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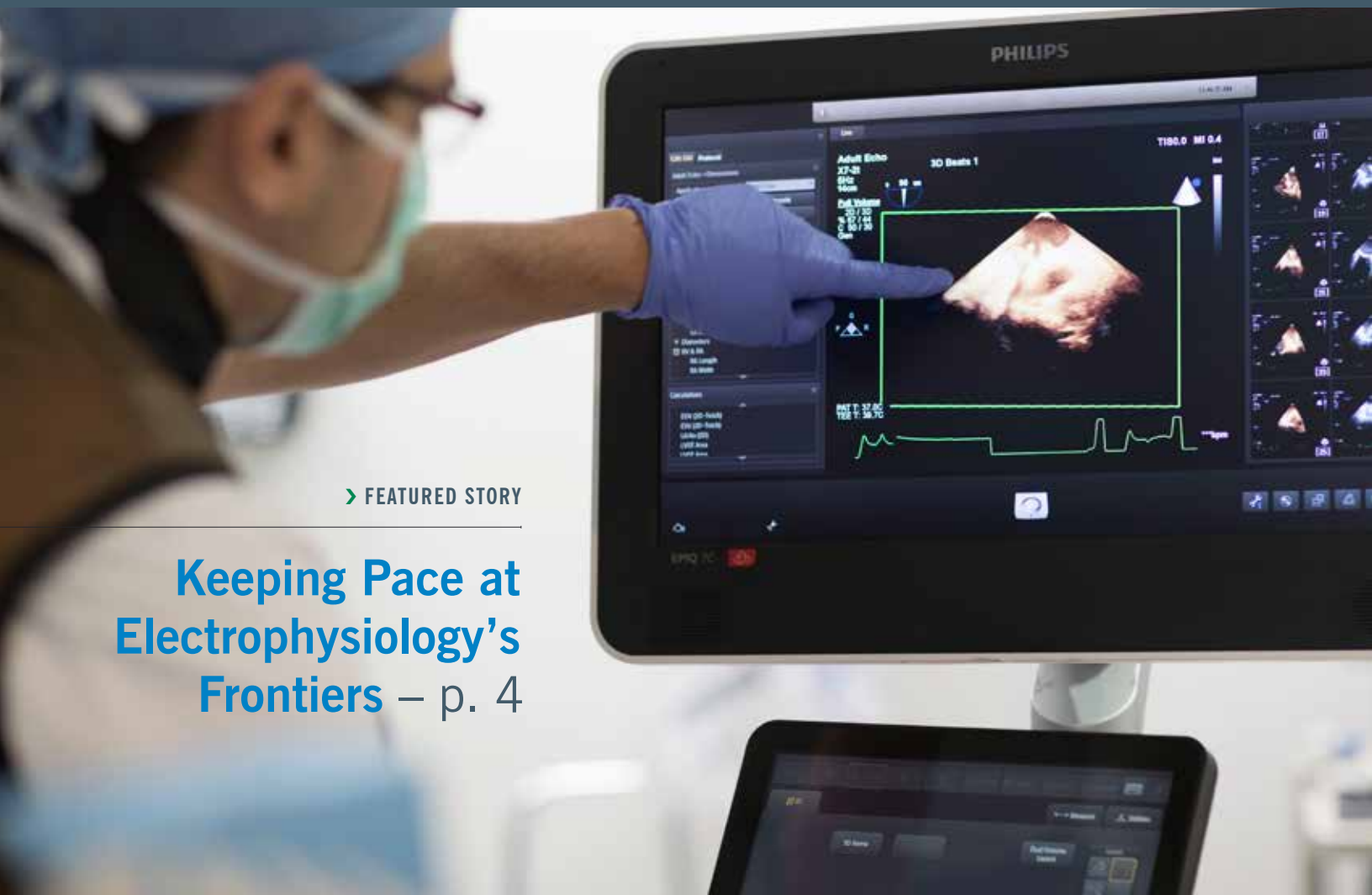
Cleveland Clinic

Cardiac Consult

Heart and Vascular News from Cleveland Clinic | Summer 2017



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Dear Colleagues,

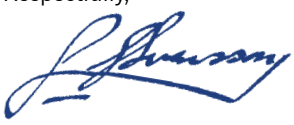
The best organizations know that maintaining a steady supply of new leaders is key to preserving their organizational excellence. That knowledge has been an essential reason why Cleveland Clinic's Miller Family Heart & Vascular Institute has now been recognized as the No. 1 cardiology and heart surgery program by *U.S. News & World Report* for 23 straight years. Identifying and cultivating new leaders is central to our culture and a secret to the successes we bring to our patients.

In this issue of *Cardiac Consult* we're pleased to share profiles of two of our program's newest leaders. On page 8, our new Chair of Thoracic and Cardiovascular Surgery, A. Marc Gillinov, MD, shares thoughts on what lies ahead for his specialty, and our cover story details some priority initiatives of Oussama Wazni, MD, as he takes on leadership of our dynamic Section of Cardiac Electrophysiology and Pacing.

Of course, leadership beyond one's own institution is equally vital. In this issue we are proud to note that the outgoing and incoming presidents of the Society for Vascular Medicine are both Cleveland Clinic physicians — John R. Bartholomew, MD, and Heather Gornik, MD. On page 12 these vascular medicine specialists — one a veteran in the field and the other a fast-rising young leader — reflect on the future of their subspecialty from their unique vantage points.

We at Cleveland Clinic look forward to working with our cardiovascular colleagues across the nation to continue to elevate the future leaders of our specialty areas. When leadership remains fresh and vibrant, the benefits to our disciplines extend beyond institutional borders to touch patients far and wide.

Respectfully,



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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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Heart & Vascular Vitals:
Focus on Cardiothoracic Surgery

A sampling of Cleveland Clinic's Miller Family Heart & Vascular Institute outcomes and volumes. This issue's focus is cardiothoracic surgery. For more outcomes data, visit **clevelandclinic.org/E15**.

3 for 3 in STS Adult Cardiac Surgery Database

Cleveland Clinic achieved a 3-star (highest) rating in all 3 surgical categories of the Society of Thoracic Surgeons (STS) National Adult Cardiac Surgery Database for the period ending 12/31/2016 (1-year period for CABG; 3 years for other categories). The rating applies to Cleveland Clinic's main campus and Fairview and Hillcrest regional hospitals.

1.3% Only 14 (1.3%) of the 1,068 STS Adult Cardiac Surgery Database site participants achieved this distinction.

CABG	AVR	AVR+CABG
★ ★ ★	★ ★ ★	★ ★ ★

3 Stars in Lobectomy, Too

Cleveland Clinic also achieved a 3-star overall rating for lobectomy for lung cancer in the STS General Thoracic Surgery Database for the 3-year period ending 12/31/2016. It was among only 10 (5.4%) of 186 ranked participating sites to achieve this distinction.

More Stats of Note

1/3 Mortality was one-third the expected rate across the 3 procedure categories in the STS Adult Cardiac Surgery Database in 2016 (0.6% vs. 1.9%)

0% Mortality for isolated mitral valve repair for 2014-2016 (vs. 0.9% expected [STS])

1.6% Mortality for pediatric congenital surgery in 2016 (vs. 3.1% expected [Vizient])

4,471 Cardiac surgeries in 2016 — most to date

3,039 Valve surgeries in 2016 — most to date

1,724 Thoracic surgeries in 2016 — most to date

265 Thoracic endovascular aortic repairs in 2016 — most to date

110 Lung transplants in 2016 — 2nd-highest volume in U.S.

87 Aortic valve-sparing LGS reimplantation operations in 2016 — most to date

Keeping Pace at Electrophysiology's Frontiers:

New Leadership Looks to Link Research with Practice to Tackle Complex Cases

When Oussama Wazni, MD, takes over as head of Cleveland Clinic's Section of Cardiac Electrophysiology and Pacing in September 2017, he'll be leading a vibrant, internationally recognized team committed to advancing the standard of care for patients with abnormal heart rhythms and related complications.

Dr. Oussama Wazni and a colleague during a WATCHMAN implantation.

"I'm excited to continue our leading-edge clinical work and build on our research efforts," says Dr. Wazni, who has been a member of the section since 2006, most recently directing its outpatient clinic. "We have the capability to study a clinical problem from the bench to the preclinical lab and then ultimately in patients."

Translation in Practice

That translational approach is well-represented by work done within the section's Atrial Fibrillation Center, a multidisciplinary specialty treatment group devoted to addressing both paroxysmal and persistent atrial fibrillation (AFib) using new mapping technology, lead removal when devices go awry and new approaches to stroke prevention.

"It's an exciting time for ablation," says Atrial Fibrillation Center Director Walid Saliba, MD. "We're acquiring new tools to make our work easier, safer and more efficient. For the first time we're using sophisticated mapping to help us understand what goes on during AFib. There's a long way to go, but we hope that improved understanding can yield better ablation success rates."

Management of ventricular tachycardia (VT) is another area of expertise — one in which a major initiative has been mapping and ablation in patients with severe forms of VT who are often turned away by other centers. "At Cleveland Clinic, because of our close collaboration with heart failure colleagues and cardiac surgeons, we're able to tackle the most complex cases of VT, with encouraging outcomes," Dr. Wazni says.

A Multidisciplinary Take on Stroke Prevention

In the realm of stroke prevention, Cleveland Clinic's Atrial Fibrillation Stroke Prevention Center has helped pioneer the use of implanted devices designed to close the left atrial appendage to prevent clot migration in patients with nonvalvular AFib who are at high risk for bleeding. In addition to

electrophysiologists, the center is staffed by interventional cardiologists, imaging cardiologists, neurovascular medicine specialists and gastroenterologists with expertise in the bleeding complications of anticoagulants.

"The whole concept of the center — and of closing the left atrial appendage for stroke prevention — is new," Dr. Saliba notes.

The center is currently participating in a head-to-head trial of two left atrial appendage closure devices — the FDA-approved WATCHMAN™ and the investigational AMPLATZER™ Amulet™. "These devices work similarly but have different designs, and their implantation is different," Dr. Wazni notes. "We're hopeful that both will perform well."

Mapping and Intervening When AFib Persists

Another major research effort centers on elucidating the mechanisms behind persistent AFib. "We know a lot about paroxysmal AFib, but uncertainty remains around persistent AFib," Dr. Wazni explains. "We've put intense effort into understanding persistent AFib, as it continues to be a clinical problem without a very good solution."

Last year, Cleveland Clinic researchers published a study demonstrating the importance of performing catheter ablation as soon as possible following diagnosis of persistent AFib (*Circ Arrhythm Electrophysiol.* 2016;9:e003669). And in a separate study published this year (*J Cardiovasc Electrophysiol.* 2017;28:483-488), they found that the use of contact force sensing in persistent AFib ablation is associated with shorter procedure times and fewer arrhythmia recurrences.

Cleveland Clinic electrophysiologists are also among a select few to work with several different manufacturers to employ the latest multielectrode 3-D mapping technology for both clinical use and research into AFib and VT. "We map AFib with the goal of understanding where it's coming from," Dr. Wazni observes. "Several different systems will likely yield the answer, but we don't yet know which ones."

The team has also developed expertise in "redo" ablations for patients who continue to experience AFib despite a prior ablation. In these cases, the redo is typically needed because the pulmonary veins weren't completely ablated (see sidebar), arrhythmias other than AFib are at play or the patient may have post-ablation atrial flutter, which requires further mapping to localize and eliminate, Dr. Saliba explains.

Taking Lead Management Beyond Extraction

While many U.S. centers place cardiac implantable electronic devices (CIEDs) to treat arrhythmias, Cleveland Clinic is one of far fewer with expertise in removal of the devices' leads in the event of infection, recall or malfunction. But this focus on leads extends beyond simple extraction, according to Bruce Wilkoff, MD, Director of Cardiac Pacing and Tachyarrhythmia Devices.

"We tend to talk about 'lead management,' or how to plan for lifelong therapy with pacemakers and defibrillators with leads," he says. "We continue to work on reducing the need for lead extraction while improving the safety of doing so if it's necessary."

In one such effort, Cleveland Clinic is serving as lead center in a randomized, prospective, international study of nearly 7,000 CIED recipients to learn whether the TYRX™ antibiotic-releasing absorbable envelope for CIEDs reduces the risk of infection during the year following implantation. The study is nearly fully enrolled and will continue for another year, says Dr. Wilkoff, who chairs its steering committee.

When **AFib** Recurs After Long-Term Success

When patients achieve long-term success with AFib ablation, it's reasonable to think they have well-isolated pulmonary veins, but that's not always the case. So found a recent analysis of a prospective registry of more than 10,000 patients who underwent AFib ablation at Cleveland Clinic from 2000 to 2015. Fortunately, the study also showed that these patients stand to benefit from redo ablations.

The analysis identified 137 patients who had initially enjoyed freedom from AFib for more than 36 months after ablation (median, 52 months) before undergoing repeat ablation for recurrent AFib.

In the redo ablations, reconnections along at least one pulmonary vein were found in 81 percent of patients. Additional ablations were performed at the veins, as well as in the substrate, as deemed necessary. After median follow-up of 17 months, 75.2 percent of patients were arrhythmia-free after their redo ablation.

The finding raises questions such as how quickly pulmonary vein reconnections develop after ablation, says Cleveland Clinic electrophysiologist Ayman Hussein, MD, who presented the study at the Heart Rhythm Society's 2017 annual scientific sessions. He notes that Cleveland Clinic is designing multiple studies to identify the mechanisms behind persistent arrhythmias. "We hope to achieve more durable pulmonary vein ablations," he says. For more, see **consultqd.clevelandclinic.org/afib**.

Data Diving to Promote Extraction Safety

Another focus involves the use of a novel compliant endovascular balloon device during transvenous lead extraction in the unlikely event of a tear in the superior vena cava. While such tears happen in less than 2 percent of procedures, the case fatality rate due to rapid bleeding is roughly 50 percent. Approved by the FDA in February 2016, the Bridge™ Occlusion Balloon temporarily occludes the torn vessel to give a surgeon sufficient time to repair the damage.

Dr. Wilkoff and colleagues searched the FDA's Manufacturer and User Facility Device Experience (MAUDE) database for superior vena cava tears related to lead extraction procedures during the final six months of 2016. The sample was small — 35 tears in all — but the results were striking: 100 percent of patients (9/9) were discharged alive when the balloon was used, compared with 50 percent (13/26) when it wasn't.

Those data were presented at the Heart Rhythm Society's 2017 scientific sessions and simultaneously published in *Heart Rhythm* (2017 May 13 [Epub ahead of print]). "This device is just beginning to be employed on a regular basis," says Dr. Wilkoff. "We're working to establish best practices for its safe use."

Balancing Future and Present

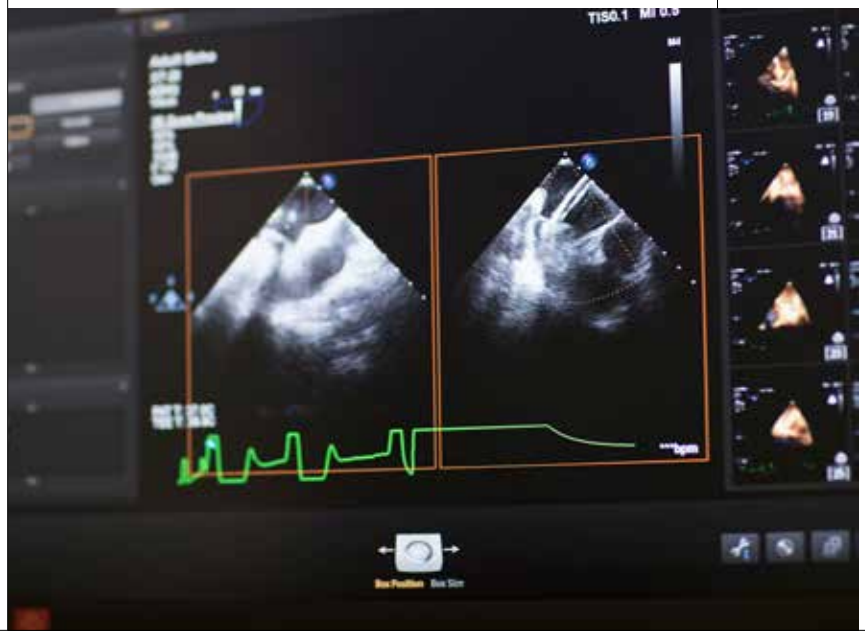
While Cleveland Clinic cardiologists are also involved in several trials of leadless pacemakers, those devices are currently limited to single-chamber right ventricular pacing, whereas many patients require dual- or triple-chamber pacing. "Leads are going to be around for a long time to come," Dr. Wilkoff remarks.

Improving Response to CRT Nonresponders

Cardiac resynchronization therapy (CRT) has been a godsend for patients with advanced heart failure, but as many as one-third of patients fail to respond. Those individuals are the target population of a CRT optimization clinic recently launched under the leadership of electrophysiologist John Rickard, MD, MPH, Director of Cleveland Clinic's CRT Program.

In the absence of a thorough multidisciplinary assessment, patients who don't respond to CRT are at increased risk for poor exercise tolerance, repeat hospitalizations and early death, says Dr. Rickard. In response, he explains, the CRT optimization clinic is designed to "troubleshoot the care of the sickest patients" with a collaborative approach that employs a comprehensive algorithm-driven evaluation to systematically identify possible reasons for CRT nonresponse.

The clinic uses a multidisciplinary model — with input from electrophysiologists, heart failure and imaging cardiologists, cardiothoracic surgeons and sometimes other subspecialists — to assess findings from the algorithm-driven examination, determine potential reasons for CRT nonresponse and establish a treatment plan to optimize long-term outcomes. "Our goal is to leave no stone unturned," says Dr. Rickard. For more, see **consultqd.clevelandclinic.org/crt**.



Indeed, he is co-chairing a panel working on a consensus document on lead management, which will be published as an upcoming Heart Rhythm Society guideline.

These endeavors and others (see sidebar) contribute to Dr. Wazni's vision for the Section of Cardiac Electrophysiology and Pacing under his leadership. "We'll continue to aspire toward impactful research that both informs the field and directly improves patient care." ■

Contact Dr. Wazni at waznio@ccf.org, Dr. Saliba at salibaw@ccf.org and Dr. Wilkoff at wilkofb@ccf.org.

Tracking TMAO's Trail in Cardiometabolic Disease: **Not for the Weary**

New studies implicate the gut microbial metabolite in more and more conditions.

For the better part of a decade, the Cleveland Clinic research team led by Stanley Hazen, MD, PhD, has been following where the gut microbial metabolite TMAO leads.

It's taken them — by way of studies in *Nature*, *New England Journal of Medicine*, *Cell* and more — to evidence of a contributory role for TMAO (trimethylamine-*N*-oxide) in cardiometabolic disorders ranging from atherosclerosis to heart failure to chronic kidney disease. Now they've published two new studies extending TMAO's reach further still, finding that TMAO from dietary choline is prothrombotic in humans and demonstrating that high TMAO levels are associated with increased incidence of type 2 diabetes.

Evidence of Prothrombotic Effects

In an April 2017 paper in *Circulation* (2017;135:1671-1673), Dr. Hazen and colleagues showed for the first time in a human intervention study that the dietary nutrient choline (abundant in animal products) exerts a direct prothrombotic effect via elevated levels of TMAO, a byproduct of choline digestion. They also found that the heightened platelet responsiveness mediated by elevated TMAO appears to be attenuated by low-dose aspirin.

The findings come from studies in 18 healthy subjects who took oral choline supplements for two months. As subjects' plasma TMAO levels rose with choline supplementation, the rise corresponded with significantly enhanced mean platelet aggregation responses to submaximal adenosine diphosphate in a dose-dependent fashion. Effects were seen in omnivores and vegans/vegetarians alike.

"TMAO appears to supercharge platelet function," says Dr. Hazen, Chair of Cellular and Molecular Medicine and Section Head of Preventive Cardiology and Rehabilitation. "These studies are consistent with our prior animal studies, and they further support a direct mechanistic link between TMAO levels and risk for clotting events such as myocardial infarction and stroke."

Next the omnivores from the initial study (n = 10) were started on low-dose aspirin (81 mg/day) for one month, after which they received two months of choline supplementation while aspirin was continued.

Relative to baseline, fasting plasma TMAO and platelet aggregation responses increased after choline supplementation. Notably, however, the degrees of TMAO rise and platelet hyperresponsiveness during this second study, when subjects received aspirin, were significantly attenuated compared with the initial study ($P < .01$ for both measures).

"These results suggest that the platelet hyperresponsiveness that's mediated by increased TMAO can be reduced by low-dose aspirin," says Dr. Hazen. "Further research is needed, but it appears that patients without known cardiovascular disease but with elevated TMAO levels might benefit from both aspirin and diet modification to prevent blood clotting."

Clearest Linkage with Obesity, Diabetes to Date

In a separate paper (*Cell Rep*. 2017;19:2451-2461), a Cleveland Clinic colleague, J. Mark Brown, PhD, collaborated with Dr. Hazen's team to show that the TMAO-generating pathway is linked to obesity and energy metabolism. They did so in complementary studies in mice and humans.

In mice the researchers focused on the host enzyme FMO3, which produces the active compound, TMAO, from a gut microbe-generated precursor. They found that mice with a missing or silenced gene encoding for FMO3 were protected from obesity despite being fed a high-fat, high-calorie diet and eating the same amount of food as control mice. Moreover, FMO3-negative mice showed higher expression of genes associated with beige adipose tissue, which is more metabolically active than white adipose tissue.

To establish clinical relevance in humans, the researchers analyzed plasma TMAO levels in 435 patients undergoing cardiac risk evaluation. They found that TMAO levels were significantly higher, in a dose-dependent fashion, in subjects with type 2 diabetes.

"Obesity, diabetes and cardiovascular disease are strongly linked," says Dr. Brown. "These findings are among the earliest evidence of how gut bacteria influence obesity. They shed light on a possible way to therapeutically manipulate the microbiome to combat both obesity and diabetes." ■

For more, see consultqd.clevelandclinic.org/prothrombotic and consultqd.clevelandclinic.org/fmo3.

Q&A Meet Our New Chair of Cardiothoracic Surgery, A. Marc Gillinov, MD

In April 2017, Cleveland Clinic appointed **A. Marc Gillinov, MD**, as Chair of its Department of Thoracic and Cardiovascular Surgery. Since joining Cleveland Clinic's cardiothoracic surgery staff in 1997, Dr. Gillinov has specialized in mitral valve repair, robotically assisted mitral valve surgery, aortic valve surgery and atrial fibrillation. He has one of the world's largest practices in robotic and minimally invasive mitral valve repair.

In addition to his clinical responsibilities, Dr. Gillinov (shown above) serves as Chief Experience Officer of the Miller Family Heart & Vascular Institute and holds The Judith Dion Pyle Chair in Heart Valve Research. Several of his surgical innovations have been granted patents, and he is a widely published researcher and active lecturer.

"Marc is an innovative surgeon who grew up in Cleveland, showed an early interest in heart surgery as a research assistant at Cleveland Clinic during high school, and went on to become an internationally recognized leader in mitral valve surgery," says Heart & Vascular Institute Chair Lars Svensson, MD, PhD. "The robotic surgery team he's led achieved the unequalled result of an operative risk of less than one-tenth of 1 percent across more than 1,500 robotic mitral valve surgeries. I have no doubt our overall cardiothoracic team will continue to make major contributions to heart care under his leadership."

Cardiac Consult caught up with Dr. Gillinov for a Q&A on his vision for the department, the future of his specialty and collaboration in cardiovascular care.

Q: Taking the helm of a department as celebrated as this one must be daunting. How will you maintain the tradition of excellence?

A: We already have the best surgeons and teams, and this motivates everyone to operate at the highest level. Today there are a variety of novel challenges that accompany the delivery of first-class surgical care. These include expanding requirements for documentation, complex insurance issues and the pervasive requirement to improve affordability. We will approach these challenges with creativity and innovation.

Q: Continuous improvement is at the heart of the Cleveland Clinic ethic. How would you like this department to further improve under your leadership?

A: Patients often come thousands of miles to see us, and we must ensure that they receive the best care at every stage of their surgical experience. This means ensuring that we employ evidence-based best practices across the board. The optimal way of doing things changes over time, so we have added a new element to our biweekly staff meeting: We update each other on new developments in our specialty, ensuring that we disseminate our collective knowledge to the group so that each of us may provide the most innovative and successful care.

Q: Which forces impacting cardiac surgery are likely to be most important over the next decade?

A: Innovation in the treatment of structural heart disease is ongoing. Traditionally, surgeons were the experts in this area, but today, cardiologists and heart surgeons are both experts and work together. This requires changes in both the way we consider a patient's treatment and the resources needed to deliver care. In order to provide multidisciplinary care, right now we are building more hybrid operating rooms with new imaging capabilities, including three-dimensional echocardiography.

Q: Should cardiac surgeons view the expansion of transcatheter procedures as a threat?

A: That depends on where you are and how your organization is structured. The Cleveland Clinic model renders such innovation an advantage. Because surgeons and cardiologists are all part of our Heart & Vascular Institute, transcatheter approaches are not viewed as a threat but rather as an addition to the armamentarium of treatments we can offer patients.

Q: How is robotically assisted cardiac surgery likely to evolve or expand over the next decade?

A: Robotic cardiac surgery is expanding at Cleveland Clinic. We are committed to this technology. It is optimal for mitral valve repair, cardiac tumor excision and closure of atrial septal defects. We have the most experienced robotic team in the world, by a wide margin. We just recruited Per Wierup, MD, PhD [from Lund University in Sweden], one of Europe's pre-eminent robotic surgeons. This gives us a total of three cardiothoracic surgeons with robotics expertise in Cleveland and three more at our Cleveland Clinic Abu Dhabi location in the Middle East. A second surgical robot was just added, so we now have a dedicated robot for cardiac cases and one for thoracic cases.

Q: Does reality match rhetoric when it comes to a multidisciplinary heart team approach to complex patients?

A: Here at Cleveland Clinic, we feel that the multidisciplinary approach is very valuable, particularly when we have high-risk patients for whom traditional surgery may not be appropriate. We discuss these patients in multidisciplinary case conferences, which allows us to choose the best treatment option. All team members are part of the Heart & Vascular Institute, and since our practice model focuses on quality and does not provide rewards for procedural volume, we have a single incentive: To do everything we can to determine the best strategy for an individual patient.

Q: What do you want your external colleagues to know about your department?

A: We have the single most important asset: The best people. We will deploy them in the most focused and collaborative environment in order to build and improve on our program. ■

Contact Dr. Gillinov at gillinom@ccf.org.

Two Glimpses of Dr. Gillinov

Two recent developments showcase a few of the leadership talents Dr. Gillinov will be bringing to bear in his new chairman's role.

Research Leadership

In May, he reported results from a Cardiothoracic Surgical Trials Network (CTSN) study that used weekly transtelephonic monitoring to evaluate the effect of lesion set on atrial fibrillation (AFib) ablation outcomes in patients with persistent AFib who also required mitral valve surgery. The randomized trial (originally published in the *New England Journal of Medicine*) found higher rates of freedom from AFib among patients who underwent ablation with the biatrial maze procedure compared with those undergoing pulmonary vein isolation (PVI).

"It's safe to say the biatrial maze procedure is superior to PVI in mitral valve surgery patients who also need surgical ablation of AFib," says Dr. Gillinov, who served as principal investigator and presented the findings as a late-breaking trial at the American Association for Thoracic Surgery annual meeting. "I am now more likely to do a biatrial maze than a PVI in these patients." For more, see **consultqd.clevelandclinic.org/ctsn**.

Thought Leadership

Also in May, Dr. Gillinov teamed with two other Cleveland Clinic cardiac surgeons — Stephanie Mick, MD, and Rakesh Suri, MD, DPhil — to make the case in a *Journal of the American College of Cardiology* editorial that mitral valve repair should be viewed as a recognized specialty within cardiac surgery — and that a subset of surgeons should be encouraged to develop deep expertise in mitral repair and maintain it through consistently high procedural volumes.

"No examination of this topic has ever found … that surgeons' volume or experience fails to influence repair rates and results," Dr. Gillinov and his colleagues wrote. "The weight of these data strongly supports the notion that valve repair for degenerative disease is a specialty."

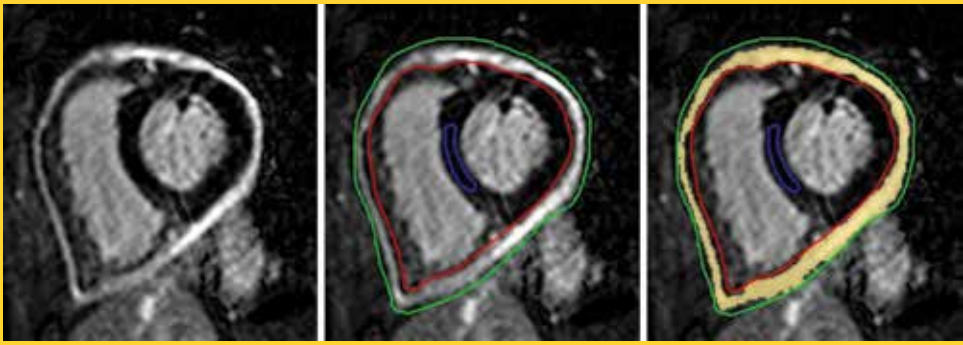
While acknowledging that their call for overt specialization in mitral valve repair will generate controversy, the editorialists noted that it's a fundamentally data-driven position in service of optimal patient outcomes: "Surgeon volume matters," they concluded. For more, see **consultqd.clevelandclinic.org/mitralspecialty**.

Quantitative Pericardial DHE:
A Helpful Clinical Tool in Recurrent Pericarditis?

Incremental prognostic value is demonstrated for the first time.

Among patients with multiple pericarditis recurrences, higher quantitative delayed hyperenhancement (DHE) on cardiac magnetic resonance imaging (CMR) indicates a longer clinical course. So concludes a recent Cleveland Clinic study in *JACC: Cardiovascular Imaging*, the first to show the incremental prognostic value of adding quantitative DHE to other clinical variables in patients with recurrent pericarditis.

"Pericardial DHE on CMR may last beyond the acute phase of pericarditis, suggesting ongoing pericardial inflammation despite treatment," says senior author Allan Klein, MD, Director of Cleveland Clinic's Pericardial Disease Center. "We undertook this study to determine the value of quantitative assessment of DHE in predicting the clinical course of recurrent pericarditis in patients with multiple recurrences by the time of presentation."



Post-gadolinium DHE images, produced using a quantitative approach, from a patient with severe inflammation.

Study Recap

He and colleagues retrospectively identified 159 patients with recurrent pericarditis who underwent DHE imaging at Cleveland Clinic from 2007 to 2015 and were followed for at least six months. They quantified inflammation on short-axis DHE sequences by contouring the pericardium, using normal septal myocardium as a reference region and then quantifying the pericardial signal that was more than six standard deviations above the reference. Clinical remission was the primary end point; time to recurrence and recurrence rate were secondary outcomes.

Over a median follow-up of 23 months, 20 percent of patients achieved clinical remission. Multivariate analysis showed that lower quantitative pericardial DHE was independently associated with clinical remission ($P = .008$).

Notably, adding quantitative DHE to background clinical and lab variables yielded incremental prognostic value, providing better discrimination for clinical remission ($P = .004$). Additionally, higher pericardial DHE values were associated with shorter times to recurrence ($P = .012$) and higher six-month recurrence rates ($P = .026$).

Implications for Practice and Research

"This study demonstrates that quantitative pericardial DHE may offer insight into pericarditis duration and expected response to treatment," remarks Dr. Klein. "Qualitative assessment is done in clinical practice but was not as robust as the quantitative approach in our study."

He adds that the prognostic value of inflammatory markers tends to be lower among patients with recurrent pericarditis, who are often on intense anti-inflammatory regimens when evaluated. "In such presentations," he notes, "a baseline assessment of pericardial DHE may be of value, especially since traditional prognostic markers for acute pericarditis — such as fever and pericardial effusion — were not associated with clinical outcomes in our cohort."

Dr. Klein points out that this study was hypothesis-generating and future investigations are needed to definitively guide use of quantitative pericardial DHE. "Clinical trials examining the interval change in pericardial DHE in patients with recurrent pericarditis, with correlation to symptoms and inflammatory markers, could help elucidate the precise changes in medication dosing that would be indicated," he says.

In an accompanying editorial, Italian cardiologist Massimo Lombardi, MD, concurred. "The data presented [in this study], if confirmed, may push clinicians to modify their diagnostic workflow," he wrote, adding that a randomized trial is needed "to transform this initial thought-provoking suggestion into a consolidated clinical procedure for adoption." ■

Contact Dr. Klein at kleina@ccf.org.

Fixing Failed EVAR:
How Do Open and Endovascular Options Stack Up?

As rates of failed endovascular aortic aneurysm repair (EVAR) rise, so does the need to define optimal methods of managing failed EVAR cases. Results of a large Cleveland Clinic analysis presented at the Society for Vascular Surgery's 2017 Vascular Annual Meeting in June show that open and endovascular management methods are comparable in 30-day reintervention and mortality rates but tend to be used for different modes of EVAR failure.

"Cleveland Clinic is seeing more and more patients present with failed standard EVAR that we need to repair," explains the study's principal investigator, Matthew Eagleton, MD, of the Department of Vascular Surgery. "We've traditionally taken two completely different approaches to these cases, so we wanted to compare them to assess any differences between the two modes of therapy."

The investigation was a retrospective analysis of 247 patients treated for failed EVAR at Cleveland Clinic from 1999 to 2016. Patients (mean age, 75) underwent open surgical explantation (n = 162) or endovascular therapy with fenestrated-branched EVAR (FB EVAR) (n = 85), which was performed under a physician-sponsored investigational device exemption (IDE).

Various patient characteristics — demographics, clinical presentation, failure etiology, perioperative management — and short-term rates of reintervention and mortality were statistically compared between the two methods.

Results: Differing Presentations, Similar Outcomes

There were no significant differences between the explant group and the FB EVAR group in graft manufacturer for the primary EVAR, and endoleak was the most common reason for primary EVAR failure in both groups. Beyond that, the groups differed significantly in EVAR failure etiology and other key clinical factors, as follows:

In the FB EVAR group, the mean time from primary EVAR was longer, and failure of the primary EVAR was more likely to involve a type I endoleak and to include graft migration and neck degeneration/disease progression.

In the explant group, a higher share of patients required urgent/emergent surgery, aortic rupture was more prevalent and the presence of primary EVAR graft infection was more common (17 percent vs. 0 percent). Additionally, failure of the primary EVAR in the explant group was more likely to involve a type II endoleak and to involve aneurysm enlargement.

Analysis of outcomes showed no significant differences between the two management methods:

- 30-day reintervention rates were 21 percent with explant and 10.6 percent with FB EVAR (P = .14)
- 30-day mortality was 13 percent with explant and 4.7 percent with FB EVAR (P = .11).

The absence of significant differences in reintervention or mortality rates was not altered by subset analysis excluding emergent/compassionate-use cases and cases involving infections and ruptures.

Two Necessary Options

"These results suggest that explants and fenestrated-branched EVAR are both useful and necessary options for patients with failed EVAR," says Dr. Eagleton. "Different modes of primary EVAR failure may point to a preferred method of treatment, but short-term outcomes are comparable between these options."

He notes that the findings are reassuring in that they suggest "there's no reason to hesitate in undertaking FB EVAR in a high-risk patient who's not likely to tolerate open surgery, while in healthier patients we can safely proceed with open repair and expect very good long-term survival."

He says future studies should help match specific modes of failure with the best treatment option and better assess long-term outcomes. "Meanwhile surgeons should individualize management of EVAR failure according to the patient's presentation and the resources available," he advises. ■

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Q&A Vascular Medicine in 2017: The View from SVM's Outgoing and Incoming Presidents

Q&A with Drs. John R. Bartholomew and Heather Gornik

In June, Cleveland Clinic cardiologist and vascular medicine specialist **Heather Gornik, MD**, became the first female president of the Society for Vascular Medicine (SVM), succeeding **John R. Bartholomew, MD**, Cleveland Clinic's Section Head of Vascular Medicine, who had been SVM president for the prior two years. The two physicians, shown above, recently sat down for a Q&A to discuss the future of vascular medicine.

Q: What are the biggest challenges that vascular medicine faces?

Dr. Bartholomew: Recruiting more vascular medicine physicians. I was SVM president-elect for two years and then president for two more, and growth has been a challenge throughout that period. The society now has about 500 members.

Dr. Gornik: One barrier to recruitment is the fact that there are not a lot of programs that can train vascular medicine specialists. Here at Cleveland Clinic we've had a comprehensive one-year fellowship program in clinical vascular medicine for decades, but that's not the case at most centers.

Dr. Bartholomew: Another challenge is that the American Board of Internal Medicine has not yet recognized vascular medicine as a subspecialty, despite our petitioning for this recognition. Disciplines like sleep medicine and palliative care have been recognized, and I think ours is equally important.

Q: What are some of the biggest opportunities in vascular medicine?

Dr. Gornik: Because our field is small and there's so much work that needs to be done, there are abundant opportunities for research and to make one's mark, especially for young doctors. For instance, there are many common and rare vascular diseases that are woefully understudied, underdiagnosed and undertreated. A great example is peripheral artery disease, which has been examined substantially less than coronary artery disease. There are also rare diseases that are very poorly understood, and for which vascular medicine specialists have led the way in research.

Q: What might vascular medicine specialists do to elevate the specialty?

Dr. Bartholomew: We need to continue to enhance our presence at the national level by speaking at major meetings like those of the American Heart Association, the American College of Cardiology, the American College of Physicians and the American College of Chest Physicians, to name a few.

Q: What do other specialties need to recognize about vascular medicine?

Dr. Bartholomew: That we are often the go-to doctors when a colleague doesn't know what's going on with a patient. All vascular medicine physicians are internists, but we also offer subspecialty expertise in cardiology, hematology, vascular surgery and many other areas. In addition, most of us are experts in anticoagulation, managing clotting problems and managing leg edema, which a lot of physicians tend to overlook.

Q: Dr. Bartholomew, what was one of the key accomplishments during your term?

A: We worked with other medical and surgical societies to convince the Centers for Medicare & Medicaid Services (CMS) to reimburse for a rehabilitation walking program for patients with peripheral artery disease [see sidebar]. This will be important for many older patients with the condition, who will now be able to work with exercise therapists or physical therapists to improve their walking capacity, much like heart attack patients have benefited from Medicare reimbursement for cardiac rehab.

Q: Dr. Gornik, what are some priorities for your term?

A: While SVM president, I want to help fill the pipeline of early-career internal medicine physicians and even medical students who might be interested in vascular medicine. I also plan to work with colleagues to achieve recognition of vascular medicine as a formal subspecialty of internal medicine. I plan to engage SVM members to accomplish these priorities, looking to past presidents and senior providers to help, as well as the next generation of "fresh out of fellowship" vascular medicine specialists. We need everyone to work for our cause.

Q: Dr. Gornik, will you continue as editor-in-chief of SVM's journal, *Vascular Medicine*?

A: Absolutely. It's a unique opportunity for me personally and for the organization. Staying on as editor also ensures that my commitment to the society will continue for years beyond the end of my presidential term. As editor, I'm able to keep my finger on the pulse of research. This role has also allowed me to grow relationships between the journal and the society and use the journal to advocate for the specialty through some of the content we publish. ■

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CMS Decision on Exercise Therapy for PAD: A Clear Win for Patients

The recent CMS decision to cover supervised exercise therapy for symptomatic peripheral artery disease (PAD) and intermittent claudication will enable many patients to improve their walking ability without surgery or an interventional procedure. So says Society for Vascular Medicine president and Cleveland Clinic cardiologist Heather Gornik, MD.

"Exercise is the single most effective therapy for claudication," says Dr. Gornik. "Research has shown over and over that supervised exercise increases both total and pain-free walking distance. It's the first treatment that should be tried for these patients."

Cleveland Clinic vascular surgeon Lee Kirksey, MD, shares that enthusiasm. "It's very exciting," he says. "You can get the same benefits with exercise as with a procedure — sometimes better. Not only can exercise save the cost of an expensive procedure, but patients often enjoy benefits in recovery of walking function and quality of life."

The CMS coverage decision will allow for up to 36 physician-supervised sessions over a 12-week period. The sessions must last 30 to 60 minutes, be conducted in a hospital outpatient setting or physician's office, be delivered by qualified personnel and be supervised directly by a physician or midlevel provider trained in life-support techniques.

Though the decision allows coverage to be extended for an additional 36 sessions at the discretion of CMS, Dr. Gornik feels the goal for most patients should be to complete 36 sessions and then transition to a community- or home-based exercise program. "We want to empower patients to exercise on their own," she says, a goal that's possible after patients learn how exercise improves their ability to enjoy life and handle everyday tasks with less pain.

Cleveland Clinic has offered exercise therapy for PAD for years, but since the intervention was reimbursed by few commercial insurers, its use was limited. Following the lead of CMS, more carriers are likely to extend coverage to patients with PAD.

Research Roundup Quick Takes on Recent Cardiovascular Studies of Note

ROADMAP: Outcomes Remain Intact at Two Years

Decision-making for patients with non-inotrope-dependent heart failure has just gotten better-informed, thanks to publication of two-year results of the ROADMAP trial comparing LVAD therapy with optimal medical management (OMM) (*JACC Heart Fail.* 2017;5:518-527). Results of the prospective, nonrandomized study showed that LVADs' advantage over OMM on the primary end point of survival on original therapy with improvement in six-minute walk distance, first reported at 12 months, extends out to two years. New treatment-guiding insights emerged too, including evidence of a reduction in adverse events with LVAD therapy in the second (vs. first) year of follow-up and evidence that there's no rise in mortality with delaying LVAD implantation among OMM patients who are monitored closely by a heart failure specialist.

"Until a randomized trial of these strategies is undertaken," says lead investigator Randall Starling, MD, MPH, of Cleveland Clinic, "ROADMAP provides data to help physicians counsel patients on which treatment option makes the most sense for them in terms of both survival and quality of life." More at consultqd.clevelandclinic.org/roadmap.

Sutureless Aortic Bioprosthesis Shines in Low-Risk Patients

Lower-than-predicted stroke and mortality rates and an excellent effectiveness profile at one year support growing use of the first sutureless, self-expanding aortic bioprosthesis approved in the U.S. for patients with aortic stenosis. So concluded investigators with the multicenter Perceval IDE trial in a late-breaking presentation at the American Association for Thoracic Surgery's 2017 centennial meeting.

The 300-patient, single-arm trial assessed use of the Perceval valve in patients at low surgical risk; prior studies had been in high-risk patients. Key results of the new study included a 96.3 percent implant success rate, 1.0 percent operative mortality, a 1.0 percent stroke rate at 12 months and a significant, stable reduction in transvalvular gradient. "Low-risk patients are a population for whom this valve is ideally suited," says the trial's principal investigator, Rakesh Suri, MD, DPhil, of Cleveland Clinic Abu Dhabi. "This includes younger patients and those with bicuspid valves." More at consultqd.clevelandclinic.org/perceval.

Women Overlooked for CIEDs Despite Better Survival

A nationwide cohort analysis of 269,471 patients receiving cardiac implantable electronic devices (CIEDs) found that women account for less than 30 percent of high-voltage implants and less than half of low-voltage implants. Yet the rationale for this lower use in females is questionable, since survival after receiving an implantable cardioverter-defibrillator or pacemaker was found to be similar between the sexes over median follow-up of 2.9 years. Moreover, survival was 27 percent *higher* for women than men among patients receiving cardiac resynchronization therapy (CRT) defibrillators and 31 percent *higher* for women than men among those receiving CRT pacemakers.

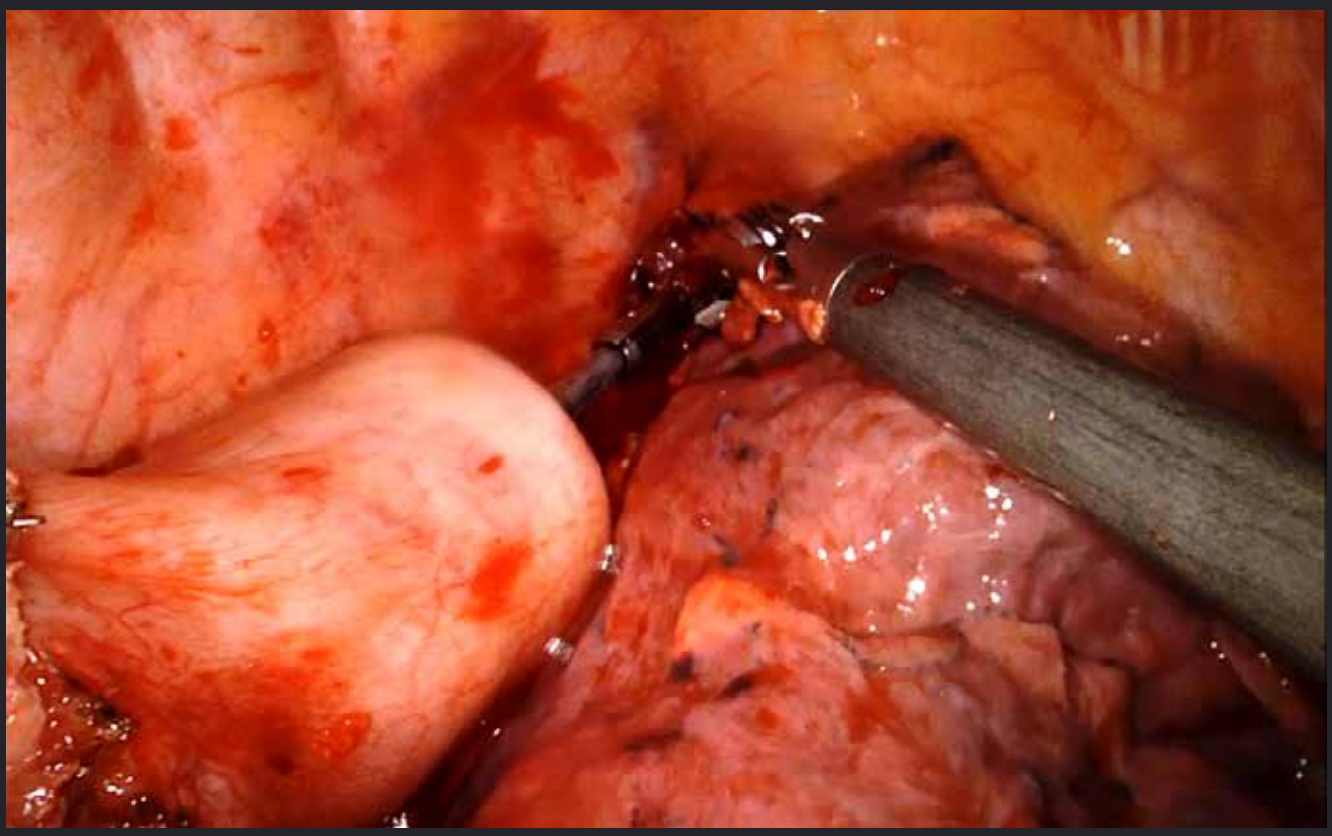
"Our results contradict the notion that women derive less benefit from CIED therapy," write the investigators (*J Am Heart Assoc.* 2017;6:e005031), led by Cleveland Clinic cardiologist Niraj Varma, MD, PhD. They call for resolving "barriers in candidate selection to lessen disparate care as a function of sex in patients eligible for device therapy." More at consultqd.clevelandclinic.org/crackedcode.

SYNTAX: CABG's Edge Over PCI Extends to Long-Term QoL

Four years ago, final clinical results from the multicenter SYNTAX trial showed that patients with three-vessel or left main coronary artery disease (CAD) who undergo bypass surgery fare better with respect to five-year major adverse cardiovascular outcomes than their matched counterparts who undergo percuteaneous coronary intervention (PCI) with a first-generation drug-eluting stent. Now a health status substudy of SYNTAX has found that the bypass recipients are also more likely to enjoy a higher quality of life over the long term.

The results (*J Am Coll Cardiol.* 2017;69:2039-2050) provide additional support for CABG as the preferred revascularization option for patients with anatomically complex three-vessel or left main CAD. "Both CABG and PCI with a drug-eluting stent were associated with substantial and sustained quality-of-life benefits over five years of follow-up," explains the study's first author, Cleveland Clinic cardiologist Mouin Abdallah, MD. "But CABG provided greater angina relief at five years, primarily due to an advantage in patients with anatomically complex disease as reflected by higher SYNTAX scores." More at consultqd.clevelandclinic.org/syntax.

Image of the Issue



USING ROBOTICS TO EXPAND ESOPHAGECTOMY OPTIONS

As one of a limited number of cardiothoracic surgery programs that offer esophageal procedures, Cleveland Clinic's Department of Thoracic and Cardiovascular Surgery has seen its esophageal surgery volumes rise in recent years, surging to 261 cases in 2016.

Esophagectomy for esophageal cancer is one procedure where volume-based expertise is yielding the greatest outcome dividends: Across 153 esophagectomies from July 2013 through June 2016, Cleveland Clinic surgeons achieved among the lowest risk-adjusted combined morbidity and 30-day mortality rates in the entire country, with a standardized incidence ratio of 0.55 (95% CI, 0.38-0.75), according to the Society of Thoracic Surgeons General Thoracic Surgery Database.

Now Cleveland Clinic surgeons are increasingly turning to robotics to offer a minimally invasive option to patients requiring esophagectomy. A snapshot of robotic esophagectomy is presented above, showing engagement of an end-to-end anastomosis stapler to connect the gastric conduit with the proximal esophagus.

"Minimally invasive esophagectomy is a complex operation and requires a multidisciplinary approach and very careful patient selection," says Sudish Murthy, MD, PhD, Section Head of Thoracic Surgery.

"The best way to achieve excellent results after esophagectomy is to tailor the operation for the patient and his or her cancer," adds Siva Raja, MD, PhD, Surgical Director, Center for Esophageal Disorders. "We are facile in performing all the variations of esophagectomy, even in the setting of chemotherapy and radiation, to help our patients achieve their cure." ■

For more on robotic esophagectomy at Cleveland Clinic, contact Dr. Murthy at murthys1@ccf.org or Dr. Raja at rajas@ccf.org.

Cleveland Clinic

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Cardiac Consult

Live CME Spotlight Don't miss these **CME** offerings this fall.

Controversies in the Management of Cardiovascular Disease

Fri., Oct. 6, 2017, 7 a.m. to 5 p.m.
The Roosevelt Hotel | New York, New York

Information/registration: northwell.edu/cme

Cleveland Clinic Cardiovascular Update 2017

Thu.-Fri., Oct. 26-27, 2017
Global Center for Health Innovation | Cleveland, Ohio

Information/registration: ccfcme.org/cvupdate17

Treatment of Coronary Artery Disease: Past, Present and Future (Celebrating the 50th Anniversary of CABG)

Fri., Nov. 3, 2017, 8 a.m. to 5:30 p.m.
InterContinental Hotel & Conference Center | Cleveland, Ohio

Thirty expert faculty from Cleveland Clinic and around the world discuss and apply the latest data and practices in CABG and PCI. The fast-paced agenda features "How I Do It" videos," pro/con debates and much more.

Information/registration: ccfcme.org/cabg50years

2nd Annual Advances in Pediatric & Congenital Heart Care Summit: Navigating Shone's Complex

Thu.-Sat., Nov. 9-11, 2017
InterContinental Hotel & Conference Center | Cleveland, Ohio

Comprehensive is the word for this 2.5-day exploration of Shone's complex over the lifespan, from diagnosis in utero through survival into adulthood. Highlights include weighing catheter vs. surgical interventions, common extracardiac problems and quality metrics for Shone's-related care.

Information/registration: ccfcme.org/pediatric-congenital17

Mastering the Mitral Valve

Fri.-Sat., Dec. 1-2, 2017
JW Marriott Essex House New York | New York, New York

Two dozen leading experts in mitral valve disease come together for this 1.5-day course to share the very latest in mitral valve guidelines, assessment, diagnosis and timing of treatment, including MIS and percutaneous approaches, surgical techniques, devices and long-term results.

Information/registration: ccfcme.org/mitralmasters

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

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