Current concepts in the management of carotid stenosis
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Abstract

Several large randomized clinical trials in North America and Europe concluded over a decade ago that carotid endarterectomy plus medical management was significantly better than medical management alone for stroke prevention in either symptomatic or asymptomatic patients with severe carotid stenosis. Percutaneous carotid angioplasty now represents another treatment option that currently seems most appropriate either in the context of prospectively randomized trials or for patients who are at a higher than average risk for conventional surgical treatment.

Introduction and context

Few modern clinical problems have provoked as much controversy as extracranial carotid artery disease. Prompted by concern that carotid endarterectomy (CEA) was being performed for uncertain indications during the 1980s, four randomized clinical trials (RCTs) were sponsored by the National Institutes of Health in the United States and by the Medical Research Council in the United Kingdom in order to determine the benefit of CEA in symptomatic patients and for asymptomatic carotid stenosis [1–7]. These included the North American Symptomatic Carotid Endarterectomy Trial (NASCET), the European Carotid Surgery Trial (ECST), the Asymptomatic Carotid Atherosclerosis Study (ACAS) and the Asymptomatic Carotid Surgery Trial (ACST), all of which remain the foundation for proper patient selection and should be thoroughly familiar to clinicians who recommend or perform any kind of carotid intervention.

Table 1 contains data from these four important investigations. It must be noted that the methods for estimating the percentage of carotid stenosis differed in the North American (NASCET, ACAS) and the European (ECST, ACST) trials; the former used the diameter of the uninvolved internal carotid artery distal to the index lesion as the denominator, whereas the latter employed the projected normal diameter of the internal carotid bulb. Nevertheless, the conclusions reached by these trials were reasonably consistent and can be summarized as follows.

First, the 30-day combined stroke or mortality rates for CEA were two to three times higher in symptomatic patients than in patients who had asymptomatic carotid stenosis. This may reflect the potential of symptomatic lesions to cause intraoperative cerebral emboli during carotid manipulation.

Second, the benefit of CEA was greater and became obvious within shorter periods of follow-up in patients who had previous symptoms in conjunction with severe carotid stenosis measuring at least 70% of lumen diameter. The relative risk reduction associated with CEA for 50–69% stenosis was only marginally significant (P = 0.045) in the NASCET, and the ECST showed no risk reduction at all for CEA in this particular group of patients.

Third, in comparison to symptomatic patients in the NASCET and ECST, patients with asymptomatic carotid stenosis in the ACAS and the ACST had lower long-term event rates irrespective of whether they were randomized to CEA or medical management. Furthermore, while CEA provided a significant overall reduction of relative risk in the ACAS, this benefit seemed substantially less
impressive in women (17 versus 66% in men, $P = 0.10$), probably because they tended to have a higher incidence of perioperative stroke or death (3.6 versus 1.7%, $P = 0.12$).

Fourth, the ACST did not substantiate the apparent lesser benefit of CEA that was found in asymptomatic women by the ACAS, but this might be explained by the fact that the ACST excluded the risk for perioperative stroke or death (3.6% in women, 2.5% in men) from its subset analyses. The ACST also reported that unoperated patients with 60–79% stenosis were as likely as those with 80–99% stenosis to have future strokes. The ACAS did not further stratify its criterion of 60–99% stenosis, but other non-randomized case series strongly suggest that asymptomatic 60–79% stenosis has a very low risk for stroke and can be kept under surveillance by duplex scanning [8].

Fifth, the 'number needed to treat' (NNT) is defined as the number of patients who would have to undergo CEA in order to prevent one long-term adverse event. In the NASCET, this ranged from an NNT of 6 for patients who had 70–99% stenosis, to an NNT of 15 for patients with 50–69% stenosis [1,2]. The corresponding NNT was 19 for all patients in the ACAS, and it undoubtedly was even higher in women [6].

Recent advances
Percutaneous carotid angioplasty (PCA) was described in isolated case reports during the late 1970s and has since been the topic of more than 20 large case series, over a dozen industry-sponsored registries, and a few independent trials [9]. Many of these studies became obsolete almost immediately because of additional refinements in endovascular technology, such as carotid stents and over-the-wire cerebral embolic protection devices [10].

Table 1. Major RCTs in North America and Europe (1980s to mid-1990s) comparing carotid endarterectomy versus medical management alone for stroke prevention

| RCT       | Severity of stenosis (%) | 30-day surgical CSM (%) | Reported follow-up period (years) | Long-term event rate | Relative risk reduction (%) | $P$-value |
|-----------|--------------------------|-------------------------|----------------------------------|----------------------|---------------------------|-----------|
|           | Carotid endarterectomy   | Medical management      |                                  |                      |                           |           |
| Symptomatic patients |                         |                         |                                  |                      |                           |           |
| NASCET [1]  | 70–99                    | 5.8                     | 2                                | 9.0$^a$             | 26.0$^a$                 | 65        | <0.001    |
| NASCET [2]  | 50–69                    | 6.7                     | 5                                | 15.7$^b$            | 22.2$^b$                 | 29        | 0.045     |
| ECST [3]    | 70–99                    | 7.5                     | 3                                | 12.3$^b$            | 21.9$^b$                 | 45        | <0.01     |
| ECST [4,5]  | 50–69                    | 7.9                     | 8                                | 18.4$^a$            | 15.6$^a$                 | None      | -         |
| Asymptomatic patients |                     |                         |                                  |                      |                           |           |
| ACAS [6]    | 60–99                    | 2.3                     | 5                                | 5.1$^c$             | 11.0$^c$                 | 53        | 0.004     |
| ACST [7]    | 60–99                    | 3.1                     | 5                                | 6.4$^c$             | 11.8$^c$                 | 46        | <0.0001   |

*Includes 30-day strokes and deaths but only ipsilateral late strokes. $^a$Includes 30-day strokes and deaths and all late strokes. $^b$Includes 30-day strokes (but not deaths) and all late strokes. ACAS, Asymptomatic Carotid Atherosclerosis Study; ACST, Asymptomatic Carotid Surgery Trial; CSM, combined stroke and/or mortality rate; ECST, European Carotid Surgery Trial; NASCET, North American Symptomatic Carotid Endarterectomy Trial; RCT, randomized controlled trial.

CAVATAS
Conducted from 1992 to 1997, the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS) was the earliest trial of PCA versus CEA to be independently funded and to capture international attention. Each of the participating centers had to designate one or more radiologists with prior training in angioplasty techniques, but there was no requirement for previous experience with the carotid artery. The CAVATAS showed no long-term outcome differences between PCA and CEA in symptomatic patients, but its credibility was eroded by a 30-day stroke or mortality rate for CEA (9.9%) that was much worse than generally had been reported. Moreover, carotid stents were used in only 26% of the patients who received PCA, a factor that could have contributed to a high incidence of recurrent ≥70% stenosis (18 versus 5.2% for CEA, $P = 0.0001$) at just 1 year of follow-up [17]. Cerebral embolic protection devices were unavailable at that time, so this adjunct was not used in the CAVATAS.

SAPPHIRE
The Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial was funded by industry and for this reason may not have quite the cache of an independent RCT. It enrolled asymptomatic patients with ≥80% stenosis in addition to symptomatic patients with ≥50% stenosis, and it employed a unique primary end point of stroke, death...
and/or myocardial infarction (MI). This represented a departure from the traditional composite endpoint of stroke and/or death, especially since it included asymptomatic elevations in cardiac isoenzyme and troponin levels that had not been measured in most previous studies of CEA. The SAPPHIRE trial did have a number of practical features, however. First, it only accepted patients who were less than ideal surgical candidates because of serious cardiac disease (e.g. recent MI or unstable angina, congestive heart failure, <30% ejection fraction) or treacherous local anatomy, such as high carotid lesions near the skull base, prior cervical irradiation, or recurrent stenosis after prior CEA. Second, its interventionalists were strictly vetted and had a median past experience with 64 PCAs. Third, every PCA procedure in the trial was done using a cerebral embolic protection device and a carotid stent, both of which were manufactured by the sponsor (Cordis Corporation).

Much of the difference in 30-day end points could be attributed to a higher incidence of ‘chemical’ MIs after CEA, but the ultimate conclusion of the trial was that PCA provided an equivalent alternative in patients who were perceived to be at high risk for CEA. The SAPPHIRE trial has been criticized on the grounds that the majority (70%) of its patients were asymptomatic, that too many were entered into a non-randomized PCA registry because they were considered unsuitable for CEA, and that the unconventional primary end points were potentially misleading [18]. Asymptomatic carotid disease is the most common indication for CEA or PCA in the United States [19], however, and not just for the convincing severity of stenosis (80–99%) that this trial required. In addition, participating surgeons may have been understandably reluctant to randomize certain patients who had multiple high-risk factors for CEA. Finally, although the inclusion of clinically unsuspected MIs was a novel approach to early outcome assessment, it is difficult to argue logically that these events should have been allowed to go undetected.

**SPACE**

The Stent-Supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy (SPACE) trial is a non-inferiority study that was designed to demonstrate equivalence between PCA/stenting and CEA. In order to participate, interventionalists had to show proof of at least 25 successful consecutive PCA procedures. The virtues of the SPACE trial are its large size (1,200 symptomatic patients), which thusfar exceeds any similar RCT, and the fact that it has been supported predominantly by independent resources. Its perceived liabilities are that cerebral embolic protection was used during only 27% of the PCA procedures, and that recruitment was prematurely stopped for lack of funding after it was discovered that more than 2,500 patients would be necessary to confirm its interim results with adequate statistical power. At that time, the 30-day risk for death or ipsilateral stroke appeared comparable for CEA and CEA (6.8 and 6.3%, respectively), but the *P*-value for non-inferiority was only 0.9. No long-term event rates are available for the SPACE trial, but its trialists have stated that these outcomes will be published in the form of a meta-analysis in conjunction with other European RCTs [14].

**EVA-3S**

The Endarterectomy Versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis (EVA-3S) trial is the most recent study summarized in Table 2 and could conceivably serve as a proxy for the evolution of PCA in other large population bases. Sponsored by the French

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**Table 2. Selected data from recent RCTs comparing carotid endarterectomy to percutaneous carotid angioplasty**

| RCT                 | Clinical features | Angioplasty adjuncts | 30-day surgical or procedural CSM | Long-term event rate |
|---------------------|-------------------|----------------------|-----------------------------------|----------------------|
|                     | Symptoms (%)      | Stenosis (%)         | Stent (%) | CEP (%) | CEPA (%) | PCA (%) | *P*-value | CEA (%) | CA (%) | *P*-value |
| CAVATAS [11]        | 97                | Mean: 85±10          | 26       | None    | 9.9     | 10      | NS        | 14.2    | 14.3    | NS        |
| SAPPHIRE [12,13]    | 29                | ≥50 (symptomatic)    | 100      | 100     | 9.8     | 4.8     | 0.09      | 26.9    | 24.6    | 0.71      |
| SPACE [14]          | 100               | ≥80 (NASCET)         | 100      | 27      | 6.3     | 6.8     | 0.09      | NR      | NR      | -         |
| EVA-3S [15]         | 100               | ≥70 (ECST)           | 100      | 92      | 3.9     | 9.6     | 0.01      | 4.2     | 10.2    | 0.008     |

*Death or disabling stroke within 3 years. bIndustry sponsored (Cordis Corporation). cDeath, stroke or myocardial infarction. dDeath, stroke or myocardial infarction within 30 days or death or ipsilateral stroke within 3 years. eDeath or ipsilateral ischemic stroke. fAny death or stroke. gAny death or stroke within 30 days plus ipsilateral stroke between 31 days and 6 months. CAVATAS, Carotid and Vertebral Artery Transluminal Angioplasty Study; CEA, carotid endarterectomy; CEP, cerebral embolic protection; CSM, combined stroke and/or mortality rate; EVA-3S, Endarterectomy Versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis trial; NR, not reported; NS, not significant; PCA, percutaneous carotid angioplasty; RCT, randomized controlled trial; SAPPHIRE, Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy trial; SPACE, Stent-Supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy trial.
Ministry of Health in 20 academic and 10 non-academic medical centers, this trial permitted the use of a variety of approved catheter devices. Carotid stenting was mandatory, but cerebral embolic protection (ultimately used in 92% of patients) was not routinely recommended until the 30-day stroke rate was discovered to be 3.9 (95% confidence interval, 0.9 to 16.7) times higher without embolic protection (27%, 4 out of 15) than with protection (8.6%, 5 out of 58) in the initial 73 patients treated by PCA [20]. Perhaps the most controversial element of this trial is that interventionalists who had no previous experience with PCA still were permitted to perform it in randomized patients under the supervision of tutors until they acquired the requisite number of 12 PCAs (or only five PCAs plus another 30 stenting procedures in aortic arch vessels) for full accreditation. Interventionalists also could begin using a new catheter device within the trial as soon as they had gained some familiarity with it in just two other cases.

Trial enrollment was stopped on the basis of safety and futility once the 30-day stroke or mortality rate in the first 527 treated patients was found to be so much higher for PCA (9.6 versus 3.9% for CEA; relative risk, 2.5; 95% confidence interval, 1.2 to 5.1; P = 0.01) that more than 4,000 patients would have been necessary to demonstrate its non-inferiority to CEA. The EVA-3S trial has been criticized for the inexperience among its interventionalists and the lack of a standardized technique for PCA, but the flaws that some might find in this trial - the mix of community hospitals as well as referral centers, the mid-course changes to new or improved equipment, the low procedural volumes or on-the-job training by more experienced colleagues - are ubiquitous and may make its results more relevant to 'real world' practice [21]. The French trial was limited to symptomatic patients, but another national dataset also has shown that PCA/stenting was associated with higher risks for stroke or death than CEA in both symptomatic and asymptomatic patients in the United States during 2003 and 2004 [19].

**Ongoing trials**

The International Carotid Stenting Study (ICSS), or CAVATAS 2, and the Carotid Revascularization Endarterectomy versus Stent Trial (CREST) are two major independent RCTs currently underway in Europe and North America, respectively. No outcome data are available from the ICSS, but the CREST has reported early results for a total of 749 patients who underwent PTA/stenting with routine embolic protection during a lead-in phase that was used to credential interventionists. The 30-day stroke or mortality rate was significantly higher (12%, P < 0.0001) in octogenarians than it was in patients who were 70 to 79 (5.3%), 60 to 69 (1.3%) or less than 60 (1.7%) years of age [22]. Others have confirmed the unfavorable influence of advancing age on the risk of PCA in device regulatory trials [23] and have attributed this to the arterial tortuosity and calcification that often occur in elderly patients, thus making catheter-directed devices more likely to provoke cerebral emboli [24].

**Implications for clinical practice**

Citing much of the material covered in this review as well as additional sources in the literature, the Society for Vascular Surgery recently published clinical practice guidelines for the management of atherosclerotic carotid artery disease [25]. This document reconfirms the continued importance of the NASCET, ECST, ACAS and ACST in the selection of patients for either surgical or catheter-based intervention, emphasizing that patients who have symptomatic <50% stenosis or asymptomatic ≤60% stenosis are well suited to optimal medical management alone. These guidelines also propose that CEA plus medical therapy should remain the primary option for patients with more severe stenosis unless the ICSS and the CREST eventually prove otherwise. On the basis of current uncertainties, PCA generally seems most appropriate in the setting of these or similar trials until it has been shown conclusively to have the same safety and durability as CEA. In the meantime, exceptions favoring PCA can be justified for patients whose medical comorbidities or cervical anatomy make them questionable candidates for CEA.

**Abbreviations**

ACAS, Asymptomatic Carotid Atherosclerosis Study; ACST, Asymptomatic Carotid Surgery Trial; CAVATAS, Carotid and Vertebral Artery Transluminal Angioplasty Study; CEA, carotid endarterectomy; CREST, Carotid Revascularization Endarterectomy versus Stent; ECST, European Carotid Surgery Trial; EVA-3S, Endarterectomy Versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis; ICSS, International Carotid Stenting Study; MI, myocardial infarction; NASCET, North American Symptomatic Carotid Endarterectomy Trial; NNT, number needed to treat; PCA, percutaneous carotid angioplasty; RCT, randomized clinical trial; SAPPHIRE, Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy; SPACE, Stent-Supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy.

**Competing interests**

The author was a participating surgeon in the SAPPHIRE trial but had no role in the design of the trial, the
management or the interpretation of its data, or the preparation of its published reports.

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, 325:455-53.

2. Barnett HJ, Taylor DW, Eliasziw M, Fox AJ, Ferguson GG, Haynes RB, Rankin RN, Clagett GP, Hashinski VC, Sackett DL, Thorpe KE, Meldrum HE, Spence JD: Benefit of carotid endarterectomy in patients with symptomatic moderate or severe stenosis. North American Symptomatic Carotid Endarterectomy Trial Collaborators. N Engl J Med 1998, 339:1415-25.

3. European Carotid Surgery Trialists’ Collaborative Group: MRC European Carotid Surgery Trial: interim results for symptomatic patients with severe (70–99%) or with mild (0–29%) carotid stenosis. Lancet 1991, 337:123-43.

4. European Carotid Surgery Trialists’ Collaborative Group: Endarterectomy for moderate symptomatic carotid stenosis: interim results from the MRC European Carotid Surgery Trial. Lancet 1996, 347:1591-3.

5. 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.

6. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study: Endarterectomy for asymptomatic carotid artery stenosis. JAMA 1995, 273:1421-8.

7. Halliday A, Mansfield A, Marro J, Peto C, Peto R, Potter J, Thomas D: Long-term results of carotid stenting versus carotid endarterectomy in symptomatic patients with severe carotid stenosis. Lancet 1998, 334:491-502.

8. Olin JW, Fonseca C, Childs MB, Piedmonte MR, Hertzler, NR, Young JR: The natural history of asymptomatic moderate internal carotid artery stenosis by duplex ultrasound. Vasc Med 1998, 3:101-18.

9. Goodney PP, Powell RJ: Carotid artery stenting: what have we learned from the clinical trials and registries and where do we go from here? Ann Vasc Surg 2008, 22:48-58.

10. Kastrup A, Gröschel K, Krapf H, Brehm BR, Dichgans J, Schulzt JB: Early outcome of carotid angioplasty and stenting with and without cerebral protection devices: a systematic review of the literature. Stroke 2003, 34:813-9.

11. CAVATAS Investigators: Endovascular versus surgical treatment in patients with carotid stenosis in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS): a randomised trial. Lancet 2001, 357:1729-30.

12. Yadav JS, Wholey MH, Kunze RE, Fayad P, Katzen BT, Mishkel GJ, Bajwa TK, Whitlow P, Strickman NE, Jaff MR, Popma JJ, Sneed DB, Curtin DE, Firth BG, Oursel K: Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy Investigators: Protected carotid-artery stenting versus endarterectomy in high-risk patients. N Engl J Med 2004, 351:1493-501.

13. Gurm JS, Yadav JS, Fayad P, Katzen BT, Mishkel GJ, Bajwa TK, Ansel G, Strickman NE, Wang H, Cohen SA, Massaro JM, Curtin DE: SPHAPPRE Investigators: Long-term results of carotid stenting versus endarterectomy in high-risk patients. N Engl J Med 2008, 358:1572-9.

14. SPACE Collaborative Group, Ringleb PA, Allenberg J, Bruckmann H, Eckstein HH, Fradrich G, Hartmann M, Hennerici M, Jansen O, Klein G, Kunze A, Marx P, Niederkorn K, Schmiedt W, Solymosi L, Stingele R, Zeumer H, Hacke W: 30 day results from the SPACE trial of stent-protected angioplasty versus carotid endarterectomy in symptomatic patients: a randomised non-inferiority trial. Lancet 2006, 368:1239-47.

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15. Mas JL, Chatellier G, Beyssen B, Branchereau A, Moulin T, Becquemin JP, Larrue V, Lièvre M, Leys D, Bonneville JF, Watelet J, Pruvot JP, Albucher JF, Viguier A, Piquet P, Garnier P, Viader F, Touze E, Giroud M, Hosseini H, Pilette JC, Favrole P, Neau JP, Ducrocq X: EVA-3S Investigators: Endarterectomy versus stenting in patients with symptomatic severe carotid stenosis. N Engl J Med 2006, 355:1660-71.

F1000 Factor 6.0 Must Read Evaluated by Norman Hertzler 27 Jul 2007

16. Branchereau A, Macdonald S, Wholey MJ, Busquet J, Green R, Gray W: Perspectives on recent CAS trial data. Endovascular Today 2007, February: 22-49. [http://www.evtoday.com/PDFArticles/0207/EVT0207_01.pdf]

17. McCabe DJ, Pereira AC, Clifton A, Bland JM, Brown MM, CAVATAS Investigators: Restenosis after carotid angioplasty, stenting, or endarterectomy in the Carotid and Vertebral Artery Transluminal Angioplasty Study (CAVATAS). Stroke 2005, 36:281-6.

18. Thomas DJ: Protected carotid artery stenting versus endarterectomy in high-risk patients reflections from SAPPHIRE. Stroke 2005, 36:912-3.

19. McPhee JT, Hill JS, Ciocca RG, Messina LM, Eslami MH: Carotid endarterectomy was performed with lower stroke and death rates than carotid artery stenting in the United States in 2003 and 2004. J Vasc Surg 2007, 46:1112-8.

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20. Mas JL, Chatellier G, Beyssen B, EVA-3S Investigators: Carotid angioplasty and stenting with and without cerebral protection devices: clinical alert from the Endarterectomy Versus Angioplasty in Patients With Symptomatic Severe Carotid Stenosis (EVA-3S) trial. Stroke 2004, 35:e18-20.

21. Naylor AR: Where next after SPACE and EVA-3S: ‘the good, the bad and the ugly’. Eur J Vasc Endovasc Surg 2007, 33:44-7.

22. Hobson RW 2nd, Howard VJ, Roubin GS, Brott TG, Ferguson RD, Popma JJ, Graham DL, Howard G, CREST Investigators: Carotid artery stenting is associated with increased complications in octogenarians: 30-day stroke and death rates in the CREST lead-in phase. J Vasc Surg 2004, 40:1106-11.

23. Stanziale SF, Morone LC, Boules TN, Brimmeier JA, Hill K, Makaroun MS, Wholey MH: Carotid artery stenting in octogenarians is associated with increased adverse outcomes. J Vasc Surg 2005, 43:297-304.

24. Lam RC, Lin SC, DeRubertis B, Hyneczek R, Kent KC, Faries PL: The impact of increasing age on anatomic factors affecting carotid angioplasty and stenting. J Vasc Surg 2007, 45:875-80.

25. Hobson RW 2nd, Mackey WC, Ascher E, Murad MH, Calligaro KD, Comerota AJ, Montori VM, Eskandari MK, Massop DW, Bush RL, Lal BK, Perler BA: Society for Vascular Surgery: Management of atherosclerotic carotid artery disease: clinical practice guidelines of the Society for Vascular Surgery. J Vasc Surg 2008, 48:480-6.