Se supplementation exclusively for male patients. Now the study conducted by Nawrot et al. describes the fourth sexual dimorphic major health effect of Se, beyond fertility, cancer, and sepsis. One hesitates and wonders how and why Selene shines on men only.

The Se status is dominated by a hepatically derived Se transport serum protein, i.e. selenoprotein P (SePP). We and others have demonstrated that SePP controls Se distribution within the body and that SePP-KO mice display sex-specific Se-deficiency symptoms. SePP attaches to endothelial cells and protects from peroxynitrite-mediated damage in plasma. Moreover, we have just demonstrated that biosynthesis of selenoenzymes including SePP displays pronounced sex-specific differences, and male livers have a superior potency to translate mRNA into functional selenoproteins. Remarkably, these differences are not constant but Se-dependent.

If larger groups of people with a more divergent Se status were analysed, we would not expect such a linear correlation of blood Se with blood pressure as depicted in Figure 1. At higher Se status, all selenoproteins become maximally expressed and independent from the trace element. This kind of saturable effect has been similarly observed in both cancer prevention and sepsis studies mentioned earlier, in which participants with low baseline Se status always profited most. Consequently, successful Se supplementation will stabilize blood pressure in a healthier range.

Unfortunately, large supplementation trials are conducted mainly in the USA, where baseline Se levels are already replete because of better nutritional supply. Given the clear-cut and appealing correlation shown in the manuscript, some large-scale prospective analyses are clearly needed in Europe in order to benefit our hearts and health insurance systems. Such trials should necessarily include both men and women who are at risk of a low Se status, such as chronically ill patients, people on regular dialysis or with eating disorders, and vegans and vegetarians. Hopefully, financial support can be raised for such eagerly awaited large-scale European supplementation trials. The future shines bright, less pressure is in sight, especially at night.

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Concerns on carotid stenting in octogenarians

Zahn et al. should be complimented for creating an inter-hospital carotid artery stenting (CAS) registry and for presenting their 10 year experience, including many procedures performed on octogenarians. Although their analysis is retrospective in nature and unbalanced (321 patients >80 years vs. 2557 patients <80 years), it shows that in-hospital outcome or death rates increase significantly with older age, but the complication rate in octogenarians is not excessively high. The Zahn et al. article raises some concerns, however.

First, no distinction was drawn between ischemic and haemorrhagic strokes (as far as we know haemorrhagic stroke is not due to carotid disease) or between the various types of ischemic strokes (atheroembolic, cardioembolic, or lacunar infarction), so that patients with non-atheroembolic strokes should have been excluded from this analysis (it is worrying to see atrial fibrillation significantly more often in octogenarians than in the younger group). The proportions of smokers and diabetic patients or patients with hyperlipidemia were lower among the octogenarians included in the study than among younger patients, so the former would be at lower risk of atherothrombotic stroke. So, how can the authors be sure that all 184 symptomatic octogenarians had symptoms related to the carotid stenosis?

Secondly, no mention was made of the timing of CAS vis-à-vis symptom onset, and “it is an incontestable fact that carotid endarterectomy (CEA) confers the maximum benefit provided it is undertaken as soon as possible after the onset of symptoms”. We were among the first groups to demonstrate as much in a 4 year prospective study on 86 patients with minor stroke, 45 of them randomized to undergo early CEA while 41 had delayed CEA.

Thirdly, since elderly patients were less likely to undergo CAS while on statin therapy, it would be interesting to know why the asymptomatic octogenarians underwent CAS, although some of them were on sub-optimal medical therapy.

Fourthly, since only in-hospital data were recorded, failure to report the event rate at 30 days prevents any comparison with other studies and casts a shadow of doubt over the study as a whole. The authors’ conviction that “clinical events are extremely low after the first days of stent implantation” is debatable. CAS was aborted in 6.9% of octogenarians and there was a residual stenosis in 10%: whatever the reasons, these should be defined as cases of treatment failure and added to all the patients who had in-hospital events after CAS.

Finally, why should octogenarians be treated with CAS? It is particularly important to demonstrate that the interventional procedure adopted is safe, and therefore that the patient would be at a higher risk of stroke if said treatment is withheld, but the results of Zahn et al. analysis do not support this conclusion. A few years ago, in a study on octogenarians with contralateral carotid artery occlusion, we demonstrated that these patients can undergo CEA with no more risks or complications than younger patients with contralateral carotid occlusion, and we suggested that—until prospective, randomized trials to evaluate the role of CAS have been completed—CEA should remain the standard treatment for such patients.

References


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Concerns on carotid stenting in octogenarians: reply

Barracchini and Ballotta\(^1\) point out some important issues concerning our registry data on carotid artery stenting (CAS) as well as on CAS in general.

They mention that a distinction neither between ischemic and haemorrhagic stroke nor between different types of ischemic strokes was made. We also regret not to have collected this information. However, concerning stroke as a complication of CAS or endarterectomy (CEA), the large, randomized studies on this issue also summarized all strokes into the primary endpoint of death or stroke.\(^2\)\(^-\)\(^4\) This makes sense because either CAS or CEA could be complicated by an excess of haemorrhagic strokes, for example, by the use of heparin in CAS.

In concordance with Barracchini and Ballotta,\(^1\) we are not sure that all symptoms in the symptomatic patients were as a result of carotid disease; however, this was the judgement of the treating physicians, which we have to accept in such a registry.

We also agree that timing of CAS or CEA in symptomatic patients with carotid stenoses is of crucial importance, which is emphasized in recent guidelines.\(^5\) In 84.5% (91.6% in octogenarians and 83.2% in non-octogenarians) of our symptomatic patients, symptoms occurred within 180 days before CAS.

The decision to treat a patient with CAS was left to treating physician. Although we share the caution of Barracchini and Ballotta\(^1\) to treat octogenarians for carotid stenoses at all, especially the asymptomatic ones, this is true for CAS as well as CEA. As pointed out in our discussion\(^5\): “The results of the Asymptomatic Carotid Surgery Trial (ACST)\(^6\) showed, that CEA was superior to medical treatment only in patients with high-grade but asymptomatic carotid stenoses. However, in patients older than 74 years, there was no advantage of CEA, mainly due to a high mortality rate in the following years in both groups. Thus the selection of more symptomatic patients in our registry may already reflect the restriction of the treating physicians to high risk candidates of stroke in the very old”. Our data also reflect only the use of CAS in our registry, not the practice or conviction of the authors.

We do not believe that a residual stenosis after CAS of about 10% is a treatment failure, for we do not have data to show us that such minor residual stenoses are associated with a worse outcome after CAS. The proportion of aborted procedures in this intention-to-treat CAS registry is an important quality measurement of this registry.

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