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Measurement of the brain atrophy index to predict mortality: a 'no brainer'?

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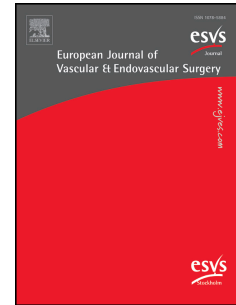
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1 **Measurement of the brain atrophy index to predict mortality: a ‘no brainer’?**

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13 In this issue of the European Journal of Vascular and Endovascular Surgery Lauksia et al present a
14 multivariate analysis of preoperative brain atrophy as a predictor of long-term mortality after carotid
15 endarterectomy¹. [REFERENCE TO BE CORRECTED, in PubMed first and last names inverted]. In the field
16 of carotid revascularization various prediction models have been developed in the past in order to assist
17 in stratifying patients into groups at high and low risk for periprocedural complications or long-term
18 stroke risk. An evaluation of the external performance of 23 short-term and 7 long-term outcome
19 models showed that these models do not reliably predict outcome after carotid revascularization, and
20 concluded that new prediction models are needed.² A more recent evaluation of 9 prediction models
21 using a validation cohort of 26293 patients showed that the Ontario Carotid Endarterectomy Registry
22 risk model had the most reliable predictions of procedural stroke or death after CEA³. However, this
23 study did not assess long-term outcomes.

24 It is well established that brain atrophy is a strong predictor for functional disabilities, cognitive decline,
25 and dementia, and these disorders by themselves are already associated with an increased risk for
26 mortality.⁴ Since patients with cardiovascular disease have a higher risk of recurrent cardiovascular
27 events and mortality it was hypothesized in the SMART study (using MRI) that brain atrophy in
28 combination with cardiovascular disease could be associated with an additional increase in mortality⁴. In
29 this MRI-based study of a group of 1215 patients, several measurements were performed (brain
30 parenchymal fraction, sulcal cerebrospinal fluid fraction and ventricular fraction). It was found, after
31 adjusting for cardiovascular risk factors and the presence of vascular brain lesions, that there was a
32 statistically significant association between brain atrophy and mortality risk. The measurements as
33 obtained in the SMART study were performed using an imaging modality that is not routinely used in the
34 workup of patients prior to carotid intervention. Furthermore, the measurements that were performed
35 were quite complex, which renders this method relatively unfriendly for use and application in daily
36 clinical practice. A 'threshold' of the point at which the mortality risk increased significantly was not

37 provided in the SMART study. The authors of the current paper therefore need to be complimented to
38 propose the use of the brain atrophy index (BAI), that can be easily calculated from a (non-contrast
39 enhanced) CT scan without the use of dedicated software. It needs to be mentioned that the use of this
40 index is not entirely novel. The BAI (originally described and developed for the evaluation of multiple
41 sclerosis patients^{5,6}) has also been used in a recent study that evaluated the association of brain atrophy
42 and mortality (in combination with masseter sarcopenia) in trauma patients⁷, and in a study originating
43 from the same institution as the current paper in patients after mechanical thrombectomy in acute
44 (anterior circulation) stroke⁸. Inter-observer reliability in determining the BAI was evaluated in both
45 studies and an excellent reproducibility was found, although this was based on a relatively small number
46 of patients (364 and 204 patients respectively). Unfortunately, in the current study no correction for
47 other cardiovascular risk factors was made, as was done in the SMART study. Further validation of this
48 index in a larger cohort of patients, correcting for these factors is therefore probably needed before
49 starting to use the BAI as parameter in (crucial) decision making.

50 What is new in this paper is the establishment of a threshold of the BAI that is related to mortality, and
51 this makes this method potentially useful for risk stratification and patient selection. Limitation remains
52 the small number of patients that was available to determine this cut-off point. In the future, the BAI, in
53 combination with other variables, may be able to identify differences in 'numbers needed to treat'
54 between patients in order to have them benefit from carotid endarterectomy. Therefore, the BAI may
55 be able to provide a more granular evaluation of patients, and a more personalized healthcare offering
56 in the future, instead of applying the same 'number needed to treat' on the entire population. The
57 establishment of a patient oriented 'number needed to treat' is especially of importance in
58 asymptomatic patients, taking also into account the quality of life after a surgical procedure, as an
59 integral part of an approach towards optimization of patient selection and optimal use of healthcare
60 resources. In this study there is a preponderance of symptomatic patients where the issue of long-term

61 survival is probably of less importance as compared to asymptomatic patients. It would therefore be
62 interesting to evaluate asymptomatic patients only, but the total number of asymptomatic patients in
63 this cohort is likely too small to draw any conclusion. Larger studies focusing on the use of BAI in
64 asymptomatic patients are therefore warranted.

65 Although sarcopenia and dental status are mentioned in the methods these aspects have not been
66 evaluated thoroughly in this paper, and this should be part of future research. In the abovementioned
67 study on older trauma patients the evaluation of both brain atrophy and masseter sarcopenia were
68 cumulatively (but also independently) associated with increased mortality, and it would be interesting to
69 explore this further⁷.

70 One of the questions that comes to mind is whether it is the brain volume reduction in itself that is
71 contributing to the increased mortality, or whether the effect can be explained by the shared underlying
72 cardiovascular risk factors⁴, and this issue is unfortunately not addressed by the authors.

73 In addition to its application in patients with carotid artery disease the concept of incorporating the BAI
74 may be applied and developed in other areas of vascular disease (e.g. chronic limb threatening ischemia
75 where oftentimes in the older patient the difficult decision of primary amputation needs to be made),
76 and become part of the 'frailty index' calculation⁷.

77 The findings of this study are interesting but the true value needs to be evaluated in a larger cohort in
78 order to be able to develop a (multi-variable) scoring system that can help in deciding whether to
79 operate or not. It is unlikely that the BAI can be used as a stand alone parameter especially for such an
80 important decision of whether to offer a patient carotid endarterectomy or not. Therefore the BAI will
81 not be the holy grail that helps in the decision to refrain from surgery or not, but will certainly be a part
82 of future scoring systems.

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