Cardiac arrhythmias are a major public-health problem in the United States, contributing to mortality as well as a diminished quality of life. New procedures and techniques for managing these difficult conditions are improving the outlook for many patients, with the UCLA Cardiac Arrhythmia Center a national leader in this effort.

Ventricular arrhythmias cause the majority of sudden cardiac deaths in the United States — some 300,000 each year. Approximately 150,000 new cases of atrial fibrillation are diagnosed annually, often after a patient suffers a stroke, which is five times more likely in people with the condition. Standard treatments for arrhythmias — including medications, pacemakers and implantable
**UCLA Clinical Updates**

Learn about the Latest Advances from UCLA

**Polycystic Kidney Disease**
The fragmentation of patient services for polycystic kidney disease has been a longstanding challenge for both PKD patients and healthcare providers. At UCLA, a multidisciplinary team offers comprehensive care.

**Pulmonary Arterial Hypertension**
Increased research efforts into pulmonary arterial hypertension have yielded significant advances in the field of pulmonary vascular disease, and new therapies offer hope of better outcomes.

**UCLA Brain PET in Westlake Village**
Brain PET can often provide a level of diagnostic certainty that is not possible with other imaging technologies. UCLA Nuclear Medicine is now offering a NeuroPET clinic in Westlake Village.

**MRI-guided Radiotherapy Enables Physicians to Target Tumors in Real Time**
UCLA is one of the first three locations in the world for the ViewRay MRI-guided radiotherapy system, and the first in the Western United States with the technology, which enables physicians to see and accurately target cancerous tumors and make immediate adjustments in treatment delivery as needed in real time.

**Ketogenic Diet Effective in Treating Pediatric Epilepsy**
While many individuals with epilepsy respond to pharmacologic treatment, 20 to 30 percent develop medically refractory epilepsy. Alternative nonpharmacologic treatments, including the ketogenic diet, can sometimes be more beneficial than further trials of seizure medications.

**Pediatric Growth Disorders**
UCLA is a major center for the evaluation and treatment of pediatric growth disorders and is among the leaders in advancing treatment of these conditions, having made significant contributions to hormone-dose monitoring practices.

**Pediatric ACL Injury Repair**
With both pediatric and sports-medicine orthopaedic surgeons working in collaboration, UCLA offers a full range of reconstructive options, including advanced techniques that preserve the integrity of the phys in younger patients, who have more growth remaining, and established reconstruction techniques suitable for teen and collegiate athletes who are closer to skeletal maturity.

**Immunodeficiency Diseases in Children**
In recent years, advances in immunology have contributed to an enhanced understanding of primary immunodeficiency disease (PID) and a greatly expanded number of disease-related genes. Dozens of major and minor immunodeficiency illnesses are now identifiable in children.

To download these and other clinical advances at UCLA Health, go to: uclahealth.org/clinicalupdates

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**News from UCLA Health**

**Immunotherapy drug to treat advanced lung cancer**
The largest study to date using immunotherapy to treat lung cancer has found pembrolizumab (Keytruda) to be safe and effective in arresting tumor growth in people with advanced non-small cell lung cancer.

uclahealth.org/immunotherapylungcancer

**Clot removal device improves outcomes in acute ischemic stroke**
A study led by a UCLA investigator finds that a new device to remove obstructing blood clots can significantly improve outcomes for people who suffer an acute ischemic stroke. The stent retriever device significantly reduced post-stroke disability and increased the percentage of patients who were independent in daily function after three months.

uclahealth.org/clotremoval

**Method helps to validate stem cells created in a lab**
Two UCLA stem cell researchers have received a patent for their method of verifying that stem cells created in a lab using adult donor cells have potentially reached a pluripotent state, which means they are capable of turning into any other cell in the body. Validating the pluripotent state of stem cells has become a critical step in ensuring that stem cell research studies are accurate.

uclahealth.org/labstemcells

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**Continuing Medical Education: Save the Date**

**Fifth Fetal Echocardiography Symposium at UCLA**

**When:** October 24, 2015

**Where:** Tamkin Auditorium, Ronald Reagan UCLA Medical Center

**What:** This program will review key aspects of how to optimize image quality, how to scan and evaluate the normal fetal heart, and how to evaluate abnormalities of the four-chamber view, outflow tracts and the three-vessel view.

**Cost:** $275 – Physicians / $150 – Sonographers/Nurses / $100 – Trainees

**Register:** Go to cme.ucla.edu/courses and select “Fifth Fetal Echocardiography Symposium”

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UCLA HEALTH.ORG 1-844-4UCLA6DR (1-844-482-5237)
Heart Disease in Women Presents Differently than in Men

Heart disease is the leading killer of women in the United States, with important and often overlooked physiological and clinical differences that distinguish it from the disease in men.

While most risk factors for heart disease affect both genders, some more actively promote the disease in women, says Karol Watson, MD, director of the UCLA Women’s Cardiovascular Center. “As physicians, we need to be aware of the risk factors that are especially important in women and be especially aggressive in identifying and addressing them,” Dr. Watson says. In particular, metabolic risk factors, which are risk factors often linked to overweight and obesity — including insulin resistance, overweight/obesity and high triglycerides — appear to be much more harmful to women’s hearts than men’s.

Traditional risk factors such as smoking, high blood pressure and high blood cholesterol can increase a woman’s risk of cardiovascular disease by at least 10-fold, notes Marcella Calfon Press, MD, PhD, co-director of the center. Studies also suggest that physical activity and healthful eating are particularly important for women. “The good news is that basic lifestyle changes can have dramatic impacts on a woman’s risk,” Dr. Calfon Press says.

Studies also have indicated that mental stress, anxiety and depression play a greater role in development of heart disease in women and are more likely to contribute to worsened cardiovascular-disease outcomes. “We need to take a holistic approach to counseling women on implementing lifestyle changes that will reduce stress levels and improve mood,” says Tamara Horwich, MD, co-director.

The presentation of coronary artery disease also tends to be different; a heart attack for a woman can be very different from what a man experiences. For men, “It’s like a bomb going off — you get a dramatic chest pain that sends you to your knees,” Dr. Watson says. “But for women, it tends to be more of a plaque erosion, which produces more subtle types of symptoms.” Because women’s symptoms are likely to be more atypical and vague — such as pain in the jaw, arm or neck, or simply nausea and fatigue — they are underreported and under-recognized, and consequently many women don’t receive a diagnosis that could bring them lifesaving therapies.

Because of this more subtle presentation — and the fact that tests for detecting heart disease have been based on studies done in men — diagnosis in women can be more challenging. Dr. Watson says. Stress tests tend to be less accurate in women, and an angiogram also is less reliable. A standard angiogram doesn’t show the microvessels that arise from the inside of the heart, supplying about one-third of the blood flow, and microvascular dysfunction is more common in women. In men, an angiogram tends to show discrete blockages in the coronary arteries. “That’s the way we’ve traditionally thought about heart disease, but that’s really male coronary artery disease,” Dr. Horwich says. “Women tend to have more diffuse disease in their coronary arteries, as well as diseases of their smaller vessels that aren’t visible on an angiogram.” Advanced imaging techniques, including specialized PET scans and cardiac MRI, are able to detect microvascular disease, she notes.

There are differences, too, in the realm of therapies. Risk, not gender, dictates the value of statin therapy, but low-dose aspirin is recommended in women only after the age of 65, according to American Heart Association guidelines. Women are more likely than men to have trouble tolerating statins and other medications, which doesn’t mean they shouldn’t receive the therapy if they are at the appropriate level of risk, but it may require adjusting doses.
New procedures and techniques are improving the outlook for many patients with cardiac arrhythmias. The UCLA Cardiac Arrhythmia Center also has developed new catheter-based technologies for managing VT.

STORY HIGHLIGHTS

- New procedures and techniques are improving the outlook for many patients with cardiac arrhythmias.
- The UCLA Cardiac Arrhythmia Center also has developed new catheter-based technologies for managing VT.

UCLA has a dedicated program for patients with inherited arrhythmia conditions such as Long QT Syndrome and Brugada Syndrome, who are prone to life-threatening ventricular arrhythmias.

(continued from cover)

cardioverter-defibrillators (ICDs) — are available, but when these treatment options fall short, the UCLA Cardiac Arrhythmia Center offers advanced treatment modalities such as complex catheter ablations and surgical options.

“There are significant limitations to pharmacologic approaches, both in their ability to manage the arrhythmia and their side effects,” says Kalyanam Shivkumar, MD, PhD, director of the UCLA Cardiac Arrhythmia Center. “Driven by the needs of patients who have come to us with complex arrhythmias from all over the world, we have developed new techniques for treating and curing arrhythmias.”

The center, for example, uses catheter-based ablation procedures to treat life-threatening and symptomatic arrhythmias. “Ablation is usually a good choice for symptomatic patients who have not been successfully managed pharmacologically,” says Noel G. Boyle, MD, PhD, the center’s director of cardiac electrophysiology labs. Dr. Boyle adds that many patients seen at UCLA for ventricular tachycardia (VT) often have been transferred from other hospitals after presenting with multiple shocks from their ICDs — called VT storms.

With the aid of advanced cardiac-mapping techniques pioneered by Dr. Shivkumar, the center’s team sends controlled electrical burns to cure arrhythmias from both inside and outside the heart. “Catheter ablation of ventricular tachycardia is a specialized procedure that aims to eliminate arrhythmogenic areas within scar tissue,” explains Roderick Tung, MD, director of the center’s specialized program in ventricular tachycardia. The UCLA team performs endocardial and epicardial ablations to manage these patients, with an overall success rate of about 70 percent. “We have one of the largest experiences of epicardial ablation of such patients, which is a technique that enables us to map and ablate the outer wall and lining of the heart by introducing a needle underneath the breastbone. This technique has been shown to improve outcomes in patients with recurrent VT,” Dr. Tung says.

The center also is a leader in developing new methods for eliminating VTs that arise from deep within the heart muscle. “By using coils, we have been able to find and embolize small blood vessels that feed the deep portion of the muscle wall to treat arrhythmias,” Dr. Tung says.

Another major development to treat arrhythmias involves neuromodulation therapy, including cardiac sympathetic denervation — cutting nerves that go to the heart. The center recently launched the Neurocardiology Research Center of Excellence to develop treatment options for patients with refractory ventricular tachycardia when death is imminent. “Neuromodulatory interventions represent a new avenue of therapies for treatment of ventricular arrhythmias,” says Marmar Vaseghi, MD, cardiac electrophysiologist and director of clinical and translational research for the center, who is helping to spearhead the effort. “Specifically, ablation on the surfaces of the heart has limitations in reaching substrates that may be lying within the heart muscle. The
cardiac sympathetic nerves initiate and maintain ventricular arrhythmias. Cardiac sympathetic denervation, a surgical technique involving removal of the lower third to half of the stellate ganglia and cardiac thoracic ganglia, has been shown to reduce the burden of life-threatening ventricular arrhythmias and defibrillator shocks in patients with recurrent arrhythmias and heart failure.”

To help patients with inherited arrhythmia conditions such as Long QT Syndrome and Brugada Syndrome, the center now has a dedicated program for patients who are at risk for life-threatening ventricular arrhythmias. “These patients often require extensive diagnostic testing and in some cases may need an implantable cardiac defibrillator (ICD) for prevention of sudden cardiac death, or they may benefit from interventions such as radiofrequency ablation or cardiac sympathetic denervation,” says Jason Bradfield, MD, director of the UCLA Inherited Cardiac Arrhythmia Program. “Most importantly, these patients need to be followed in a specialized clinic that offers comprehensive assessment and care, which may involve consultation by multiple providers during one visit.”

The newly established UCLA Inherited Arrhythmia Clinic provides this comprehensive care and will serve as a vital referral center for patients and their families with these complex disorders in California and nationally, Dr. Bradfield says.

“Driven by the needs of patients who have come to us with complex arrhythmias from all over the world, we have developed new techniques for treating and curing arrhythmias.”
What is meant by a chronic total occlusion of the coronary arteries, and how do CTOs develop?

CTOs are 100-percent obstructions of coronary arteries that have been present for more than three months. Typically, there is no downstream blood flow from the main lumen of the artery. They tend to develop in one of two ways. It can be as a silent heart attack, in which the patient experienced symptoms but didn’t seek care, or the symptoms were so weak that he or she didn’t realize what was happening and only later was discovered on an angiogram. The other way of developing a CTO is that a blockage progresses over time — going from 70 to 80 to 90 to 100 percent. When it gets to that point, the patient may or may not have any symptoms.

How commonly are CTOs discovered on a coronary angiogram, and what is the urgency of treating them?

In 10-to-20 percent of angiograms, patients have no blockages at all — the stress test was falsely positive or it turns out their symptoms are unrelated to the heart. Patients with blocked arteries undergoing a coronary angiogram have up to a one-third incidence of having a CTO. In terms of the urgency, some studies have shown that if you leave the CTOs untreated, these patients can have more damage to the heart muscle, potentially leading to congestive heart failure and a higher three-year mortality. On the other hand, successfully reopening a CTO in the presence of a viable heart muscle has been associated with improvement in symptoms, left ventricular function and survival.

Using advanced technology and specialized training, UCLA interventional cardiologists are improving outcomes of percutaneous coronary intervention for patients with chronic total occlusions of the coronary vessels. Ravi Dave, MD, director of interventional cardiology at UCLA, explains how a small number of centers are taking advantage of the new technology to advance treatment for a challenging problem.

Ravi Dave, MD
How has the approach to CTO treatment changed?

The way we are opening these blood vessels is completely different from what we were doing before. Previously, the focus was to go through the lumen of the artery and re-enter past the blockage. Now, we are much more comfortable creating a diversion within the wall of the artery. The artery wall has three layers, and sometimes the blockage in the lumen of the artery is so tight that the wires can’t poke through. So we create a breakage in the layers of the wall, then we go in and re-enter downstream of that 100-percent blockage. Once we’ve created that small diversion, we place a stent. So, instead of the artery running straight, we would turn a bit to the left, run parallel, turn back right and re-enter the artery.

What is required to perform this procedure?

It’s a complex angioplasty procedure that is not something every center can do. You need to have special training and specific technology. This includes special types of wires and balloons to negotiate through and open the 100-percent blockages. At UCLA, we have dedicated ourselves to the training and technology, and it has led to significant improvements.

How has this affected patient outcomes?

Before we had this technology, the rate of success at reopening CTOs nationally was less than 50 percent, and at UCLA it was about 60 percent. Now, with this combined percutaneous approach, our success rate at UCLA is more than 85 percent.

Which patients are candidates?

Any patient with a chronic total occlusion who has symptoms, or who has an abnormal stress test suggesting a reduced blood flow, may be a candidate. We don’t necessarily go after every CTO. We determine whether it’s causing the patient to have reduced blood flow in an area of the heart that’s not adequate, and the heart muscle has to be viable in that area. But if that’s the case and you open the blockage up, it has been shown that the patient’s symptoms improve, heart muscle function improves and patient survival goes up.

“Successfully reopening a CTO in the presence of a viable heart muscle has been associated with improvement in symptoms, left ventricular function and survival.”
Recent advances in cardiac catheterization have transformed the treatment of infants, children and adults with congenital heart disease (CHD). At UCLA, physicians in the Congenital Cardiac Catheterization Laboratory have pioneered efforts to enable heart valves to be replaced without surgery, as well as through minimally invasive procedures developed and performed in collaboration with cardiac surgeons.

“Many doctors are surprised to learn how much we can now achieve with valves, stents and closure devices,” says Daniel Levi, MD, director of the UCLA Pediatric Cardiac Catheterization Laboratory.

In the field of transcatheter valve replacement, the UCLA Congenital Cardiac Catheterization Laboratory has taken technology designed specifically for aortic-valve replacement and applied it to the replacement of dysfunctional mitral, tricuspid and pulmonary valves without open surgery — enabling patients to leave the hospital the next day. The laboratory also is a leading center for more common procedures used to treat congenital heart disease, including the use of stenting to open blockages, balloons to open valves and devices to close holes in the heart. For example, Dr. Levi notes, most atrial septal defects are now treated using transcatheter devices.

UCLA’s congenital cardiac catheterization lab is applying these advances to smaller patients and larger structural defects — in some cases taking premature infants and other newborns straight from the delivery room to the catheterization lab.
to perform the procedures. The lab also treats children of all ages and a large population of adult CHD patients, many of whom would not have survived their childhood without the recent advances.

Before the revolution in cardiac surgery that enabled surgeons to operate using cardiopulmonary bypass, “the majority of people born with severe forms of congenital heart disease died before reaching adulthood,” says Jamil Aboulhosn, MD, director of UCLA’s Ahmanson Adult Congenital Heart Disease Center. “Now, cardiac surgery has become the gold standard — replacing and repairing valves, transplanting hearts and lungs. But repeat surgeries come at a cost and carry risk. That has led to the current revolution in which we use catheters, balloons and various occlusion devices to perform interventions that previously required open-heart surgery. This has led to shorter hospital stays, less pain, more patient satisfaction and improved quality of life,” he says.

UCLA’s interventional cardiologists work closely with surgeons to minimize the morbidity and mortality risk for CHD patients, most notably in the development of hybrid procedures that combine catheter-based interventions with surgical approaches. For example, in cases where accessing the vein or the artery for a catheter-based procedure is difficult, the surgeon will make a small incision in the chest to provide access to the heart for the interventional cardiologist to use wires and balloons for a repair, then will suture and close the incision after the repair is complete.

“We all work as a team — interventional cardiologists, electrophysiologists, cardiothoracic and vascular surgeons, the OB/GYNs who diagnose conditions in utero, adult cardiologists, pulmonologists and interventional radiologists,”

For CHD patients who need surgery, there is a continuing trend toward improved outcomes in the most complex cases, says Brian Reemtsen, MD, chief of congenital heart surgery and chief of pediatric heart transplantation at UCLA. Most dramatic are the improvements seen in patients with hypoplastic left heart syndrome, one of the most common congenital heart defects, in which the left side of the heart fails to form correctly. “This is a disease that had a mortality rate as high as 25-to-30 percent even a few years ago and is now down to less than 10 percent at UCLA,” Dr. Reemtsen says. Another major advance at UCLA and elsewhere has been the use of tissue scaffolds for intra- and extra-cardiac repair of congenital heart defects, Dr. Reemtsen adds.

As advances in surgical and nonsurgical treatments continue to enable CHD patients to live longer lives, the importance of pediatric and adult surgeons, interventional cardiologists and other team members working together has become critical, Dr. Reemtsen notes. The Ahmanson-UCLA Adult Congenital Heart Disease Center was the first clinic of its kind in the United States, founded in 1980; today, there are an estimated 1.5 million adults in the United States with CHD.

“We all work as a team — interventional cardiologists, electrophysiologists, cardiothoracic and vascular surgeons, the OB/GYNs who diagnose conditions in utero, adult cardiologists, pulmonologists and interventional radiologists,”

“Patients who in the past wouldn’t have survived infancy are living longer and even having children of their own thanks to the advances in care,” says Dr. Aboulhosn. “The adult congenital population is growing, and many of them require repeat interventions. That means we need to work closely with our pediatric colleagues in treating these patients as they transition to adulthood, and to continue to improve on techniques that will minimize morbidity and improve outcomes.”
The ventricular assist device (VAD) becomes a “destination” therapy offering a potentially lifesaving option for some end-stage heart-failure patients. The UCLA advanced-heart-failure program is developing shared-care sites to assist community physicians in managing this growing patient population.

The emergence of the left ventricular assist device (VAD) as “destination” therapy rather than a temporary bridge to transplantation offers a potentially lifesaving option for end-stage heart-failure patients who are not candidates for transplantation. Moreover, the expected continued improvement and growing demand for VADs will be invaluable in meeting the needs of the advanced-heart-failure population in the face of the limited supply of donor organs, says Mario C. Deng, MD, medical director of the Advanced Heart Failure, Mechanical Circulatory Support and Heart Transplant Program at Ronald Reagan UCLA Medical Center.

“The ventricular assist device continues to improve as it moves into its second and third generations, to the point that it is now rivaling the one-year and five-year outcomes after heart transplantation,” Dr. Deng says. “Given that transplantation can’t come close to meeting the needs of the large advanced-heart-failure population, we need to spread the word that lifetime mechanical support is a very viable long-term option. And because we expect the demand for this therapy to grow dramatically in the years ahead, we are working with community physicians to develop a shared-care infrastructure to care for these patients.”

“For patients whose only option in the past would have been hospice, we can now offer the left ventricular assist device for destination therapy,” says Ali Nsair, MD, a UCLA interventional cardiologist and associate director of mechanical circulatory-support-device services. “To maximize the potential benefit of the therapy, we need to be engaged in their care earlier than in the past.” Dr. Nsair recommends that end-stage heart-failure patients who are no longer tolerating cardiac-protective medications, as well as older patients or those with co-morbidities that would make them poor transplant candidates, should be referred for evaluation and potential co-management with the UCLA heart-failure team.

When VADs were first introduced, in the 1960s, they were bulky and came with a significant risk of side effects that led to serious complications, Dr. Deng notes. In the ensuing years, the devices have become smaller, safer and more reliable, with fewer complications and improved quality of life and survival outcomes. But until 2010, they were offered only as a bridge to heart transplantation. That changed when the U.S. Food and Drug Administration approved the HeartMate II, a left ventricular assist device manufactured by Thoratec, for use as destination therapy.

“The VAD can now be used for patients who are not heart-transplant candidates,” says Richard Shemin, MD, Robert and Kelly Day Chair in Cardiothoracic Surgery, chairman of cardiothoracic surgery at Ronald Reagan UCLA Medical Center.
Medical Center and co-director of the UCLA Cardiovascular Center. “This third-generation device is very reliable compared to previous ones, with outcomes in certain patients that are as good as a heart transplant at two years.” He notes that more than 10,000 patients in the U.S. have had the VAD implanted as destination therapy, and that the devices are quite durable and selected patients have lived with them for a decade.

“For patients whose only option in the past would have been hospice, we can now offer the left ventricular assist device for destination therapy.”

“In many ways, the VAD market has mirrored the consumer electronics market — the devices have gotten smaller and battery support has gotten better,” says Murray Kwon, MD, UCLA cardiothoracic and transplant surgeon. “Decades ago, a VAD would hang outside the body and you would be connected to a console the size of a refrigerator — which might have been conducive to support for someone critically ill, but not very meaningful for patients who wanted to lead independent lives outside the hospital. Now, they are smaller, more implantable, and their controllers have shrunken to the point that many can be worn as a fanny pack, with batteries that last much longer between charges.”

Patients with VAD as destination therapy face specific challenges, including the need to be on anticoagulation therapy for life and to properly manage their driveline — where the power cord comes out of their skin and connects to the battery. To assist community physicians in managing this growing patient population, the UCLA advanced-heart-failure program is developing shared-care sites where practicing internists and cardiologists are trained in the intricacies of caring for patients, in collaboration with the UCLA team, pre- and post-VAD implant.

Within the next several years, Dr. Kwon says, a new generation of destination VADs may include implantable batteries that can be charged subcutaneously, eliminating the driveline and its associated risks. “Once we have a device that is fully implantable, it becomes a very attractive alternative to transplant,” Dr. Kwon says. “The options for destination therapy will only increase as these devices become smaller and better tolerated, and the burden for us as healthcare practitioners will be to identify appropriate candidates who would benefit from this therapy.”

When VADs were first introduced in the 1960s, they were bulky and came with a significant risk of side effects. Today’s devices, like this one for a UCLA patient, are much smaller, safer and more reliable, and they have been approved for use as destination therapy.
UCLA Physician Access Line

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