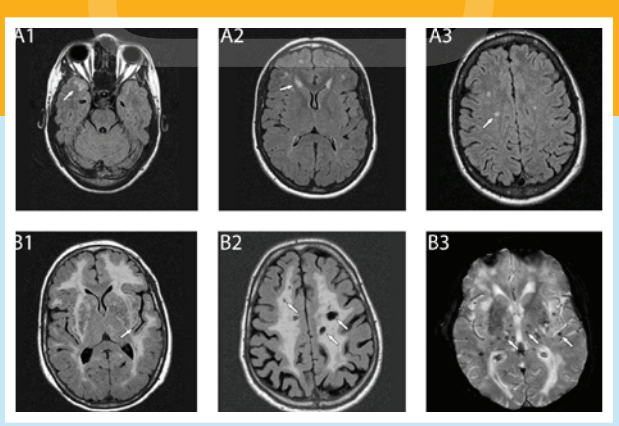
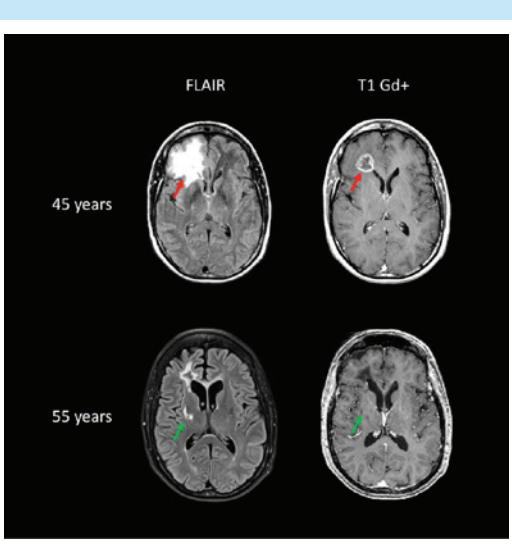
European Academy of Neurology

Guideline on monogenic cerebral small vessel disease (cSVD)



- cSVD is the most common cause of heritable stroke related to single gene disorders
- Many additional genes responsible for cSVD have recently been identified, and apart from Fabry disease, there are currently no available disease-modifying therapies
- Evidence to support the diagnosis and management of monogenic cSVD is lacking
- Most treatment focuses on symptomatic management, using approaches for which there is often no clear evidence

- Used the Delphi methodology to provide recommendations on genetic testing, clinical and neuroradiological diagnosis, and management, and a framework for clinicians
- 14 experts identified the causes, the clinical features and diagnosis, and the management of cSVD
- Endorsed by the Stroke and Neurogenetics Panels of the European Academy of Neurology

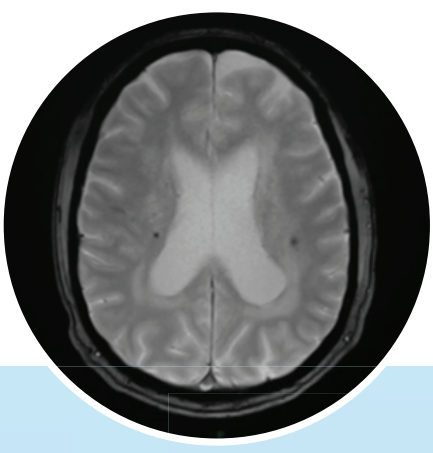


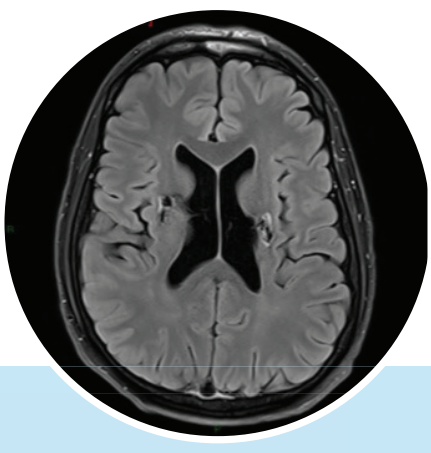
DIAGNOSIS

To check at the consultation

- Family history
- Young age at onset
- Being a blood relative of a patient diagnosed with cSVD
- Suggestive extra cerebral/systemic features

- Clinical phenotype characteristics of a specific monogenic disease
- Neuroimaging features characteristic of a specific monogenic disease
- At risk for conventional vascular diseases





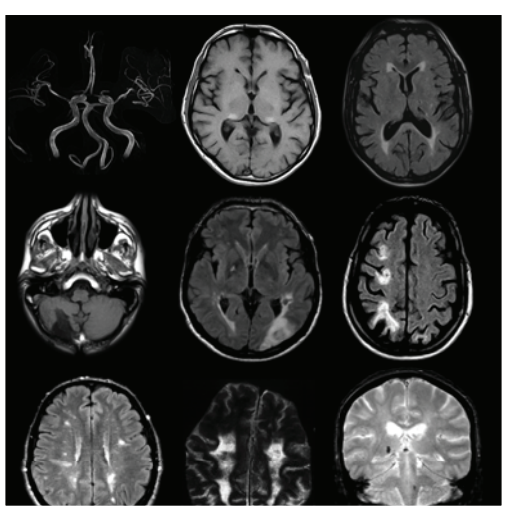
MANAGEMENT

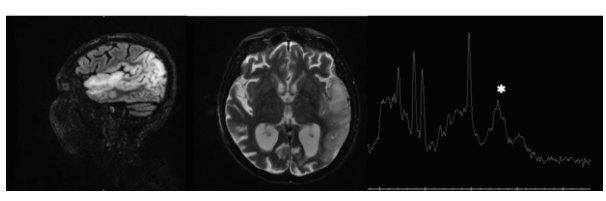
- Patients should be followed up by specialised centres and/or by an expert neurologist
- Genetic counselling should include discussion of family planning, comprising the option of prenatal diagnosis and pre-implantation genetic diagnosis
- Family members should be offered at least one consultation with a clinical geneticist or equivalent for genetic counseling

- At genetic diagnosis, patients should be offered psychological support if needed
- The vascular risk factor profile of patients should be carefully evaluated, and life-style changes should be advised
- Patients should have an annual evaluation of their vascular risk factor profile
- A cerebral MRI should be considered, irrespective of signs or symptoms

RECOMMENDATIONS

- CADASIL should be considered in the differential diagnosis of multiple sclerosis
- Carriers of heterozygous HTRA1 variants do not manifest with CARASIL but with a different form of heritable cSVD





- The gold standard for diagnosis is the genetic test. Skin biopsy is not useful for CARASIL diagnosis since it is not disease specific and do not reveal GOM
- Pathogenic frame-shift variants in TREX1 cause protein truncation in the C-terminus, which leads to subcellular mis-localisation of the protein, but does not affect enzyme activity

Read the Guideline in full in the *European Journal of Neurology* at **http://bit.ly/StrokeGL**

WILEY