INSIDE THIS ISSUE



Cleveland Clinic

# Cardiac Consult

Heart and Vascular News from Cleveland Clinic | 2019 | Issue 2

## How Data Science Is Shaping Cardiothoracic Surgery

– p. 4

# Dear Colleagues,

The clinicians who began building Cleveland Clinic's Cardiovascular Information Registry back in 1971 were farsighted individuals, but there was no way they could have imagined their efforts would one day serve as the underpinning of advanced data techniques like machine learning. Yet that's precisely what happened, as outlined in the cover story of this issue of *Cardiac Consult*.

Beyond growing into one of the world's largest and longest-running cardiovascular databases, the registry has provided invaluable longitudinal data to fuel sophisticated algorithms offering insights on everything from how to intervene in ischemic cardiomyopathy to advanced analysis of valve disease.

An essential player in these innovative uses of our registry has been our longtime Head of Clinical Investigations, Eugene Blackstone, MD. The cover story outlines how Gene's passion for new fields of statistical endeavor has led him to assemble a team of data experts who collaborate with our cardiothoracic surgeons to generate fresh practice insights from novel analyses of reams of clinical data. The beneficiaries have been patients here at Cleveland Clinic and around the world.

This issue also shares other developments from across our Heart & Vascular Institute, from the results of the Cleveland Clinic-led global WRAP-IT trial of an antibiotic-eluting envelope for cardiac implantable electronic devices to the management of a fascinating case of thoracic dystrophy. As always, we welcome your feedback and inquiries on collaboration.

Respectfully,

**Lars G. Svensson, MD, PhD**

CHAIRMAN | Sydell and Arnold Miller Family Heart & Vascular Institute

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In 2018, Cleveland Clinic was ranked a top U.S. hospital in *U.S. News & World Report*'s "Best Hospitals" survey. The survey ranks Cleveland Clinic among the nation's top 5 hospitals in 12 specialty areas, and the top hospital in heart care (for the 24th consecutive year) and urologic care.



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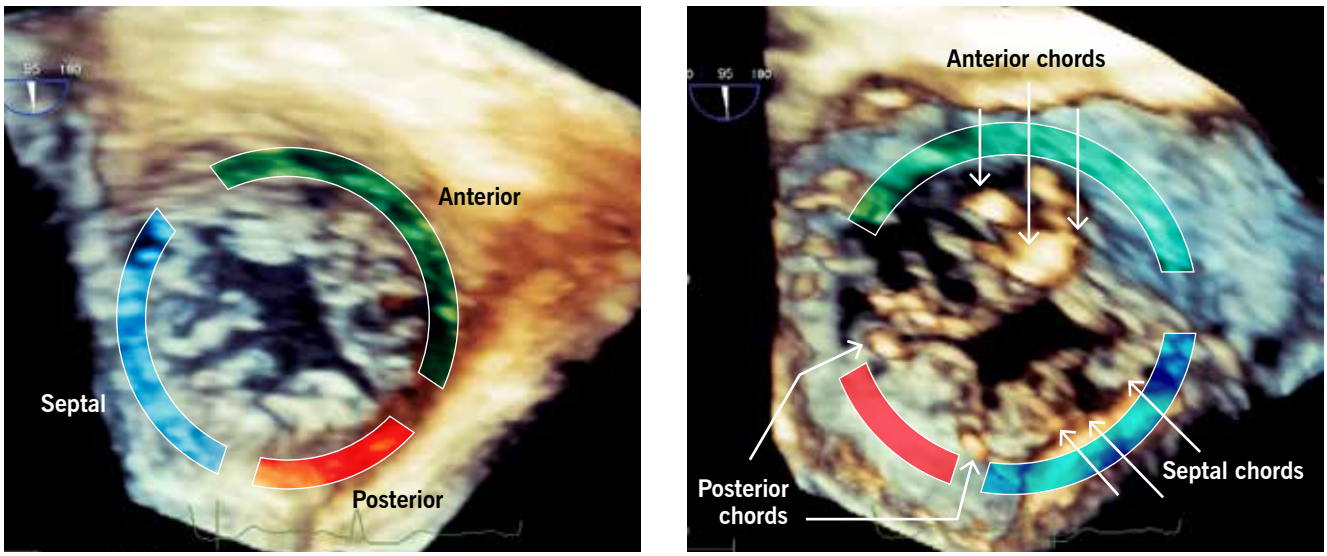
# Image of the Issue




3D transesophageal echo images showing atrial (left) and ventricular (right) views of the tricuspid valve in systole.

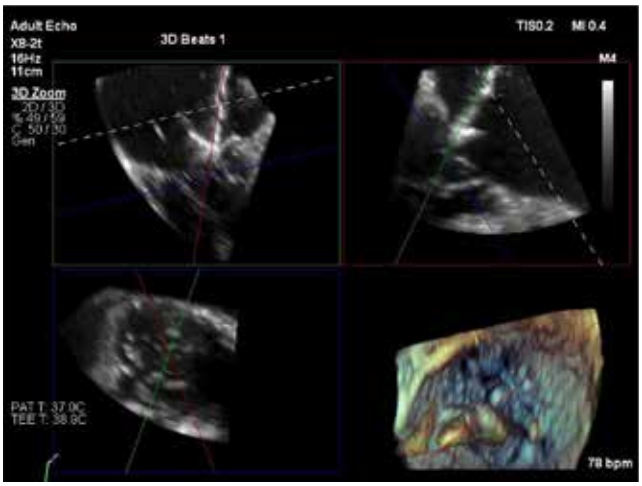
## 3D TEE OF THE TRICUSPID VALVE: A NEW WINDOW INTO COMPLEX, HIGHLY VARIABLE ANATOMY

The tricuspid valve is a complex, highly variable structure that has been historically challenging to image with transesophageal echocardiography (TEE). As percutaneous options for tricuspid valve interventions have increased, so has the need for high-quality tricuspid imaging for use in preprocedural planning and intraprocedural guidance.

Cleveland Clinic is using state-of-the-art three-dimensional (3D) TEE to obtain high-resolution images to detail tricuspid anatomy. The number of leaflets, orientation and subvalvular apparatus can be identified clearly, as demonstrated in the representative images above.

Furthermore, the use of live 3D multiplanar reconstruction has allowed us to provide highly detailed and accurate simultaneous 2D and 3D imaging for intraprocedural guidance of transcatheter tricuspid valve interventions, as reflected in the sample images to the right.

For patients, 3D TEE technology translates into provision of the highest-quality imaging available for both the diagnosis and treatment of complex valvular heart disease. ■

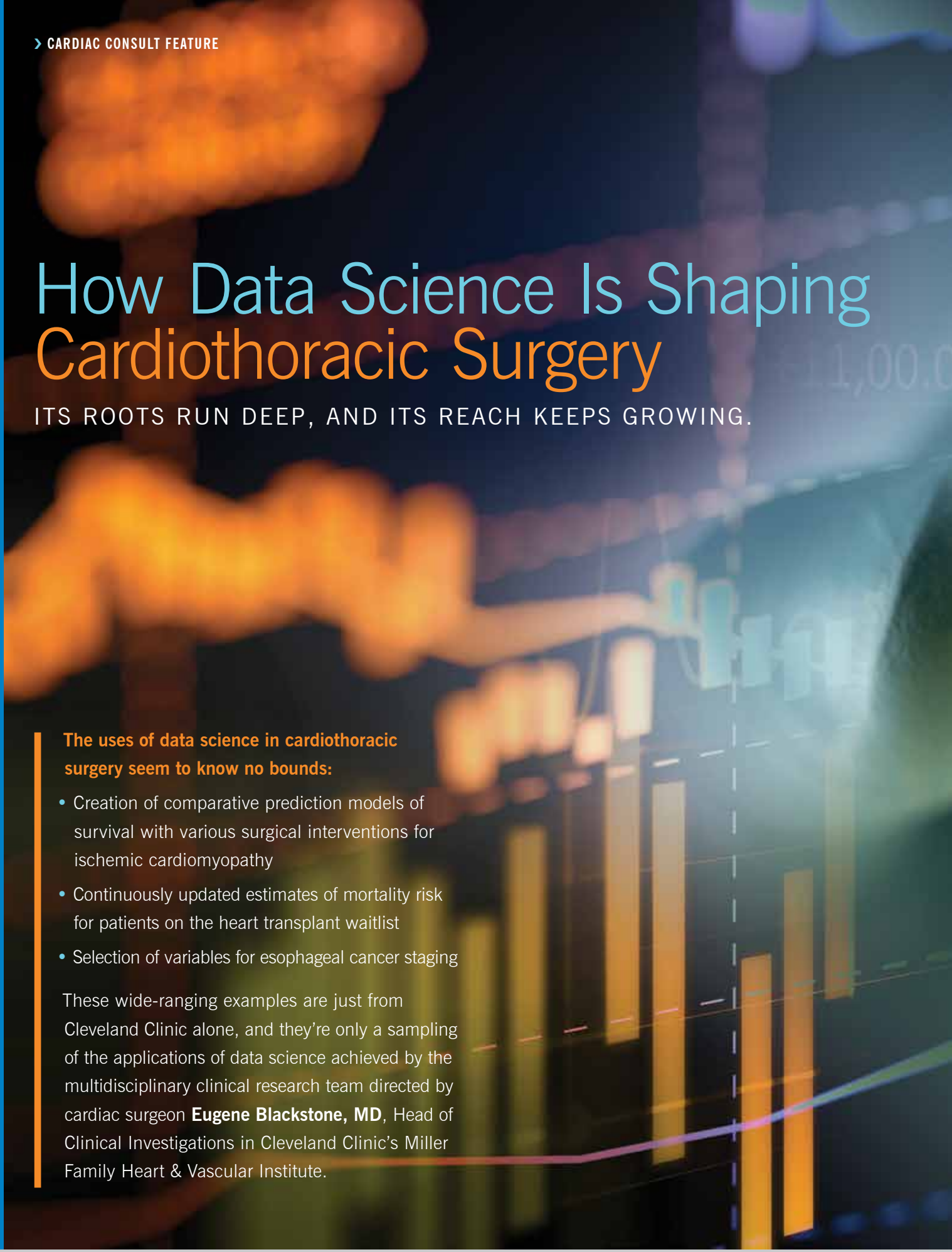



Live 3D multiplanar reconstruction allows for accurate, real-time 3D image guidance.

**Images and text supplied by Rhonda Miyasaka, MD, a staff physician in Cleveland Clinic's Section of Cardiovascular Imaging. Contact her at 216.442.2304.**

# How Data Science Is Shaping Cardiothoracic Surgery

## ITS ROOTS RUN DEEP, AND ITS REACH KEEPS GROWING.



**The uses of data science in cardiothoracic surgery seem to know no bounds:**

- Creation of comparative prediction models of survival with various surgical interventions for ischemic cardiomyopathy
- Continuously updated estimates of mortality risk for patients on the heart transplant waitlist
- Selection of variables for esophageal cancer staging

These wide-ranging examples are just from Cleveland Clinic alone, and they're only a sampling of the applications of data science achieved by the multidisciplinary clinical research team directed by cardiac surgeon **Eugene Blackstone, MD**, Head of Clinical Investigations in Cleveland Clinic's Miller Family Heart & Vascular Institute.

### Seeds planted decades ago

Yet they all can be traced back to a handful of consequential developments several decades ago.

First was the launch of Cleveland Clinic's Cardiovascular Information Registry, established in 1971 to collect data on every cardiovascular surgery patient at the institution. The result is the oldest and one of the largest computerized databanks of cardiovascular information, which has served ever since as the foundation of Cleveland Clinic's pioneering cardiovascular outcomes research. For instance, the registry was instrumental in confirming the internal thoracic artery as the conduit of choice for coronary bypass grafting, as reported by Loop and colleagues in a landmark 1986 *New England Journal of Medicine* publication.

Next was Dr. Blackstone's recruitment to Cleveland Clinic in 1997 as Head of Clinical Research for the Department of Thoracic and Cardiovascular Surgery. He arrived after many years at the University of Alabama at Birmingham, where he collaborated with John Kirklin, MD, a pioneer of data-driven cardiothoracic surgery research and practice who helped put the subspecialty in the vanguard of clinical outcomes analysis. Dr. Blackstone brought extensive statistical expertise and a passion for novel mathematical models and algorithmic approaches, which he was eager to apply to Cleveland Clinic's treasure trove of data.

Another key development was the start of a long-standing collaboration between Cleveland Clinic and IBM to construct an optimal medical record based on ontology, or the metaphysical concept of grouping things according to similarities and differences. "The aim was to capture information on patients in terms of values or variables, rather than as long stories, to promote interoperability and use anywhere in the world, regardless of language," explains Dr. Blackstone. IBM's efforts in this realm began at the University of Alabama in 1993 when Dr. Blackstone was still working there, but they continued at an accelerated pace starting in 1997 when Dr. Blackstone began to help pair IBM's data capabilities with Cleveland Clinic's Cardiovascular Information Registry.

"Cleveland Clinic was one of only perhaps five medical centers in the world with a serious interest in data science dating back to the early 1970s," he says. "This institution was ahead of the curve in carving out a role like mine and consistently supporting it for so many years."

### The wide reach of data science in CT surgery

That support has allowed Dr. Blackstone, who is also staff in Cleveland Clinic's Department of Quantitative Health Sciences, to assemble a team of statisticians, computer scientists, mathematicians and other data experts to support his cardiothoracic surgery colleagues in a wealth of research and outcomes endeavors. They draw on methodologies ranging from machine learning to data management to artificial intelligence to help surgeons improve clinical decision-making and assess appropriateness of care through long-term follow-up. The following paragraphs present a sampling of a few projects the group has undertaken in recent years to shape practice.

*Continued next page* ›

› **Prediction models for decision support in surgical management of ischemic cardiomyopathy.** About a decade ago, Dr. Blackstone's team worked with clinical colleagues to develop and validate comparative prediction models of survival following four different surgical intervention strategies for ischemic cardiomyopathy (*J Thorac Cardiovasc Surg.* 2010;139:283-293). Using a robust, nonparametric algorithmic method called Random Survival Forests, they transformed the models into a computer-based strategic decision aid to facilitate personalized decision-making. "The idea was to quantitatively make decisions with a model that could go down many different paths rather than the norm of going down each path individually," Dr. Blackstone explains. "These methods have since morphed into a formal set of machine learning tools that allow clinicians to test alternative treatment scenarios to recommend the one that maximizes an outcome, such as length of life."

› **Classification of bicuspid aortopathy.** In work published just last year (*J Thorac Cardiovasc Surg.* 2018;155:461-469), Dr. Blackstone and colleagues applied unsupervised clustering algorithms to a data set of 656 patients with bicuspid aortic valves who underwent ascending aorta surgery at Cleveland Clinic over a 12-year period. This method finds similarities in uncategorized data and then groups similar data points, allowing processing of a large number of variables to uncover underlying patterns. The result was a new classification of bicuspid aortopathy that for the first time established a statistical relationship between the shapes of bicuspid valves and patterns of aortic aneurysms.

› **Selection of variables for esophageal cancer staging and precision cancer care.** Cleveland Clinic thoracic surgeons and data scientists gathered data on patients with esophageal cancer from all six inhabited continents to develop a data-driven approach to staging for the seventh and eighth editions of the cancer staging manual of the American Joint Committee on Cancer. "Survival of individual patients with esophageal cancer is all over the map, which means 'average survival time' is not very meaningful," Dr. Blackstone says. "We used machine learning algorithms — specifically, Random Survival Forests — to enable much more precise prediction of which treatments will promote longer survival at the individual patient level. This approach is generally applicable in many other conditions as well."

› **Longitudinal assessment of valve function.** In the past, emphasis has been on clinical events, like death and stroke, that occur during follow-up after heart surgery. Today, however, fully half of the analyses done by Dr. Blackstone's group focus on longitudinal data. Examples include series of follow-up echocardiographic assessments of pressure gradient developing across a repaired heart valve or an artificial heart valve, or serial assessments of the degree of leakiness of such valves. This information can inform clinicians about the durability of the valve repair or replacement device, but it also serves to identify factors that increase or decrease the speed of developing gradients or leakage, thereby informing clinicians of who is at risk and who needs reintervention. These analytic methods, developed at Cleveland Clinic with National Institutes of Health (NIH) funding, harken back to Dr. Blackstone's early career at the University of Chicago in the late 1960s, where he helped develop the field of digital signal processing, whereby complex longitudinal data can be broken down into simple components, much like white light is broken into a rainbow of colors by a prism.

› **Continuously updated heart transplant waitlist mortality estimation.** In a recent publication (*J Am Coll Cardiol.* 2018;72:650-659), Cleveland Clinic clinicians and statisticians shared initial findings from a dynamic model that continuously updates predicted mortality based on laboratory values and other clinical measures as the conditions of patients on the heart transplant waitlist change over time. Using a newly developed method for analyzing time-related mortality, the model recomputes patients' mortality risk with each new clinical event or change in key lab values or organ function. "A model of this type that uses time-varying mortality risk estimation could reduce mortality on the waitlist and promote better utilization of the limited supply of donor hearts," Dr. Blackstone explains. "It represents a combination of traditional statistics with machine learning."

› **Identification of variables most predictive of death on the heart transplant waitlist.** In related work,

Dr. Blackstone and Cleveland Clinic heart transplant researchers have joined with colleagues from several other institutions on a project funded by a $2.8 million NIH grant to develop new machine learning methods to examine and reduce disparities in survival among heart failure patients before and after transplant. The researchers are applying machine learning to the national Scientific Registry of Transplant Recipients database to identify major risk factors for death on the waitlist and how these factors interact. The group's first publication (*Am J Transplant.* 2019 Jan 19 [Epub ahead of print]) identified the most important variables in predicting mortality on the waitlist, including a couple that are not in the current allocation system for donor hearts. "This work involves some new mathematics well suited to handling complex interactions among variable and large amounts of missing data," Dr. Blackstone observes.

### What's ahead

Dr. Blackstone sees emerging heart valve therapies as one of the most active frontiers for future data science applications in cardiothoracic surgery. "I expect that we'll be doing a lot of work to support decisions around when to do valve procedures surgically versus percutaneously, such as which approach and which valve type are best for a given patient," he says.

He notes that Cleveland Clinic can draw on the troves of data it collected as one of the data analysis centers for the PARTNER trial program for transcatheter aortic valve replacement. "We also benefit from the considerable follow-up we have done with so many cardiovascular patients at Cleveland Clinic dating back to the early 1970s," he adds. "Good data science requires the coupling of short-term data with long-term outcomes."

### Challenges and opportunities

Yet he sees follow-up as the biggest challenge now facing data science. "Patient follow-up today is much more difficult than it was 20-some years ago, in part because of patient privacy laws," he says. The result is inferior follow-up data, which he notes is exacerbated by a continuing lack of interconnectivity of health data information systems. "Our methods have ended up being better than our data."

Another challenge for a leader in his role is keeping top data science talent around for the next project. "The people who are good at this work come from a diversity of backgrounds — from traditional statistics to computer science to mathematics to computational fluid dynamics," he says. "Whoever they are, it can be a challenge to keep good data scientists around, as industry is always looking to recruit them."

Cleveland Clinic hopes its recent establishment of a cross-disciplinary Center for Clinical Artificial Intelligence will assist in attracting and keeping top talent, and Dr. Blackstone sees the center as a promising new partner.

Meanwhile, he spends time mentoring other clinician-researchers who have a shared interest in championing novel data methods to help shape cardiothoracic surgery. One current protégé is new Cleveland Clinic congenital heart surgeon Tara Karamlou, MD, who trained with him in the past.

"One way Cleveland Clinic tries to share the wealth in terms of data science expertise is through cardiothoracic surgery fellows and residents who train here," Dr. Blackstone says. "They can go back to their home institution with knowledge of how to apply new tools or methodologies. But the most fundamental step any institution can take toward advanced data techniques is to first get a handle on their data. Start by understanding your data and focusing on the quality of your outcomes. That's where Cleveland Clinic started many decades ago. Success and sophistication follow from that." ■

**Contact Dr. Blackstone at 216.444.6712.**

## In the words of a longtime colleague…

"**Gene Blackstone** has made a huge contribution to our understanding of the management of cardiothoracic surgery patients," says surgeon **Lars Svensson, MD, PhD**, Chair of Cleveland Clinic's Heart & Vascular Institute. "His work has resulted in considerably better care of patients, not only here but around the world. As we look at new fields of statistical endeavor — such as machine learning, voice recognition and interpolation for the EMR, and ultimately automated artificial intelligence — we know that Gene and his team will be at the forefront of implementing these new methods to better understand what makes for world-class cardiovascular care."

# **WRAP-IT** Reveals 40% Reduction in CIED Infections with Antibiotic Envelope

**Huge postmarketing study also shows no increase in complication rate.**

Placement of cardiac implantable electronic devices (CIEDs) inside an absorbable, antibiotic-eluting envelope reduced the incidence of major infections by 40% relative to standard-of-care CIED infection prevention strategies alone, according to results of the international WRAP-IT randomized controlled trial.

"Rates of CIED infection are generally low, but when these infections occur, they can be devastating for patients, resulting in prolonged hospitalization, removal of the device system, possible vascular injuries and sometimes fatality," says Cleveland Clinic electrophysiologist Khaldoun Tarakji, MD, MPH, global principal investigator of WRAP-IT, who reported the results in a late-breaking trials presentation at the American College of Cardiology (ACC) scientific session in March. The study was published simultaneously in the *New England Journal of Medicine.* "These findings provide strong evidence for use of the envelope to reduce CIED infection risk."

### First randomized controlled trial of the envelope

This evidence may expand adoption of the envelope (TYRX™ Absorbable Antibacterial Envelope, Medtronic), which was approved by the FDA in 2013. The product was designed to surround a CIED implanted in the chest. It consists of a knitted mesh body coated with an absorbable polymer mixed with the antibiotics minocycline and rifampin, which are eluted into local tissue for at least seven days. The envelope is absorbed by the body within about nine weeks.

"Evidence on prophylactic strategies to reduce CIED infection beyond the use of preoperative antibiotics has been limited," notes Cleveland Clinic electrophysiologist Bruce Wilkoff, MD, who served as the WRAP-IT trial's steering committee chair. "Several studies have yielded supportive evidence for local antibiotic delivery, but a large randomized trial has been lacking."

### Nearly 7,000 patients at increased infection risk

WRAP-IT, which was supported by Medtronic, was undertaken to help address that deficiency through its size and design. The study randomly assigned 6,983 patients from 25 nations to receive the envelope or not receive the envelope in addition to standard-of-care infection prevention (pre-procedure intravenous antibiotics plus sterile technique) during their CIED procedure.

Randomization was done on a 1:1 basis with patients stratified by device type — either a pacemaker/cardiac resynchronization therapy (CRT) pacemaker or an implantable cardioverter defibrillator/CRT defibrillator. Patients (mean age, 70.1 years) were blinded to their treatment group assignment, and the groups were well matched for baseline and procedural characteristics.

"Our enrollment strategy was to include individuals at increased risk for CIED infection based on literature evidence," notes Dr. Tarakji. This included those undergoing CIED generator replacement or system upgrade with or without new leads, as well as de novo CRT defibrillator implantation or pocket or lead revisions.

"Management of patients with a CIED involves more than just the implantation — there are follow-up procedures for upgrades, battery or lead changes, and the like," Dr. Wilkoff adds. "Every time the CIED pocket is revisited, there is a risk of infection."

> "This study, which is the largest global cardiac device trial ever completed, provides a realistic look at the number of device infections associated with CIEDs." — Bruce Wilkoff, MD

## WRAP-IT: Largest global cardiac device trial to date

**6,983 patients | 181 centers | 25 countries**

**Patients undergoing cardiac implantable electronic device (CIED) procedures randomized 1:1 to:**

| Standard-of-care infection prevention | Standard of care + TYRX™ antibiotic-eluting envelope to surround CIED |
|---|---|

**After 12 months…**

- 40% relative reduction in major CIED infections in envelope group
- Comparable rates of complications in envelope and no-envelope groups

**BOTTOM LINE** | With >1 million people worldwide receiving CIEDs annually, the antibiotic envelope is an effective strategy for reducing risk of devastating CIED infections.

SOURCE Tarakji KG, et al. *N Engl J Med.* 2019 Mar 17 [Epub ahead of print].

The primary end point was the incidence of major CIED infection within 12 months of the procedure, with major infections defined as those requiring system extraction or revision, requiring long-term antibiotic therapy with infection recurrence, or resulting in death. A secondary safety outcome was procedure- or system-related complications within 12 months.

### Results: Fewer infections, comparable safety

Major CIED infections occurred in 25 patients in the envelope group compared with 42 patients in the control group, for 12-month Kaplan-Meier event rate estimates of 0.7% and 1.2%, respectively (hazard ratio [HR] = 0.60; 95% CI, 0.36-0.98; $P = 0.041$), representing a 40% relative reduction in the risk of developing a major CIED infection.

On the safety front, procedure- or system-related complications occurred in 201 patients in the envelope group and 236 patients in the control group, for 12-month Kaplan-Meier event rate estimates of 6.0% and 6.9%, respectively (HR = 0.87; 95% CI, 0.72-1.06; $P < 0.001$ for noninferiority).

Mean follow-up was 20.7 months, with 89.4% of enrollees completing at least 12 months of follow-up. Across the entire follow-up period, rates of major CIED infections were again significantly lower in the envelope group than in the control group, with 36-month Kaplan-Meier event rate estimates of 0.9% and 1.6%, respectively (HR = 0.63; 95% CI, 0.40-0.98).

### Efficacy despite a low overall infection rate

"In a population at increased risk of CIED pocket infection, the antibiotic envelope was significantly more effective at preventing infection than standard infection control strategies by themselves," observes Dr. Tarakji. "The envelope was safely implanted in 99.7% of procedure attempts, and it did not increase complications despite the fact that use of the envelope may require dissection of a slightly larger CIED pocket."

The researchers called attention to two additional findings:

- The envelope's benefits were especially pronounced in patients with high-power devices relative to patients with low-power devices or those receiving de novo CRT defibrillators.
- The envelope demonstrated its treatment benefit despite a low overall infection rate across the entire study.

"This study, which is the largest global cardiac device trial ever completed, provides a realistic look at the number of device infections associated with CIEDs," says Dr. Wilkoff. "While overall infection rates were low, the envelope still provided significant benefit to patients. That's important in view of the fact that well over 1 million patients receive CIEDs worldwide every year." ■

**Contact Dr. Tarakji at 216.445.9225 and Dr. Wilkoff at 216.444.4975.**

Photo of TYRX envelope above is courtesy of Medtronic.

# Barlow's Disease: Treating the Chords, Not the Leaflets, Is Key

**The case for a minimally invasive robotic approach to this form of mitral valve disease**

Minimally invasive robotic, nonresectional mitral valve repair using neochords in Barlow's disease is safe, effective and durable. That's the consensus among Cleveland Clinic cardiothoracic surgeons, who are now using the technique on a regular basis.

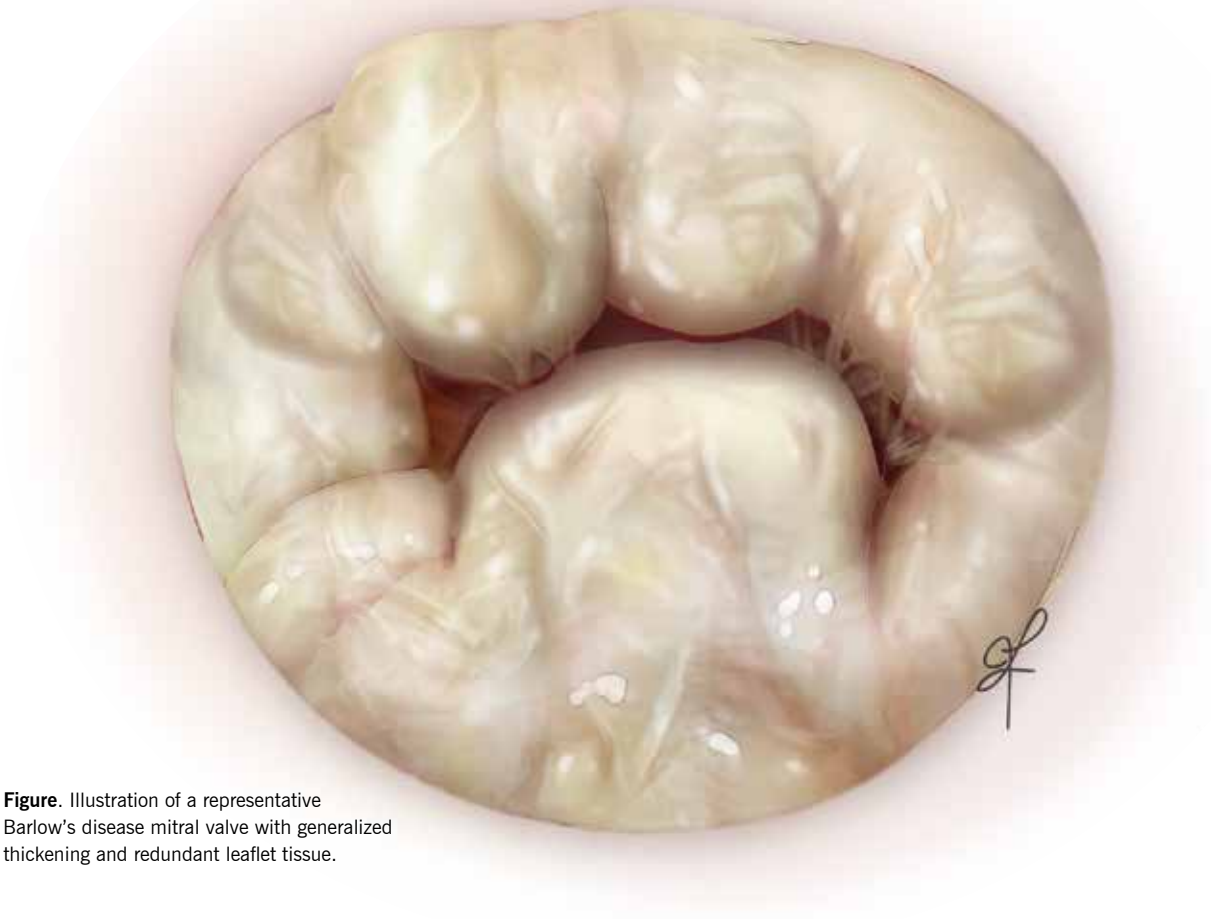


**Figure**. Illustration of a representative Barlow's disease mitral valve with generalized thickening and redundant leaflet tissue.

"The technique avoids the fibrosis and scarring caused by extensive cutting and suturing," says one of those surgeons, Per Wierup, MD, PhD. "It results in a larger opening with a lower gradient."

The procedure can be completed more quickly with a robotic approach than a conventional repair performed with a sternotomy. "Patients tolerate it very well," Dr. Wierup notes. "They require much less inotropic support and routinely only stay overnight in the ICU. Typically they can be discharged from the hospital after a few days."

## Inadequate repair techniques

Barlow's disease is one of two types of degenerative mitral valve disease causing mitral regurgitation, the other being fibroelastic deficiency. In contrast to the leaflet and chordal thinning seen in fibroelastic deficiency, Barlow's is characterized by a large valve with redundant tissue that causes the valve to appear thick and swollen (Figure). A dilated annulus and elongated chords cause the entire valve structure to prolapse into the left atrium.

> "The technique avoids the fibrosis and scarring caused by extensive cutting and suturing. It results in a larger opening with a lower gradient." — Per Wierup, MD, PhD

Surgical correction of the regurgitation in Barlow's disease offers a survival benefit when compared with optimal medical therapy or valve replacement. Conventional repair techniques used for fibroelastic deficiency have been problematic, however.

"In a conventional repair, the prolapsed sections of the valve are resected," Dr. Wierup says. "A chordal transfer may be performed, and the remaining valve is reattached."

### A better approach

More than a decade ago, Dr. Wierup began exploring how to improve on nonresectional techniques for Barlow's disease. The approach treats the chords while leaving the leaflets intact.

"Leakage is caused by valve prolapse due to elongated chords, so we replace these with Gore-Tex® neochords," he explains. "Making the chords on the anterior and posterior leaflets different lengths allows the zone of coaptation to be adjusted for perfect results."

### Supportive data from a recent review

Performing the procedure using a minimally invasive, video-assisted robotic technique offers multiple advantages over conventional sternotomy, as demonstrated by outcomes from a recent retrospective review of 102 patients who underwent repair of Barlow's disease. The results, which Dr. Wierup presented at the 2018 American Heart Association Scientific Sessions last November, included the following:

- No patient in either the sternotomy group (n = 38) or the minimally invasive robotic repair group (n = 64) required valve replacement, and no patient who underwent the minimally invasive robotic procedure required intraoperative conversion to sternotomy.
- There were no perioperative deaths or cases of >1+ mitral regurgitation at discharge in either group.
- There were no significant differences in cardiopulmonary bypass times between the groups.
- More than six hours of mechanical ventilation was required by 21% of patients in the sternotomy group versus no patients in the minimally invasive robotic repair group.
- Whereas 21% of patients in the sternotomy group remained in the ICU more than 24 hours, no patients in the minimally invasive robotic repair group did.
- Average hospital stay was 4 days following minimally invasive robotic repair versus 9 days following sternotomy.
- Postoperative atrial fibrillation occurred in 16% of the minimally invasive robotic repair group versus 42% of the sternotomy group.
- Freedom from the composite end point of death, reoperation or >1+ mitral regurgitation did not differ between the two cohorts.

### New standard of care for most patients

"Since he joined the Cleveland Clinic staff in 2017, Dr. Wierup has shared his techniques with other members of our mitral valve surgery team, increasing the options we make available to treat patients with complex mitral valve disease," says A. Marc Gillinov, MD, Chair of Thoracic and Cardiovascular Surgery.

"Minimally invasive repair using robotic assistance is now standard treatment for Barlow's disease at our institution," Dr. Wierup notes. "Patients must have a healthy aortic valve and groin blood vessels that are large enough to accommodate the cannulas required for robotic surgery. If their aortic valve is leaking or their groin vessels are too small, it is safer to perform the repair using a minimally invasive alternative approach. However, this is necessary in only a minority of patients." ■

**Contact Dr. Wierup at 216.445.1652.**

# Launching an LAAO Program: How Cleveland Clinic Assisted an Affiliated Institution

**A Missouri center turns lessons from a site visit into program success.**

Not long after Saint Francis Medical Center entered into a cardiology and cardiovascular surgery affiliation with Cleveland Clinic in early 2014, the Southeast Missouri facility turned to Cleveland Clinic to help it create a transcatheter aortic valve replacement (TAVR) program.

That experience (profiled at consultqd.clevelandclinic.org/tavrtogether) was a success, prompting the 306-bed nonprofit tertiary care institution to turn to Cleveland Clinic for guidance in launching another offering in its structural heart disease program — this time for left atrial appendage occlusion (LAAO) with the Watchman™ device.

### Site visit for firsthand observation

The effort started with a February 2018 site visit to Cleveland Clinic's main campus by several key players in the planned Saint Francis LAAO program: three physicians (an interventional cardiologist, an imaging cardiologist and an electrophysiologist) plus an advanced practice nurse serving as coordinator of the institution's structural heart program.

During the visit, the Saint Francis staff observed the Cleveland Clinic LAAO team perform a couple of Watchman procedures in the electrophysiology lab as well as manage several LAAO patients at different stages in the course of care, from workup through post-procedure discharge. The structural heart program coordinator consulted with nurse practitioners before and after LAAO procedures and visited extensively with Cleveland Clinic Heart & Vascular Institute registry, coding and billing specialists to learn the finer points of data abstraction relating to LAAO procedures for purposes of compliance, coding, billing, quality reporting and patient follow-up.

"We came prepared with questions to allow us to implement processes from Cleveland Clinic's program in a smaller organization like ours," explains Jennifer Cotner, MSN, APRN, ACNP, Structural Heart Program Coordinator at Saint Francis.

### Implementation and outcomes

The Saint Francis team applied their learnings in short order, performing their first LAAO procedure within a month after the site visit. A full-fledged program was soon up and running, with 42 patients evaluated for LAAO within the first year and 25 LAAO procedures performed. Saint Francis now performs LAAO procedures every other Tuesday. Outcomes to date have been excellent, as detailed in the table below.

**Initial LAAO Outcomes at Saint Francis Medical Center**

| | Initial Episode of Care (n = 15) | 45-Day Follow-Up (n = 13) | 6-Month Follow-Up (n = 4) |
|---|---|---|---|
| Mortality | 0% | 0% | 0% |
| Stroke (ischemic or hemorrhagic) | 0% | 0% | 0% |
| Systemic embolism | 0% | 0% | 0% |
| Evaluated for stroke using $CHA_2DS_2$-VASc score | 100% | 100% | 100% |
| Evaluated for bleed using HAS-BLED score | 100% | 100% | 100% |
| LAAO procedures that met FDA indications | 100% | 100% | 100% |

**Source:** American College of Cardiology LAAO Registry™: Standard Report ending 2018 Q3; 45-Day Follow-Up Report ending 2018 Q3; 6-Month Follow-Up Report ending 2018 Q1.


## Ongoing support

Key Cleveland Clinic team members provide ongoing support to their Saint Francis counterparts as needed. For instance, electrophysiologist Mohamed Kanj, MD, who met with Saint Francis staff during their site visit, provided at least six second opinions on Saint Francis patients who were considering an LAAO procedure during the first year of the Saint Francis program's operation. Additionally, Cleveland Clinic's LAAO registry team continues to advise and support their Saint Francis colleagues on questions of coding and reporting.

Indeed, a key aspect of the training provided to Saint Francis by Cleveland Clinic involved education relating to the American College of Cardiology's LAAO Registry™. Cleveland Clinic data specialists provided templates to assist with proper abstracting, documentation and reporting for the registry.

Additionally, as a Cleveland Clinic Heart & Vascular Institute affiliate organization, Saint Francis is entitled to complimentary attendance at Cleveland Clinic's annual Cardiac Registry and Analytics Boot Camp, a three-day event designed to share best practices in maintaining cardiac registries, data validation and accuracy, analytic outcomes reporting and physician engagement efforts. This year's boot camp is scheduled for Nov. 13-15 on Cleveland Clinic's main campus.

## Reflections on the partnership

For its part, Saint Francis is delighted with the progress it has made in just one year of offering LAAO services. "The support we have received from Cleveland Clinic has been invaluable to the development and expansion of our structural heart program," says Saint Francis interventional cardiologist Steven Joggerst, MD, who leads the LAAO program. "Dr. Kanj and his team readily shared their expertise, experience and ideas, allowing us to make a smooth transition to this technology. They have always provided timely responses to our clinical questions and concerns. It is a privilege to be affiliated with Cleveland Clinic."

"It has been gratifying to see the Saint Francis team flourish in their use of LAAO technology," observes Oussama Wazni, MD, Cleveland Clinic's Section Head of Cardiac Electrophysiology and Pacing, who met with the team during their site visit. "Through Cleveland Clinic's affiliate program, we've gained considerable experience in helping smaller centers adapt new technologies to the size and scope of their programs. This helps the affiliate centers distinguish their programs in their local markets, and it also sharpens our use of the technology by guiding another center in its use. The collaboration is inevitably a win-win." ■

**For information on affiliation and alliance opportunities with Cleveland Clinic's Heart & Vascular Institute, visit clevelandclinic.org/heartaffiliates.**

# Making Space to Breathe: A Case of Successful Surgery for Acquired Thoracic Dystrophy

A recent case from Cleveland Clinic's Section of Thoracic Surgery underscores the need for vigilance for acquired thoracic dystrophy when an adult with childhood pectus excavatum repair presents with exercise intolerance. This article recaps the case and presents a Q&A with the managing thoracic surgeon, Daniel Raymond, MD, on resulting insights about this rare condition.

## Case vignette

A 43-year-old man presented to Cleveland Clinic's Center for Chest Wall Disease with significant exercise intolerance. He was very short of breath and limited in his daily activities. Attempts to exercise led to palpitations and profuse sweating. On cardiopulmonary testing, his maximal oxygen uptake ($VO_{2max}$) was 42% of predicted.

At age 7 years, he had undergone a modified Ravitch procedure to correct a pectus excavatum defect, which entailed removal of the cartilage between the sternum and ribs. This procedure resulted in destruction of the growth plates so that his ribs stopped growing, which essentially left him with adult-sized organs squeezed within the rib cage of a 7-year-old.

Clinicians he had seen previously believed he had a recurrence of the pectus excavatum, as his sternum looked low on imaging, as if the defect had not been corrected entirely. However, CT scans at Cleveland Clinic revealed the telltale sign of acquired thoracic dystrophy: a bell-shaped chest (Figure 1) associated with a restrictive pattern on his lung function studies. Moreover, axial images showed his organs to be visibly crowded in the chest (Figure 2), restricting space for his lung tissue. In addition, the normal cartilage between his ribs had been replaced by bone, reducing his chest wall flexibility.

**Figure 1.** Preoperative image showing the classic bell-shaped chest of acquired thoracic dystrophy.

**Figure 2.** Preoperative axial image showing calcification of the medial ribs with some residual pectus deformity.

The patient was operated on at Cleveland Clinic in November 2017. The rib portions that had calcified were resected, with care taken to preserve the soft tissue underneath. His sternum was cut and bent forward since there was still a residual component of his pectus excavatum. A titanium plate was inserted to hold the sternum in its new, normal position.

Because his organs were so restricted, a bar was also used to cross his chest and push the sternum forward to create even more space in the chest (Figure 3). While bars are generally to be avoided in adults when correcting previously untreated pectus excavatum, in this case the need for additional chest wall expansion was clear. Removal of the bar is planned after two years. The plate will remain permanently.

**Figure 3.** Postoperative image showing the plate and bar placed to hold the sternum in its normal position and further increase chest volume.

## Q&A

WITH
Daniel Raymond, MD

**Q: How has the patient fared since the operation?**

**A:** He has worked hard at exercising and has improved dramatically. On repeat cardiopulmonary testing, his $VO_{2max}$ is now up to 78% of predicted. This is due not simply to the surgery but also to his vigilance: He walks every day, goes to the gym and does all the exercise we prescribed. Since he has been able to exercise, he also has lost about 30 pounds. While we made his chest wall better, he had to be the one to improve his cardiopulmonary fitness. Unfortunately, many patients don't do that. This dedication was likely central to our patient's positive result.

Interestingly, despite the improved $VO_{2max}$, his forced vital capacity and forced expiratory volume at 1 minute have not changed dramatically, remaining around 50%. We do not currently have effective technology to surgically increase the thoracic cage volume to a significant degree, and this offers an opportunity for research.

**Q: Exactly how can a modified Ravitch procedure for pectus excavatum in childhood contribute to development of acquired thoracic dystrophy?**

**A:** Pectus excavatum is a congenital chest wall deformity in which several ribs and the sternum grow abnormally, producing a concave appearance in the anterior chest wall. It occurs in about 1 in 300 births, with a male-to-female predominance of about 3:1.

In most cases, the defect is mild and doesn't require correction, but sometimes cosmetic treatment is justified in children for psychological reasons. In adults, we do not correct pectus excavatum unless there are problems with exercise intolerance, which can be overlooked. Patients are often told that pectus excavatum is only a cosmetic problem when in fact there can be real physiologic manifestations.

In the mid-1980s, pediatric surgeons recognized that pectus excavatum could be corrected without damage to the growth plates if dissection of the interface between cartilage and bone were done less aggressively. The modified Ravitch is still used, but a newer, less invasive approach called the Nuss procedure has largely replaced it.

With the Nuss, the cartilage stays in place while a bar is pushed under the sternum to force it forward. The Nuss works well in children and teens, but it tends to be more painful than the Ravitch. My practice is to not perform the Nuss in adults out of concern that rigidity of the adult skeletal system leads to rib fractures without effective correction of the defect. However, other surgeons will perform the Nuss in adults.

**Q: Does this mean acquired thoracic dystrophy will disappear as a clinical entity?**

**A:** Current awareness of the need for greater care in cartilage dissection with the modified Ravitch, along with elimination of dissection altogether with greater use of the Nuss, means we should see fewer and fewer cases of acquired thoracic dystrophy as time goes by. But we can't predict when we'll stop seeing them, since we don't know how many cases are out there.

**Q: What's needed to manage restrictive chest wall diseases like this?**

**A:** At Cleveland Clinic's Center for Chest Wall Disease, we are fortunate to be able to pool the expertise of thoracic surgeons along with clinicians in orthopaedics, radiation oncology, musculoskeletal radiology, pulmonary physiology and pain management to help these patients. We are now working on developing new technologies to more effectively expand the chest volume to treat acquired thoracic dystrophy and other restrictive diseases. ■

**Contact Dr. Raymond at 216.636.1623.**

# Stress Test Performance Beats Chronological Age in Predicting Longevity

The cliché that you're only as old as you feel just got an evidentiary boost from findings of the largest cohort of exercise stress test participants reported to date. The cohort study, published by Cleveland Clinic researchers in the *European Journal of Preventive Cardiology* in February, shows that physiological age, based on exercise stress test performance, is a better predictor of survival than chronological age.


The study evaluates a formula the researchers developed to calculate exercise performance, which they dub A-BEST (Age Based on Exercise Stress Testing), or "physiological age." It is sex-specific and consists of three components, taking into account the use of negative chronotropic medications:

- Exercise capacity (number of peak estimated metabolic equivalents of task [METs])
- Chronotropic reserve index (heart rate response to exercise)
- Heart rate recovery

"These three exercise parameters are readily available in stress test reports," explains lead author and Cleveland Clinic cardiologist Serge Harb, MD. "Our goal was to develop a mortality risk estimate that's more practical and easy to understand for patients and clinicians. The A-BEST measure can be used as a surrogate for physiological age, as it incorporates factors associated with diminishing treadmill exercise performance."

## Study essentials

The researchers applied the A-BEST formula to 126,356 consecutive patients who underwent exercise stress testing (ECG, echocardiography or myocardial perfusion imaging) at Cleveland Clinic from 1991 to 2015. Univariable and multivariable regression analyses were used to determine the association of A-BEST with all-cause mortality throughout the duration of available follow-up.

Mean patient age was 53.5 years. During mean follow-up of 8.7 years across the cohort, a total of 9,929 patients (7.9%) died.

Following adjustment for clinical comorbidities, each of the three A-BEST components was significantly associated with mortality, as follows:

- Greater exercise capacity (higher METs) was associated with lower mortality ($P < 0.001$).
- Higher chronotropic reserve index was associated with lower mortality ($P = 0.0135$).
- Abnormal heart rate recovery was associated with higher mortality ($P < 0.001$).

Consistent with the above results, the A-BEST measure itself was significantly associated with mortality, with a higher A-BEST correlating with higher mortality ($P < 0.001$). Moreover, A-BEST was significantly more predictive of death than was a patient's chronological age ($P < 0.001$).

The above findings applied to both the overall cohort and to men and women when analyzed separately.

## Helping patients better understand risk

"These findings show that estimated physiological age, based on readily available exercise stress testing parameters, performs better than chronological age in predicting all-cause mortality," Dr. Harb observes.

"The primary advantage of A-BEST is that it reliably and conveniently translates exercise variables to a risk estimate that's easily appreciated by both patients and their providers," adds senior author Wael Jaber, MD. "The hope is that this can help motivate patients to exercise more."

Simple formulas for calculating A-BEST for both men and women are presented in the *European Journal of Preventive Cardiology* study report (2019 Feb 13 [Epub ahead of print]). ■

**Contact Dr. Harb at 216.444.3316 and Dr. Jaber at 216.444.8305.**

# Research **Roundup**

**Quick Takes on Recent Cardiovascular Studies of Note**

## Increasing Inflammation Correlates with Residual Risk After ACS

Serial measurements of high-sensitivity C-reactive protein (hsCRP) following acute coronary syndrome (ACS) may help identify patients at higher risk for morbidity and mortality. So concludes a secondary analysis of the multicenter VISTA-16 trial published by a Cleveland Clinic-led group in *JAMA Cardiology*.

VISTA-16 randomized 5,145 patients to 16 weeks of the experimental anti-inflammatory drug varespladib or placebo within 96 hours of ACS. The trial was stopped early due to futility, but it lasted long enough for hsCRP levels to be obtained at baseline and weeks 1, 2, 4, 8 and 16 in over 4,200 patients. The new analysis showed that each standard-deviation increment in longitudinal hsCRP concentration was associated with a 15% increased risk of a major adverse cardiovascular event, a 25% increased risk of all-cause death and a 26% increased risk of cardiovascular death. "Monitoring hsCRP in addition to lipids after ACS may help us better identify patients at increased risk for recurrent events or death, which may prompt more intensive treatment," says senior author Rishi Puri, MD, PhD. **More at consultqd.clevelandclinic.org/vista16.**

## For Ideal STEMI Care, Look Beyond Door-to-Balloon Time

A comprehensive systems-based strategy for acute ST-segment elevation myocardial infarction (STEMI) care improves outcomes compared with a singular focus on door-to-balloon time, according to research from Cleveland Clinic investigators in *Circulation: Cardiovascular Interventions*. The study reviewed the care of 1,272 consecutive patients with STEMI treated with percutaneous coronary intervention (PCI) at Cleveland Clinic from 2011 through 2016 to assess the respective contributions of three care components: use of guideline-directed medical therapy, use of transradial primary PCI and prompt door-to-balloon time.

Each component was found to yield significant incremental outcome improvements, showing a graded association with reduced ejection fraction and reduced rates of bleeding, cardiogenic shock, and cardiovascular and all-cause mortality. "This study indicates that it's time to move beyond focusing solely on door-to-balloon time for providing quality acute STEMI care," says corresponding author Umesh Khot, MD. "We found that the best approach is to consistently achieve a range of STEMI care best practices." **More at consultqd.clevelandclinic.org/stemi.**

## Surgery for Marfan Syndrome: Support for Earlier Intervention

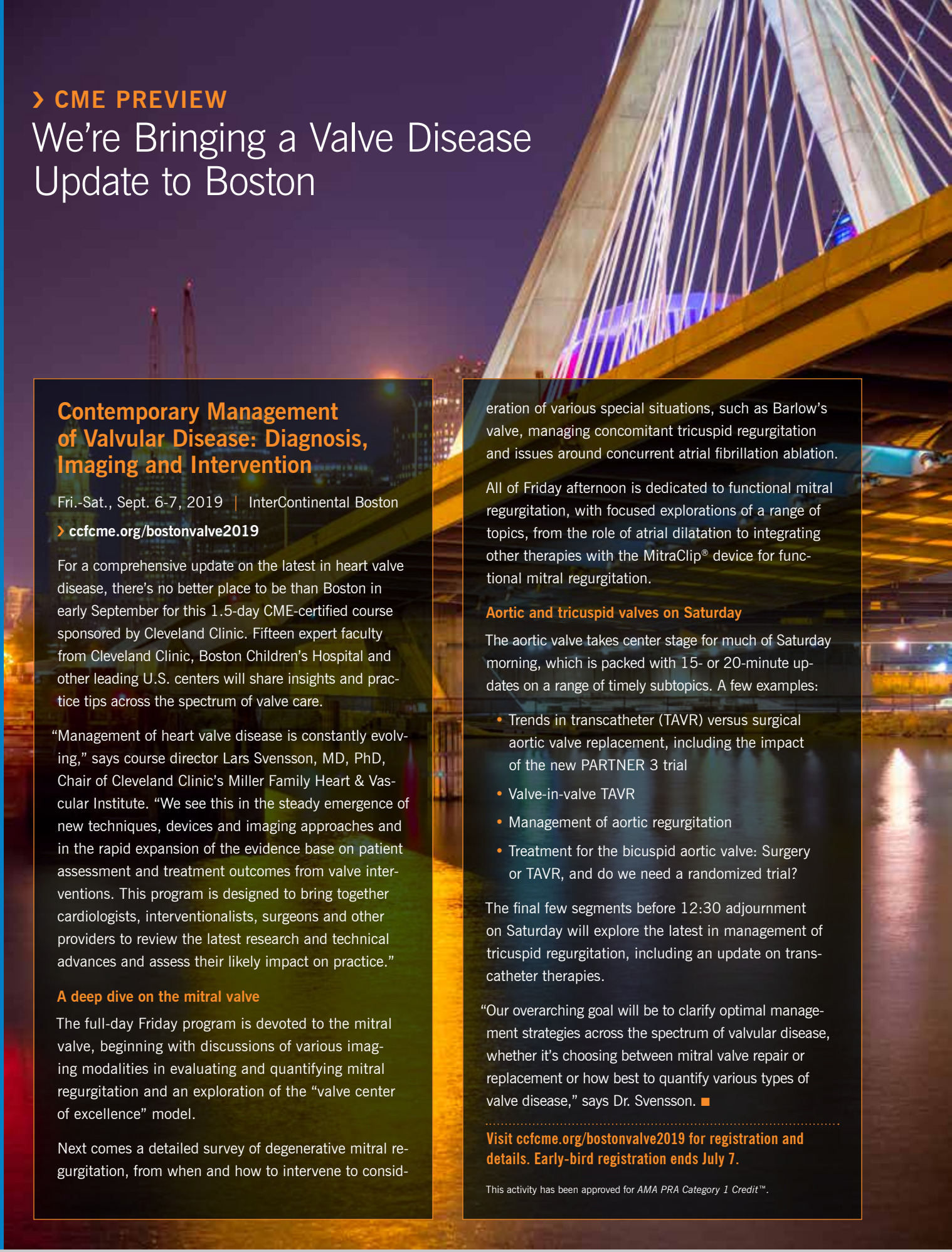
Guidelines recommend prophylactic aortic root replacement when the aortic diameter reaches 5 cm or larger (or ≥ 4 to 4.5 cm with certain risk factors), but a new observational study suggests that size threshold needs to be revisited. The study reviewed 491 adults with suspected Marfan syndrome who presented for aortic surgery at Cleveland Clinic from 1990 to 2016 who met the revised Ghent criteria and hadn't had prior aortic surgery. It found that the majority of patients who underwent emergency aortic root replacement had an aortic root diameter smaller than guideline cutoffs for prophylactic surgery. It also found that prophylactic root replacement was associated with significantly improved survival and freedom from aortic dissection compared with emergency surgery among the cohort.

"These findings suggest that Marfan syndrome patients with ascending aortopathy may benefit from prophylactic aortic root replacement surgery earlier than is indicated by current guidelines based on aortic root dilation," says senior author and cardiac surgeon Lars Svensson, MD, PhD. The study was published in the *Journal of the American College of Cardiology*. **More at consultqd.clevelandclinic.org/marfan.**

## LAA Closure Device Safe and Effective Despite Prior ICH

Placement of the Watchman left atrial appendage (LAA) closure device followed by short-term anticoagulation is effective and well tolerated in patients with atrial fibrillation and a history of intracranial hemorrhage (ICH), a Cleveland Clinic feasibility study shows. The study of 38 consecutive patients, published in *Heart Rhythm*, found that no strokes, intracranial bleeds, major cardiovascular events or deaths occurred over mean follow-up of more than a year after implantation.

"Patients with atrial fibrillation who've had a previous ICH are challenging to treat because they're at elevated risk for both stroke and recurrent bleeding," says co-author Ayman Hussein, MD, a Cleveland Clinic electrophysiologist. Yet ICH was an exclusion criterion in pivotal trials of the Watchman device. "Our study, which we believe is the largest to date in patients with ICH, suggests that short-term anticoagulation therapy, which is required perioperatively for the LAA closure device, can safely be provided to these patients." **More at consultqd.clevelandclinic.org/ichlaa.**



› CME PREVIEW

# We're Bringing a Valve Disease Update to Boston

## Contemporary Management of Valvular Disease: Diagnosis, Imaging and Intervention

Fri.-Sat., Sept. 6-7, 2019 | InterContinental Boston

› **ccfcme.org/bostonvalve2019**

For a comprehensive update on the latest in heart valve disease, there's no better place to be than Boston in early September for this 1.5-day CME-certified course sponsored by Cleveland Clinic. Fifteen expert faculty from Cleveland Clinic, Boston Children's Hospital and other leading U.S. centers will share insights and practice tips across the spectrum of valve care.

"Management of heart valve disease is constantly evolving," says course director Lars Svensson, MD, PhD, Chair of Cleveland Clinic's Miller Family Heart & Vascular Institute. "We see this in the steady emergence of new techniques, devices and imaging approaches and in the rapid expansion of the evidence base on patient assessment and treatment outcomes from valve interventions. This program is designed to bring together cardiologists, interventionalists, surgeons and other providers to review the latest research and technical advances and assess their likely impact on practice."

### A deep dive on the mitral valve

The full-day Friday program is devoted to the mitral valve, beginning with discussions of various imaging modalities in evaluating and quantifying mitral regurgitation and an exploration of the "valve center of excellence" model.

Next comes a detailed survey of degenerative mitral regurgitation, from when and how to intervene to consideration of various special situations, such as Barlow's valve, managing concomitant tricuspid regurgitation and issues around concurrent atrial fibrillation ablation.

All of Friday afternoon is dedicated to functional mitral regurgitation, with focused explorations of a range of topics, from the role of atrial dilatation to integrating other therapies with the MitraClip® device for functional mitral regurgitation.

### Aortic and tricuspid valves on Saturday

The aortic valve takes center stage for much of Saturday morning, which is packed with 15- or 20-minute updates on a range of timely subtopics. A few examples:

- Trends in transcatheter (TAVR) versus surgical aortic valve replacement, including the impact of the new PARTNER 3 trial
- Valve-in-valve TAVR
- Management of aortic regurgitation
- Treatment for the bicuspid aortic valve: Surgery or TAVR, and do we need a randomized trial?

The final few segments before 12:30 adjournment on Saturday will explore the latest in management of tricuspid regurgitation, including an update on transcatheter therapies.

"Our overarching goal will be to clarify optimal management strategies across the spectrum of valvular disease, whether it's choosing between mitral valve repair or replacement or how best to quantify various types of valve disease," says Dr. Svensson. ■

**Visit ccfcme.org/bostonvalve2019 for registration and details. Early-bird registration ends July 7.**

This activity has been approved for *AMA PRA Category 1 Credit™*.

# We're Teaming with Boston Children's in NYC to Keep You Current on CHD

## Innovations in the Management of Congenital Heart Disease: Old Problems, New Approaches

Fri.-Sat., Oct. 4-5, 2019 | JW Marriott Essex House, New York City

**› ccfcme.org/congenitalheart19**

Given that congenital heart disease is one of the most complex realms of cardiovascular practice, why not come at it with the strengths of two powerhouse heart programs instead of just one? That's the thinking behind this CME course jointly offered by Cleveland Clinic and Boston Children's Hospital.

The 1.5-day program aims to extend the knowledge and experience of 25 expert clinician faculty from Cleveland Clinic and Boston Children's to adult and pediatric providers in cardiology, cardiac surgery, pediatrics, internal medicine and beyond.

"Outcomes of both pediatric and adult patients with congenital heart disorders have improved substantially, thanks to innovations in imaging technology, research studies and surgical techniques," says course co-director Lars Svensson, MD, PhD, Chair of Cleveland Clinic's Miller Family Heart & Vascular Institute. "Yet these advances have been so rapid that it can be challenging to keep up, particularly in view of the pathophysiologic complexity of congenital heart disease."

"These challenges have informed the design of this course, which aims to improve attendees' competence and skills in diagnosing congenital heart disorders and choosing appropriate treatment strategies," adds course co-director Pedro del Nido, MD, Chair of the Department of Cardiovascular Surgery at Boston Children's. One of his Boston Children's cardiovascular surgery colleagues, John Mayer, Jr., MD, is a third co-director of the course.

The course relies on a mix of formats — short lectures, case studies, moderated discussions and more — to address its six sessions' broad topical range in a highly tailored way:

- Hypoplastic left heart syndrome, which is explored through cases focused on imaging and perioperative care as well as reviews of surgical and medical management, outcomes and issues that matter most to patients
- Innovative approaches to complex problems, including the biventricular pathway, complex heterotaxy, double-switch and cone procedures, and more
- Outcomes in congenital heart surgery, including discussions of multicenter database analyses, risk scores, quality ratings and big data
- More innovative approaches to complex problems, including 3D printing applications in interventional and surgical management, blood conservation, preoperative rhythm assessment and more
- A range of issues in preserving and restoring valvular function in congenital heart disease
- Discussions of three high-interest topics in the care of adult congenital heart disease, each with perspectives from a medical and a surgical expert

"The program was conceived to be highly multidisciplinary," says Dr. del Nido. "Most topics are addressed from a multiplicity of perspectives, including surgical, medical, imaging, interventional, perioperative, outcomes and more."

"Planning this course has been a delight," adds Dr. Svensson, "as it allows us to combine the expertise of Cleveland Clinic and Boston Children's in highly complementary ways to address congenital heart disease in both adult and pediatric populations. Attendees will benefit from the synergy that results." ■

**Visit ccfcme.org/congenitalheart19 for registration and details. Early-bird registration ends Aug. 4.**

This activity has been approved for *AMA PRA Category 1 Credit™*.

Cleveland Clinic

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# Cardiac Consult

## Live CME Events from Cleveland Clinic

### 20th Annual Intensive Review of Cardiology

**Sat.-Wed., Aug. 17-21, 2019**
InterContinental Hotel & Conference Center | Cleveland

**Info/registration:** ccfcme.org/cardioreview19

### Contemporary Management of Valvular Disease: Diagnosis, Imaging and Intervention

**Fri.-Sat., Sept. 6-7, 2019**
InterContinental Boston | Boston

**Info/registration:** ccfcme.org/bostonvalve2019
(see page 18 for more detail)

### CLE: Comprehensive Lifelong Expeditious Care of Aortic Dissection

**Thu.-Fri., Sept. 19-20, 2019**

InterContinental Hotel & Conference Center | Cleveland

**Info/registration:** ccfcme.org/aorticdissection19

### Global EP Summit 2019

**Fri.-Sat., Sept. 27-28, 2019**
Hilton Cleveland Downtown | Cleveland

**Info/registration:** ccfcme.org/globalep19

### Innovations in the Management of Congenital Heart Disease: Old Problems, New Approaches

**Fri.-Sat., Oct. 4-5, 2019**
JW Marriott Essex House | New York City

**Info/registration:** ccfcme.org/congenitalheart19
(see page 19 for more detail)

### Congenitally Corrected Transposition of the Great Arteries: Management and Outcomes from Infancy to Adulthood

**Thu.-Sat., Oct. 17-19, 2019**
InterContinental Hotel & Conference Center | Cleveland

**Info/registration:** ccfcme.org/pediatricheart19

These activities have been approved for *AMA PRA Category 1 Credit™*.



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