INVITED COMMENTARY

Antiplatelet Therapy for Carotid Interventions: Same Meat, Different Gravy or Unexplored Possibilities for Improvement?

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In this issue of *European Journal of Vascular and Endovascular Surgery,* Murphy et al. present a literature review of patients with carotid artery stenosis in an attempt to establish an evidence base for optimal antiplatelet therapy.[1] It is striking to see that robust level A evidence to guide antiplatelet treatment is still scarce, despite thousands and thousands of carotid interventions being performed annually worldwide. Many trials were, and still are, designed to compare carotid artery endarterectomy (CEA) and stenting (CAS). However, direct comparisons of different periprocedural antiplatelet regimens in high quality randomised trials are lacking.

In the trials included in the review, it seems that good old acetylsalicylic acid (ASA) was still the gold standard for periprocedural protection against ischaemic complications. However, current ESVS guidelines recommend clopidogrel 75 mg once daily, or ASA 75 mg once daily combined with dipyridamole 200 mg twice daily for optimal medical treatment in symptomatic carotid artery disease.[2] For patients waiting for CEA, dual antiplatelet therapy (ASA + clopidogrel) can be considered, and for patients treated by CAS, dual antiplatelet therapy is recommended.[2] Therefore, it is not impossible that physicians may be too overwhelmed by the different treatment options to choose the right antiplatelet regimen.

There are some other limitations and factors that should be considered regarding this topic and the currently available literature. First, there is evidence that ticagrelor might be more effective than other platelet inhibitors for the secondary prevention of ischaemic stroke in patients with cardiovascular disease.[3] However, high quality randomised trials focusing on prevention of stroke in patients with carotid artery stenosis including treatment arms with ticagrelor or newer direct oral anticoagulants, are lacking so far.

Second, high on-treatment platelet reactivity is a potential risk factor for cardiovascular events and can be tested ex vivo.[4] It seems reasonable to believe that patients with this reactivity should be prescribed alternative antiplatelet medication, but again, robust evidence is missing. Third, most of the trials focus only on clinical cardiovascular adverse events. However, asymptomatic microemboli are relevant as they were shown to be associated with cognitive decline and risk of stroke.[2,5] Use of transcranial doppler to identify microemboli, and diffusion weighted magnetic resonance imaging (dMRI) to detect subclinical brain damage should be incorporated into new trials. Last but not least, in addition to finding the optimal antiplatelet therapy to reduce stroke risks, timing of carotid interventions remains of key importance.

The next sensible step would seem to be to design a worldwide high quality trial that includes multiple treatment arms with different contemporary antiplatelet regimens and uses platelet reactivity measurements, TCD, dMRI, and timing of the intervention as important parameters. Considering the number of interventions performed annually, such a trial should be feasible. Let's join efforts for the wellbeing of our patients.

REFERENCES

1 Murphy SJX, Naylor AR, Ricco JB, Sillesen H, Kakkos S, Halliday A, et al. Optimal antiplatelet therapy in moderate to severe symptomatic and symptomatic carotid stenosis: a comprehensive review of the literature. *Eur J Vasc Endovasc Surg* 2019;**57**:199–211.
2 Naylor AR, Ricco JB, de Borst GJ, Debus S, de Haro J, Halliday A, et al. Editor's choice – management of atherosclerotic carotid and vertebral artery disease: 2017 clinical practice guidelines of the European Society for Vascular Surgery (ESVS). *Eur J Vasc Endovasc Surg* 2018;**55**:3–81.
3 Malhotra K, Goyal N, Kasunich AS, Sheth SA, Katsanos AH, Alexandrov AV, et al. Ticagrelor for stroke prevention in patients with vascular risk factors: a systematic review and meta-analysis. *J Neurol Sci* 2018;**390**:212–8.
4 Wisman PP, Roest M, Asselbergs FW, de Groot PG, Moll FL, van der Graaf Y, et al. Platelet-reactivity tests identify patients at risk of secondary cardiovascular events: a systematic review and meta-analysis. *J Thromb Haemost* 2014;**12**:736–47.
5 Markus HS, King A, Shipley M, Topakian R, Cullinane M, Reihill S, et al. Asymptomatic embolisation for prediction of stroke in the asymptomatic carotid emboli study: a prospective observational study. *Lancet Neurol* 2010;**9**:663–71.

DOI of original article: https://doi.org/10.1016/j.ejvs.2018.09.018
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https://doi.org/10.1016/j.ejvs.2018.09.021