

## 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.<sup>1</sup> 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.<sup>2,3</sup>

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

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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.<sup>6</sup> Cerebral protection with flow-reversal devices reduce brain embolisation when compared with distal filter devices.<sup>7</sup>

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.<sup>8</sup>

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.<sup>9</sup> 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.<sup>10</sup>

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.<sup>11</sup>

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)<sup>12</sup> 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 pre-occlusive 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 summarised in Table 1. Plaque echolucency was assessed in 528/831 (64%) patients and 250/528 (47%) of these were said to

**Table 1.** Baseline characteristics and plaque echolucency.

|   | Nonecholucent ( <i>n</i> = 278) | Echolucent ( <i>n</i> = 250) | <i>p</i> <sup>a</sup> | Not assessed ( <i>n</i> = 303) | <i>p</i> <sup>b</sup> |
|---|---------------------------------|------------------------------|-----------------------|--------------------------------|-----------------------|
| <b>Ipsilateral carotid diameter reduction (%)</b>   |                                 |                              |                       |                                |                       |
| <80   | 102 (36.7)                      | 92 (36.8)                    | .793                  | 113 (37.3)                     | .002                  |
| 80–89   | 121 (43.5)                      | 114 (45.6)                   |                       | 104 (34.3)                     |                       |
| 90–99   | 55 (19.8)                       | 44 (17.6)                    |                       | 86 (28.4)                      |                       |
| Mean ± SD   | 79 ± 8.5                        | 79 ± 8.5                     | .566                  | 80 ± 9.1                       | .189                  |
| <b>Contralateral carotid diameter reduction (%)</b> |                                 |                              |                       |                                |                       |
| 0–49  | 196 (70.5)                      | 162 (64.8)                   | .449                  | 159 (52.5)                     | <.001                 |
| 50–69   | 46 (16.5)                       | 47 (18.8)                    |                       | 79 (26.1)                      |                       |
| 70–99   | 18 (6.5)                        | 24 (9.6)                     |                       | 32 (10.6)                      |                       |
| Occluded  | 18 (6.5)                        | 17 (6.8)                     |                       | 33 (10.9)                      |                       |
| Mean ± SD   | 32 ± 29.5                       | 35 ± 30.5                    | .235                  | 39 ± 35.2                      | .030                  |
| <b>Side of intervention</b>                         |                                 |                              |                       |                                |                       |
| Right   | 151 (54.3)                      | 139 (55.6)                   | .767                  | 161 (53.1)                     | .618                  |
| <b>Anaesthetic technique</b>                        |                                 |                              |                       |                                |                       |
| General   | 14 (5.0)                        | 6 (2.4)                      | .113                  | 11 (3.6)                       | .908                  |
| <b>Medical history</b>                              |                                 |                              |                       |                                |                       |
| Atrial fibrillation                                 | 13 (4.7)                        | 21 (8.4)                     | .082                  | 23 (7.6)                       | .527                  |
| Renal disease                                       | 27 (9.8)                        | 29 (11.6)                    | .490                  | 27 (8.9)                       | .426                  |
| Diabetes  | 88 (31.7)                       | 73 (29.2)                    | .541                  | 84 (27.7)                      | .399                  |
| <b>Systolic blood pressure (mmHg)</b>               |                                 |                              |                       |                                |                       |
| >160  | 38 (13.7)                       | 33 (13.2)                    | .875                  | 44 (14.5)                      | .666                  |
| Mean ± SD   | 140.6 ± 16.5                    | 142.0 ± 14.9                 | .317                  | 140.2 ± 16.4                   | .386                  |
| <b>Diastolic blood pressure (mmHg)</b>              |                                 |                              |                       |                                |                       |
| >90   | 57 (20.5)                       | 49 (19.6)                    | .796                  | 54 (17.8)                      | .428                  |
| Mean ± SD   | 79.6 ± 9.7                      | 80.3 ± 8.9                   | .372                  | 78.9 ± 9.4                     | .134                  |
| <b>Medical therapy at randomization</b>             |                                 |                              |                       |                                |                       |
| Antiplatelet  | 259 (93.8)                      | 229 (92.0)                   | .403                  | 261 (86.4)                     | .002                  |
| Anticoagulant                                       | 17 (6.2)                        | 25 (10.0)                    | .102                  | 26 (8.6)                       | .398                  |
| Antihypertensive                                    | 250 (90.0)                      | 227 (91.2)                   | .816                  | 252 (83.4)                     | .001                  |
| Lipid-lowering                                      | 233 (84.4)                      | 211 (84.7)                   | .920                  | 246 (81.5)                     | .246                  |

Note.

<sup>a</sup> Between patients with echolucent and nonecholucent plaques.

<sup>b</sup> Between patients with echolucency assessed and not assessed.

have echolucent plaques (Gray–Weale type I or II). No significant differences in baseline characteristics were found between patients with echolucent and nonecholucent plaques. Severity of carotid stenosis was somewhat higher, on both ipsi- ( $p = .002$ ) and contralateral side ( $p < .001$ ), in patients where echolucency was not assessed.

### Stent design

Thirteen different stents were used. The Wallstent (Boston Scientific, Natick, MA, USA) was the most popular closed-cell stent, and the Precise (Cordis–Cardinal, Bridgewater, NJ, USA) the commonest open-cell stent (Table 2). Fifteen patients were excluded from this analysis, either because the name of the stent used is still awaited or because a membrane mesh stent was used. In the remaining 816 patients, closed-cell stents were used more often (44%) than open-cell stents (36%) and hybrid stents (20%). Thirty centres, including more than one patient (range 2–19), used the same stent in each trial patient. Of these, 17 (101 patients) used a closed stent and 13 centres (59 patients) used an open stent only. The majority (35 centres, 582 patients) used more than one stent design and only seven

**Table 2.** Stents used.

| Design   | Name (manufacturer)           | <i>n</i> (%) |
|----------|-------------------------------|--------------|
| Open     | Precise (Cordis–Cardinal)     | 108 (13.0)   |
|          | Acculink (Abbott)             | 88 (10.6)    |
|          | Protégé (Covidien–Medtronic)  | 86 (10.3)    |
|          | ViVEXX (CR Bard)              | 7 (0.8)      |
|          | Zilver (Cook Medical)         | 3 (0.4)      |
| Closed   | Wallstent (Boston Scientific) | 200 (24.1)   |
|          | XAct (Abbott)                 | 149 (17.9)   |
|          | Adapt (Boston Scientific)     | 10 (1.2)     |
| Hybrid   | Cristallo Ideale (Medtronic)  | 156 (18.5)   |
|          | Sinus RX (Optimed)            | 8 (0.9)      |
|          | Mer (Balton)                  | 1 (0.1)      |
| Membrane | Roadsaver (Terumo)            | 6 (0.7)      |
|          | CGuard (Inspire MD)           | 4 (0.5)      |
|          | Stent name awaited            | 5 (0.6)      |
| Total    |                               | 831          |

of these sites had an apparent “favourite” stent design (five preferred closed stents and two open stents).

Choice of stent design is summarized in Table 3. Stent choice significantly differed between specialties ( $p < .001$ ), with surgeons and cardiologists using a higher proportion of open-cell stents compared with IRs ( $p = .008$ ).

**Table 3.** Interventionalists' choice for open or closed design (including hybrid stent design).

|  | Open<br>(n = 292) | Closed<br>(n = 524) | Total<br>(n = 816) | p <sup>a</sup>    |
|--|-------------------|---------------------|--------------------|-------------------|
| Specialty                              |                   |                     |                    |                   |
| Surgeons                               | 143 (39.2)        | 221 (60.7)          | 364                | <.001             |
| Radiologists                           | 124 (30.2)        | 286 (69.7)          | 410                |                   |
| Cardiologists                          | 25 (59.5)         | 17 (40.5)           | 42                 |                   |
| Plaque echolucency                     |                   |                     |                    |                   |
| Nonecholucent                          | 85 (31.1)         | 188 (68.9)          | 273                | .843 <sup>b</sup> |
| Echolucent                             | 74 (30.3)         | 170 (69.7)          | 244                |                   |
| Not assessed                           | 133 (44.5)        | 166 (55.5)          | 299                |                   |
| Ipsilateral carotid diameter reduction |                   |                     |                    |                   |
| <90%                                   | 231 (36.5)        | 402 (63.5)          | 633                | .432              |
| 90–99%                                 | 61 (33.3)         | 122 (66.7)          | 183                |                   |
| Contralateral carotid disease          |                   |                     |                    |                   |
| <50%                                   | 168 (33.0)        | 341 (67.0)          | 509                | .103              |
| 50–99%                                 | 98 (40.5)         | 144 (59.5)          | 242                |                   |
| Occluded                               | 26 (40.0)         | 39 (60.0)           | 65                 |                   |

Note. Data are n (%).

<sup>a</sup> Chi-square test. Membrane mesh stents excluded from this analysis.

<sup>b</sup> Chi-square test comparing echolucency with nonecholucent.

Stent choice appeared not to be influenced by patients having ipsilateral 90–99% stenosis ( $p = .432$ ) or by the presence of contralateral stenosis >50% or occlusion ( $p = .746$ ). Plaque echolucency also seemed to have had no effect on stent choice ( $p = .843$ ). Results remained similar when hybrid stents were analysed as a separate group.

### CPDs

Ten different CPDs were used in 726/831 (87%) patients (Table 4). Filters were commonest (580/726; 80%), followed by proximal occlusion devices (142/726; 20%). Many (49/88) centres that recruited more than one patient (range 2–33) had consistent CPD usage, 37 (239 patients) using only filter devices, and in nine (64 patients) no CPD for any trial procedure. However, over half the trial patients (24 centres, 481 patients) were treated in centres that had a clear variation in types of CPD. Analysis of the use of any cerebral protection and type of CPD is summarized in Table 5. IRs used cerebral protection less frequently than other

**Table 4.** Use of cerebral protection devices (CPD).

| Type of CPD        | Name (Manufacturer)            | n (%)      |
|--------------------|--------------------------------|------------|
| Filter             | Emboshield (Abbott)            | 204 (24.5) |
|                    | Filterwire (Boston Scientific) | 159 (19.1) |
|                    | Spider (Medtronic–Covidien)    | 112 (13.4) |
|                    | AccUNET (Abbott)               | 57 (6.9)   |
|                    | Angioguard (Cordis)            | 43 (5.2)   |
|                    | Fibernet (Medtronic)           | 1 (0.1)    |
| Proximal occlusion | Filter uncategorised           | 4 (0.5)    |
|                    | Mo.Ma Ultra (Medtronic)        | 114 (13.7) |
|                    | Gore Flow Reversal (Gore)      | 28 (3.4)   |
| Distal balloon     | TwinOne (Minvasys)             | 3 (0.4)    |
|                    | Viatic (Abbott)                | 1 (0.1)    |
| None used          | –                              | 105 (12.6) |
| Total              |                                | 831        |

specialties (76% vs. 99%;  $p < 0.001$ ). The decision to use cerebral protection was not associated with any of the lesion characteristics analysed. Plaque echolucency ( $p = .871$ ) and contralateral high-grade stenosis or occlusion ( $p = .318$ ) had no effect on the type of CPD (filter or proximal occlusion) chosen by interventionalists.

### Geographical variance

Data from the six highest recruiting countries are summarized in Table 6, and there was broadly consistent practice across five of six top recruiting countries, with closed-cell stents predominating. In Italy ( $n = 189$ ), a CPD was used for all cases, echolucency was assessed most frequently (90%), and surgeons performed almost all the interventions (98%). In the UK, the second highest recruiting country, all interventions ( $n = 129$ ) were performed by IRs, but echolucency was only entered for 26% of patients and a CPD was deployed in 74% of interventions. In Sweden ( $n = 82$ ), to date, hybrid stent design was used most commonly (42%).

Clinical practice in the top-10 recruiting centres is summarized in Table 7. In these centres, all recruiting >20 patients, a minimum of three different stents was used and all centres used both open and closed stents. Highest recruiting centres used CPD in nearly all procedures (98%), but some used only one type of CPD (four of 10).

### DISCUSSION

In this cohort study of the ongoing ACST-2 trial, where patients were equally suitable for both CEA and CAS, the aim was to assess any influence of plaque echolucency, ipsilateral stenosis, and contralateral carotid disease on interventionalists' choice of stent design or cerebral protection during stenting.

From the results, no clear association between plaque characteristics and treatment choice was found. This suggests that interventionalists base their choice primarily on parameters such as vascular anatomy.

Plaque echolucency is influenced by lipid-rich necrotic core, high macrophage count, and intraplaque haemorrhage.<sup>13</sup> All have been associated with a higher risk of stroke from asymptomatic carotid stenosis,<sup>14,15</sup> and with an adverse outcome following CAS. In the Imaging in Carotid Angioplasty and Risk of Stroke in Carotid Stenting study (ICAROS), echolucent plaque (odds ratio [OR] 7.1, 95% confidence interval [CI] 2–25;  $p = .002$ ) and degree of stenosis >85% (OR 5.8, 95% CI 2–22;  $p = .01$ ) were independent predictors of periprocedural neurological complications.<sup>16</sup>

For high-risk, symptomatic or echolucent, atherosclerotic plaque, a closed stent design with a smaller free-cell area theoretically offers better embolic protection than open-cell stents. In a large study from the American Vascular Registry, where plaque type was not recorded, it was concluded that outcomes after CAS were not significantly influenced by stent design. However, in symptomatic, but not asymptomatic, patients, the open-cell stent group had a higher 30-day stroke rate than the closed-cell group.<sup>17</sup> Several other

**Table 5.** Interventionalists' choice in cerebral protection (excluding distal balloon devices).

| Specialty                                  | CPD usage         |                       | Total<br>(n = 831) | p                 | Type of CPD used           |                                 | Total<br>(n = 722) | p                 |
|--|-------------------|-----------------------|--------------------|-------------------|----------------------------|---------------------------------|--------------------|-------------------|
|  | Used<br>(n = 726) | Not used<br>(n = 105) |                    |                   | Distal filter<br>(n = 580) | Proximal occlusion<br>(n = 142) |                    |                   |
| Surgeons                                   | 365 (98.4)        | 6 (1.6)               | 371                | <.001             | 297 (81.6)                 | 67 (18.4)                       | 364                | .324              |
| Radiologists                               | 318 (76.3)        | 99 (23.7)             | 417                |                   | 246 (78.1)                 | 69 (21.9)                       | 315                |                   |
| Cardiologists                              | 43 (100)          | 0 (0)                 | 43                 |                   | 37 (86.0)                  | 6 (14.0)                        | 43                 |                   |
| Plaque echolucency                         |                   |                       |                    |                   |                            |                                 |                    |                   |
| Nonecholucent                              | 245 (88.1)        | 33 (11.9)             | 278                | .401 <sup>a</sup> | 201 (82.7)                 | 42 (17.3)                       | 243                | .888 <sup>a</sup> |
| Echolucent                                 | 226 (90.4)        | 24 (9.6)              | 250                |                   | 185 (82.2)                 | 40 (17.8)                       | 225                |                   |
| Not assessed                               | 255 (84.1)        | 48 (15.8)             | 303                |                   | 194 (76.4)                 | 60 (23.6)                       | 254                |                   |
| Ipsilateral carotid diameter reduction (%) |                   |                       |                    |                   |                            |                                 |                    |                   |
| <90  | 571 (88.4)        | 75 (11.6)             | 646                | .096              | 459 (80.8)                 | 109 (19.1)                      | 568                | .535              |
| 90–99                                      | 155 (83.4)        | 30 (16.2)             | 185                |                   | 121 (78.6)                 | 33 (21.4)                       | 154                |                   |
| Contralateral carotid disease (%)          |                   |                       |                    |                   |                            |                                 |                    |                   |
| <50  | 462 (89.4)        | 55 (10.6)             | 517                | .057              | 369 (80.2)                 | 91 (19.8)                       | 460                | .584              |
| 50–99                                      | 209 (85.0)        | 37 (15.0)             | 246                |                   | 164 (79.2)                 | 43 (20.8)                       | 207                |                   |
| Occluded                                   | 55 (80.9)         | 13 (19.1)             | 68                 |                   | 47 (85.5)                  | 8 (14.5)                        | 55                 |                   |

Note. Data are n (%).

<sup>a</sup> Chi-square test between echolucency and nonecholucency.

**Table 6.** Geographical variance of clinical practice in the six highest recruiting countries.

| Country | Patients<br>(n) | Centres<br>(n) | Centre assessment<br>of EL <sup>a</sup> | Patients with<br>EL assessed (%) | Intervention done<br>by radiologist (%) | CPD<br>used (%) | Open<br>stent (%) | Closed<br>stent (%) <sup>b</sup> | Most popular<br>stent (%) |
|---------|-----------------|----------------|---|----------------------------------|---|-----------------|-------------------|----------------------------------|---------------------------|
| Italy   | 189             | 15             | 14                                      | 90                               | 2                                       | 100             | 24                | 76                               | XAct (38)                 |
| UK      | 129             | 20             | 11                                      | 26                               | 100                                     | 74              | 36                | 64                               | Precise (30)              |
| Serbia  | 82              | 2              | 2                                       | 67                               | 100                                     | 98              | 20                | 80                               | Wallstent (38)            |
| Sweden  | 82              | 3              | 3                                       | 34                               | 68                                      | 93              | 27                | 63                               | Cristallo (42)            |
| Belgium | 45              | 6              | 4                                       | 87                               | 7                                       | 96              | 73                | 27                               | Acculink (73)             |
| Germany | 44              | 8              | 8                                       | 82                               | 41                                      | 84              | 26                | 64                               | Wallstent (50)            |

Note. EL = echolucency; CPD = cerebral protection device.

<sup>a</sup> Number of centres with at least one patient in whom echolucency was assessed.

<sup>b</sup> Including hybrid stent design.

studies also found a significantly lower periprocedural risk with closed-cell-design stents.<sup>8,18</sup> In a dual-centre (USA and Belgium) study of 701 patients, the difference in periprocedural risk between open- and closed-cell stent design was highest for symptomatic patients (11.1% vs. 3.0%, OR 4.1;  $p = .01$ ) and those with echolucent plaques (8.1% vs. 2.2%, OR 3.1;  $p = .03$ ), supporting the argument that closed-cell stent design provides more effective protection of the potentially vulnerable plaque.<sup>19</sup>

In ACST-2, use of CPD is left to interventionalists' discretion. Embolisation of debris released during the catheterisation phase of CAS may cause stroke, and use of CPD could help prevent this. It was found that IR does not use CPD in 25% of cases, while vascular surgeons routinely use CPD (98%). This difference in practice may therefore not be due to patient characteristics.

Distal filter devices (580/726; 79.9% of total CPD) preserve antegrade flow, but their main disadvantage is the need to cross the lesion before opening the filter. Smaller embolic particles can escape through the filter pores and the filter can also occlude. Proximal occlusion (PO) devices allow protection before crossing the stenotic lesion, but patients may be intolerant of flow reversal in up to 20% of cases.<sup>20</sup> PO devices also require larger

sheaths, and some imaging difficulties may be caused by flow changes in the ICA.

It was shown in the Prevention of Cerebral Embolization by Proximal Balloon Occlusion Compared to Filter Protection during Carotid Artery Stenting study (PROFI) that new brain lesions found on magnetic resonance diffusion weighted imaging are less common in patients treated with PO devices than with filters (45% vs. 87%;  $p = .001$ ).<sup>21</sup> In patients with echolucent plaques treated with distal filter-protected CAS, Montorsi et al. found that significantly higher rates of microembolization (on Transcranial Doppler (TCD)) occurred during four phases of CAS (lesion crossing, stent crossing, stent deployment, and stent dilation) when compared with PO devices.<sup>22</sup>

In the ICAROS study, use of cerebral protection reduced ipsilateral event rate (2.3% vs. 5.0%;  $p = .19$ ). However, in those with echolucent plaques, use of CPD (of which 96% were distal filters) was associated with an increased risk of stroke when compared with unprotected CAS (12.5% vs. 5.2%;  $p = .15$ ).<sup>16</sup>

These results suggest that, for echolucent plaques, it is desirable to initiate protection before crossing the lesion, and PO devices may be safer than filters, unless flow reduction is poorly tolerated.

**Table 7.** Clinical practice in top-10 recruiting centres.

| Centre | Patients (n) | Inclusion period | Specialty | Stents used (n) | Designs used | CPD used (%) | CPD type used |
|--------|--------------|------------------|-----------|-----------------|--------------|--------------|---------------|
| 1      | 92           | 2010–2015        | S         | 6               | O, H, C      | 100          | PO, DF        |
| 2      | 49           | 2009–2015        | IR        | 5               | O, H, C      | 96           | DF            |
| 3      | 41           | 2008–2015        | IR        | 7               | O, H, C, M   | 93           | PO, DF        |
| 4      | 35           | 2008–2014        | S         | 3               | O, H, C      | 94           | PO, DF        |
| 5      | 33           | 2009–2015        | IR        | 4               | O, C         | 100          | DF            |
| 6      | 33           | 2008–2015        | IR        | 5               | O, H, C, M   | 100          | PO, DF        |
| 7      | 28           | 2014–2015        | S         | 3               | O, C         | 100          | DF            |
| 8      | 27           | 2009–2015        | S         | 4               | O, H, C, M   | 100          | PO, DF        |
| 9      | 22           | 2008–2015        | S         | 6               | O, H, C      | 100          | PO, DF        |
| 10     | 21           | 2012–2015        | S         | 5               | O, H, C      | 100          | PO            |

Note. CPD = cerebral protection device; S = surgeon; O = open; H = hybrid; C = closed; PO = proximal occlusion; DF = distal filter; IR = Interventional Radiologists; M = membrane mesh.

Although closed-cell design and proximal occlusion devices may be more appropriate for patients with high-risk plaques and a filter device may be a better choice in patients with contralateral high-grade stenosis or occlusion, no association was found between the characteristics under consideration and operator choice of stent or of CPD.

This lack of association may be explained by differences in patient anatomy or clinical practice, with each centre (or individual) following its own specific protocol for stenting procedures. As guidelines do not recommend the use of certain stents or CPD according to individual patient characteristics, interventionalists often use stents and CPD they are familiar with. Filter-type CPD were introduced earlier and interventionalists therefore have more experience with these devices.

Choice of stent and CPD may, at least partly, be based on financial considerations. The financial saving after shorter hospital stay with CAS may be offset by higher device costs when compared with CEA. In the Carotid Revascularization Endarterectomy versus Stenting (CREST) trial, costs of CEA were not substantially different from CAS.<sup>23</sup> However, national reimbursement rules or hospital contracts could influence stent and CPD choice.<sup>24,25</sup>

Vascular anatomy, both in the arch and in the carotid artery itself, is important in the choice of device and use of protection and was assessed before entry in ACST-2.

The present study had several limitations. ACST-2 is an ongoing trial and data on periprocedural events will not be published until the trial is complete, so stent type and CPD choice cannot be related to periprocedural risk. Also, there was no knowledge of anatomical factors that might have influenced interventionalists in their choice of stent and CPD.

### Conclusion

In the ACST-2, patient characteristics, like plaque echolucency, ipsilateral preocclusive disease, or contralateral occlusion, did not appear to determine primarily interventionalists' choice of stent or CPD. Stent and CPD use was highly heterogeneous among participating European centres.

### CONFLICT OF INTEREST

Professor Bonati received consultancy and advisory board fees from Bayer and Claret Medical.

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