Cognitive decline and mortality in cerebral amyloid angiopathy related-inflammation: a single center longitudinal candidate predictor-finding study

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Introduction and aim

Cerebral amyloid angiopathy-related inflammation (CAA-ri) is a relapsing-remitting autoimmune disease characterized by an immune response towards cerebrovascular-deposited amyloid-beta peptides. Clinical manifestations are focal neurological signs, cognitive impairment and epilepsy. CAA-ri is associated with significant mortality and increased incidence of dementia.

This study aims at assessing prognostic markers of these outcomes in a prospective cohort of CAA-ri.

Methods

30 patients with CAA-ri presenting at the Neurology Clinic of Padova from 2012 to 2024 were enrolled in a cohort study.

Clinical findings, CSF biomarkers and brain MRI features were recorded at the time of diagnosis, while mortality, incidence of dementia (persisting MMSE <24/30) and epilepsy were recorded in the follow-up visits.

The following visual scales were applied to MRI-FLAIR and SWI images: MARS for microbleeds (1), perivascular space dilatation rating scale (2), sulcal hyperintensities and lobar oedema rating scale (3). Candidate predictors were evaluated by hypothesis tests, univariate logistic regressions, LASSO regression, Random Forests and a related algorithm; emerging candidate predictors were tested with logistic regression. Principal component analysis (PCA) was performed for MRI- derived features.

Results

At enrollment mean age was 74 ± 6.2 years, 17 women and 13 men. Mean follow up was 2.9 ± 2.9 years during which 12 patients died (survival at 2 years 76%), 16 developed dementia (survival-free 50% 24 months) and 18 epilepsy.

Survival significantly improved for patients diagnosed after publication of CAAri criteria. In the overall group, death was not significantly predicted by neither older age nor longer timelapse between onset of symptoms and diagnosis or treatment onset.

Development of **dementia** was predicted by a model including higher age at onset and increased CSF/serum albumin ratio (OR = 5.13, p = 0,05).

As for MRI data, we found three principal components that explained 48% of the variance (PC1 27%).

PC1 included variables associated to burden of lobar microbleeds, PC2 to burden of white matter lesions and PC3 mainly to subcortical small vessel disease non-CAA related. A model based on all 3 components (component 1 and 2 increased the risk, while component 3 was protective) explained 77% of the variance regarding the outcome of death, with a higher importance for the inflammatory burden (importance = 0.83).

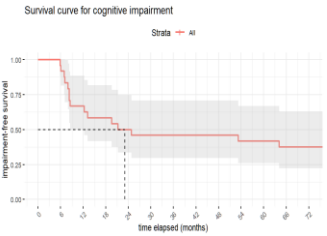

***Figure 1**: survival curve for death*

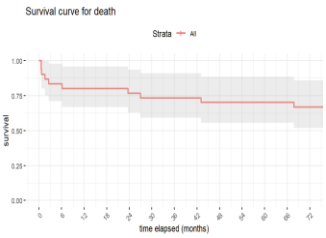

***Figure 2:** survival curve free of cognitive impairment*

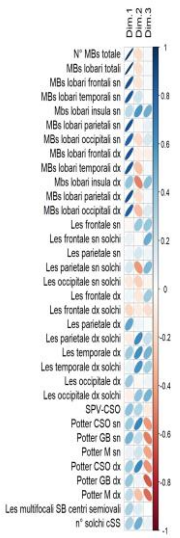

***Figure 3**: correlation between PCs and their variables*

Discussion

CAA-ri was associated with higher mortality before publication of diagnostic criteria. Burden of both inflammatory and hemorrhagic lesions are neuroimaging prognostic markers of mortality. Progression to dementia is better predicted by CSF/serum albumin ratio, a proxy measure of arteriolar barrier damage and more severe microangiopathy.
Further validation studies are needed to assess reliability of these variables in larger cohorts.

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Reference

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