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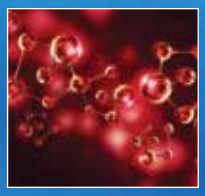

Cleveland Clinic

Cardiac Consult

Heart and Vascular News from Cleveland Clinic | Fall 2014 | Vol. XXIV No. 3

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Dear Colleagues:

Cardiac Consult is a forward-thinking publication. But in this issue's cover story (p. 10), we look back over the past 20 years of cardiovascular achievement. The piece is both a fun way to take stock of how our discipline has evolved and a not-so-subtle reminder that for every one of those 20 years, Cleveland Clinic has been ranked No. 1 for heart care in *U.S. News & World Report*'s "Best Hospitals" survey. If you wonder how Cleveland Clinic is able to consistently earn this standing year after year, the remaining articles in this issue might give some clues.

The feature on p. 3 profiles our new Cardiovascular Specialty Network and other heart care-focused affiliations and alliances with hospitals and providers nationwide. The network and affiliations are made possible by Cleveland Clinic's standardized approach to patient care. Our cardiovascular specialists strive for predictable outcomes through close observation of data, evidence-based practices and continuous quality improvement. These specialists' services are coordinated elements of a single Heart & Vascular Institute comprising cardiovascular and thoracic surgery, vascular surgery, and cardiovascular medicine.

This systemized approach is reflected by our long-standing expertise in left ventricular assist devices (LVADs), which, in turn, reflects the close collaboration of at least two generations of cardiologists and cardiac surgeons. As you'll read on p. 6, the fruits of that collaboration include the use of LVADs as a tool to improve quality of life — and not just as a last resort — in growing numbers of patients with advanced heart failure.

Collaboration is also a key subtext in the articles about our multidisciplinary approach to complex wound care (p. 14) and surgery for tetralogy of Fallot in adults (p. 17).

Teamwork and standardization are bedrocks of a system that has served us well for the past 20 years — and that continues to improve, day by day, as we meet new challenges and opportunities. We cannot point to any single member of our staff and say he or she is responsible for our continued leadership. Our success is the product of the combined efforts of all our caregivers and their commitment to give every patient the best outcome and experience.

You, as a referring physician, are an essential part of our team. We could not do anything without your trust in our expertise and your confidence in our caregiving. Thank you for making our 20-year milestone possible. We are proud to offer your patients the nation's top-ranked heart care this year and every year.

Respectfully,

Amar Krishnaswamy, MD
Staff Cardiologist, Invasive Cardiology

Michael Rocco, MD
Medical Director, Cardiac Rehabilitation and Stress Testing

W. Michael Park, MD
Staff Surgeon, Vascular Surgery

Joseph F. Sabik III, MD
Chairman, Thoracic and Cardiovascular Surgery

Cardiac Consult offers updates on advanced diagnostic and management techniques from specialists in Cleveland Clinic's Sydell and Arnold Miller Family Heart & Vascular Institute. Please direct correspondence to:

Medical Editors

Amar Krishnaswamy, MD
krishna2@ccf.org

W. Michael Park, MD
parkm3@ccf.org

Michael Rocco, MD
roccom@ccf.org

Joseph F. Sabik III, MD
sabikj@ccf.org
216.448.1026

Managing Editor
Glenn R. Campbell

Art Director
Michael Viars

Marketing Director
Megan Frankel

Marketing Associate
Jennifer Coffman

Photography & Illustrations
Cleveland Clinic Center for Medical Art and Photography

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Quality-Driven Employer Contracting Goes National

Building a National Network of Cardiac Providers Aligned Around Predictable Performance

Cleveland Clinic has launched the country's first national-scale network of affiliated cardiovascular care providers for the purpose of contracting with employers and other payers. The Cleveland Clinic Cardiovascular Specialty Network was established earlier this year and is now actively adding member provider organizations across the country.

Predictable Quality at a Predictable Price

"We're assembling a group of like-minded provider organizations aligned around quality-driven, high-performance cardiovascular care," explains Joseph Cacchione, MD, Chair of Operations and Strategy for Cleveland Clinic's Sydell and Arnold Miller Family Heart & Vascular Institute. "The aim is to present a network offering to provide predictable quality at a predictable price to large employers, health exchanges and physician-owned accountable care organizations."

The Cardiovascular Specialty Network is able to ensure predictable quality thanks to an intensive assessment process Cleveland Clinic uses to evaluate potential network members for clinical and operational quality, data integrity and cultural alignment. That process has emerged from a robust program of affiliations, alliances and consulting relationships Cleveland Clinic has forged around cardiovascular care dating back to the late 1990s. These relationships — from consulting arrangements to extensive clinical and research alliances — are outlined in the sidebar on p. 4.

Why This Approach Now?

The new network is a way to better leverage Cleveland Clinic's direct-to-employer contracts to provide cardiovascular care to large national employers such as Lowe's and Boeing and to private health insurance exchanges like Right Opt®. Those contracts now cover a couple million lives, and ongoing discussions with Fortune 500 companies aim to increase that count.

"Employers are asking for more local options," explains Daniel Towarnicke, the Heart & Vascular Institute's Director of Outreach Programs. "The idea is to work with hospitals throughout the country that demonstrate the best performance and patient experience so that our contracted employers can encourage employees to use nearby network providers when possible and appropriate."

continued next page

The Many Ways Cleveland Clinic Collaborates Around Cardiovascular Care

Consulting services — Focused engagements in which Cleveland Clinic Heart & Vascular Institute staff provide advice and insight to another hospital or health system for defined services. Services run the gamut from quality assurance reviews to physician recruitment to data auditing to clinical protocol reviews. These relationships are initiated at the request of the outside organizations, which range from small community hospitals to large academic medical centers. The Heart & Vascular Institute is typically engaged in 10 or more active consulting relationships at a given time.

Affiliations and alliances — Deeper relationships in which Cleveland Clinic establishes branding with another hospital or health system after Heart & Vascular Institute staff conduct an intense six- to 12-month assessment of the organization's cardiovascular program for quality, outcomes, data integrity and culture. Organizations that meet required criteria are designated Heart & Vascular Institute affiliates and have access to Cleveland Clinic intellectual property, protocols, care paths and clinical trials; enhanced consultation access to Heart & Vascular Institute physicians and administrative experts; and enhanced connectivity for sharing of imaging studies. Affiliates range from small community hospitals to large health systems such as Novant Health in North Carolina.

Affiliations with selected larger provider organizations are designated alliances. To date, the Heart & Vascular Institute has formed two alliances — in 2013 with MedStar Heart Institute in the Washington, D.C., area, and in 2014 with North Shore–LIJ Health System in the greater New York area. Each is Cleveland Clinic's exclusive alliance partner in its metropolitan area.

Cardiovascular Specialty Network membership — A chance for provider organizations to join Cleveland Clinic in contracting with large employers looking for a dispersed network of high-quality cardiovascular providers for their employees around the nation. The network allows Cleveland Clinic to triage cases across the nation to the network member most appropriate for them — either a nearby network affiliate for more straightforward procedures (e.g., coronary bypass surgery, mitral valve repair) or to Cleveland Clinic for highly complex surgeries like reoperative procedures. Cleveland Clinic initiates requests for network membership, and network members must be affiliates or alliance partners, though not all affiliates are network members (some do not meet the network's stricter quality requirements).

Benefits All Around

"Healthcare is often regional," adds Dr. Cacchione, who notes that a national network covering all major regions yields benefits for all stakeholders:

- Cleveland Clinic benefits through an enhanced and extended national presence and through relationships that may give patients enhanced access to Cleveland Clinic surgeons.
- Network affiliate providers benefit from their inclusion in the employer contracts and the halo effect of being affiliated with the nation's top-ranked heart program. They also gain from the sharing of data and best practices, ongoing quality improvement initiatives and supply chain savings inherent in the network.
- Employers get predictable pricing along with the assurance that their employees receive reliably high-quality care from vetted best-in-class cardiovascular providers.
- Patients covered under the network gain the ability to visit a more local provider while still having access to Cleveland Clinic for their most complex needs — all under a benefit structure designed to minimize their out-of-pocket costs.

Scrupulous Quality Standards

Many of the above benefits hinge on the Cardiovascular Specialty Network's promise of strict quality standards. Those standards cover diverse aspects of clinical and operational practice and are closely guarded by Heart & Vascular staff at every turn.

In addition to hard measures like monthly outcomes data supplied by the American College of Cardiology and the Society of Thoracic Surgeons, the intensive assessment of potential affiliates and network members includes reviews of patient experience measures, quality processes, operational and administrative procedures, and data integrity.

"Data integrity is the first thing we focus on," says Towarnicke, since it's essential to reliably documenting the other measures and has become central to the drive toward safer and more efficient care. "We have a team that does site visits to assess data infrastructure, data auditing and similar issues."

Site Visits by Top Docs

They're not the only ones who do site visits. For more than six years the Heart & Vascular Institute has been sending a diverse team of clinical and administrative experts — physicians, nurses, data analysts, continuous improvement specialists, project managers and others — to do site visits for potential affiliates and consulting clients. Each section of the Heart & Vascular Institute has one or two go-to physicians who regularly do such visits and provide ongoing consulting to affiliate hospitals.

Such involvement by physician leaders turns a lot of heads. "Cleveland Clinic is a physician group, so this is a physician-run network and affiliate program," says Dr. Cacchione. "We pay our cardiology and cardiothoracic surgery departments for a portion of their physicians' time so they can do site visits to evaluate for quality and operations. We send some of our highest-performing physicians — national experts like Dr. Stephen Ellis and Dr. Bruce Lindsay — out to do program evaluations. This network is based on quality, and physicians understand clinical quality better than anybody."

Continuous Improvement at the Cultural Core

Dr. Cacchione's team recognizes that quality can be used as both a stick and a carrot. It will terminate a relationship with an affiliate hospital that has poor outcomes — and has done so once thus far. But it likewise brings an ethic of continuous improvement to its relationship with each of its various partners. "Our range of consulting and affiliate relationships is a continuum," explains Towarnicke. "We will work with consulting clients if they aspire to qualify for affiliate status. For affiliates that don't qualify for Cardiovascular Specialty Network membership, we consult and work with them so that they might ultimately meet that quality threshold. A commitment to continuous improvement is important."

Dr. Cacchione says that commitment is the key to the "cultural fit" he looks for in potential network members. He shares the story of one hospital that said they couldn't fix a bad metric they had. "They asked me, 'You won't let us into the network just because of that one metric?' I told them it wasn't so much the bad metric as the fact that they said they can't fix it and don't seem to want to. None of us is perfect, but we all need that drive to be better every day. That's the culture we're looking for." ■

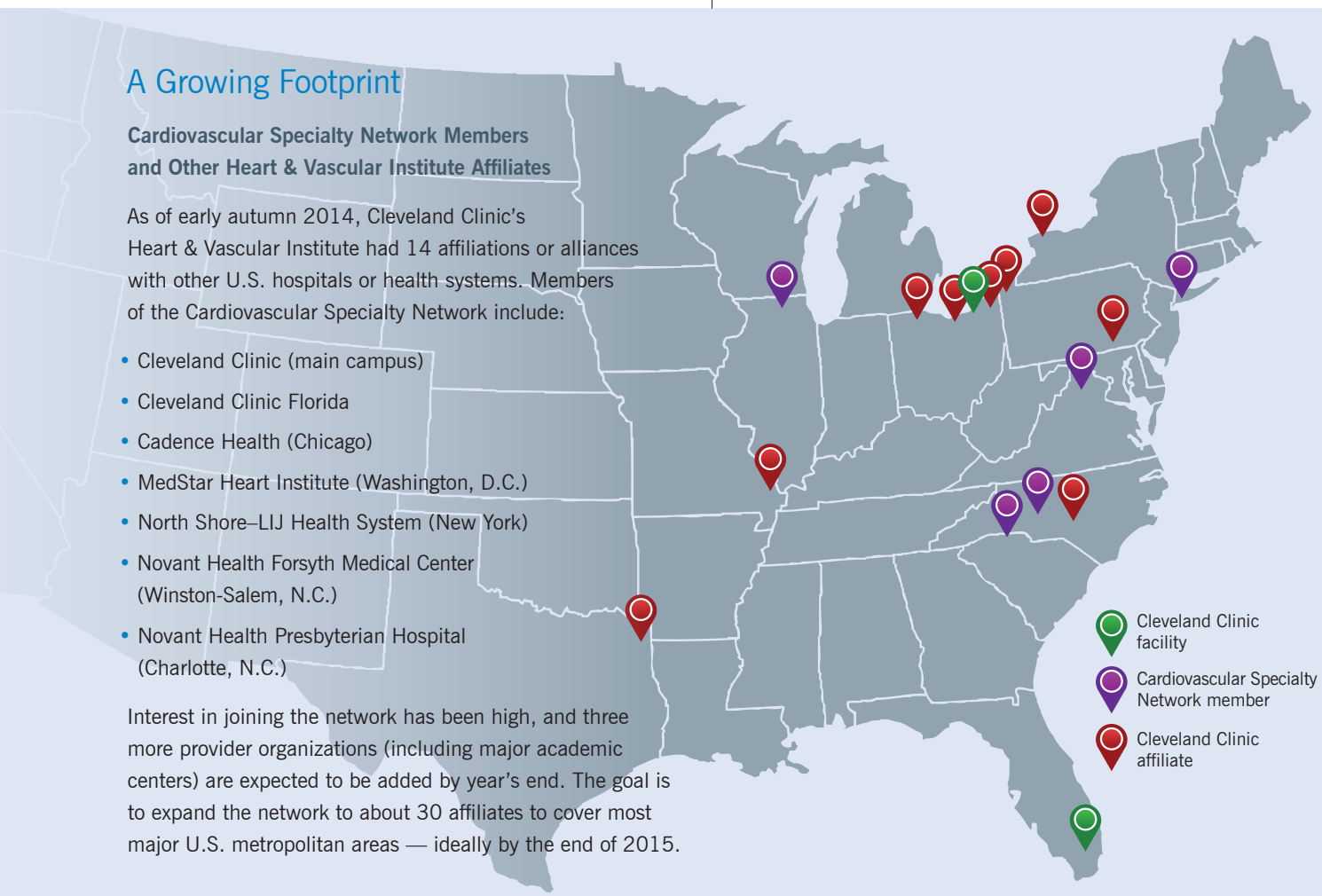
A Growing Footprint

Cardiovascular Specialty Network Members and Other Heart & Vascular Institute Affiliates

As of early autumn 2014, Cleveland Clinic's Heart & Vascular Institute had 14 affiliations or alliances with other U.S. hospitals or health systems. Members of the Cardiovascular Specialty Network include:

- Cleveland Clinic (main campus)
- Cleveland Clinic Florida
- Cadence Health (Chicago)
- MedStar Heart Institute (Washington, D.C.)
- North Shore–LIJ Health System (New York)
- Novant Health Forsyth Medical Center (Winston-Salem, N.C.)
- Novant Health Presbyterian Hospital (Charlotte, N.C.)

Interest in joining the network has been high, and three more provider organizations (including major academic centers) are expected to be added by year's end. The goal is to expand the network to about 30 affiliates to cover most major U.S. metropolitan areas — ideally by the end of 2015.



Far More than a Last Resort:

LVADs Can Benefit Many More Patients with Advanced Heart Failure

Left ventricular assist devices (LVADs) need not — and should not — be a therapy of last resort. If there's one thing about mechanical circulatory support device therapy — of which LVADs represent the vast majority — that goes underappreciated among cardiovascular specialists, that's it. So say Randall C. Starling, MD, MPH, and Nader Moazami, MD, the medical and surgical directors (respectively) of Cleveland Clinic's Cardiac Transplantation and Ventricular Assist Device Therapy Program.

"I think there may be a misperception that we have nothing to offer patients with advanced heart failure other than transplantation," says Dr. Starling. "In fact, there are many such patients not listed for transplant in whom LVAD therapy is currently extending life and substantially improving quality of life."

Help Needed to Close the Transplant Shortfall

He is referring to the use of LVADs as destination therapy, in contrast to their use as a bridge to transplantation, in which LVAD implantation is deemed necessary to provide stability to a patient on the national heart transplant waiting list until a donor heart can be obtained.

Use of LVADs for destination therapy — i.e., without plans for subsequent heart transplant — has increased in recent years, particularly as donor heart shortages have caused national heart transplant volumes to plateau around 2,200 annually. Yet that growth, which has brought the count of U.S. patients living with LVADs to 10,000 to 12,000, has barely made a dent in the population of 100,000 to 250,000 or more U.S. adults with advanced heart failure who stand to benefit from LVAD therapy.

Lifestyle Decision vs. Last Resort

A major reason for that gap, says Dr. Moazami, is that cardiologists are generally not referring patients with advanced heart failure for evaluation for LVAD destination therapy. "Many patients in end-stage heart failure are referred to us for heart transplant evaluation," he explains. "What we don't get are patients referred for evaluation for LVAD destination therapy.

Cleveland Clinic's Points of Distinction in LVAD Care

- Over 20 years of placing mechanical circulatory assist devices, with 811 devices placed through 2013
- 2013 LVAD volume nearly equally split between bridge to transplant (n = 35) and destination therapy (n = 32)
- Involved in all major clinical trials of LVADs to date
- Comprehensive research efforts, with active work in LVAD development and design, animal testing, human trials and ongoing study of everyday clinical use
- Expert clinical infrastructure for preoperative and postoperative care of LVAD patients, including highly experienced cardiac surgeons and cardiologists, specialized nurses and nurse practitioners in outpatient and inpatient settings, and rehabilitation experts specializing in LVAD patients
- Expanding clinical reach through a co-management program in which patients are implanted with LVADs at Cleveland Clinic and receive follow-up care at affiliated hospitals elsewhere in the region or nation

TABLE. SURVIVAL RATES OF LVAD PATIENTS BY ERA OF LVAD IMPLANTATION*

Post-implant follow-up	2012-2013	2010-2011	Before 2010
1 month	98%	91%	93%
6 months	91%	83%	80%
12 months	81%	78%	74%

*Includes all LVAD recipients at Cleveland Clinic, including bridge-to-transplant patients and destination therapy patients.

We'd really like to see these patients earlier, to discuss their options more fully and perhaps explore LVAD therapy outside the context of transplantation, if that makes sense for them."

Because those earlier referrals don't take place, an LVAD is too often considered only when heart failure is much more severe, perhaps after it lands the patient in the ICU. When heart transplant is contraindicated in such patients, they typically view an LVAD as their only alternative to death.

"Instead of this scenario, implantation of an LVAD as destination therapy should be a highly elective procedure," says Dr. Moazami. "When we can see patients in the outpatient setting and have time to evaluate them and discuss LVAD therapy with them, it becomes more of a lifestyle decision, and patients can really absorb what the therapy will mean for them."

Extending Life for Almost All Patients

Increasingly, what LVAD therapy means for patients is extended life and dramatically improved quality of life. Cleveland Clinic has seen its LVAD patients' survival rates rise steadily in recent years (see table) as its experience in implantation has deepened and as improved continuous-flow LVADs have displaced older pulsatile-flow device models.

And whereas the table includes all LVAD recipients — including bridge-to-transplant patients and destination therapy patients who receive LVADs as essentially a last resort — survival rates are considerably higher for patients who undergo LVAD destination therapy on a more elective basis. "Among those patients, our survival rates are close to 100 percent at one month and three months after LVAD placement," Dr. Moazami notes.

To date, most experience with chronic LVAD therapy is in patients living with the devices for one to three years, though a small but growing population of patients have lived with LVAD support for five years or more. "Mechanical failure of LVAD pumps is very rare," says Dr. Moazami. "Theoretically, these devices should be good to last for at least 10 to 15 years."

Quality of Life May Be Biggest Differentiator

Even more noteworthy is the devices' effects on patient quality of life. "We have nothing medically that compares with an LVAD as far as ability to improve the quality as well as quantity of life," notes Dr. Starling. He cites the six-minute walk test as a prime example. "Multiple studies have shown the average improvement in the six-minute walk test with LVAD therapy is about 150 meters, far greater than the average improvement of approximately 36 meters with well-established interventions like cardiac resynchronization therapy," he says.

"When I evaluate patients for LVAD therapy," adds Dr. Moazami, "I generally say the LVAD is likely to restore them to how they felt and functioned four or five years earlier. Patients tend to be highly satisfied with the strength and activity level they regain" (see patient sidebar on p. 8).

Meticulous Evaluation and Education Are Musts

That said, LVADs are not for everyone. Patients need to clearly understand what living with an LVAD involves and must have a support system to help them make the most of the device postoperatively. To that end, Cleveland Clinic's LVAD team meticulously evaluates potential LVAD recipients and spends copious time educating them about LVAD surgery and what they can expect when living with the device.

Patients meet with a full complement of providers — cardiac surgeon, cardiologist, social worker, dedicated VAD nurses and specialized nurse practitioners — as well as a fellow patient now living with an LVAD. "We educate patients at all these levels because each of us provides a different perspective on the LVAD experience," explains Dr. Moazami.

So What Should Trigger Referral for LVAD Evaluation?

To ensure that more patients who would benefit from LVADs actually get the devices, Dr. Starling advises cardiologists to consider referring advanced heart failure patients for possible LVAD evaluation if they meet the following conditions:

continued next page

- Hospitalized for heart failure once or twice in prior 12 months
- Becoming winded and needing to stop after walking one block or climbing one flight of stairs

He adds that repeated use of inotropic therapy or being discharged on inotropic therapy also signals that a patient with advanced heart failure may be ready for evaluation for LVAD placement. "Additionally, an inability to tolerate ACE inhibitors and beta blockers due to low blood pressure and/or worsening kidney function is another marker that a patient could perhaps benefit from an LVAD," Dr. Starling notes.

"Not all these patients will be candidates, but they all deserve a chance to learn what can be offered to them," adds Dr. Moazami. "These are the patients who are not being referred to LVAD programs now." ■

To refer a patient for LVAD evaluation, please call 216.444.3472.

LVAD Keeps a Farmer Plowing Ahead

Duane Olin is a testament to how LVAD destination therapy can restore a patient's quality of life. The crop farmer from upstate New York received an LVAD at Cleveland Clinic in November 2013 at age 74. After a long history of cardiovascular disease, Mr. Olin was referred in 2013 for evaluation for advanced therapy for systolic heart failure after testing revealed very low exercise capacity and an ejection fraction of 10 to 15 percent.

"Before the LVAD, I was in trouble," he says. "I hardly had any energy and wasn't able to do what I do on my farm on a daily basis. But now I'm back running the bulldozer and other equipment and doing all sorts of farm-related work. I'm 200 percent better after the LVAD, not just 100 percent.

"It was a little ticklish starting out with the LVAD, like anything new, and my wife has to change my wound dressing daily, but it's become relatively routine for us. It's made a huge difference in my lifestyle. I send a big 'thank you' to the LVAD team at Cleveland Clinic."

Cleveland Clinic Florida Launches Heart Transplant Program

Cedric Sheffield, MD

Cleveland Clinic Florida has hired Cedric Sheffield, MD, as surgical director of its new adult heart transplantation program. The move follows the facility's June 2014 receipt of United Network for Organ Sharing (UNOS) approval to begin offering heart transplant services.

Dr. Sheffield, a prominent heart transplant surgeon who recently served as director and CEO of the Tampa Transplant Institute, completed a fellowship in thoracic surgery and transplantation at Cleveland Clinic in 1999. He continued as a Cleveland Clinic associate staff physician until 2001.

Cleveland Clinic Florida launched its overall transplant program at its 155-bed hospital in Weston, Florida, in 2013 with adult liver and kidney transplant services. It had completed more than 50 such transplants as of mid-2014.

The program operates under a "one program" model with Cleveland Clinic's Transplant Center in Cleveland through shared protocols, some shared staff, joint patient selection meetings, shared EMR and transplant databases, and regular and frequent communications.

"We have recruited an outstanding team of transplant professionals," says Andreas Tzakis, MD, PhD, Director of Cleveland Clinic Florida's transplant program and a world-renowned transplant surgeon. "They are filling a critical need for highly specialized services from a growing number of patients who might otherwise have to seek care outside South Florida." ■

For heart transplant referrals to Cleveland Clinic Florida (in Weston), please call 954.659.5133.

Study Sizes Up New System Designed to Bag Type II Endoleaks in AAA Repair

Endoleaks have proved to be one of the few downsides to endovascular aneurysm repair (EVAR), but a novel approach being studied at Cleveland Clinic and elsewhere could significantly reduce the risk of endoleaks and stent graft migration.

EVAR: Even Revolutionary Treatments Can Spring a Leak

EVAR has revolutionized abdominal aortic aneurysm (AAA) treatment. The technique delivers a fabric-covered stent to the aneurysm site via a catheter, after which the stent is expanded inside the aneurysm sac to provide a new conduit for blood flow. The stent graft seals the aortic blood flow from entering the aneurysm, but it cannot prevent blood flow from small branches that perfuse the aneurysm.

In typical endograft treatment of AAA, about 15 to 20 percent of patients develop this type of flow into the aneurysm sac, referred to as a type II endoleak. It is not strictly a leak, as the flow is still in the vascular system, but it is in the aneurysm, outside the endograft. "These 'leaks' can lead to pressurization of the aneurysm sac and, in some instances, to continued increase in the aneurysm's size," explains Daniel Clair, MD, Chair of Vascular Surgery at Cleveland Clinic. "In fact, in studies of patients with these types of leaks, the risk of complications and mid- to long-term graft failure is increased."

A New Approach to Fixing Leaks — Endobags

Preventive solutions for stent graft migration and leaks from the proximal seal zone include the experimental use of screw-type anchors to close the proximal seal. But to address type II endoleaks, a wholly novel approach is now being studied at Cleveland Clinic and other centers — one that could significantly cut the risk of endoleaks and stent migration in infrarenal stent grafts.

The investigational Nellix® EndoVascular Aneurysm Sealing System (Endologix) deploys twin catheters to the site of the infrarenal aneurysm. Balloons expand bilateral stents whose distal portions extend into the common iliac arteries. The stents are surrounded by endobags, which are pumped full of a fast-hardening biostable polymer. The polymer bags fill the aneurysmal sac and then anchor and seal the grafts — at the proximal end and at the bifurcation. The pressure of the endobags against the blood vessel walls seals off the opening of branches into the aneurysm sac, thus preventing type II endoleaks and limiting stent migration.

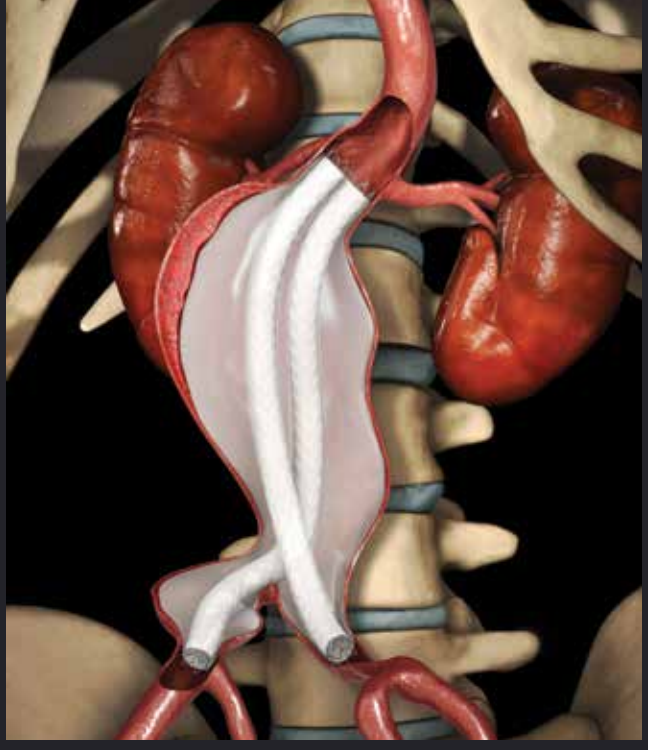


Illustration of the deployed Nellix system. Courtesy of Endologix.

Placement of the system takes about 30 minutes and can be performed through a percutaneous approach.

Potential to Broaden the Patient Pool

The Nellix system can be used "out of the box." Because it is able to accommodate a wider range of anatomies than can conventional EVAR, it holds the potential to expand the pool of patients who are eligible for endovascular AAA treatment.

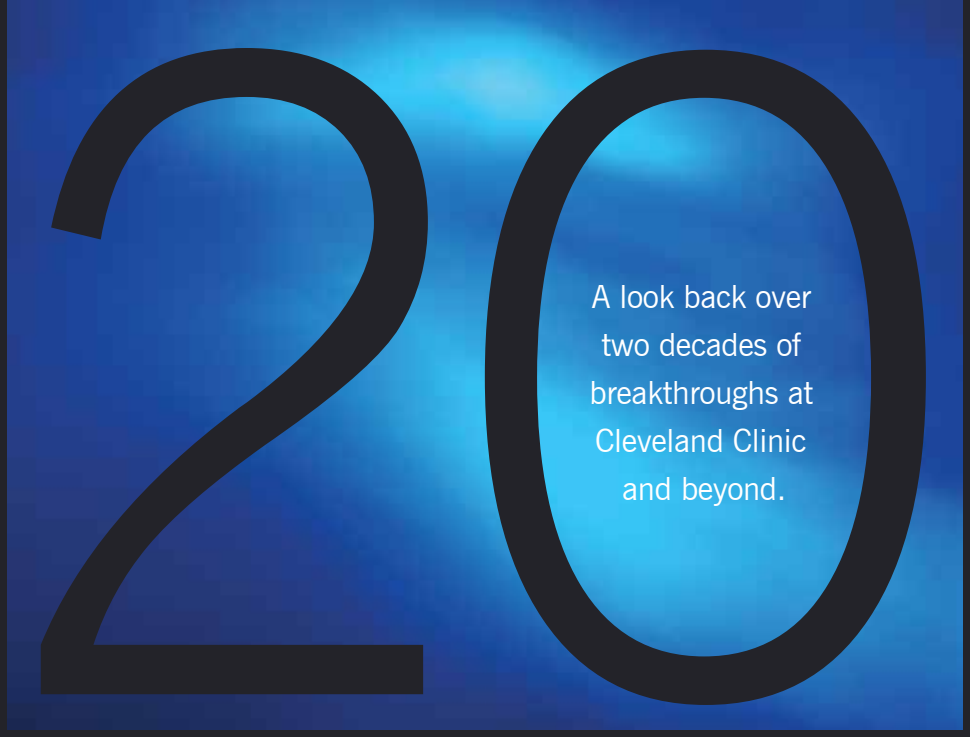
Early studies suggest that the system may be able to drastically reduce the risk of late aneurysm rupture and decrease the need for secondary intervention or CT surveillance. An initial series of 34 patients in New Zealand demonstrated 100 percent technical success with the system, with no ruptures, endoleaks or need to convert to conventional repair.

Multicenter Trial Enrolling Patients

Now a prospective multicenter trial — known as EVAS IDE — is underway to evaluate the safety and device performance of the Nellix system for the treatment of infrarenal AAAs. "Because this technology offers the possibility to completely mitigate endoleaks, patients may ultimately require less intense follow-up," says Dr. Clair, who is site PI for the trial at Cleveland Clinic. "And the hope is that the long-term risk from these type II endoleaks may be eliminated." ■

Enrollment in the EVAS IDE trial is ongoing at Cleveland Clinic; to refer a patient for trial evaluation, call 216.445.3608.

Taking Heart from 20 Years of Cardiovascular Progress



This year, Cleveland Clinic marks its 20th anniversary as the nation's top-ranked center for cardiology and heart surgery in *U.S. News & World Report*'s "Best Hospital" rankings. The cardiovascular specialties have seen remarkable changes over that time. Many treatments that seemed to hold high promise in 1994 have lost favor. New and unexpected hypotheses have emerged. Some long-standing controversies continue to simmer. Others have been laid to rest by rigorous studies.

"The past 20 years have been among the most exciting in the history of cardiac care," says Steven Nissen, MD, Chair of the Robert and Suzanne Tomsich Department of Cardiovascular Medicine. "We know more and can do more to prevent and treat cardiovascular disease than ever before."

Joseph Sabik, MD, Chair of the Department of Thoracic and Cardiovascular Surgery, adds: "Every aspect of cardiac surgery has improved over the past 20 years. Mortality continues to fall, patients go home sooner, and we can operate on many more patients previously ineligible because of age and comorbidities."

Abundant Advances, Stubborn Challenges

Many advances come to mind. Minimally invasive alternatives are well-established for many common cardiovascular procedures. Multidimensional imaging techniques promise new, noninvasive diagnostic capabilities. Cardiac assist devices have become a destination therapy. Implantable electrophysiology devices have increased in effectiveness. Genomics and big data are expanding the boundaries of cardiovascular knowledge. The roles of inflammation, plaque rupture, gut flora, metabolic syndrome and — of course — diet and lifestyle as contributors to cardiovascular disease have become more firmly accepted by clinicians and the public alike.

The continuing overall decline in deaths from cardiovascular disease is proof that cardiovascular specialists have not labored in vain over the past 20 years. Yet cardiovascular disease is still the developed world's top cause of death. And demographic projections suggest that without significant breakthroughs, the realities of age, obesity and harmful lifestyles will soon overwhelm providers with cases of diabetes, coronary disease and heart failure. Much more remains to be done.

But now is a good time to take heart from some of the major advances in our field over the past 20 years — and to take stock of a few surprising bumps along the road to progress. The following pages present a (far from comprehensive) sampling. We've thrown in some relevant covers from past *Cardiac Consult* issues as signposts along the way.

Two Decades, 50 Developments

INSIGHTS, ADVANCES AND COURSE CORRECTIONS FROM 20 YEARS OF CARDIOVASCULAR PRACTICE

- The plaque-rupture hypothesis is widely accepted as the cause of heart attacks.
- Ventricular assist devices (VADs) get smaller, more efficient and more implantable.
- A new generation of totally implantable artificial hearts is under development at Cleveland Clinic and other centers, including several nonpulsatile devices.

❮ *Fall 1995 Issue*

As pacemakers and other implantable devices proliferate, Cleveland Clinic and other centers refine the complex procedures for extracting device leads that become defective or infected. Success rates for lead extraction now approach 99 percent.

- Stenting becomes a commonplace adjunct to angioplasty in the treatment of coronary disease. Stents themselves progress — from bare-metal designs to coated and drug-eluting models and then to bioabsorbable designs — in the quest to slow restenosis.
- Perception of HDL's role in atherosclerosis is drastically revised as studies fail to prove that raising HDL levels can control cardiovascular disease. Closer investigation reveals a "bad" form of HDL that contributes to the formation of unstable plaques. Cleveland Clinic-led studies provide essential data.

❮ *Spring 1997 Issue*

Open heart surgery, the very definition of a major operation, is challenged by minimally invasive approaches, including robotic, thoracoscopic and beating-heart procedures. Today many operations have minimally invasive alternatives.

- Research at Cleveland Clinic and other centers comes to focus more on understanding inflammation and oxidant stress in the development of atherosclerosis.
- Hybrid operating rooms enable new combinations of exo- and endocardiac procedures. Thoracic aortic repair, transvascular aortic valve replacement, coronary artery bypass plus angioplasty, and other procedures can now be performed simultaneously or in sequence.
- Cardiac troponin T levels are found by Cleveland Clinic researchers to be a powerful independent risk marker for patients with acute myocardial infarction.
- As new cancer therapies improve survival, more patients live long enough to suffer the negative effects of damage to the heart from radiation and chemotherapy — and cardio-oncology emerges as a new subspecialty.
- Studies at Cleveland Clinic uncover an association between the use of COX-2 inhibitors and death from heart disease. The drugs' use is restricted, preventing millions of premature deaths.
- Portable defibrillators become common in stadiums, airports and other public places.
- Endovascular stent grafting increasingly replaces open surgical repair of abdominal aortic aneurysms. Key innovations take place at Cleveland Clinic.
- The cardioprotective benefits of aspirin are generally accepted, but broad consensus remains elusive on who should take regular aspirin and at what doses.

Spring 2004 Issue ❯

Intravascular ultrasound becomes a powerful research tool, enabling precise measurements of plaque regression in high-profile clinical trials designed and led at Cleveland Clinic.

- The time it takes the heart rate to return to normal after exercise is found to be a valuable diagnostic and prognostic tool by Cleveland Clinic-led research.
- The left atrial appendage becomes a target for surgical and endovascular closure techniques designed to prevent the escape of stroke-causing blood clots. A left atrial appendage clip designed at Cleveland Clinic is approved by the FDA.

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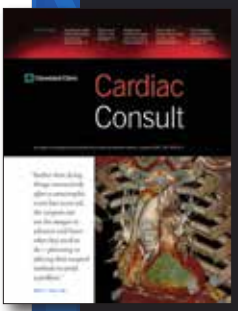
- Niacin gains favor for its ability to raise HDL levels, then loses favor as later studies suggest health risks.
- Awareness of women's heart disease increases, along with recognition of its particular manifestations and the need for more woman-specific heart disease studies.
- Studies show that statins can reduce the risk of a major cardiac event in patients with diagnosed disease. Key research is designed and led at Cleveland Clinic.
- High-dose statin therapy is proven by Cleveland Clinic studies to halt and even reverse the progression of atherosclerosis and improve survival by reducing LDL levels and possibly lowering inflammation.



‹ *Summer 2008 Issue*

Cardiac imaging modalities expand to include echo, nuclear imaging, cardiac magnetic resonance and CT. Cross-training among these options is encouraged, as specialists work to find the most efficient and effective mix of options for each patient.

- Dyspnea is linked to coronary artery disease in Cleveland Clinic-led research and is shown to be a significant independent predictor of death from this and other causes.
- The special risk posed by trans fats in the diet is recognized.
- C-reactive protein emerges as a potent marker of inflammation and heart disease.
- Adult stem cells can, for the first time, be guided into becoming cardiac cells capable of repairing damaged tissue.
- Transfused red cells stored more than two weeks are found by a Cleveland Clinic study to be associated with greater postoperative complications and mortality.
- Reduction left ventriculoplasty (the Batista procedure) to surgically reduce ventricular mass in patients with congestive heart failure is introduced to America; when it does not achieve acceptable outcomes, most hospitals discontinue its use.
- Beating-heart surgery techniques improve. Today 15 to 20 percent of all coronary artery bypass operations worldwide are performed on a beating heart.
- Large-scale, prospective, randomized, multicenter international trials demonstrate their power to assess and compare the effectiveness of a multitude of treatments. Studies led by Cleveland Clinic's C5 Research (STAMPEDE, REVERSAL, EPISTENT, CAMELOT, GUSTO V and many more) define what works and what doesn't.
- Carotid stenting emerges as a complementary alternative to endarterectomy for treating patients with carotid artery stenosis, offering outcomes similar to those with the surgical approach for many patients who are less well-suited to surgery.
- Surgeons develop blood-sparing and blood-free techniques for major cardiac procedures. Cleveland Clinic research shows that the risk of complications and mortality rises with blood transfusions.

***Fall 2010 Issue* ›**

Branched endovascular stent grafts are successfully implanted to treat complex aneurysms in the aortic arch.

- Recognition mounts of the persistence of heart health disparities among socio-economic groups, with disadvantaged patient groups having greater disease burden and poorer treatment outcomes.
- Vest-like, wearable cardioverter defibrillators are successfully used in patients with heart rhythm disorders.
- High-volume cardiac surgery centers like Cleveland Clinic are able to repair 99 out of 100 cases of mitral valve regurgitation due to prolapse, with minimum mortality.
- New oral anticoagulants — i.e., direct thrombin and direct factor Xa inhibitors — join vitamin K antagonists like warfarin for the medical prevention of stroke-causing blood clots.
- Normothermic ex vivo perfusion-based organ care systems ("heart in a box") enable procurement teams to travel longer distances to collect suitable hearts and lungs for transplant.
- Cleveland Clinic surgeons improve meticulous techniques for removal of infective endocarditis from heart tissue, neutralizing the formerly high risk of operating on a patient with an active infection.

‹ *Spring 2013 Issue*

As more patients live longer with cardiac surgery, the number of reoperations increases at centers like Cleveland Clinic, where mortality rates for these challenging procedures are below 1 percent, even for second, third or fourth reoperations.

- Cleveland Clinic studies show that gut flora linked to consuming meat and eggs is associated with increased cardiac risk in humans, amplifying the negative cardiac effects of dietary cholesterol.
- Cleveland Clinic researchers develop an automated system that extracts the centerlines of the aorta and branch vessels from a patient's CT scan and builds a complete mathematical model of the relevant vasculature for 3-D printing.
- A sealable cardiac port device (Kapsus) undergoes development at Cleveland Clinic to provide safe, transapical access to the heart chambers for percutaneous aortic and mitral valve replacement.
- 3-D echocardiography aids the diagnosis of complex valve problems for the surgical and percutaneous repair of structural heart conditions.
- Robotic catheter navigation helps improve the safety and effectiveness of complex catheter ablation procedures.
- Robotic arms developed for automobile assembly lines are adapted to hold X-ray equipment on C-arms in the catheterization lab.
- Increasing numbers of complex interventions begin to be performed percutaneously, including aortic valve replacement, mitral valve repair, and closure of patent foramen ovale, atrial septal defects and paravalvular leaks.
- The safety of percutaneous coronary intervention improves dramatically.
- Improvements in diagnosis and treatment contribute to a dramatic overall decline in STEMI in all age groups except younger women.

The Beat Goes On

While old controversies are laid to rest, healthy debate continues on subjects of major importance to patients and physicians:

- What is the role of coronary CT angiography in screening patients for cardiovascular disease?
- Which is better for stable angina — medical treatment or interventions like angioplasty, stenting and coronary artery bypass?
- Have recent studies permanently eroded confidence in renal ablation to treat resistant hypertension, or is there still hope for this once-promising technology?

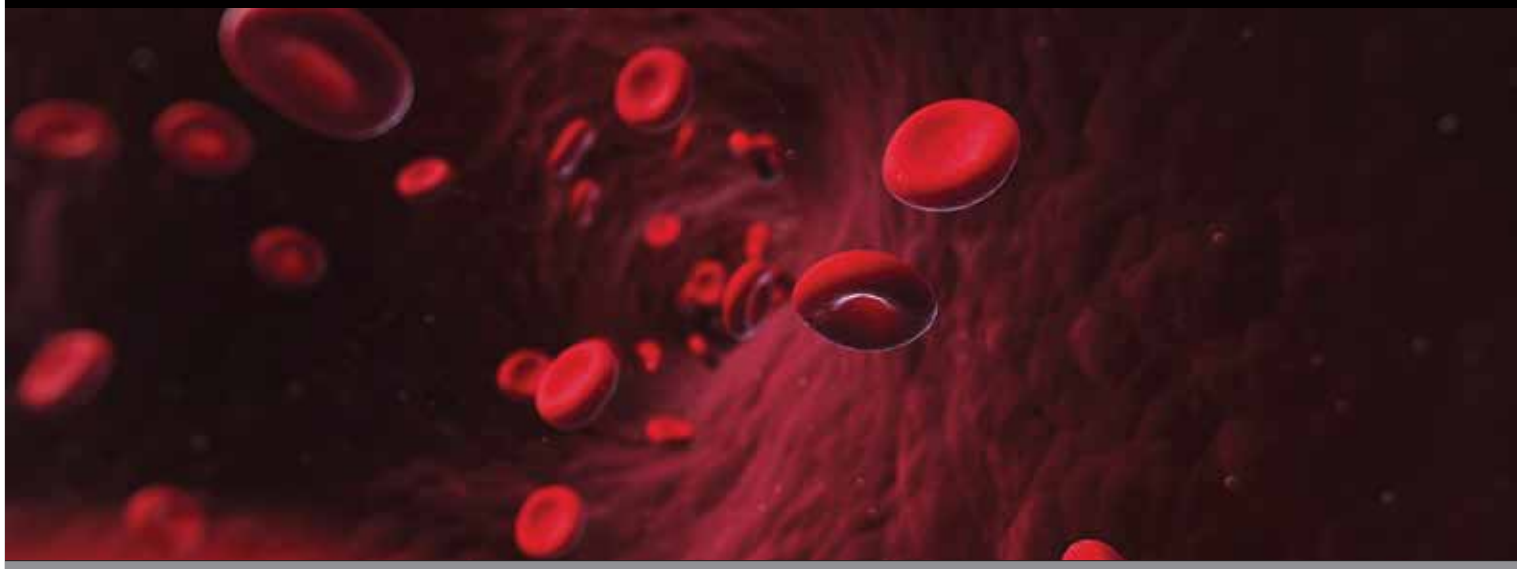
There's been no shortage of excitement and innovation in the cardiovascular specialties over the past two decades. Physicians and researchers are still driven by the recognition that cardiovascular disease remains the leading cause of death in the developed world. They also know that as their work transforms cardiovascular disease from a fatal to a chronic condition, the challenges and costs of long-term management loom.

The most powerful lesson we can take from the past 20 years is that the best approach to curbing cardiovascular disease is still prevention. A tobacco-free lifestyle that includes regular exercise, mindful eating, stress reduction and maintenance of a healthy weight can be achieved by almost everyone and can reduce heart disease risk for most people by as much as 50 percent.

Sounds like a good prescription to keep us all around to work on the next 20 years of progress. ■

For 'No Option' Wound Patients, a Versatile, Multidisciplinary Approach Can Still Save Limbs

Novel techniques and products open blocked arteries and expedite healing in complex cases.



A multidisciplinary team of dedicated wound-care specialists at Cleveland Clinic takes a "no holds barred" approach to the treatment of complex, nonhealing wounds. By employing novel techniques for limb salvage and new products to encourage wound healing, they are often able to prevent or delay the need for amputation in the sickest patients (see example case in "Image of the Issue," p. 16).

"When others decide amputation is the only option, that is the patient we want to see," says Mehdi Shishehbor, DO, an interventional cardiologist and Director of Endovascular Services in Cleveland Clinic's Heart & Vascular Institute.

Dr. Shishehbor and vascular podiatrist Michael Maier, DPM, Director of the Lower Extremity Wound Clinic in the Department of Cardiovascular Medicine, evaluate patients together and formulate treatment plans for healing the wound and revascularizing the limb.

"There is no wait for consultative services," says Dr. Maier. "If a patient has tissue loss, the sooner we restore blood flow, the better the chance the patient will heal."

It Takes a Team

The vast majority of wounds treated at Cleveland Clinic are large, deep wounds complicated by infection and poor circulation. For successful healing, contributory factors must be treated aggressively and thoroughly. The treatment plan often involves specialists in other disciplines.

"What differentiates our wound care program is the breadth and depth of experts who are committed to these challenging patients," says Dr. Shishehbor. The team includes key colleagues in vascular surgery, infectious disease, diabetology, nutrition, plastic surgery, and foot and ankle surgery, as well as orthotists and prosthetists.

Individualizing Options to Restore Blood Flow

Patients with peripheral arterial disease constitute 90 percent of Cleveland Clinic's lower extremity wound care population. The remaining 10 percent generally have venous insufficiency or both conditions.

Due to the severity of ischemia typically encountered, the wound care team offers a variety of approaches to restore blood flow. These include endovascular treatment with angioplasty and stenting, bypass surgery and a novel technique known as combined antegrade-retrograde tibiopedal reconstruction.

"The optimal procedure depends on the severity and location of blockages and is not necessarily an either/or decision,"

says vascular surgeon Lee Kirksey, MD, referring to stenting and bypass surgery. "Sometimes a hybrid approach, which involves using a balloon in one leg and performing bypass surgery in the other, can produce the most durable result and is less stressful than a larger operation."

Combined Antegrade-Retrograde Intervention

When a total obstruction cannot be crossed with a wire using a conventional antegrade approach, and the patient is too high-risk or not a candidate for bypass surgery, a retrograde approach via the foot arteries often achieves perfusion and can prevent amputation. Dr. Shishehbor is one of a handful of U.S. physicians skilled in performing combined antegrade-retrograde tibiopedal reconstruction.

Using a micropuncture needle, he accesses the small tibial or pedal arteries in the lower leg or the foot and introduces very low-profile wires (the same ones used to treat blockages in the heart) into the vessels. Multiple wire exchanges may be needed. A support catheter is introduced into the lumen and the lesion is crossed in the retrograde fashion. The intervention is then performed using femoral access.

"About 30 percent of patients cannot be treated with the typical antegrade approach. Using the combined antegrade-retrograde approach increases the success rate to 93 percent," says Dr. Shishehbor, who teaches the technique nationally and internationally. He, Dr. Maier and other Cleveland Clinic colleagues recently published positive early results with this approach in patients with high-risk critical limb ischemia (*Ann Vasc Surg*. 2014;28[6]:1439-1448).

Innovative Treatment of Nonhealing Wounds

Sophisticated nonsurgical treatments include the use of advanced wound-care products containing local mediators of wound healing and synthetic skin grafts.

"If we improve circulation and cure infection, but cytokines and other local mediators of wound healing have been depleted, healing is rare," explains Dr. Kirksey. "So we replenish the extracellular matrix with a product that restores proteins and growth factors."

Synthetic skin grafts made from porcine tissue and human cells are used to regenerate tissue and encourage healing of large wounds. (See **clevelandclinic.org/skingraft** for a short video of Dr. Kirksey applying one of the many types of synthetic skin graft products to a wound patient.)

When Amputation Is the Best Option

When amputation is the most appropriate treatment, it must be performed properly. "The patient should be able to be fitted with a prosthetic and resume a meaningful life," says Dr. Kirksey.

Ongoing Research to Improve Limb Perfusion

Dr. Shishehbor has received industry funding for two research projects: $500,000 to evaluate the impact of the platelet aggregation inhibitor ticagrelor (Brilinta®) on microcirculation in the foot, and $25,000 to test a novel microperfusion assessment tool currently used in breast reduction and gastric bypass surgery.

"We hope the tool will allow us to better assess whether a patient needs revascularization and whether a revascularization was successful," he says. "Right now, tools to evaluate perfusion at the level of the foot are limited. We still have a lot to learn."

After a partial amputation, orthotists ensure the foot will bear weight when fitted with an appropriate shoe.

Amputation leaves a patient with a large wound that often requires assistance in healing. A post-acute team of physicians and nurse practitioners follows patients to skilled nursing and rehabilitation facilities after discharge to monitor healing in these settings.

A Continuum of Care

When the healing process starts in the hospital, it continues in the ambulatory setting. For patient convenience, Cleveland Clinic offers wound care and ongoing treatment of underlying factors, including diabetes, obesity and cardiovascular disease, in its community hospitals.

"We can't simply hope a wound will heal," says Dr. Kirksey. "We must continue to be aggressive and diligent, or 60-day readmission rates can be as high as 35 percent."

"If we do a complex intervention, and the patient has poorly controlled diabetes or blood pressure, the vessels will reocclude in short order," says Dr. Maier. "The goal of treatment is ongoing management of cardiovascular risk factors and surveillance of peripheral arterial disease."

"We are in it for the long haul," he adds. ■

Contact Dr. Shishehbor at shishem@ccf.org or 216.636.6918.
Contact Dr. Maier at maierm@ccf.org or 216.445.6042.
Contact Dr. Kirksey at kirksel@ccf.org or 216.444.2892.

Image of the Issue

FROM MICHAEL MAIER, DPM, AND MEHDI SHISHEHBOR, DO

FROM DEHISCENCE TO HEALING:
WOUND CARE IN A COMPLEX LVAD PATIENT

Photos of a dehisced transmetatarsal amputation (left) in Cleveland Clinic's longest-living left ventricular assist device (LVAD) patient and the healed wound at one-year follow-up (right) illustrate how a dedicated effort can prevent below-the-knee amputation in a highly complex patient.

Five years after receiving a permanent LVAD, the 64-year-old male patient developed an interdigital pressure ulcer. CT angiography revealed severe infrapopliteal arterial disease, with occlusion in the anterior and posterior tibial arteries. Due to comorbidities — including ischemic cardiomyopathy, heart failure, hypertension, end-stage renal disease, diabetes and sleep apnea — the patient was not a candidate for bypass surgery.

Recanalization was accomplished through a combined antegrade-retrograde approach (see preceding article for description). Nevertheless, the third digit progressively declined, requiring a partial third ray amputation.

The site failed to heal, and a transmetatarsal amputation was performed. The wound dehisced. Angiography revealed recurrent occlusive disease, and arterial intervention was repeated to restore perfusion.

The amputation site was surgically revised, with debridement of soft tissue and bone. The patient was placed on an extended course of IV meropenem. Through dedicated use of negative-pressure therapy and a full complement of advanced wound-healing products derived from porcine tissue and human cells, the wound body slowly healed. Today, the patient is able to walk without pain.

Cleveland Clinic's wound care team (see preceding article) continues to watch the lower extremity while monitoring the patient's other leg and his cardiovascular risk factors. ■

FOR MORE INFORMATION, CONTACT MICHAEL MAIER, DPM, AT MAIERM@CCF.ORG OR 216.445.6042.

Tetralogy of Fallot in Adults:

What to Do When the Diagnosis Is — and Is Not — a Surprise

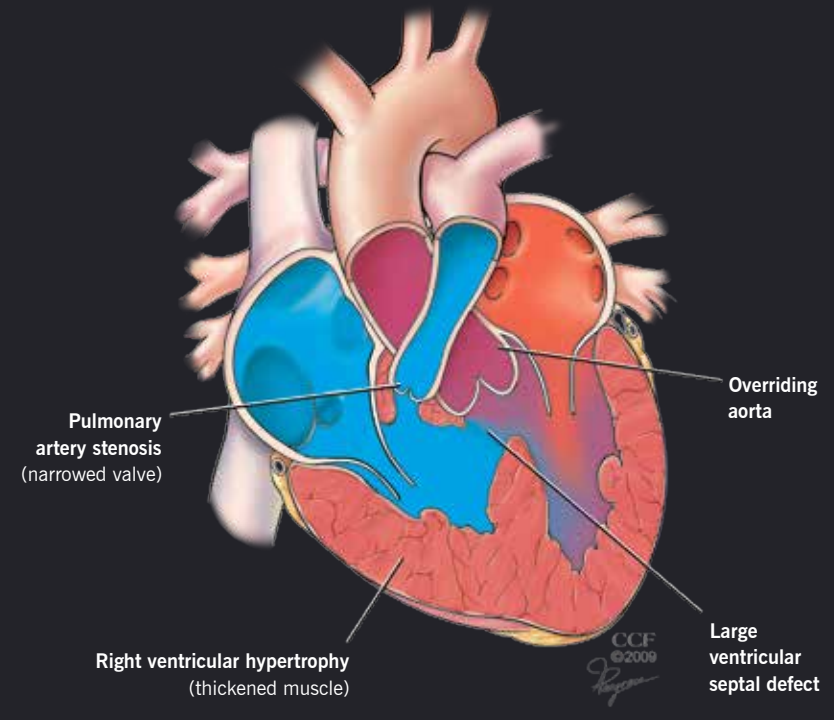
By Gösta Pettersson, MD, PhD, and Richard Krasuski, MD

Tetralogy of Fallot (ToF) is the most common complex lesion seen in adults with congenital heart disease (CHD). The condition usually is diagnosed at birth or shortly thereafter in response to its hallmark cyanosis. It is sometimes treated with a shunt, and palliative surgery typically is performed between 3 and 9 months of age. These techniques can relieve symptoms for years, often well into adulthood, until more definitive surgical repair is needed. If necessary, a valve repair (or replacement) to open the outflow tract can be performed starting from approximately age 5 or 6 years.

In keeping with the above, the large majority of adults with ToF evaluated at Cleveland Clinic's Adult Congenital Heart Disease Center have undergone palliative or corrective surgery for the condition during childhood. Yet the occasional patient with ToF reaches adulthood without prior diagnosis or surgical repair; these patients may or may not be symptomatic when referred.

During the past several years, we have seen a handful of adults with ToF who were not previously diagnosed — or fully diagnosed — and thus had not undergone surgical correction. One such case is presented in the following sidebar (p. 18) as a model of issues encountered in the management of these unusual cases where precedent is hard to come by.

continued next page



Tetralogy of Fallot at a Glance

ToF is a conotruncal defect resulting from anterior malalignment of the infundibular septum that classically involves four defects:

- A large ventricular septal defect
- Aortic valve overriding the ventricular septum
- Narrowing of the right ventricular outflow tract, typically caused by pulmonary, subpulmonic and/or right ventricular outflow tract stenosis
- Right ventricular hypertrophy

Case Presentation

The patient was a 24-year-old woman who had been diagnosed with a ventricular septal defect as a child. She was referred to our center with exertional dyspnea, chest pain and palpitations, all of which had worsened over the prior six months. She had been prescribed a beta blocker, which improved her palpitations, but her other symptoms persisted. She had not undergone any surgical correction of her ventricular septal defect.

Diagnosis

After examination and diagnostic workup (Figure 1), we suspected the patient also had the other three defects that constitute ToF. An MRI clinched the diagnosis, and we recommended surgical correction.

Surgical Intervention

The patient was an excellent candidate for surgical repair. The narrowing of her right ventricular outflow tract was caused by thickened muscle obstructing the outflow tract; we resected the muscle and opened up the outflow tract. She had a good pulmonic valve and did not require a replacement. The ventricular septal defect was closed through the tricuspid valve with a patch.

Four months after the operation, she developed atrial flutter, which was immediately treated successfully with ablation. Because we could preserve her own good pulmonary valve, it is unlikely she will require any future surgeries related to her CHD.

Outcome

The patient, now 31, had a follow-up appointment and echocardiogram earlier this year. The echo was perfect (Figure 2), showing normal function of both ventricles and no outflow tract obstruction. Because she has fewer physical limitations than before her surgery, she has become more active and lost a significant amount of weight.

In the seven years since the surgery, the patient delivered one healthy child, now 4 years old, and was in the third trimester of another pregnancy at the time of this writing. We referred her for preconception counseling, which confirmed that she did not carry the specific genetic abnormality (a deletion in chromosome 22q11) implicated in about 15 percent of ToF cases. Fetal echoes during her pregnancies have also been normal.

The patient recently described her physical limitations prior to her diagnosis and surgical correction as follows: "I played softball, but I knew I couldn't hit a home run because I wouldn't be able to make it to home plate. I've become much more active since the surgery — I can keep up with my preschooler, and I've even run a 5K. My quality of life has greatly improved. I didn't really realize what I was missing until I had the surgery." ■

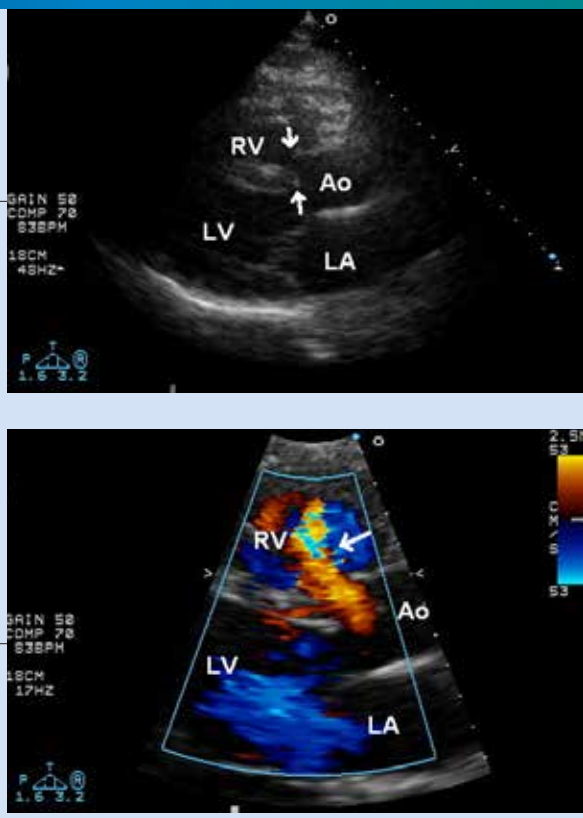


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Figure 1. Presurgical parasternal long-axis echocardiographic views of the patient showing an overriding aorta (arrows in top image) with a large ventricular septal defect (arrow in bottom image).

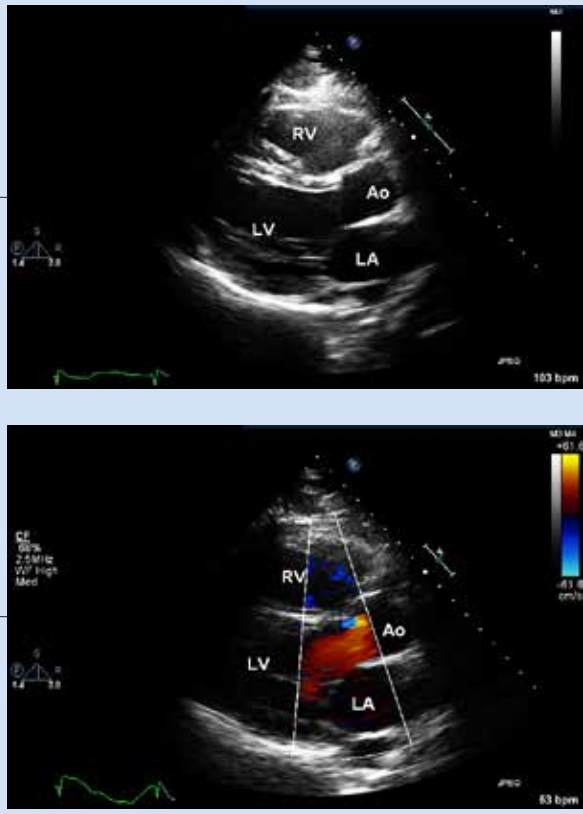

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Figure 2. Similar postsurgical views showing closure of the ventricular septal defect with no residual flow across the ventricular septum.

The Exception Proves the Rule

While it is highly unusual for ToF to go undiagnosed until adulthood, it does happen — typically in cases such as this when there is a perfect balance in childhood between the narrowing of the pulmonic valve and the ventricular septal defect so that cyanosis does not occur.

This patient was fortunate to have avoided the complications that can be associated with uncorrected ToF, which include atrial clot formation, increased risk of infections and abscesses, or even sudden death.

Managing Adult ToF in Its More Common Presentations

Much more commonly, the adults we see with ToF were diagnosed early in life due to cyanosis, and they have received palliative — and most often also corrective — surgery. We see these patients for routine follow-up and for long-term complications that can arise from either the disease or prior surgeries.

When ToF is repaired in childhood, we try to spare the pulmonic valve, but more often the pulmonic valve is opened up and an outflow patch is placed, which compromises the valve's function. (Valve placement in childhood is rare because it is not necessary in the short term and the available valves have very limited life spans.) Therefore, leaky valves are the most common reason these patients are referred for surgical repair in adulthood.

We determine and continually monitor the need for a valve repair or replacement based primarily on symptoms such as cyanosis or fatigue, physical ability and size of the right ventricle. Some patients may never need a reoperation.

However, it is important that surgical intervention, if needed, occur before the right ventricle becomes too stretched.

We always strive for valve-sparing surgeries; in cases when the pulmonary arteries and right ventricle are in good condition, patients can go through life without ever requiring a prosthetic valve. Occasionally we are able to implant a valve without performing surgery, but the ability to replace the valve percutaneously is often limited by the large size of the pulmonary outflow tracts or by other structural defects that need to be concomitantly corrected.

In certain cases in which we know additional strain may be placed on the heart in the near future — such as a planned pregnancy — we may recommend valve replacement surgery sooner than we otherwise would.

Specialization Matters

Regardless of when ToF is diagnosed, patients who require interventional or surgical procedures are best served at centers with a specialized multidisciplinary adult CHD center, as recommended by the American College of Cardiology/American Heart Association guidelines on adult CHD. Because this specialty is fairly uncommon, at least 30 percent of the patients seen at our center come from out of state.

When performed by an experienced CHD surgeon, surgical repair of ToF in adults has a high success rate, and most patients will not need further surgical treatment. ■

Contact Dr. Pettersson, Section Head of Pediatric and Adult Congenital Heart Surgery, at 216.444.2035 or petterg@ccf.org. Contact Dr. Krasuski, Director of the Adult Congenital Heart Disease Center, at 216.445.7430 or krasusr@ccf.org.

Clinical Trials Enrolling Patients

Here are a few of the many clinical research trials underway in Cleveland Clinic's Heart & Vascular Institute. For information on enrolling a patient in these or other trials, call 216.445.3608.

CARDIOTHORACIC SURGERY

PERIGON: Medtronic Pericardial Surgical Aortic Valve Replacement Pivotal Trial

Site PI: Joseph Sabik, MD (also national PI)

Description: Nonrandomized phase 3 trial evaluating the safety and effectiveness of the Medtronic Model 400 aortic valve bioprosthesis

Population: Patients requiring replacement of their native or prosthetic aortic valve (with or without concomitant procedures such as CABG surgery)

Sponsor: Medtronic Cardiovascular

Clinical Investigation of the Perceval S Sutureless Heart Valve

Site PI: Eric Roselli, MD

Description: Nonrandomized prospective study of the safety and effectiveness of the Perceval S heart valve to replace a diseased or dysfunctional native or prosthetic aortic valve

Population: Patients scheduled to undergo planned aortic valve replacement

Sponsor: Sorin Group USA

eMESH I: Study of External Saphenous Vein Support Using eSVS® Mesh in CABG Surgery

Site PI: Joseph Sabik, MD

Description: Randomized prospective study to assess the feasibility, initial safety and performance of the eSVS Mesh as an external vein support device for use over saphenous vein grafts (SVGs) during CABG surgery. Each enrollee receives an SVG without the mesh (control) and an SVG with the mesh (treatment).

Population: Patients requiring CABG surgery with SVGs to the right coronary artery system and the left circumflex artery system, with ≥ 70 percent stenosis in each system

Sponsor: Kips Bay Medical

ELECTROPHYSIOLOGY

LEADLESS II IDE: Safety and Effectiveness Trial for the Nanostim™ Leadless Pacemaker

Site PI: Daniel Cantillon, MD

Description: Phase 3 study of the safety and effectiveness of the Nanostim leadless pacemaker

Population: Patients with indications for a VVI pacemaker

Sponsor: St. Jude Medical

Micra Transcatheter Pacing Study

Site PI: Bruce Wilkoff, MD

Description: Phase 3 study to evaluate the safety and efficacy of the leadless Micra™ Transcatheter Pacing System and assess its long-term performance

Population: Patients with a class I or II indication for implantation of a single-chamber ventricular pacemaker

Sponsor: Medtronic Cardiac Rhythm Disease Management

reMARQable: nMARQ™ Pulmonary Vein Isolation System for the Treatment of Paroxysmal Atrial Fibrillation

Site PI: Bruce Lindsay, MD

Description: Randomized phase 3 trial evaluating the safety and effectiveness of the nMARQ Catheter System vs. ThermoCool® Navigation Catheters in treating drug-refractory symptomatic paroxysmal atrial fibrillation (AF)

Population: Patients with symptomatic paroxysmal AF who have had at least one AF episode in the prior year and failure of at least one antiarrhythmic drug

Sponsor: Biosense Webster

HEART FAILURE

FIGHT: Functional Impact of GLP-1 for Heart Failure Treatment

Site PI: Wilson Tang, MD

Description: Randomized, double-blind phase 2 trial testing whether treatment with a subcutaneously delivered GLP-1 agonist in the period after acute heart failure syndrome discharge is associated with greater clinical stability (measured by a composite clinical endpoint) at six months compared with placebo

Population: Patients recently hospitalized for heart failure with an LVEF < 40 percent

Sponsors: Duke University and NHLBI

GUIDE-IT: Guiding Evidence Based Therapy Using Biomarker Intensified Treatment

Site PI: Wilson Tang, MD

Description: Randomized open-label trial to determine the efficacy of a strategy of biomarker-guided therapy compared with usual care in high-risk patients with left ventricular systolic dysfunction

Population: Heart failure patients with a recent LVEF < 40 percent and recent hospitalization or ED visit for heart failure

Sponsors: Duke University and NHLBI

NEAT: Nitrate's Effect on Activity Tolerance in Heart Failure with Preserved Ejection Fraction

Site PI: Wilson Tang, MD

Description: Randomized, double-blind, placebo-controlled crossover study assessing the effect of isosorbide mononitrate with upward dose titration on activity tolerance as assessed by accelerometry

Population: Heart failure patients with preserved ejection fraction

Sponsors: Duke University and NHLBI

IMAGING

HCMR: Novel Markers of Prognosis in Hypertrophic Cardiomyopathy

Site PI: Milind Desai, MD

Description: Patient registry study to develop a predictive model of cardiovascular outcomes in hypertrophic cardiomyopathy (HCM) by using data mining to identify demographic, clinical and novel cardiovascular magnetic resonance, genetic and biomarker variables associated with outcomes

Population: Adults up to age 65 with an established diagnosis of HCM defined as unexplained left ventricular hypertrophy

Sponsors: University of Virginia and NHLBI

VANISH: Valsartan for Attenuating Disease Evolution in Early Sarcomeric HCM

Site PI: Harry Lever, MD

Description: Randomized, double-blind, placebo-controlled phase 2 trial assessing the safety and efficacy of valsartan in attenuating disease evolution in early hypertrophic cardiomyopathy (HCM)

Population: Patients with a pathogenic or likely pathogenic HCM sarcomere mutation

Sponsors: New England Research Institutes and NHLBI

INTERVENTIONAL CARDIOLOGY

ABSORB IV: A Clinical Evaluation of Absorb™ BVS, the Everolimus Eluting Bioresorbable Vascular Scaffold, in the Treatment of Subjects with De Novo Native Coronary Artery Lesions

Site PI: Russell Raymond, DO

Description: Randomized, controlled, single-blind evaluation of the Absorb BVS everolimus-eluting bioresorbable vascular scaffold compared with XIENCE stents for the treatment of de novo native coronary artery lesions

Population: Patients with de novo native coronary artery lesions

Sponsor: Abbott Vascular

SALUS: The Direct Flow Medical Transcatheter Aortic Valve Replacement System: A U.S. Pivotal Trial

Site PI: Samir Kapadia, MD

Description: Open-label study to assess the safety and effectiveness of the Direct Flow Medical aortic valve system for patients with severe aortic stenosis who are not well enough to undergo surgical repair

Population: Patients with severe symptomatic aortic stenosis at high risk or deemed not suitable for surgery following evaluation by a cardiac surgeon

Sponsor: Direct Flow Medical

PREVENTIVE CARDIOLOGY

GAUSS-3: Trial of Patients with Statin Intolerance Randomized to PCSK9 vs. Zetia

Site PI: Michael Rocco, MD

Description: Randomized, double-blind, controlled phase 3 study of AMG 145 (evolocumab) in statin-intolerant individuals with dyslipidemia to assess side effects and efficacy in lowering LDL cholesterol and increasing HDL cholesterol

Population: Patients ages 18 to 80 who are not at goal LDL cholesterol, have fasting triglycerides ≤ 400 mg/dL, have a history of intolerance to at least two statins, and currently are not on a statin or are on a stable low dose

Sponsor: Amgen

GRADY: Gut Flora Metabolite Reduction After Dietary Intervention

Site PIs: Wilson Tang, MD, and Stanley Hazen, MD, PhD

Description: Randomized, open-label phase 1/2 study investigating the ability of dietary intervention to modulate TMAO levels with and without TMAO levels being provided to subjects for guidance

Population: Patients with elevated TMAO metabolizers (> 5 μM), based on a screening test, who are willing to follow a modified Mediterranean diet for 12 weeks

Sponsor: Cleveland Clinic

STRENGTH: Outcomes Study to Assess Statin Residual Risk Reduction with Epanova® in High CV Risk Patients with Hypertriglyceridemia

Site PI: Michael Rocco, MD

Description: Double-blind, controlled, parallel-group phase 3 study randomizing 13,000 patients to either Epanova (omega-3 carboxylic acids) plus statin therapy or corn oil plus statin therapy for three to five years to assess for major adverse cardiovascular events

Population: Eligible adults considered to be at high risk for atherosclerotic cardiovascular disease

Sponsor: AstraZeneca, with Cleveland Clinic as collaborator

continued next page

VASCULAR MEDICINE

ATTRACT: Acute Venous Thrombosis: Thrombus Removal with Adjunctive Catheter-Directed Thrombolysis

Site PI: Heather Gornik, MD

Description: Randomized open-label study to determine whether pharmacomechanical catheter-directed thrombolysis prevents post-thrombotic syndrome and improves quality of life in patients with DVT compared with optimal standard DVT therapy alone

Population: Patients ages 16 through 75 with symptomatic proximal DVT involving the iliac, common femoral and/or femoral veins

Sponsor: Washington University School of Medicine

PRYME: Prospective Registry of Young Women with MI: Evaluating the Prevalence and Long-term Impact of Nonatherosclerotic CAD

Site PI: Heather Gornik, MD

Description: Prospective observational registry study to evaluate the long-term outcome of young women with non-atherosclerotic coronary artery disease (CAD) relative to those with atherosclerotic CAD over five years of follow-up

Population: Women 55 or younger with a troponin-positive acute coronary syndrome who have a coronary angiogram

Sponsors: Cardiology Research UBC and University of British Columbia

VASCULAR SURGERY

EVAS IDE: Safety and Effectiveness Study of Endovascular Abdominal Aortic Aneurysm Repair Using the Nellix® System

Site PI: Daniel Clair, MD

Description: Prospective single-arm study assessing the safety and effectiveness of the investigational Nellix System for the endovascular repair of infrarenal abdominal aortic aneurysms

Population: Patients with abdominal aortic aneurysms

Sponsor: Endologix

Lutonix® Drug Coated Balloon Versus Standard Balloon Angioplasty for Treatment of Below-the-Knee Arteries

Site PI: Sean Lyden, MD

Description: Randomized single-blind study comparing the Lutonix Drug Coated Balloon with standard balloon angioplasty for safety and efficacy in the treatment of stenosis or occlusion of native below-the-knee arteries

Population: Patients with stenosis or occlusion of native below-the-knee arteries

Sponsor: C.R. Bard

SCAFFOLD: GORE® Carotid Stent Clinical Study for the Treatment of Carotid Artery Stenosis in Patients at Increased Risk for Adverse Events from Carotid Endarterectomy

Site PI: Daniel Clair, MD

Description: Prospective single-arm study comparing efficacy and safety with the GORE Carotid Stent to a performance goal developed from carotid endarterectomy outcomes

Population: Patients with stenosis of the carotid arteries at high surgical risk

Sponsor: W.L. Gore & Associates

Save the Date for CME

COMPREHENSIVE CARDIOVASCULAR MEDICINE

Friday, Jan. 16, 2015
Bonaventure Hotel
Ft. Lauderdale, Florida

Expert faculty from Cleveland join their colleagues from Cleveland Clinic Florida to present this comprehensive daylong course focused on issues in office-based cardiovascular practice that impact patient care on a day-to-day basis.

Information/registration:
ccfcme.org/GoCVMedicine

More CME … at Your Convenience

Cleveland Clinic is working with **theheart.org/Medscape Cardiology** to offer engaging online educational programs on high-interest cardiology topics. For the activities below, visit medscape.org and enter "Cleveland Clinic" in the site's search box.

- **Ischemic Events in ACS: Unmet Needs in the Antiplatelet World**, a video expert panel discussion of the pros and cons of antiplatelet therapy for ACS patients undergoing PCI
- **A Systems Approach to VTE: Highlighting Best Practices to Ensure Optimal Outcomes**, a video expert panel discussion of anticoagulation therapy in VTE and systems-based barriers to optimal treatment

theheart.org | Medscape EDUCATION CARDIOLOGY

Beyond this collaboration, the Cleveland Clinic Center for Continuing Education website offers a wealth of complimentary CME activities — webcasts, case-based lessons, online journal articles and more — in all aspects of cardiovascular practice. Some take as little as 15 minutes. Check them out at **ccfcme.org** and choose "Cardiology" under "Browse by Specialty."

RESOURCES FOR PHYSICIANS

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Consult QD – Heart & Vascular

A blog featuring insights and perspectives from Cleveland Clinic experts. Visit today and join the conversation.

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Establish a secure online DrConnect account at clevelandclinic.org/drconnect for real-time information about your patients' treatment.

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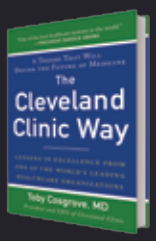
Outcomes Data
View Outcomes books at clevelandclinic.org/outcomes.

CME Opportunities
Visit ccfcme.org for convenient learning opportunities from Cleveland Clinic's Center for Continuing Education.

Executive Education
Learn about our Executive Visitors' Program and two-week Samson Global Leadership Academy immersion program at clevelandclinic.org/executiveeducation.



The Cleveland Clinic Way
By Toby Cosgrove, MD, CEO and President, Cleveland Clinic

Great things happen when a medical center puts patients first. Visit clevelandclinic.org/ClevelandClinicWay for details or to order a copy.

About Cleveland Clinic
Cleveland Clinic is an integrated healthcare delivery system with local, national and international reach. At Cleveland Clinic, more than 3,000 physicians and researchers represent 120 medical specialties and subspecialties. We are a main campus, more than 75 northern Ohio outpatient locations (including 16 full-service family health centers), Cleveland Clinic Florida, Cleveland Clinic Lou Ruvo Center for Brain Health in Las Vegas, Cleveland Clinic Canada, Sheikh Khalifa Medical City and Cleveland Clinic Abu Dhabi.

In 2014, Cleveland Clinic was ranked one of America's top four hospitals 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 20th consecutive year) and urologic care.

Cleveland Clinic

The Cleveland Clinic Foundation
9500 Euclid Ave./AC311
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