

Appendix

Check list to assess methodological and informative quality of studies

Patient selection

1. Consecutive patients with symptomatic lacunar stroke were included.
2. Description of exclusion criteria, e.g. connective tissue disease (in case of inflammatory markers and absence of carotid lesions (in case of cerebrovascular reactivity).

Patient characteristics

3. Definition of lacunar stroke syndrome
 - a. Using TOAST, OCSP or NINDS Classification (1 point)
 - b. Subtyping by combination of clinical and radiological data (2 points)
4. Imaging by
 - a. CT (1 point)
 - b. MRI in all patients (2 points)
5. Assessment of imaging by validated scale (e.g. modified Fazekas scale) and by 2 radiologists (1 point for each criterion).
6. Description of vascular risk factor profile in patients and controls
7. Controls
 - a. Population-based healthy controls with or without vascular risk factors (2 points)
 - b. Patients with non-lacunar stroke (1 point)
 - c. Both healthy controls and patients with non-lacunar stroke (2 points)

Patient material

8. Time of sample drawing (or diagnostic test) and method of testing can be extracted from the paper.
9. Sequential samples or sample extraction (or diagnostic test) several months after the event (not applicable in studies on polymorphism).

Follow-up

10. Registration of vascular events in patients and controls (clinical follow-up).
11. Follow up by imaging of new symptomatic and asymptomatic infarcts in patients and controls

Treatment

12. Possibly confounding medication reported (statins, anticoagulants) (1 point) and corrected for in analysis (2 points).

Analysis

13. Significance levels or confidence intervals
14. Description of crude data

Unless commented on in checklist; 'Yes' = 2 points and 'not clear/no' = 0 points. Maximum of 28 points. In studies on polymorphism a maximum of 26 points, because item 9 ('repeated sampling') is not relevant.