MAYO CLINIC

CARDIOVASCULAR UPDATE

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Endovascular Stent Graft Repair of Thoracic Aortic

Kevin L. Greason, MD

Thoracic aortic aneurysm is a life-threatening condition that causes considerable short- and long-term mortality because of the potential for both rupture and dissection. The natural history of thoracic aortic aneurysm is incompletely understood, and the prevalence is increasing as the population ages. In fact, aneurysms affect an estimated 6 patients per 100,000 persons per year, an estimated 21,000 patients yearly in the United States. Unfortunately, these patients frequently have comorbid conditions such as chronic obstructive pulmonary disease, coronary artery disease, or renal insufficiency that can complicate standard open operative repair.

Despite advances in anesthetic, surgical, and critical care practices and technologies, open thoracic aortic surgery is still associated with severe pain and extensive morbidity and mortality. A new technology has emerged in the management of thoracic aortic aneurysm previously treated only with open surgery—the endovascular stent graft. Successful stent graft treatment of a descending thoracic aortic aneurysm has the potential to avoid the deleterious effects of a thoracotomy, aortic cross-clamp placement, and major blood loss.

Open repair of a thoracic aortic aneurysm classically involves induction of general anesthesia and thoracotomy. The patient is placed on left-heart bypass, the aorta is clamped above and below the aneurysm, and the abnormal segment of aorta is replaced with an artificial graft. The average intensive care unit stay is about 5 days, with a total hospital stay of 14 days.

The major perioperative complications associated with open surgical replacement of the descending thoracic aorta include lower extremity paralysis, stroke, and death. In the hands of well-trained and experienced surgeons, an average lower extremity paralysis rate of 3.4%, stroke rate of 2.7%, and mortality rate of 4.8% can be expected for an open surgical procedure today. Estimates of 5- and 10-year survival are 60% and 38%, respectively. In addition, recovery from a thoracotomy can be difficult; postoperative symptoms of fatigue, dyspnea, and pain can persist for several months in some patients.

Endovascular stent graft placement for treatment of a thoracic aortic aneurysm is usually performed with the patient under general anesthesia but can be accomplished with regional or managed anesthetic care with local anesthesia. Following percutaneous puncture of the femoral artery, a guidewire is passed across the dilated portion of the aorta, and the stent graft is advanced over the wire. Once adequate position of the stent graft has been achieved, the constraining device around the stent graft is released and the graft is expanded to exclude the aneurysm (Figure). The delivery device is removed from the femoral artery, which can be repaired using a percutaneous suture device. The average intensive care unit stay is about 3 days with a total hospital stay of 7 days.

Perioperative major morbidity and mortality are not notably less with endovascular stent graft placement than with open thoracotomy repair. Reported outcomes after endovascular stent graft repair include an average lower extremity paralysis rate of 1.5%, stroke rate of 2.9%, and mortality rate of 5.7%. The 5-year survival estimate is 68%. Because endovascular stent graft repair is a relatively new technology, 10-year survival data are not readily available. However, all-cause 5-year survival is similar between endovascular and open surgical repair.

Despite reasonably low neurologic morbidity and mortality rates, endovascular and open repair are not otherwise equal because some complications do occur with endovascular stent graft repair that are specific to the technique. Not uncommonly, vascular access injury occurs in 14% of patients and can result in extensive associated morbidity and mortality. Endoleaks—when blood perfuses between the stent graft and the native aorta—are reported in 10% to 20% of patients. As long as the endograft is present, it is at risk to develop endoleak, and more than 70% of such leaks occur in a location that puts the aneurysm at risk of rupture. Other less common complications include stent graft migration, stent fracture, and infection.

Endovascular stent graft repair is less invasive than the open surgical technique, intensive care unit and hospital stays are shorter, a higher percentage of patients are discharged to home rather than to nursing homes, and

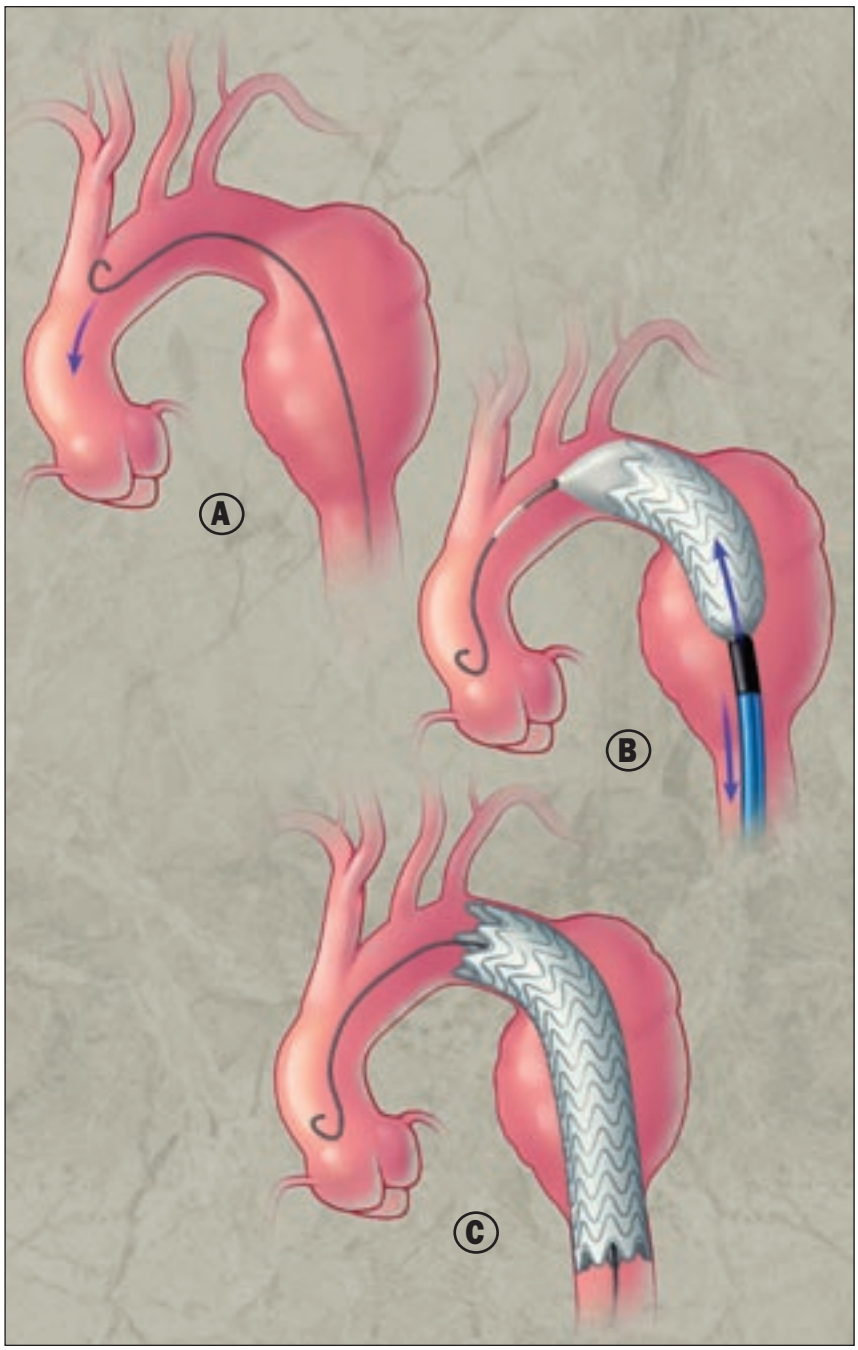

Figure. Stent Placement. A, Advancement of guidewire past descending aortic aneurysm. B, Stent-mounted balloon is advanced over guidewire and positioned so that, when deployed, the stent completely covers the aneurysm. C, The proximal and distal portions of the deployed endovascular stent extend beyond the aneurysm to unaffected segments of the aorta.

patients have a faster return to normal level of function. The perceived advantages of the less invasive stent graft placement are such that it is rapidly being applied to other aspects of thoracic aortic disease to include acute descending thoracic aortic dissection and traumatic aortic rupture.

In up to 10% of patients presenting with acute dissection of the descending thoracic aorta, a complication develops related to the dissection such as rupture of the aorta or malperfusion of a branch vessel (ie, mesenteric, renal, or extremity vessel). These patients have more than 50% likelihood of dying and require emergency treatment. Unfortunately, open operation is associated with extreme morbidity and mortality. Reported outcomes include a spinal cord ischemia rate of 7%, stroke rate of 7%, and mortality rate of 22%. Additional complications include vocal cord paralysis rate of 40%, pulmonary morbidity rate of 14%, and cardiac morbidity rate of 43%.

Endovascular stent graft repair offers the relatively recent ability to simply cover the primary tear site and to restore blood flow down the true lumen of the aorta, thus relieving the body of malperfusion and preventing rupture without the insult of open thoracotomy. Initial reports are promising, with a reduced mortality rate of 11%. Unfortunately, morbidity remains high, with a reported spinal cord ischemia rate of 7%. Emergency stent graft repair for patients with life-threatening complications of acute descending thoracic aortic dissection may save many lives, and this could well become the most clinically valuable application of thoracic aortic stent graft techniques in the future.

Emergency open surgical repair of traumatic aortic rupture of the proximal descending thoracic aorta is associated with substantial morbidity and mortality. Reported outcomes include a spinal cord ischemia rate of 7% and mortality rate of 21%. Endovascular repair confers advantages in perioperative morbidity and mortality over traditional open repair, with some centers reporting no spinal cord ischemia or mortality. Unfortunately, the current technology of endovascular stent graft placement is not applicable to all affected patients.

Traumatic aortic rupture often occurs in young patients who, by nature, have a smaller diameter aorta with more acute angulation of the aortic arch than older patients who present with degenerative thoracic aneurysm or dissection. These 2 findings can make safe placement of the endograft difficult. Catastrophic endovascular collapse can occur, resulting in acute aortic coarctation syndrome and death. It must also be kept in mind that stent grafts have been designed to have a durability of 10 years. Long-term durability is unknown. The consequences of placing a stent graft in a young person who has not reached full maturity or someone with a life expectancy of more than 10 years are not known.

Endovascular stent graft repair represents an exciting new technology in the treatment of many descending thoracic aortic diseases. It offers a less invasive treatment option than open thoracotomy, with relatively equal morbidity and mortality rates for aneurysm repair. There may be more benefit in the treatment of acute dissection and aortic rupture. Ultimately, the decision to offer a patient with descending thoracic aorta aneurysm, dissection, or rupture either open or endovascular repair must balance the patient's expected prognosis and life expectancy against the risk of undergoing the procedure.

National Marfan Foundation Conference Comes to Mayo Clinic Rochester

Heidi M. Connolly, MD

The National Marfan Foundation (NMF) is a nonprofit patient advocacy organization founded by individuals with Marfan syndrome and their loved ones, with the strong support of the medical community. The organization is dedicated to saving lives and improving the quality of life for individuals and families affected by Marfan syndrome and related disorders. Each year the NMF conducts a unique educational conference bringing together patients, family, and health care providers. This year the NMF will celebrate its 25th anniversary during its meeting August 6-9, 2009, at Mayo Clinic in Rochester, Minnesota.

Expected are approximately 500 attendees, including patients, their families, and health care providers with special interest in the Marfan syndrome and related disorders. "Patients will be offered clinical evaluations as well as formal and informal educational sessions by world-renowned doctors and researchers," according to Heidi M. Connolly, MD, codirector of the Marfan and Thoracic Aortic Clinic at Mayo Clinic Rochester. "Children and teens with Marfan syndrome or related disorders will enjoy a fun-filled and educational weekend while sharing experiences with others in the supportive environment of the NMF conferences."

Each year an important component of the annual NMF meeting is the Marfan clinic day. During this clinic, about 60 patients (prescreened by the NMF) with suspected or confirmed Marfan syndrome will have about 180 consults (adult and pediatric cardiology, genetics, ophthalmology, orthopedics, pulmonary, pain, dental, obstetrics, internal medicine, cardiac surgery, and vascular surgery). External national and international experts volunteer their time and will be seeing these patients in conjunction with Mayo staff.

Health care providers will have an opportunity to interact with these same experts informally in addition to a formal CME program. Because Marfan syndrome is an uncommon condition in most physicians' practices, equally valuable may be the opportunity to meet and interact with the patients and their families. It is perhaps this aspect more than any other that makes the annual NMF meeting unique.

More information about the NMF and the 2009 NMF conference can be obtained at http://www.marfan.org/nmf or by writing Marfan2009@mayo.edu.

UNDER THE STETHOSCOPE

by Clarence Shub, MD

Physical Findings in Thoracic Aortic Dissection

- The correct diagnosis of acute aortic dissection can be elusive, especially in elderly patients and in patients with atypical or subtle manifestations. It may be misdiagnosed as acute myocardial infarction, stroke, acute peripheral arterial occlusion, and even various acute abdominal conditions.
- In the presence of chest, back, and/or abdominal pain, an aortic diastolic murmur suggests dissection involving the ascending aorta. If such a patient presents emergently, an appropriate diagnostic test should be obtained as soon as possible.
- Even though patients with acute aortic dissection may appear pale and sweaty, as if in shock, approximately 70% of patients have elevated blood pressure, which is the most common physical finding in patients with acute aortic dissection.
- Reduced or absent arterial pulses in 1 or more extremities may be noted, and at times, severe ischemia of an extremity may occur.

Amiodarone, the Thyroid, and Amiodarone Thyrotoxicity

Michael D. Brennan, MD, and Yong-Mei Cha, MD

Amiodarone was introduced in Europe in the late 1960s and in the United States more than a decade later for the management of refractory atrial and ventricular arrhythmias. Michael D. Brennan, MD, of the Division of Endocrinology, Diabetes, Metabolism, and Nutrition at Mayo Clinic in Rochester, explains: "It is a heavily iodinated compound—a 200-mg tablet contains 75 mg of iodine—10% of which is liberated as free iodide daily, resulting in tremendous expansion of the iodine pool. Amiodarone is very lipophilic, which accounts for its extremely long biologic half-life—measured in months." Although it is an effective antiarrhythmic agent, its use carries serious potential adverse effects, including pulmonary toxicity, liver dysfunction, and neuropathy. Amiodarone also has a number of effects on thyroid hormone economy and metabolism, as well as direct effects on the thyroid gland.

Some predictable effects of amiodarone treatment include the following:

- Increased thyroid gland iodine content and a histologic appearance of abundant colloid and flattened follicular epithelium.
- Inhibition of type 1 deiodinase in the liver, muscles, and other tissues, resulting in a 10% increase in serum free thyroxine (T_4), a 60% decrease in serum triiodothyronine (T_3), and a 150% increase in serum reverse T_3.
- Inhibition of type 2 deiodinase in the pituitary gland, resulting in a modest increase in serum thyrotropin (TSH). However, in the absence of underlying autoimmune thyroid disease, TSH concentration usually remains within the normal range.
- A 30-fold increase in urinary iodine excretion, a 50-fold increase in plasma inorganic iodide concentration, and a decreased thyroid uptake of administered radioactive iodine (^{131}I).
- Patients treated with amiodarone are at risk for development of either hypothyroidism or hyperthyroidism—both of which have serious implications among patients with underlying cardiac disease. The onset of both conditions is unpredictable. Screening for certain identified predisposing risk factors for thyroid disease should be done before initiation of therapy with amiodarone (Table 1).

Amiodarone-Induced Hyperthyroidism

Two types of amiodarone-induced hyperthyroidism (AIT)—referred to as type I and type II—have been identified. The incidence of AIT is higher in Europe (15%) than in more iodine-replete regions of the world, such as North America (3%). "It is important to distinguish between AIT type I and type II, because management options may differ," says Dr Brennan. AIT type I occurs among patients with preexisting nodular goiter and frequently in areas of relative or absolute iodine deficiency. The nodules of such thyroid glands lose the ability to autoregulate the amount of iodine that is trapped, organified, and incorporated into thyroid hormone. Thus, patients should be assessed for the presence of nodular goiter before amiodarone administration. The presence of a goiter is not of itself a contraindication to the administration of amiodarone, but careful monitoring of thyroid function is essential, particularly during the early weeks and months of therapy.

AIT type II occurs abruptly and without warning in patients who do not have recognizable preexisting thyroid disease. The onset may occur months or even years after initiation of amiodarone therapy; the average interval is 12 months. Weight loss, muscle weak-

TABLE 1
Checklist for the Clinician Before Initiation of Amiodarone Therapy

- Medical history: discuss any history of thyroid disease
- Physical examination: thyroid palpation (eg, size, consistency, nodules)
- Blood tests: TSH, thyrotropin, thyroperoxidase antibodies, free thyroxine

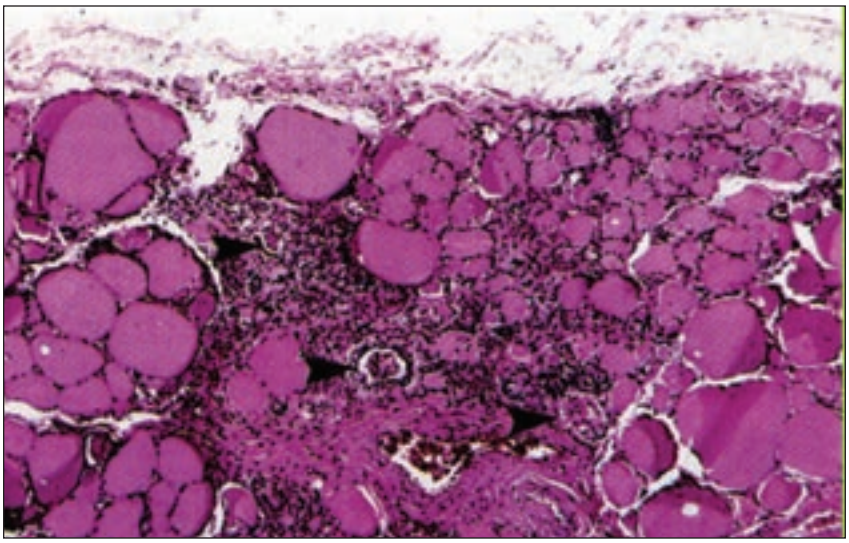

Figure. The pathology of the thyroid in amiodarone hyperthyroidism includes involution of thyroid follicles consistent with a high iodine intake with zones of follicular disruption.

ness, and the reemergence of cardiac arrhythmias are the most frequent symptoms. In these cases, the thyroid gland is nontender and may be mildly enlarged. Laboratory testing shows decreased serum TSH concentration and increased concentrations of total T_4 and free T_4. Thyroid ultrasound in patients with AIT type II shows decreased or absent vascularity, whereas patients with AIT type I typically exhibit thyroid nodules and increased thyroid vascularity (Figure).

The management of AIT is challenging because treatment options are limited by the marked drug-induced expansion of the iodine pool, resulting in ^{131}I uptake of 1% to 2%—levels that preclude its use in therapy for most but not all patients. In addition, antithyroid drugs (eg, thioamides) are less effective in states of high thyroid iodine content. Potassium perchlorate may hasten recovery in some patients, but it is now difficult to obtain. Antithyroid drugs are more effective in AIT type I than in AIT type II and, if used, require relatively high doses. Glucocorticoids are usually rapidly effective but must be used with caution in patients with cardiac decomposition. Thyroidectomy rapidly reverses hyperthyroidism and has been adopted successfully in selected cases.

Amiodarone-Induced Hypothyroidism

In contrast to AIT, the prevalence of hypothyroidism among amiodarone-treated patients is higher in iodine-replete regions, such as North America. Preexisting autoimmune thyroid disease—such as Hashimoto thyroiditis—is a recognized risk factor because the thyroid glands of such patients have an impaired autoregulatory capability. It is prudent, therefore, to screen for the presence of thyroperoxidase antibodies, in addition to serum TSH, before starting amiodarone treatment (Table 1). If thyroperoxidase antibodies are present, close monitoring for evidence of hypothyroidism is recommended. Amiodarone-associated thyroid failure is treated in a manner similar to treatment of other forms of hypothyroidism, although slightly higher serum TSH values may be expected and tolerated while taking levothyroxine therapy.

Despite its serious potential adverse effects, amiodarone is a valuable antiarrhythmic drug. "From a cardiac standpoint, it is the safest and most effective drug for many patients," says Yong-Mei Cha, MD, an electrophysiologist at Mayo Clinic in Rochester. "Its efficacy in the treatment of atrial and ventricular arrhythmias, its minimal proarrhythmic effect especially in patients with severe ventricular dysfunction, and the limited number of antiarrhythmic drugs available make amiodarone an important tool in the pharmacologic treatment of many arrhythmias." When starting patients on amiodarone, it is important that they understand all the potential adverse effects of the drug and the importance of following monitoring recommendations (Table 2). "Thyroid function abnormalities are among the most frequent adverse effects we see in patients taking amiodarone," says Dr Cha. "Close collaboration between the cardiologist and the endocrinologist is key to the optimal management of these patients."

TABLE 2
Recommended Monitoring of Patients on Amiodarone

- Liver function and thyroid function tests: baseline and semiannually
- Chest x-ray and ECG: baseline and annually
- Ophthalmologic examination and pulmonary function tests: baseline and if suggestive symptoms develop

Cardiovascular Innovations

Dear Colleagues:

In this issue of Cardiovascular Update, *we launch a new feature, "Cardiovascular Innovations." Innovation has been an increasingly important and productive endeavor for the cardiovascular diseases and cardiovascular surgery divisions at Mayo Clinic Rochester. This section will feature new ideas intended to impact clinical patient care, including new devices, biological molecules, and methods of health care delivery and risk assessment—ideas that may lead to health care solutions where none currently exists.*

At present more than 90 innovation projects are under way, at various stages of development, from concept to bedside. In this column, we will share ongoing developments in our quest to revolutionize medical care for our patients.

Samuel J. Asirvatham, MD

Vice Chair for Innovation
Cardiology and Therapeutic Area Team Leader
Research Translation Program
Division of Cardiovascular Diseases
Mayo Clinic Rochester

Reducing Stroke Incidence by Ligating the Left Atrial Appendage

Background

The left atrial appendage is a common site for left atrial thrombus formation and subsequent stroke in patients with atrial fibrillation. On the basis of transesophageal echocardiographic (TEE) studies, it has been estimated that more than 95% of thromboembolisms in patients with atrial fibrillation arise from this structure. Given the widespread prevalence of atrial fibrillation, this thrombus formation is expected to afflict 16 million patients by 2050. The best established therapy for preventing thromboembolism has been warfarin, which has been proven to reduce stroke risk in patients eligible for anticoagulation. Multiple problems with warfarin therapy, including frequent blood draws, bleeding risk, and drug-dietary interactions, result in its underutilization.

Because of these difficulties, new strategies have been directed at preventing left atrial appendage thrombus by excluding this structure from the circulation. These tactics include surgical exclusion; however, because of the morbidity associated with invasive surgical procedures, percutaneous approaches have been the focus of recent innovation. Placement close to the ostium of

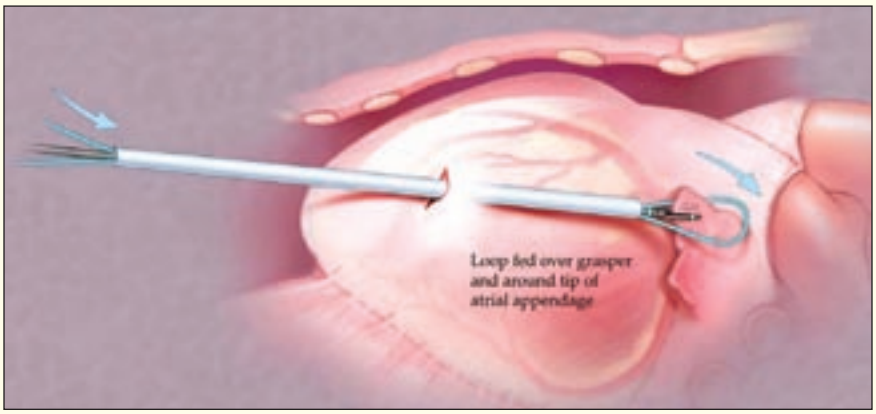

Figure 1. Pericardial access with sheath placement. Through the sheath, the electrogram-directed grabber is advanced to stabilize the left atrial appendage. Over this, a loop that converts to a ligature at the base of the appendage is advanced.

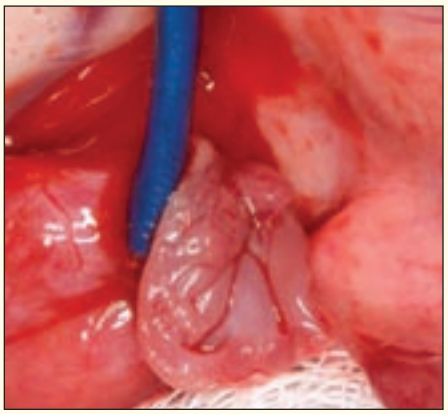

Figure 2. Following closed-chest pericardial placement of the ligature, the chest was opened to reveal successful placement of the ligature at the appendage base.

the left atrial appendage of a self-expanding nitinol cage with a permeable fabric covering as well as epicardial approaches without thoracotomy are being evaluated. An ideal approach, perhaps, is closure of the atrial appendage at the level of the ostium without exposure of any portion of the device to the left-sided circulation.

Paul A. Friedman, MD
Samuel J. Asirvatham, MD
Charles J. Bruce, MD

The Invention

Mayo Clinic Rochester cardiologists Paul A. Friedman, MD, Charles J. Bruce, MD, and Samuel J. Asirvatham, MD, have developed a system that involves ligation of the left atrial appendage via a percutaneous subxiphoid approach using a novel hollow suture concept. With the aid of local electrograms and fluoroscopy, the appendage is grabbed with an electrode-containing device. The ligator is then placed over the appendage and the hollow suture is tightened (Figure 1), with TEE documentation of adequate appendage closure.

Experimental Results

In 4 live acute closed-chest canine experiments, the device successfully ligated the left atrial appendage. In this initial proof of concept study, there was no evidence of trauma to the left atrial appendage or pericardium (Figure 2).

In these experiments, TEE and fluoroscopic visualization were used to ensure closure of the appendage ostium when the ligature was applied. Additional parameters included the loss of atrial electrograms measured by the electrical mapping plant when closure was achieved. The investigators are continuing to evaluate the system in closed-chest long-term survival experiments.

Potential Application and Impact of Innovation

If further validated with long-term animal and subsequent human data, this minimally invasive percutaneous epicardial approach to ligate the left atrial appendage may eliminate or decrease the risk of thromboembolism in patients with atrial fibrillation. Further, this may be done without having an endovascular structure in the left-sided circulation.

Upcoming Courses

Continuing Medical Education, Mayo Clinic

To request additional information or to register, unless noted otherwise, please call 800-323-2688, e-mail cme@mayo.edu, or visit www.mayo.edu/cme.

19th Annual Advances and Controversies in Clinical Nutrition
Apr 17-19, 2009, Amelia Island, FL
Phone: 800-462-9633; e-mail: cme-jax@mayo.edu

Topics in Complementary and Alternative Medicine: Evidence-Based Information for Your Practice
Apr 23-25, 2009, Scottsdale, AZ

Controversies in Cardiovascular Disease
May 2-3, 2009, Saint Paul, MN

30th Annual Practice of Internal Medicine
May 4-8, 2009, Rochester, MN

Controversies in Women's Health
Jun 18-20, 2009, Wisconsin Dells, WI

Mayo Clinic International Vascular Symposium
Jun 27-30, 2009, Budapest, Hungary

Putting Prevention Into Practice: Individualized Approach to Preventing Cardiovascular Disease
Jun 29-Jul 1, 2009, La Jolla, CA
Phone: 800-283-6296; e-mail: cvcme@mayo.edu

Success With Failure: New Strategies for the Evaluation and Treatment of Congestive Heart Failure
Aug 9-12, 2009, Whistler, BC
Phone: 800-283-6296; e-mail: cvcme@mayo.edu

Mayo Echocardiography Review Course for Boards and Recertification
Aug 22-25, 2009, Rochester, MN

Pulmonary Hypertension Update 2009
Aug 29, 2009, Jacksonville, FL
Phone: 800-462-9633; e-mail: cme-jax@mayo.edu

Cerebrovascular Course
Sep 10-12, 2009, Amelia Island, FL
Phone: 800-462-9633; e-mail: cme-jax@mayo.edu

Self-Study CME

Mayo Clinic's 2008 Review Courses

(Interventional Cardiology, Electrophysiology, and Echocardiography)

Available on DVD at http://www.mayo.edu/cme/self-study.html

RECOGNITION

Donald B. Hunninghake, MD (right), from the University of Minnesota, delivered the Third Annual Gerald T. Gau Lecture. Dr Gau is on the left.

Mayo Interventional Cardiology Board Review
Oct 2-4, 2009, Rochester, MN

Mayo Cardiovascular Review Course for Cardiology Boards and Recertification
Oct 3-8, 2009, Rochester, MN

Electrophysiology Review for Boards and Recertification
Oct 7-11, 2009, Rochester, MN

Continuing Medical Education, Cosponsored With American Society of Echocardiology

To request additional information or to register, unless noted otherwise, please phone 507-266-6703 or e-mail echocme@mayo.edu.

Echocardiography in the Nation's Capital: Focus for the Physician
Apr 27-29, 2009, Falls Church, VA

Echocardiography in the Nation's Capital: Focus for the Sonographer
Apr 30-May 2, 2009, Falls Church, VA

2009 Echo Fiesta: An In-Depth Review of Adult Echocardiography for Sonographers and Physicians
May 7-9, 2009, San Antonio, TX

17th Annual Echocardiography for the Sonographer 2009
Sep 20-22, 2009, Rochester, MN

19th Annual Cases in Echocardiography: TEE, Doppler and Stress—Interpretation and Clinical Decision Making for the Advanced Echocardiographer
Oct 28-31, 2009, Napa, CA

Other Education Opportunities

6th Annual Team Echocardiography: The Heart of Cardiovascular Medicine
Apr 23-26, 2009, Hilton Head Island, SC
Phone: 336-716-4505; e-mail: cmu@wfubmc.edu

20th Annual ASE Scientific Sessions: Special Emphasis on Cardiovascular Ultrasound Core Curriculum
Jun 6-10, 2009, Washington DC
Web: www.aseecho.org

25th Annual National Conference on Marfan Syndrome and Related Disorders
Aug 6-9, 2009, Rochester, MN
Phone: 800-8-MARFAN; e-mail: marfan2009@mayo.edu; Web: www.marfan.org

Mayo Clinic Cardiovascular Update

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