Eur J Vasc Endovasc Surg (2016) 51, 336–342

Antiplatelet Therapy in Carotid Artery Stenting and Carotid Endarterectomy in the Asymptomatic Carotid Surgery Trial-2

A. Huibers [a,c], A. Halliday [a,*], R. Bulbulia [b], G. Coppi [d], G.J. de Borst [c], on behalf of the ACST-2 Collaborative Group

[a] Nuffield Department of Surgical Sciences, University of Oxford, John Radcliffe Hospital, Oxford, UK
[b] Clinical Trial Service Unit, University of Oxford, Oxford, UK
[c] Department of Vascular Surgery, University Medical Center Utrecht, Utrecht, The Netherlands
[d] Department of Vascular Surgery, Nuovo Ospedale S. Agostino Estense, University of Modena, Modena, Italy

WHAT THIS PAPER ADDS

Strokes are infrequent but potentially serious complications following carotid intervention, but antiplatelet therapy can reduce these risks. There are currently no specific guidelines on dose and duration of peri-procedural antiplatelet treatment to help clinical proposal design for patients undergoing carotid intervention. The Asymptomatic Carotid Surgery Trial-2 (ACST-2) is the largest clinical trial of interventional treatment for asymptomatic carotid disease, randomising patients to either carotid endarterectomy (CEA) or carotid artery stenting (CAS). The present study reports the "real-world" practice in peri-procedural antiplatelet therapy among collaborators in ACST-2.

Objective: Strokes are infrequent but potentially serious complications following carotid intervention, but antiplatelet therapy can reduce these risks. There are currently no specific guidelines on dose or duration of peri-procedural antiplatelet treatment for patients undergoing carotid intervention. Within the ongoing Asymptomatic Carotid Surgery Trial-2 (ACST-2), this study aimed at assessing the current use of antiplatelet therapy before, during, and after CEA and CAS in patients with asymptomatic carotid stenosis.
Methods: Questionnaires were sent to ACST-2 collaborators seeking information about the use of antiplatelet therapy during the pre-, peri-, and post-operative periods in patients undergoing carotid intervention at 77 participating sites and also whether sites tested for antiplatelet therapy resistance.
Results: The response rate was 68/77 (88%). For CAS, 82% of sites used dual antiplatelet therapy (DAPT) pre-operatively and 86% post-operatively with a mean post-procedural duration of 3 months (range 1–12), while 9% continued DAPT life-long. For CEA only 31% used DAPT pre-operatively, 24% post-operatively with a mean post-procedural duration of 3 months (range 1–5), while 10% continued DAPT life-long. For those prescribing post-procedural mono antiplatelet (MAPT) therapy (76%), aspirin was more commonly prescribed (59%) than clopidogrel (6%) and 11% of centres did not show a preference for either aspirin or clopidogrel. Eleven centres (16%) tested for antiplatelet therapy resistance.
Conclusion: There appears to be broad agreement on the use of antiplatelet therapy in ACST-2 patients undergoing carotid artery stenting and surgery. Although evidence to help guide the duration of peri-procedural antiplatelet therapy is limited, long-term treatment with DAPT appears similar between both treatment arms.

Article history: Received 12 August 2015, Accepted 1 November 2015, Available online 21 December 2015
Keywords: Carotid artery stenosis, Carotid artery stenting, Carotid endarterectomy, Antiplatelet therapy

INTRODUCTION

Stroke is a leading cause of morbidity and mortality worldwide.[1] Randomised trials in patients with carotid artery narrowing have shown that carotid endarterectomy (CEA) with medical treatment reduces 5 and 10 year stroke risk compared with medical treatment alone.[2,3] A feared peri-operative complication is embolism from the narrowed carotid plaque leading to distal vascular occlusion and ischaemic stroke.[4,5] Antiplatelet therapy reduces the risk of occlusive vascular events, but can also cause bleeding (the risk of which may be increased substantially with more intensive regimens).[6,7] There are no specific guidelines on dose and duration on peri-procedural antiplatelet treatment to help clinical proposal design for patients undergoing carotid intervention.[8,9] In previous carotid trials comparing CEA and CAS, single antiplatelet therapy (usually

* Corresponding author. Nuffield Department of Surgical Sciences, University of Oxford, Level 6 John Radcliffe Hospital, Oxford OX3 9DU, UK.
E-mail address: alison.halliday@nds.ox.ac.uk (A. Halliday).
1078-5884/
http://dx.doi.org/10.1016/j.ejvs.2015.11.002

aspirin) was used for CEA, and dual antiplatelet therapy (usually clopidogrel and aspirin) was either recommended or mandated.[10–12]

The Asymptomatic Carotid Surgery Trial-2 (ACST-2) is the largest clinical trial of interventional treatment for asymptomatic carotid disease, randomising patients to either CEA or carotid artery stenting (CAS). ACST-2 will compare the immediate hazards of both procedures and subsequent stroke rates over the next 5–10 years.[13] Collaborators from 26 countries worldwide are experienced surgeons and interventionists, and the choice of peri-procedural antithrombotic treatment is at the clinicians' discretion. This gives a unique opportunity to study "real-world" practice in peri-procedural antiplatelet therapy. Therefore, the aim of the present study was to describe the use of antiplatelet therapy for both carotid surgery and stenting among collaborators in the ACST-2 trial.

METHODS

ACST-2

The aims and methods used in ACST-2 have been described previously.[13] Briefly, patients with severe asymptomatic carotid stenosis in which revascularisation is felt to be indicated, are randomised in a 1:1 fashion between CAS and CEA. The trial is multicentre and international, thereby facilitating large-scale recruitment of an appropriately heterogeneous and representative group. However, the majority of recruiting centres (93%) are located in Europe and therefore the study largely reflects antiplatelet therapy in Europe. The trial protocol states that all patients should receive appropriate medical treatment, including antiplatelet therapy, but the use and dose of specific antiplatelet drugs (and other drugs) are left to the discretion of the treating physician.

Study

This study questionnaire was administered in August 2014 and addressed four areas of practice: (1) pre-procedural antiplatelet therapy (in CAS and CEA); (2) intra-procedural antiplatelet therapy (CAS and CEA); (3) post-procedural antiplatelet therapy (CAS and CEA); and (4) testing of antiplatelet resistance; Collaborators who failed to respond were sent a reminder e-mail to participate in the study after 4 and 8 weeks. Seventy-seven of the currently active and recruiting centres in ACST-2 were studied; these studies had recruited a total of 1645 patients to ACST-2. In these centres, 75 performed both CAS and CEA and two performed CEA only.

Statistical analysis

Statistical analysis was performed using SPSS (IBM version 22, 2013). If an answer to duration of antiplatelet therapy was given as a range, the midpoint was taken for the subsequent analysis. Chi-square test was applied to compare pre-, intra- and post-procedural antiplatelet therapy, and a Mann-Whitney *U* test was used to compare means between two treatments. A *p*-value was considered significant when $<.05$.

RESULTS

Response

This study was completed in 66 of 75 centres (88% for CAS) and 61 of 77 centres (79% for CEA). These centres had randomised 1407/1645 patients in ACST-2 (85% of the overall randomisation) from 20 different countries.

Carotid artery stenting

Nearly all responding collaborators who performed CAS had a specific protocol for pre-procedural antiplatelet therapy (65/66 [98%]). The majority treated patients with dual antiplatelet therapy (DAPT) prior to stenting (53/65 [82%]). In nearly all centres (52/53 [98%]) DAPT consisted of aspirin and clopidogrel. One centre prescribed aspirin in combination with either clopidogrel or ticagrelor. Other pre-procedural treatment regimens consisted of aspirin only (3/65 [5%]), clopidogrel only (6/65 [8%]), or triple antiplatelet therapy (3/65 [5%]).

During CAS, all patients received heparin and pre-procedural antiplatelet therapy was continued. One centre also routinely used intra-procedural dextran.

After stenting, all patients received at least aspirin or clopidogrel as life-long therapy. The majority of centres (51/66 [77%]) used DAPT for a defined period post-stenting, followed by life-long single antiplatelet therapy. The drug of preference for life-long treatment was aspirin in 68% of the centres (45/66) and clopidogrel in 6/66 centres (9%). In 51 centres, 12 (24%) administered DAPT for up to 4 weeks and 39 centres (76%) extended DAPT beyond the procedural period (median 3; range 1–12 months). A small proportion of respondents stated that they would give life-long DAPT (6/66 [9%]) or just use life-long single antiplatelet therapy (5/66 [8%]). Four centres treated patients with 9 months of prasugrel or cilostazol (4/66 [6%]) in addition to DAPT (Table 1).

Carotid endarterectomy

For CEA, collaborators had a protocol for pre-operative antiplatelet therapy protocol in 55 out of the 61 responding centres (90%). The remaining six centres continued baseline therapy at randomisation.

Prior to the procedure, most patients received aspirin as single antiplatelet therapy (36/55 [65%]). In 17 centres (31%) dual antiplatelet therapy was used. The number of centres that prescribed DAPT prior to CEA was significantly lower than the use of DAPT prior to CAS ($p < .05$). DAPT consisted of aspirin and clopidogrel in 14 centres. Three centres prescribed aspirin in combination with dipyridamole. In one centre (2%) clopidogrel was used as a single antiplatelet agent. Other pre-procedural treatments consisted of triple antiplatelet therapy in one centre. Patients undergoing CEA received similar intra-operative antiplatelet treatment to patients undergoing CAS: in all centres heparin