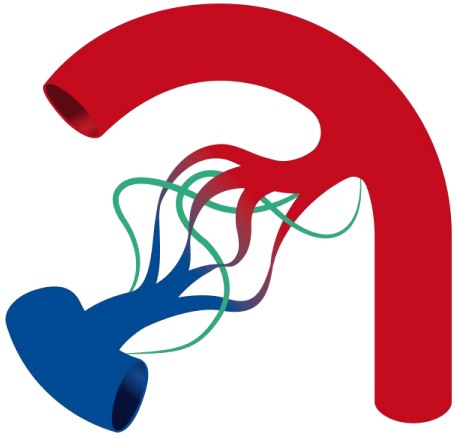
European Reference Network

for rare or low prevalence complex diseases

Network Vascular Diseases (VASCERN)



CADASIL

Final Approved Patient Pathway by the Neurovascular Diseases (NEUROVASC) Working Group – 18/07/2024

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Disclaimer

- This document is an opinion statement reflecting strategies put forward by the experts and patient representatives involved in the Neurovascular (NEUROVASC) Rare Disease Working Group of VASCERN.
- It is preferred that patients are evaluated in a multidisciplinary center specialized in the diagnosis and management of rare cerebrovascular diseases.
- This pathway is issued on 18/07/2024 and will be further validated and adjusted as needed.
- Responsibility for the care of individual patients remains with the treating physician.

SVD DIAGNOSED ON MRI (WITH OR WITHOUT SYMPTOMS)

Asymptomatic, but the MRI results are suggestive of a sporadic or genetic ischemic SVD*

Symptomatic with one or more of the following symptoms:
- Migraine with aura
- Transient ischemic attack(s)
- Ischemic (SVD type), rarely hemorrhagic stroke
- Motor or gait/balance disturbances
- Mood and/or behavioral disturbances
- Cognitive decline / dementia

with MRI data suggestive of a sporadic or genetic ischemic SVD (i.e. temporal lobes)*

- Full family history of stroke, cognitive decline, dementia (at least 1st and 2nd degree relatives)
- Collect age at onset of symptoms, age at death, any other diagnoses or genetic information
- Ask for consent to obtain clinical records and MRI data from affected family members

- Check for any vascular risk factors (HT, diabetes, hypercholesterolemia)

- Status of cervical and intracranial arteries
- Cardiac ultrasound and ECG
- Blood tests (blood count, creatinine, glucose level, LDL cholesterol, sedimentation rate, CRP)

- Complete neurological assessment
- Cognitive tests, disability assessment
- MRI (3DT1, FLAIR./T2, T2*/SWI, DWI, 3DTOF)

SVD of undetermined cause or familial SVD***:**
- Discrepancy between microvascular lesion load on MRI with age and CVRF burden
- Positive family history of stroke at young age, dementia, or migraine with aura

DNA testing for genetic SVD (gene or panel)

Announcement of test results

Absence of NOTCH3 variant → CADASIL excluded: search for another cause

NOTCH3 variant of undetermined significance (VUS) → Refer to a clinical geneticist

Pathogenic variant in NOTCH3 gene**** → Dedicated consultation (neurologist and/or clinical geneticist) to discuss consequences, NOTCH3 risk category, expected disease course and variability, informing at-risk family members, option of predictive DNA testing and family planning

*These patients are usually seen by a neurologist (but may also be seen by a psychiatrist, a clinical geneticist, a geriatrician, or others).

**These patients are usually seen by a clinical geneticist (but may also be seen by a neurologist).

***This step may vary depending on procedures and resources.

**** Typical cysteine altering NOTCH3 variant

***** De novo NOTCH3 variant can occur

AT RISK HEALTHY INDIVIDUAL, NO MRI DATA

Asymptomatic, no MRI, genetic diagnosis of CADASIL confirmed in the family**

Dedicated pre-symptomatic consultation (geneticist and/or neurologist, psychologist) to evaluate the nature and context of the request

Reflection time

Consultation including potential predictive DNA testing for the familial NOTCH3 variant***

Consultation for genetic results (physician ± psychologist + accompanying person)

Proposal of follow up

Follow-up consultation and MRI assessment if needed

Psychological support

LEGEND: Clinical evaluation | Investigations | Genetics | Management

Version 1

European Reference Network

VASCERN

Gathering the best expertise in Europe
to provide accessible cross-border healthcare
to patients with rare vascular diseases

VASCERN, the European Reference Network on Rare Multisystemic Vascular Diseases, is dedicated to gathering the best expertise in Europe in order to provide accessible cross-border healthcare to patients with rare vascular diseases (an estimated 1.3 million concerned). These include arterial diseases (affecting aorta to small arteries), arterio-venous anomalies, vascular malformations, and lymphatic diseases.

VASCERN currently consists of 48 expert teams from 39 highly specialised multidisciplinary Healthcare Providers (HCPs) from 19 EU Member States and of various European Patient Organisations and is coordinated in Paris, France.

Through our 6 Rare Disease Working Groups (RDWGs) as well as several thematic WGs and the ePAG – European Patient Advocacy Group, we aim to improve care, promote best practices and guidelines, reinforce research, empower patients, provide training for healthcare professionals and realise the full potential of European cooperation for specialised healthcare by exploiting the latest innovations in medical science and health technologies.

More information available at: www.vascern.eu

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