**Supplementary material**

*Musiałek P, Grunwald IQ. How asymptomatic is “asymptomatic” carotid stenosis? Resolving confusion(s) – and confusions yet to be resolved. Pol Arch Intern Med. 2017. doi:*

Please note that the journal is not responsible for the scientific accuracy or functionality of any supplementary material submitted by the authors. Any queries (except missing content) should be directed to the corresponding author of the article.

**ESC/ESVS/ESO joint guidelines 2017**

The recent joint guidelines[1] of the European Society of Cardiology and European Society of Vascular Surgery, endorsed by the European Stroke Organization, provide an important attempt to resolve at least some of the key decision-making issues in asymptomatic CSS. Some fundamental postulates have been addressed,[1] including the postulate of a multispecialty (Neuro-)Vascular Team decision-making[2,3] and the recognition of specific risk factors for CS stroke[3]. This is not new since such an approach has already been operational in leading cardiovascular centers in the last decade[3]. Another issue that has been addressed is what constitutes OMT in patients with CS.[3,4] Moreover, the postulate[2] to intensify work to develop risk evaluation scores in CS similar to those in, for instance, in atrial fibrillation (such as the CHA₂DS₂-VASC scale) is also reflected in the 2017 joint guidelines.[1]

The new guidelines[1] list most (unfortunately not all) of the identified (and easily applicable) CS increased risk signs and features. The missed ones include, for instance, plaque irregularities/ulceration(s), plaque thrombus, diabetes, or occlusion of the contralateral internal carotid artery.[1-3] On the other hand, the practical role of some guideline-listed[1] ones, such as transcranial Doppler high intensity transient signals (HITS) remains controversial due to contradictory data,[5,6] problems with acquisition protocol(s) standardization and labor intensity or impracticality. Furthermore, contemporary evidence
indicated that the HITS test accuracy may be greatly blurred by today’s medical therapy since, for instance, today only about 6% patients with a very recent CS stroke or TIA show spontaneous embolization on transcranial Doppler (an estimated 4.1-fold reduction with double antiplatelet therapy; 95% confidence interval, 1.5–10.7; \( P = 0.0047 \)).[7] The rejection of ACST-1 data[6,8] but the simultaneous enthusiasm to press for applying the HITS “evidence” (generated at the same time as ACST-1[6,9]) in asymptomatic CS decision-making today[1,10] is another example of a highly selective approach to evidence.

According to the body of knowledge that we have in the public domain today, rather than “asymptomatic,” “not-yet-symptomatic” or “at risk of symptomatic transformation” would be a more accurate label for a proportion of patients with CS. Risk stratification in “asymptomatic” CS, and evaluation of the revascularization role, are in the center of intensive research in cardiovascular medicine today. For instance, following the initial data obtained a decade ago,[11,12] evidence is now accumulating for the beneficial role of (safe, associated with minimized cerebral embolism) carotid revascularization on cognitive function.[13-15]

Conclusions

It is fundamental to realize that today it is only an assumption that OMT might be noninferior to OMT plus intervention in asymptomatic CS. [16,17] Thus, today routinely limiting the management of the “asymptomatic” CS patient to medical therapy (against ACST-1 level-1 evidence) is, strictly speaking, an experimental approach that, where applied, should rather be subjected to the ethical boards review.

The Carotid Revascularization Endarterectomy Versus Stenting Trial 2 (CREST-2) continues to randomize subjects with “asymptomatic” CS to OMT + surgical revascularization vs OMT or to OMT + endovascular revascularization vs OMT [16,17]. In addition, the CREST-2 substudy evaluates cognitive function. [16] The success of CREST-2 will be critically dependent on effective inclusion of the whole spectrum of CS patients. [18]
It may be difficult, however, to routinely convince the patients with increased stroke risk features to accept the watchful waiting strategy. If high-risk patients become treated with an intervention (which appears right ethically but it is wrong scientifically) while the lower-risk patients get randomized, the trial will provide answers for the low-risk patients only (and, unsurprisingly, it might come out “negative” [18]). It is important to understand, however, that then the data will not be applicable to decision making in the trial-non-represented (higher risk) “asymptomatic” patients with CS.[18]

Other important developments on the endovascular side come from the progress in device technology. Today, with cerebral diffusion-weighted magnetic resonance imaging acting as a quality control and study endpoint,[18-20] optimized cerebral protection is available. This includes not only optimized (proximal) systems for intraprocedural neuroprotection [18,20-22] but also by novel carotid stents such as the embolic prevention stent system covered with a Micro-Net that can effectively insulate the plaque,[21,23] resulting in minimized intraprocedural and nearly-eliminated postprocedural embolism.[23]

Indeed, mesh-covered stents have been shown to offer an overall 30-day intervention risk at the level of about 1% in more than 550 patients presenting with or without the symptoms of cerebral ischemia in relation to CS.[2,21] Notwithstanding the importance of OMT, these developments translate into better serving our patients with “asymptomatic” CS.[21] Rather than awaiting “a sentence of fate”, we are now increasingly able to safely prevent strokes in relation to CS that continue to occur today despite OMT. [2,21,24-26]

References
1 Aboyans V, Ricco JB, Bartelink MEL, et al. 2017 ESC Guidelines on the Diagnosis and Treatment of Peripheral Arterial Diseases, in collaboration with the European Society for


8 Abbott AL. Medical (nonsurgical) 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-e583.


18 Musiałek P. TASTE-less endpoint of 30-day mortality (and some other issues with TASTE) in evaluating the effectiveness of thrombus aspiration in STEMI: not the "evidence"


