HARRINGTON HEART & VASCULAR INSTITUTE INNOVATIONS

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Patients deemed extremely elderly are a growing segment of the American public. The U.S. Census Bureau estimates that the number of Americans age 90 and older will quadruple by the year 2050.

As the population of older Americans grows, so, too, do the numbers of extremely elderly patients with aortic stenosis.

In the past, some structural heart disease experts have been hesitant to refer these patients for surgical procedures – even minimally invasive ones. However, recent studies are challenging these perceptions.

Results from the PARTNER I trial, published in the Annals of Thoracic Surgery in 2015, showed that transcatheter aortic valve replacement (TAVR) can result in acceptable short- and mid-term outcomes among patients age 90 and older.

Its investigators concluded that “age alone should not preclude referrals for TAVR in nonagenarians.” A single-institution study, also from 2015, reached a similar conclusion. Its group of 95 nonagenarian patients undergoing TAVR had a 30-day mortality rate of 3.2 percent – far less than the 14.5 percent mortality rate for this age group predicted by The Society of Thoracic Surgeons.

“When it comes to TAVR, advanced age alone is not a disqualifying factor. Our group confirmed that in a report that will appear soon in the American Journal of Cardiology,” says Guilherme Attizzani, MD, an interventional cardiologist and part of the Valve & Structural Heart Disease Center at University Hospitals Harrington Heart & Vascular Institute.

Dr. Attizzani and UH cardiac surgeon Basar Sareyupoglu, MD, recently had the opportunity to emphasize this point. Their patient, a 102-year-old woman, was admitted to UH Case Medical Center after a week of dizzy spells, shortness of breath and an episode of syncope. Her echocardiogram revealed severe aortic stenosis, with a peak gradient of 73 mmHg and a mean gradient of 40 mmHg.

The patient underwent a TAVR procedure under conscious sedation, as has been standard practice at UH since 2012. Although the minimalist approach to TAVR is used routinely in Europe, nearly 95 percent of U.S. hospitals still subject their TAVR patients to general anesthesia. The UH Harrington Heart & Vascular Institute heart team has pioneered the minimalist approach in the U.S. and recently reported the outcomes of the first 207 TAVR patients. Results show that the minimalist approach was not only safe and effective, but also significantly lowered costs and patients’ length of stay, compared with TAVR performed under general anesthesia. The Valve & Structural...
Success with 102-year-old patient shows the value of minimalist approach to TAVR among the extremely elderly

Heart Disease Center at UH has performed more than 600 TAVR procedures and is the nation’s first training site for the minimalist, percutaneous, conscious-sedation approach to TAVR.

Although research shows this approach benefits nearly all patients, it may have even more advantages for those who are elderly.

“Recovery is easier for patients who already may be debilitated or frail,” says Angela Davis, RN, BSN, Nurse Coordinator, Valve & Structural Heart Disease Center, who worked with this patient. “Many have impaired renal function. Not having to clear the medications used for general anesthesia can reduce their length of stay by up to a day. Patients this age may also be experiencing some dementia or memory loss. They don’t want to worry about anything that might exacerbate that.”

After her TAVR procedure, the patient’s echocardiogram showed normal aortic valve prosthesis structure and function, with no evidence of aortic valve regurgitation. “She’s now back to her normal routine,” Dr. Attizzani says.

For more information about the minimally invasive approach to TAVR employed at UH or to refer a patient, please call 216-844-3800.

2011: 20 procedures
2012: 31 procedures
2013: 67 procedures
2014: 150 procedures
2015: 216 procedures

TAVR VOLUME AT UH Harrington Heart & Vascular Institute
Dr. Dan Simon: I’m talking today with Dr. Sahil Parikh, one of our interventional cardiologists specializing in vascular medicine and endovascular therapy, who treats many patients with PAD. What is research telling us about the role of anti-thrombotic therapy for these patients?

Dr. Sahil Parikh: Sadly, PAD remains underdiagnosed by primary care physicians and cardiologists because many patients are asymptomatic despite evidence of obstructive atherosclerosis. PAD prevalence increases with age and concomitant cardiovascular risk factors. Most contemporary cardiovascular practices have a prevalence of upward of 30 percent. Moreover, the natural history of PAD can be misleading. Only a small percentage of patients with obstructive PAD will have severe enough symptoms to merit revascularization; however, up to 75 percent will go on to die from cardiovascular causes, primarily MI and stroke. An abnormal ankle brachial index (ABI) confers a 10-year risk of cardiovascular morbidity approaching 50 percent.

Because of the systemic nature of atherosclerosis, patients with PAD should be considered candidates for secondary prevention strategies that include aggressive risk factor modification and antiplatelet therapy. In fact, recently published data suggests that adherence with guideline-based medical therapy can reduce major adverse cardiac events and major adverse limb events (MACE and MALE, respectively) by over 40 percent. Unfortunately, we know that patients with PAD are undertreated with regard to the use of lipid-lowering and antiplatelet drugs, when compared with patients who have coronary artery disease. We simply have to do better.

Dr. Simon: With that in mind, tell me about the results of a new PAD subgroup analysis of the PEGASUS trial indicating that the addition of a second antiplatelet agent, the P2Y12 inhibitor ticagrelor, not only reduced major adverse cardiovascular events, but also reduced “limb-specific” events.

Dr. Parikh: As you recall, the PEGASUS-TIMI 54 trial evaluated the efficacy and safety of ticagrelor in patients with prior MI. It included 21,162 patients with prior MI (one to three years), who were randomized to ticagrelor 90 mg BID, 60 mg BID or placebo, all with low-dose aspirin. History of PAD was obtained at baseline. This new subgroup analysis focused on 1,143 patients with known PAD and looked at the occurrence of MACE (defined as cardiovascular death, MI or stroke) as well as MALE (defined as acute limb ischemia or peripheral revascularization for ischemia) during follow-up.
**Dr. Simon:** What did the subgroup analysis show?

**Dr. Parikh:** There are several remarkable findings. First, in the placebo or aspirin-only arm, those with PAD had higher rates of MACE at three years, compared with those without. These differences persisted after adjusting for baseline differences. Patients with known PAD randomized to aspirin only also had higher rates of acute limb ischemia (1.0% vs 0.1%) and peripheral revascularization procedures (9.15% vs 0.46%). Second, ticagrelor reduced MACE, but because of their higher absolute risk of MACE, patients with PAD had a greater absolute risk reduction of 4.1 percent, resulting in a highly favorable number needed to treat of only 25. The absolute excess of TIMI major bleeding was quite low at 0.12 percent, corresponding to a number needed to harm of NNH 834. Third, and perhaps most important, ticagrelor (doses pooled) reduced the risk of major adverse limb outcomes by 35 percent.

**Dr. Simon:** This is very impressive. Do you think this will change clinical practice? Are you initiating dual antiplatelet therapy in your patients with PAD?

**Dr. Parikh:** This adds to our knowledge that potent P2Y12 antagonists in patients with known PAD and MI may have strong grounds for prolonged therapy with ticagrelor on the basis of not just reduction of MACE but also MALE. However, I would caution against over-extrapolating these results. In the coming year, we expect results of the EUCLID study, which has randomized more than 13,000 PAD patients to either clopidogrel or ticagrelor monotherapy in secondary prevention, looking at the incidence of MACE and MALE after three years. Moreover, we’re humbled by the results of the SOCRATES trial, which was recently published in The New England Journal of Medicine. In this study, more than 13,000 patients were randomized to receiving ticagrelor or aspirin after ischemic stroke or TIA and were followed for achievement of a primary endpoint composite of stroke, MI or death at 90 days. There was no statistically significant difference between the two groups.

**Dr. Simon:** What about other antiplatelet agents, such as the PAR-1 thrombin receptor antagonist vorapaxar?

**Dr. Parikh:** That’s a great question, but we have incomplete clinical trial data to guide us here. The Clopidogrel vs. Aspirin in Patients at Risk of Ischemic Events (CAPRIE) trial compared clopidogrel 75 mg with aspirin 325 mg daily in approximately 19,000 patients with recent MI, recent ischemic stroke or PAD. The PAD group was large with 6,452 patients and included patients with claudication and an ankle brachial index value of 0.85 or less, history of claudication with previous peripheral bypass surgery, angioplasty or amputation. Clopidogrel was associated with an overall reduction of 8.7 percent in the primary endpoint of fatal or nonfatal ischemic stroke, fatal or nonfatal myocardial infarction or death from other vascular causes. In fact, clopidogrel appeared to be most effective in the PAD subgroup, reducing the primary endpoint by 23 percent. This result led to FDA approval of clopidogrel for secondary prevention of atherosclerotic events in patients with atherosclerosis, including those with PAD. EUCLID will evaluate ticagrelor vs. clopidogrel alone in patients with PAD. We’ll see if the results are similar to the retrospective findings in PEGASUS.
Patients at University Hospitals Harrington Heart & Vascular Institute have access to a new multidisciplinary center that provides coordinated evaluations and treatment options for aortic pathologies. The new Aortic Center, led by UH vascular surgeon Vikram S. Kashyap, MD, and UH cardiac surgeon Yakov Elgudin, MD, PhD, also draws on the expertise of other experienced vascular and cardiac surgeons, as well as interventional cardiologists and experts in cardiovascular medicine, imaging and genetics.

“Aortic pathologies are very often complex,” says Dr. Kashyap. “They require a multidisciplinary team with highly trained and experienced subspecialists working side by side.”

“Patients with aortic root and ascending aortic and arch aneurysms or dissections require long-term follow-up and frequently complex interventions on descending thoracic and abdominal aorta,” adds Dr. Elgudin. “Cardiac and vascular surgeons at our center work closely together to make sure the follow-up is provided and required interventions are performed in a timely fashion.”

Advanced imaging available at the Aortic Center includes coronary computed tomography angiography (CTA), magnetic resonance angiography (MRA), angiography and intravascular ultrasound (IVUS). Therapies include leading-edge surgical techniques, such as complex aortic root reconstructions (including valve-sparing aortic root replacement) and surgical reconstruction of ascending aneurysms, arch pathologies and thoraco-abdominal aneurysms. At the same time, the Aortic Center also offers innovative technologies in endovascular therapy, providing minimally invasive stent therapies for aneurysms, dissections and other aortic pathologies. Complex endovascular therapies include endovascular aortic repair (EVAR), fenestrated endovascular aortic repair (FEVAR) and thoracic endovascular aortic repair (TEVAR). To treat descending aortic aneurysms, the Aortic Center at UH offers the staged and combined surgical-endovascular “elephant trunk” procedure. In addition, the center offers surgical and stent-graft treatment options for type A and type B aortic dissections.

“We have extensive experience in endovascular therapies for abdominal aortic aneurysm (AAA), thoracic aortic aneurysm (TAA) and transcatheter aortic valve replacement (TAVR),” Dr. Kashyap says. “In addition, we have excellent results and large experience in treating acute aortic dissection.”

One hallmark of the new Aortic Center is its participation in clinical research. Appropriate patients treated for AAA or TAA with a Gore endovascular device are enrolled in the Global Registry for Endovascular Aortic Treatment (GREAT) registry, which is collecting 10 years of patient and device performance data. The Aortic Center at UH is also one of just 11 national sites participating in the Rehearsal clinical trial, a multicenter, randomized study to compare the performance of endovascular AAA procedures with and without prior rehearsal using a virtual
procedure rehearsal studio. Select AAA patients at UH are also enrolled in the LEOPARD (Looking at EVAR Outcomes by Primary Analysis of Randomized Data) trial. This post-market study aims to test which endovascular device approach is best for AAA patients – one that employs fixation of the endograft on the aortic bifurcation or one that relies on penetrating hooks and barbs for device fixation within the aorta.

**Beyond surgical and endovascular approaches, the Aortic Center at UH offers medical therapies for vasculitis and nonatherosclerotic occlusive disease of the aorta and branches.**

In addition, through the Center for Cardiovascular Genetics within UH Harrington Heart & Vascular Institute, the Aortic Center offers genetic evaluation and counseling for patients and families affected by Marfan’s syndrome and Loeys-Dietz syndrome and other aortopathies.

“This is the beauty of a ‘virtual center’ such as ours,” Dr. Kashyap says. “Each member or component within UH Harrington Heart & Vascular Institute continues to see patients at the usual venue. But then we collaborate across disciplines to review cases and get the best outcomes for our patients.”

If you have a patient who would benefit from the multidisciplinary approach of the Aortic Center at UH, please call Anette Martin at 216-844-3013. For emergency transfers, please call 216-844-1111.

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**Aortic Pathologies Treated at the Aortic Center**
- Aorto-annular ectasia
- Aortic root aneurysm
- Aneurysms of the ascending aorta, aortic arch, and descending thoracic and abdominal aorta
- Thoraco-abdominal aortic aneurysms
- Aortoiliac occlusive disease
- Acute and chronic aortic dissections
- Penetrating aortic ulceration
- Intramural hematoma
- Aortic atherosclerosis
- Marfan’s syndrome
- Loeys-Dietz syndrome
- Vasculitis

For more information from University Hospitals, visit [UHDoctor.org](http://UHDoctor.org). This new online resource center features relevant content for physicians and other clinicians, covering clinical practice, patient care, research and education. Visit [UHDoctor.org](http://UHDoctor.org) today.
At University Hospitals Harrington Heart & Vascular Institute, patients with cardiovascular disease have access to more than 90 clinical trials. Here are some details about three leading-edge trials under way here:

**Momentum 3**: This trial is comparing a next-generation left ventricular assist device (LVAD), HeartMate 3, with its predecessor, HeartMate 2, both as a bridge to heart transplantation and as destination therapy for patients with advanced refractory left ventricular heart failure. Investigators are determining whether the new device offers comparable survival and quality of life benefits as the older device, as well as whether the new, smaller device may reduce adverse events.

HeartMate 3 received CE Mark approval in Europe in October 2015. It uses magnetic levitation, allowing the device’s rotor to be suspended by magnetic forces. This design aims to reduce trauma to blood passing through the pump, reduce friction and “wear-and-tear” on the rotor and improve outcomes for patients. HeartMate 3 also provides pulsatility.

Heart failure specialist Guilherme Oliveira, MD, and cardiac surgeon Benjamin Medalion, MD, are leading the Momentum 3 trial at UH.

“I think HeartMate 3 is going to be a significantly better device, with less infection and less thrombosis,” Dr. Oliveira says. “It has no bearing, so it’s less thrombogenic and therefore likely safer. It has pulsatility, which we think will be beneficial to patients. Overall, I believe that this device will result in longer event-free survival compared with HeartMate 2.”
TACT 2: In 2013, the Trial to Access Chelation Therapy (TACT) 1 study showed a striking decline in recurrent cardiovascular events among post-MI diabetic patients, with results published in JAMA. Now, investigators on the TACT 2 study are seeking to replicate these findings among this high-risk population.

“The first TACT trial showed a modest benefit for all post-MI patients, but among diabetic subjects, a substantial improvement in survival free of recurrent heart disease was observed. This was a big surprise and has prompted a follow-up trial to validate these findings,” says interventional cardiologist David A. Zidar, MD, PhD, who is leading the TACT 2 trial at UH.

Patients eligible for the TACT 2 trial include people with diabetes, age 50 or older, who’ve had a prior MI. They’re randomly assigned to one of four groups: active chelation plus twice-daily high-dose oral multivitamins and multiminerals (OMVM); active chelation plus oral placebo; placebo chelation plus OMVM; and placebo chelation plus oral placebo. Chelation therapy (or placebo) sessions occur weekly for 40 weeks.

“This study could have significant ramifications for people with diabetes,” Dr. Zidar says. “Chelation is well-tolerated, but it is done weekly, so it does become a substantial commitment on the part of patients. And the design will also show us whether vitamins are an essential part of chelation therapy.”

RADIANCE-HTN trial: Methodological problems with the SYMPLICITY HTN-3 trial made the results difficult to interpret. Although the trial showed no differences between the catheter-based renal denervation and a sham procedure in addressing treatment-resistant hypertension, differing hypertension drug regimens and medication compliance rates confounded the results. The new RADIANCE-HTN trial aims to clear up these issues – potentially opening a new treatment avenue for millions of people with treatment-resistant hypertension.

Interventional cardiologist Sahil Parikh, MD, is leading the RADIANCE-HTN trial at UH, along with UH hypertension authority Jackson Wright, MD, PhD.

The new RADIANCE-HTN trial has two arms: Patients in the solo cohort are included if their hypertension is such that they can safely discontinue their hypertension medications for a short time. Patients with resistant hypertension are enrolled in the trio cohort. They discontinue their individual hypertension regimens and instead receive a single, three-medicine pill once a day. Both groups are randomly assigned to the denervation procedure with a new, ultrasound-based device, or to a renal angiogram “sham” procedure.

“The FDA has had a strong hand in designing this and other renal denervation trials, and we’re better positioned to get the answers we need,” Dr. Parikh says. “Treatment-resistant hypertension is an incredibly important problem. For carefully selected patients, this trial gives them options.”

If you have a patient whom you believe would benefit from any of these clinical trials, please contact Stacey Mazzurco, BSN, RN, CCRP, Director, Clinical Trials, at 216-844-3130 or Stacey.Mazzurco@UHhospitals.org.

HeartMate 2 and HeartMate 3 left ventricular assist devices. Images courtesy of St. Jude Medical.
Multidisciplinary approaches to managing coronary artery disease (CAD) are relatively rare.

“Patients are typically referred either to surgery or to percutaneous coronary intervention (PCI),” says Hiram Bezerra, MD, PhD, an interventional cardiologist with University Hospitals Harrington Heart & Vascular Institute. “That’s the model for 99 percent of hospitals.”

According to Dr. Bezerra, this model is long overdue for disruption. He and UH cardiac surgeon Yakov Elgudin, MD, PhD, are launching a new multidisciplinary Coronary Clinic at UH, with equal participation from surgeons and interventionalists. The goal is to create a deliberative process where all the best and most contemporary options for revascularization are considered.

“For patients with more complex anatomy, it’s important to use all the resources available,” Dr. Elgudin says. “It’s not uncommon that cardiologists and surgeons will disagree about the management of patients. By pulling people together, we can discuss issues directly and make the best possible decisions, given all the available options possible in the setting of a high-level quaternary center.”

In evaluating patients, the Coronary Clinic team relies not only on clinical experience, but also on newer evidence-based tools that bring outcomes data into the mix.

“There’s a lot of evidence in the literature today suggesting that you can make some of these decisions in almost a quantitative way,” Dr. Bezerra says. He references the SYNTAX and clinical SYNTAX risk score models, which were developed to predict the risk of adverse events.

“These scoring systems address the complexity of anatomy for intervention,” Dr. Bezerra says. “Our team will not only entertain qualitative conversations, we’ll also be able to systematically score patients for surgical risk vs. PCI risk in a way that is more reproducible.”

Advanced services provided to patients within the Coronary Clinic include minimally invasive coronary surgery done through a small thoracotomy.

“Advanced services provided to patients within the Coronary Clinic include minimally invasive coronary surgery done through a small thoracotomy. Other leading-edge options available within the Coronary Clinic are advanced approaches to chronic total occlusion (CTO) and protected PCI using the Impella LVAD to provide hemodynamic support. For percutaneous treatment of CTO, Dr. Bezerra uses a streamlined, methodical approach of advanced imaging evaluation to select the best strategy and leading-edge tools. “It really has become a subspecialty,” he says. “It’s not a matter of experience but specialization. Even highly experienced operators should consider referring patients to specialized CTO programs, because novel techniques have dramatically increased success rates of CTO interventions.”

Complex PCI procedures can now be performed with the safety of LV hemodynamic protection with the Impella device.

The catheter is advanced into the heart and connected to an external pump. It then aspirates blood from the left ventricle and releases it into the aorta, aiding the weakened heart muscle by increasing cardiac output.

“This is the high end of catheter-based therapy, and we are pleased to offer it to our most complex patients with CAD,” Dr. Bezerra says.

For more information about the new Coronary Clinic at UH or to refer a patient, please call Dr. Bezerra at 216-983-5746 or Dr. Elgudin at 216-844-3992 or 216-844-4004.
University Hospitals Harrington Heart & Vascular Institute has partnered with Procter & Gamble (P&G) to promote heart health to patients who might benefit from Meta Daily Heart Health, an over-the-counter supplement that can help lower total and LDL cholesterol. P&G is launching the product in the Cleveland area beginning this month. It contains 100 percent natural psyllium husk, and is available online nationally or at selected retailers in the Cleveland and Tampa areas as a powder mix; in convenient, easy-to-dose powder packets; and in capsules.

The key dietary ingredient in Meta Daily Heart Health is psyllium husk. The psyllium husk in Meta Daily Heart Health lowers cholesterol by forming a gel and trapping and eliminating some bile via the stool. In response, the liver removes cholesterol from the bloodstream to make more bile, lowering serum total and LDL cholesterol.

Randomized, double-blind placebo-controlled clinical studies have demonstrated that psyllium is a useful adjunct to dietary intervention, lowering total cholesterol (-4 percent to -6 percent) and LDL cholesterol (-5 percent to -9 percent). Greater reductions in total cholesterol (-15 percent) and LDL cholesterol (-20 percent) have been observed with psyllium in studies with a usual, unrestricted/uncontrolled diet.

For more information on Meta Daily Heart Health, visit MetaDailyHeartHealth.com.

\*Diets low in saturated fat and cholesterol that include 7 grams of soluble fiber per day from psyllium husk, as in Meta Daily Heart Health, may reduce the risk of heart disease by lowering cholesterol. One serving of Meta Daily Heart Health powder has 3.6 grams of this soluble fiber. One serving of Meta Daily Heart Health capsules has 1.8 grams of this soluble fiber.

References:
Marco Costa, MD, PhD, MBA, Named New President of UH Harrington Heart & Vascular Institute

University Hospitals Harrington Heart & Vascular Institute leadership has selected Marco Costa, MD, PhD, MBA, as its new President.

Dr. Costa succeeds Daniel I. Simon, MD, who served as the institute’s first President, and is now the President of UH Case Medical Center. Dr. Simon was pivotal in shaping and strengthening the institute into one of the premier institutes in the country, with more than 1,000 employees delivering the highest-quality of care in 18 hospitals across Northeast Ohio.

The appointment follows an extensive search for a highly qualified individual to lead the institute.

“Dr. Costa’s scientific accomplishments, combined with a talent for developing creative solutions to some of medicine’s biggest challenges, are valuable assets as he begins his new leadership role at UH Harrington Heart & Vascular Institute,” says Jeffrey Peters, MD, Chief Operating Officer, University Hospitals. “We look forward to the future of the institute with Dr. Costa and his team as we continue to deliver the highest-quality care and extraordinary experience to our patients.”

Since 2007, Dr. Costa has worked alongside Dr. Simon leading the Interventional Cardiovascular Center to become a regional market leader and a national center of excellence. He will continue his prominent medical practice treating patients with the most complex and advanced heart and vascular diseases through catheter-based, minimally invasive approaches.

Dr. Costa is among a select group of physician investigators whose work has helped change medical practice worldwide. He was one of the pioneers of drug-eluting stents, a revolutionary technology at the time and now standard treatment for coronary artery disease. His reputation as a world-class physician-investigator is supported by an impressive number of original manuscripts published in top scientific journals and invited lectures around the world. More recently, Dr. Costa helped develop intravascular optical coherence tomography, an imaging technology capable of acquiring micron-scale images of human blood vessels. He is currently leading global studies of new therapies for patients with valve disease and heart failure.

He is also actively engaged in promoting global health, having performed the first minimally invasive heart and vascular procedures in Uganda.

Dr. Costa received his executive MBA degree from the MIT Sloan School of Management, and has successfully applied modern principles of strategy and management during his tenure at the helm of UH’s Executive Office of Innovation. In his new role, Dr. Costa will oversee UH Harrington Heart & Vascular Institute’s clinical, educational, research and administrative programs. He will continue to serve as Chief Innovation Officer at University Hospitals.