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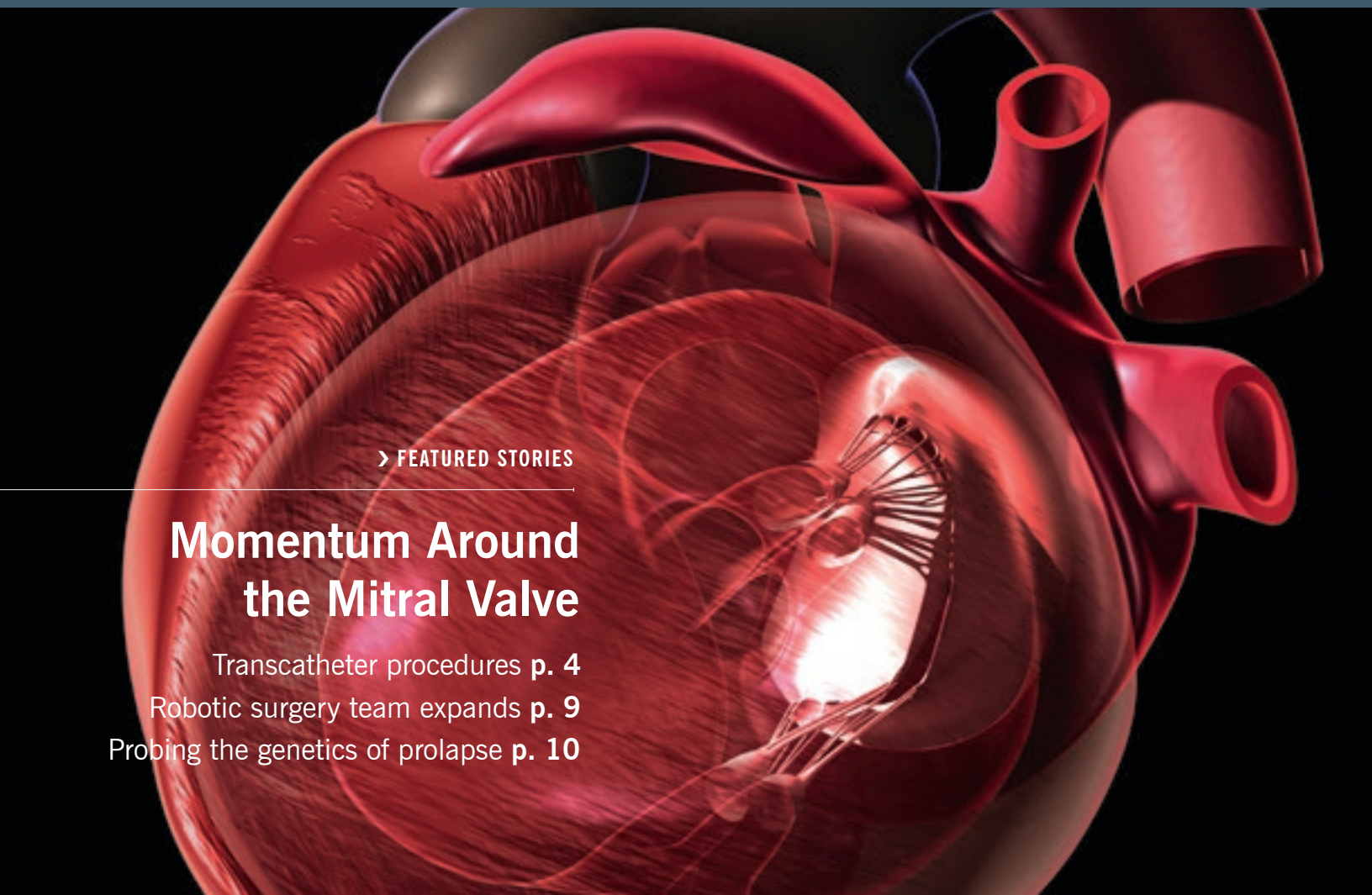
Cleveland Clinic

Cardiac Consult

Heart and Vascular News from Cleveland Clinic | Fall 2017



› FEATURED STORIES

Momentum Around the Mitral Valve

Dear Colleagues,

About 5 percent of the U.S. population has some degree of mitral valve disease. As the busiest mitral valve center in North America, Cleveland Clinic is acutely aware of just how large mitral valve disease looms within the realm of cardiovascular care. But if we had forgotten, this issue of *Cardiac Consult* serves as a clear reminder.

As this issue came together, nearly half of it ended up focusing on aspects of mitral valve disease. The cover story (p. 4) provides a useful update on the state of transcatheter procedures for mitral valve disease, from the flurry of related research activity to the technical challenges that remain. Another article (p. 10) outlines a study our staff have underway to analyze blood from 500 patients with mitral valve prolapse to look for genetic markers for the condition. It's the largest population-based study of the genetics of mitral valve prolapse to date.

In between those articles we have a profile of one of our newest cardiothoracic surgeons, Per Wierup, MD, PhD, who joins us from a stellar career in Sweden to further grow the capacity of our robotic mitral valve surgery program, the largest in the world. And the mitral valve even crops up in our Image of the Issue feature (p. 15), which showcases the emerging utility of four-dimensional CT for evaluating structural causes of bioprosthetic mitral valve dysfunction.

Whether it's for a challenging mitral valve patient or any other exceptionally complex case, our cardiovascular team at Cleveland Clinic is always honored by the opportunity to consult for or assist you, our colleagues across the nation.

Respectfully,

Lars G. Svensson, MD, PhD

CHAIRMAN | Sydell and Arnold Miller Family Heart & Vascular Institute

Cardiac Consult is produced by Cleveland Clinic's Sydell and Arnold Miller Family Heart & Vascular Institute.

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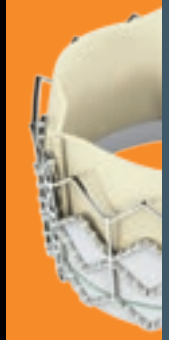
Vitals

Heart & Vascular Vitals: Focus on Cardiovascular Medicine

A sampling of Cleveland Clinic's Miller Family Heart & Vascular Institute outcomes and volumes. This issue's focus is cardiovascular medicine. For more outcomes data, visit **clevelandclinic.org/outcomes**.

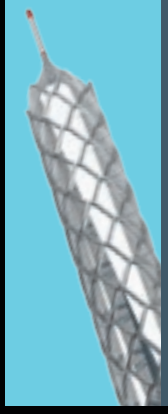


374

Number of TAVR procedures in 2016

0%

In-hospital TAVR mortality in 2016 (vs. 2.9% expected from national benchmark database)



48

Median door-to-balloon time (in minutes) for treatment of STEMI patients in 2016 (N = 76), better than the 90th percentile for comparable hospitals

(Source: ACC National Cardiovascular Data Registry [NCDR] database)

99%

Procedural success rate for left atrial appendage occlusions (LAAOs) in 2016 (N = 101)

0%

Intra- and postprocedure event rate for LAAOs in 2016 (N = 101)

(Source: NCDR LAAO Registry™)

>90th

Percentile ranking for risk-adjusted in-hospital complication rate for ICD implants in the four quarters ending Q1 2016. Our rate of 1.03 compares with 50th and 90th percentile all-hospital rates of 1.40 and 1.08, respectively.

(Source: NCDR ICD Registry™)

1,750

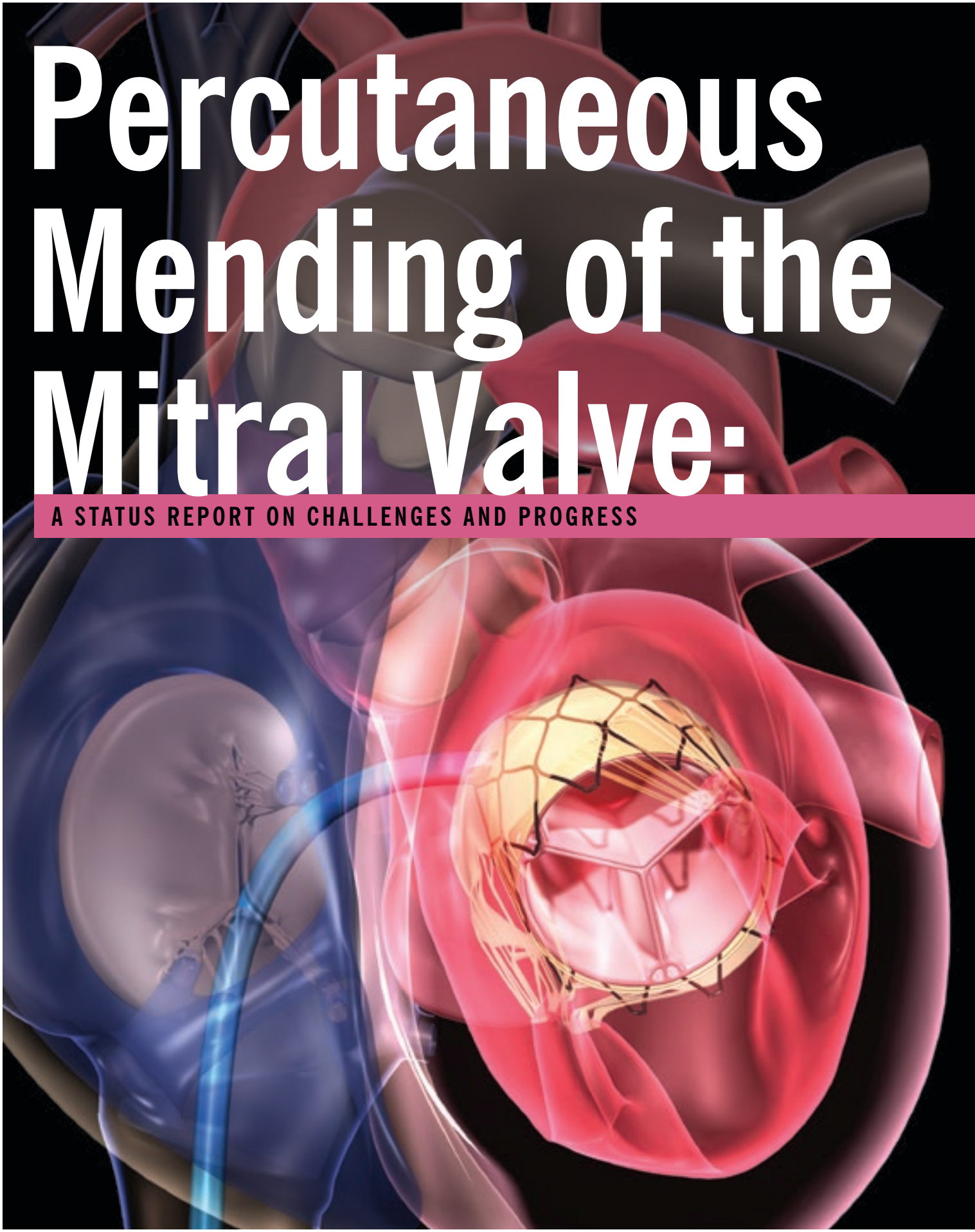
Lead extractions performed, 2012-2016

97.6%

Clinical success rate across those 1,750 lead extractions

Percutaneous Mending of the Mitral Valve:

A STATUS REPORT ON CHALLENGES AND PROGRESS



The use of catheter-based procedures rather than open surgery for treating structural heart disease has taken hold in the past decade, so much so that it's now routinely considered for many cases of aortic valve replacement. But when it comes to mitral valve disease, percutaneous procedures are not so easy, simply because the mitral valve poses greater anatomic challenges for a transcatheter approach.

Those difficulties are compounded by the fact that most patients with mitral valve disease prefer repair of the valve to replacement, explains Cleveland Clinic Cardiothoracic Surgery Chairman A. Marc Gillinov, MD. "To replicate the repair with a catheter is challenging," he says, "because it requires many maneuvers. You tend to not get the kind of results with a catheter that you get with surgery."

Even so, he and Cleveland Clinic colleagues are among those leading efforts to overcome these challenges and offer minimally invasive options for patients with mitral valve disease. "Not all patients are candidates for surgery," notes cardiothoracic surgeon Stephanie Mick, MD, "so it's important to develop nonsurgical options so we can offer treatment to more patients."

"Mitral valve interventions are among the most exciting innovations in interventional cardiology, and they're evolving rapidly," adds Samir Kapadia, MD, Section Head of Interventional Cardiology.

Efforts Focus Largely on Functional MR

As the busiest center for mitral valve repair and replacement in North America, Cleveland Clinic manages more than enough cases to know that open surgery is safe and effective for most patients with degenerative mitral valve regurgitation (DMR). Yet for individuals with DMR who have comorbidities that render surgery too risky, the percutaneously placed MitraClip® device has proved a welcome option since its FDA approval in late 2013 as a repair device for severe DMR.

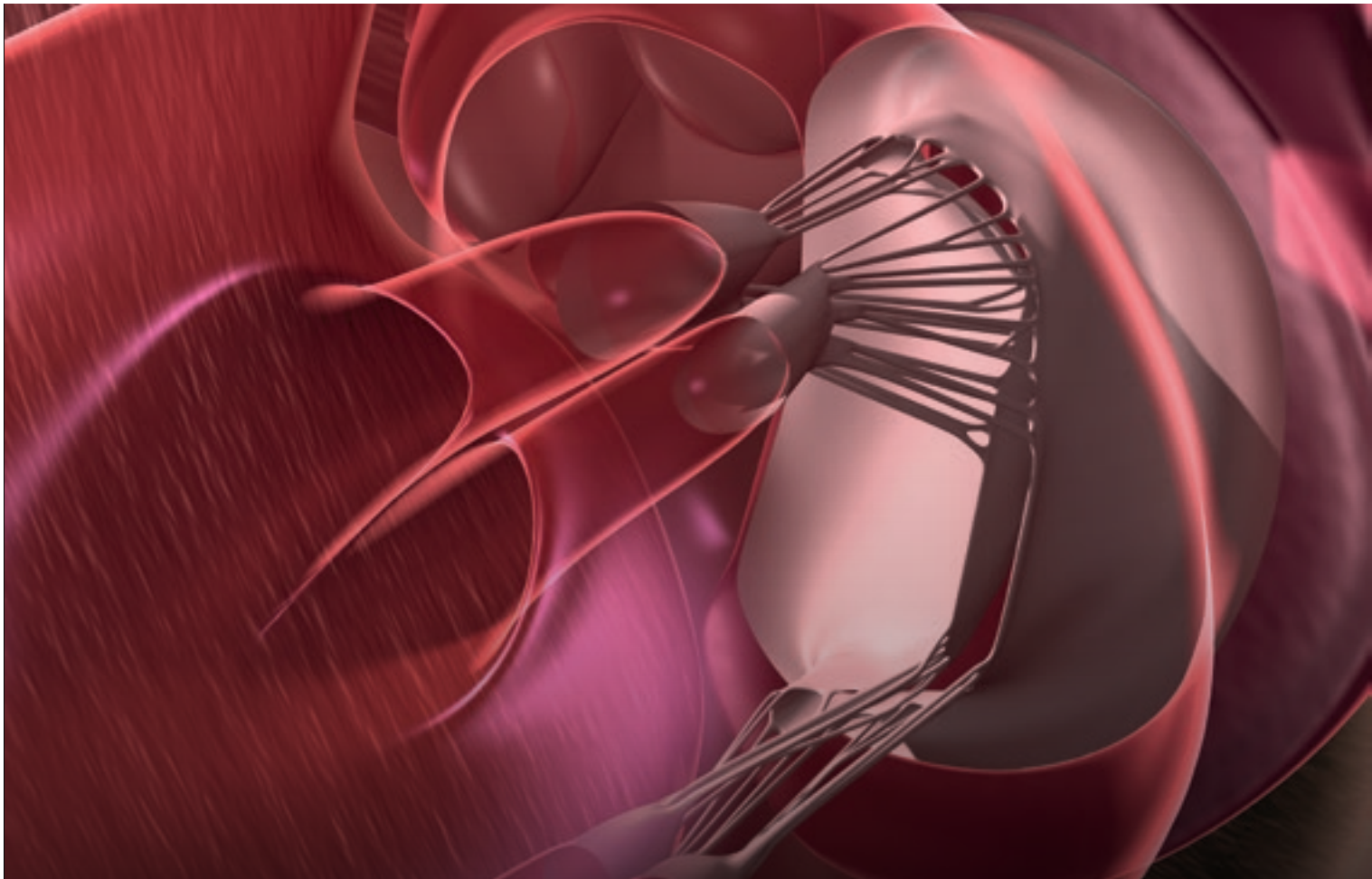
However, for most patients with functional mitral valve regurgitation (FMR) — resulting from factors outside the leaflets themselves — surgery poses a greater risk and is typically less effective. But for these patients no minimally invasive repair or replacement options are currently available in the U.S.

"This has prompted much research into new device technologies largely targeting the population with FMR," notes interventional cardiologist Amar Krishnaswamy, MD. Cleveland Clinic is leading or participating in at least six trials of percutaneous repair or replacement devices for FMR, all aiming for eventual FDA approval. Three of these studies are summarized immediately below.

Percutaneous Mitral Valve Repair: Edge-to-Edge, Direct or Indirect Annuloplasty

COAPT trial. This study is investigating use of the MitraClip device for patients with moderate-to-severe or severe FMR who are deemed inappropriate candidates for surgery. The device is a V-shaped clip delivered via the femoral vein, closing the mitral valve leaflets in an edge-to-edge fashion. Over 600 subjects were randomized in COAPT, with about half receiving the study device and all receiving standard care. The study has reached its 12-month safety and 24-month effectiveness end points, but no data have yet been presented. Cleveland Clinic is one of 83 study sites. Dr. Kapadia is on the trial's steering committee, and Dr. Gillinov is on the central eligibility committee.

Continued next page ›



Transcatheter Treatment of Functional Mitral Regurgitation trial. This prospective, randomized, double-blind trial is assessing the investigational Carillon® Mitral Contour System® for treating subjects with FMR associated with heart failure (control patients are being managed medically). The study device uses an indirect annuloplasty approach, with a nitinol wire placed in the coronary sinus via the internal jugular vein. The study launched in autumn 2017 with a target enrollment of 400 and expected completion in 2020. Drs. Kapadia and Gillinov join Cleveland Clinic's Randall Starling, MD, MPH, as co-principal investigators.

ACTIVE. The ACTIVE trial is assessing transcatheter mitral valve repair with the Cardioband™ annuloplasty system plus guideline-directed medical therapy versus guideline-directed medical therapy alone in patients with FMR and heart failure. Cardioband is an adjustable sutureless band that's placed in the posterior annulus (i.e., direct annuloplasty) via the femoral artery. Adjustment can be performed on a beating heart to optimize correction of mitral regurgitation. The study began in 2017, with an estimated enrollment of 375 patients and planned completion by December 2023. Cleveland Clinic is a participating center.

Dr. Kapadia reflects on these three trials by noting that while MitraClip is a safe device, it may limit future options for transcatheter mitral valve replacement if mitral regurgitation recurs or persists after treatment. In contrast, the devices in the other two trials potentially will allow for future transcatheter valve replacement. "It may be helpful not to burn bridges," he says. "With MitraClip, you may not be able to go back later and replace the valve percutaneously. The Carillon and Cardioband devices may be more compatible with future options."

(Early) Studies of Transcatheter Mitral Valve Replacement

Use of percutaneous techniques has been slower for replacement than for repair of the mitral valve. That has much to do with basic logistics of replacement in this setting: In contrast to aortic valve replacement, the native mitral valve cannot simply be pushed aside without risking left ventricular outflow tract obstruction.

"The question is how to avoid this obstruction in a percutaneous procedure," Dr. Kapadia explains. "Transcatheter mitral valve replacement is an important tool in our armamentarium, but it will take time to become extremely safe and reproducible. Until then, repair may be considered as a first step as long as it doesn't prevent future options."

"Cleveland Clinic has always fostered strong collaboration among interventional cardiologists, cardiac surgeons and the imaging cardiologists who help visualize the structures of importance during these procedures." – Amar Krishnaswamy, MD

"It's fair to say that transcatheter mitral valve replacement is still in its infancy," adds Dr. Mick, "but we're pleased to be involved in several early trials." Those studies are detailed below.

Early Feasibility Study of the Tendyne Mitral Valve System. This trial is designed to "generate initial insights" on the safety and performance of the Tendyne valve, a self-expanding prosthesis with porcine pericardial leaflets. It's delivered transapically and held in place by a tether from the valve to the left ventricular apex. The study includes up to 110 adults with symptomatic mitral regurgitation who aren't candidates for conventional valve repair or replacement. Follow-up continues through two years after implant. Approximately 30 centers, including Cleveland Clinic, are participating. Completion is expected in 2018.

CardiAQ Early Feasibility Study. This 28-patient phase 1 study is evaluating the safety and function of the CardiAQ™ transcatheter mitral valve for both DMR and FMR. The valve is constructed of bovine pericardium and can be delivered via a transseptal or transapical route. Trial completion is expected in 2021. Cleveland Clinic is a participating center.

PRELUDE. This phase 1, single-arm study is assessing the Caisson TMVR system for treating patients with severe symptomatic MR (primary or secondary). The system consists of a self-expanding nitinol frame with a trileaflet porcine pericardial valve that nests in a D-shaped anchor designed to grip the native valve annulus. Delivery is via a transfemoral route. The study began in 2016 and is expected to end in 2021. Dr. Kapadia is study co-director.

Teamwork Will Be Paramount

Despite all these efforts to percutaneously tame mitral valve disease, Dr. Gillinov says widespread transcatheter mitral valve repair and replacement "remains some years off" and is likely to never be as prevalent as transcatheter aortic valve replacement (TAVR) has become. "Percutaneous mitral valve procedures are going to be much more specialized, especially for repairs," he says. "They will need to be extremely team-based."

Dr. Krishnaswamy welcomes this emphasis on teamwork. "Cleveland Clinic has always fostered strong collaboration among interventional cardiologists, cardiac surgeons and the imaging cardiologists who help visualize the structures of importance during these procedures," he explains. "Such collaboration helped us become pioneers in TAVR, and we're committed to building on it to help make transcatheter mitral valve procedures a beneficial option for many patients." ■

Contact Dr. Gillinov at gillinom@ccf.org, Dr. Mick at micks@ccf.org, Dr. Kapadia at kapadis@ccf.org and Dr. Krishnaswamy at krishna2@ccf.org.

Another Front: Valve-in-Valve Procedures

Another area of exploration is the use of transcatheter aortic valve replacement prostheses in patients with degeneration of a prior mitral valve prosthesis or ring. These valve-in-valve and valve-in-ring procedures have been done successfully at Cleveland Clinic, and the valve-in-valve application is FDA-approved. As left ventricular outflow tract obstruction is also a risk, patient eligibility for this option (vs. reoperation) requires in-depth assessment of clinical and anatomic factors.

Heart Surgeon Tomislav Mihaljevic, MD,
Named Cleveland Clinic CEO and President

Cleveland Clinic's Miller Family Heart & Vascular Institute is proud to report that one of its own — cardiothoracic surgeon **Tomislav (Tom) Mihaljevic, MD** — has been appointed the next CEO and president of Cleveland Clinic, effective Jan. 1, 2018.

Dr. Mihaljevic joined Cleveland Clinic in 2004 as a cardiothoracic surgeon specializing in minimally invasive and robotically assisted cardiac surgeries, helping to build the institution's robotic heart surgery practice into the world's largest. Since 2015, he has served as CEO of Cleveland Clinic Abu Dhabi, directing its strategy and operations as the first U.S. multispecialty hospital to be replicated outside North America. In that role he led more than 5,000 caregivers and managed the 364-bed facility.

Dr. Mihaljevic is a native of Croatia and a naturalized American citizen who began practicing in the United States in 1995, initially at Brigham and Women's Hospital.

He will succeed fellow cardiothoracic surgeon Toby Cosgrove, MD, who has served as CEO and president since 2004 and will continue to serve Cleveland Clinic in an advisory role. ■

Q&A Meet the Newest Member of Our Robotic Surgery Team: Per Wierup, MD, PhD

One of Europe's pre-eminent cardiothoracic surgeons, **Per Wierup, MD, PhD**, has joined Cleveland Clinic's Department of Thoracic and Cardiovascular Surgery. A versatile surgeon with broad expertise, he's opted to concentrate on further expanding the world's largest robotic valve surgery practice and a robust program in endocarditis surgery.

Since completing an advanced cardiothoracic fellowship at Cleveland Clinic in 1998-99, Dr. Wierup has held leadership positions at major Swedish and Danish institutions — most recently at Sweden's Lund University Hospital — in many subspecialties, including adult cardiac surgery, pediatric cardiac surgery, and heart and lung transplantation. He helped introduce the maze procedure to Scandinavia, along with valve-sparing aortic surgery and a more modern method of mitral valve repair for use in nearly any patient with mitral regurgitation. He also developed minimally invasive surgery programs using video-assisted thoracotomy as well as robotics to perform the repairs.

Cardiac Consult took a moment to catch up with Dr. Wierup as he settled in at Cleveland Clinic.

Q: Why make this change at this point in your career?

A: Europeans know Cleveland Clinic as the best heart hospital in the world, and you want to play on the best team. I knew the possibilities to thrive and develop from my fellowship year here. When I was in Scandinavia, I was asked to do virtually everything you can do to a heart. As a result, I don't get into clinical situations I don't recognize or know how to handle. I'm now ready to narrow my focus, and the opportunities at Cleveland Clinic are perfectly aligned with my main interests.

Q: What will you be focusing on?

A: My main interest is advanced valve repair, mainly but not exclusively in mitral valves. Reoperations will also be a focus, especially for endocarditis. These are technically complex surgeries that require in-depth understanding of the heart's structure to determine where the infection is, how to clean it out and how to reconstruct the heart.

Q: What about Cleveland Clinic attracted you?

A: I've been back at least 10 times since 1999 for observational fellowships. I've also referred patients. Whenever

I felt a patient could be better cared for here, I referred them and came along. I always learned a lot. I also was drawn by the team approach here. I've joined an exceptional team of surgeons with robotics expertise that includes Marc Gillinov and Stephanie Mick, plus anesthesiologists, cardiologists, nurses, perfusionists and others with expertise in this area. There's a second robotics team at Cleveland Clinic Abu Dhabi established by Rakesh Suri and our next Cleveland Clinic CEO, Tomislav Mihaljevic.

Q: How has Cleveland Clinic changed since the late '90s?

A: The facilities are nice and new. Otherwise there's been no change — and that's good! I see so many familiar faces. People tend to want to stay here. During my fellowship, I was struck by Cleveland Clinic's "patients first" mantra and promoted it wherever I went. I returned knowing that Cleveland Clinic and I were aligned on this thinking. I don't accept "good" results — I want excellent results. ■

For the full interview, see **consultqd.clevelandclinic.org/wierup**.

Contact Dr. Wierup at wierupp@ccf.org.

Probing the Genetics of Mitral Valve Prolapse with the Largest Population Study to Date

The search is on for genetic markers in a 500-patient sample.

The genetics of mitral valve (MV) prolapse pose a bit of a mystery. The condition usually isn't present at birth and generally develops over the course of many decades, yet at least three specific areas of the genome have been associated with prolapse in familial studies reported in the literature.

Cleveland Clinic researchers have published extensively over the past 15 years on various mechanisms by which MV prolapse develops, and now they're turning their attention to how much of a genetic underpinning there is to prolapse development by conducting the largest population-based study of the question to date.

"We have gathered blood samples on 500 individuals with significant mitral valve prolapse that are now being evaluated to determine whether there are specific genetic markers in this population," says Brian Griffin, MD, Cleveland Clinic's Section Head of Cardiovascular Imaging and leader of the research project. "We're looking for genetic signals that can help determine who is at risk for developing prolapse severe enough to require surgical intervention."

"Mitral valve prolapse is one of the most common reasons that people require mitral valve surgery," adds co-investigator A. Marc Gillinov, MD, Chairman of Cardiothoracic Surgery. "While we know how to repair these valves, we don't know what causes the problem. This research aims to unlock that mystery at the genetic level."

Exploiting Sizable Patient Volumes

The study builds on Cleveland Clinic's enormous volume of patients evaluated and treated for MV prolapse each year. Over a period of approximately two years, 500 Cleveland Clinic patients with significant MV prolapse — most of whom required corrective surgery — consented to giving blood samples for genetic analysis. Their samples are being compared with blood from 1,000 control individuals without MV prolapse to look for any areas of the genome where they differ.

"If we find specific areas of interest, we will do a deep dive into those areas to see which genes are implicated and whether they may be involved in the synthesis of proteins within the mitral valve or are otherwise related to valve function," Dr. Griffin explains.

Building on Small Family Studies

The study will include examination of the three genome sites previously shown to be associated with MV prolapse in families with members from multiple generations affected by the condition. Dr. Griffin notes that those prior studies included roughly 20 or 30 individuals within a family, some of whom had prolapse and some of whom didn't. "So those genome sites might be specific to those families," he says. "We hope to learn whether they are or if they apply to mitral valve prolapse more generally."

The study will also look for additional genome sites of interest, which Dr. Griffin says may emerge from this much larger sample in which most patients have MV prolapse severe enough to require surgery. "Ours is the first population study rather than a family-based study," he observes.

In addition to co-investigator Dr. Gillinov, key collaborators on the project include cardiologist W.H. Wilson Tang, MD, Director of Cleveland Clinic's Center for Clinical Genomics, and two of Dr. Griffin's cardiovascular imaging colleagues, Patrick Collier, MD, PhD, and Serge Harb, MD.

The team expects to have data by spring 2018 and to publish findings later next year. "If we get a signal without the statistical power to clearly determine whether it's real, we plan to enroll more patients," Dr. Griffin says. "That's one of the advantages of our sizable mitral valve patient population."

Potential Applications Abound

The researchers are hopeful this study will yield insights for eventual application on several fronts, including:

- **Screening,** through identification of one or more markers for use in pinpointing at-risk individuals before they develop severe MV disease. The aim would be to follow such individuals more closely and potentially offer them earlier intervention.
- **Better pathophysiologic understanding.** The findings may suggest that there is a process underlying MV prolapse — whether it's metabolic, synthetic or something else — that wasn't understood before, and which could guide further research.
- **Potential new interventions.** Though this development is likely the furthest off, Dr. Griffin says it's the most exciting possibility. "For patients today, when the mitral valve develops severe leakage, the horse is out of the barn," he notes. "At that point it's a structural problem that requires surgery. But if we find that somewhere along the line there's a process that leads to eventual disruption of the valve, we might be able to target that process via medications or other interventions to prevent or slow the disruption before valve damage occurs. That could transform the therapeutic approach to mitral valve prolapse."

Dr. Griffin adds that this new genetic study complements his team's prior research on mechanisms behind the development of MV prolapse — such as the disproportionate part played by chordae weakening and the role of glycoproteins — by exploring whether these mechanisms have genetic underpinnings. "It's like a detective story," he observes. ■

Contact Dr. Griffin at griffib@ccf.org and Dr. Gillinov at gillinom@ccf.org.

"When the mitral valve develops severe leakage, the horse is out of the barn and it's a structural problem that requires surgery. But if we find that somewhere along the line there's a process that leads to eventual valve disruption, we might be able to target that process." – Brian Griffin, MD

Cath Lab Leadership Summit Shares Strategies, Successes in Overcoming Obstacles to Efficiency

In modern catheterization labs, the challenges are all about maximizing efficiency, and most solutions involve communication and accountability from the leadership level down. That's the takeaway from a recent daylong retreat convened by the affiliate program team of Cleveland Clinic's Miller Family Heart & Vascular Institute.

The event — the "Cath Lab Leadership Summit: Driving Financial Success in the Procedural Area" — was held in May at Cleveland Clinic's main campus and drew 63 participants from the cath lab leadership teams of 18 hospitals or health systems across the U.S. that have entered into affiliate or alliance relationships with the Heart & Vascular Institute.

The aim was to showcase financial best practices for the cath lab and share what's worked (or hasn't) when implementing changes to boost patient satisfaction, care quality and staff engagement — all while pursuing lower-cost care delivery. This was done through presentations and panel discussions involving leaders of all cath lab stakeholder groups — physicians, nurses, administrators and supply chain managers.

"A systematic and collaborative approach is necessary for achieving the highest level of efficiency and quality in the cath lab," says Samir Kapadia, MD, Director of Cleveland Clinic's Cardiac Catheterization Laboratory. "This is the type of learning we should share more often."

Presenters and discussants came from Cleveland Clinic's main campus and regional hospitals and from several organizations with an affiliation or alliance with Cleveland Clinic, including MedStar Health in the Washington-Baltimore metro area, UPMC Susquehanna in Pennsylvania, and Valley Health in New Jersey. Lively discussion sessions encouraged sharing from all summit participants, representing large academic centers and smaller community hospitals alike.

Consensus Around Challenges

Cath lab discussion topics ranged from administrative, physician and nursing leadership roles to radial access, nursing strategies, optimizing case scheduling, metrics of efficiency, supply chain best practices, business review processes and best practices in documentation.

Common cath lab challenges surfaced in the discussions. These included ensuring consistent tracking of efficiency metrics, variations in schedule processing, lack of communication between electronic medical records and physician

Summit participants from UPMC Susquehanna, an affiliate of Cleveland Clinic's Heart & Vascular Institute. They shared how a high-functioning leadership team has been central to their cardiovascular program's success in achieving an 83 percent market share in their region.

Cleveland Clinic's **Samir Kapadia, MD** (left), chats at the summit with **John Wang, MD**, of MedStar Union Memorial Hospital, one of Cleveland Clinic's allied provider organizations. Each physician directs his institution's cath lab.

"Solid leadership is needed in all three key areas of cath lab operations: administration, physician staffing and nursing."

– Christopher Bajzer, MD

office computers, conflicting policies and procedures, lack of compliance and enforcement, and delays in receiving patient throughput logistics. Further discussion identified themes behind these challenges — built-in obstacles to efficient work flows and an overall lack of accountability for efficiency — and pointed to an overarching key to solutions: strong, coordinated, transparent cath lab leadership.

"The consensus was that solid leadership is needed in all three key areas of cath lab operations: administration, physician staffing and nursing," says Christopher Bajzer, MD, Director of Cardiovascular Medicine, Cleveland Clinic Affiliate Network. "There was further consensus that these leaders must work together and share the same goals for efficiency, with a focus on accountability for achieving those goals."

Presenters from MedStar Union Memorial Hospital shared a compelling example: They overcame poor physician cath lab scheduling practices by implementing what they call a "competitive scheduling process" that rewards physicians for being on time for cases and having pre-procedure paperwork and labs completed and available. The process likewise holds accountable physicians who are late for cases or not prepared.

"Leadership is of utmost importance," said John Wang, MD, chief of the cath lab at MedStar Union. "Physician leaders must lead by example and enforce rules fairly and consistently. In the end, physicians will end up losing credibility if they fail to be on time. That's accountability."

More to Come

This summit followed a 2016 gathering for affiliate and alliance programs focused on electrophysiology lab management. Stay tuned for word on future summits on other high-interest challenges in cardiovascular care. ■

For more on Cleveland Clinic's affiliate and alliance program, see ahsproviders.com.

Do You Realize How Far Our Field Has Come in 50 Years?

1967 was a watershed year in cardiovascular practice, as it witnessed the world's first heart transplant and the development of modern coronary bypass surgery.

That's why 1967 is the starting point for "The Beat Goes On: 50 Years of Heart Health," a multimedia timeline created by T Brand Studio in partnership with Cleveland Clinic. The timeline walks through a multitude of advances of the past half-century that have dramatically reduced heart disease risk and expanded treatment options. Key events are linked to *The New York Times*' contemporary coverage of them via the newspaper's TimesMachine digital archives tool.

Visit the timeline at **cle.clinic/2fcvBg2**. It'll leave you with enhanced pride for our discipline.

Cleveland Clinic Welcomes Boston Children's to Its Cardiovascular Specialty Network

Agreement expands access to complex heart care for contracted employers' pediatric beneficiaries.

Boston Children's Hospital has joined Cleveland Clinic's national Cardiovascular Specialty Network as a joint provider for complex pediatric heart services. The Cleveland Clinic-led network is the first national-scale network of selected high-value cardiovascular care providers for the purpose of contracting with employers and payers.

Boston Children's Hospital
Until every child is well℠

The collaboration brings together two highly renowned clinical programs:

- Cleveland Clinic's cardiology and heart surgery program, rated the No. 1 U.S. program in this category for each of the past 23 years in *U.S. News & World Report*'s "Best Hospitals" rankings
- Boston Children's, rated the top children's hospital in *U.S. News & World Report*'s "Best Children's Hospitals" honor roll for 2017-18, with the No. 2 pediatric cardiology and heart surgery program in the same report

"Teamwork in many forms is the next phase of American medicine," says Hani Najm, MD, Chair of Pediatric and Congenital Heart Surgery at Cleveland Clinic. "We're finding new ways to combine our individual strengths for better patient care and higher value."

As part of the collaboration, Boston Children's has been given special status in the network, including:

- Participation in leadership of the pediatric program along with Cleveland Clinic
- Sharing in the establishment and management of best practices related to patient care, outcome measurement, quality reporting and clinical research for cardiovascular care in children

"Together, our goal to develop and provide consistently high-quality outcomes will drive ongoing improvement and spur innovations for the benefit of patients and families," says Boston Children's Chief of Cardiac Surgery, Pedro J. del Nido, MD, of the agreement. "The collaboration between our organizations offers access to high-quality, cost-effective care for employers' families who need the most complex heart care." ■

For more about Cleveland Clinic's Cardiovascular Specialty Network and related cardiovascular advisory services, visit ahsproviders.com.

New Leader for Cleveland Clinic's Heart Affiliate/Alliance Program

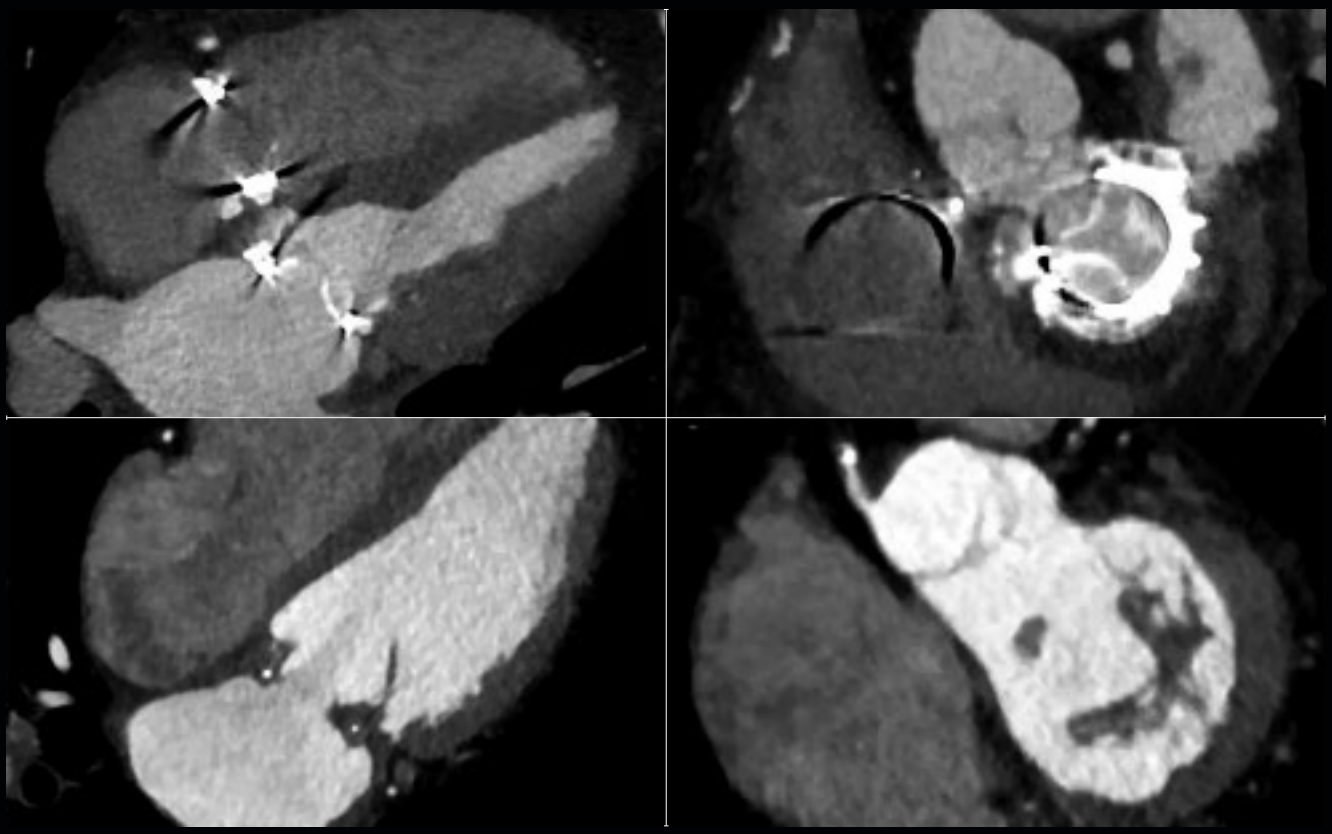
Few physicians understand healthcare value and the changing healthcare environment better than **Jeffrey Rich, MD**. That's why Cleveland Clinic appointed him Chairman of Operations and Strategy for its Miller Family Heart & Vascular Institute a few months ago. A key part of the job is overseeing Cleveland Clinic's growing network of cardiovascular and cardiac surgery affiliate and alliance relationships.

Dr. Rich has held a variety of notable positions focused on quality improvement and payment reform. Among these, he ran Medicare's fee-for-service program in the George W. Bush administration, held leadership positions with the National Quality Forum and testified before Congress on payment models that reward quality over volume.

While practicing cardiac surgery at Sentara Heart Hospital in Virginia, he helped launch a quality initiative for sharing data and outcomes among all Virginia hospitals with cardiovascular programs. They used a clinical financial tool to develop evidence-based protocols to reduce complications and costs, saving the hospitals hundreds of millions of dollars.

"Dr. Rich is well-suited to spearhead our affiliate and alliance relationships," says Heart & Vascular Institute Chair Lars Svensson, MD, PhD. For a Q&A with Dr. Rich, see **consultqd.clevelandclinic.org/drrich**.

Image of the Issue



AN EMERGING USE OF FOUR-DIMENSIONAL CT

Echocardiography is the mainstay for assessing bioprosthetic mitral valve function, but when it comes to assessing structure, there's an emerging role for four-dimensional (4-D) CT. That's particularly the case when there's a diagnostic question of whether the predominant pathology is calcification versus valve thrombosis.

The 4-D CT images above highlight this point. The top two images are from a patient with symptomatic bioprosthetic mitral valve stenosis. On the left, the reconstructed apical four-chamber view shows hyperattenuated bioprosthetic valve leaflets, representing severe calcification. On the right, the short-axis reconstruction also shows leaflet hyperattenuation, consistent with calcification.

In contrast, the bottom two images are from a case of subacute bioprosthetic valve thrombosis in a patient with symptomatic mitral stenosis. On the left, the apical four-chamber reconstruction shows layering hypoattenuation along the sewing ring, indicating thrombus. On the right, the short-axis reconstruction shows prominent hypoattenuation and increased leaflet thickness, illustrating the extension of thrombus onto the leaflets.

Imaging calcium is a strength of CT and a relative weakness of echocardiography, despite the overall strength of echo to assess the severity of bioprosthetic mitral valve dysfunction. The above images highlight how helpful 4-D CT can be in evaluating structural causes of bioprosthetic mitral valve dysfunction, especially for distinguishing between calcification and thrombus. ■

Images and commentary are from Paul Cremer, MD (cremerp@ccf.org), of the Section of Cardiovascular Imaging.

Cardiomyopathy: The Thick and the Thin

Bulk is a defining characteristic of hypertrophic cardiomyopathy (HCM). A thick heart is a dysfunctional heart. But an increasing number of patients are being identified as having all the dysfunction with little or none of the thickness. How can this be? And how do you treat these patients when the best strategy, debulking, is no longer an option? Cleveland Clinic specialists are collaborating on the answers to these questions, and in the process they're opening up a new world of knowledge about HCM in all its manifestations.

Insights from Imaging

"Imaging is the key to our understanding of HCM," says cardiologist Milind Desai, MD, Professor of Medicine at Cleveland Clinic Lerner College of Medicine, "and echocardiography is the mainstay of diagnosis."

Echocardiography confirms that about 70 percent of patients with HCM have left ventricular outflow tract obstruction (LVOTO). In most cases, LVOTO is largely responsible for the symptoms of HCM — i.e., dyspnea, fatigue, chest pain, syncope, etc. — thus explaining the alternate nomenclature *hypertrophic obstructive cardiomyopathy* (HOCM).

Dr. Desai recently led a Cleveland Clinic study (*Circ Cardiovasc Imaging.* 2015;8:e003132) that sought to understand LVOTO in 121 patients with HCM without thick walls. The retrospective study used advanced echocardiography and a newer modality, cardiac magnetic resonance (CMR), to quantify the features of mitral valve and papillary muscle abnormalities in patients with HCM and then confirm whether these abnormalities could be responsible for LVOTO in these patients.

Using these data, Dr. Desai and co-authors substantiated the independent effect of three factors:

- Greater anterior mitral leaflet length
- Abnormal chordal attachment
- Increased bifid papillary muscle mobility

"We used the strengths of each modality," explains Dr. Desai. "Echocardiography was useful in delineating highly mobile mitral valve leaflets, while CMR allowed us to characterize papillary muscle morphology and apical displacement, and to quantify systolic mobility."

Building on previous reports, this study is the largest published analysis of HCM without severe septal hypertrophy.

Dynamic Interplay

"The idea that there could be obstruction without thick walls is relatively new — it's only been around about six or seven years," observes study co-author Harry Lever, MD, a cardiologist in Cleveland Clinic's Section of Cardiovascular Imaging.

A Genetic Disease

Hypertrophic cardiomyopathy (HCM) is the most common genetic heart disease. It affects 1 in every 500 adults. It often runs in families, with inheritance from either parent, and never skips a generation. But it also can appear as a sporadic mutation.

Patients with HCM should be referred for genetic counseling. If the causative mutation can be identified, the patient's siblings and children can also be screened for the disease.

Individuals who are aware that they carry the mutation can opt for regular monitoring, implantable defibrillators or lifestyle changes to mitigate their risk of heart failure or sudden cardiac death. HCM is closely associated with the deaths of young athletes in competitive sports. Those with a family history of HCM may be counseled to avoid vigorous activity.

Individuals who know they carry the mutation can reduce their risk of passing it on to the next generation by having children through in vitro fertilization and using a technique that identifies embryos without the mutation for implantation in the womb.

MRI of a patient with severe obstruction but minimal septal hypertrophy.

"The mechanism is to be found in the dynamic interplay among the mitral valve leaflets, chordae and papillary muscles."

A key factor is the anterior mitral valve leaflet, which was found to be abnormally long in many of the patients studied. The long leaflet buckles toward the septum during systolic contraction. This obstructs the left ventricular outflow tract. Another factor is a structural anomaly known as bifid papillary muscle. Excessive mobility of the bifid papillary muscle distorts the movement of the mitral leaflet during systole. These factors, along with anomalies of the chordae, all contribute to LVOTO.

Refractory HCM is traditionally addressed through a septal myectomy, which restores normal systole dynamics and provides almost immediate relief of symptoms. Alcohol ablation, which may take weeks to relieve symptoms, is used to shrink the septal wall in patients who are not eligible for myectomy.

Neither of these alternatives will help patients who have severe obstruction with thin walls. In the absence of better choices, patients are often offered mitral valve replacement alone or with a light myectomy. Valve replacement resolves some LVOTO issues but is considered less than ideal for what is generally a younger patient population that should be spared the rigors of lifelong anticoagulation.

'Plastic Surgery for the Heart'

Using the knowledge quantified in the study led by Dr. Desai, Cleveland Clinic has developed a multidisciplinary approach to the treatment of thin-wall HCM. Cardiovascular surgeon Nicholas Smedira, MD, Professor of Surgery at Cleveland Clinic Lerner College of Medicine and a co-author of the study, works with colleagues like Drs. Lever and Desai to develop treatment strategies for patients with thin-wall LVOTO.

"Mitral valve replacement is to be avoided," says Dr. Smedira. "If the problem is the length of the anterior mitral valve leaflet, we can go in and shorten it. This reduces contact with the septum during systole, and spares the native valve."

In patients in whom bifid papillary muscle mobility is the larger issue, Dr. Smedira surgically reorients the papillary muscles away from the septum. Dr. Lever describes these techniques as "plastic surgery for the heart."

Drawing the Septal Curtain

The study by Dr. Desai and colleagues goes a long way toward drawing back the septal curtain that obscures the independent factors contributing to LVOTO. Through use of multimodality imaging, it has produced a more nuanced picture of HCM — and lays the groundwork for future progress.

"Our findings strengthen our commitment to personalizing treatment for HCM — and to ensuring that every patient gets the most appropriate treatment for his or her condition," says Dr. Desai. "Advanced echocardiography combined with CMR provides a rich core of data to help us make treatment decisions that are in the patient's best interest." ■

Contact Dr. Desai at desaim2@ccf.org, Dr. Lever at leverh@ccf.org and Dr. Smedira at smedirn@ccf.org.

The Experience Edge

The surest way to reduce surgical risk is to have an operation done at a center that frequently performs that surgery. This is particularly true for complex cardiac procedures like septal myectomy, valve repair and papillary muscle realignment.

Cleveland Clinic cardiovascular surgeons have performed more than 3,000 septal myectomies over the past 50 years. More than 2,000 of these have been performed by Nicholas Smedira, MD, a cardiovascular surgeon with a strong interest in HCM.

"We often do 200 or more myectomies a year," says Dr. Smedira. "I'm pretty certain that's the largest number of any medical center in the United States."

In fact, Dr. Smedira and colleagues performed 207 surgical myectomies in 2016. And mortality for septal myectomy at Cleveland Clinic is consistently well below the expected rate, coming in at approximately 0.2 percent over the past 10 years.

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

Differential BP Effects with Chronic Use of 3 NSAIDs

Among patients taking daily NSAID therapy for arthritis, the nonselective NSAID ibuprofen was associated with a significant rise in systolic blood pressure (BP) and a higher incidence of new-onset hypertension compared with the selective COX-2 inhibitor celecoxib. So finds a new substudy of the large PRECISION trial published in late 2016. The substudy, dubbed PRECISION-ABPM, set out to evaluate the BP effects of celecoxib versus ibuprofen and another nonselective NSAID, naproxen, which had BP effects intermediate to those of the other two drugs.

"These findings concur with the primary outcomes of the overall PRECISION trial and could impact clinical outcomes for patients who use NSAIDs chronically," says co-author Steven Nissen, MD, of Cleveland Clinic, who chaired PRECISION. "Just as clinicians weigh GI safety risks when considering NSAIDs, they need to do so for blood pressure risks, especially with ibuprofen." The study was published in the *European Heart Journal*. More at consultqd.clevelandclinic.org/precision-abpm.

Diabetes, CABG Graft Patency and Long-Term Survival

Diabetes doesn't compromise the long-term patency of grafts used in coronary artery bypass (CABG), yet long-term survival is worse in CABG patients who have diabetes versus those who don't. Those are the somewhat surprising findings of an unprecedentedly large observational study from a Cleveland Clinic database examining CABG outcomes by patients' diabetes status over more than 20 years of follow-up. Nearly 16,000 postoperative angiograms were assessed for graft patency.

Notably, the study also showed that while internal thoracic artery (ITA) graft patency remained high and stable over time across the cohort, saphenous vein graft patency declined progressively for diabetic and nondiabetic patients alike. "This argues for use of ITA grafts whenever possible, regardless of diabetes status," says Cleveland Clinic cardiac surgeon Faisal Bakaeen, MD, a study co-author. He adds that while the causes of reduced survival among diabetic CABG patients remain uncertain, lower graft patency isn't one of them. The study is published in the *Journal of the American College of Cardiology*. More at consultqd.clevelandclinic.org/cabgdiabetes.

Hope for Fully Percutaneous Bypass of Long Fem-Pop Lesions

Long-segment femoropopliteal (fem-pop) lesions may be treatable with a fully percutaneous bypass procedure, according to a subset analysis of the multicenter DETOUR I study. The analysis involved 50 patients with extremely long fem-pop blockages — 25 to 45 cm — treated with a procedure using the investigational Detour system to provide fully percutaneous bypass. Six-month results of the single-arm investigation showed a 76.9 percent overall primary patency rate (88.9 percent with optimal device placement) with a low rate of major adverse events (2 percent) and no significant impact on venous health.

"These outcomes suggest that a fully percutaneous bypass procedure has potential to fill the traditional gap between the durability of open surgery and the reduced invasiveness of endovascular approaches in the setting of fem-pop blockages of 25 to 45 cm," says Cleveland Clinic vascular surgeon Sean Lyden, MD, who presented the results at the VIVA 17 conference in September. More at consultqd.clevelandclinic.org/fem-pop.

Heart Med Price Spikes Are Far from Benign, Analysis Shows

Despite arguments to the contrary, dramatic U.S. price increases for two critical inpatient heart drugs — nitroprusside and isoproterenol — have resulted in large declines in these drugs' utilization. So concludes a Cleveland Clinic study published in the *New England Journal of Medicine*. From 2012 to 2015, wholesale acquisition costs rose 30-fold for nitroprusside and nearly 70-fold for isoproterenol. "It's been claimed in testimony to Congress that these price increases would not reduce access to or utilization of these two vital drugs," explains Cleveland Clinic cardiologist Umesh Khot, MD, the study's lead author.

But his team's analysis of a database of 47 U.S. hospitals showed otherwise, demonstrating declines of 46 percent (per 1,000 inpatients) and 53 percent (absolute) in use of nitroprusside from 2012 to 2015 and declines of 40 percent (per 1,000 inpatients) and 35 percent (absolute) in use of isoproterenol over the same period. "Physicians have decreased their use of these drugs, for which there are no direct therapeutic equivalents," says Dr. Khot. "Our findings show that these price hikes have not been benign." More at consultqd.clevelandclinic.org/pricespikes.

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About Cleveland Clinic

Cleveland Clinic is an integrated healthcare delivery system with local, national and international reach. At Cleveland Clinic, more than 3,500 physicians and researchers represent 140 medical specialties and subspecialties. We are a main campus, more than 150 northern Ohio outpatient locations (including 18 full-service family health centers and three health and wellness centers), Cleveland Clinic Florida, Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas, Cleveland Clinic Canada and Cleveland Clinic Abu Dhabi.

In 2017, Cleveland Clinic was ranked the No. 2 hospital in America in *U.S. News & World Report*'s "Best Hospitals" survey. The survey ranks Cleveland Clinic among the nation's top 10 hospitals in 13 specialty areas, and the top hospital in heart care (for the 23rd consecutive year) and urologic care.

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Fri., Feb. 9, 2018, 7 a.m. to 5 p.m.
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Info/registration: events.medtelligence.net/CV18.html

8th Annual Case-Based Approach to Controversies in Cardiovascular Diseases

Fri.-Sat., Feb. 16-17, 2018
Mohammed Bin Rashid Academic Medical Center | Dubai, UAE

Offered in partnership with Mayo Clinic

Info/registration: cvuae.com

Valve Disease, Structural Interventions, and Diastology Summit

Fri.-Sun., March 2-4, 2018
Marriott Harbor Beach Hotel
Ft. Lauderdale, Florida

Offered in collaboration with Atlantic Health System/Morristown Medical Center and in cooperation with the American Society of Echocardiography

Info/registration: ccfcme.org/echo

Managing Valvular and Thoracic Aortic Disease: What Every Cardiologist Should Know in 2018

Fri., March 9, 2018, 7-9:30 p.m.
Hilton Orlando | Orlando, Florida

An independent certified session at the ACC's 67th Scientific Session (ACC.18)

Info/registration: ccfcme.org/aorticacc

Case-Based Approach to the Heart Failure Patient: Getting from the Start to the Finish Line Successfully

Fri., March 9, 2018, 7-9:15 p.m.
Rosen Centre | Orlando, Florida

An independent certified session at the ACC's 67th Scientific Session (ACC.18)

Info/registration: ccfcme.org/ephfacc

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