Yoga has gained increased popularity for the promotion of both mental and physical health. A 2012 national survey found that approximately 10 percent of U.S. adults (21 million) practiced yoga. Matthew T. Drake, M.D., Ph.D., with Endocrinology, Diabetes, Metabolism, and Nutrition at Mayo Clinic’s campus in Rochester, Minnesota, says: “Importantly, yoga has found significant traction among more older adults, with a recent report that more than 20 percent of U.S. yoga practitioners are older than 60 years, perhaps in part due to reports that the regular performance of yoga has the potential to improve balance and to limit falls.

The relative safety of yoga in at-risk populations, however, remains largely undetermined. Thus, between 2001 and 2014, nearly 30,000 visits to U.S. emergency rooms were related to yoga-associated injuries, with 13 percent of injuries occurring in those age 65 years or older. Further, injury rates in the older adults increased from 6.9 to 57.9 per 100,000 participants over this same time frame.

“However, it has been difficult to estimate and characterize the yoga-specific associated risks, define the at-risk populations for yoga-associated injuries, and identify potential protective measures to limit injuries.”

Mehrsheed Sinaki, M.D., M.S., with Physical Medicine and Rehabilitation at Mayo Clinic’s campus in Minnesota, comments: “Whether the effects of yoga on the skeleton are beneficial or harmful remains a subject of debate. While a recent report suggested that daily yoga exercises may increase bone mineral density over two years, it was not clear that fracture risk was diminished. Further, a recent systematic review identified the musculoskeletal system as the most common site of yoga-associated injuries. Given both that many yoga exercises involve significant spinal flexion, extension and torsion and that many yoga adherents are aged and...
thus likely to be at increased fracture risk, it is of potential concern that some yoga exercises may surpass the biomechanical competence of the spine and result in vertebral compression fractures (VCFs).”

Jad G. Sfeir, M.D., with Endocrinology, Diabetes, Metabolism, and Nutrition at Mayo Clinic’s campus in Minnesota, explains: “To address this concern, we recently published a study in the European Journal of Physical Rehabilitation Medicine where we evaluated 33 consecutive patients with back pain that began after yoga exercise. Plain radiographs and medical records were reviewed to ascertain the relationship between the development of acute pain with associated VCFs and the yoga exercise. Nine patients met all criteria. All patients described a yoga-associated spinal flexion exercise as causative of the acute back pain that preceded their VCF diagnoses.

“Consistent with the increased popularity of yoga in the general population, six of the nine people had initiated yoga without a medical recommendation. Collectively, the group included eight women and one man. Median age was 66 years (range, 53 to 87 years), and eight people were Caucasian. The primary basis for presentation in all people was back pain, which ranged from four to 48 months in duration. VCF occurred one to 72 months after yoga exercise initiation, with four patients having fractures within one year of starting yoga. VCFs were identified in the thoracic (n = 6), lumbar (n = 4) and cervical (n = 1) spine.

“Dual energy X-ray absorptiometry (DXA) assessment performed at a median of 10.5 months prior to the index VCF showed that only four patients had osteoporosis by bone mineral density criteria, while one additional patient was classified as having osteoporosis due to a history of a prior fragility fracture. In only one patient was a secondary cause (primary hyperparathyroidism) for osteoporosis identified. Notably, four patients sustained a VCF in the setting of normal or near-normal bone mineral density.”

Dr. Sinaki highlights: “Spinal flexion exercises are common in yoga and produce increases in both torque pressures and compressive mechanical loading forces applied to individual vertebral bodies. These forces may be additive or multiplicative and result from a diminished ability of the intervertebral disks to absorb the simultaneous combination of forces from upper body weight, spinal flexure muscle contraction and spinal longitudinal ligament strain.

“Importantly, these issues may be particularly acute in older people, in whom age-associated degenerative changes in the intervertebral disks are common. While there is good evidence that appropriate exercise and rehabilitation programs can significantly reduce fracture risk, the incorporation of safe exercise practices is essential for balancing progressive skeletal loading activities within biomechanical limits. Accordingly, the implementation of personalized exercise programs, ideally aimed at strengthening both the back extensor and core abdominal muscles to increase overall balance and stability while simultaneously avoiding excess spinal strain, becomes crucial.

“The figure (Figure, page 1) demonstrates yoga poses that generally should be avoided in at-risk patients given the extreme flexion, extension and torsional strains involved. Also included in the figure are yoga poses that will increase balance and muscle strengthening without imposing significant spinal forces.”

Dr. Drake concludes: “In sum, yoga has unfortunately been misconceived as a one-size-fits-all prescription based on scientific and media reports that continue to advertise yoga as a purely bone protective activity. Instead, the cornerstone for fracture prevention and benefit from yoga should be the appropriate selection of patients and provision of an appropriate yoga poses prescription.”

For more information
Ethanol Ablation for the Treatment of Cystic and Predominantly Cystic Thyroid Nodules

With the increased use of high-resolution neck ultrasonography, thyroid nodules are commonly detected in clinical practice. When a thyroid nodule is cystic, the American Thyroid Association advises that pure cysts are of negligible malignancy risk (less than 1 percent) and partially cystic nodules with no suspicious features are considered very low suspicion (less than 3 percent risk of malignancy). Once malignancy has been excluded, treatment paths are dictated by the presence or absence of symptoms, such as compressive symptoms.

Marius N. Stan, M.D., with Endocrinology, Diabetes, Metabolism, and Nutrition at Mayo Clinic’s campus in Rochester, Minnesota, says: “Treatment options for symptomatic benign cystic or predominately cystic thyroid nodules include needle aspiration, minimally invasive techniques or surgical resection. With needle aspiration the recurrence rates are high (60 to 90 percent). Although surgical management is definitive, it can be associated with complications — leading some patients to decline this treatment option. In addition, in some patients (because of medical comorbidities) surgery is contraindicated.

“In these clinical scenarios, a minimally invasive treatment option, such as percutaneous ethanol injection (PEI) under ultrasound guidance, generally should be considered. With thyroid cyst PEI, the ethanol results in permanent tissue damage with subsequent necrosis, fibrosis and thrombosis of cyst wall blood vessels.”

M. Regina Castro, M.D., with Endocrinology, Diabetes, Metabolism, and Nutrition at Mayo Clinic’s campus in Minnesota, says: “We recently published a study in Mayo Clinic Proceedings where we determined the safety and efficacy of PEI in the treatment of cystic thyroid nodules.” Nicole M. Iñiguez-Ariza, M.D., a research fellow with Endocrinology, Diabetes, Metabolism, and Nutrition at Mayo Clinic’s campus in Minnesota, explains: “In the study, safety was defined as either no adverse events or minor adverse events such as temporary pain. Efficacy was defined as symptom relief, reduction in nodule volume by 50 percent or more, or both. Twenty patients with cystic thyroid nodules were treated with PEI; eight patients had pure thyroid cysts and 12 patients had complex cystic thyroid nodules — nodules that had more than 50 percent cystic component.”

Robert A. Lee, M.D., with Radiology at Mayo Clinic’s campus in Minnesota, notes: “The largest median diameter of the thyroid cyst was 4.5 cm (range, 2.3 to 8.0 cm); the median volume before PEI was 19.6 mL.

Figure. Example of a thyroid cyst before and at follow-up after percutaneous ethanol injection (PEI). Panels A and B, transverse and longitudinal views of cystic nodule before PEI; 1.4 x 1.4 x 2.7 cm and volume of 2.77 cc. Panels C and D, transverse and longitudinal views of the cystic nodule 12 months after PEI; 1.1 x 0.85 x 0.88 cm and volume of 0.43 cc (84 percent volume reduction).
The median amount of cystic fluid drained prior to PEI was 13.5 mL, and the median amount of ethanol administered was 3 mL (range, 0.5 to 20 mL). At follow-up (median follow-up was two years), 89 percent of patients were asymptomatic, and 70 percent had a 50 percent or greater reduction in nodule volume (Figure, page 3). The median decrease in volume was 75.6 percent. Four patients (20 percent) had mild and temporary side effects such as vagal reaction, slight pain and bleeding into the cyst.”

Dr. Castro concludes: “Our study demonstrates that PEI is a safe and effective treatment option in patients with large, benign, symptomatic cystic nodules. In the era of minimally invasive treatments and shared decision-making, the availability of PEI for treatment of otherwise benign thyroid disease is an attractive treatment option. Our findings can be used to counsel patients interested in alternative treatment options to surgery.”

For more information

Artificial Pancreas: The Journey Continues

Among the various types of diabetes, type 1 diabetes is the most common type to be associated with complete or near complete lack of endogenous insulin secretion and require a basal-bolus insulin therapy program. Such insulin delivery could be achieved either through multiple daily insulin injection (MDI) or an insulin pump. MDI or insulin pump therapy guided by conventional blood glucose meters was implemented in the Diabetes Control and Complications Trial, which demonstrated that improved glycemic control was associated with decreased target organ damage. Trial results were published in the New England Journal of Medicine in 1993. However, the therapy was associated with glucose variability with daily hyperglycemia and hypoglycemia. Thus, unless blood glucose is measured frequently and insulin delivery is modified to respond to changes in glucose status, the basal-bolus insulin programs significantly impact daily life for patients with type 1 diabetes (Table, page 5).

Yogish C. Kudva, M.B.B.S., an endocrinology consultant at Mayo Clinic’s campus in Rochester, Minnesota, says: “The development and maturation of continuous glucose monitoring to provide real-time glucose measurements every five minutes, the development of insulin pumps and insulin analogs, and the acceleration in the speed of computing have all combined to make an artificial pancreas (AP) that is capable of 24/7 modulation of insulin delivery a practical solution for patients with type 1 diabetes.

“In 2005, the Food and Drug Administration (FDA) established a critical pathway for approval of therapies for type 1 diabetes. The critical pathway mechanism empowered the FDA to work with sponsors to develop clinical...
trials of experimental therapies with the aim of expediting approval. Through this pathway, the low-glucose insulin suspend system (530G) manufactured by Medtronic was approved by the FDA in September 2013—just 90 days after submission of the application.

“The next significant development in the field was the FDA approval of the hybrid closed loop system (670G) in September 2016. This system was also approved 90 days after submission of the application. The trial involved 124 people and was a single-arm three-month study. The study showed an 8.2 percent increase in time spent in target glucose range (70 to 180 mg/dL) and 44 percent and 11 percent respective decrease in times spent in the hypoglycemic and hyperglycemic ranges. However, simultaneous with the approval, the FDA encouraged conduct of a randomized clinical trial to test the 670G system.”

Medtronic is currently conducting a multi-center randomized trial that will involve more than 1,100 patients at about 30 clinical centers, most in the U.S. and some abroad. Patients from three different cohorts (listed below) will be randomized to use the 670G AP system or persist with their current therapy:

• Continuous subcutaneous insulin infusion (CSII)
• Continuous glucose monitoring sensor-augmented insulin pump (SAP)
• Multiple daily insulin injection (MDI)

Dr. Kudva comments: “Mayo Clinic in Rochester, Minnesota, is a site for this study and is currently enrolling patients. The trial will seek to demonstrate superior glucose control compared to the control arms. The MDI cohort has not started patient enrollment. Trial duration will be six months. Following their participation, patients can enter an extension phase. Details of this period are being developed at this time.

The NIH has funded four academic center-industry partnerships to develop more AP options for patients with type 1 diabetes. Dr. Kudva explains: “Of the four partnerships, the University of Virginia effort is currently the most advanced. This consortium will conduct a randomized controlled trial that will use the Dexcom G6 CGM System integrated with the Tandem t:slim X2 insulin pump. The trial will randomize 168 patients at seven medical centers in the U.S. to SAP or the Tandem AP system with Basil-IQ technology. Enrollment started in July 2018. Patients enrolled can be on SAP, CSII or MDI. Following a run-in period that will be of variable duration depending on patient characteristics, patients will be randomized on a 2-to-1 basis to six months of AP or SAP. Following their participation, patients can enter an extension phase.

“This randomized controlled trial seeks to show superior glucose control with the AP system. The advantages for patients seeking enrollment include free access to advanced therapeutic technology, guaranteed supplies for the duration of the study, engagement with the study team and active participation in the research process with the ability to provide feedback to improve the patient-oriented features of the system. A negative factor for those who participate in this study would be the time spent during research visits.”

Dr. Kudva continues: “At Mayo Clinic, we are also initiating studies aimed at developing the next-generation AP that will include nonglucose signals impacting glucose control such as physical activity and emotional stress. Such data will be captured during a state-of-the-art AP study of nine weeks duration. This study is expected to start in December 2018. Subsequently, we hope to conduct clinical trials of the next-generation AP systems. This is an exciting time for therapeutic device development for type 1 diabetes. Mayo Clinic in Rochester, Minnesota, is delighted to be an active site in this clinical therapeutic research space.”

For more information

Medtronic Diabetes. Multi-center Trial in Adult and Pediatric Patients With Type 1 Diabetes Using Hybrid Closed Loop System at Home. ClinicalTrials.gov.

<table>
<thead>
<tr>
<th>Complex insulin administration programs</th>
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<tbody>
<tr>
<td>670G = hybrid closed loop system</td>
</tr>
<tr>
<td>AP = artificial pancreas</td>
</tr>
<tr>
<td>CSII = continuous subcutaneous insulin infusion</td>
</tr>
<tr>
<td>MDI = multiple daily insulin injection</td>
</tr>
<tr>
<td>SAP = continuous glucose monitoring sensor-augmented insulin pump</td>
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Table. Basal–bolus insulin programs significantly impact daily life for patients with type 1 diabetes, unless blood glucose is measured frequently and insulin delivery is modified to respond to changes in glucose status.
A 37-year-old woman was referred for evaluation of a right adnexal mass in the setting of severely elevated blood pressure and hypokalemia. She was previously healthy and had regular menses since age 11. She had four healthy pregnancies without any complications and had completed childbearing. Four months prior to presentation, her blood pressure during a routine physical exam was 96/54 mm Hg, which was consistent with past blood pressure readings.

One month prior to the initial evaluation, the patient developed menometrorrhagia and sought care from her local gynecologist. At the initial assessment, her blood pressure was 232/105 mm Hg. A physical exam revealed a solid right adnexal mass. Endometrial biopsy showed no evidence of hyperplasia or carcinoma. Subsequent assessment by a local nephrologist included a normal renal artery ultrasound. Computed tomography (CT) of the abdomen and pelvis revealed a large complex solid and cystic right adnexal mass (7.5 by 7.5 by 6.5 cm), located anterior to the uterus and superior to the urinary bladder (Figure 1). There was no abdominal or pelvic lymphadenopathy, and the adrenal glands appeared normal bilaterally.

Laboratory evaluation (Table) showed potassium of 2.7 mmol/L (reference range, 3.6 to 5.2 mmol/L), serum aldosterone of 47 ng/dL (reference range, less than 28 ng/dL), plasma renin activity of 76 ng/mL/hr (reference range, 0.25 to 5.82 ng/mL/hr) and estradiol of 379 pg/mL (reference range, 15 to 350 pg/mL). The patient was started on clonidine 0.1 mg twice daily, metoprolol 50 mg twice daily, spironolactone 50 mg twice daily and potassium chloride 20 mEq three times a day. Despite multiple antihypertensive medications, her blood pressure remained uncontrolled. The patient was then referred to Mayo Clinic for further evaluation and management of the right adnexal mass, secondary aldosteronism and menometrorrhagia. CT angiography was obtained and ruled out stenosis of the intrarenal arteries. During the initial visit at our institution, her blood pressure was 193/133 mm Hg. Lisinopril 5 mg daily was added to the regimen. The following day, after the second dose of lisinopril, the patient’s blood pressure was 90/60 mm Hg and she was experiencing lightheadedness. A renin- and estradiol-producing ovarian tumor was suspected.

The patient underwent laparoscopic right oophorectomy. A 2-cm vertical infraumbilical skin incision was made to avoid morcellation of this hormonally active tumor. The peritoneal surfaces, omentum, liver and bowel peritoneum were all normal. The uterus and cul-de-sac peritoneum appeared normal, as did the left fallopian tube and ovary. The right ovary contained a 9-by-7.5-by-6.5-cm mass that was completely covered with normal ovarian surface (Figure 2, page 7). There was a sizable portion of the ovary at the periphery of this mass that appeared normal. The right fallopian tube appeared normal, indicating no spread of the tumor beyond the ovary. The specimen was resected and placed

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**Blood test** | **Reference range** | **Before surgery** | **1 day after surgery**
--- | --- | --- | ---
Potassium | 3.6-5.2 mmol/L | 2.7 mmol/L | 4.4 mmol/L |
Creatinine | 0.6-1.3 mg/dL | 0.80 mg/dL | 0.5 mg/dL |
Serum aldosterone | < 28 ng/dL | 47 ng/dL | 8.4 ng/dL |
Plasma renin activity | 0.25-5.82 ng/mL/hr | 76 ng/mL/hr | 2.9 ng/mL/hr |
Cortisol | 7-25 mcg/dL | 14 mcg/dL |
Estradiol | 15-350 pg/mL | 379 pg/mL | < 10 pg/mL |
Metanephrine, free | < 0.50 nmol/L | < 0.20 nmol/L |
Normetanephrine, free | < 0.90 nmol/L | 0.33 nmol/L |
FSH | 1.8-5.1 IU/L (luteal) | < 0.3 IU/L (luteal) |
LH | 1.2-12.9 IU/L (luteal) | < 0.3 IU/L (luteal) |
Prolactin | 4.8-23.3 ng/mL | 7.4 ng/mL |
Testosterone, total | 8-60 ng/dL | 19 ng/dL | < 7.0 ng/dL |
Testosterone, bioavailable | 0.8-10 ng/dL | 3.4 ng/dL | < 0.7 ng/dL |
HCG | < 5.0 IU/L | < 0.5 IU/L |
AFP | < 15 ng/mL | 6.4 ng/mL |
CA 125 | < 35.0 U/mL | 13 U/mL |

**Table.** Laboratory evaluation results. Abbreviations used: AFP, alpha-fetoprotein; FSH, follicle-stimulating hormone; HCG, human chorionic gonadotropin; LH, luteinizing hormone.
in a large bag and removed through the infraumbilical incision. There were no intraoperative complications. Histopathological evaluation demonstrated a steroid cell tumor of the ovary, not otherwise specified (NOS), with no cytologic atypia (Figure 3).

One day after surgery, her blood pressure was 138/95 mm Hg with clonidine monotherapy. Laboratory studies showed normalization of serum potassium (4.4 mmol/L), serum aldosterone (8.4 ng/dL) and plasma renin activity (2.9 ng/mL/hr), and the estradiol level was undetectable. The patient will return for follow-up imaging and laboratory studies in three months.

Discussion
As highlighted in articles in the *American Journal of Surgical Pathology* and the *Journal of Ovarian Research*, steroid cell tumors are exceedingly rare sex cord-stromal tumors of the ovary. Sex cord-stromal tumors comprise three steroid cell tumor subtypes (steroid cell tumors, NOS; stromal luteomas; and Leydig cell tumors) and account for 5 percent of ovarian tumors and 2 percent of malignant ovarian tumors. As opposed to Leydig cell tumors, steroid cell tumors, NOS, lack crystals of Reinke in the cytoplasm.

Steroid cell tumors typically affect adults with a mean age at diagnosis of 47 years, although cases in young girls (2 to 13 years old) have been described. Approximately 75 percent of steroid cell tumors produce steroid hormones. The most common symptoms include hirsutism and virilization occurring in 56 to 77 percent of patients. Estrogen secretion is reported in 6 to 23 percent of patients. Steroid cell tumors have also been associated with Cushing syndrome in 6 to 10 percent of patients. An elevated renin level, which can produce hypertension and hypokalemia, also has been reported. Although ovarian steroid cell tumors are usually benign, approximately 25 to 43 percent of steroid cell tumors are malignant.

The diagnosis of steroid cell tumors may be challenging. In addition to careful history, physical examination and biochemical testing, CT imaging may identify an adrenal or ovarian mass. Likewise, transabdominal and vaginal ultrasound can be useful in evaluating ovarian size and morphology. If no obvious mass is found on imaging studies, as highlighted in a recent article in the *Journal of Clinical Endocrinology & Metabolism*, venous sampling of the adrenal and ovarian veins may localize small steroid-producing tumors.

Similar to other ovarian stromal tumors, surgery is the main treatment for ovarian steroid cell tumors with a goal to achieve a complete resection. Conservative surgery with unilateral oophorectomy and proper staging generally should be performed in women with stage I disease who desire future fertility. For women who have completed childbearing, total abdominal hysterectomy with bilateral salpingo-oopho-
rectomy and complete surgical staging is indicated. Hormonal levels should be monitored as part of the patient's postoperative follow-up. Adjuvant chemotherapy should be based on the histologic appearance of the tumor and on its surgical staging.

For more information
