Journal Pre-proof

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

Jos C. van den Berg, MD PhD

PII: S1078-5884(22)00865-6

DOI: https://doi.org/10.1016/j.ejvs.2022.12.023

Reference: YEJVS 8618

To appear in: *European Journal of Vascular & Endovascular Surgery*

Received Date: 20 October 2022

Revised Date: 17 December 2022

Accepted Date: 19 December 2022

Please cite this article as: van den Berg JC, Measurement of the brain atrophy index to predict mortality: a 'no brainer'?, *European Journal of Vascular & Endovascular Surgery*, https://doi.org/10.1016/j.ejvs.2022.12.023.

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

Jos C. van den Berg MD PhD

CENTRO VASCOLARE TICINO

Ospedale Regionale di Lugano, sede Civico

Via Tesserete 46

6903 Lugano

Universitätsinstitut für Diagnostische, Interventionelle und Pädiatrische Radiologie

and Interdisziplinäres Zentrum für vaskuläre Interventionen, Inselspital Universität Bern

Bern

Switzerland

No conflict of interest related to this contribution

In this issue of the European Journal of Vascular and Endovascular Surgery Lauksia et al present a multivariate analysis of preoperative brain atrophy as a predictor of long-term mortality after carotid endarterectomy[1]. [REFERENCE TO BE CORRECTED, in PubMed first and last names inverted]. In the field of carotid revascularization various prediction models have been delevoped in the past in order to assist in stratifying patients into groups at high and low risk for periprocedural complications or long-term stroke risk. An evaluation of the external performance of 23 short-term and 7 long-term outcome models showed that these models do not reliably predict outcome after carotid revascularization, and concluded that new prediction models are needed.[2] A more recent evaluation of 9 prediction models using a validation cohort of 26293 patients showed that the Ontario Carotid Endarterectomy Registry risk model had the most reliable predictions of procedural stroke or death after CEA[3]. However, this study did not assess long-term outcomes.

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

provided in the SMART study. The authors of the current paper therefore need to be complimented to propose the use of the brain atrophy index (BAI), that can be easily calculated from a (non-contrast enhanced) CT scan without the use of dedicated software. It needs to be mentioned that the use of this index is not entirely novel. The BAI (originally described and developed for the evaluation of multiple sclerosis patients[5,6]) has also been used in a recent study that evaluated the association of brain atrophy and mortality (in combination with masseter sarcopenia) in trauma patients[7], and in a study originating from the same institution as the current paper in patients after mechanical thrombectomy in acute (anterior circulation) stroke[8]. Inter-observer reliability in determining the BAI was evaluated in both studies and an excellent reproducibility was found, although this was based on a relatively small number of patients (364 and 204 patients respectively). Unfortunately, in the current study no correction for other cardiovascular risk factors was made, as was done in the SMART study. Further validation of this index in a larger cohort of patients, correcting for these factors is therefore probably needed before starting to use the BAI as parameter in (crucial) decision making.

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

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

Although sarcopenia and dental status are mentioned in the methods these aspects have not been evaluated thoroughly in this paper, and this should be part of future research. In the abovementioned study on older trauma patients the evaluation of both brain atrophy and masseter sarcopenia were cumulatively (but also independently) associated with increased mortality, and it would be interesting to explore this further[7].

One of the questions that comes to mind is whether it is the brain volume reduction in itself that is contributing to the increased mortality, or whether the effect can be explained by the shared underlying cardiovascular risk factors[4], and this issue is unfortunately not addressed by the authors.

In addition to its application in patients with carotid artery disease the concept of incorporating the BAI may be applied and developed in other areas of vascular disease (e.g. chronic limb threatening ischemia where oftentimes in the older patient the difficult decision of primary amputation needs to be made), and become part of the 'frailty index' calculation[7].

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

References

1. Iisa L, Linda W, Iisa L, et al. Multivariable Analysis of Preoperative Brain Atrophy as a Predictor of Long-Term Mortality after Carotid Endarterectomy. *Eur J Vasc Endovasc Surg.* 2022.
2. Volkers EJ, Algra A, Kappelle LJ, et al. Prediction Models for Clinical Outcome After a Carotid Revascularization Procedure. *Stroke.* 2018;49(8):1880-1885.
3. Poorthuis MHF, Herings RAR, Dansey K, et al. External Validation of Risk Prediction Models to Improve Selection of Patients for Carotid Endarterectomy. *Stroke.* 2022;53(1):87-99.
4. van der Veen PH, Muller M, Vincken KL, et al. Brain volumes and risk of cardiovascular events and mortality. The SMART-MR study. *Neurobiol Aging.* 2014;35(7):1624-1631.
5. Bermel RA, Bakshi R, Tjoa C, Puli SR, Jacobs L. Bicaudate ratio as a magnetic resonance imaging marker of brain atrophy in multiple sclerosis. *Arch Neurol.* 2002;59(2):275-280.
6. Sharma J, Sanfilipo MP, Benedict RH, Weinstock-Guttman B, Munschauer FE, 3rd, Bakshi R. Whole-brain atrophy in multiple sclerosis measured by automated versus semiautomated MR imaging segmentation. *AJNR Am J Neuroradiol.* 2004;25(6):985-996.
7. Tanabe C, Reed MJ, Pham TN, Penn K, Bentov I, Kaplan SJ. Association of Brain Atrophy and Masseter Sarcopenia With 1-Year Mortality in Older Trauma Patients. *JAMA Surg.* 2019;154(8):716-723.
8. Lauksio I, Lindstrom I, Khan N, et al. Brain atrophy predicts mortality after mechanical thrombectomy of proximal anterior circulation occlusion. *J Neurointerv Surg.* 2021;13(5):415-420.