

From the Editors

The Story of Anybody, Somebody, Nobody and Everybody

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“There was an important job to be done. Everybody thought Somebody would do it. Anybody could have done it; but Nobody did it. Somebody got angry because he thought it was Everybody’s job to do it. In the end; Everybody blamed Somebody, when Nobody did what Anybody could have done!”

ANON

In this issue of the *EJVES*; ACST-2 publishes safety data in asymptomatic patients following carotid endarterectomy (CEA) and carotid artery stenting (CAS), observing that the 30-day combined rate of death, disabling stroke or fatal myocardial infarction was 1%.¹ There are no parallel data from CREST,² but the 30-day rate of death/any stroke following CAS and CEA in ACST-2 is currently about 3.3%, compared to 1.9% in CREST.² Accordingly, while the overall procedural risks are not dissimilar to those following CEA in ACST-1,³ the ACST-2 Trial Collaborators can be confident that their interventions are conferring a low risk of death/disabling stroke.

So how does this data inform the current debate? The management of asymptomatic carotid disease remains enduringly controversial. Despite 2011 American Heart Association (AHA) Guidelines advising that CAS could now be considered as an alternative to CEA in ‘average risk’ asymptomatic patients,⁴ there is still much disagreement as to how best to treat these patients. This was evident when the Centres for Medicare & Medicaid Services (CMS) convened a January 2012 meeting of the Medicare Evidence Development & Coverage Advisory Committee (MEDCAC) to determine whether CAS coverage should be expanded to include ‘average risk’ patients with asymptomatic carotid disease.⁵

The MEDCAC panel considered the same evidence base as the AHA, but when asked whether they were confident that there was adequate evidence to determine whether CAS, CEA or best medical therapy (BMT) was the favoured strategy in the ‘average risk’ Medicare population with

asymptomatic carotid disease, the pooled consensus was that there was low confidence that CEA or CAS was appropriate. There was, however, a significantly higher level of confidence that BMT was preferable.⁵ This interpretation of the literature is very similar to what was reported previously in an online audit in the *NEJM* where 50% of 5000+ respondents said they would not subject an asymptomatic patient to CEA or CAS.⁶

The main reason for the lack of confidence regarding the evidence for supporting either CEA or CAS at MEDCAC was a growing awareness that the modern concept of BMT has probably reduced the average annual rate of stroke in patients with asymptomatic carotid disease,⁷ to the extent that ACAS and ACST data may no longer be relevant in the modern era.^{3,8} Data suggest that there has been a sustained decline in the annual rate of ‘any’ and ipsilateral stroke, irrespective of stenosis severity at baseline.⁹ In addition, and notwithstanding the excellent ACST-2 safety data, evidence suggests that even if it were possible to perform CEA or CAS with a zero percent risk, about 93% of all interventions in asymptomatic individuals would still prove ultimately unnecessary.⁹

At this moment in time, three randomised trials are recruiting patients with asymptomatic carotid disease (ACT-1, ACST-2 and SPACE-2). A fourth (CREST-2) is currently in preparation and an application for funding is expected shortly. Each have different methodologies, though it has been suggested that this degree of heterogeneity should be viewed as a positive feature as it enables clinicians to identify a trial that best suits their equipoise. For example; if you believe that your asymptomatic patient does require an intervention (but are not sure whether it should be CEA or CAS), he/she can be randomised within ACT-1 or ACST-2. If, however, you are uncertain as to whether any intervention is appropriate, these patients can be randomised within SPACE-2. This is because, unlike ACT-1 and ACST-2, SPACE-2 includes a limb for BMT. SPACE-2 initially planned to compare intervention (CEA or CAS) vs BMT alone, but a recent protocol change means that patients will now be randomised to either CEA vs BMT or CAS vs BMT (according to clinician preference). By contrast, CREST-2 plans to have a three-arm trial that will include randomisation to CEA, CAS or BMT alone.

So will the combination of these four studies enable Guideline makers and any future MEDCAC panel decide how best to treat patients with asymptomatic carotid disease? Unfortunately, the answer is probably no as there is still an ‘elephant in the room’. Notwithstanding the claim by ACST-2 that their trial is suitable for clinicians who are

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confident that their patient requires an intervention (but not which), the inescapable fact is that no one has developed any validated criteria for identifying this type of patient (i.e. high risk for stroke and hence will benefit from intervention). Secondly, it would seem that neither SPACE-2 nor CREST-2 intend to include any form of risk-stratification (beyond stenosis severity) that might enable 'high risk for stroke' patients to be identified in those that are randomised to BMT. Unfortunately, simply recruiting asymptomatic patients based upon stenosis severity is a failed experiment as was evident in both ACAS and ACST.^{3,8}

Accordingly, there is a very real risk that a lot of money and a great deal of effort could be expended in the performance of large-scale randomised trials with the very real possibility that exactly the same questions (posed to MEDCAC) regarding roles for CEA, CAS and BMT in 'average risk' asymptomatic patients will remain unanswered. It is now too late for ACT-1 and ACST-2 to change their protocol and include a risk-stratified medical limb (their methodology and funding was secured well before the current debate intensified) and there does not (currently) seem to be any realistic prospect of SPACE-2 being able to secure the additional funding required to evaluate risk stratification based on imaging protocols in medically treated patients. That leaves CREST-2. Their final protocol has not been made public, but it may be the only realistic chance of performing an appropriately powered study to identify imaging features that might be capable of identifying the relatively small cohort of 'high risk for stroke' patients in whom to target CEA or CAS. There are a number of potential (and not unduly complex) imaging strategies for consideration in CREST-2 including; silent infarction on baseline CT/MRI, stenosis progression, baseline cerebral vascular reserve, computerised ultrasound plaque analysis, MR diagnosed intra-plaque haemorrhage and, most importantly, spontaneous embolisation on transcranial Doppler ultrasound.

Yes; the inclusion of imaging will incur increased trial costs, but these pale into insignificance compared to the cost of doing nothing. If we assume that the ACAS data do retain some relevance in 2013, performing 1000 CEA (or CAS) procedures with a 2% procedural risk will only prevent 50–60 strokes at five years,⁹ meaning that about 950 interventions (95%) were ultimately unnecessary. For US Health Providers, this equates to about \$2 billion being spent on unnecessary interventions each year.¹⁰ Surely they might consider that investing a tiny fraction of this amount

towards helping identify a small but high-risk cohort who would then benefit from CEA or CAS is good business?

Alas; Everybody knows that a really important question needs to be answered. Unfortunately, Nobody seems willing to deal with it, but Somebody has to take responsibility. Is Anybody listening or will Everybody continue to blame Somebody, when Nobody did what Anybody could have done?

CONFLICT OF INTEREST

None.

REFERENCES

- Halliday AH, Bulbulia R, Naughten A, den Hartog AG, Delmestri A, Wallis CM, et al. Is carotid intervention in trials becoming safer?: Some early results from the ACST-2 (Asymptomatic Carotid Surgery trial). *Eur J Vasc Endovasc Surg*.
- Silver FL, Mackey A, Clark WM, Brooks W, Timaran CH, Chiu D, et al. Safety of stenting and endarterectomy by symptomatic status in the Carotid Revascularization Endarterectomy Versus Stenting Trial (CREST). *Stroke* 2011;42:675–80.
- Asymptomatic Carotid Surgery Trial Collaborators. The MRC Asymptomatic Carotid Surgery Trial (ACST): carotid endarterectomy prevents disabling and fatal carotid territory strokes. *Lancet* 2004;363:1491–502.
- Goldstein LB, Bushnell CD, Adams RJ, Appel LJ, Braun LT, Chaturvedi S, et al. Guidelines for primary prevention of stroke. Guideline for healthcare professionals from AHA/ASA. *Stroke* 2011;42:517–84.
- <http://.bmctoday.net/evtoday/2012/01/article.asp%3ff%3dcm-s-advisory-panel-meets-to-consider-evidence-for-coverage-of-carotid-artery-disease-treatments> [accessed 28.10.12].
- Klein A, Solomon CG, Hamel MB. Management of carotid stenosis—polling results. *N Engl J Med* 2008;358:e23.
- Abbott AL. Medical (non-surgical) intervention alone is now best for prevention of stroke associated with asymptomatic severe carotid stenosis: results of a systematic review and analysis. *Stroke* 2009;40:e573–83.
- Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid artery stenosis. *J Am Med Assoc* 1995;273:1421–8.
- Naylor AR. Time to rethink management strategies in asymptomatic carotid disease. *Nat Rev Cardiol* 2011;9:116–24.
- Naylor AR, Gaines PA, Rothwell PM. Who benefits most from intervention for asymptomatic carotid stenosis: patients of professional? *Eur J Vasc Endovasc Surg* 2009;37:625–32. *Corrigendum Eur J Vasc Endovasc Surg* 2009;38:657.

Everybody, somebody, anybody and nobody are four important indefinite pronouns. We use them all the time. This anonymous story is often quoted in business advice books and websites. There was an important job to be done and Everybody was sure that Somebody would do it. Anybody could have done it, but Nobody did it. Somebody got angry about that, because it was Everybody's job. Everybody thought Anybody could do it, but Nobody realized that Everybody wouldn't do it. It ended up that Everybody blamed Somebody when Nobody did what Anybody could have done. (Everybody, somebody, anybody and nobody are four important indefinite pronouns. We use them all the time. This anonymous story is often quoted in business advice books and websites.) This is a little story about four people named Everybody, Somebody, Anybody, and Nobody. There was an important job to be done and Everybody was sure that Somebody would do it. Anybody could have done it, but Nobody did it. Somebody got angry about that because it was Everybody's job. Everybody thought that Anybody could do it, but Nobody realized that Everybody wouldn't do it. It ended up that Everybody blamed Somebody when Nobody did what Anybody could have done. Who wants Change? Once there were four people named Everybody, Somebody, Anybody, Nobody who wanted change. So, Everybody said "I want change". Somebody said "If only anybody would start to change, I will join." But nobody said "I will change." This is a story about four people named Everybody, Somebody, Anybody and Nobody. There was an important job to be done and Everybody was sure that Somebody would do it. Anybody could have done it, but Nobody did it. Somebody got angry about that, because it was Everybody's job. Everybody thought Anybody could do it, but Nobody realized that Everybody wouldn't do it. It ended up that Everybody blamed Somebody when Nobody did what Anybody could have done. The story may be confusing but the message is clear: no one took responsibility so nothing got accomplished. It's a story that plays out often in organizations and companies and on teams anywhere there is culture that lacks accountability. Everybody thought Somebody would do it. Anybody could have done it; but Nobody did it. Somebody got angry because he thought it was Everybody's job to do it. In the end; Everybody blamed Somebody, when Nobody did what Anybody could have done!" Discover the world's research. Despite scepticism amongst some surgeons of the time these particular randomized trials have stood the test of time and remain the cornerstone of virtually every guideline of practice to this day. The carotid randomized trials became a beacon for using "evidence" rather than "intuitive reasoning" and randomized trials have now been used to determine optimal practice in a plethora of carotid surgery and stenting trials, lower limb revascularization and numerous aortic aneurysm based studies.