MAYO CLINIC

Clinical Update

Current Trends in the Practice of Medicine

Vol. 26, No. 2, 2010

Radiosurgery: An Effective Treatment for Benign Intracranial Tumors

INSIDE THIS ISSUE

The Challenge

Benign intracranial tumors occur about as often as primary malignant brain tumors. Most benign tumors are noninvasive, well defined and well visualized on MRI, and have a slow rate of progression. Each of these features makes them good candidates for radiosurgery. Radiosurgery can deliver a destructive dose of radiation to the target with little or no radiation effects on adjacent structures. Proper patient selection for this procedure is critical.

Defining Selection Criteria

With 2 decades of experience performing radiosurgery, Mayo Clinic neurosurgeons have accumulated a depth of expertise and a vast database that includes patient characteristics, radiosurgical dosimetry, and outcomes. After reviewing more than 1,400 cases of meningiomas, vestibular schwannomas, and pituitary adenomas, Mayo clinicians observe that radiosurgery is an excellent choice when these types of benign tumors are small, occur in critical locations, or have recurred following previous surgery.

Radiosurgery is also well tolerated and of particular utility in elderly patients with medical conditions that put them at risk for an open procedure. Additionally, radiosurgery does not preclude an open procedure, should that be necessary at a later time.

Points to Remember

- Radiosurgery is focused delivery of radiation to an image-defined target performed in 1 to 5 sessions.
- When used as an alternative to or in conjunction with open neurosurgical techniques, radiosurgery is an effective, less invasive option for treating many benign intracranial tumors, including meningiomas, vestibular schwannomas, and pituitary adenomas.

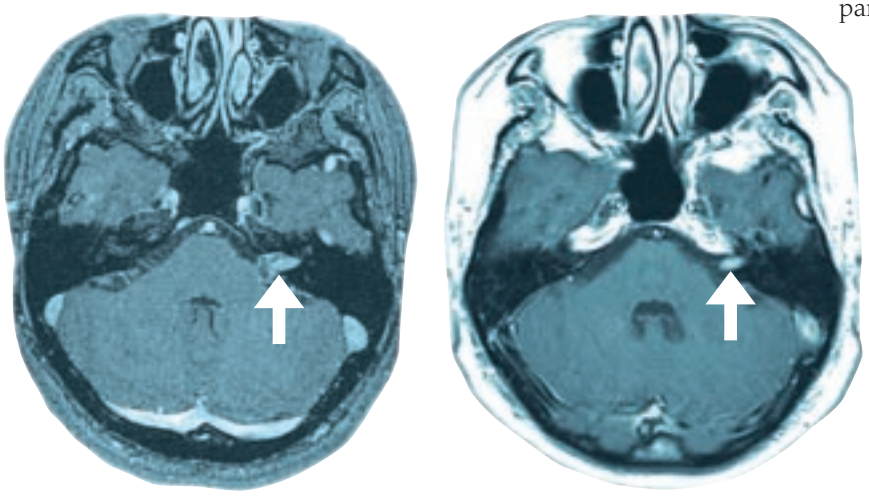

Figure. *A patient with a vestibular schwannoma before radiosurgery (left, December 1997) and almost 12 years later (right, March 2009).*

Radiosurgery for Meningiomas

The rate of recurrence for a surgically removed meningioma is about 18% to 25% at 10 years. For this reason, Mayo neurosurgeons recommend maintaining extended surveillance of meningiomas. In contrast, radiosurgery has been found to reduce the risk of recurrence or progression. Tumor progression outside the field of radiation and tumor histology can affect both long- and short-term outcomes. Tumors that can be clearly imaged and those that are benign and without atypical histology have a far greater rate 5-year progression-free survival. Radiosurgery is also an effective therapy for cavernous sinus meningiomas, except when there is symptomatic mass effect, an unusual clinical presentation, or nontypical features on imaging. Radiosurgery is typically not recommended for convexity and parasagittal meningiomas.

Radiosurgery for Vestibular Schwannomas

Several studies report that radiosurgery for small to moderate-sized vestibular schwannomas is associated with higher rates of hearing preservation and improved facial nerve outcomes when compared to surgical removal. This conclusion was supported by a Mayo Clinic study comparing surgical resection and radiosurgery for vestibular schwannomas with an average diameter of less than 3 cm. These Mayo investigators also found that the radiosurgical patients experienced less postprocedure dizziness. The Figure on page 1 shows a patient with a vestibular schwannoma before and after radiosurgery.

Radiosurgery for Pituitary Adenomas

Radiosurgery is considered safe and effective for hormone-secreting pituitary adenomas. When compared with radiotherapy, radiosurgery appears to shorten by more than half the time required to achieve biochemical remission and normal hormone levels. Controversy remains over whether pituitary-suppressive medications at the time of surgery have a negative impact on tumor control. However, several studies, including a series of 46 acromegaly cases at Mayo Clinic, found that patients were more than 4 times as likely to reach normal hormone levels if they were taken off such medications before surgery.

At Mayo Clinic, patients with over-secretion of growth hormone or adrenocorticotropic hormone and patients who experience new or progressing visual field deficits are referred for surgical resection. However, patients with tumors that extend into the cavernous sinuses and patients with recurrent tumors after prior surgery are generally treated with radiosurgery if the tumor does not directly involve the optic nerves and chiasm.

Across Mayo Clinic's 3 sites in Arizona, Florida, and Minnesota, patients are seen by neurosurgeons who have expertise in both open procedures and radiosurgery. When used as an alternative to or in conjunction with traditional neurosurgery, radiosurgery is an effective, noninvasive option for treating benign intracranial tumors.

Holmium Laser Enucleation of the Prostate Provides Faster Relief and Maximum Benefit for BPH Patients

The Challenge

Benign prostatic hyperplasia (BPH) is a noncancerous enlargement of the prostate gland that often leads to bladder outlet obstruction and restriction of urine flow. Symptoms may include frequent urination (especially at night), urgency, burning or pain during urination, leakage of urine, and diminished stream. An estimated 40% of men in their 50s and 90% of men in their 80s experience symptoms of BPH. When medications and minimally invasive office-based procedures fail to provide lasting benefits, surgical intervention may be necessary.

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.

Laser ablation procedures vaporize the obstructive portion of BPH, while minimizing the risk of damage to healthy tissue impotence or prolonged incontinence. Ablative procedures can be performed on an outpatient basis and offer quick recovery time. Although they can

provide swift symptom relief, some laser ablation procedures may result in prostate swelling with temporary need for catheterization. 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.

A New Approach

HoLEP is typically performed with the patient under general anesthesia. The surgeon uses the laser to enucleate the entire adenoma, leaving just the capsule in place (Figure). The surgeon pushes the excised adenoma into the bladder and then uses a morcellation device to grind up and remove the tissue.

Advantages of HoLEP include

- Performance of the procedure on any size prostate gland.
- Complete excision of the obstructing prostate tissue down to the prostate's encapsulating structure, resulting in a retreatment rate of less than 2%.
- Same day or next day hospital discharge when the procedure is performed in a 23-hour observation setting.
- Nearly immediate symptom relief and fast return to normal activity. Next-day catheter removal with limited swelling generally allows patients to void painlessly and immediately.
- 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.
- 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 develop 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.

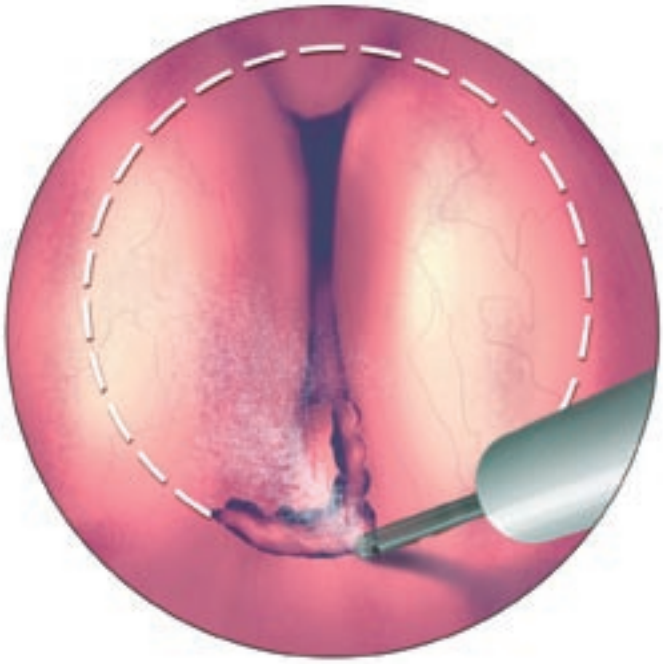

Figure. *Shown is the urologist's view through the laser resectoscope looking through the prostatic urethra into the bladder. Demonstrated is the initial incision through the prostate adenoma to the prostate capsule with the holmium laser fiber depicted at the 6-o'clock position.*

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.

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 adenoma and the prostate capsule.
- HoLEP allows complete resection of all adenomatous tissue, minimizing the need for future retreatment.

Evaluation and Management of the Incidentally Found Pituitary Mass

The Challenge

You review the MRI scan of a patient who presented with headaches after head trauma. No brain injury is present, but a mass is visible in the pituitary gland (Figure)—a pituitary incidentaloma, or an asymptomatic mass in the pituitary gland found on imaging done for an unrelated reason. What tests, if any, should you obtain? Does the pituitary mass need treatment, or may it be monitored rather than treated?

To answer these questions and to develop rational recommendations for testing and follow-up, the physician needs to 1) confirm that the patient is asymptomatic, 2) consider the possible etiologic factors of the mass, and 3) consider the potential for and the clinical impact of hormone deficiency, hormone excess, and mass growth. Most pituitary incidentalomas are less than 1 cm in largest diameter and prove to be pituitary adenomas or Rathke cleft cysts.

Points to Remember

- Autopsy and head MRI studies indicate that the prevalence of incidentally discovered pituitary masses is approximately 10%.
- Determining whether the patient is asymptomatic, possible underlying causes of the mass, and the potential impact of hormone excess or deficiency and mass growth are important tools in formulating management strategies.

Potential for Hormonal Hyperfunction

Prolactin-producing pituitary adenomas are common (12%-28%) in patients with pituitary incidentalomas. Prolactinomas have potential for morbidity, testing is easy, and treatment is safe and effective. The incidence of growth hormone (GH) production by an incidentally found pituitary mass is between 2% and 8%. Patients whose pituitary incidentaloma is detected early in the course of disease may have GH-related symptoms and physical findings that are subtle. However, there is potential for serious morbidity and increased risk of death when GH excess is undiagnosed. In addition, the likelihood of surgical cure for a GH-secreting pituitary adenoma is greater when the tumor is small. Testing for corticotropin excess in asymptomatic patients with pituitary incidentaloma is not recommended because of the low prevalence of disease and the high false-positive rates associated with the case detection tests used for this disorder. There is no reliable preoperative biochemical test to detect gonadotroph adenomas, which represent approximately 4% of pituitary adenomas discovered at autopsy. Thyrotropin (TSH)-secreting pituitary adenomas are exceedingly rare, and patients with these tumors usually present with signs and symptoms of hyperthyroidism.

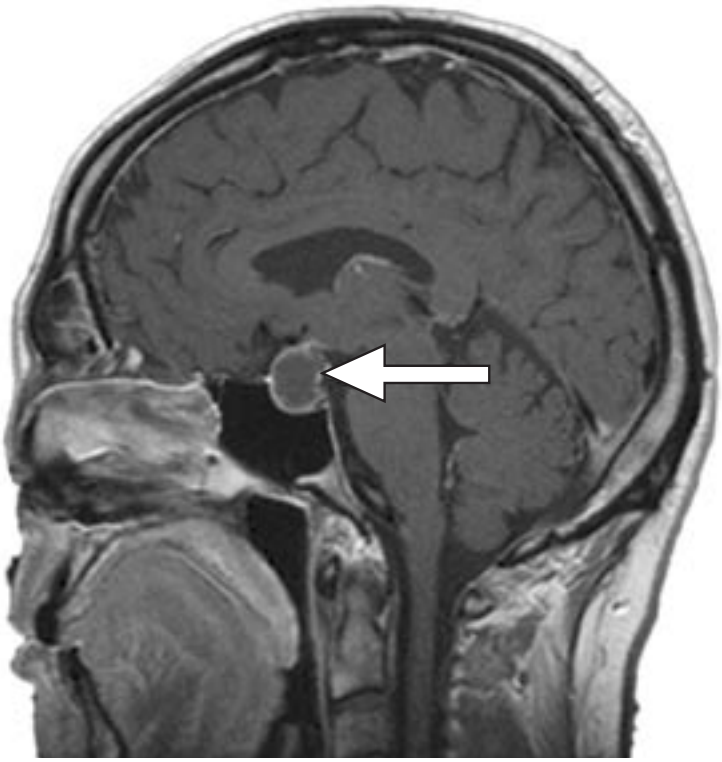

Figure. *MRI scan (sagittal image) showing an incidentally discovered 2-cm pituitary mass (arrow).*

Potential for Hormonal Hypofunction or Growth

Pituitary microadenomas (≤10 mm in largest diameter) have a very low probability of being associated with hormonal hypofunction of the neighboring pituitary gland. However, macroadenomas (>10 mm in largest diameter) (Figure) are frequently (15%-57%) associated with varying degrees of pituitary hypofunction. Both microadenomas and macroadenomas have the potential to increase in size over time, even after several years of apparent stability. Growth of a macroadenoma is more likely to be detected

Table. *Recommended Laboratory Studies for Patients With Pituitary Incidentalomas*

	To Assess Subclinical Hormone Excess		To Assess Subclinical Hormone Deficiency	
Blood Tests	**Microadenoma[a]**	**Macroadenoma[b]**	**Microadenoma[a]**	**Macroadenoma[b]**
Prolactin	X	X		
IGF-1[c]	X	X		X
FT_4, TSH				X
Testosterone (men)				X
8 AM cortisol[c]				X

Abbreviations: FT_4, free thyroxine; IGF-1, insulinlike growth factor 1; TSH, thyrotropin.

[a] Adenoma ≤10 mm in largest diameter.

[b] Adenoma >10 mm in largest diameter.

[c] IGF-1 and 8 AM cortisol levels may not be sufficient to indicate normalcy or deficiency, and dynamic studies may be necessary.

during imaging follow-up than growth of a microadenoma. Any increase in the size of a macroadenoma is associated with an increased probability of clinically important mass effects (eg, hypopituitarism, vision loss).

Recommended Management for Pituitary Incidentaloma

To exclude excess hormone production, measurement of prolactin and insulinlike growth factor 1 (IGF-1) should be obtained in all patients with pituitary incidentalomas (Table). Laboratory testing to exclude pituitary hormone deficiencies is not needed for patients with microadenomas. However, the following blood tests should be obtained for patients with macroadenomas: TSH, free thyroxine, cortisol measured at 8 AM, prolactin, and IGF-1. A menstrual history should be obtained for women and serum testosterone concentration should be measured for men. Baseline blood levels of cortisol and IGF-1 may not be sufficient to indicate normalcy or deficiency, and dynamic studies may be necessary. Quantitative perimetry to assess visual fields should be obtained when a macroadenoma is near or in contact with the optic chiasm.

Observation is appropriate when there is no evidence of pituitary hormone hyperfunction or hypofunction and when the pituitary mass is not causing or threatening vision loss. Reevaluation with pituitary-directed MRI should be completed 6 to 12 months after the initial scan, annually for 2 to 4 years, and periodically thereafter. All follow-up scans should be compared with the baseline scan in addition to the prior scan, since slow changes in size may not be appreciated from one year to the next. The follow-up for pituitary macroadenomas should also include formal visual field assessment, since the decision to remove a nonfunctioning macroadenoma rests primarily on the development or risk of vision loss.

For more information about evaluation and management of pituitary incidentalomas, call the referring physician service at the number listed on page 8.

Cardiologists' Input Critical to Integrated Management of Peripheral Artery Disease

The Challenge

Although 70% of patients with PAD may be asymptomatic at any given time, the presence of PAD is a powerful predictor of cardiovascular morbidity and mortality. The presence of asymptomatic PAD should therefore provide motivation for both patients and clinicians to aggressively reduce cardiovascular risk factors in an attempt to limit events. Conversely, the presence of coronary or carotid disease should alert the physician to consider the coexistence of PAD (Figure 1).

The Role of Cardiologists in a Global Vascular Care Plan

Specific peripheral vascular disorders may also affect the management of cardiac disease. Renal artery stenosis (RAS) is the most common secondary cause of hypertension in patients with atherosclerosis. Moreover, renovascular hypertension is often resistant to medical therapy, thus increasing cardiovascular risk. Bilateral RAS may produce flash pulmonary edema in patients with normal left ventricular function. Subclavian artery stenosis may lead to angina or even myocardial infarction by compromising inflow to left or right internal mammary bypass grafts. Claudication from lower extremity artery disease may limit mobilization and impair the effectiveness of cardiac rehabilitation programs. Iliac and subclavian artery stenoses may limit access for cardiac catheterization and percutaneous coronary intervention.

Situations such as these have led to an increasing role for the input of cardiologists in the recognition and medical management of global vascular disease, as well as in therapeutic endovascular approaches for noncoronary revascularization. Mayo Clinic uses an integrated approach, bringing together endovascular specialists from vascular medicine, vascular radiology, vascular surgery, and interventional cardiology, to individualize an optimal patient treatment plan.

Points to Remember

- Peripheral artery disease (PAD) affects between 8 million and 12 million people in the United States, and its prevalence will likely reach 20 million in 10 years.
- The poor prognosis of PAD (disease affecting any of the upper or lower extremity carotid, renal, and mesenteric arteries) confers a markedly increased risk of subsequent ischemic cardiac and cerebrovascular events, reflecting the coexistence of often asymptomatic, but extensive coronary and carotid disease.
- The notable overlap of incidence, natural history, and treatment outcomes between coronary and noncoronary atherosclerosis highlights the importance of cardiologists' participation in management of patients with PAD.

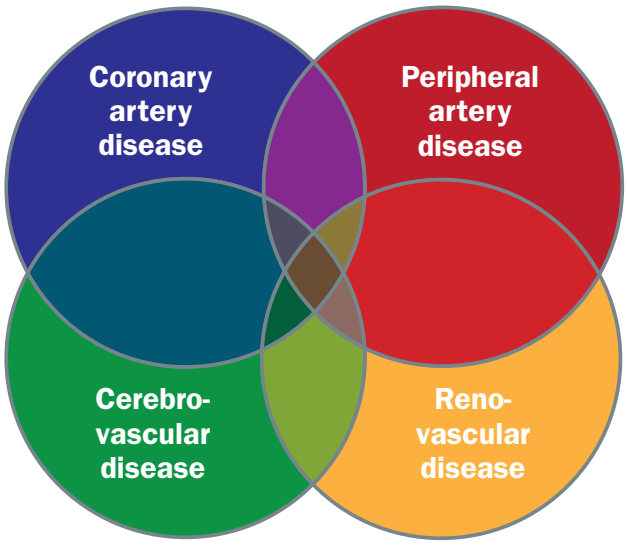

Figure 1. *Atherosclerotic artery disease, a global problem.*

Claudication

The mainstay of therapy is risk factor modification in conjunction with antiplatelet therapy. A supervised exercise program along with pharmacologic therapy with phosphodiesterase inhibitors has additional proven benefit. Revascularization has typically been reserved for patients with persistent lifestyle limitations.

An increasing number of patients now undergo an endovascular rather than a surgical approach for revascularization of occlusive lower extremity artery disease. Patients who previously were considered too high risk for surgery are now eligible for percutaneous approaches, with the advantages of rapid recovery time and reduced morbidity. In patients with severe obstructive disease or occlusions throughout a limb, treatment of proximal level stenoses alone often cures or markedly reduces claudication symptoms, despite residual high-grade occlusive disease more

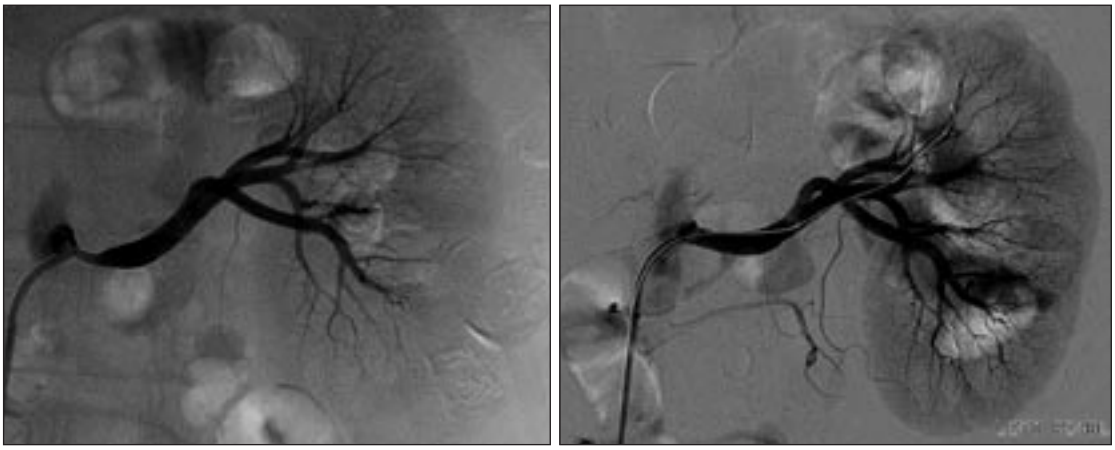

Figure 2. *Assessment and treatment of renal lesions. Several technologies from the cardiac arena can help refine the definition of physiologically relevant RAS and tailor revascularization for those patients with the greatest likelihood of benefit. A 58-year-old woman presented with resistant hypertension, despite using 5 antihypertensive agents; her serum creatinine had increased from 1.0 mg/dL to 2.0 mg/dL over the preceding year. Her hypertension had been well controlled on 2 agents 2 years earlier. Bilateral elevated renal artery velocities were identified on ultrasound with normal-sized renal arteries. Angiography, pressure wire assessment, and intravascular ultrasound confirmed physiologically important, high-grade stenoses bilaterally (left). Both renal arteries were dilated (right radiograph of opened left renal artery), and blood pressure control began to improve within 24 hours. At follow-up 1 month later, she had returned to controlled hypertension using 2 pharmacologic agents, and her creatinine level had normalized.*

distally. In other circumstances of complex disease patterns, a hybrid endovascular-surgical approach may be considered.

Critical Limb Ischemia

The presence of rest pain, nonhealing ulcer, or gangrene may represent critical limb ischemia (CLI). CLI is associated with mortality in 25% of patients and limb loss in 50% at 1 year. The optimal treatment for CLI is prompt revascularization. The therapeutic goal is to reestablish single-vessel, in-line (uninterrupted) arterial flow to the foot. This often requires multiple level dilation and endovascular reconstruction of at least a single infrapopliteal vessel. Endovascular treatment of proximal disease alone to optimize collateralization of occluded infrapopliteal vessels may not always be sufficient for healing of distal extremity ulcers. However, if patency is maintained for even a short period, wound healing and limb salvage can be achieved.

Renal Artery Stenosis

The presence of atherosclerotic RAS is a risk factor for cardiovascular disease and is a strong predictor of mortality. RAS may lead to hypertension, deterioration of renal function, and irreversible renal tissue injury (ischemic nephropathy). It can be difficult to determine whether the relationship between RAS and hypertension or renal impairment is causative. Renal lesions can now be comprehensively assessed for both stenosis severity and downstream end-organ impact using tools from the coronary arena (Figure 2).

The incorporation of cardiac interventional techniques has expanded the treatments available for these challenging patients with vascular disease. For additional information or to refer a patient, please call 507-255-4244.

Table. *Clues to Renal Artery Stenosis*

- **Known atherosclerosis**
- **Onset of hypertension before the age of 30 years or after the age of 55 years**
- **Worsening of previously controlled hypertension**
- **Malignant or resistant hypertension**
- **Abdominal bruit**
- **Discrepancy of renal size**
- **Azotemia not otherwise explained or worsened by angiotensin-converting enzyme inhibitors or angiotensin II receptor blockers**
- **Recurrent congestive heart failure or flash pulmonary edema in a hypertensive patient, particularly with preserved systolic left ventricular function**

Mayo Clinic
Clinical Update

Medical Editor:
Scott C. Litin, MD

Editorial Board:
Robert P. Shannon, MD
Douglas M. Peterson, MD

Contact Us

Referrals and Consultations

Arizona
866-629-6362

Florida
800-634-1417

Minnesota
800-533-1564

www.mayoclinic.org/medicalprofs

Mayo Clinic Offers Online Services for Referring Physicians

Mayo Clinic Online Services for Referring Physicians is a secure, user-friendly Web site that provides a window into the care of patients referred to Mayo Clinic through Online Services.

Online Services allows health care providers to

- Make appointment requests electronically, 24 hours a day, 7 days a week.
- View and print Mayo Clinic medical documents for patients referred through Online Services, including consultative and surgical notes, laboratory and radiology reports, and hospital discharge summaries.

To view a demonstration, go to www.mayoclinic.org, click the tab for Online Services, then select Physicians Outside Mayo Clinic.

To register to use Online Services contact one of Mayo Clinic's Referring Physician Offices:

Jacksonville, Florida
800-634-1417

Rochester, Minnesota
800-881-9764

Scottsdale/Phoenix, Arizona
866-629-6362

E-mail: rponlineservice@mayo.edu

MAYO CLINIC

4500 San Pablo Road
Jacksonville, FL 32224

200 First Street SW
Rochester, MN 55905

13400 East Shea Boulevard
Scottsdale, AZ 85259

MC2024-0410

www.mayoclinic.org