MAYO CLINIC

Clinical Update

Current Trends in the Practice of Medicine

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PARTNER Investigators Announce Dramatic Trial Results for the Treatment of Aortic Stenosis

The Challenge

Surgical replacement, either with tissue or mechanical valve prostheses, has been the "gold standard" for treatment of extensive valve stenosis. Improvements in surgical technique, durable valve prostheses, and better anticoagulation regimens have resulted in excellent patient survival and functional status. Nevertheless, approximately a third of individuals with symptomatic aortic stenosis are not candidates for open surgical replacement or repair because of advanced age, the presence of comorbid conditions, or both. Complications such as renal failure, prolonged ventilator dependence, and wound-healing problems occur more frequently in these high-risk patients.

Evaluating a Nonsurgical Approach

Mayo Clinic in Rochester, Minnesota, is now participating in a multicenter, prospective, randomized trial—the Placement of Aortic Transcatheter Valve Trial (PARTNER)—to evaluate a new cardiac valve designed to be placed without the need for a median sternotomy. This new valve is a balloon-expandable, stented bioprosthesis designed to be delivered through either the transfemoral or the transapical route. It has been approved in some European countries and has been placed in almost 4,000 patients worldwide.

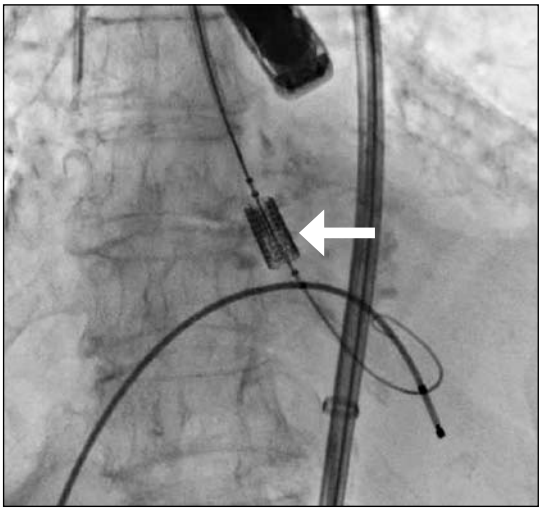

Figure 1. *Deployment of percutaneous aortic valve bioprosthesis. Arrow indicates investigational valve mounted on a balloon catheter.*

Conducted at 21 centers in the United States, Canada, and Germany, the PARTNER study is comparing in parallel 2 large patient cohorts. Cohort A will directly compare the transfemoral or transapical placement of the investigational

Points to Remember

- As many as 300,000 individuals in the United States currently have symptomatic aortic stenosis, and the prevalence is increasing as the population ages.
- Approximately a third of individuals with symptomatic aortic stenosis are not candidates for open surgical replacement or repair because of advanced age, the presence of comorbid conditions, or both.
- Mayo Clinic is participating in a randomized clinical trial—the Placement of Aortic Transcatheter Valve Trial (PARTNER)—to evaluate a new balloon-expandable cardiac valve designed to be placed through the transfemoral or the transapical route, without the need for a median sternotomy.

prosthesis (Figures 1 and 2) with traditional surgical aortic valve replacement (via median sternotomy); cohort B will compare transfemoral prosthesis implantation with standard medical management (which can include balloon valvuloplasty if clinically indicated) in patients whose medical condition precludes them from being candidates for open surgical replacement.

Preliminary Results

The PARTNER study has released results for the 358 patients in cohort B (investigational valve placement vs medical therapy only), while the surgical arm of the trial is ongoing. Although the 30-day rates of stroke and vascular complications were higher in the cohort B patients treated with the investigational valve, survival at 1 year was dramatically higher in this group (69.3%) than in patients who received only medical therapy (49.3%). Furthermore, patients who received the investigational valve had significantly fewer hospitalizations and improved symptom relief when compared with those receiving standard medical therapy.

Some patients are not candidates for the investigational valve, due to characteristics of the valve annulus or because they have severe peripheral vascular disease. However, Mayo researchers believe that the new valve's design and improved delivery systems should enable the deployment of percutaneous valves in more of these patients in the future, with a reduced risk of stroke, vascular damage, and major bleeding.

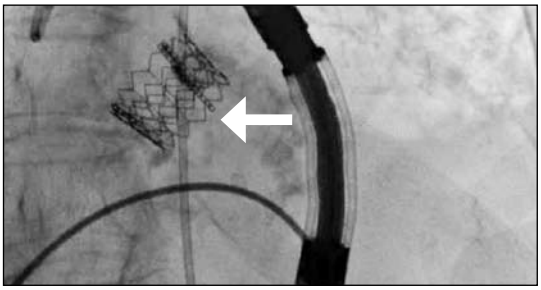

Figure 2. *Investigational aortic valve (arrow) after deployment.*

Mayo researchers also stress that the results of this cohort should not be extrapolated to other patient groups, as the long-term durability of this investigational valve is as yet unknown. Until the results of the surgical cohort provide further insight, the standard surgical approach to aortic valve replacement and repair may still be the best option in patients with low operative risk. Ultimately, trials in other patient subsets and long-term patient follow-up will determine the role of percutaneous valves in the treatment of valvular heart disease.

Potential PARTNER study candidates may be referred directly to the Mayo Clinic Valvular Heart Disease or Interventional Clinics (507-284-3994 or 800-471-1727) or by contacting the Mayo Clinic trial coordinator at 507-255-7100.

Treating Trigeminal Nerve Pain

The stabbing, lancinating, recurrent facial pain associated with trigeminal neuralgia (TN) is considered one of the most painful sensations in human experience. It can impact mood, sleep, overall health, and employment and, in some cases, has led to suicide. Treatment ranges from drug therapy to surgery. Therapeutic success is particularly dependent on differential diagnosis to distinguish classic TN from other types of facial pain, some of which share clinical features with TN.

Differentiating TN From Other Types of Facial Pain

TN1, or classic TN, generates repetitive volleys of piercing, paroxysmal pain that can last seconds or minutes and sometimes hours. It is almost always unilateral and typically occurs in the mandibular and maxillary divisions of the trigeminal nerve. TN1 can be triggered by everyday activities that stimulate the nerve, such as eating, speaking, or touching the face. Pain-free intervals range from several days to years, but typically the pain increases in frequency and severity over time.

TN1 is most often caused by vascular compression at the trigeminal nerve root. In rare cases, the nerve root may be compressed by a tumor, an aneurysm, or an arteriovenous malformation. Over time, demyelination of the nerve due to compression may generate random, spontaneous afferent discharges.

Sometimes misdiagnosed as dental pain, the pain in TN2 is distinguished by a throbbing, burning sensation that is constant rather than episodic. Some patients with TN2 report

Points to Remember

- Trigeminal neuralgia (TN) occurs in the distribution of the trigeminal nerve, is of sudden onset, and is excruciating. Its 2 subcategories—TN1 and TN2—have distinct etiologies and symptoms.
- TN can occur at any age but is most common after the age of 50 years, with a higher incidence rate in women than men. Its most distinguishing clinical feature is the nature of the pain.
- Mayo Clinic neurologists, neurosurgeons, and neuroradiologists are highly experienced in the diagnosis and management of TN, allowing an individualized approach to each patient's problem.

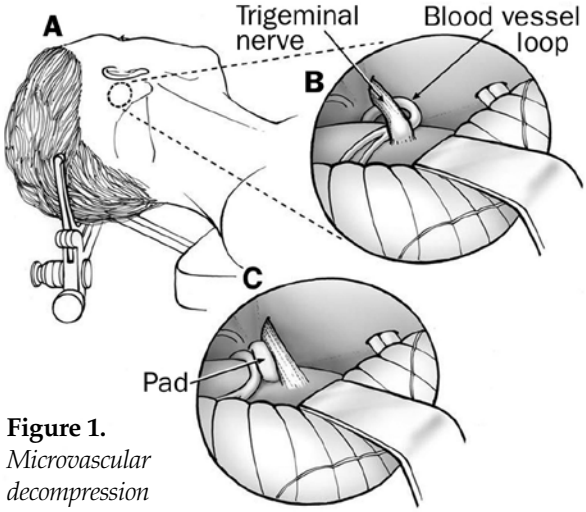

Figure 1. *Microvascular decompression for classic TN1.*
A, Illustration showing patient positioning and location of incision behind the ear. B, Magnified view of pertinent anatomy as seen through the operating microscope. C, Illustration of a completed microvascular decompression. Padding prevents the vascular loop from touching the trigeminal nerve.

the shooting pain of TN1 as occurring within a background of chronic dull pain.

TN2 can arise from various sources, including the following:

- Structural anomalies, such as tumors or arteriovenous malformations
- Inflammatory conditions, such as multiple sclerosis and herpes zoster
- Trigeminal nerve injury caused by stroke or dental procedures
- Deafferentation arising from intentional denervating procedures used to treat TN1 (eg, anesthesia dolorosa)

Although demyelinating disease and structural anomalies may be evident on high-resolution magnetic resonance imaging, neurovascular compression may not always be seen. For this reason, the clinical examination is critical in determining the best approach to treatment.

Management of TN and other types of neurologically based facial pain is best served by a team approach with close communication between neurologists and neurosurgeons.

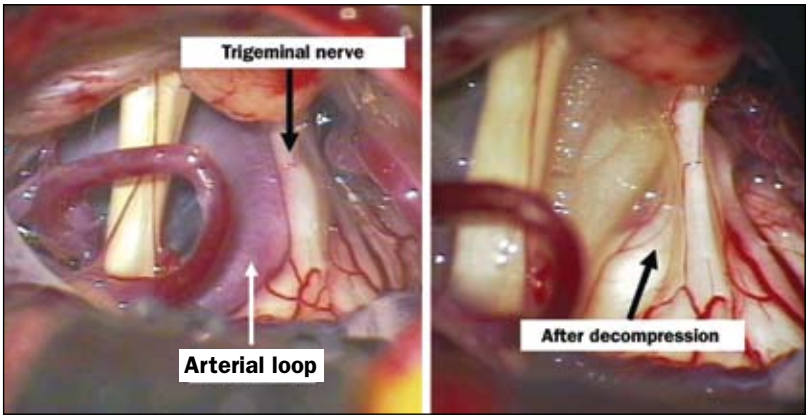

Figure 2. *Surgery directed at the site of microvascular compression. Trigeminal nerve and arterial loop (left panel) and the same area after surgical decompression (right panel).*

Treatment Options

Medical Management

In TN, the goal of pharmacologic intervention is to block or suppress painful trigeminal nerve discharges. TN1 does not respond well to analgesics but does to antiepileptic drugs such as carbamazepine, sometimes at lower doses than those used to treat epilepsy. Although initial pain control usually can be achieved within days to weeks, the effect may wear off. Incremental dosing helps prevent dose-dependent adverse effects that might discourage patients from continuing a pharmacologic approach when it could be of great benefit.

Surgical Management

Depending on the probable cause of TN, surgical options include microvascular decompression for classic TN1

(Figure 1) and percutaneous denervating procedures or stereotactic radiosurgery to block the pain signal. For cases of microvascular compression, surgery directed at the site of compression (Figure 2) can stop the pain immediately and have excellent long-term durability. One advantage of this approach is that it minimizes the risk for facial numbness, a complication associated with ablation techniques.

Percutaneous ablation techniques, such as balloon compression or the injection of an alcohol-like substance into the nerve (glycerol rhizotomy), are less invasive but also are less durable because the nerve may recover over time. Stereotactic radiosurgery, another ablative technique, is the least invasive surgical approach, with excellent outcomes. All ablative techniques intentionally damage the nerve and thus increase the patient's risk for facial numbness. Motor cortex stimulation is not used for TN1, but it has been found effective for selected cases of intractable trigeminal neuropathic pain arising from deafferentation or previous nerve injury in TN2.

Aspirin for Multiple Sclerosis–Related Fatigue

Fatigue is one of the most common and debilitating symptoms of multiple sclerosis (MS). It can affect concentration, muscle strength, and psychosocial well-being. The mechanisms are not understood and may differ among patients. Few medications are available, and even these may be ineffective for many patients.

Mayo Clinic neurologists advise that before prescribing medications, it is important to rule out common factors that may contribute to fatigue in MS patients such as depression, drug therapies, and problems that disturb sleep, including nocturia and sleep apnea. Current medications for MS-related fatigue include amantadine, modafinil, and other stimulants, but none of them addresses underlying fatigue mechanisms.

Ten years ago, Mayo Clinic neurologists noted that some patients taking moderately high doses of aspirin for coexisting conditions such as rheumatoid arthritis reported more energy and less fatigue. They also reported that with reduced doses of aspirin, fatigue worsened. For many years, researchers have postulated that since MS is an autoimmune disease, inflammation might be a key factor in the pathogenesis of MS-related fatigue. The well-understood anti-inflammatory mechanisms of aspirin may thus help researchers understand the relevant mechanisms in MS.

From this clinical observation, the Mayo team designed a pilot study of 30 patients. Fatigue levels were measured by patient self-report, and results showed aspirin was effective compared with a placebo. To replicate, expand, and further objectify their findings, the team is now conducting a larger study, funded by the National Multiple Sclerosis Society and carried out at all 3 Mayo Clinic sites.

Points to Remember

- Researchers have postulated that since multiple sclerosis (MS) is an autoimmune disease, inflammation might be a key factor in the pathogenesis of MS-related fatigue.
- Mayo Clinic neurologists have noted that some patients taking moderately high doses of aspirin for coexisting conditions such as rheumatoid arthritis reported more energy and less fatigue.
- After conducting a small pilot study, Mayo Clinic researchers are enrolling patients in a larger study funded by the National Multiple Sclerosis Society to determine the efficacy and magnitude of the effect of aspirin on MS-related fatigue.

Open Clinical Trial

The primary goal of the current study is to determine the efficacy and magnitude of the effect of aspirin on MS-related fatigue. A secondary goal is to more precisely quantify fatigue in order to develop objective measures of therapeutic

Mayo Clinic Clinical Trial on Aspirin for MS-Related Fatigue

Contacts and Additional Information

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Minnesota: Darcy Rauchwarter, RN, 507-284-9360

More information, including inclusion and exclusion criteria, is available at

http://clinicaltrials.mayo.edu/clinicaltrialdetails.cfm?trial_id=100795&title=ASA%20for%20MS

outcome. In addition to a standard self-report questionnaire, participants will be given cognitive tests of memory and concentration, blood tests to measure inflammation markers, and at the Arizona site, tests of muscle fatigue conducted in a biomechanics laboratory.

To participate, patients must be between 18 and 65 years old, have confirmed relapsing-remitting or secondary progressive MS, be ambulatory for a distance of at least 100 meters without assistance, have had persistent fatigue for 8 weeks not attributable to causes other than MS, and be able to complete cognitive testing and questionnaires. Exclusionary criteria include medical contraindications for aspirin, factors related to other causes of fatigue, and general health problems. Participants who meet enrollment criteria are placed in 1 of 3 groups and given a high dose (1,300 mg/day) or low dose (162 mg/day) of aspirin or a placebo over an 8-week course.

The Mayo research team hopes that in addition to the stated goals, the study will shed light on the role of inflammation in MS-related fatigue.

Transoral Robotic Surgery Broadens Oral Cancer Treatment Options

The Challenge

Oral cancer tends to affect otherwise healthy people in their 20s through 50s and is often in an advanced stage when diagnosed. Standard surgical approaches, chemotherapy, and radiation therapy are only moderately successful in treating oral cancer, and traditional surgery can involve splitting the jawbone open to fully access and remove malignancies. This approach is associated with a lengthy hospital stay, difficulty swallowing, impaired speech, and extended feeding via gastric tube.

A New Approach

Transoral robotic surgery is a recent development in minimally invasive surgical techniques and offers improved cure rates and fewer complications. During the procedure, an assistant is positioned at the patient's head to provide suction or traction or other support. The surgeon manipulates controls inside a workstation

Points to Remember

- Transoral robotic surgery is emerging as a less invasive surgical alternative for treatment of selected patients with oral cancers.
- The robotic system provides 3-dimensional imaging and articulated instruments that enhance a surgeon's precision when navigating challenging anatomy.
- Mayo Clinic surgeons have performed more than 100 procedures using the transoral robotic approach to treat cancers of the tonsil, palate, base of tongue, throat, and pharynx.

Figure 1. *While looking though binoculars equipped with a high-resolution 3-D stereoscopic imaging system, the surgeon manipulates controls that guide robotic endoscopic instruments docked at the operating table.*

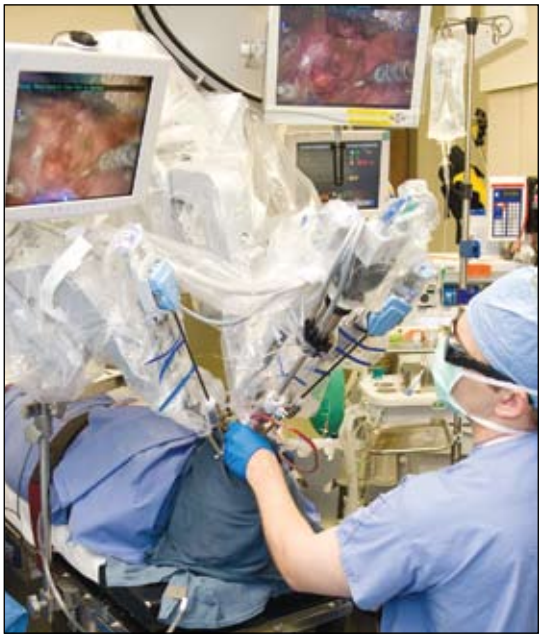

Figure 2. *At Mayo Clinic, surgeons now use the robotic system to remove tumors from the tonsil, palate, base of the tongue, throat, and pharynx that are hard to access with other modalities.*

console several feet from the operating table while looking though binoculars equipped with a high-resolution 3-D stereoscopic imaging system. These controls guide robotic instruments, including graspers and cautery instruments, docked at the operating table.

Surgical robots help overcome some of the challenges associated with conventional surgical procedures by allowing surgeons to operate with more precision and flexibility. The master controls at the surgeon's console relay the exact movements of the surgeon's hands and fingers to the instruments and filter out any hand tremor. The surgical instruments are equipped with articulating tips and wrist mobility that improve precision. This sensitivity enhances a surgeon's ability to navigate challenging anatomy, to deftly perform microresection, and to precisely place sutures.

Surgical Indications and Benefits

When performed by experienced high-volume surgeons, the robotic approach provides an effective option for a wide range of patients. At Mayo Clinic, surgeons now use the robotic system to remove tumors from the tonsil, palate, base of the tongue, throat, and pharynx that are hard to access with other modalities.

A dedicated team of Mayo Clinic surgeons has developed a surgical technique using the robotic system. In 2009, Mayo surgeons studied a group of 45 patients with tonsil and base of tongue cancers to evaluate the safety and efficacy of the transoral robotic approach. Study participants included 26 patients who had base of tongue primary tumors and 19 patients who had tonsillar fossa tumors, all of whom underwent surgery using the robotic approach. Mayo researchers recorded data on surgical time, blood loss, surgical complications, tracheostomy tubes, feeding tubes and resumption of oral diet, speech, swallowing, and tumor recurrence.

No major complications occurred, and no procedure was stopped due to inability to remove the tumor. The average hospital stay for these 45 patients was 2.3 days, while patients undergoing traditional oral surgery for the same diagnosis typically require 7 to 10 days in the hospital. Additionally, the removal of feeding tubes in patients undergoing robotic surgery occurred an average of 7 to 10 days after surgery, while patients undergoing traditional surgery typically require 2 to 3 months of feeding tube use.

Mayo Clinic surgeons have now performed more than 100 transoral robotic surgeries and have adopted this as their technique of choice for patients with tumors of the tonsil and base of tongue. They are also exploring the use of the robotic approach for the removal of voice box polyps and tumors in the larynx and other regions difficult to access through the mouth and for the treatment of obstructive sleep apnea and Zenker diverticulum.

Pain Medicine: A State-of-the-Art Course in Pain Management for the Non-Pain Specialist

February 28-March 4, 2011

Koloa, Kauai, Hawaii

Multidisciplinary course that will target the integration of pain services across disciplines to address the national and international movement toward improved pain control in acute, chronic, and cancer pain populations. This course also provides an update on critical issues in the management of chronic pain. Contact: 800-323-2688.

7th Annual Women's Health Update

March 10-12, 2011

Scottsdale, Arizona

This course consists of 3 half-days with afternoon workshops and focuses on reviewing the latest medical updates pertinent to women's health care. The intended audience includes primary care physicians, general internists, gynecologists, and specialists in preventive medicine. Participants gain comprehensive insight into recent initiatives, as well as a basic approach to addressing and improving common health concerns for women. Contact: 480-301-4580.

Clinical Reviews—A Family Medicine and Internal Medicine Update

March 23-26, 2011

Scottsdale, Arizona

Clinical Reviews: A Family Practice and Internal Medicine Update provides a comprehensive review of the most important advances recently made in internal and family medicine. The emphasis is on progress and management strategies made in major subspecialties, which include gastroenterology, endocrinology, neurology, pulmonology, and cardiology. An audience response system is used. Contact: 480-301-4580.

32nd Annual Practice of Internal Medicine

May 2-6, 2011

Rochester, Minnesota

This postgraduate course provides general internists, internist-subspecialists, family medicine physicians, and other primary care professionals with a state-of-the-art update in internal medicine. Topics represent some of the most commonly encountered problems in clinical practice. Contact: 800-323-2688.

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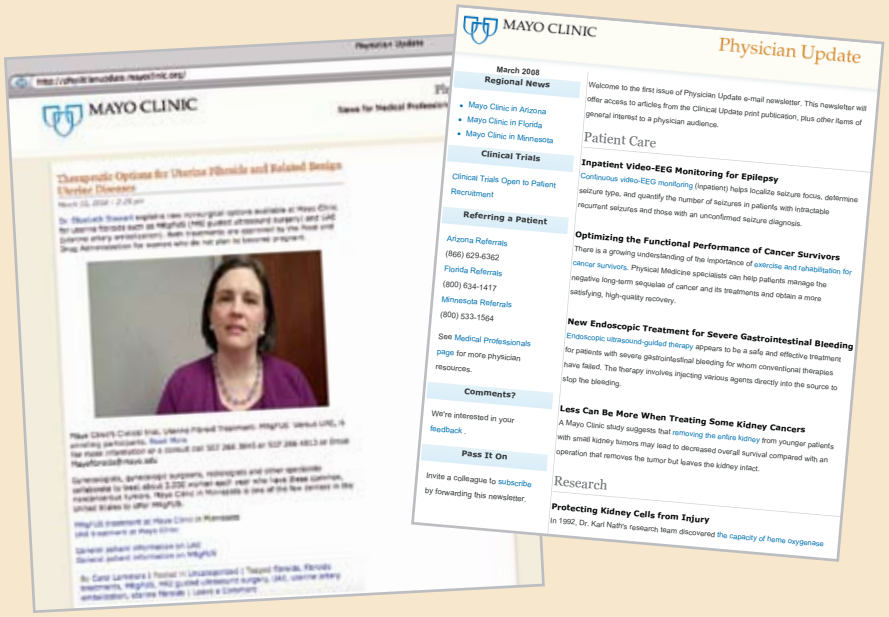

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