MAYO CLINIC

Neurosciences Update

Focus on Cerebrovascular Medicine and Surgery

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Mayo Clinic Intracranial Aneurysm Practice Specializes in Medical, Surgical, and Endovascular Treatments

INSIDE THIS ISSUE

Intracranial aneurysms are common disorders, occurring in approximately 2% of the general population. They can be either asymptomatic or symptomatic, presenting acutely with a subarachnoid or intracerebral hemorrhage. When an aneurysm ruptures, it is fatal in approximately 40% of patients.

Because of this high potential mortality, expert, immediate, and comprehensive aneurysm management is a medical imperative. Explains Fredric B. Meyer, MD, a neurosurgeon at Mayo Clinic in Rochester, Minnesota: "If a patient survives the initial hemorrhage, then the optimal outcome is obtained by a multispecialty approach that commences in the emergency department and extends through the time of treatment of the lesion, subsequent management in the intensive care unit, and then recovery in a rehabilitation unit if necessary."

Dr Meyer adds that optimal outcomes of all aneurysm cases—not just ruptures—are best achieved through an advanced multidisciplinary team approach. Among the larger referral practices for the treatment of aneurysm in North America, Mayo Clinic neurosciences physicians manage all manifestations of this complex clinical presentation. Team members have special expertise and extensive experience treating all forms, especially skull base, posterior circulation, and giant aneurysms, and can quickly apply the most effective and least invasive treatment. The severity of the health threat depends on many variables, including size, location, patient age, and prior neurologic history. "Hence, there are differences between small, asymptomatic aneurysms in the anterior circulation compared with similar-sized aneurysms in the posterior circulation or large, complex giant aneurysms," Dr Meyer says. "Accordingly, not all aneurysms necessarily require treatment. Furthermore, the risks of intervention must be balanced against the predicted natural history of the aneurysm if left untreated."

To Treat or Observe?

When a patient is referred to the Mayo Clinic

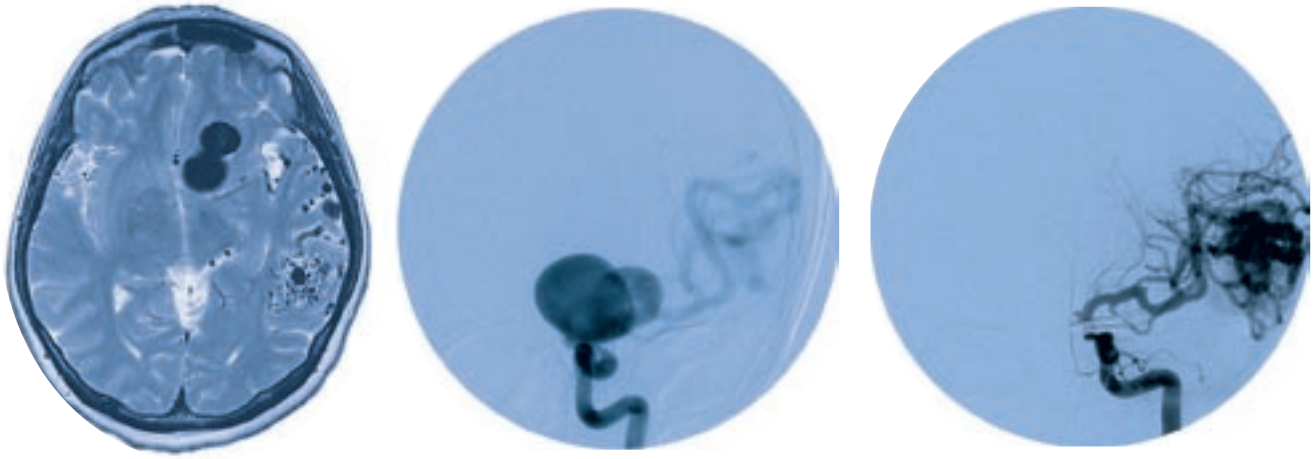

Figure 1. *Giant left internal carotid artery aneurysm associated with ipsilateral arteriovenous malformation (left and middle). The aneurysm was treated with direct clipping, and the postoperative angiogram shows complete exclusion of the aneurysm with no compromise of distal flow (right). The arteriovenous malformation was subsequently treated with Gamma Knife.*

Fredric B. Meyer, MD

Cerebrovascular Clinic for treatment of an intracranial aneurysm, the first step is to carefully consider whether to treat or observe the aneurysm. When an aneurysm is large or symptomatic or when the patient has a history of subarachnoid hemorrhage, treatment usually is advocated because these characteristics place the patient at greater risk of hemorrhage, especially in the posterior circulation (Figure 1). However, in older patients who harbor a small asymptomatic aneurysm, proceeding with treatment poses a more difficult question. Recent prospective clinical research suggests that aneurysms smaller than 7 mm in the anterior circulation have a lower risk of hemorrhage. Therefore, the decision to treat also must take into account patient age, the presence of comorbid conditions, and neurologic function. Sometimes, the safer approach is observation, with control of hypertension if present, smoking cessation if the patient is a smoker, and intermittent repeat imaging to be sure the aneurysm is not changing.

Surgery

In direct surgical repair with the patient under general anesthesia, the aneurysm is approached through a craniotomy. The advantages of the surgical approach are that the surgeon can visualize the aneurysm, and treatment is most often definitive and curative. The disadvantages are that surgery is invasive, carries the risks of any invasive procedure, and requires 3 to 5 days of recovery time in the hospital.

Endovascular Obliteration

Coil embolization is performed by an interventional team. A catheter is passed through the femoral artery into the cerebral circulation, and wire coils are inserted into the aneurysm, detached from the supporting wire left in place after proper positioning is carefully checked under radiographic control. Sometimes balloons or stents are used with the coils.

Giuseppe Lanzino, MD

The advantage of endovascular treatment is that it is less invasive than direct surgery and therefore generally better tolerated by patients. "Endovascular treatment is rapidly gaining ground as a valid alternative to open surgery in an increasing number of patients with intracranial aneurysms," observes Giuseppe Lanzino, MD, a neuosurgeon at Mayo Clinic in Rochester, Minnesota. Dr Lanzino has dual subspecialty training in endovascular and open vascular neurosurgery. A disadvantage of endovascular treatment is that the aneurysm may not be obliterated completely and repeated imaging follow-up may be required. At Mayo Clinic, all patients who undergo endovascular aneurysm occlusion procedures are followed at regular intervals to ensure that there is no recurrence.

Combined Treatment

Some complex aneurysms are difficult to treat and require advanced surgical and endovascular skills. In addition to size, these lesions often have broad necks that incorporate the origin of perforators or major blood vessels. Sometimes these aneurysms are dolichoectatic, a term used to describe giant fusiform aneurysms of a major blood vessel, most commonly the internal carotid, middle cerebral, basilar, or posterior cerebral arteries (Figure 2). Direct occlusion of a fusiform aneurysm by default would cause loss of the parent blood vessel.

In these circumstances, straightforward clipping or endovascular occlusion is often not an option because of the risk of stroke. Intervention often requires advanced techniques such as intracranial vascular reconstruction using microsurgical techniques, bypass surgery, or resection of the aneurysm under deep hypothermia. A final alternative is a combined interventional surgical approach in which an intracranial bypass graft is constructed first, followed by endovascular proximal vessel occlusion or embolization.

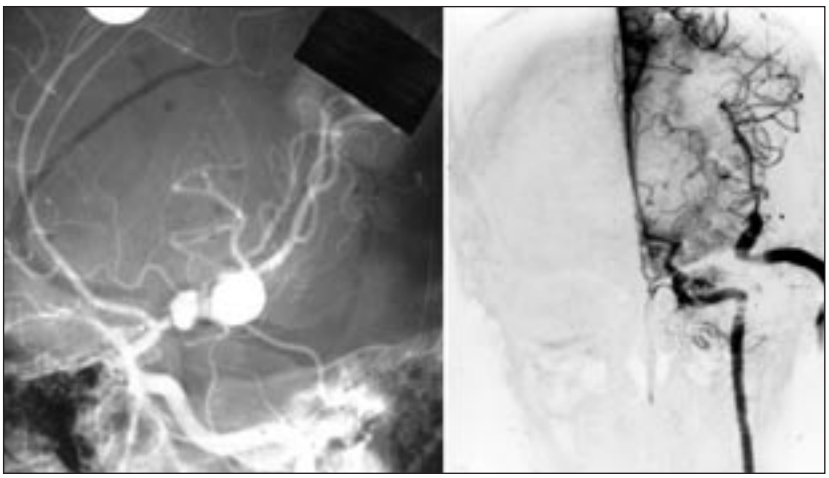

Figure 2. *A fusiform middle cerebral artery aneurysm. Left, Before treatment. Right, After treatment by saphenous vein bypass and trapping.*

The Continuum of Care

"Patients who undergo treatment for aneurysms that have hemorrhaged or for complex aneurysms often require special care in the neurology intensive care unit. Patients are aggressively treated to avoid potential sequelae of aneurysmal subarachnoid hemorrhage, including hydrocephalus, vasospasm, and cardiopulmonary complications," Dr Meyer explains. After recovery, all patients are seen in the Cerebrovascular Clinic to make sure they have no delayed complications. For incompletely obliterated aneurysms, a follow-up plan is developed to watch for possible aneurysm regrowth.

Carotid Angioplasty With Stent Placement

Carotid angioplasty with stent (CAS) placement is an emerging alternative to carotid endarterectomy for the treatment of patients with carotid artery occlusive disease. Mayo Clinic neuroradiologists began using it in 1996 for patients at high risk for surgery.

"The Cerebrovascular Clinic in the Department of Neurology has a multidisciplinary CAS placement protocol in which a vascular neurologist, an interventionalist, and a neurosurgeon meet with the patient to help clarify the best treatment approach. Cardiology colleagues may also be involved if the patient has cardiac symptoms. This is not uncommon, since so many patients with carotid occlusive disease also have coronary artery occlusive disease," says neurologist Robert D. Brown Jr, MD. Adds Harry Cloft, MD, PhD, a neuroradiologist: "The protocol has been highly successful in allowing us to select patients carefully and appropriately as we move forward with this emerging technology."

Indications and Procedure for CAS Placement

"Candidates for CAS placement are patients with a severe narrowing of the carotid artery who have had symptoms such as transient ischemic attacks or cerebral infarction, and also selected patients who have severe narrowing of the carotid artery without symptoms," say Dr Brown and neurosurgeon Giuseppe Lanzino, MD.

Most patients arrive at the Cerebrovascular Clinic at Mayo Clinic in Rochester, Minnesota, after carotid ultrasonography, magnetic resonance angiography, or computed tomographic angiography has shown narrowing of the carotid artery. After thoroughly examining the patient, the multidisciplinary neuroscience team members decide whether CAS placement is the appropriate treatment. If it is, the patient proceeds to the interventional neuroradiology suite in Saint Marys Hospital for further evaluation.

The patient is sedated but awake, and a small plastic catheter is inserted in a groin artery and tracked through the aorta to the carotid arteries. Next, contrast material is injected to delineate the anatomy. If the angiogram confirms severe narrowing that could be best treated with CAS placement, then the procedure begins.

First, a protection device may be deployed distally in the carotid artery. This device functions something like a tiny mesh umbrella to catch material that may break free during the angioplasty. Then the angioplasty balloon is advanced across the plaque and inflated to push the plaque aside, thus reducing arterial narrowing. The stent—a small metallic scaffolding device—is put in place to keep the artery open. The procedure ends with withdrawal of the distal protection device and the catheter.

Typically, the patient is hospitalized for 1 day. Aftercare involves taking clopidogrel and aspirin daily for 1 month to prevent blood clots from

Robert D. Brown Jr, MD

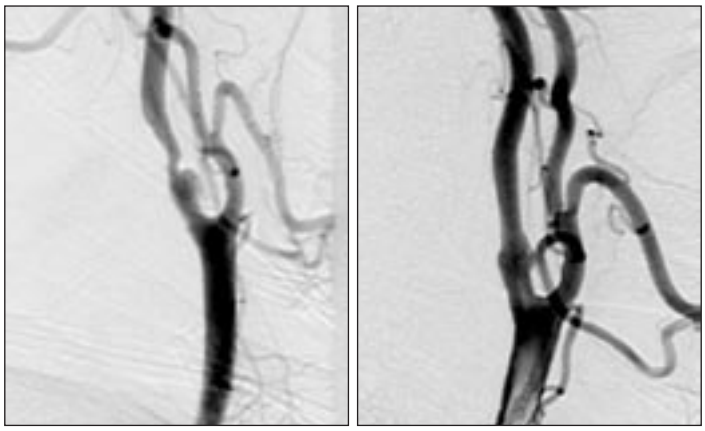

Figure. *Left, Preoperative image of narrowed carotid artery. Right, Postoperative image showing stent in place and open artery after CAS placement.*

forming at the stent site and then aspirin alone indefinitely thereafter. Mayo Clinic specialists follow each patient long term, both to assess durability of the stent and to determine whether narrowing recurs. Follow-up includes annual carotid ultrasonography that begins several months after the procedure.

Results, Risks, and Complications

The concept of CAS placement is a logical extension of the balloon stenting used for coronary artery disease. Initially, in the early 1990s, CAS placement was performed on patients who were at high risk for conventional surgery. The outcomes of these early cases were excellent, and the risk of stroke and death was extremely low. Because these measures of success were so similar to those of the standard treatment, carotid endarterectomy, the use of CAS placement was cautiously and carefully expanded.

Since then, Mayo Clinic experience with CAS placement suggests that, when performed by an experienced, multispecialty team on carefully selected patients, the procedure is approximately equal to carotid endarterectomy in terms of effectiveness, risks, and complications.

Future Directions

The National Institutes of Health selected Mayo Clinic to participate with other US medical centers in the formal evaluation of CAS placement in the Carotid Revascularization Endarterectomy vs Stent Trial (CREST). The goal of CREST is to determine how CAS placement compares with carotid endarterectomy, the standard treatment for carotid artery stenosis. A key question is whether the risk of recurrent narrowing after CAS placement is as low as the extremely low risk of recurrent narrowing after carotid endarterectomy.

CREST will also evaluate the comparative risks of stroke associated with CAS placement and carotid endarterectomy. Because CAS placement requires the interventionalist to work within the artery, the possibility exists for stroke during the procedure. Carotid endarterectomy, when performed by an experienced neurosurgeon or vascular surgeon, also carries the risk of stroke. The goal of the CREST protocols is to determine these issues conclusively. CREST completed patient recruitment in the summer of 2008, and the final results will be available in the near future.

Mayo Clinic's Cerebrovascular Clinic is a full-time clinic, providing consultations for patients with carotid stenosis and all other types of cerebrovascular disorders. To refer a patient for evaluation, call the Cerebrovascular Clinic at 507-284-1588.

Managing Arteriovenous Malformations

Michael J. Link, MD

An arteriovenous malformation (AVM) is a congenital, abnormal tangle of blood vessels occurring within any area of the brain that commonly presents with spontaneous hemorrhage, seizure, or intense headache. Only 1 or 2 persons per 100,000 are diagnosed annually with a brain AVM. Most AVMs do not cause any symptoms until the third decade of life.

Because of the variability inherent in each AVM and in each patient, treatment is highly individualized. Treatment—by conventional surgery, stereotactic radiosurgery, endovascular embolization, or a combination of these methods—is most effective when performed by an experienced team of neurosurgeons, neurologists, and interventional neuroradiologists who have training in the latest techniques, access to the most advanced equipment, and appreciation of a collaborative approach to care that assures each patient receives the best treatment for an optimal outcome.

Michael J. Link, MD, a neurosurgeon at Mayo Clinic in Rochester, Minnesota, comments: "The cerebrovascular team at Mayo Clinic has experience treating thousands of patients with AVMs and a variation of AVM, dural arteriovenous fistula. Given this broad and deep base of experience, we believe we are well poised to respond fully to the uniqueness of each case." Adds Mayo Clinic interventional neuroradiologist Harry Cloft, MD, PhD: "The treatment for any particular AVM has to be carefully individualized to minimize risk to the patient and maximize the chance for completely obliterating the lesion. Surgery, radiosurgery, or embolization, alone or in com-

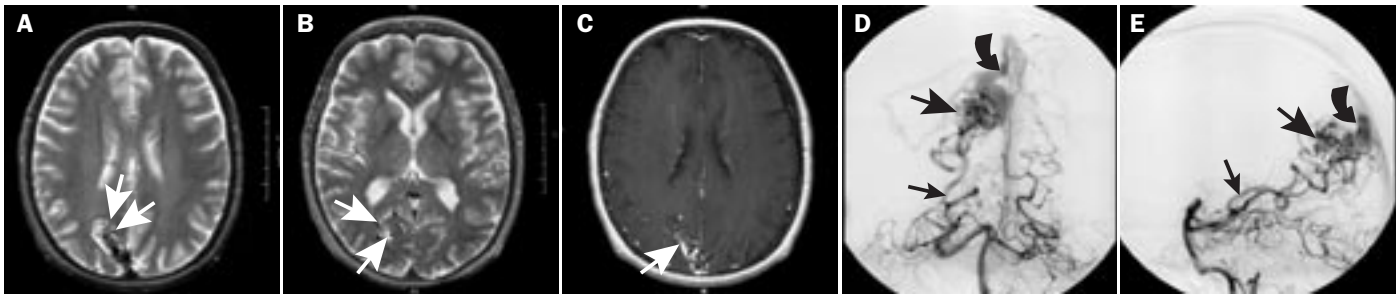

Figure. *A and B, Right parieto-occipital AVM shown in T2-weighted MRIs with flow voids consistent with AVM (arrows). C, T1-weighted MRI with contrast that partially enhances the parieto-occipital AVM (arrow). D and E, Anteroposterior and lateral arteriograms with vertebral injection show posterior cerebral artery feeders (small arrows) to the AVM (large arrows), with a large draining vein into the superior sagittal sinus (curved arrows). Reprinted with permission from Mayo Clinic Proceedings. 2005;80:269-281.*

bination, may be advisable, depending on the location and size of the AVM and the general health of the patient. Each of these variables requires thorough and expert evaluation, which is why a multidisciplinary treatment model works best for AVMs."

First AVM Symptoms

About 50% of patients with AVMs come to medical attention because of a spontaneous hemorrhage. The hemorrhage is most commonly in the brain surrounding the AVM. This may result in headache, unilateral weakness or numbness, trouble with speech, or alteration of consciousness, depending on the size and location in the brain where the hemorrhage occurs. Between 80% and 90% of patients who experience a hemorrhage from an AVM survive the initial rupture.

The second most common presentation of an AVM is a seizure, which occurs in about 25% of cases. All types of seizures have been reported in association with AVMs, and most are well controlled with anticonvulsant medication.

Other common presenting symptoms include headache not associated with hemorrhage and progressive neurologic deficit. The headaches are believed to be due to stretching of the covering of the brain and venous channels, which have many pain sensing fibers. (The brain itself has no pain sensing fibers.) Although the headaches may be similar to migraine headaches, migraine sufferers are not at increased risk of AVM. Progressive neurologic deficits may occur in association with an AVM because the brain does not have time to extract adequate oxygen from the fast-flowing blood. The malformation is therefore "stealing" blood from the surrounding brain, and this can result in symptoms that mimic a stroke. As in the case of hemorrhage, these symptoms depend on where the malformation is located in the brain.

Diagnosis of AVM

A hemorrhage from an AVM is usually detected by obtaining a CT scan when the patient comes to the hospital. Calcification within the AVM may also be demonstrated on a CT scan. After intravenous administration of contrast, the nidus may "light up" and become apparent. MRI and magnetic resonance angiography are even more sensitive in demonstrating the AVM vessels. MRI also provides essential anatomic information about where in the brain the AVM is located, which is important for treatment planning and risk assessment (Figure).

Angiography remains the "gold standard" in demonstrating the AVM, the feeding arteries, and the draining veins. Angiography is performed by radiologists. A catheter is inserted into a leg artery and routed to the vessels that supply the brain or spinal cord. Contrast dye is then injected as radiographic pictures are taken. This imaging technique provides a detailed "road map" of the AVM and other blood vessels. Angiography is usually done using local anesthesia, with minimal pain and only a small risk. It is crucial in deciding on therapy for an AVM.

Treatment Options for AVM

The 3 main forms of intervention to treat an AVM are surgical removal, stereotactic radiosurgery, and endovascular embolization.

The size and location of the AVM largely determine how safely surgery can be performed. The many advances in surgical technique in the past 20 years have improved results, and many AVMs can safely and effectively be removed surgically. These improvements include advances in neuroanesthesia, the operating microscope, the development of improved microinstruments, a better understanding of the potential causes of complications, and preventive and corrective measures of these complications.

Harry Cloft, MD, PhD

Stereotactic radiosurgery involves delivering high-dose radiation to a defined area, such as an AVM nidus. Radiosurgery is usually performed as an outpatient procedure and does not require general anesthesia or an incision. The Leksell Gamma Knife uses cobalt radiation sources to accomplish this precise delivery of radiation. The radiation causes the AVM vessels to slowly close during the ensuing 1 to 3 years until the AVM is completely obliterated. This form of treatment works best for small AVMs and AVMs that have not recently caused a life-threatening hemorrhage.

In endovascular embolization, performed like an angiogram, a catheter is introduced into the leg artery and threaded through the vascular system to the brain arteries. The catheter is positioned in one of the feeding arteries to the AVM. Instead of injecting dye to take a picture of the AVM, small particles or a glue-like substance are injected to occlude the vessel and reduce the blood flow into the AVM. This is often done before surgery to reduce the chance of a bleeding complication during the operation or to reduce the overall size of the AVM to make it more responsive to stereotactic radiosurgery. In some large AVMs that are considered inoperable, embolization may reduce the stroke-like symptoms caused by the stealing phenomenon by diverting blood back to the normal brain. In rare cases, endovascular embolization may completely obliterate or cure the AVM, eliminating the need for any other therapy.

Risks of Not Treating an AVM

The risk of hemorrhage from an AVM is between 2% and 4%. About 10% to 20% of patients die from their AVM-related brain hemorrhage. The risk of severe permanent neurologic problems is 2% to 3%. Notes Dr Link: "While the day-to-day risk of hemorrhage or other problems is small, over time the risk adds up, and therefore treatment is usually recommended for otherwise healthy young people discovered to have AVMs."

Secondary Stroke Prevention

Toward Nurse-Based, Physician-Directed Management to Close the Evidence-Practice Gap in Stroke Care

Kelly D. Flemming, MD

Stroke is the leading cause of disability in the United States and the third leading cause of death. It is therefore an important factor in both health care budgets and the "emotional economy" of families. Although much is known about modifying risk factors to prevent first stroke (primary prevention) or recurrent stroke (secondary prevention), too often a consistent, systematic assessment of stroke risk factors is lacking in clinical practice. Underutilization of stroke risk assessment strategies creates a gap between existing evidence and actual practice. "This gap is especially concerning for patients after they have already had a stroke, because of the risk of recurrent stroke and the increased likelihood of certain medical disorders," explains Kelly D. Flemming, MD, a Mayo Clinic neurologist who is investigating the use of new clinical models for stroke prevention.

Among the serious consequences of stroke—

- Subsequent stroke. An estimated 30% of survivors of an initial ischemic stroke will have a subsequent stroke within 5 years, 18% of which will be fatal.
- Cardiac involvement. Stroke carries with it a serious risk of cardiac involvement: 5% of cerebral infarction (CI) patients have myocardial infarction (MI) within the first year after CI; more than 3% of patients have MI annually for the first 10 years after CI.
- Depression. Often depression is unrecognized by both caregivers and family members. Yet data suggest that nearly 40% of stroke patients will experience depression sometime during the first year after the stroke.

Secondary stroke prevention is well suited to a new model of care aimed at preventing long-term morbidity and mortality for 2 main reasons: 1) risk modification strategies can lessen the likelihood of recurrent stroke or other adverse outcomes, and 2) those patients with initial stroke can be readily identified. One promising new model is the stroke prevention clinic modeled after cardiac rehabilitation clinics (Table).

The Stroke Prevention Clinic Concept

To help close the evidence-practice gap in stroke prevention—and to prepare for the changing demographics of stroke as the population ages and more people are at risk of stroke—Mayo Clinic in Minnesota is evaluating a physician-led, nurse-assisted stroke management program. It is currently being assessed for its long-term effectiveness to manage cerebrovascular disease. The program aims to achieve with stroke the success that cardiac rehabilitation clinics have obtained with secondary prevention of coronary heart disease. Through this approach, neurologists play a leading role in meeting the emerging demand for preventive stroke services by obtaining training in management of atherosclerotic risk factors; by making stroke risk factor modification a part of the neurologic evaluation; and by providing long-term follow-up and appropriate care in the setting of a physician-led, nurse-assisted stroke prevention clinic. The neurologic team can closely collaborate with the patient's primary care provider to optimize management.

Data for similar nurse-assisted, physician-led clinics—such as the Stanford Coronary Risk Intervention Project—have shown that this approach can improve patient outcomes while reducing use of medical resources. In the Mayo Clinic secondary stroke prevention initiative, nurses guided by physicians provide intensive multiple risk factor reduction counseling and support in the outpatient setting. This outpatient clinic is the next step in the continuum of care of the stroke patient, after acute treatment and evaluation have been provided in the Saint Marys Hospital inpatient stroke center and, if needed, a stay in the stroke rehabilitation unit. The goals of this ongoing outpatient care are to support lifestyle changes known to reduce the risk factors of stroke, to prescribe appropriate medications to assist in reducing these risk factors, and to enhance use of appropriate antithrombotic agents.

Table. Individual Stroke Risk Factors To Be Addressed in a Stroke Prevention Clinic

Risk Factor	Clinical Intervention
Hypertension control	Physicians manage prescription medications (eg, diuretics, ACE inhibitors), and nurses educate on lifestyle changes. Antihypertensive medications are considered for every patient with ischemic stroke or transient ischemic attack (TIA).
Cholesterol level control	Physicians evaluate the need for statin drugs in patients with atherosclerotic stroke.
Tobacco cessation counseling	Interventions range from patient education to outpatient and inpatient treatment.
Weight loss, increased exercise, metabolic syndrome	Educating, motivating, and supporting dietary changes and daily activity levels.
Diabetes mellitus	Tight control of diabetes may not reduce stroke risk; however, important in these patients are tight blood pressure control and cholesterol lowering, with a goal of <70 mg/dL.
Atrial fibrillation	Abnormal cardiac contractions can lead to thrombus formation. The physician evaluates the need for warfarin therapy, which can reduce relative risk of stroke by 70% to 80% in the highest-risk groups.
Asymptomatic carotid artery stenosis	Selection of patients for carotid endarterectomy or carotid angioplasty with stenting is highly individualized, and many factors should be considered.
Elevated homocysteine level	Data are not conclusive that lowering this amino acid reduces stroke. However, in young patients with early atherosclerosis, screening for this amino acid and treatment with vitamin B_6, vitamin B_{12}, and folate may be considered.
Sleep apnea	If oximetry results suggest sleep apnea, the physician may order a polysomnogram for definitive diagnosis; continuous positive airway pressure or other treatments are available.
Hormone therapy	Research on this topic is changing, but patients with history of stroke should be advised against hormone therapy without a medically compelling reason.
Stress	Nurses educate on the negative effects of stress and offer ways to improve stress levels.

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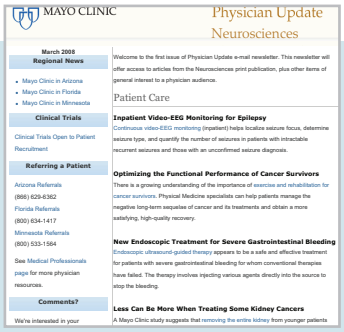
Mayo Clinic Cerebrovascular Practice

Mayo Clinic has one of the largest cerebrovascular practices in the United States. Every year, more than 4,000 cerebrovascular patients receive care from Mayo Clinic's multidisciplinary team of specialists. The team includes vascular neurologists and neurosurgeons, interventional neurosurgeons, critical care neurologists, neuroradiologists, and endovascular surgical neuroradiologists with a specific interest in cerebrovascular disease, cerebrovascular-specialist physiatrists, speech pathologists, physical, occupational, and speech therapists, neuropsychometrists, emergency medicine physicians, critical care physicians, subspecialty-trained nurses, nurse practitioners, and physicians in other disciplines working together in an extraordinarily integrated manner to provide the highest level of care.

All 3 Mayo Clinic locations are Joint Commission–certified Primary Stroke Centers. Patients benefit from access to outpatient and inpatient cerebrovascular and rehabilitation services and the cutting-edge knowledge contributed by Mayo Clinic's extensive cerebrovascular research program.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Inpatient Video-EEG Monitoring for Epilepsy
Continuous video-EEG monitoring (inpatient) helps localize seizure focus, determine seizure type, and quantify the number of seizures in patients with intractable recurrent seizures and those with an unconfirmed seizure diagnosis.
Optimizing the Functional Performance of Cancer Survivors
There is a growing understanding of the importance of exercise and rehabilitation for cancer survivors. Physical Medicine specialists can help patients manage the negative long-term sequelae of cancer and its treatments and obtain a more satisfying, high-quality recovery.
New Endoscopic Treatment for Severe Gastrointestinal Bleeding
Endoscopic ultrasound-guided therapy appears to be a safe and effective treatment for patients with severe gastrointestinal bleeding for whom conventional therapies have failed. The therapy involves injecting various agents directly into the source to stop the bleeding.
Less Can Be More When Treating Some Kidney Cancers
A Mayo Clinic study suggests that removing the entire kidney from younger patients

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