. **Right**, Preoperative duplex scan without contrast enhancement.

He then underwent a three-dimensional contrast-enhanced carotid duplex examination after infusing OPTISON (Perflutren Protein-Type A Microspheres Injectable Suspension, USP; GE Healthcare, Waukesha, Wisc) in the preoperative holding unit. A

significant area of the vasa vasorum was illuminated within a large irregular plaque suggestive of IPH (Fig 2).

In the absence of other potential etiologies for his recurrent strokes, he consented to undergo left CEA. An uneventful left



**Fig 3.** Operative findings. Note hemorrhagic plaque.

CEA was performed in the operating room under general anesthesia with the use of an intraluminal shunt. The dissection was carried distally and proximally using sharp and blunt dissection. The carotid bulb was very soft and mildly dilated, with thinned adventitia and lipid-colored underlying plaque. We estimated the degree of stenosis approached 50%. Great care was taken to not disturb the bulb in the dissection. We identified a large lipid-laden hemorrhagic plaque (Fig 3).

A conventional CEA was performed, and the artery repaired with a Dacron (DuPont, Wilmington, Del) patch. A completion carotid duplex scan demonstrated normal flow velocities in the left common, internal, and external carotid arteries.

The patient was then awoken from general anesthesia. He exhibited temporary weakness and dysarthria, but this returned to his baseline  $\leq 15$  minutes. A neurology consult was requested, and they agreed that he did not have a temporary ischemic accident but that his symptoms were more consistent with “stunned brain” after CEA in a symptomatic patient. A head computed tomography scan did not show any additional findings. The remainder of his postoperative course was uneventful, and he was discharged home to his family the next day.

## DISCUSSION

The anatomic severity of a carotid stenosis has been the primary metric for defining the indications for CEA. Level I evidence supports intervention for symptomatic patients with a  $>50\%$  stenosis. Rarely, however, clinicians encounter patients with symptomatic disease and  $<50\%$  stenoses. Previous studies have indicated that echolucent plaques with abundant lipid and inflammatory cell content may be unstable and more vulnerable to rupture.<sup>3-5</sup> As a result of the decreased collagen formation and increased collagen degradation, the plaque’s thin fibrous cap is more easily disrupted by the increasing wall shear stress.<sup>6</sup>

To better identify these high-risk plaques, MRI has been used to evaluate plaque morphology. Specifically, IPH can be difficult to distinguish from a lipid core on conventional T1- or T2-weighted images.<sup>7</sup> Many have argued that the accuracy is improved when time of flight is added.<sup>8</sup>

However, Wasserman et al<sup>9</sup> of our institution demonstrated that the use of a mask sequence at 3 T revealed higher specificity compared by those with 1.5 T for IPH detection. Even further, ulceration can be easily distinguished from IPH with this technique. We found that technology very informative in this case. In fact, Altaf et al<sup>10</sup> prospectively analyzed the recurrence of ischemic events in patients with symptomatic mild stenosis (30%-49%) and found that during a 28-month period, MRI detected IPH in 25% of these patients. Similarly, among symptomatic patients with low-grade carotid stenoses, Yoshida et al<sup>11</sup> found ischemic recurrence in 44% of medically treated patients with a high-signal plaque during a 16-month period. When Wasserman et al<sup>12</sup> studied 47 patients in vivo, they demonstrated that IPH and neovascularity are both independently associated with previous cerebrovascular events.

Neovascularization is proposed to precede the development of increased intima-media thickness and therefore atherosclerosis at its earliest stage of development.<sup>13,14</sup> To further develop the recognition of neovascularity, contrast-enhanced ultrasound has recently emerged as a valuable advancement in carotid artery surveillance. The adjunctive contrast is used to identify neovascularization within the adventitial layer.<sup>13</sup> The contrast is well tolerated by patients, and because of the incorporation of three-dimensional imaging, the need for operator-dependent probe maneuvers to capture three planes is eliminated.

This technology clearly represents another tool to more accurately characterize plaque morphology. We believe it may provide another means of identifying patients with asymptomatic carotid disease who would be at increased risk of stroke and therefore candidates for CEA. One can only speculate, and further study will be required, to determine if this technology might allow better case selection of patients for carotid stenting vs CEA.

## CONCLUSIONS

Evidence is accumulating that plaque morphology indicative of plaque instability, including echolucency, ulceration, or the presence of IPH, should be considered when offering CEA to a patient with symptomatic low-grade stenosis. Although most patients who present with morphologic plaque features indicative of plaque instability tend to be severely stenotic, infrequently one will encounter a patient with hemodynamically insignificant disease without the conventional accepted anatomic indications for intervention but in whom an unstable plaque is etiologically responsible for stroke. The current case illustrates how contrast-enhanced MRA and ultrasound examinations can help identify appropriate candidates for carotid intervention in the absence of hemodynamically significant disease.

## REFERENCES

1. North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic

- patients with high-grade carotid stenosis. *N Engl J Med* 1991;325:445-53.
- European Carotid Surgery Trialists' Collaborative Group. Randomised trial of endarterectomy for recently symptomatic carotid stenosis: final results of the MRC European Carotid Surgery Trial (ECST). *Lancet* 1998;351:1379-87.
  - Giannoukas AD, Sfyroeras GS, Griffin M, Saleptsis V, Nicolaidis AN. Association of plaque echostructure and cardiovascular risk factors with symptomatic carotid artery disease. *J Cardiovasc Surg (Torino)* 2010;51:245-51.
  - Gronholdt ML, Nordestgaard BG, Wiebe BM, Willhjelm FE, Sillesen H. Echolucency of computerized ultrasound images of carotid atherosclerotic plaques are associated with increased levels of triglyceride-rich lipoproteins as well as increased plaque lipid content. *Circulation* 1998;97:34-40.
  - Gronholdt ML, Wiebe BM, Laursen H, Nielsen TG, Schroeder TV, Sillesen H. Lipid-rich carotid artery plaques may appear echolucent on ultrasound B-mode images and may be associated with intra-plaque haemorrhage. *Eur J Vasc Endovasc Surg* 1997;14:439-45.
  - Davies MJ, Richardson PD, Woolfe N, Katz DR, Mann J. Risk of thrombosis in human atherosclerotic plaques: role of extracellular lipid, macrophage, and smooth muscle cell content. *Br Heart J* 1993;69:377-81.
  - Fayad ZA. MR imaging for the noninvasive assessment of atherothrombotic plaques. *Magn Reson Imaging Clin N Am* 2003;11:101-13.
  - Yuan C, Mitsumori LM, Ferguson MS, Polissar NL, Echelard D, Ortiz G, et al. In vivo accuracy of multispectral magnetic resonance imaging for identifying lipid-rich necrotic cores and intraplaque hemorrhage in advanced human carotid plaques. *Circulation* 2001;104:2051-6.
  - Qiao Y, Etesami M, Malhotra S, Astor BC, Virmani R, Kolodgie FD, et al. Identification of intraplaque hemorrhage on MR angiography images: a comparison of contrast-enhanced mask and time-of-flight techniques. *AJNR Am J Neuroradiol* 2011;32:454-9.
  - Altaf N, Daniels L, Morgan PS, Auer D, MacSweeney ST, Moody AR, et al. Detection of intraplaque hemorrhage by magnetic resonance imaging in symptomatic patients with mild to moderate carotid stenosis predicts recurrent neurological events. *J Vasc Surg* 2008;47:337-42.
  - Yoshida K, Sadamasa N, Narumi O, Chin M, Yamagata S, Miyamoto S. Symptomatic low-grade carotid stenosis with intraplaque hemorrhage and expansive arterial remodeling is associated with a high relapse rate refractory to medical treatment. *Neurosurgery* 2012;70:1143-50.
  - Qiao Y, Etesami M, Astor BC, Zeiler SR, Trout HH 3rd, Wasserman BA. Carotid plaque neovascularization and hemorrhage detected by MR imaging are associated with recent cerebrovascular ischemic events. *Am J Neuroradiol* 2012;33:755-60.
  - Feinstein SF. Contrast ultrasound imaging of the carotid artery vasa vasorum and atherosclerotic plaque neovascularization. *J Am Coll Cardiol* 2006;48:236-43.
  - Byrnes KR, Ross CB. The current role of carotid duplex ultrasonography in the management of carotid atherosclerosis: foundation and advances. *Int J Vasc Med* 2012;2012:187872.

Submitted Feb 2, 2015; accepted Mar 1, 2015.