Diagnosis of cerebral amyloid angiopathy-associated lobar intracerebral haemorrhage: diagnostic test accuracy simulation study

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Background & Aims

- Cerebral amyloid angiopathy (CAA) is a diffuse small vessel disease associated with lobar intracerebral haemorrhage (ICH)
- Cortical biopsy is the pathological reference standard in life
- But potentially results in false negatives (CAA missed by biopsy) and false positives (CAA in the biopsy but sparse in the whole brain).
- We aimed to compare simulations of cortical biopsy against autopsy for CAA diagnosis.

Methods

- We identified adults with first-ever symptomatic ICH, who died and underwent research autopsy between 01/06/2010 and 04/01/2018 as part of a prospective, population-based, inception cohort in Lothian, Scotland
- We compared two published pathological approaches to rating the tissue block obtained from the lobe affected by ICH (simulated cortical biopsy –index tests) against the whole-brain reference standard at autopsy
- A neuropathologist staged and graded CAA using a standardised consensus rating scale
- We defined lobar ICH as CAA-associated if global cerebral summed parenchymal CAA score was ≥ 9

Results

- Among 69 adults with 1st-ever lobar ICH (median age 83 years [IQR 78–86], 26 [38%] men), 42 (61%) were CAA-associated at research autopsy
- Presence of any CAA in simulated cortical biopsy (Vonsattel grade ≥ 1) was 100% (95%CI 90-100) sensitive for CAA-associated ICH, but 70% (95%CI 50-86) specific
- Presence of complete replacement of a vessel wall with amyloid in simulated cortical biopsy (Vonsattel grade ≥ 2) was 95% (95%CI 83-99) sensitive & 78% (95%CI 57-91)

Conclusions & future plans

Cortical biopsy appears sensitive enough to rule out CAA-associated lobar ICH, but its specificity is moderate in comparison to whole-brain assessments

Vonsattel grade ≥ 1 in simulated cortical biopsy of the lobe affect by ICH vs autopsy reference standard

Vonsattel grade ≥ 2 in simulated cortical biopsy of the lobe affect by ICH vs autopsy reference standard