Practice Current

How do you manage patients with a “hot carotid”?

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Neurology: Clinical Practice December 2018 vol. 8 no. 6 527-536 doi:10.1212/CPJ.0000000000000562

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Abstract

Patients presenting with acutely symptomatic carotid stenosis (a “hot carotid”) are known to be at a high up-front risk of recurrent strokes. Uncertainties remain regarding the appropriate management of such patients in the acute period, particularly with respect to anti-thrombotic treatment as they await revascularisation with carotid endarterectomy (CEA) or angioplasty/stenting (CAS). Decision-making is further complicated when intraluminal thrombi are encountered on vessel imaging. Given these uncertainties, and the paucity of high-quality data in the literature, we sought expert opinion from around the globe on how to manage patients with a “hot carotid” as they await CEA/CAS, with a focus on anti-thrombotic treatment options. Similar questions were posed to the rest of our readership in an online survey, the results of which are also presented.

Carotid atherosclerosis causes about 15%–20% of ischemic stroke and TIAs,^{1,2} primarily via thromboembolism from ruptured plaque and sometimes from low-flow states.³ Carotid endarterectomy (CEA), or the alternative of carotid angioplasty and stenting (CAS), are used for revascularization of the symptomatic extracranial carotid artery.^{4,5} A meta-analysis of data from the European Carotid Surgery Trial (ECST) and North American Symptomatic Carotid Endarterectomy Trial (NASCET) demonstrated that the benefit of CEA is time-sensitive: greatest when performed within 2 weeks of the last ischemic event and falling rapidly with increasing delay.⁴ This urgency of treatment underscores the high upfront risk of recurrent strokes in patients presenting with acutely symptomatic carotid stenosis (a “hot carotid,” defined pragmatically for our purpose as a recent stroke/TIA [within hours–days of symptom onset] and thought to be etiologically related to the carotid artery stenosis).⁶ In a meta-analysis of data from 1,709 patients in 4 population-based studies, patients with large artery disease (likely a majority with hot carotids) had 37% of all early recurrent strokes within 7 days of the initial event, despite accounting for only 14% of the patients.⁷ In the Oxford Vascular Study, patients with TIA or minor stroke and $\geq 50\%$ symptomatic carotid stenosis had about a 20% risk of stroke in the first 2 weeks.⁸

The beneficial effect of single antiplatelet therapy for recurrent stroke prevention is well-established.⁹ During the last 20 years, major advances have been made in medical therapy for stroke prevention, including other antiplatelets like clopidogrel, statin therapy (not available when NASCET and ECST were recruiting), as well as antihypertensive agents, raising questions about what should constitute “best medical therapy” for stroke prevention, including in those patients awaiting CEA/CAS. The Clopidogrel in High-Risk Patients with Acute Nondisabling Cerebrovascular Events (CHANCE) and Platelet-Oriented Inhibition in New TIA and Minor Ischemic Stroke (POINT) trials have demonstrated the added benefit of dual antiplatelet therapy (DAPT) with clopidogrel and aspirin compared to aspirin alone when used for 21 and 90 days, respectively, in a broad population of patients with TIA or minor stroke, with most of the recurrent events occurring within the first week.^{10,11} Patients with hot carotids were mostly excluded from these

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Funding information and disclosures are provided at the end of the article. Full disclosure form information provided by the authors is available with the full text of this article at Neurology.org/cp.

trials by design. Trials of intracranial atherosclerosis like the Warfarin-Aspirin Symptomatic Intracranial Disease Trial (WASID) and Stenting and Aggressive Medical Management for Preventing Recurrent Stroke in Intracranial Stenosis (SAMMPRIS) have respectively shown that warfarin is associated with higher adverse events with no benefit over aspirin and that aggressive medical management with DAPT in addition to statin therapy and management of hypertension is associated with a low risk of recurrent events (which was lower than the aspirin arm of WASID).^{12,13} The generalizability of these findings to patients with cervical carotid atherosclerosis is unclear. Uncertainties therefore remain regarding the optimal antithrombotic regimen for hot carotid patients, particularly as they await revascularization with CEA/CAS, with the key tradeoff being between optimizing recurrent ischemic stroke prevention vs minimizing hemorrhagic risk within infarcted brain.

There is observational evidence that early DAPT may be associated with a reduction in recurrent events and spontaneous embolization prior to CEA, without a significant increase in major perioperative bleeding complications.¹⁴ However, a recent systematic review and meta-analysis¹⁵ of 7 observational studies and 3 randomized controlled trials (RCTs)¹⁶⁻¹⁸ reporting comparative outcomes of dual vs single antiplatelet therapy in CEA/CAS found that DAPT demonstrated advantages in patients with TIA (but not stroke), only in patients undergoing CAS, based on only 150 total procedures from a pooled sample of 2 RCTs. There were no differences in stroke/TIA/death incidence between single and dual antiplatelet therapy in the setting of CEA, based on a larger pooled sample of 36,881 procedures, but with only 100 cases from a single RCT and the rest from observational studies. There was significantly increased major bleeding and neck hematoma with DAPT in patients undergoing CEA. The quality of evidence for each outcome was deemed to be moderate or low, underpinning the need for further research on this topic. Whereas some studies have used non-contemporary agents like ticlopidine,¹⁷ newer antiplatelet agents like ticagrelor have not been studied for this indication.

Decision-making is further complicated when intraluminal thrombi (ILT) are encountered on vessel imaging, the management of which is clouded in additional uncertainty.^{19,20} Uncertainty about the optimal antithrombotic regimen is further heightened when one considers the possibility of combining or substituting antiplatelet agents with preoperative and perioperative anticoagulation, including a variety of options, namely heparin, warfarin, and direct oral anticoagulants, all of which carry their own unique balance of risks vs benefits.

Given these uncertainties, and the paucity of high-quality data in the literature, we sought expert opinion from around the globe on the question of how to best manage patients with a hot carotid as they await CEA/CAS, with a focus on antithrombotic treatment options. We acknowledge that practice patterns and traditions can become established in medicine even in the absence of evidence, and adoption of such paradigms by

For a long time in Calgary, we have been using dual aspirin and clopidogrel therapy in these patients. We load them in the ER if we identify significant carotid stenosis with CTA acutely. (M. Hill)

physicians can prevent them from recognizing their own fallibility. On the other hand, we sought to better elucidate existing expert perspectives on this topic to identify areas of agreement and disagreement that could help clinicians critically examine and refine their own practice patterns, in addition to potentially informing further studies in this area.

Expert opinion

Questions were posed to experts from 3 different continents, representing differing medical systems and patient populations. The following summary of their responses addresses their preferred imaging and revascularization approaches for patients with a hot carotid, their preferred antithrombotic regimens in these patients, and clinical or imaging characteristics that influence their management decisions. Similar questions were posed to the rest of our readership in an online survey using a representative case (appendix e-1, links. www.com/CPJ/A70 for case and multiple-choice questions), the results of which are presented following the expert commentaries.

In alphabetical order:

Michael Hill, MD, MSc, FRCPC (Canada)

Preferred imaging modality

My preferred imaging modality in acutely symptomatic patients is CT/CT angiography (CTA). Based on this routine imaging, we can not only rapidly identify patients with significant carotid stenosis, but can also have great anatomic insight into key characteristics like the presence of non-occlusive thrombus on top of a plaque, a carotid web,^{21,22} dissection, or old pseudoaneurysm, and so on. There is the known limitation of interpreting CTA in patients with heavy calcification. In that setting, if there appears to be a tight stenosis, I would probably favor revascularization anyway. Using an additional imaging modality like ultrasound in that setting is not always helpful as it can run into similar challenges.

Preferred revascularization procedure

Based on the data we have from the acute carotid stenting trials, I favor CEA, when that is possible. In Calgary, we were involved in the Carotid Revascularization Endarterectomy vs

Stenting Trial (CREST)²³ and whereas the inclusion of MI in the combined endpoint of CREST was controversial, when stroke and death are considered, CEA is superior. However, timing is important, so if there is going to be a delay to CEA on the order for weeks for example, and CAS can be arranged sooner, it is better to do CAS. In other words, the differences between the 2 techniques are not so large that you can afford to delay acute intervention. There are technical situations in which CEA appears to be superior to CAS, such as patients with aortic arch calcifications, very tight stenosis, or those who cannot have DAPT (e.g., cancer patients with upcoming surgeries and bleeding risks) or who are unwilling to quit smoking (restenosis risk). There are other situations in which CAS may be safer than or superior to CEA, such as in patients who have a contralateral tight stenosis or occlusion, a higher location of stenosis, or an isolated circle of Willis.

With respect to timing, at our center, the angiography laboratory is controlled by the interventionalists and there is a greater degree of freedom to get urgent patients into the laboratory due to less demand from other conditions. On the other hand, the operating rooms as a resource are shared with other surgical specialties and there can be delays for CEA; but if we need to get urgent carotid surgery we can get that without too much difficulty. We can generally get CEA/CAS done within a couple of days and sometimes even on the same day for minor events. For TIA or minor stroke, the ideal timing would be within a day. For a large infarct, the ideal timing may be even a few weeks later. The timing of surgery in the setting of an uncertain anatomic lesion remains poorly established. If the plaque on imaging looks unremarkable and smooth, then our surgeons do not mind operating early; if the plaque looks ugly and ratty and ulcerated or there is thrombus on it, then there is worry about operating hyperacutely because of a perceived higher risk of ipsilateral stroke. To me, plaque appearance itself is not relevant to the timing of surgery; biologically it may be a contributor but at present I do not have any compelling evidence to support a change in timing. However, with plaques that have associated thrombi, I would delay the procedure until further reassessment (see below).

We generally manage patients with symptomatic carotid stenosis <50% medically, but we have had a couple of younger patients who have had recurrent events despite stenosis of 30%–40%, in which case we have operated on them. The decision to operate has been driven by the recurrent events and not by plaque characteristics like ulceration.

Approach to antithrombotic management

For a long time in Calgary, we have been using DAPT with aspirin (81 mg after 160 mg load) and clopidogrel (75 mg after 300 mg load) in these patients, in large part because of our experience with the Fast Assessment of Stroke and Transient Ischaemic Attack to Prevent Early Recurrence

(FASTER) trial.²⁴ FASTER was ultimately a pilot trial and nonconclusive statistically, but we have been proven to be correct with the evolution of CHANCE and POINT.^{10,11} We load patients with aspirin and clopidogrel in the emergency room if we identify significant carotid stenosis, based on routine CT/CTA acutely.

Some of our surgeons are more reluctant to operate on patients on DAPT, based particularly on the CURE study²⁵ in coronary disease, which found that patients on DAPT with aspirin and clopidogrel had a higher risk of bleeding at the time of surgery. This reluctance is based on the reasonable concern of increased risk of a perioperative wound hematoma or hematoma on the carotid with DAPT. I am not sure that it truly makes a difference, and in fact some surgeons will operate with DAPT on board.

In choosing an antithrombotic regimen, I have never made a distinction based on imaging features like whether a plaque was ulcerated, or demographic features like age. Bleeding risk would be the only point to consider; if the patient has an underlying bleeding diathesis or something like an active (or recently active) duodenal ulcer, that would reduce my enthusiasm for DAPT. If the patient comes in already on aspirin, I would still give them DAPT. Although there has been some theoretical discussion about the concept of aspirin resistance and that maybe in some patients taking higher doses of aspirin you overcome the potential biochemical aspirin resistance, the bedside tests for platelet function do not seem to correlate well with clinical events. Patients with symptomatic stenosis <50% also receive DAPT.

Approach to ILT

One of the things we are all interested in as a group is whether we should be anticoagulating some of these patients. Is there a subset—for example, those with apparent nonocclusive thrombus—who might be good candidates for anticoagulation, such as with simple unfractionated heparin, before moving on to CEA? There are some preliminary post hoc data from NASCET that suggest that if there is evidence of free-floating thrombus then that might carry a poor prognosis at the time of surgery, but these are old data, many of the patients were operated on much later from stroke onset than they are today, and the degree of antithrombotic usage was less. It is a false argument in some ways to say you do not want to operate because you think there is fresh thrombus there on imaging when in fact there is always fresh thrombus on every single plaque when examined ex vivo pathologically. My rough guess is that it is likely a good idea to provide 2–4 days of medical treatment to cool off a hot plaque and then proceed to CEA. For example, there are times when someone appears to have quite a tight carotid lesion with some fresh thrombus, but when you anticoagulate them, 5 days later it is only a 30% lesion, which could then be managed medically without surgery. It would be helpful to have some prospective studies to try to

understand what people do and then figure out whether there is an opportunity to intervene and do studies on some of these patients.

Typically, I use aspirin and an unfractionated IV heparin drip, and then the duration of therapy would be guided by repeat imaging in 5 days to look for thrombus resolution or change. The majority of times, there is resolution or partial resolution, whether due to the treatment or due to natural history. The timing of the patient's surgery in relation to all this varies depending on the surgeon. If it has been 8–10 days and the thrombus has not resolved, then I give DAPT and operate, or if the patient has been event-free, implying that this is not perhaps fresh thrombus, I might put the patient on aspirin or DAPT and send him or her home. If recurrent events have occurred, then this suggests a more malignant stenosis, supporting revascularization. The decision will also depend on the nature of the event (TIA/minor stroke vs larger stroke, as discussed above). If the thrombus has not resolved with aspirin and heparin by the second imaging, that does not necessitate a third scan and I might proceed with surgery at that point. The second scan is primarily intended to decide whether surgery is still indicated, given that thrombus resolution might reveal a lesser extent of stenosis that could be medically managed. At this point, we have not been performing magnetic resonance plaque or thrombus imaging, which may help; one would expect the signal characteristics on high-resolution MRI of the carotid to be different for plaque vs associated thrombus. Complementary information on thrombi may be provided by ultrasound imaging, but I do not typically use it for this indication.

Keith W. Muir, MD, FRCP (United Kingdom) **Preferred imaging modality**

My preferred investigation of these patients typically involves a CT or MRI brain and CTA. We have less access to Doppler ultrasound and therefore CTA has been the preferred modality to establish the degree of carotid stenosis in the last 10 years.

Preferred revascularization procedure

My preference is CEA. We have good and fast surgical input and we have not found cases where we think there is a clear indication for CAS over CEA. However, it is important to note that our understanding of TIA and stroke has changed since the time of the CEA trials: we did not yet appreciate the very high short-term risk and so patients were randomized within 6 months of the event instead of hyperacutely, modern statin therapy and DAPT were not used, and hypertension was not well-managed.

With respect to timing, if the patient has come in with a minor stroke or TIA and is a high-risk patient, imaging would usually be completed within 24–48 hours, and if the patient has a stenosis potentially eligible for CEA, he or she would usually be reviewed by vascular surgery on the same

or next day. CEA is usually then performed in eligible patients within 24–72 hours depending on the time of the week. For those with larger strokes where there are residual deficits, that time scale is a bit more variable depending on the patient's individual condition (still usually within a few days as we do not require full resolution of deficits), and for outpatients it is a little bit longer because it will typically take some time for patients to present first to their general practitioner and then be referred onwards. The CEA timing is ultimately a joint decision among the surgeon, the stroke team, and the patient, so we need people to have capacity to understand what is involved such that they would be able to give informed consent.

Approach to antithrombotic management

The default preference for poststroke or TIA management would be aspirin 300 mg daily for 14 days or until discharge per the International Stroke Trial (IST),²⁶ which is easily implemented. Patients often initially get a plain CT head and a CTA later, so most patients start on aspirin initially. Once they have had a CTA (usually within 24 hours) identifying significant carotid stenosis or irregular plaque or tandem intracranial disease (irrespective of the degree of stenosis), I then initiate DAPT, adding clopidogrel to the aspirin. There may be some delay in the formal measurement of the degree of stenosis from radiology, so we will often initiate DAPT based on our somewhat qualitative assessment. Patients continue this right up until the day before surgery, and then resume it fairly soon afterwards, with some variation in resumption timing. I think most vascular surgeons are comfortable with patients being on DAPT. I would continue DAPT for 30 days before reverting to monotherapy, usually with clopidogrel 75 mg indefinitely. The Clopidogrel and Aspirin for Reduction of Emboli in Symptomatic Carotid Stenosis (CARESS) trial was fairly persuasive by demonstrating that DAPT is effective at reducing platelet emboli as detected by transcranial Doppler (TCD).²⁷ It would be helpful to have an easily applicable system of TCD monitoring to determine when emboli have flared or settled, allowing for a more individualized approach than what we currently do based on a single snapshot of the arteries.

Other factors may modify the approach; for example, if the patient has additional small vessel disease, and if I am uncertain about the mechanism, I may defer starting DAPT until I have better clarity such as through an MRI to look at the pattern of ischemic change. If the mechanism of the event seems likely to be large artery embolism, then even with some background small vessel disease and markers like microbleeds, I would probably favor DAPT. However, if the mechanism is unclear and it could be a small vessel etiology, the presence of some atherosclerosis would not make me start DAPT and I would favor aspirin. Swallowing in the acute poststroke phase may be an issue with giving DAPT, as might renal insufficiency. Systemic bleeding problems would promote caution, but if the patient just has a milder history of

poorly defined gastric upset, then I would view the risk period for DAPT as being relatively short and cover the patient with a proton pump inhibitor in the meantime. The patient having previously been on aspirin would not change my approach; the occurrence of an event on aspirin does not mean the treatment was ineffective as we cannot know what other events were prevented.

There is a high prevalence of coronary artery disease in the population of patients with carotid disease, so a certain proportion of these patients are already taking DAPT or have indications for it, like coronary stents. I do not see any biological plausibility for the degree of stenosis to be the sole determining factor for whether or not a given large artery is responsible for embolism, so if the patient has irregular ulcerated plaque and no alternative source with what looks like an embolic event, I would still put him or her on 30-day DAPT with high-dose statins even if the degree of stenosis is <50%. However, there is no evidence at present for CEA in these patients, as the original trials were performed using the degree of stenosis as the main guiding parameter. As for CAS in such patients, if the stent is designed to restore flow, it makes more sense in a high-grade stenosis rather than a non-flow-limiting mild stenosis, and there may be an increase in disease at either end of the stent. Placing a stent over an acutely thrombotic plaque also seems risky.

There is recent evidence from the Acute Stroke or Transient Ischemic Attack Treated with Aspirin or Ticagrelor and Patient Outcomes (SOCRATES) trial that ticagrelor might have some advantages in patients with carotid disease,²⁸ but as stroke specialists we have been biased by having only seen complications of ticagrelor rather than the cardiovascular prevention benefits previously seen by our cardiologist colleagues.

Approach to ILT

Determining what is truly ILT is difficult; one person's stenosis is another person's thrombus. For example, you might be looking at hemorrhage into the wall of the stenotic vessel, which may have some density to it. If I am sure that it is a thrombus hanging free in the lumen, I would tend to use anticoagulation rather than DAPT, and defer surgery until we have a less acute image of the vessel wall to better assess the degree of underlying stenosis. After anticoagulating for a period of a few weeks, the vessel may go from apparent 90% stenosis to 30% and the clot often disappears. I prefer to use low molecular weight heparin, and potentially transition to one of the oral anticoagulants like warfarin. I would continue to use heparin if there are potential hemorrhagic risks or if the patient might go for CEA soon. I would probably reimaging with CTA 4–6 weeks later. Factors like the patient's general health and vascular vs hemorrhagic risk factors may influence earlier vs later review. The longer you wait, the less benefit there is with CEA, but this process is also evaluating whether CEA is the most appropriate option for this patient. If the

thrombus is still present on reimaging, this triggers another conversation with the radiologist and surgeon. If I am still confident that this is an ILT, then our vascular surgeons may sometimes operate, but more commonly, there is less certainty about what we are actually seeing and so there may be greater impetus to operate depending on the passage of time.

P.N. Sylaja, MD, DM, FRCP, FESO (India)

Preferred imaging modality

We prefer to image these patients with CTA and MRI with diffusion-weighted imaging if the CT does not show any infarcts. Sometimes patients referred from other centers come with an MRI angiography already performed; however, if the quality is poor, we will obtain a CTA or a carotid Doppler.

Preferred revascularization procedure

Our standard of care is CEA. Only patients who are not considered candidates for endarterectomy are taken for CAS—these include patients with significant cardiac or lung disease. Patient preference is also taken into account. Many patients are reluctant to have surgery, especially if they have only had a TIA or minor stroke and have recovered from their deficits and have only 50%–69% stenosis. Overall the data are not very clear for benefit of CEA in patients with moderate stenoses when they present after 2 weeks. If we find they have high-risk features like an ulcerated plaque, or recurrent events, then we are more enthusiastic for revascularization procedures in this group. However, we often tend to see patients who present 2 months or more after their event, and if the patient only had a TIA and no recurrent events, we then prefer to keep them on medical treatment alone given the uncertain benefit of surgery at that point. For patients with <50% carotid stenosis per CTA, we do not provide revascularization procedures.

Patients who present acutely may wait between 1 and 5 days, but patients who are referred to our service a month or more after their event usually wait 2–4 weeks.

Approach to antithrombotic management

We would ideally prefer to keep these patients on DAPT (aspirin and clopidogrel). Previously, we had done CEA on patients with dual antiplatelets on board especially when they presented within 24–48 hours, but some of these patients developed a wound hematoma, so the surgeons are now particular about stopping clopidogrel 4–5 days prior to the procedure, and then by the fifth day they will take the patient for CEA. In patients who have had a single ischemic event, even if there is an ulcerated plaque or associated thrombus, we feel comfortable taking off the clopidogrel pre-CEA. But if they have had a recurrent TIA/stroke on medical treatment, then we do not take off the clopidogrel.

Patients who are taken for CAS are continued on DAPT in the perioperative period. In patients with significant

hemorrhagic transformation of the infarct, we tend to take them for CAS after 3 weeks.

We have encountered situations where patients had recurrent events even when on DAPT. In such cases, we have switched these patients from clopidogrel to heparin (in addition to aspirin) and then stopped the heparin 12 hours prior to surgery. If patient is having recurrent hemodynamic events or progressing stroke, we will take them earlier for CEA.

Patients who are on single antiplatelet therapy (aspirin typically) and going for CEA will continue this lifelong. Continuation of DAPT in these patients beyond the procedure depends on various factors. Most of these patients have concomitant significant coronary artery disease, so most of the time we leave it to the cardiologist to decide when they should stop the clopidogrel. Patients with <50% carotid stenosis are given DAPT for 3 months and then switched over to single antiplatelet therapy.

Approach to ILT

In patients with ILT, particularly in the carotids, we do not know whether there is benefit in keeping them on heparin in addition to aspirin. If this is seen on CTA, then we perform Doppler imaging to determine whether the thrombus is mobile.

We favor keeping those with a mobile thrombus on heparin plus aspirin, and we prefer to wait for 2 weeks to reimage them before performing CEA. In these patients, we usually prefer CEA over CAS. If the thrombus is not mobile, then we treat as per our routine practice (as discussed above).

Lower/middle-income country challenges

Some families are reluctant for the patient to undergo a surgery and they can be difficult to convince, especially if the patient is older, and had a single TIA or minor stroke. Families often do not want to be aggressive in their management. Financial barriers to treatment used to be a much larger issue in the past (although government hospitals provide free-of-cost health care facilities, in practice, Indian patients are often served in the private health care sector with expenses paid out of pocket rather than through private insurance, contributing to a high financial burden for families).²⁹ However, in the last few years, health care assistance being provided has improved markedly and CEA and CAS costs are covered by the government. For secondary stroke prevention, financial barriers do not come into play for medical management, as most of the noncommunicable disease clinics provide aspirin, clopidogrel, and statins. But the major challenge is adherence to medical treatment. Most of our patients stop treatment after 3–6 months, and then their risk factor control is very poor. Currently, through the Indian Stroke Clinical Trial Network (InSTRUCT) funded by the Indian Council of Medical Research, we are conducting a semi-

interactive stroke secondary prevention package trial for recurrent stroke prevention in patients with ischemic stroke.

Preliminary survey results (October 12, 2018): Section Editor: Luca Bartolini, MD

We collected a total of 384 complete responses since September 6, 2018, primarily from board-certified neurologists (62%) who have been in practice for less than 10 years (44%); 24% of respondents were trainees, 5% were advanced-care providers, and 32% more senior neurologists who have been in practice for more than 10 years.

The majority of survey-takers practiced in a hospital-based setting (82%) outside of the United States (73%). Consistent with previous surveys, the most represented countries were India (10%), Brazil (10%), Spain (9%), Germany (7%), and Italy (7%). Within the United States, the 3 states that collected more responses were New York (14%), Florida (10%), and California (8%).

The clinical case was a 65-year-old man presenting with acute onset of right-sided hemiparesis lasting several hours who is found to have 80% left-sided extracranial internal carotid artery stenosis. For vascular imaging, responders chose CTA (71%) and Doppler ultrasound (57%), while a minority opted for MRA (14%) or digital subtraction angiography (11%).

While CEA was the procedure of choice for 69% of survey takers, almost one-third chose CAS, primarily outside of the United States (figure 1, A and B).

Uncertainty prevailed, both within (figure 2A) and outside the United States (figure 2B), regarding the timing for carotid revascularization: 38% chose 3–7 days, 36% more than 7 days, and 27% 2–3 days. While waiting for the procedure, most respondents chose aspirin (44% low-dose and 42% high-dose) and clopidogrel (44%), either alone or in combination. The majority of survey takers opted for heparin (36%), clopidogrel (25%), or low-molecular-weight heparin (23%) in the presence of an intravascular thrombus.

Most respondents would feel more inclined to add additional agents beyond a single antiplatelet and statin if the patient had multiple TIAs (58%), was already on antithrombotic (45%), or planned procedure was CAS instead of CEA (35%). Imaging features that would increase the likelihood of additional agents were intraluminal thrombus (59%), ulcerated plaque (54%), and microembolic signals on Doppler (48%).

IV tissue plasminogen activator or endovascular therapy more than 24 hours prior would lower the likelihood of additional agents for 41% of responders combined. The same was true for planned CEA vs CAS (22%) or either procedure

Figure 1 Interactive map shows preferred revascularization procedure for patients with significant symptomatic carotid stenosis

(A) In United States. (B) Outside United States.

planned within 2 days (21%), presence of microbleeds on MRI (59%), lesser degree of stenosis (36%), or larger (35%) or lacunar (26%) stroke on imaging.

The accompanying editorial by Dr. Seemant Chaturvedi³⁰ helps to put these results into context and highlights the critical need for new treatment trials of patients with a hot carotid, since available data from NASCET date back to

1991. We are hopeful that initiatives such as this international survey will facilitate this endeavor.

Discussion

To the practicing neurologist, the management of the patient with a hot carotid is complicated by the absence of

Figure 2 Interactive map shows timing for carotid revascularization after symptomatic event

(A) In United States. (B) Outside United States.

definitive evidence relating to the preoperative and perioperative period, despite the high volume of CEA/CAS and stroke prevention-related literature. The 3 experts interviewed all preferred CTA for primary vascular imaging in hot carotids and CEA for carotid revascularization. Complementary information about associated thrombi, such as their mobility, may be provided by

ultrasonography. The 3 experts also noted the benefit of DAPT in preventing recurrent events in this population. They recognized concerns expressed by surgeons regarding increased bleeding risk in patients with DAPT undergoing CEA but were also aware of varying preferences of surgeons in this regard (some surgeons were comfortable operating on DAPT while others were not).

They often reverted to single antiplatelet therapy (aspirin) during the perioperative period in patients offered CEA, while acknowledging the uncertainty of evidence in this area, and differed in the duration that they would hold off DAPT. They would generally avoid revascularization procedures in patients with <50% stenosis but differed in their approach to patients with ulcerated plaques. They generally favored anticoagulation in addition to aspirin in patients with ILT but differed in the type and duration of anticoagulation and the extent to which they would defer/reevaluate revascularization procedures in the interim. Differences were also seen in the dose of aspirin used (81 vs 300 mg), with implications for the relative safety and efficacy of aspirin in patients with different body sizes.³¹

In addition to providing some guidance on areas of relative agreement on hot carotid management for clinicians, the areas of relative disagreement identified by our survey and expert interviews may help inform the design of future RCTs. Such RCTs will need to be based on an understanding of the practice patterns and attitudes of physician stakeholders in order to successfully recruit patients and help resolve practical uncertainties.

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Michael Hill, MD, MSc, FRCPC, is a stroke doctor from Calgary. Dr. Hill is Professor for the Departments of Clinical Neurosciences, Community Health Sciences, and Medicine and Radiology, University of Calgary. He is Director of the Stroke Unit for the Calgary Stroke Program, Foothills Hospital at Alberta Health Services. He trained at McGill University, University of Ottawa, University of Toronto, and finally at the University of Calgary, where he joined the faculty in 2001. He served as Associate Dean (Clinical Trials) at University of

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Author contributions

A. Ganesh was involved in the conception, writing, and revising of the paper as well as interviewing of expert opinion contributors. J.H. Wong was involved in the conception and revising of the paper. B.K. Menon was involved in the conception, writing, and revising of the paper.

Acknowledgment

The authors thank Lori Herard and Dr. Malavika Varma for assistance in transcribing expert interviews and Drs. David J.T.

Campbell, Abdulaziz Al-Sultan, and Ravinder-Jeet Singh for assistance in formulating questions posed to experts.

Study funding

This study was funded by a Heart and Stroke Foundation Professorship held by Dr. Bijoy K. Menon, the senior study investigator.

Disclosure

A. Ganesh is a member of the editorial team of the Resident & Fellow Section of *Neurology*[®]; has received speaker honoraria from The Meritas Seminar Series, Oxford; has served as a consultant for Adkins Research Group and Genome BC; has received research support from The Rhodes Trust and Wellcome Trust; and holds stock/stock options from SnapDx, TheRounds.ca, and Advanced Health Analytics (AHA Health Ltd.). J.H. Wong reports no disclosures. B.K. Menon has received travel honoraria from Penumbra Inc.; is a member of the Steering and Executive Committee for ESCAPE trial (received support from Covidien Inc.) and is Site Principal Investigator for SOCRATES trial (sponsored by Astra Zeneca); is a member of the Editorial Board of *Stroke*; is a member of the Program Committee and lead for the acute nonendovascular section of the International Stroke Conference; has received research support from Canadian Institute for Health Research, Heart and Stroke Foundation of Canada, Alberta Innovates Health Solutions, Hotchkiss Brain Institute, and Faculty of Medicine, University of Calgary; and has a patent pending on systems of triage in acute stroke. Full disclosure form information provided by the authors is available with the full text of this article at Neurology.org/cp.