CAVERNOUS MALFORMATION:
Guide for Primary Care Providers

NEW CONSENSUS CARE GUIDELINES FOR CAVERNOUS MALFORMATION

PUBLISHED MAY 2025 – PMID: 40396744

We greatly appreciate your care of patients with cavernous malformation (CM)!

Please find recent updates on CM treatment and management relevant to primary care practice. The new guidelines include:

NEW DATA ON MEDICATIONS AND CM RISKS

- Statins
- Beta blockers
- Vitamin D

NEW WOMEN'S HEALTH CONSIDERATIONS

- Female hormones
- Pregnancy planning

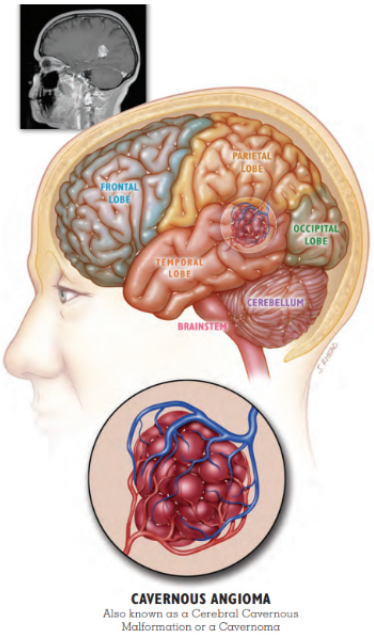
NEW LIFESTYLE RECOMMENDATIONS

- Physical activity
- Diet
- Tobacco
- Alcohol
- Blood pressure
- Mental health

Refer your patients to the Alliance to Cure Cavernous Malformation! www.alliancetocure.org

- Designated Centers of Excellence and Clinical Centers
- Patient Educational Webinars & Care Navigation
- Virtual Support Group
- CCM Patient Registry

CAVERNOUS MALFORMATION (CM)



DEFINITION

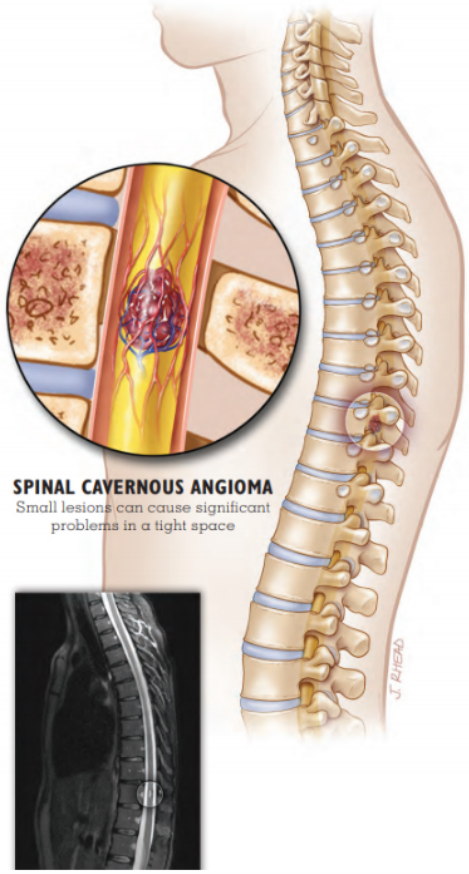
A cavernous malformation (CM) is a blood vessel abnormality of closely clustered, dilated, leaky capillary caverns in the brain and spinal cord. CMs impact as many as 1 in 500 individuals.

Other names: cavernous angioma, hemangioma, cavernoma, or cerebral cavernous malformation (CCM)

CAUSES

Most CMs occur sporadically (80%) with a single lesion and no family history. A history of radiation therapy to the brain can increase the risk of developing a CM.

Less commonly, CMs can happen due to a genetic condition (20%), familial cerebral cavernous malformation (FCCM). Individuals with FCCM are at increased risk of developing multiple CMs and typically will have multiple affected relatives. Pathogenic or likely pathogenic variants in the KRIT1, CCM2, or PDCD10 genes can cause FCCM.



Common Hispanic Mutation (*KRIT1* c.1363C>T (p.Q455*)

There is a form of FCCM that is prevalent in the U.S. Southwest and Northern Mexico related to a *KRIT1* gene founder mutation. As many as 30,000 people may live in New Mexico and surrounding areas with FCCM related to the *KRIT1* gene.

SYMPTOMS

Typical symptom onset in the 20s to 50s. Most common presenting symptoms for cerebral cavernous malformations (CCM) include:

- Seizures (50%)
- Stroke due to intracranial hemorrhage (25%)
- New focal neurologic deficits (25%)
- Headaches (may be as high as 52%)

Spinal cord cavernous malformations may present with sudden or slowly progressive weakness or sensory disturbance in the limbs, pain, and/or sphincter disturbance.

DIAGNOSIS (PREFERRED ICD-10: D18.03 HEMANGIOMA OF INTRACRANIAL STRUCTURES)

Imaging is key to diagnosis. Brain MRI is strongly recommended for diagnosis and clinical follow-up of suspected or known CM. Brain MRI with susceptibility weighted imaging (SWI) sequences can detect very small lesions. Follow-up imaging is essential for guiding treatment decisions or investigating new symptoms. After CM diagnosis, follow-up images do not generally require contrast. In emergencies, CT may be appropriate to evaluate the presenting neurologic symptom, but it may not detect all lesions visible by MRI. Repeat MRI should be considered with new or worsened symptoms to assess for new CM lesions, lesion growth, or hemorrhage.

Given the increased availability of MRI scans, many asymptomatic CMs are identified incidentally. Among incidentally detected cases of CMs, the risk of intracranial hemorrhage is very low (0.08% per person-year).

CCM TREATMENT AND MANAGEMENT

CCM CENTER OF EXCELLENCE AND CLINICAL CENTER NETWORK

Patients with CMs may benefit from expert consultation at a multidisciplinary CCM Center of Excellence or Clinical Center. The Alliance to Cure Cavernous Malformation offers this special designation to hospitals with expertise in CMs, multidisciplinary staffing, and commitment to CM research, patient engagement, and medical education. More information available here: https://www.alliancetocure.org/home/for-patients/centers-of-excellence/

NEUROSURGICAL EVALUATION

Referral to neurosurgery can be considered for the management of CMs. Surgical intervention is not appropriate for all patients or circumstances. Surgical decision-making should involve consideration of the individual patient's location, size, hemorrhage history, and symptoms. Surgical approaches may include open brain or spinal surgery or more minimally invasive techniques. Given the minimal hemorrhage risk for these lesions, surgery is not typically recommended for incidental CMs.

NEW DATA ON MEDICATIONS AND CM RISKS

Antithrombotic Medications

Risk of hemorrhage in patients needing antithrombotics is low; the presence of CMs should not preclude use.

Thrombolytic Medications

For patients presenting with acute ischemic stroke who are known to harbor an unruptured and untreated CM, the risk of thrombolysis is not well established. Intravenous thrombolytics may be considered in patients with CM after weighing the risks and benefits in an individual patient, which may include the severity of the ischemic stroke, recent symptoms related to the CM, and alternative options.

Statins

The long-term efficacy of statins for reducing CM hemorrhage risk or preventing new CM development is unknown. According to standard medical use guidelines, a statin can be considered in patients with CM and elevated cholesterol.

Beta blockers

Propranolol is safe and tolerable at low doses in patients with familial CM. The long-term efficacy of propranolol for reducing CM hemorrhage or preventing new CM formation in familial CM is not clear.

Cholecalciferol

Vitamin D supplementation should be considered for bone health in CM patients with vitamin D deficiency; the effects on CM hemorrhage are less clear. Vitamin D supplementation is reasonable in CM patients with unknown 25-OH-vit D levels, especially those on antiseizure medications or with risk for deficiency.

NEW WOMEN'S HEALTH CONSIDERATIONS

Female hormones

Sex hormones (including exogenous oral estrogen and progesterone) may increase the risk of CM hemorrhage in some patients, and caution regarding their use is recommended. Research is ongoing to define which patients may be at the highest risk.

Pregnancy planning

Genetic counseling should be considered for FCCM. Risk for neurological symptoms is not thought to be different from the nonpregnant state. Vaginal delivery is appropriate for most patients.

NEW LIFESTYLE RECOMMENDATIONS

Physical Activity

Aerobic activity is reasonable for patients with CM.

Diet

A diet low in processed foods or emulsifiers may be considered to reduce gut leakiness, which has implications for CM development.

Alcohol and Tobacco

Recommend against tobacco use and binge drinking.

High Blood Pressure

Limited data suggest that blood pressure is a risk factor for CM hemorrhage. Assessment and treatment are recommended according to standard guidelines.

Mental Health

Patients with CMs may have higher anxiety than the general population—assessment and referral to appropriate resources recommended

"Guidelines for the Diagnosis and Clinical Management of Cavernous Malformations of the Brain and Spinal Cord: Consensus Recommendations Based on a Systematic Literature Review by the Alliance to Cure Cavernous Malformation Clinical Advisory Board Experts Panel" (Akers, 2025; PMID: 40396744)