Carotid endarterectomy: The procedure of choice for carotid stenosis

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ABSTRACT

Ischemic stroke is the commonest cause of neurological morbidity and mortality. Carotid endarterectomy has been shown to be beneficial in preventing ischemic strokes in patients with significant stenosis of the carotid artery, both in symptomatic and asymptomatic patients. Carotid artery stenting has been proposed as an alternative to CEA for this population. This paper reviews the available literature on carotid endarterectomy comparing it to the best medical therapy and carotid artery stenting in the prevention of ischemic strokes in patients with carotid stenosis. The use of newer imaging techniques and tools to redefine the existing idea of "asymptomatic" stenosis and post procedural strokes has also been reviewed. We present a concise review of existing data that shows unequivocally that endarterectomy still remains superior to stenting and best medical therapy as of now.

Key words: Carotid artery, endarterectomy, revascularization, stroke

INTRODUCTION

Stroke is the third leading cause of death and probably the most important cause of long-term disability in the United States.[1,2] This may be even higher in the developing world with significantly disabled patients in the low and middle income countries. According to various studies done in India, the prevalence of stroke varies from 145-450/100,000 population.[3,4]

Eighty-five per cent of strokes are ischemic, and it has been reported that in conscious patients with an acute ischemic stroke requiring admission to a stroke unit, 76% had angiographic evidence of complete occlusion of the internal carotid artery, the middle cerebral artery or one of its branches.[5,6] The concept of prevention of further strokes in patients who had been diagnosed with either a transient ischemic attack (TIA), amaurosis fugax, or an ischemic stroke stems from the fact that recurrent strokes may occur with a risk of 3.1% at 30 days (95% CI 1.7 to 4.4%) and 26.4% at 5 years (95% CI 20.1 to 32.8%).[7]

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The evolution of medical therapy has reduced the 5 year stroke rate by almost 50% from the 1960s to the present day in asymptomatic patients.

Extracranial carotid artery disease is one of the major treatable causes of stroke. Studies have shown that large vessel atherosclerotic disease accounts for about 20% of all ischemic stroke patients, out of which about half is due to extracranial carotid artery disease. The recognition of the fact that carotid stenosis and occlusion were the major cause of cerebral vascular insufficiency led to the targeting of the carotid artery in order to prevent recurrent strokes.

In 1953, DeBakey in Texas described the successful abolition of recurrent left cerebral hemispheric ischemic symptoms in a bus driver who underwent CEA in 1953, and in 1954, Eastcott in London successfully treated a 66-year-old housewife with comparable symptoms by resection and repair of her carotid stenosis.[8,9] Since 1954, the underlying principle of resection of the luminal atheromatous plague within the carotid artery has been the foundation of various variations and modifications of CEA. It may be performed under either local or general anaesthesia with little difference in results; however, the use of local anaesthesia gives the added advantage of monitoring of the patient for the evolution of possible focal neurological signs during the procedure.[10] The use of intraoperative shunting during the endarterectomy was

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also advocated especially for patients with contralateral carotid disease, but this too did not appear to significantly influence outcome.[11,12] Closure of the carotid following resection of the plaque may be through primary closure, by prosthetic patch, or by vein graft. There is limited evidence that patch closure may reduce late restenosis and perioperative stroke.[13]

Carotid artery stenting (CAS) has emerged as a potential alternative for patients with symptomatic and asymptomatic carotid artery stenosis. In this paper, we review the literature and present the current evidence regarding the controversy between CAS and CEA.

CEA VERSUS MEDICAL THERAPY

The major randomized trials that compared CEA with best available medical therapy to prevent recurrent strokes in patients with symptomatic carotid occlusive disease were NASCET, ECST, and the Veteran Affairs trail 309.[14-16] The third trial was terminated when the results of NASCET were announced. Patients were classified as symptomatic if they had a TIA or a non disabling stroke in the carotid distribution in the preceding 6 months (for NASCET, the preceding 4 months) [Table 1]. Additionally, NASCET classified the degrees of stenosis as low moderate (<50%), high moderate (50-69%), and severe (70-99%).[14]

North American Symptomatic Carotid Endarterectomy Trial randomized 659 symptomatic patients of severe (70-99%) stenosis and found that the 2-year ipsilateral stroke risk was 26% in the medically treated patients and 9% in the medical therapy plus CEA group (P<0.001) with an absolute risk reduction (ARR) was 17.0%.[17] In the high moderate stenosis group, 858 patients were recruited and the trial showed that the 5-year rate of ipsilateral stroke was 15.7% in patients treated with medical therapy plus CEA and 22.2% in patients who received medical therapy alone (ARR 6.5%, P<0.045). The results were however not consistent across all patient subgroups. There was a greater benefit from CEA in men than in women although this finding was not statistically significant. For prevention of an ipsilateral stroke of any severity or for prevention of a disabling stroke, the number needed to treat was 12 and 16 for men and 67 and 125 for women. Moreover, patients with retinal stroke or retinal TIA in that subgroup did not benefit from surgical treatment.[15]

In patients with less than 50% stenosis the results were not statistically significant, with a 5-year rate of ipsilateral stroke of 14.9% in the CEA group and 18.7% in the medical therapy group (P<0.16).[14]

The ECST trial used a different method of determining the degree of stenosis but the results were consistent with those of NASCET. The 5-year risk reduction of "stroke or surgical death" in ECST patients with 70-99% stenosis randomized to CEA rather than medical treatment was 21.2% (95% CI 12.9 to 29.4%). In patients with 50-69% stenosis, the risk reduction was 5.7% (95% CI 0 to 11.6%).[15]

A combined analysis of the symptomatic trials-ECST, NASCET, and the Veterans affairs trial 309, which included 6092 patients with 35 000 patient-years of follow-up, was performed by Rothwell.[18] In this analysis, individual patient data were included, the angiograms were reassessed, and the outcomes were standardized. Due to differences in the trials in terms of definitions, the combined analysis used the following NASCET definitions, viz.

1) Stroke was defined as any cerebral or retinal event with symptoms lasting longer than 24 h; and
2) Disabling stroke was defined as a stroke that resulted in a Rankin score of 3, or an equivalent rating, at a defined follow-up interval.

For all these studies, the outcome was ipsilateral stroke or perioperative (30 days) stroke or death.

The major conclusions were as follows:
A benefit for CEA was shown for 50-69% stenosis with an ARR of 4.6% (over 5 years). A stenosis of >70% (excluding near occlusion) demonstrated an ARR of 16% (over 5 years). Patients with near occlusion had an ARR of 5.6% over 2 years (P<0.19) but only 1.7% (P<0.9) over 5 years.[18]

Table 1: Trials for symptomatic carotid stenosis-Endarterectomy *vs.* Medical management

Trial	Total patients	Degree of stenosis (%)	Stroke rate (CEA)	Stroke rate (medical)	ARR	*P* value
NASCET[14]	2885	50-69	15.7	22.5	6.5	<0.045
		70-99	8.9	28.3	19.4	<0.001
ECST[19] (reanalysed)	3024	50-69	6.8	12.5	5.7	0.05
		70-99	10.5	31.7	21.2	<0.001
VA 309[16]	189	>50	7.7	19.4	11.7	<0.011

ECST – European Carotid Surgery Trial; ARR – Absolute risk reduction

ASYMPTOMATIC CAROTID STENOSIS

While patients with history of TIA or amaurosis fugax have a significantly increased risk of a disabling stroke, patients of asymptomatic carotid stenosis have a lower risk of developing stroke. However, two major trials have been conducted on asymptomatic patients with significant carotid stenosis to ascertain the potential benefit from CEA in these patients – ACAS – Asymptomatic Carotid Atherosclerosis Study and ACST – Asymptomatic Carotid Surgery Trial.[20,21]

The ACAS enrolled and randomized 1662 patients with an asymptomatic carotid stenosis of 60% or greater (measured using NASCET criteria) as detected on cerebral angiography or computerized tomography angiogram either to daily aspirin and management of risk factors or to CEA with medical management. The primary comparison was the rate of ipsilateral stroke or any perioperative stroke or death. CEA reduced the rate of this outcome from 11.0 to 5.1%, a relative risk reduction of 53% (95% CI 22 to 72%).[20] The study was halted by the Data Safety and Monitoring Board after 2.7 years because of the projected 5.9% ARR at 5 years favoring CEA.

The Asymptomatic Carotid Surgery Trial randomized 3120 patients with 60-99% carotid stenosis to either immediate endarterectomy, *i.e.,* half of patients being operated on within 1 month after randomization and 88% within the first year, or indefinite deferral of CEA until a clinician considered there to be a clear indication for surgery. In ACST, the degree of stenosis was measured by Doppler ultrasound of the neck. Combining the perioperative events (stroke and death within 30 days) and the non-perioperative strokes, the net 5-year risks were 6.4% (immediate CEA) *versus* 11.8% (deferred CEA) for all strokes ($P<0.0001$) and 3.5% versus 6.1% for fatal or disabling strokes ($P<0.004$). Subgroup analyses demonstrated significant benefits for patients <65 years, and those between 65 and 74 years, but uncertain for those >75 years. Both men and women benefited from CEA. The 5-year benefit of CEA appeared to be as great for those with approximately 70, 80, and 90% carotid artery narrowing on ultrasound. There was no significant difference in results in those patients who were never symptomatic (7.1% absolute 5-year gain) compared with those with symptoms greater than 6 months previously (4.6% absolute 5-year gain).[21] A recent report of long-term results of the ACST has shown a sustained benefit of CEA for patients under the age of 75.[22]

A meta-analysis of these trials and the Veteran Affairs Cooperative Studies[23] show that the practice of endarterectomy for asymptomatic carotid stenosis does reduce the risk of ipsilateral stroke over 3 years.[24] It is important, however, to note that in subgroup analyses, surgical intervention appeared to benefit men more than women and younger patients more than older. When the outcome of any stroke or any death is examined, the risk reduction seen with CEA is not statistically significant (RR 0.92, 95% CI 0.83 to 1.02), and thus the benefit is less substantial here than in symptomatic patients.[24]

Medical therapy for atherosclerosis has substantially improved over the past 20 years and thus the results of the ACAS and ACST should be looked at in present light with care. With best medical therapy the risk of stroke in patients of >50% stenosis is about 0.34% per year, as compared to 2-5% risk in major trials quoted above.[25] Statin therapy, for instance has been shown to reduce the need for revascularization by almost half.[26] Re-evaluation of the long-term risk of stroke on modern medical therapy *versus* CEA is now being addressed by two ongoing trials, namely SPACE-2[27] and the European Carotid Surgery Trial 2 (www.ecst-2.com). In addition, the newer trials comparing endarterectomy and stenting in asymptomatic patients also have a medical arm (TACIT trial).

CEA VERSUS STENTING - EARLY TRIALS

Carotid angioplasty was described in the late 1960s and 70s as a possible alternative to open surgery.[28,29] Various modifications in technique and evolution of stents led to interest in this procedure and by 2003 over 10 000 patients had undergone endovascular treatment of carotid stenosis.[30]

The earliest moderately well-designed trials to compare CEA with CAS were SAPPHIRE – Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy and CAVATAS – Carotid and Vertebral Artery Transluminal Angioplasty Study.[31,32]

CAVATAS included patients with anterior circulation symptoms and carotid artery stenosis as well as those with posterior circulation symptoms and vertebral artery stenosis and patients were randomized to either angioplasty or endarterectomy. The 30-day rate of stroke with symptoms persisting more than 7 days or death was almost identical between the two randomized groups, but during extended follow-up, there was a non-significant increase in the 8 year incidence of ipsilateral non perioperative stroke, which was 11.3% in the endovascular group compared to 8.6% in the endarterectomy group.[33] The study was therefore

considered underpowered to detect a significant difference in treatment effect (*n*=504). Also, during the course of the trial the angioplasty procedure evolved to include the routine deployment of a carotid stent.[33]

The SAPPHIRE trial looked at patients who were considered "high risk" for endarterectomy. These included those with cardiac disease, respiratory disease, contralateral carotid occlusion, contralateral laryngeal nerve palsy, recurrent stenosis, previous radical neck surgery or radiation therapy to the neck, or advanced age (over the age of 80 years).[31] Symptomatic patients were enrolled if they had stenosis of at least 50%, and asymptomatic patients if they had stenosis of at least 80%. Stenting patients received a cerebral protection device. The trial was of non-inferiority design, testing the hypothesis that CAS was not inferior to CEA. At 1 year, the specified endpoint of death, stroke, or MI was reached by 12.2% of stenting and 20.1% of endarterectomy patients with 95% confidence intervals for the difference that included equality of the two treatments. At 3 years, there was no statistically significant difference in the rate of stroke, death, or MI between the groups.[34] This trial enrolled a large proportion of asymptomatic patients, and thus extrapolation of the results to a purely symptomatic population, which carries a higher procedural risk of stroke that is not possible.

CEA VERSUS STENTING - RECENT TRIALS

Four major trials are considered here SPACE, EVA-3S, ICSS, and CREST [Table 2].

The Stent-Protected Angioplasty *versus* Carotid Endarterectomy (SPACE) study was carried out in Central Europe. This trial was of non-inferiority design, and analysis of 1183 patients provided 30-day complication rates of 6.84% death or ipsilateral stroke associated with CAS and 6.34% with CEA (absolute difference 0.51%, 90% CI − 1.89 to 2.91%, one-sided *P* value for non-inferiority 0.09).[35] Continuing follow-up to 2 years, the SPACE investigators found similar rates in both groups for recurrent ipsilateral stroke, although it was noted that recurrent carotid artery stenosis was more common in the CAS group.[36]

The French EVA-3S (Endarterectomy *versus* Angioplasty in Patients with Symptomatic Severe Carotid Stenosis) trial was also of non-inferiority design, and the early safety results were reported around the same time as the results of SPACE.[37] After 527 patients had been randomized, recruitment was stopped early on the recommendation of the safety committee because the primary endpoint of peri-procedural stroke or death occurred in 9.6% of the stenting group (95% CI 6.4 to 14.0%) compared to just 3.9% of the endarterectomy group (95% CI 2.0 to 7.2%). Follow-up was continued up to 4 years after randomization and showed that the subsequent longer-term risk of recurrent ipsilateral stroke after the periprocedural period was "low and similar in both treatment groups."[38] This trial also showed significant early post procedural morbidity in patients who underwent stenting without a protection device.

The International Carotid Stenting Study initially randomized 1713 patients with stenosis >50%. The interim intention to treat analysis has recently been reported and the main safety end points – stroke, death, or procedural MI at 120 days – were 8.5% and 5.2% for CAS and CEA, respectively (*P*<0.006).[39] At 30 days, the incidence of disabling stroke was the same in both groups (1.7%), but the incidence of fatal and non disabling stroke was significantly greater in CAS-treated patients. Of periprocedural strokes, 74% in CAS-treated patients and 44% in CEA-treated patients occurred on the day of the procedure. Risks of any stroke (65 *vs.* 35 events) and all-cause death (19 *vs.* 7 events) were greater in the stenting group than in the endarterectomy group. Long-term follow-up has not yet been completed in this study, with interim results suggesting CEA to be the treatment of choice.[39]

The latest trial to date to compare CEA with CAS is the Carotid Revascularization Endarterectomy *vs.* Stenting Trial - CREST. The study design was to test for superiority with the null hypothesis as the equivalence of

Table 2: Trials comparing CEA with CAS in symptomatic carotid stenosis

Trial	Sample size	Primary treatments	Outcome	Rate of outcome at 30 days post procedure (%)
EVA-3S[37,38]	527	CAS+CPD CEA	Any periprocedural stroke or death	9.6 *vs.* 3.9 (*P*=0.01) by intention to treat
SPACE[35,36]	1183	CAS +/- CPD CEA	Any periprocedural ipsilateral ischemic stroke or death	6.84 *vs.* 6.34 (*P*=0.09 for non-inferiority) by intention to treat
ICSS[39]	1,713	CAS +/- CPD CEA	Any periprocedural stroke, MI, or death	7.4 *vs.* 4.0 (P=0.003) per protocol
CREST (symptomatic patients)[40]	1,321	CAS+CPD CEA	Any periprocedural stroke, MI, or death	6.7 *vs.* 5.4 (*P*=0.3) by intention to treat

CAS – Carotid artery stenting; ICSS – International carotid stening study; SPACE – Stent-protected angioplasty versus carotid endarterectomy)

the two treatments.[40] The study enrolled 2502 patients at 117 centres in the United States and Canada. Both surgeons and interventionalists had to have minimum acceptable outcome results for inclusion in the study.[41] The protocol specified the use of a single stenting system and, when feasible, the same embolic protection device in CAS-treated patients. The primary end points for the study were any periprocedural stroke, MI, death, or post procedural ipsilateral stroke up to 4 years after intervention (similar to ICSS). MI was defined by specifically timed cardiac enzyme increase (creatine kinase and troponin) and electrocardiographic changes and was independently reviewed by a cardiologist who was blinded to the treatment. CREST also included a measurement of functional health and well-being by including the Short-Form Health Survey (*i.e.,* SF-36) at 2 weeks, 1 month, and 1 year after the procedure, hitherto not examined in other studies.[40]

There was no significant difference in the rates of the primary end points between CAS and CEA (7.2 *vs.* 6.8%; hazard ratio; $P<0.51$) at a mean follow-up of 2.5 years.[42] On subgroup analysis, change in treatment effect with age was significant ($P<0.02$). Outcomes, interestingly, were slightly better with CAS for patients aged <70 years with greater benefit the younger the patient and better with CEA for patients aged >70 years, with an increase in age demonstrating an increase in benefit. The periprocedural (30-day incidence) end point did not differ for CAS and CEA, but there were statistically significant differences in the components for CAS and CEA treated patients (stroke 4.1% *vs.* 2.3%, $P<0.012$; and MI 1.1% *vs.* 2.3%, $P<0.032$).[42]

In summary, CEA is superior to CAS in respect to the outcomes of ischemic stroke, perioperative stroke, or death in both asymptomatic and symptomatic patients. However, addressing the primary end point of any stroke, MI, or death up to 4 years after intervention, the two interventions were comparable with no significant statistical difference.[42]

The inclusion of asymptomatic cardiac ischemia as a primary end point in CREST has been criticized by a number of commentators.[43] The clinical relevance of including silent cardiac events is questionable because results from the Health Survey (SF-36) in CREST showed no adverse effects on the quality of life as the result of cardiac events. Furthermore, without inclusion of asymptomatic cardiac ischemia in CREST as a primary end point, CEA would be a safer procedure because of a greater incidence of perioperative strokes and death in the CAS group. This difference is still significant at 4 years.[43-45]

A meta-analysis of three large trials comparing CEA and CAS has found that perioperative risk of stroke or death was significantly higher with CAS (8.9% [153/1725]) than with CEA (5.8%[99/1708]) (relative risk, 1.53; 95% confidence interval, 1.20-1.95, $P=0.0006$).[46] The investigators concluded that CAS for treatment of people with symptomatic carotid artery stenosis should be avoided among people older than 70 years. Data on the safety and potential efficacy of CAS in younger patients were insufficient to draw a conclusion. The findings of an age relationship for safety and efficacy of CAS in the meta-analysis generally are in agreement with those found in CREST. Amerenco *et al.* concluded that CEA should be considered safer than CAS, particularly when looking at the end points of prevention of ischemic stroke and perioperative stroke or death.[44]

CEA VERSUS CAS IN ASYMPTOMATIC PATIENTS

The SAPPHIRE, CREST, and TESCAS-C trials had significant cohorts of asymptomatic patients who were randomized to CAS and CEA. A meta-analysis of these patients revealed a trend toward worse outcome with CAS in asymptomatic patients in the short-term with respect to periprocedural stroke or death, and in the intermediate to long term with respect to periprocedural death or stroke plus ipsilateral stroke thereafter. However, because the total number of patients studied is low, the increased event rate does not reach statistical significance.[47]

NEW DIFFUSION LESIONS ON MRI

The ICSS, in its interim analysis did give evidence that stenting has a higher rate of non disabling strokes than endarterectomy for symptomatic patients with carotid stenosis. The follow-up assessment was not blinded to treatment and therefore it was decided to include imaging in the follow-up of a subset of patients. It has been shown in many earlier reports of non-randomized studies that stenting has a higher rate of new lesions appearing on MRI post procedure.[48,49]

The results of this study were published recently.[50] ICSS enrolled 231 patients in a magnetic resonance imaging (MRI) sub-study examining the incidence of new diffusion-weighted imaging (DWI) lesions post-treatment with either stenting ($n=124$) or endarterectomy ($n=107$). The adjusted odds ratio for finding at least one new DWI lesion on a post-treatment scan (performed on a median of 1 day after treatment) was 5.21 (95% CI 2.78 to 9.79) after CAS compared with CEA.[50] Half of

the patients (50%) who underwent stenting developed a new lesion when compared to 17% of patients who underwent endarterectomy. More importantly, in many of these patients, these diffusion lesions persisted, and were seen as FLAIR positive lesions at an MRI done at 1 month. At 1 month, there were new changes in FLAIR in 28 (33%) of the 86 patients in the stenting group and six (8%) of the 75 in the CEA group. In the patients who underwent stenting with protection devices, 73% had at least one diffusion positive lesion on post-treatment scans, compared to 34% in the patients who were treated without a protection device.

In another systematic review of literature, Schnaudigel *et al.* reviewed 32 studies (1363 CAS and 754 CEA procedures). The incidence of any new DWI lesion was significantly higher after CAS (37%) than after CEA (10%) ($P<0.01$).[49] Similar results were obtained in a meta-analysis focusing on those studies directly comparing the incidence of new DWI lesions after either CEA or CAS (OR 6.1; 95% CI, 4.19 to 8.87; $P<0.01$).[50]

In the light of these findings, many authors now suggest that akin to including asymptomatic MI as a primary end-point in the trials comparing CEA and CAS, the newer trials should also include asymptomatic stroke (new diffusion lesions after the procedure of FLAIR positive lesion at 1 month) as the end-point. As of now, the new diffusion lesions are of unclear significance, but there is clearly a much higher incidence of both asymptomatic and symptomatic stroke in the stenting group.

HYPERPERFUSION AND INTRACEREBRAL HEMORRHAGE

The outcomes studied in all of the trials that have compared CEA with CAS have been non-disabling or disabling ischemic strokes and death. The rate of intracerebral hemorrhage as a complication following intervention has not been studied in any of the trials. This is because the studies are not powered to bring out the differences between the two as regards to ICH following the two procedures. However, large systematic inpatient samples would bring out these differences.

A study conducted by McDonald *et al.* addressed this by retrospectively relating all intracerebral hematomas in the National Inpatient Sample (NIS) of the United States to prior CEA/CAS.[51] This would be the "real life scenario," as practised in the US. They compared the data between 215 012 CEA and 13 884 CAS procedures in the NIS sample between 2001 and 2008. Symptomatic presentations represented minority of CEA (5%) and CAS cases (10%). ICH occurred significantly more frequently after CAS than CEA. Among symptomatic presentations, the frequency of hemorrhage was 6-fold higher among CAS procedures, relative to CEA procedures (4.4 *vs.* 0.8%, $P<0.0001$). In asymptomatic patients, intracranial hemorrhage rates were 10-times higher among cases undergoing CAS *versus* CEA (CEA, 0.06%; CAS, 0.5%; $P<0.0001$). Similar to earlier studies, in-hospital mortality rates were higher among symptomatic patients who underwent CAS (6.2 *vs.* 4.0%; $P<0.0001$). Patients <70 years had lower in-hospital mortality than patients 70 years or older, irrespective of clinical presentation or revascularization procedure. In contrast, symptomatic patients who underwent CAS <70 years had higher rates of intracranial hemorrhage compared to similarly treated individuals 70 years or older (5.0 *vs.* 3.3%). In all other subgroups (asymptomatic CAS recipients, symptomatic CEA recipients, asymptomatic CEA recipients), patients 70 years or older had higher rates of ICH relative to younger patients.[51]

The cause has been postulated to be either surgical handling of the carotid, reperfusion injury, or the use of two antiplatelet drugs while stenting as opposed to one following endarterectomy.

CURRENT OPINION

CEA has been the established treatment of choice for patients with symptomatic and asymptomatic internal carotid artery stenosis.[43] The total combined morbidity and mortality of open surgery by experienced surgeons is now <3% and the risk of recurrent stenosis after surgery has been reported to be <0.5% in large series.[52,53] CEA therefore should be offered to symptomatic patients with 50% stenosis and for asymptomatic patients with over 70% carotid occlusion.[54]

CAS has similarly undergone enormous changes in the last decade, with an improvement of endovascular techniques, materials, and an availability of more experienced and skilled interventionalists.[55,56] In addition, new antiplatelet therapies, such as clopidogrel and treatment options for dyslipidemia in the form of various statins have been added to the armamentarium. These medical improvements have not systematically been studied and given the clear superiority of CEA and medical therapy *versus* medical therapy alone in earlier randomized controlled trials,[11] contemporary medical therapy may be of interest in patients with asymptomatic stenosis of 50% or more, given the low incidence of stroke in this patient group.[57]

The results of the CREST trial showed an increased risk of cardiac events in the CEA cohort and this must

be interpreted in the light of two factors. The first is the effect of current antiplatelet therapies, where CEA is usually performed under the administration of only one antiplatelet agent and CAS on double antiplatelet therapy. And second, in the CREST study, CEA was commonly performed under generally anaesthesia (90%) with CAS being performed preferentially under local anaesthesia resulting in more cardiac events in the surgical group (2.3 *vs.* 1.1%).[40]

Currently, CEA by the experienced surgeon remains the gold standard for treatment of patients with carotid occlusive disease. The complication rate and durability of CEA (with respect to restenosis) is superior to that reported for stenting at this time. This fact suggests that it may be more beneficial in patients <70 years. The data from the CREST trial and a large meta-analysis of pooled individual patient data from the EVA-3S trial, the SPACE trial, and the ICSS all suggest lower risk in older patients with CEA.[40,46] This may be due to a more friable plaque in older patients.[58] Additionally, retrospective data have been published that demonstrate that CEA risk does not increase with age of a patient.[59]

Good indications for stenting at this time include patients with recurrent carotid stenosis and vocal-cord paresis. The Carotid Stenting Trialists' Collaboration study of their meta-analysis of pooled individual patient data of 3433 randomized patients with symptomatic internal carotid artery stenosis demonstrates that the risk of any stroke or death occurring within 120 days of randomization was greater in the stent group (8.9%) than in the CEA group (5.8%), a result that is statistically highly significant,[46] even though 5.8% surgical complication rate is well above that reported by many experienced surgeons.

The future may see better prediction of stroke risk in apparently asymptomatic patients with the use of more sensitive measures of cerebral perfusion, such as magnetic resonance angiography, fludeoxyglucose-positron emission tomography, computed tomography angiography, or transcranial Doppler monitoring of high-intensity transient. More aggressive use of cognitive assessment as a measure of chronic cerebral ischemia may also change the existing definition of "asymptomatic."[60]

Evolution in medical management may obviate the need for any kind of intervention in patients with asymptomatic carotid stenosis and reserve surgery or endovascular intervention for patients with symptomatic occlusions.

As with stenting, there are significant variations in technique of plaque removal, closure of the arteriotomy, and the use of cerebroprotective agents across various centers in the world. This leads to some discrepancy in surgical results especially while looking at morbidity. A more in depth and objective analysis of these are required to determine the best possible treatment within the various options of endarterectomy itself. This can only lead to a further reduction in morbidity in an otherwise excellent procedure.

Surgical treatment of extracranial carotid disease *via* endarterectomy still remains the mainstay and gold standard of treatment for atherosclerotic carotid occlusive disease. Many trials have shown stenting to be inferior when compared to CEA in terms of neurological outcome. Till further data are available therefore, it is recommended to offer endarterectomy by an experienced surgeon to these patients.

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