MAYO CLINIC

ClinicalUpdate

Current Trends in the Practice of Medicine

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Update on Transcatheter Aortic Valve Replacement

Approximately a third of individuals with symptomatic aortic stenosis are not candidates for open surgical replacement because of advanced age, the presence of comorbid conditions, or both. Transcatheter aortic valve replacement (TAVR) has been available as an option for select patients since 2008. The many developments in the past year related to TAVR include publication of 2-year outcome data of the Placement of Aortic Transcatheter Valve (PARTNER) trial cohorts and approval by the US Food and Drug Administration (FDA) of the Edwards Sapien prosthetic aortic valve for inoperable patients. The development of paravalvular aortic valve regurgitation is a new concern that has been identified in patients receiving these valves (Figure).

On November 2, 2011, the FDA approved the Sapien valve for patients with senile aortic valve stenosis, but use is restricted to those whose condition is considered inoperable by conventional standards for severe, symptomatic aortic stenosis. The FDA approved the valve for all transarterial avenues, and in general, suitable vascular access can be identified in almost all patients.

In the PARTNER trial, 699 patients in cohort A were randomly assigned to TAVR (348 patients) or standard operative valve replacement (351 patients). Of the TAVR patients, those with inadequate peripheral vascular access had transaortic valve replacement (104 patients). The 2-year survival data of high-risk patients (ie, those who were otherwise operable) in the PARTNER trial, published in the May 3, 2012, issue of *New England Journal of Medicine*, support TAVR as an alternative to surgery in high-risk patients. Mortality from any cause was similar in the TAVR and standard aortic valve replacement groups (P=.41). At 2 years, mortality was 34% in the transcatheter group and 35% in the standard surgery group (P=.78).

Encouragingly, the risk of stroke associated with TAVR appears to level off after the initial spike associated with valve replacement. The original PARTNER high-risk TAVR cohort experienced an increased rate of stroke at 30 days compared with patients treated with standard aortic valve replacement (5.5% vs 2.4%; P=.04), and this difference persisted at 1 year (8.3% vs 4.3%; P=.04). At 2-year follow-up, however, the frequency of all strokes did not differ signifi-

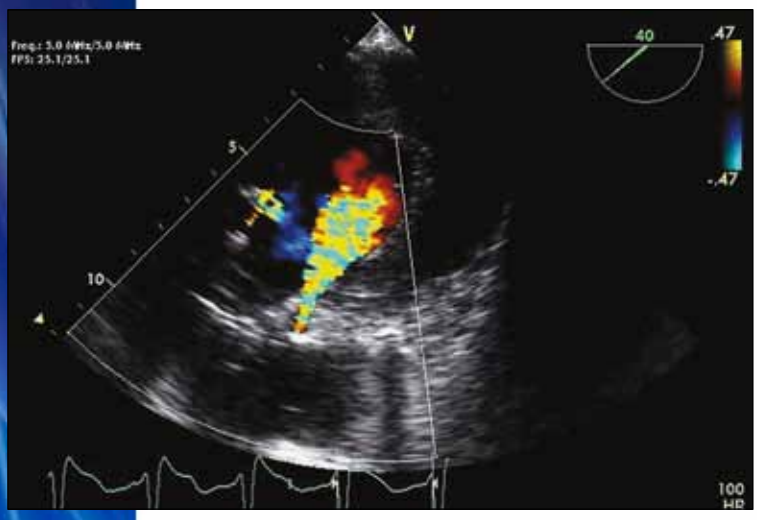

Figure. *Transesophageal echocardiographic image demonstrating paravalvular regurgitation in a patient who received a transcatheter prosthetic aortic valve.*

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.
- Transcatheter aortic valve replacement (TAVR) involves placement of a balloon expandable cardiac valve via a transfemoral, a transaortic, or a transapical route, usually without the need for cardiopulmonary bypass. The Placement of Aortic Transcatheter Valve (PARTNER) trial documented patient outcomes associated with TAVR.
- The 2-year survival data of high-risk patients in the PARTNER trial support TAVR as an alternative to standard aortic valve replacement in high-risk patients. PARTNER trial data also show that paravalvular regurgitation has emerged as a major concern associated with TAVR.

cantly between the 2 groups (P=.52). It appears that the constant hazard of late stroke is unrelated to the mode of valve replacement. Current efforts are directed at reducing the perioperative risk of stroke (ie, with use of embolic protection devices), thereby making the procedure safer. Earlier this year, a procedural stroke incidence of only 2% was reported in the PARTNER 1A transapical continuing access registry.

According to Mayo Clinic interventional cardiologists participating in the PARTNER trial, paravalvular regurgitation has emerged as a major concern associated with TAVR. The first reports of this procedure acknowledged that approximately 77% of patients had some degree of paravalvular regurgitation at 30 days. Recent data indicate that at 2-year follow-up, paravalvular regurgitation was unchanged in 46% and worse in 22%. Importantly, the presence of paravalvular aortic valve regurgitation was associated with increased late mortality (P<.001). The effect of aortic valve regurgitation on mortality was proportional to the severity of the regurgitation, but even mild aortic valve regurgitation was associated with an increased rate of late deaths.

According to Mayo Clinic cardiovascular surgeons participating in the PARTNER trial, it is unclear whether paravalvular aortic valve regurgitation causes late mortality or is simply associated with other causative factors. There are 3 reasons why paravalvular aortic valve regurgitation develops after TAVR: 1) asymmetric or excessive calcification of the aortic valve annulus; 2) improper assessment of the aortic valve annulus size; and/or 3) valve design. Mayo Clinic investigators are evaluating the first 2 causes with 3-dimensional transesophageal echocardiography and multidetector computed tomography. A better understanding of the dynamic, 3-dimensional structure of the aortic valve annulus throughout the cardiac cycle and how it relates to the emergence of paravalvular regurgitation may improve patient selection.

Mayo Clinic specialists also note that it is likely that not all patients will have the right valve or annulus size to safely undergo transcatheter valve replacement. Technological advances in the current generation of valve prostheses may better address the problem. As much as the transcatheter technology has enhanced patient care, more important is the creation of the multidisciplinary heart team to deliver the technology. Cardiologists and cardiac surgeons have combined their talents with remarkable results. When patients are evaluated by the team, the best technology, the best access, and the best technique for aortic valve replacement are identified for the individual patient.

Update on Holmium Laser Enucleation of the Prostate: Faster Relief and Maximum Benefit for Patients With Benign Prostatic Hyperplasia

The Challenge

For decades, transurethral resection of the prostate (TURP) has been the gold standard surgical treatment for BPH. However, depending on surgeon experience, up to 25% of patients may experience some type of complication after TURP, including bleeding, hyponatremia, urinary incontinence, and erectile dysfunction. TURP also subjects patients to risks inherent in any surgical procedure, as well as a hospital stay of 1 to 4 days and recovery time of 4 to 6 weeks.

Although laser ablation can provide swift symptom relief and quick recovery and minimize the risk of damage to healthy tissue, impotence, or prolonged incontinence, some procedures may result in prostate swelling

Points to Remember

- Holmium laser enucleation of the prostate (HoLEP) is a minimally invasive treatment for benign prostatic hyperplasia (BPH). Its short- and long-term outcomes are superior to those associated with transurethral resection of the prostate and suprapubic prostatectomy.
- HoLEP is performed transurethrally, using a holmium laser to separate the plane between the prostate gland tissue and the prostate capsule. This procedure allows complete resection of all adenomatous tissue, minimizing the need for future re-treatment.
- Mayo Clinic researchers are testing the use of HoLEP for men with hypocontractile or acontractile bladders and BPH.

with temporary need for catheterization. Additionally, the long-term durability of ablative procedures has not been widely assessed, and there is a risk of prostate regrowth requiring repeat surgical intervention in some cases.

Holmium laser enucleation of the prostate (HoLEP) is a minimally invasive treatment for BPH. With the patient under general anesthesia, the surgeon uses the laser to enucleate the prostate gland tissue, leaving just the capsule in place (Figure). The surgeon pushes the excised prostate gland tissue into the bladder and then uses a morcellation device to grind up and remove the tissue.

HoLEP offers some distinct advantages:

1. Treatment of any size prostate gland.
2. Complete excision of the obstructing prostate tissue down to the prostate's encapsulating structures, resulting in a re-treatment rate of less than 2%.
3. Early, immediate symptom relief and fast return to normal activity. Next-day catheter removal with limited swelling generally allows patients to void painlessly and immediately. Same-day or next-day hospital discharge is possible when the procedure is performed in a 23-hour observation setting.
4. Tissue preservation for pathologic examination. Because adenomatous tissue is excised rather than ablated, surgeons can examine specimens for prostate cancer or other abnormalities. Cancer is found in about 10% of HoLEP procedures, even in patients previously screened. In many cases, the cancer identified is of low malignant potential.
5. Fewer potential complications. The low depth of penetration of the holmium laser causes little damage to healthy tissue, and the risk of excessive bleeding and erectile dysfunction associated with traditional surgical approaches is reduced.

Some studies have shown that patients who underwent HoLEP actually had improved erectile function after surgery, but almost all had retrograde ejaculation. All patients experience hematuria for 1 to 2 weeks after the procedure, but the need for blood transfusion is low, around 1%. Since normal saline irrigation is used for the procedure, there is no risk of hyponatremia, regardless of prostate size. Transient urinary incontinence is common, but permanent incontinence at 1 year after the procedure occurs in approximately 1% to 2% of patients, depending on the definition and type of incontinence.

Ongoing HoLEP Research

Detrusor acontractility is viewed as a relative contraindication to surgical intervention for men with bladder outlet obstruction secondary to BPH. Mayo Clinic researchers are testing the use of HoLEP for men with hypocontractile or acontractile bladders. In a prospective trial of men aged 53 to 85 years, Mayo urologists performed HoLEP on 15 participants with evidence of BPH and bladders that had very

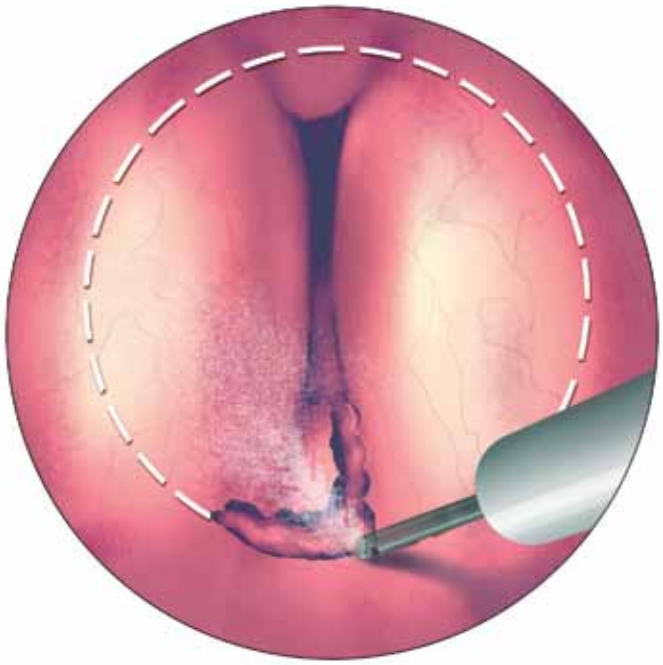

Figure. *A urologist's view through the laser resectoscope looking through the prostatic urethra into the bladder. The initial incision through the prostate adenoma to prostate capsule with the holmium laser fiber is depicted at the 6-o'clock position.*

little function or contraction ability. Preoperatively, all participants had catheter-dependent urinary retention for a median of 5 months (range, 3-60 months). Postoperatively, all men were able to void spontaneously without need for intermittent catheterization, with 13 participants displaying a return of detrusor contractility, and 2 participants voiding exclusively by Valsalva efforts. At their 6-month postoperative follow-up, all participants were still able to urinate. Although these findings are preliminary, they suggest that HoLEP may be a viable treatment option for men with BPH and hypocontractile or acontractile detrusor muscle.

Widely acknowledged as a benchmark BPH procedure, HoLEP requires specialized skills and training. Mayo Clinic is among the few medical centers in the United States that performs HoLEP procedures at its campuses in Minnesota and Arizona.

Surgical Management of Intractable Seizures in Children With Epilepsy

The Challenge

One in 5 children with epilepsy has intractable seizures—defined as seizures that fail to respond to at least 2 appropriate antiseizure medications. Surgery may be an option, but the path to that decision is complex. At many institutions, the evaluation process can take months.

At Mayo Clinic in Rochester, Minnesota, the surgical work-up can be done in 1 or 2 weeks and includes state-of-the-art functional brain mapping and seizure focus studies. If the child is documented to be a good surgical candidate and the family decides to proceed, surgery can then be scheduled promptly. The typical range for most epilepsy patients is 2 to 4 weeks from initial consult to surgery.

Points to Remember

- Mayo Clinic's multidisciplinary epilepsy team includes pediatric epileptologists, pediatric neurosurgeons, neuroradiologists, and pediatric neuropsychologists.
- Surgical candidates undergo continuous electroencephalographic monitoring, which may take from 24 hours to several days to record a sufficient number of seizures.
- Depending on the nature of the problem, surgical options include cortical resection; peri-insular hemispherotomy; endoscopic surgery; radiosurgery or microsurgical resection; or neuromodulation.

Determining Surgical Candidacy

A pediatric epileptologist determines the frequency, severity, and duration of seizures; whether the seizure onset is focal; and whether other conditions coexist. An MRI, scalp electroencephalography (EEG), and blood tests help identify seizure etiology (eg, cortical dysplasia, vascular malformations, arteriovenous malformation, tumor, trauma, stroke, rare metabolic conditions) and the presence (or absence) of a specific lesion and its location. A pediatric neuropsychologist then evaluates baseline cognitive function and helps establish lateralization of function. Other tests to localize function may include functional MRI, positron emission tomography, or intracarotid sodium amobarbital (Wada) testing.

Inpatient Pediatric EEG Monitoring

Surgical candidates then undergo continuous EEG monitoring in the Eugenio Litta Children's Hospital, the 85-bed pediatric facility located within Mayo's Saint Marys Hospital. Four rooms, as well as the pediatric intensive care unit, are hardwired with ceiling cameras for behavioral observation and continuous EEG monitoring via external or intracranial EEG leads (Figure 1). Inpatient video-EEG monitoring is needed to record several seizures by EEG and video and to minimize risks of medication withdrawal, a process that is often required to record seizures. Monitoring may take from 24 hours to several days to record a sufficient number of seizures. The single-patient rooms allow parents to stay with their child throughout the child's hospitalization and provide continuous monitoring by trained technicians.

Localizing Seizure Focus Through SISCOM

Pioneered at Mayo Clinic, SISCOM is an advanced imaging technology that fuses an MRI image with a SPECT image, an innovation

Figure 1. *Mayo Clinic's video-EEG monitoring unit is specifically designed for children and families and provides 24/7 monitoring by trained technicians.*

particularly useful in localizing seizure focus when seizures have a focal onset. A radioactive tracer is injected as soon as possible during a seizure. The first imaging study is performed shortly after the seizure; the second is done after 24 hours of seizure freedom. SISCOM can be very helpful in pediatric epilepsy in which the MRI frequently does not show a clear structural abnormality.

If imaging studies establish a clear focus that is not in an area of critical brain function, the child may have surgery for resection. If the focus cannot be precisely localized or if it is in an area of eloquent cortex, intracranial electrodes may be implanted. Further seizures are then recorded to improve localization of seizure onset. Electrical stimulation can be performed to map important motor and language functions.

Multiple Surgical Options

Depending on the nature of the problem, the patient may have surgical resection or disconnection. Resections are generally conducted for tumors, vascular malformations, and areas of cortical dysplasia. Cortical disconnection (corpus callosotomy) is used to treat drop attacks. For patients whose epilepsy arises from an entire hemisphere, Mayo neurosurgeons may perform a peri-insular hemispherotomy instead of the traditional hemispherectomy. Rather than removing the entire hemisphere, a hemispherotomy involves a much smaller resection monitored by image-guidance technology to disconnect the diseased hemisphere from the healthy one (Figure 2). As a result, there are fewer postoperative complications such as hydrocephalus and superficial siderosis.

Other options include endoscopic surgery in the rare case of a patient with gelastic or laughing seizures, in which there is a third ventricle hypothalamic hamartoma; radiosurgery or microsurgical resection for seizure-causing arteriovenous malformations; and neuromodulation using vagus nerve stimulation, deep brain stimulation, or cortical stimulation for focal, multifocal, and generalized seizures.

Mayo Clinic's multidisciplinary epilepsy team individualizes the most appropriate management strategy for each child seen and evaluated.

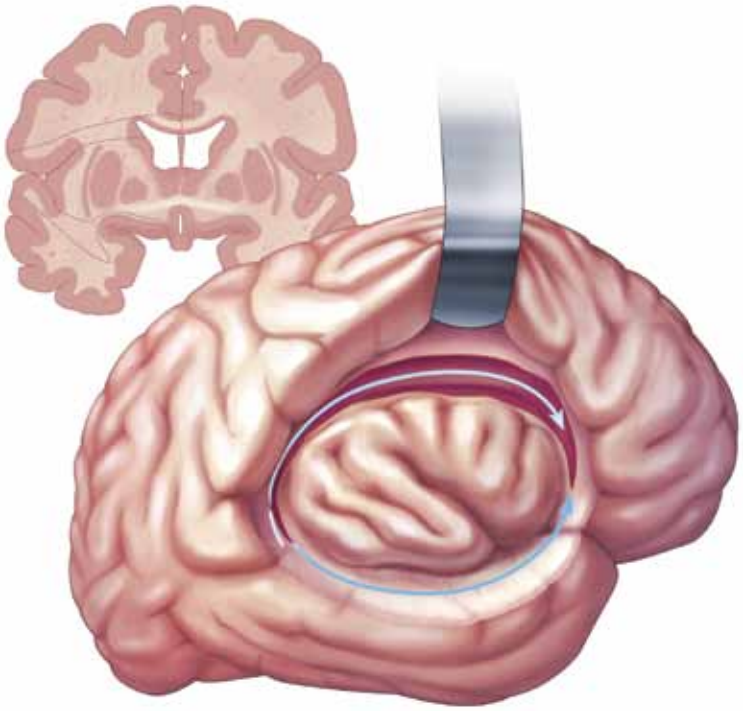

Figure 2. *Rather than removing the entire hemisphere, a hemispherotomy involves a much smaller resection (arrows) followed by image-guidance technology to disconnect the diseased hemisphere from the healthy one.*

Endovascular Repair of Abdominal Aortic Aneurysms

The Challenge

Abdominal aortic aneurysm (AAA) affects an estimated 12 to 15 per 100,000 persons per year and causes considerable risk for mortality because of the potential risk of rupture. First introduced in 1991, endovascular aortic aneurysm repair (EVAR) using a stent graft now provides a less invasive alternative to open repair. The procedure has excellent results in appropriately selected patients with good anatomy.

Monitoring and Treatment

Because aneurysms are often asymptomatic, they are frequently discovered via examination of the abdomen or through an x-ray examination, CT scan, or ultrasound study of the abdomen performed for another purpose. If the aneurysm is less than 5 cm in diameter and there are no symptoms, monitoring annually with Doppler ultrasound is recommended. Optimal medical management should include blood pressure control and smoking cessation.

Repair is usually recommended for aneurysms with a diameter of 5 cm or more in women and 5.5 cm or more in men, or if there has been growth of more than 0.5 cm in a year. During EVAR, the femoral arteries can be exposed using small incisions, or the procedure may be performed totally percutaneously. Following puncture of the femoral artery, a guide wire is passed across the dilated portion of the aorta, and the stent graft is advanced over the wire (Figure). Once the stent graft is correctly positioned, the device is released and the graft expands to exclude the aneurysm just below the renal arteries.

To ensure a proper seal between the stent graft and the aorta, most stents currently available require the aneurysm to have a proximal neck length of at least 1.0 to 1.5 cm below the renal arteries. However, repair can be done

Points to Remember

- Screening for abdominal aortic aneurysm via CT scan or ultrasound is recommended for all men aged 65 years or older and for women aged 65 years or older who have been or still are tobacco users or whose parent or sibling had an aortic aneurysm. Screening for men is recommended at age 55 years if a parent or a sibling had an aortic aneurysm.
- Repair is considered for aneurysms with a diameter of 5 cm or more in women and 5.5 cm or more in men or if the aneurysm has enlarged by more than 0.5 cm in a year.
- Endovascular aortic aneurysm repair (EVAR) is the preferred treatment for patients with suitable anatomy. EVAR is particularly advantageous for patients older than 65 years, patients who are considered to be at high risk because of other medical conditions, and patients who have undergone prior abdominal operations.
- Percutaneous EVAR is feasible and will increase in frequency as endograft technology improves.

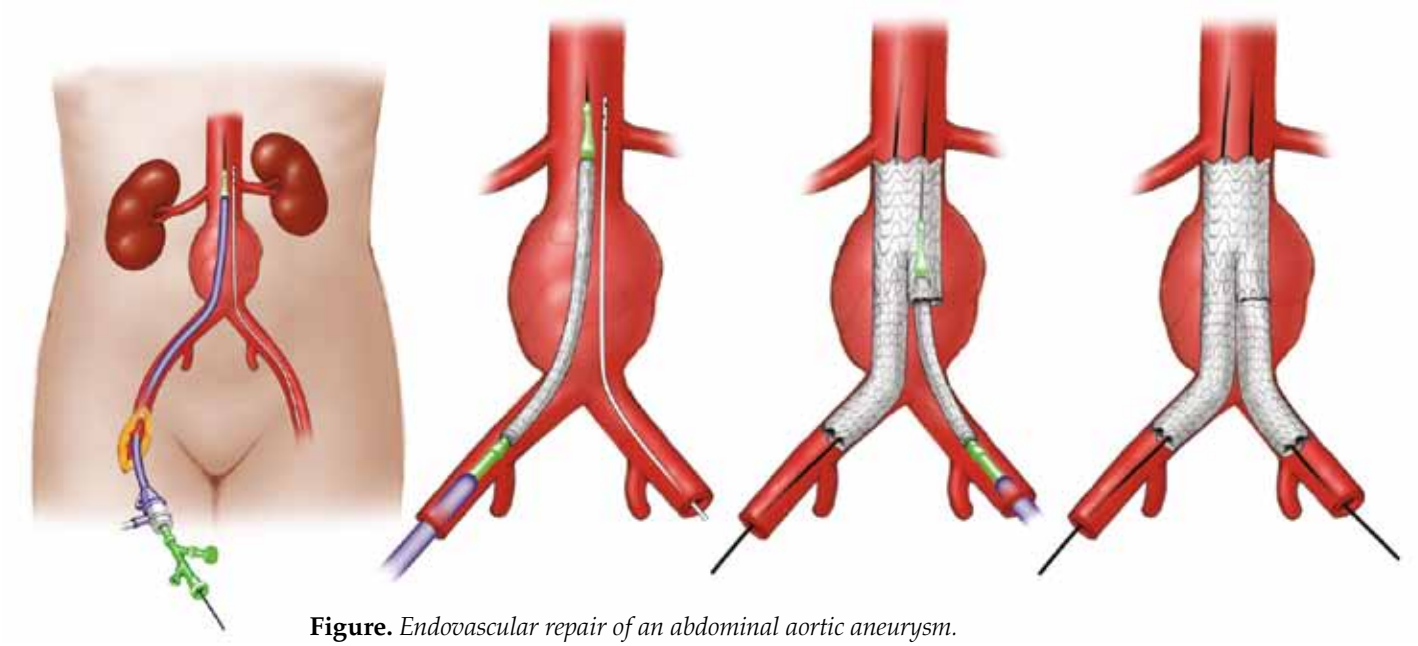

Figure. *Endovascular repair of an abdominal aortic aneurysm.*

in patients with aneurysms that have shorter necks by using a fenestrated stent graft with side holes and branches to the renal or intestinal arteries. Suitable iliac arteries are required for introduction of the devices, although deployment through a polyester "chimney" graft sutured to the iliac artery via a small retroperitoneal incision has increased the number of candidates for EVAR.

Using a Mayo Clinic aortic registry, Mayo Clinic researchers recently analyzed data from 1,008 consecutive patients (133 women and 875 men) who received endovascular repair between 1997 and 2011. Patients ranged in age from 49 to 99 years, with a mean age of 76 years. Thirty-day mortality after repair of nonruptured aneurysms was 0.2% in low-risk patients and 2.2% in high-risk patients. The 5-year survival rate was 72% for low-risk patients and 51% for those at high risk; three-fourths of those in either group were free from early and late complications, which can include postprocedure bleeding, blood clots, or problems with the repair. Age and high surgical risk were associated with complications and early and all-cause death. Women were more likely than men to have complications but were not at higher risk of death.

Most patients treated with EVAR no longer require admission to the intensive care unit and are dismissed home the day after surgery. A higher percentage of patients undergoing EVAR are discharged directly home rather than to nursing homes, and patients have a faster return to normal level of function, with post-discharge recovery time of 1 to 2 weeks.

The current prognosis for healthy patients who undergo elective aneurysm repair is excellent. Follow-up imaging studies at regular intervals are required to look for rare late complications such as graft migration or leaks around the stent (endoleaks). If a significant leak around the stent is discovered, the aneurysm sac still can rupture if no procedure to correct this is performed.

However, with low rates of operative and early (30-day) mortality, even among high-risk patients, EVAR represents an exciting and cost-effective advance in the treatment of patients with suitable anatomy.

Physician Update

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Education Opportunities

T Denny Sanford Pediatric Symposium
April 5, 2013, Mayo Clinic, Rochester, MN
The series of presentations and discussions will address the needs of regional clinicians in primary care, covering recent breakthroughs in topics of significant complexity and specifically topics that involve the consideration of working with a pediatric subspecialist. For more information or to register, please call 800-323-2688 or email cme@mayo.edu.

Pediatric Fundamental Critical Care Support Course
April 18-19, 2013, Rochester, MN
This 2-day course provides an exposure to the basic principles of pediatric critical care. The primary goals are to enhance the ability of the primary care practitioner in performing the initial assessment of critically ill pediatric patients and then augment their skills in managing and stabilizing them in anticipation of transport to a tertiary care center. For more information or to register, please call 800-323-2688 or email cme@mayo.edu.

34th Annual Practice of Internal Medicine
April 29-May 3, 2013, Rochester, MN
This course will focus on the management of a variety of medical issues seen in areas of gastroenterology, infectious diseases, general internal medicine, rheumatology, geriatrics, emergency medicine, pulmonary, endocrinology, cardiology, neurology, and women's health. For more information or to register, please call 800-323-2688 or email cme@mayo.edu.

20th Annual Clinical Reviews and Primary Care Update
June 17-21, 2013, Amelia Island, FL
This program is intended for the continuing education of general internists, family physicians, physician assistants, nurse practitioners, and nurses in primary care medicine. For more information or to register, please call 800-462-9633 or email cme-jax@mayo.edu.

Internal Medicine Board Review: Certification and Maintenance of Certification
July 15-19, 2013, Rochester, MN
This intensive course is designed to provide a comprehensive overview of all areas in internal medicine for practicing physicians. For more information or to register, please call 800-323-2688 or email cme@mayo.edu.

Internal Medicine Review for Nurse Practitioners, Physician Assistants, and Primary Care Providers
September 18-20, 2013, Rochester, MN
This annual interdisciplinary course offers participants an overview of current topics in internal medicine, including interactive case studies using an automated audience response system. Interdisciplinary speakers present diverse clinical topics chosen for applicability to NP/PA and primary care physician practice settings. As care of complex patients transitions to the outpatient arena, current guideline-based medicine typically in the hospital setting continues to be important as patients are managed outside the hospital setting. For more information or to register, please call 800-323-2688 or email cme@mayo.edu.

16th Annual Mayo Clinic Internal Medicine Update: Sedona 2013
October 10-13, 2013, Sedona, AZ
This 4-day course offers primary care physicians, nurse practitioners, and physician assistants a practical update on a variety of subspecialty topics, including allergy, cardiovascular diseases, dermatology, endocrinology, gastroenterology, hematology, infectious diseases, integrative medicine, neurology, psychiatry, pulmonary, renal disease, rheumatology, and others applicable to today's practice and patients. It is also offered on October 24-27, 2013. For more information or to register, please call 480-301-4580 or email mca.cme@mayo.edu.

Update in Hospital Medicine, 2013
November 6-9, 2013, Tucson, AZ
The course is designed to provide a review of the most recent medical updates relevant to the care of hospitalized patients. Using an interactive, case-based format, the key highlights from all major areas of internal medicine and its specialties will be presented. An expert panel of distinguished Mayo Clinic academic physicians will present didactic lectures and address questions from the audience. For more information or to register, please call 480-301-4580 or email mca.cme@mayo.edu.

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