# Carotid Revascularization: Current Practice and Future Directions

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# Abstract

#### **Keywords**

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Carotid stenosis is responsible for approximately 15% of ischemic strokes. Carotid revascularization significantly decreases patients' stroke risk. Carotid endarterectomy has first-line therapy for moderate-to-severe carotid stenosis after a series of pivotal randomized controlled trials were published almost 30 years ago. Revascularization with carotid stenting has become a popular and effective alternative in a select subpopulation of patients. We review the current state of the literature regarding revascularization indications, patient selection, advantages of each revascularization approach, timing of intervention, and emerging interventional techniques, such as transcarotid artery revascularization.

Severe carotid stenosis is one of the most significant risk factors for ischemic stroke. Carotid stenosis is the causative etiology for approximately 15% of ischemic strokes, and approximately 1 to 3% of the population has moderate- to high-grade carotid stenosis.<sup>1,2</sup> Management of carotid stenosis involves optimization of medical stroke risk factors (e.g., hypertension, hypercholesterolemia, diabetes, tobacco use), antithrombotic medication, and revascularization via carotid endarterectomy (CEA) or carotid artery stenting (CAS). Extensive and high-quality literature investigating carotid revascularization has developed over the past three decades. Since the pivotal trials published in the 1990s, CEA has been established as the first-line therapy for symptomatic standard-risk patients with carotid stenosis between 50 and 99%.<sup>3,4</sup> Over the past 10 years, CAS use has increased and now constitutes approximately 17% of all carotid revascularization procedures in the United States.<sup>5,6</sup> This article aims to review the current state of practice regarding these procedures and the future directions of interventional management of carotid stenosis.

### Indication for Revascularization

#### Symptomatic Carotid Stenosis

The 2014 American Heart Association/American Stroke Association (AHA/ASA) guidelines and the 2017 European Society for Vascular Surgery (ESVS) guidelines recommend carotid revascularization via CEA for patients with severe (70-99%) extracranial carotid stenosis with attributable symptoms, such as infarct, transient ischemic attack, or amaurosis fugax, in the past 6 months. This recommendation was based on the positive results of the three pivotal trials that compared CEA to best medical therapy-the European Carotid Surgery Trial (ECST), the North American Symptomatic Carotid Endarterectomy Trial (NASCET), and the Symptomatic Veterans Affairs Cooperative Study Trial.<sup>7,8</sup> In pooled analyses of these trials, which includes over 6,000 symptomatic patients, CEA produced a 16% absolute risk reduction and an approximately 50% relative risk reduction in ipsilateral ischemic stroke at a follow-up of 5 years.<sup>9</sup> The number of patients needed to treat was only six to avoid ipsilateral

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Issue Theme Neurointerventions; Guest Editors, Venu Vadlamudi, MD, RPVI, FSIR, FSVM, FASA and Martin Radvany, MD Copyright © 2020 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel: +1(212) 760-0888. DOI https://doi.org/ 10.1055/s-0040-1709154. ISSN 0739-9529. carotid territory ischemic stroke, operative stroke, or death in these patients with severe stenosis.

Patients with nearocclusion of their carotid, defined as 95 to 99% stenosis on catheter angiogram with distal internal carotid artery (ICA) collapse or "trickle flow," did not experience any stroke risk reduction with CEA in the pooled analyses, and the European guidelines suggest reserving revascularization for those patients with near-occlusive carotid stenosis who experience recurrent ischemic symptoms despite optimal medical therapy. If only Doppler imaging is used to evaluate candidacy for revascularization, it is possible to confuse near-occlusive carotid disease with conventional high-grade stenosis if a normal caliber distal ICA lumen cannot be visualized. This error can be avoided by recognizing that near-occlusive disease is associated with low peak systolic velocities and absent end-diastolic flow on Doppler, and nearocclusive stenosis should not have a normal caliber ICA distal to the stenosis on computed tomography angiography (CTA).<sup>10</sup>

These pivotal trials demonstrated clinical benefit with CEA with less-severe stenosis of 50 to 69%, though the risk reduction was less robust with an absolute risk reduction of 4% for ipsilateral stroke or death in the pooled analyses. As such, the AHA/ASA and ESVS guidelines recommend considering CEA in patients with moderate stenosis (50-69%), recent attributable ischemic symptoms, and standard surgical risk if the surgeon's rate of perioperative stroke or death is less than 6%, which is thought to be the risk of periprocedural stroke or death among surgeons in the general population.<sup>11</sup> If 1,000 patients with symptomatic 50 to 69% stenosis underwent CEA, Naylor et al estimated that only 78 strokes would have been prevented at 5 years postprocedure using the pooled data from NASCET and ECST.<sup>10</sup> Because the understanding of medical risk factor management has improved significantly since these trials were published in 1991 (e.g., increased use of dual-antiplatelet therapy and highdose statins, and different glucose and blood pressure goals), it is likely that the benefit of revascularization in these symptomatic patients with moderate stenosis may even be more modest, and there are several ongoing randomized controlled trials (RCTs) comparing contemporary optimal medical therapy with revascularization via CEA or CAS.

In an attempt to better identify a population with symptomatic moderate carotid occlusive disease who might benefit from revascularization, studies have attempted to define clinical and imaging features that place patients with symptomatic stenosis at high risk for recurrent ischemic events. Older patients enjoy a greater stroke risk reduction after CEA.9,12,13 The 5-year absolute risk reduction after CEA was 5.6% in patients with 50 to 99% stenosis who were younger than 65 years, and 19.6% in patients older than 75 years.<sup>10</sup> Thus, advanced age should not be a contraindication to revascularization, provided the patient's life expectancy is greater than 3 to 5 years, which is the minimum amount of time for the benefit of revascularization to outweigh the procedure-related risks of stroke and death. Male patients with 50 to 99% carotid occlusive disease benefit much more than females after CEA with a 5-year absolute risk reduction of 11% versus 2.8%.<sup>12</sup> Patients presenting with ocular symptoms have lower risk reduction with of

CEA than those with hemispheric symptoms (5-year absolute risk reduction of 5 vs. 15–18%). Imaging features associated with increased benefit of CEA include irregular plaque, tandem intracranial stenosis, and poor collateral supply of the affected hemisphere on catheter angiography.<sup>9,14,15</sup>

#### Asymptomatic Carotid Stenosis

Indications for carotid revascularization in those with asymptomatic carotid stenosis are controversial and vary widely among practice locations. For example, results from a billing database sample suggest that more than 90% of carotid revascularization procedures in the United States are for asymptomatic carotid stenosis, though others argue that the poor quality of the underlying database may inflate this proportion.<sup>16,17</sup> Simultaneously, no patients in Denmark undergo carotid revascularization for asymptomatic carotid occlusive disease.<sup>18</sup> Data supporting the use of carotid revascularization in asymptomatic patients come largely from two large studies: the Asymptomatic Carotid Atherosclerosis Study (ACAS) and the Asymptomatic Carotid Surgery Trial (ACST).<sup>19,20</sup> These trials enrolled patients with greater than 60% stenosis, randomized them to CEA or best medical therapy, and followed up patients for an average of 2.7 years (ACAS) and 9 years (ACST). Both described a statistically significant decreased risk of stroke with CEA with an absolute risk reduction of 4 to 6%, which suggests 40 to 60 strokes prevented per 1,000 CEAs performed in this patient population over 10 years of follow-up.<sup>21</sup> Advocates for carotid revascularization in asymptomatic patients point to the gradual improvement in procedural safety profile, which would improve the absolute risk reduction with revascularization compared with the estimates provided by these older studies. Critics of treating asymptomatic carotid stenosis with CEA or CAS point to the improved results of optimal medical therapy over time, which would decrease the expected benefit of revascularization. A metaanalysis of 6 RCTs and 35 observational studies that investigated asymptomatic patients with carotid stenosis who were treated with medical therapy alone found that the incidence of ipsilateral stroke was 2.3 per 100 person-years in studies completed before the year 2000 and 1.0 per 100 person-years in studies completed after the year 2000, which lends credence to the proposition that improvements in medical therapy since the pivotal asymptomatic carotid stenosis trials may limit the application of their findings today.

Certain subgroups of asymptomatic patients with carotid stenosis may be at higher risk for stroke, and therefore more likely to benefit from revascularization. While increasing stenosis and contralateral occlusion strongly increased ipsilateral stroke risk in the population with symptomatic stenosis, the same relationship between stenosis severity and stroke risk was not observed in the asymptomatic population in the ACAS/ACST trials. In the meta-analysis of asymptomatic patients undergoing medical therapy, the risk of ipsilateral stroke was 1.9/100 person-years in patients with moderate stenosis and 2.1/100 person-years in those with severe stenosis (p = 0.43), suggesting that the thresholds used for symptomatic patients may not risk-stratify

asymptomatic patients.<sup>22</sup> Those whose stenosis became more severe over time were at significantly higher risk of ipsilateral stroke. The 8-year risk of ipsilateral stroke was 0% in patients whose stenosis improved, 9% in those whose stenosis was largely stable, and 16% in those whose asymptomatic stenosis progressed.<sup>23</sup> Asymptomatic patients with echolucent carotid plagues, plagues with multiple microulcers, intraplaque hemorrhage, or cerebral microemboli detected by transcranial Doppler are at increased risk of ipsilateral stroke.<sup>24–26</sup> Patients with asymptomatic carotid stenosis and ipsilateral "silent" infarction are at increased risk of stroke.<sup>27</sup> In contrast to symptomatic carotid stenosis in which the stroke reduction benefits of CEA increase with patient age, there was an inverse relationship between stroke risk reduction and age in asymptomatic patients in ACST-1 at 5-year follow-up. When periprocedural risks were included, there was no benefit to CEA in asymptomatic patients older than 75 years.<sup>19</sup>

The ESVS guidelines suggest that carotid revascularization via CEA should be considered, and CAS may be considered, in average surgical risk patients with asymptomatic carotid stenosis of 60 to 99% if they have imaging or clinical characteristics that increase stroke risk (e.g., large plaque area, ipsilateral silent infarction, stenosis progression), if periprocedural risk of stroke or death is under 3% and if the patient's life expectancy is greater than 5 years. Guidelines will likely provide more clarity as the ongoing large RCTs investigating revascularization versus best medical therapy in patients with asymptomatic carotid stenosis share their results.

# Choice of Carotid Endarterectomy versus Stenting

To date, there have been 20 RCTs investigating the efficacy and safety of endarterectomy and stenting for carotid stenosis.<sup>28,29</sup> There is variability among these studies with respect to enrollment criteria, clinical endpoints, antithrombotic regimen after revascularization, and their requirements regarding CAS experience among the involved interventionalists. Despite the different study designs, these RCTs and their meta-analyses have yielded similar results: CEA has a lower risk of periprocedural stroke; CAS has lower risk of periprocedural myocardial infarction (MI), lower risk of cranial nerve injury, and lower risk of serious access-site hematomas. Once periprocedural strokes are excluded (i.e., those strokes that occur within 30 days of the intervention), neither CAS nor CEA has demonstrated superior long-term results in lowering ipsilateral stroke risk in patients with symptomatic carotid occlusive disease.<sup>30</sup>

Because the long-term stroke reduction is not statistically different between CAS and CEA, the countervailing risks of MI and periprocedural stroke drive much of the discussion regarding revascularization approach, and it is worthwhile to discuss them in more depth. The inclusion of MI, which was defined as an elevation of serum biomarkers (e.g., troponin elevation) or clinical infarction with electrocardiogram changes, was controversial as it had not been included in the primary endpoint in several earlier studies.<sup>31,32</sup> Ratio-

nale for including MI in the primary composite endpoint in the CREST trial relied on the understanding that myocardial injury, even when detected at subclinical levels via serum assays, increases mortality risk. Indeed, patients in CREST who experienced clinical MI symptoms or myocardial biomarker elevation had significant increase in late mortality (odds ratios: 3.4 and 3.6, respectively, p < 0.05). However, increased mortality was also noted in patients with postprocedural stroke (odds ratio: 2.78, 95% confidence interval [CI]: 1.63-4.76). A meta-analysis revealed that CAS is associated with 0.4% decreased risk of MI but a 1.7% increased risk of periprocedural stroke.<sup>33</sup> The relationship between CAS and periprocedural risk is less clear in high-risk patients. In the SAPPHIRE trial, which only included patients with high surgical risk, carotid stenting was associated with a 3.6% decreased risk of MI and 0.6% increased risk of stroke. It appears that the increased MI risk with CEA treatment is due to the effects of general anesthesia. In patients who undergo CEA with locoregional anesthesia, the risk of MI is no different than those who undergo CAS with locoregional anesthesia, and as expected, use of general anesthesia with CAS greatly increases MI and in-hospital morbidity.<sup>34,35</sup>

Periprocedural stroke, but not periprocedural MI, had a significant impact on quality of life 1 year after revascularization in the CREST trial.<sup>36</sup> The risk of periprocedural stroke increases sharply in elderly patients. A meta-analysis of 16 trials including 7,572 patients demonstrated that the odds ratio for periprocedural stroke was 1.16 (95% CI: 0.80–1.67) in patients younger than 70 years and 2.20 (95% CI: 1.47–3.29) in those older than 70 years.<sup>29</sup> Importantly, there was no significant difference in periprocedural stroke risk in those patients younger than 70 years.<sup>37</sup> Those with a greater burden of agerelated white matter changes are at higher risk of periprocedural stroke.<sup>38</sup> This age-dependent risk profile informs the guidelines from the AHA/ASA and the ESVS,both of which recommend against CAS in patients older than 70 years for whom CEA is an option.

Several technical developments have improved the safety profile of CAS. The use of embolic protection devices, which have been demonstrated to decrease risk of embolism during stenting, is now common practice.<sup>39</sup> Protection devices were associated with a 38% decrease in relative risk of periprocedural stroke in a systematic review of 134 studies including more than 23,000 patients.<sup>40</sup> Interventionalists realized earlyon that open-cell stent design doubled the risk of postprocedural stroke in the SPACE and ICSS trials, and so modern stents used for carotid revascularization are closedcell in design.<sup>41,42</sup> Techniques that have a high risk of causing stroke during the CAS procedure, such as dilating after stent deployment, have been identified so that interventionalists can make informed decisions regarding use of these techniques.<sup>43</sup> CAS is safest when performed in a multidisciplinary environment with an experienced team.<sup>44–46</sup> The literature has not determined a threshold number of CAS cases needed to decrease risk, but there is a consistent finding across several studies that low-volume centers are associated with worse outcomes. For example, in a large study of Medicare beneficiaries that included 24,701 procedures by more than 2,000

interventionalists, those operators who performed fewer than six cases per year had almost double the periprocedural rate of stroke and death as those who performed more than 24 cases per year.<sup>47</sup>

CAS is indicated as an alternative to CEA in the presence of factors that increase the risk of open surgery, such as high carotid bifurcation, prior neck irradiation, contralateral carotid occlusion, contralateral vocal cord paralysis, tracheostomy, carotid dissection, and those who cannot medically tolerate anesthesia. CAS may be considered for those with standard surgical risk and symptomatic carotid stenosis if there are factors that decrease the risk of endovascular intervention such as age less than 70 years, last symptomatic episode more than 2 weeks prior, low burden of age-related white matter changes, experienced interventionalist team, a single short noncalcified plaque without intraluminal thrombus, favorable aortic arch anatomy without significant atheromatous burden, etc.

# **Timing of Carotid Revascularization**

Some early studies suggested delaying CEA in patients with symptomatic carotid stenosis due to the perceived increased perioperative stroke risk in the days following initial presentation.<sup>37</sup> Others suggested that delaying revascularization for more than 4 weeks was optimal in those with evidence of cerebral infarction on CT to avoid hemorrhagic transformation.<sup>48,49</sup> Some guidelines published in the 1990s recommended revascularization within 6 months of presentation with symptomatic carotid stenosis. We now know that patients with symptomatic carotid stenosis are at increased risk of recurrent ischemic event shortly after their index event, and that there is a critical window in which revascularization may provide improved stroke risk reduction without jeopardizing safety. In those who present with symptomatic carotid stenosis and are eligible for revascularization, more than 10% will suffer another ischemic event within the 14 days following their index presentation, suggesting a need for more urgent surgical management.<sup>50</sup> Pooled data from ECST and NASCET demonstrated that the benefit of revascularization decreased as the surgery was delayed for 2 weeks.<sup>12</sup> The absolute risk reduction of recurrent stroke was 30% in those patients who underwent CEA for severe symptomatic carotid stenosis within 2 weeks, 17% in those who underwent CEA between 2 and 4 weeks, and 11% if the delay was between 1 and 3 months.

In patients who have received intravenous thrombolysis for the treatment of acute ischemic stroke due to carotid thromboembolism, early CEA can be performed safely provided there is evidence that the volume of brain that completed infarction is small (i.e., the patient's neurologic status has improved, the area of infarction is less than a third of the MCA territory, there is evidence of recanalization of the previously occluded large vessel after thrombolysis, there is no intraparenchymal hemorrhage or significant brain edema).<sup>51–53</sup> Patients with large volume infarcts (e.g., greater than one-third of the MCA territory) are at much higher risk for periprocedural stroke, and therefore the ESVS guidelines recommend deferring revascularization to minimize the risk of intraparenchymal hemorrhage.<sup>7</sup> Revascularization with endarterectomy can be performed safely on an urgent (<24 hours) basis in patients with crescendo transient ischemic attacks or "stroke-in-progress".<sup>54,55</sup>

Several studies have evaluated timing of revascularization in patients undergoing CAS.<sup>56–59</sup> There is consensus among the studies that there is significant risk of periprocedural stroke with early stenting. When compared with CEA performed during the same interval, CAS within 7 days of presentation with symptomatic carotid stenosis was associated with threefold greater periprocedural stroke risk and CAS within 14 days doubles periprocedural stroke risk.<sup>57</sup> The ESVS guidelines recommend performing CEA rather than CAS if revascularization is to happen within 14 days of presentation. Due to the limited number of small single-institution reports, there is insufficient evidence in the literature to support the use of urgent CAS in lieu of CEA for those patients who present after intravenous thrombolysis.<sup>60–62</sup>

# Carotid Revascularization during Thrombectomy for Acute Stroke

Management of tandem carotid occlusion or high-grade stenosis encountered during emergent endovascular thrombectomy (EVT) for ischemic stroke poses a distinct clinical challenge that has confronted interventionalists in an increasing rate since the simultaneous publication of several large RCTs in 2015, which cemented EVT with stent-retriever as first-line therapy for acute ischemic stroke with large vessel occlusion.<sup>63</sup> Atherosclerosis with possible superimposed thrombus constitutes approximately 80% of the cases of tandem occlusion, with dissection causing the remainder.<sup>64</sup> These tandem occlusions, which are found in approximately 15 to 20% of patients with acute ischemic stroke, are associated with adverse clinical outcomes after intravenous thrombolysis.<sup>65,66</sup> The pivotal EVT trials of 2015 do not provide clear guidance on the management of tandem occlusions because patients with extracranial carotid occlusive disease comprised only 10% of enrolled subjects, and were excluded from two of the trials, EXTEND IA and SWIFT PRIME.<sup>63</sup> Given the lack of high-quality evidence, there is a spectrum of practice among the interventional community, with 40% of practitioners in one recent international survey reporting that they never perform CAS acutely during thrombectomy.<sup>67</sup> Even if one adopts a conservative strategy for the management of tandem occlusion, angioplasty or stenting may be necessary in up to 31% of cases, simply to provide access to the intracranial lesion.<sup>68</sup>

Those that prefer to avoid stenting advocate angioplasty only to provide access to the intracranial vasculature for thrombectomy. They point to the single-center studies that suggest high in-stent thrombosis and intracranial hemorrhage rates, which may be due to the antithrombotic medications used in stenting.<sup>69–71</sup> Larger studies, however, have suggested that stentmanagement of tandem occlusions during EVT may improve clinical outcomes without significantly altering the risk profile of the procedure. The HERMES meta-analysis of the five pivotal 2015 EVT trials demonstrated that those with tandem occlusion benefit functionally from thrombectomy at the same rate as those without extracranial severe carotid stenosis.<sup>63</sup> In a registry of 1,000 patients who underwent EVT with the Solitaire device, 54% of the 147 patients with tandem occlusion underwent CAS.<sup>66</sup> Stenting did not change rates of cerebral reperfusion or increase mortality or intracranial hemorrhage rate significantly. CAS of tandem occlusion did result in a substantially higher proportion of patients with good functional clinical outcome, defined as modified Rankin's score of 0 to 2, which was achieved in 42% of those who were not stented, 37% of those who underwent angioplasty alone, and 68% of those who underwent angioplasty and stenting (p = 0.003). Another large multi-institution registry study with 482 patients with acute ischemic stroke and tandem occlusion demonstrated that stenting significantly improved intracranial revascularization rate. There was a trend toward improved functional outcome that was statistically nonsignificant upon multivariate analysis.<sup>72</sup>

Just as there is no agreement regarding the benefit of stenting for tandem occlusion, there is no consensus on how the stenting should be performed: whether the extracranial lesion should be treated before thrombectomy ("neck-first" vs. "head-first"). Those who recommend thrombectomy before stenting claim that the time to intracranial recanalization may be shorter by up to an hour, that extracranial stenting may be unnecessary if an adequate channel has been formed through the carotid atheromatous plaque, and that potentially harmful antithrombotic medications can be avoided if injury to the intracranial vessels are encountered during thrombectomy.<sup>73,74</sup> In addition, some fear interaction between the deployed cervical stent and the catheters being used for the thrombectomy.<sup>75</sup> Those that advocate for neck-first suggest that increasing intracranial inflow may aid in recanalization by increasing access to the distal lesion and may minimize intraprocedural distal embolism by stabilizing the plaque. No prospective study has compared the two approaches. A 2018 meta-analysis of 33 studies, which included 316 patients for whom the sequence of the procedure was known, demonstrated no improvement in successful recanalization rates and no difference in patients' functional outcome.<sup>76</sup>

The 2018 AHA/ASA guidelines on the management of acute ischemic stroke state that EVT may be reasonable in the setting of tandem occlusion, but there is insufficient evidence for the guideline to recommend a single method for treatment of the extracranial pathology.<sup>77</sup> In addition, the optimal antithrombotic regimen for carotid stenting during EVT has not been defined.

### **Future of Carotid Revascularization**

The field of carotid revascularization continues to develop at break-neck pace. Transcarotid artery revascularization (TCAR) was developed to perform CAS without the risk of embolism from atheroma dislodged during passage of a catheter over the aortic arch and supra-aortic arteries. In 2015, the FDA awarded premarket approval for the ENROUTE system (Silk Road Medical Inc., Sunnyvale, CA), which consists of a carotid sheath, inserted via cut-down on the artery, and a dynamic flow controller, which reverses flow and passes blood through a 200-µm filter to a femoral vein return sheath. A carotid stent can be deployed through the carotid sheath under flow reversal. The industry-sponsored multicenter ROADSTER trial, which provided the data supporting FDA approval, was a single-arm design with a lead-in phase of five procedures that enrolled patients with symptomatic carotid stenosis with greater than 50% stenosis or asymptomatic stenosis with greater than 70% stenosis who were at high risk for complication with CEA. Of the 141 patients in the intent-to-treat analysis, there were 2 deaths, 2 nondisabling strokes, and 1 MI, for a 30-day complication rate of 3.5%.<sup>78</sup> A 1-year follow-up study of 165 patients, which excluded the periprocedural period, found 1 ipsilateral stroke and 7 deaths, none of which were neurological in etiology.<sup>79</sup> The PROOF trial, which was designed to obtain approval for use in Europe, included 75 patients and no device-related periprocedural major adverse event was noted.<sup>80</sup> Seventy-five percent of patients in this study had MRI before and after the procedure, and 18% of patients were found to have new diffusion-restricting lesions after TCAR, which is notable given that 73% of patients in the CAS group of the large ICSS trial were noted to have new diffusionrestricting lesions postprocedure.<sup>81</sup> Although age over 70 was found to be a significant predictor of periprocedural stroke risk in the various CAS studies, the average age of patients in the ROADSTER and PROOF studies were older than 70years. A propensity-matched study of TCAR versus CEA demonstrated that TCAR had a similar safety profile to CEA with no significant difference in periprocedural or 1year rates of stroke or death.<sup>82</sup> Taken together, this literature suggests that TCAR may be an effective and safe method for carotid revascularization, though no direct RCT has been performed comparing this new therapy with CEA and CAS.

Interventionalists have successfully used other approaches for CAS as well. The transradial approach for cerebral angiography has been gaining popularity as an alternative to transfemoral access. The transradial approach has become the standard in coronary angiography, and proponents of the approach report that it may result in fewer access site complications and earlier ambulation. The majority of patients with exposure to both approaches prefer transradial access.<sup>83</sup> In addition, some patients who are candidates for CAS cannot undergo transfemoral approach due to aortoiliac occlusive disease or aberrant aortic arch morphology. Many retrospective and several prospective studies have demonstrated that transradial CAS is feasible and safe.<sup>84–86</sup> A meta-analysis of 723 patients in seven studies describing transradial approach reported a procedural success rate of 90%.<sup>87</sup> There were 3 deaths, no MIs, 5 major periprocedural neurological complications, 16 periprocedural minor neurological complications, and 2 major access-site complications (1 symptomatic radial artery occlusion in a patient with Buerger's disease and 1 pseudoaneurysm). Of the 66 procedural failures described in the study, 8 were caused by difficulty with radial artery access due to spasm, radial artery loop, or subclavian stenosis. The remainder of failures were due to difficulty cannulating the

carotid. Asymptomatic radial artery occlusion was noted in approximately 6% of patients. As expected given the right radial artery access, attempted access of the left carotid had higher risk of failure, especially in nonbovine aortic arch morphology. The single RCT comparing transradial and transfemoral approaches for CAS had 130 patients in each arm, and demonstrated no difference in access complications or periprocedural death, stroke, or cardiac complications.<sup>85</sup> There was a statistically significant increase in radiation in the transradial approach. Crossover from transradial to transfemoral was more common than viceversa (10 vs. 1.5%). These studies suggest that right transradial approach for CAS may expand the technical armamentarium of the interventionalist by allowing endovascular access in those with aortoiliac stenoocclusive disease and in some of those with difficult aortic arch anatomy, though there is no indication that transradial approach decreases the rates of periprocedural stroke.

Ongoing carotid revascularization trials such as CREST-2, ECST-2, and ACST-2 will hopefully shed additional light on optimal revascularization strategies for asymptomatic carotid artery stenosis. CREST-2 will specifically evaluate modern aggressive medical management strategies with either CEA or CAS but will have a subgroup of medical management alone. The ECST-2 and ACST-2 trials are complementary but with different study designs. ECST-2 will randomize patients with asymptomatic carotid artery stenosis to medical management alone versus medical management with immediate revascularization. ACST-2 will study patients with asymptomatic carotid artery stenosis for whom revascularization has been decided but seeks to address whether CEA or CAS is better for these patients, all of whom are medically managed.

# Conclusion

Carotid revascularization substantially decreases risk of ischemic stroke from moderate and severe carotid stenosis. CEA remains the first-line therapy for revascularization in patients whose stenosis is symptomatic, but carotid stenting is an acceptable alternative in a subpopulation of patients with significant surgical and anesthetic risk factors. The role for CEA or CAS in the asymptomatic patient with moderate or severe carotid stenosis is less clear since the benefit over modern medical therapy has yet to be demonstrated, but ongoing trials seek to answer this question. Several technical developments, such as TCAR and transradial carotid stenting, may provide additional tools to the interventionalist's armamentarium.

# **Conflict of Interest**

Dr. Priest is a consultant for Medtronic Neurovascular, Stryker Neurovascular, and Cerenovus Neurovascular (a division of Johnson and Johnson).

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