MAYO CLINIC

Clinical Update

Current Trends in the Practice of Medicine

Vol. 28, No. 3, 2012

INSIDE THIS ISSUE

Endoscopic Management of Dysplasia and Early Cancer in Barrett Esophagus

Two decades ago, the primary treatment for high-grade dysplasia and early cancer in Barrett esophagus (BE) was esophagectomy, a complicated surgical procedure associated with considerable morbidity and even mortality. Since then, tremendous advances in the field have provided doctors and patients with far less invasive options. Today, endoscopic management of esophageal dysplasia and early (stage T1a) adenocarcinomas is the standard of care for most people.

Radiofrequency ablation (RFA), which uses targeted thermal energy to destroy abnormal tissue, is a safe, effective, and durable way to eradicate intestinal metaplasia and dysplasia in patients with BE. For many patients, RFA, which usually requires 2 or 3 treatments, is preferable to long-term surveillance with multiple biopsies and is certainly preferable to surgery.

Arguably one of the most important advances in the field of BE management is the treatment of early-stage cancers with organ-sparing endoscopic therapies, primarily endoscopic mucosal resection (EMR), but also, in some cases, endoscopic submucosal dissection.

EMR snares and removes well-contained, superficial cancer smaller than 1.5 to 2 cm. Endoscopic submucosal dissection can meticulously dissect lesions up to 9 cm). Both procedures show cure rates similar to esophagectomy in cohort studies, although no randomized trials have been performed (Figures 1 and 2).

EMR and endoscopic submucosal dissection are potentially simple outpatient procedures with a rapid recovery and few complications. Despite improved techniques using robots and other minimal access procedures, the recovery after esophagectomy is lengthy, and the complication rate remains high, up to 50%.

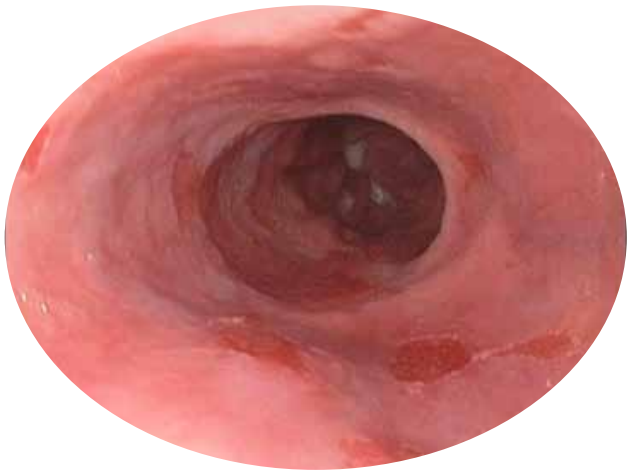

Figure 1. *Barrett esophagus before treatment with endoscopic mucosal resection.*

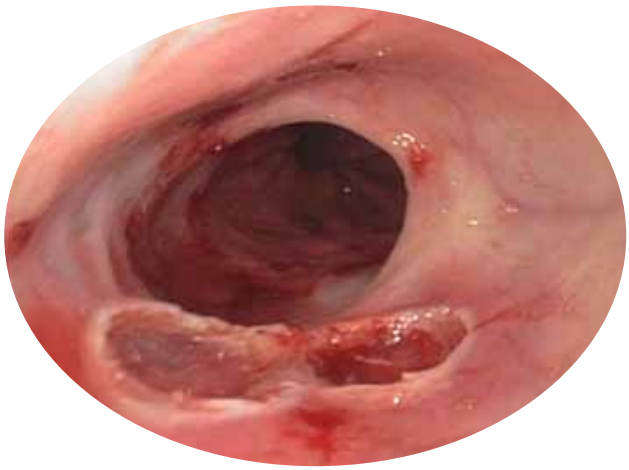

Figure 2. *Barrett esophagus after treatment with endoscopic mucosal resection.*

Optical Imaging, Molecular Testing

Equally important are novel techniques that improve the detection of neoplastic changes. Standard endoscopy, for instance, shows few details of the mucosal surface, but high-resolution magnifying endoscopes can enhance the appearance of the esophageal mucosa 300 times, revealing microvascular and pit patterns.

Also expanding the capabilities of endoscopy are optical imaging technologies—narrow band imaging, autofluorescence, and optical coherence tomography among them—which better identify areas of dysplasia or scan large areas of the mucosa in a single pass. These methods allow for better-targeted biopsies, reducing the number of random samples needed and increasing diagnostic yield.

Mayo Clinic gastroenterologists are also convinced that finding alternatives to traditional biopsy is crucial. One technique with potential is confocal laser endomicroscopy, which relies on tissue fluorescence to examine mucosal histology in real time. The confocal laser microscope probe magnifies 400 times, providing optical biopsies of any accessible surface in vivo.

Emerging technologies such as angle-resolved low-coherence interferometry, which uses patterns of scattered light to locate abnormal cells in situ while avoiding observer error, may provide even better results. A procedure currently in use that addresses the difficult problem of interpretation error is molecular testing. Fluorescent in situ hybridization (FISH), for instance, which bypasses the unreliability of histology by analyzing cytology specimens, uses fluorescent probes to detect abnormal genetic changes in cells. These tests are valuable in helping identify patients with progressive neoplasia who will benefit from further treatment.

The Goal: Better Patient Care

In addition to novel diagnostic and therapeutic options for BE and esophageal cancer, research on the etiology of these disorders is ongoing. Mayo experts agree that the confluence of so many breakthroughs make today an exciting time to be in this field.

In the past, patients with BE-related adenocarcinoma faced difficult surgery, 2 to 4 weeks in the hospital, a 6-month recovery at home, lifelong dietary restrictions, and a 50% chance of serious complications—and that was if everything went well. Today, physicians remove the cancer, and the patient goes home the same day, is eating a regular diet the next day, and has a completely normal quality of life.

Points to Remember

- The treatment of early-stage cancers with radiofrequency ablation and organ-sparing endoscopic therapies such as endoscopic mucosal resection and endoscopic submucosal dissection are important advances in the treatment of Barrett esophagus.
- The use of high-resolution magnifying endoscopes, which improve the detection of neoplastic changes, and optical imaging technologies allow for better-targeted biopsies, reduce the number of random samples needed, and increase diagnostic yield.
- Alternatives to traditional biopsy with potential include confocal laser endomicroscopy, which relies on tissue fluorescence to examine mucosal histology in real time, and angle-resolved low-coherence interferometry, which uses patterns of scattered light to locate abnormal cells in situ.

American Brain Tumor Association and Mayo Clinic Create Patient Education Program

The American Brain Tumor Association (ABTA) and Mayo Clinic have established a program to provide educational support for patients coping with the diagnosis and treatment of brain tumors. The program includes 1-on-1 coaching for patients and their families. Announced at the ABTA annual meeting in July 2011, this program provides a dedicated nurse educator and enhanced patient education materials exclusively for brain tumor patients and their families

at Mayo Clinic. With both organizations working together to improve outcomes for patients with brain tumors, these enhanced services reflect a shared commitment to providing optimal education and support to brain tumor patients and their families.

The nurse educator provides individual coaching and education to patients and their families. Patient education materials, including the ABTA Brain Tumor Primer, publications on individual tumor types and treatments, and other ABTA resources, will be available at the Stephen and Barbara Slaggie Family Cancer Education Center, on the main floor of the Gonda Building at Mayo Clinic in Rochester (Figure). The ABTA Website and electronic resources and its patient support phone line, CareLine, are available at easily accessible computer workstations and phones in the Cancer Education Center and patient care areas in the Gonda Building.

The program includes an annual assessment of the nurse educator and enhanced training on patient learning needs, health literacy, cultural barriers, age-specific approaches to education, learning styles, and teaching strategies. The feedback will also help guide the ABTA as it enhances its patient education materials and services.

Points to Remember

- The American Brain Tumor Association (ABTA) and Mayo Clinic have established a program to provide individual coaching and educational support for patients coping with the diagnosis and treatment of brain tumors.
- Also included are an annual assessment of the nurse educator and enhanced training on patient learning needs, health literacy, cultural barriers, age-specific approaches to education, learning styles, and teaching strategies. The feedback will also help guide the ABTA as it enhances its patient education materials and services.

Support for the joint effort is being provided to ABTA by proceeds from the annual Humor to Fight the Tumor gala in Minneapolis. The event is organized by brain tumor survivor Joelle Syverson and a committed group of individuals and families affected by a brain tumor diagnosis.

Figure. *Stephen and Barbara Slaggie Family Cancer Education Center.*

Pediatric Head Trauma: To Scan or Not to Scan

The Challenge

Each year, 600,000 children in the United States are seen in emergency departments for head trauma. Approximately half of them receive CT scans. Yet less than 1% of pediatric head injuries are serious, raising increased concerns about unnecessary exposure to ionizing radiation.

Although the exact numbers are a matter of debate, it's estimated that 1 in 1,000 to 1 in 5,000 CT scans will cause a fatal brain cancer. The risk is greatest for children whose brains are still developing. To help reduce the number of unnecessary scans (those with negative or noncontributory findings), Mayo Clinic has adopted imaging guidelines for minor head trauma (Figure). These guidelines draw on a landmark study published in *The Lancet* in 2009. This large, multicenter study involved 42,000 children at 25 hospitals. Using study data, researchers established decision rules for identifying cases where scans are not needed. One rule was established for children under the age of 2 years and another for children aged 2 to 18 years.

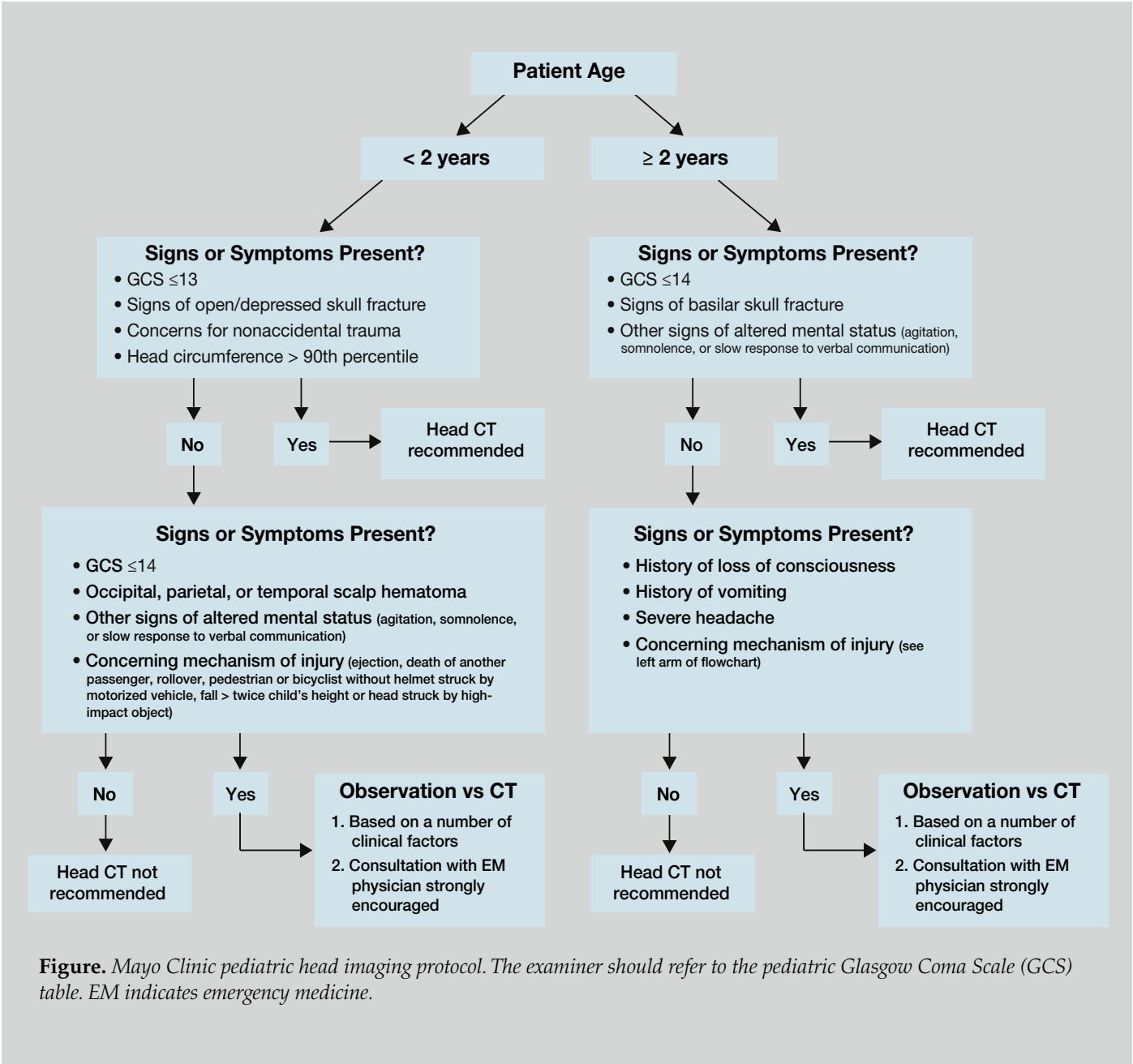

Figure. *Mayo Clinic pediatric head imaging protocol. The examiner should refer to the pediatric Glasgow Coma Scale (GCS) table. EM indicates emergency medicine.*

Points to Remember

- Although the exact numbers are a matter of debate, an estimated 1 in 1,000 to 1 in 5,000 CT scans will cause a fatal brain cancer. The risk is greatest for children whose brains are still developing.
- To help reduce the number of unnecessary CT scans in children, Mayo Clinic has adopted imaging guidelines for minor head trauma that draw on a landmark study published in *The Lancet* in 2009.

Predictive Factors

Six predictive factors apply to each group. For children younger than 2 years, these factors include either Glasgow Coma Scale (GCS) score of ≤14 (at Mayo Clinic, this threshold is ≤13), or 1 or more of these 6 predictors:

- Altered mental status
- Skull fracture
- Loss of consciousness for more than 5 seconds
- Nonfrontal scalp hematoma
- Severe mechanism of injury (outlined in detail in *The Lancet*)
- Abnormal behavior based on parental reporting

The guideline for children aged 2 years or older includes some key differences. In addition to altered mental status and mechanism of injury, it cites basilar skull fracture, any loss of consciousness, vomiting, and severe headache.

In both age groups, if none of these factors is present, no imaging studies are performed. Because the guidelines have essentially a 100% negative predictive value, Mayo Clinic emergency medicine and pediatrics staff feel very comfortable not having scans performed on these children.

How to proceed with children who have 1 or more predictors depends on the clinical situation and age of the patient. In general, any child who has a change in mental status and visible signs of a skull fracture is scanned. But most children are simply observed for a brief period in the emergency department to watch for worsening or improving symptoms. According to these guidelines, only a small subset of children need imaging studies. Mayo Clinic staff note that they can identify children with severe injuries without needlessly exposing the children to radiation. In another study published in the *Annals of Emergency Medicine* in 2011, researchers concluded that patients with negative CT scans do not need to be admitted for observation if the indication for admission is solely for neurologic observation.

Central Obesity Can Double the Risk of Death in Patients With Coronary Artery Disease

One of the largest studies of its kind has found that people with coronary artery disease (CAD) and central obesity, measured by waist circumference and waist-hip ratio, are at higher risk for death than people whose fat collects elsewhere. The effect was observed even in patients with a normal body mass index (BMI). The findings of this analysis were published in the May 10, 2011, issue of *Journal of the American College of Cardiology*.

The researchers reviewed the literature from 1980 to 2008 and asked experts in the field for unpublished data on patients meeting the inclusion criteria: 1) CAD at baseline; 2) measures of waist circumference or waist-hip ratio; 3) mortality data; and 4) a minimum follow-up of 6 months.

The final sample consisted of 15,923 subjects with CAD involved in 5 studies from the United States (Rochester, Minnesota, San Francisco, California), Denmark, France, and South Korea. There were 5,696 deaths after a median follow-up of 2.3 years. Central obesity was associated with mortality (hazard ratio

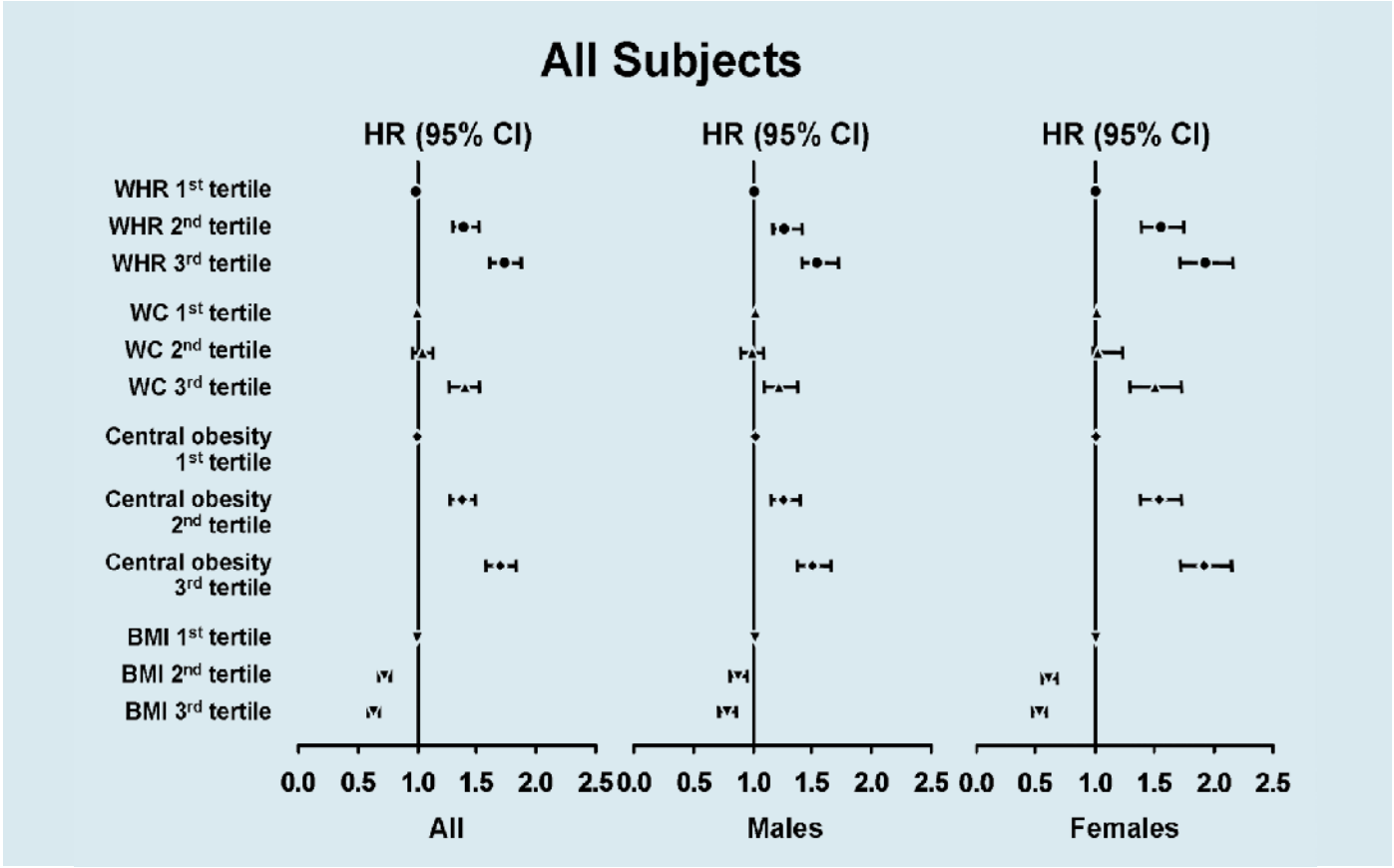

Figure 1. *Mortality on the basis of tertiles of measures of central and total obesity in all subjects. BMI indicates body mass index; CI, confidence interval; HR, hazard ratio; WC, waist circumference; WHR, waist-hip ratio.* Reprinted, with permission, from *J Am Coll Cardiol.* 2011;57:1877-86.

[HR], 1.70), whereas BMI was inversely associated with mortality (HR, 0.64). Central obesity was also associated with higher mortality in the subset of subjects with normal BMI (HR, 1.70) and BMI of 30 kg/m^2 or higher (HR, 1.93) (Figures 1 and 2). Thus, the researchers found that those with CAD and central obesity, measured by waist circumference and waist-hip ratio, had up to twice the risk of dying.

The question of which measure of obesity better predicts survival in patients with CAD is controversial. The findings refute the obesity paradox, a puzzling finding in many studies that show that patients with a higher BMI and chronic diseases such as CAD have better survival odds than normal-weight individuals. In this analysis, the researchers suspected that the obesity paradox was occurring because BMI is not a good measure of body fatness and gives no insight into the distribution of fat. The report noted that visceral fat has been found to be more metabolically

Points to Remember

- The question of which measure of obesity better predicts survival in patients with coronary artery disease (CAD) is controversial.
- Researchers at Mayo Clinic and 4 collaborating institutions examined the association of central obesity (measured by waist circumference and waist-hip ratio) and total obesity (measured by body mass index [BMI]) with mortality in CAD patients.
- In a sample of 15,923 subjects with CAD, researchers found that central obesity but not BMI is directly associated with mortality.

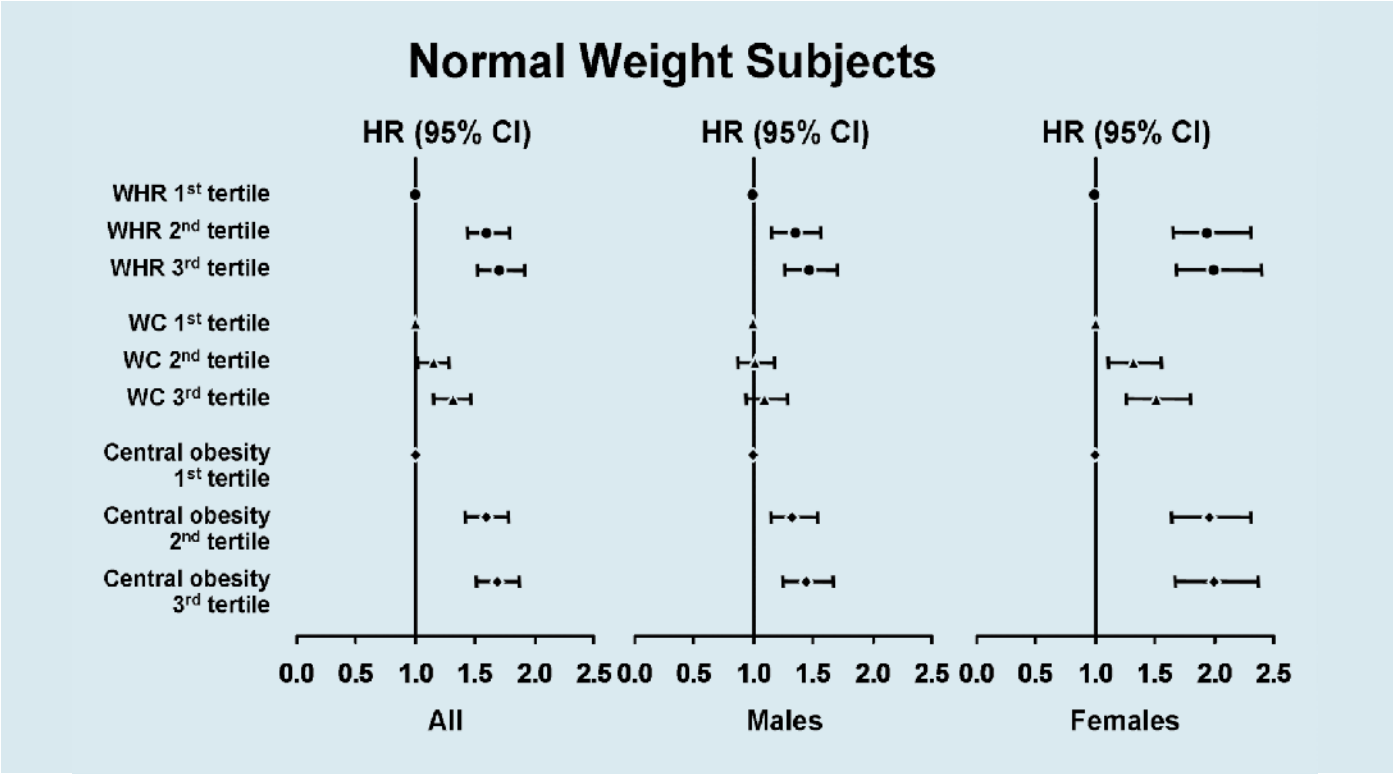

Figure 2. *Mortality on the basis of tertiles of measures of central obesity in normal-weight subjects. BMI indicates body mass index; CI, confidence interval; HR, hazard ratio; WC, waist circumference; WHR, waist-hip ratio.* Reprinted, with permission, from *J Am Coll Cardiol.* 2011;57:1877-86.

active, producing more changes in cholesterol, blood pressure, and blood glucose. However, people who have fat mostly in other locations in the body, specifically, the legs and buttocks, do not show this increased risk.

Mayo researchers suggest that physicians counsel CAD patients who have normal BMIs to lose weight if they have a large waist circumference or a high waist-hip ratio. These measures are easy to use, as they require only a tape measure and 1 minute to measure the perimeter of a patient's waist and hips.

Physician Update

An e-mail newsletter and a physician video blog. Visit www.mayoclinic.org/medicalprofs for more details.

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Clinical Update

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- Clinical trials
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Education Opportunities

Mayo Clinic Symposium on Concussion in Sport
September 28-29, 2012, Scottsdale, Arizona

Concussion is a major public health priority that transcends age, gender, and sport. This state-of-the-art symposium highlights the epidemiology of concussion in sport; the pathophysiology of concussion; sideline and outpatient clinical evaluation; standard and novel diagnostic strategies; and implementation of return-to-activity guidelines. The format includes platform lectures, small group workshops, panel discussions, and live 2-way remote audio/video concussion evaluations using robotic teleconcussion technology. The faculty is composed of scientific and clinical experts in the field of concussion from Mayo Clinic and leading US academic medical centers.
For information or to register, phone 480-301-4580.

Individualizing Medicine 2012: Transforming Patient Care With Genomics
October 1-3, 2012, Rochester Minnesota

This conference will explore the promise and challenges of incorporating genomics tools into clinical care. These emerging technologies are already changing the way we diagnose and treat disease. With the rapid pace of discovery and translation, Mayo Clinic hosts this conference to discuss the clinical implications and what it means for the patient. For more information, visit http://individualizingmedicineconference.mayo.edu.

15th Annual Mayo Clinic Internal Medicine Update: Sedona 2012
October 11-14, 2012, and October 25-28, 2012, Sedona, Arizona

Mayo Clinic's 15th Annual Internal Medicine Update: Sedona 2012 is a unique 4-day course offering 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. For information or to register, phone 480-301-4580.

86th Annual Clinical Reviews
October 29-31, 2012, and November 12-14, 2012, Rochester, MN

Clinical Reviews seeks to update physicians on the latest recommendations involving the medical subspecialties important for the primary care physician through a comprehensive program consisting of lectures, panel and roundtable discussions on problems of general interest in various areas of medicine, surgery, and pediatrics relevant to clinical practice. For information or to register, phone 800-323-2688.

Movers and Shakers in Neurology: Epilepsy and Movement Disorders
November 3, 2012, Jacksonville, Florida

This program is intended for neurologists, physicians in internal medicine, family practice and general practice, pediatricians, physician assistants, nurses, and allied health professionals who are involved in the care of patients with seizures, epilepsy, and movement disorders. There have been significant advances in the understanding and management of these disorders. This course will address the gap between these advances and their application in the treatment of epilepsy and movement disorders. The course will consist of an interactive and didactic format, including multimedia presentations, and will allow audience participation. Additionally, this course will offer opportunities for participants to ask questions about the cases discussed and/or present their own cases to the faculty panels. For information or to register, phone 904-307-2605.

To view all continuous professional development opportunities offered by Mayo Clinic, visit www.mayo.edu/cme/.

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