MUSCLE DAMAGE CONNECTED WITH PELVIC ORGAN PROLAPSE

Researchers do not endorse more elective C-sections based on findings

The study—appearing in the February issue of the journal Obstetrics & Gynecology and funded by the National Institute of Child Health & Human Development, part of the National Institutes of Health—found major defects of the levator ani, an important muscle that supports the bladder and uterus, among 55 percent of women with prolapse and just 16 percent of women who don’t have prolapse.

“Our findings are an important step forward in the search to identify what causes pelvic organ prolapse and subsequent difficulties with other problems, such as incontinence,” says lead author John O. L. DeLancey, M.D., the Norman F. Miller Professor of Obstetrics and Gynecology at the U-M Medical School and director of pelvic floor research.

“The next step is for researchers to look at ways of preventing and treating these injuries of the levator ani muscle in order to reduce the rate of pelvic organ prolapse later in life,” he says.

Pelvic organ prolapse can mean the falling of the bladder, uterus, vagina or lower bowel. One of the most common effects of the condition is urinary incontinence—that is, the inability to control the release of urine. Many women with prolapse experience a protrusion or bulging in the vaginal area. The condition is common; one of nine women has surgery to correct prolapse and other pelvic floor disorders in her lifetime.

The U-M researchers studied 151 women with prolapse and compared them with 135 women who do not have prolapse. MRI was used to determine the extent of damage to the levator ani muscles. The women’s vaginal closure force at rest and while contracting her pelvic muscle also was measured.

Women with prolapse were found to have a much higher rate of major levator ani damage than women without prolapse (55 percent compared with 16 percent). When they asked women to contract their muscles, the muscles were 40 percent weaker in women with prolapse.

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CRANIAL BASE TUMORS: SYMPTOMS, DIAGNOSES AND TREATMENT

New surgical techniques and treatment options are helping patients live longer and more fully.

**Lateral Cranial Base**

Most lateral cranial base lesions present with seemingly innocuous symptoms: hearing loss, tinnitus, and/or pain. The key is unilaterality. If a patient complains of unilateral hearing loss or a sensation of aural fullness, otoscopy, tuning fork testing and audiometry can help ascertain if the loss is conductive or sensorineural. If there is no obvious etiology, an imaging study is usually indicated.

Likewise, persistent unilateral tinnitus may indicate a lateral cranial base lesion. Unilateral pulsatile tinnitus, in particular, can be due to glomus tympanicum or jugulare tumors, arteriovenous malformations, skull base vascular problems, or other rare tumors.

The most common cranial base neoplasm is a vestibular schwannoma (acoustic neuroma) and usually presents with a combination of unilateral sensorineural hearing loss and tinnitus. Other lesions to be considered include meningioma, cholesteatoma, chondrosarcoma, endolymphatic sac tumor, epidermoid cysts, and hemangioma.

Unilateral otalgia is a common complaint, often without an obvious etiology. If it is persistent, thorough evaluation is warranted. Neoplasms of the temporal bone, the infratemporal fossa, and the nasopharynx can present with ear pain. Neoplasms of the upper aerodigestive tract, such as laryngeal, pharyngeal or tonsillar carcinoma can result in pain referred to the ear. Workup for persistent otalgia should involve an imaging study of the cranial base and neck, and/or upper airway endoscopy.

Unlike unilateral hearing loss and tinnitus, facial paralysis is seldom ignored. The most common cause of acute facial paralysis is Bell’s palsy, which has an excellent prognosis, recovering to normal or near normal in about 87% of cases. It is critical to remember, however, that facial paralysis can also be caused by cranial base or parotid neoplasms. Indicators include slow onset paralysis, fluctuating facial weakness, and lack of recovery.

**Anterior Cranial Base**

The most common symptoms of tumors of the anterior cranial base are nasal congestion, epistaxis, facial pressure mimicking sinusitis, or propstosis. These complaints suggest nasal cavity or paranasal sinus neoplasms. Visual acuity change, diplopia, anosmia, personality changes, or temporal masses may occur with intracranial lesions but will be seen in advanced stages of nasal and sinus tumors. Those presenting with clear, but unexplained rhinorrhea should be tested for cerebrospinal fluid using the beta-2 transferrin analysis. Patients may present with one or more complaints, depending upon the location of the lesion. Should a tumor be suspected, a CT scan will help with the diagnosis. Patients with unexplained facial pain should be investigated with an MRI to evaluate for intracranial pathology.

To provide the optimal approach to skull base tumors in the anterior, middle and posterior skull base regions, coordination of care is recommended and should involve both neurosurgeons and subspecialists in otolaryngology and neuro-otology. This allows for the wide circumferential resection of skull base tumors and for the prevention of cerebrospinal fluid fistulae with vascularized tissue flaps.

**Dr. Lawrence J. Marentette (photo right)**

Dr. Lawrence J. Marentette has fellowship training in craniomaxillofacial surgery from the University of Zurich, Switzerland and specializes in anterior skull base lesions and facial reconstruction. He received his M.D. from Wayne State University and also completed his residency there.

**Dr. H. Alexander Arts**

Dr. H. Alexander Arts is a graduate of Baylor College of Medicine. He completed his residency at the University of Washington and has fellowship training in otorhinolaryngology and neurotology at the University of Virginia. Dr. Arts specializes in lateral and posterior skull base lesions. His clinical interests range from cranial base surgery and cochlear implants to general ear surgery, Meniere’s disease, and facial nerve disorders.

**Dr. Jason Heth**

Dr. Jason Heth’s clinical interests include skull base surgery, complex cranial reconstruction, CSF leaks and glioma treatment. His research efforts include participation in clinical trials to treat gliomas and brain metastasis as well as quality of life issues for brain tumor patients. Dr. Heth received his M.D. from the University of Iowa, completed his residency at the University of Iowa Hospitals and Clinics, and received a fellowship for Skull Base Neurosurgery at the University of Arkansas for Medical Sciences.

**Dr. Stephen Sullivan**

Dr. Stephen Sullivan specializes in adult neurosurgery at the University of Michigan Medical Center and is an expert in anterior cranial base surgery and endoscopic intracranial surgery. His clinical interests include meningiomas, brain tumors, pituitary tumors, spinal cord tumors, Arnold Chiari malformation and Von-Hippel-Landau syndrome, among others. Dr. Sullivan received his M.D. from the University of Chicago and completed his residency at the University of Michigan.

**Dr. Greg Thompson**

Dr. Greg Thompson has been instrumental in the development of hearing preservation techniques in acoustic neuroma surgery and he leads the University of Michigan Neurovascular program. He received his M.D. from the University of Kansas, completed his residency at the University of Pittsburgh and received a research fellowship for Neurological Disease and Stroke from the National Institutes of Health. Dr. Thompson’s specialty is adult neurosurgery. Arteriovenous malformations and carotid endarterectomy/carotid occlusive disease are among his many clinical interests.
New Treatments and Ongoing Research

The Cranial Base Program at the University of Michigan is exploring and creating innovative treatment options for patients.

Induction chemotherapy has been used to downstage large tumors prior to resection. The result is an improvement in surgical salvage and local control of disease.

Biological markers are now being studied to advance the scope of practice with such tumors. Tumors are being evaluated for the presence of erbB2 and EGFR and the use of Cetuximab and Trastuzamab have been incorporated into practice. In addition, U-M researchers are studying the use of novel agents in skull base tumors, including mTOR inhibitors in patients with advanced sinonasal carcinomas.

Intensity modulated radiotherapy (IMRT) uses radiation fields whose intensity varies across the field, depending on the thickness of the target and the existence of critical organs or noninvolved tissue in their paths. Multiple beams of varying intensity allow a relatively uniform dose in an irregularly shaped target while avoiding a high dose to the surrounding structures. The anatomy of the skull base is complex and contains many critical, radiation-sensitive organs, e.g., the salivary glands, the mandible, and the pharyngeal musculature. In the cases of nasopharyngeal and paranasal sinus cancer, critical normal tissue that may be partly spared using IMRT include the inner and middle ears, the temporomandibular joints, temporal brain lobes, and the optic pathways.

These advances, coupled with earlier diagnoses and a multidisciplinary approach to treatment can mean fuller, longer life for patients with cranial tumors.

FIND MORE ON THE WEB
www.med.umich.edu/cranialbase
Obesity is taking a hefty toll on the health of children and young adults, leaving more Americans facing the burden of a lifetime of diabetes care and management.

A new study—published in the December issue of *Diabetes Care*—finds that the number of children and young adults with diabetes who were hospitalized from 1993 to 2004 increased 38 percent. During that period, hospital charges for diabetes care for children and young adults also swelled, from $1.05 billion in 1993 to $2.42 billion in 2004.

Plus, researchers say, rates of hospitalization were higher among young women with diabetes than for young men.

Joyce Lee, M.D., MPH  
Assistant Professor and Pediatric Endocrinologist  
Child Health Evaluation and Research (CHEAR)  
U-M Division of General Pediatrics

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Lead study author Joyce Lee, M.D., MPH, assistant professor, pediatric endocrinologist and member of the Child Health Evaluation and Research (CHEAR) Unit in the U-M Division of General Pediatrics, says these findings reflect the recent epidemic of childhood obesity and the increasing burden of diabetes among young adults.

“The number of young adults hospitalized with diabetes in the U.S. has increased significantly over the past decade, along with the rate of childhood obesity,” says Lee. “Today’s young adults experienced childhood and adolescence in the leading edge of the childhood obesity epidemic in the 1970s and 1980s. Our findings suggest that we are now just beginning to see the first manifestation of a related ‘diabetes epidemic’ among these young adults.”

For the study, Lee and her colleagues used the Nationwide Inpatient Sample—a nationally representative annual sample of discharges from nonfederal, short-term, general and other specialty hospitals in the U.S.—to access trends from 1993 to 2004 in hospitalizations associated with a diabetes diagnosis.

Among other trends, the study reported a rapid growth in health care expenditures as the result of diabetes-related hospitalizations. In 2004 alone, hospital charges were estimated to be $924 million for Medicaid, and $849 million for private payers.

The number of young adults hospitalized with diabetes in the U.S. has increased significantly over the past decade, along with the rate of childhood obesity.
“With the growing epidemic of childhood obesity and increasing trends in type 2 diabetes among young adults, the economic burden of diabetes will only continue to rise, affecting public and private insurance plans alike,” says Lee.

Lee says this study points to the need for further research to examine trends in diabetes prevalence among young adults, as well as how the U.S. childhood obesity epidemic may further amplify such trends in health care. Those trends—and their associated costs—also “may provide third-party payers with a strong impetus to cover more services focused on disease prevention and the treatment of childhood obesity,” she says.

In addition to Lee, co-authors are: from the University of California, San Francisco: Megumi J. Okumura, M.D.; and from the University of Michigan C.S. Mott Children’s Hospital: Gary L. Freed, M.D., MPH, Percy and Mary Murphy Professor of Pediatrics and Child Health Delivery, and chief of the Division of General Pediatrics; Ram K. Menon, M.D., professor, Department of Pediatrics and Communicable Diseases, and director of Pediatric Endocrinology; and Matthew M. Davis, M.D., M.A.P.P., associate professor of general pediatrics and internal medicine, and associate professor of public policy at the Gerald R. Ford School of Public Policy.

This study was supported by the National Institutes of Health (National Institute of Child Health and Human Development) Pediatric HSR Training Grant, and the Clinical Sciences Scholars Program.

The biostatistics core of the Michigan Diabetes Research and Training Center was funded by the National Institute of Diabetes and Digestive and Kidney Diseases Grant.

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Radiation for cancer treatment involves targeting intense beams in a very precise fashion to a relatively small area. But despite efforts to align a patient beforehand, a cough, a wiggle, a deep breath or any other number of small movements could dramatically alter where the treatment is being delivered.

To help eliminate the error associated with treating a moving target, the University of Michigan’s Radiation Oncology department has begun using a new system designed to detect in real time the location of a tumor. The system, called the Calypso 4D Localization System, will be used within the U-M Comprehensive Cancer Center to guide treatment during external beam radiation therapy for prostate cancer. U-M is the first cancer center in Michigan to purchase the device and one of a few cancer centers in the country involved in the clinical study evaluated by the U.S. Food and Drug Administration.

“During the treatment, if there’s any change in the prostate’s location, we’ll know instantly and can correct the treatment. We know these movements occur, but presently we have no way of detecting them during the treatment,” says Howard Sandler, M.D., professor of radiation oncology and urology at the U-M Medical School.

With the new Calypso System, radiation oncologists implant three small electromagnetic sensors, about the size of a grain of rice, into a patient’s prostate. The sensor is a passive device until it is coupled with the Calypso System during treatment. The sensor is implanted in a simple outpatient procedure, similar to a biopsy. Currently, doctors implant gold seeds in the prostate, which show up on X-rays to mark where the radiation needs to be delivered. But the X-rays
“During the treatment, if there’s any change in the prostate’s location, we’ll know instantly and can correct the treatment. We know these movements occur, but presently we have no way of detecting them during the treatment.”

represent the prostate’s location only at the moment in which they were taken. If the patient coughs or takes a deep breath, the prostate could move.

The Calypso System and the implanted transponders generate electromagnetic signals that tell the radiation therapist when the tumor target is perfectly aligned. A computer system allows the therapist to monitor in real time where the prostate is, noting if it moves outside the area targeted to receive radiation. If it moves outside that zone, the therapist can stop the treatment and either wait until the prostate moves back or reposition the patient.

Typically, patients who receive radiation are carefully positioned on the table, at times using restraints around the ankles to prevent leg or pelvis movement. Small tattoos and laser guided lights help the technician align the patient in a consistent location. One-third of the treatment session can involve positioning the patient.

Once positioned, patients typically have X-rays taken to show where the prostate is sitting. From day to day, a prostate tumor can move more than one centimeter—a big difference when pinpoint beams of radiation are being delivered. The Calypso System eliminates the need for X-rays, exposing patients to less ionizing radiation and removing one more step out of the daily radiation therapy process. Prostate cancer patients can receive radiation daily for six to eight weeks.

U-M was among the first centers to test the Calypso System in an FDA clinical study, enrolling 10 patients. The device will now also be used as part of a research protocol. Calypso Medical currently has clearance from the FDA only for prostate cancer, although U-M radiation oncologists hope to study the device in other cancer types as well.

More than 1.2 million Americans a year receive radiation treatment for cancer. According to the American Cancer Society, 218,890 men will be diagnosed with prostate cancer this year and 27,050 will die from the disease.

FOR MORE INFORMATION call Cancer AnswerLine at 1-800-865-1125 or visit www.mcancer.org
In addition, about 52 percent of the women in the study with prolapse recalled having forceps used during childbirth, nearly twice the amount (about 27 percent) of women in the study who do not have prolapse who remembered that forceps were used. Thirty-one percent of women with prolapse reported a family history of the condition, compared with 13 percent of the women without prolapse.

The researchers from the Department of Obstetrics and Gynecology have joined forces with a colleague in the U-M College of Engineering, James A. Ashton-Miller, Ph.D., who has helped to create the intricate computer simulations necessary for understanding how the levator ani muscles are damaged. The computer modeling is a vital part of this line of research, DeLancey notes.

The senior author of the paper is Ashton-Miller, Ph.D., director of the Biomechanics Research Laboratories. The researchers are asbestos research scientist, Mechanical Engineering Department, U-M College of Engineering, and senior research scientist, U-M Institute of Gerontology; and Daniel M. Morgan, M.D., Dee E. Fenner, M.D., Rohna Kearney, M.D., Kenneth Guire, M.S., Janis M. Miller, R.N., A.N.P., Ph.D., Hero Hussain, M.D., Wolfgang Umek, M.D., and Yvonne Hsu, M.D. All are from the pelvic floor research group at U-M. Kearney also has an appointment with University College Hospital, London, and Umek has an appointment at Medical University, Vienna, Austria.