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Choices of Stent and Cerebral Protection in the Ongoing ACST-2 Trial: A Descriptive Study

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WHAT THIS PAPER ADDS

Technical innovations in stent design and cerebral protection (CPD) may improve the outcome of carotid artery stenting (CAS). The present study reports whether interventionalists tailor their choice of stent and CPD according to plaque echolucency or severity of stenosis in the Asymptomatic Carotid Surgery Trial-2 (ACST-2), the largest interventional trial comparing CAS with carotid endarterectomy.

Objective/Background: Several plaque and lesion characteristics have been associated with an increased risk for procedural stroke during or shortly after carotid artery stenting (CAS). While technical advancements in stent design and cerebral protection devices (CPD) may help reduce the procedural stroke risk, and anatomy remains important, tailoring stenting procedures according to plaque and lesion characteristics might be a useful strategy in reducing stroke associated with CAS. In this descriptive report of the ongoing Asymptomatic Carotid Surgery Trial-2 (ACST-2), it was assessed whether choice for stent and use or type of CPD was influenced by plaque and lesion characteristics.
Methods: Trial patients who underwent CAS between 2008 and 2015 were included in this study. Chi-square statistics were used to study the effects of plaque echolucency, ipsilateral preocclusive disease (90–99%), and contralateral high-grade stenosis (>50%) or occlusion of the carotid artery on interventionalists' choice for stent and CPD. Differences in treatment preference between specialties were also analysed.
Results: In this study, 831 patients from 88 ACST-2 centres were included. Almost all procedures were performed by either interventional radiologists (50%) or vascular surgeons (45%). Plaque echolucency, ipsilateral preocclusive disease (90–99%), and significant contralateral stenosis (>50%) or occlusion did not affect the choice of stent or either the use of cerebral protection and type of CPD employed (i.e., filter/flow reversal). Vascular surgeons used a CPD significantly more often than interventional radiologists (98.6% vs. 76.3%; $p < .001$), but this choice did not appear to be dependent on patient characteristics.
Conclusion: In ACST-2, plaque characteristics and severity of stenosis did not primarily determine interventionalists' choice of stent or use or type of CPD, suggesting that other factors, such as vascular anatomy or personal and centre preference, may be more important. Stent and CPD use was highly heterogeneous among participating European centres.

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INTRODUCTION

In Europe, despite advances in medical therapy and a reduction in smoking, stroke remains the third leading cause of mortality and the most important cause of long-term disability. Carotid artery stenosis is thought to cause up to 20% of all ischaemic strokes.[1] Randomised controlled trials have shown that both carotid endarterectomy (CEA) and carotid artery stenting (CAS) are effective in preventing long-term stroke caused by tight carotid stenosis.[2,3]

Concerns remain about the higher periprocedural (<30 days) stroke rate following CAS.[4] Analysis of the underlying pathophysiological mechanism of these procedural strokes has shown that most strokes occur on the day of the procedure.[5]

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Better patient selection and technical developments could make stenting as safe as surgery. Technical advances in stenting include use of cerebral protection devices (CPD), which have been shown to reduce brain embolisation during CAS.[6] Cerebral protection with flow-reversal devices reduce brain embolisation when compared with distal filter devices.[7]

Stent design might also influence outcome of CAS. Closed-cell stents are thought to prevent extrusion of vulnerable plaque through the stent, while open-cell stents provide more flexibility in tortuous vessels. The use of closed-cell stent design has shown to reduce post-procedural stroke when compared with open-cell design.[8]

Interventionalists will be influenced by patient anatomy and may be influenced by other patient characteristics in their choice of stent type and/or CPD use. Plaque echolucency is thought to be a marker of plaque vulnerability and has been associated with higher periprocedural risk.[9] High-grade contralateral disease might make proximal occlusion devices less suitable because of relatively long endovascular occlusion time. During filter-protected CAS, patients with echolucent, vulnerable plaque, or preocclusive ipsilateral disease may be at higher risk of ipsilateral stroke.[10]

As a consequence, although anatomical characteristics are of great importance when choosing stent and CPD, tailoring this choice to individual lesion characteristics might reduce periprocedural risk in CAS. In the ongoing second Asymptomatic Carotid Surgery Trial (ACST-2), choice of stent and cerebral protection device is left to interventionalists' discretion. The aim was to assess whether interventionalists' choices are influenced by the reported plaque and lesion characteristics.

METHODS

Trial protocol and patient selection

ACST-2 is an ongoing, large-scale, randomised controlled trial comparing CEA with CAS in patients with asymptomatic carotid stenotic disease (i.e., no ipsilateral stroke, transient ischaemic attack or amaurosis fugax in the past 6 months). The trial protocol has been described previously.[11]

Patients are eligible for ACST-2 when there is tight carotid stenosis, revascularization is thought to be necessary, and there is substantial uncertainty as to whether CEA or CAS is the more appropriate treatment. Carotid imaging must be done before randomisation in order to show that the anatomy is appropriate for both procedures and patients should reasonably expect to have at least 5 years of good-quality life following intervention.

In the present study, patients who had undergone CAS and had a verified 1-month follow-up, which included the details of the procedure, were included. This analysis includes data collected up to December 2015, when >2000 patients had been enrolled in ACST-2.

ACST-2 was approved by the East of England Cambridgeshire and Hertfordshire Ethics Committee. Individual collaborating centres also obtained approval from their local ethics committees before patients could be included in the trial.

CAS

ACST-2 is designed to reflect everyday clinical practice and therefore all interventionalists participating in ACST-2 should follow their locally approved protocol for CAS. All CE-marked stents and cerebral protection devices can be used in ACST-2. Interventionalists performing CAS have to have independently approved track records, documenting their experience and success with the procedure.

Stents in the trial may be of open-cell, closed-cell, or hybrid design. New generation, double-layer membrane mesh stents are now also being used in ACST-2, but were excluded from this analysis owing to low numbers at time of data extraction. The use of CPD was recorded for all patients. Three main types of CPD being used in ACST-2 include distal filters, proximal occlusion, and distal balloon occlusion, but distal balloon devices were excluded from analysis of CPD type, again owing to low numbers.

Plaque echolucency, defined as Gray—Weale type I (uniformly anechoic or hypoechoic) or type II (predominantly [>50%] hypoechoic)[12] and the severity of ipsi- and contralateral stenosis was determined by duplex ultrasonography. Angiographic data was not collected by the trial office.

Statistical analysis

Statistical analysis was performed using SPSS (Version 22, 2013; IBM, Armonk, NY, USA). Baseline characteristics of patients with echolucent and nonecholucent plaques were compared using a chi-square test, and a two-sample *t* test was used to compare the mean of continuous variables. For the analysis of stent design, hybrid stents were combined with closed-cell stent design. Chi-square testing was used to analyse whether plaque echolucency, ipsilateral preocclusive disease (90—99%), and contralateral high-grade stenosis (>50%) or occlusion influenced stent choice or use of CPD. Differences in treatment preferences by specialty of interventionalists were also analysed. As ACST-2 is an ongoing trial scheduled to report initial results in 2020, influence of stent and CPD choice on procedural outcome cannot be analysed at this stage. A p-value $< .05$ was considered significant for all analyses.

RESULTS

Patient characteristics

Between January 2008 and December 2015, 2045 patients were randomized in ACST-2. At the time of analysis, the trial office had received and verified information on the procedure for 878 patients who underwent CEA and for 831 who had undergone CAS.

The 831 patients in this study were recruited from 88 centres in 27 countries. Interventional radiologists (IRs; 50%) and vascular surgeons (45%) performed the majority of procedures, while the remaining 5% was performed by cardiologists. Baseline patient characteristics are summarized in Table 1. Plaque echolucency was assessed in 528/831 (64%) patients and 250/528 (47%) of these were said to

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