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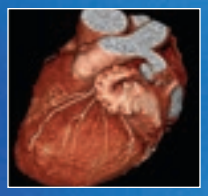

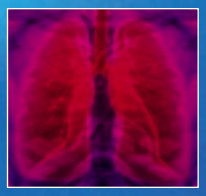

Cleveland Clinic

Cardiac Consult

Heart and Vascular News from Cleveland Clinic | Fall-Winter 2018

› CARDIAC CONSULT FEATURE

What's on the Horizon in Cardiovascular Care?

Dear Colleagues,

Cardiovascular practice and technology are evolving fast. That's the premise of our cover feature stories in this issue of *Cardiac Consult*. Experts from across our Miller Family Heart & Vascular Institute weigh in on developments and trends they see on the horizon in three dynamic areas of practice: transcatheter valve procedures, heart failure and mechanical circulatory support, and endovascular therapy for aortic and peripheral vascular disease.

While these rapid advancements are overwhelmingly positive for our patients, they shouldn't distract us from the reality that some constants are needed among all the change. One such constant is the abiding importance of a heart team approach, particularly in the setting of advising patients on transcatheter versus surgical approaches for a valve procedure. The collaborative input of all subspecialty members of the team — surgeons, interventionalists, imaging specialists and others — is required to ensure that each patient is guided to the treatment strategy best suited to his or her particular situation and needs. This will only become more true as advancements and options continue to proliferate.

Our Heart & Vascular Institute remains deeply committed to a comprehensive heart team approach across the full spectrum of complex cardiovascular disease. We welcome opportunities to work with you to offer this approach to patients with challenging cases that may require referral.

Respectfully,

Lars G. Svensson, MD, PhD

CHAIRMAN | Sydell and Arnold Miller Family Heart & Vascular Institute

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

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

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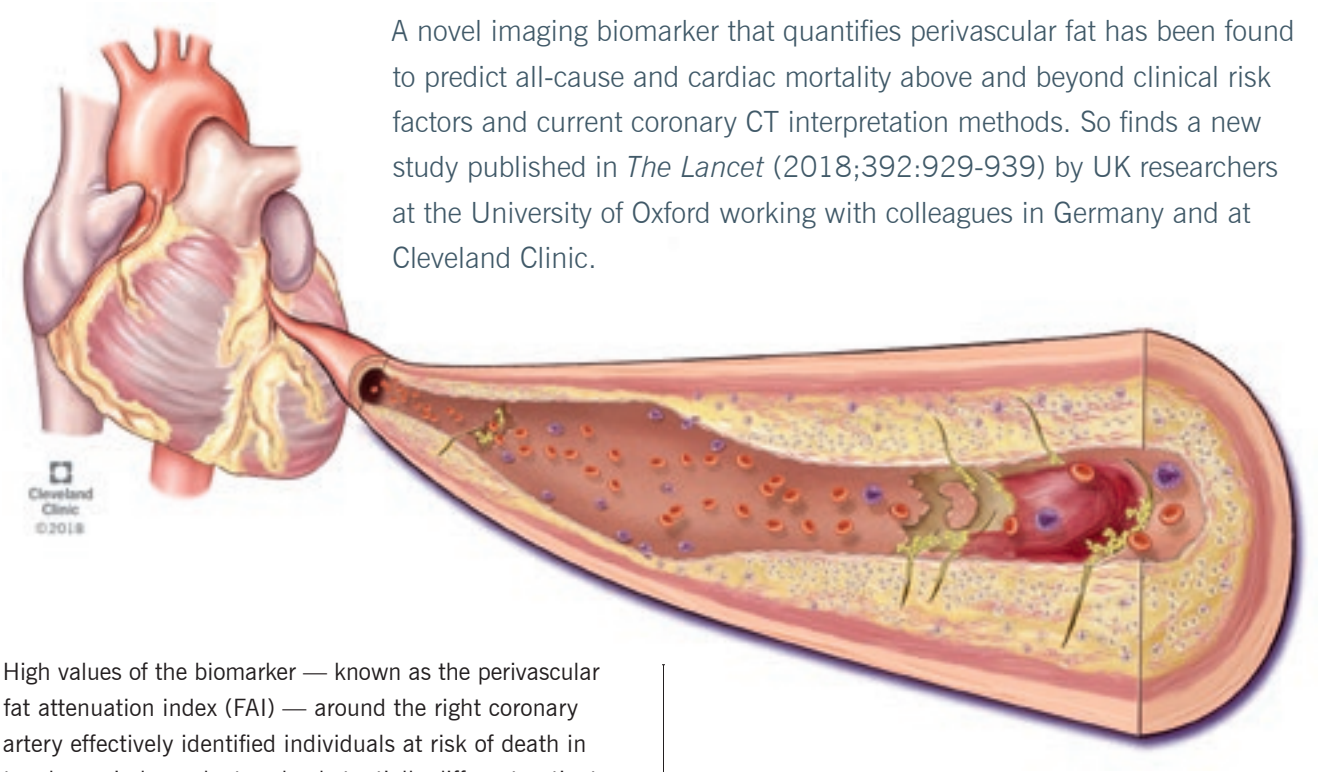
New Imaging Biomarker of Coronary Inflammation Shows Prognostic Value Exceeding All Current Noninvasive Measures

Perivascular fat attenuation index could transform primary and secondary prevention.



A novel imaging biomarker that quantifies perivascular fat has been found to predict all-cause and cardiac mortality above and beyond clinical risk factors and current coronary CT interpretation methods. So finds a new study published in *The Lancet* (2018;392:929-939) by UK researchers at the University of Oxford working with colleagues in Germany and at Cleveland Clinic.

High values of the biomarker — known as the perivascular fat attenuation index (FAI) — around the right coronary artery effectively identified individuals at risk of death in two large, independent and substantially different patient cohorts: a derivation cohort in Erlangen, Germany, and a validation cohort at Cleveland Clinic.

"The perivascular fat attenuation index is the first noninvasive biomarker of coronary inflammation measured by traditional coronary CT angiography," says co-first author Milind Desai, MD, Professor of Medicine at Cleveland Clinic Lerner College of Medicine and a Cleveland Clinic cardiologist. "Our study validates the prognostic role of this index over and above the presence of coronary stenosis or calcification. We now have, for the first time, a biomarker derived from a fairly routine imaging study that measures residual cardiovascular risk with independent and incremental value over modern risk scores and other noninvasive tests. This could have transformative effects on primary and secondary prevention."

Homing in on signals in perivascular fat

The investigation, known as the Cardiovascular Risk Prediction using Computed Tomography (CRISP-CT) study, builds on recent work by the Oxford researchers showing that coronary artery inflammation inhibits adipogenesis in adjacent perivascular fat. Specifically, signals released from the inflamed coronary artery spread to perivascular adipose tissue, impeding local adipogenesis.

The researchers developed the perivascular FAI as an imaging biomarker to quantify inflammation-induced changes in perivascular fat, enabling early detection of coronary inflammation via routine coronary CT angiography. But the index's utility for clinical risk stratification was uncertain, prompting the CRISP-CT study.

"We hypothesized that the perivascular FAI could predict future adverse events among patients undergoing coronary CT angiography — independent of the extent of coronary stenosis or other components of risk scores — and thereby flag high-risk patients who stand to benefit from more aggressive therapeutic management," Dr. Desai explains.

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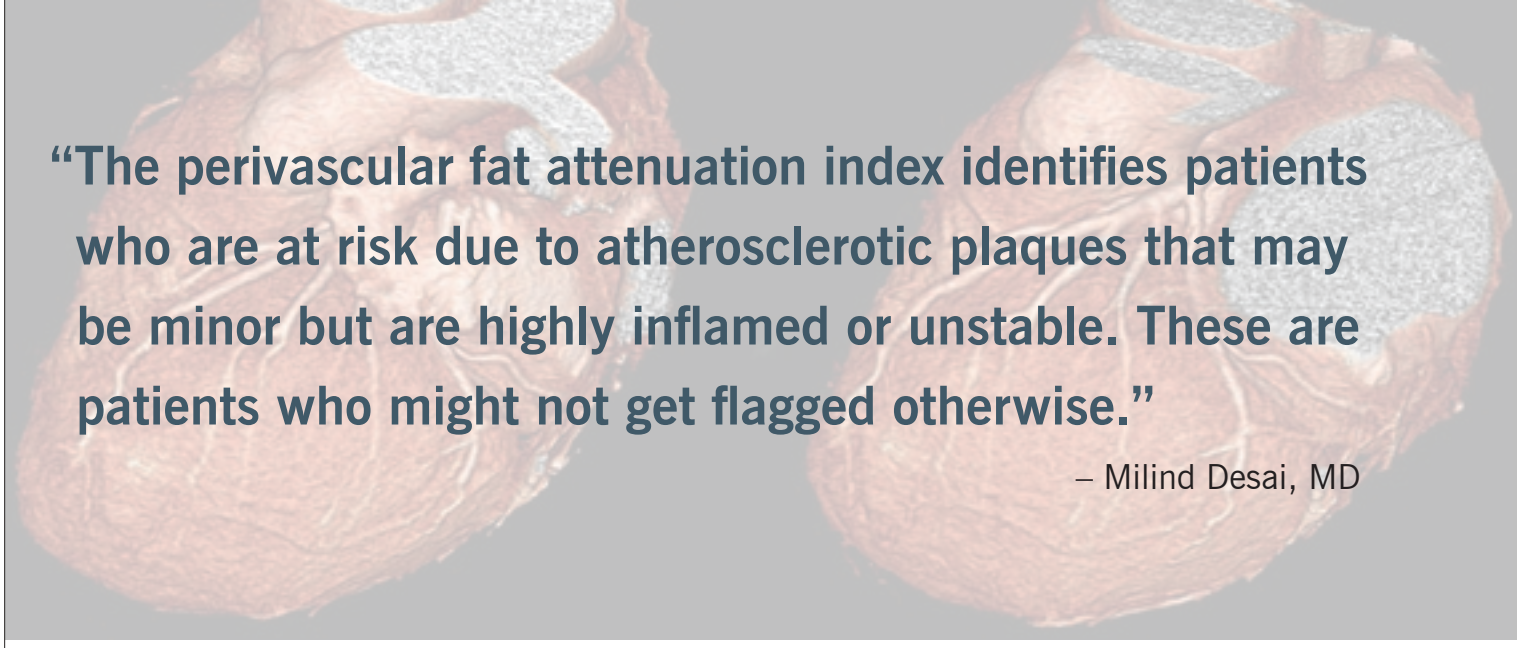


"The perivascular fat attenuation index identifies patients who are at risk due to atherosclerotic plaques that may be minor but are highly inflamed or unstable. These are patients who might not get flagged otherwise."

– Milind Desai, MD

Similar findings in two large cohorts

To test this hypothesis, the researchers prospectively collected data from the two cohorts of consecutive patients undergoing coronary CT angiography — 1,872 patients in Germany from 2005 to 2009 (derivation cohort) and 2,040 patients at Cleveland Clinic from 2008 to 2016 (validation cohort). Median patient age in the cohorts was 62 and 53 years, respectively.

Perivascular fat attenuation was mapped around the three major coronary arteries — proximal right, left anterior descending and left circumflex. The prognostic value of the perivascular FAI was assessed for all-cause and cardiac mortality in multivariate regression models. Median follow-up was 72 months in the derivation cohort and 54 months in the validation cohort.

In each cohort, perivascular FAI values around the proximal right coronary artery and left anterior descending artery — but not around the left circumflex artery — were predictive of all-cause and cardiac mortality and correlated strongly with one another. In view of this, the researchers used the perivascular FAI value around the right coronary artery as a representative marker of global coronary inflammation (hazard ratio [HR] for cardiac mortality of 2.15 [95% CI, 1.33-3.48] in the derivation cohort and 2.06 [95% CI, 1.50-2.83] in the validation cohort).

Further analysis showed that the optimal perivascular FAI cutoff in the derivation cohort was –70.1 Hounsfield units (HU) or higher (HR = 9.04 [95% CI, 3.35-24.40] for cardiac mortality and HR = 2.55 [95% CI, 1.65-3.92] for all-cause mortality). This cutoff value was confirmed in the validation cohort (HR = 5.62 [95% CI, 2.90-10.88] for cardiac mortality and HR = 3.69 [95% CI, 2.26-6.02] for all-cause mortality).

"Among patients undergoing coronary CT angiography, a perivascular FAI cutoff of –70.1 HU or higher identified those at a fivefold to ninefold elevated adjusted risk for cardiac death," observes Dr. Desai. "This association remained robust after appropriate sensitivity and subgroup analyses. Most notably, the perivascular FAI significantly improved risk discrimination in both cohorts beyond current risk models."

Implications for primary and secondary prevention

Dr. Desai and his co-investigators note that their findings are particularly important because half of myocardial infarctions occur in the absence of substantial coronary stenosis and most coronary CT angiograms do not reveal relevant coronary atherosclerosis.

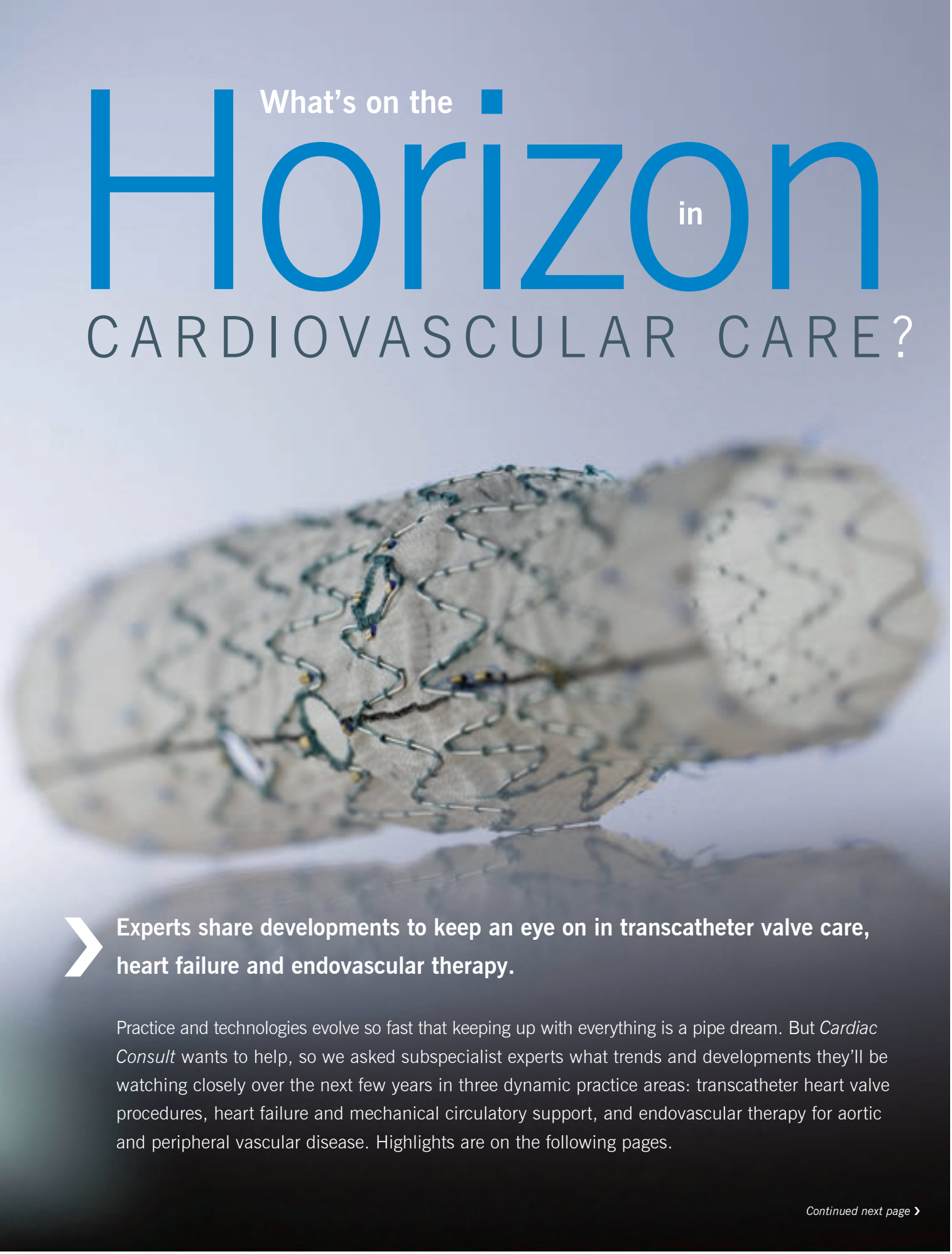
"The perivascular FAI identifies patients who are at risk due to atherosclerotic plaques that may be minor but are highly inflamed or unstable," says Dr. Desai. "These are patients who might not get flagged otherwise. This biomarker could help guide early deployment of intensive measures of primary prevention."

The findings also suggest that routine coronary CT angiography could potentially help identify the residual inflammatory risk that's captured by the perivascular FAI. "Future studies are justified to explore whether targeting this marker by intensifying existing therapies or developing newer therapies could help modify risk of future coronary events," he says. "Such trials could confirm whether the perivascular FAI is the highly sought noninvasive biomarker to guide personalized medicine in this secondary prevention setting."

He concludes: "Notably, this study also demonstrates the value of cross-continent collaboration to develop and validate newer technologies." ■

Contact Dr. Desai at 216.445.5250.

What's on the Horizon in CARDIOVASCULAR CARE?



Experts share developments to keep an eye on in transcatheter valve care, heart failure and endovascular therapy.

Practice and technologies evolve so fast that keeping up with everything is a pipe dream. But *Cardiac Consult* wants to help, so we asked subspecialist experts what trends and developments they'll be watching closely over the next few years in three dynamic practice areas: transcatheter heart valve procedures, heart failure and mechanical circulatory support, and endovascular therapy for aortic and peripheral vascular disease. Highlights are on the following pages.

Continued next page ›

› Transcatheter Valve Care

TAVR: Three things to watch for

1 **Expanding indications and populations.** "There's no doubt that transcatheter aortic valve replacement [TAVR] is going to expand more and more, because it's less invasive," says cardiac surgeon and early TAVR pioneer Lars Svensson, MD, PhD, Chair of Cleveland Clinic's Miller Family Heart & Vascular Institute. Some 168,000 TAVR procedures are projected to be performed annually in the U.S. by 2026, he notes. That growth is likely to stem largely from the following expanding indications, our experts say:

› **Aortic stenosis in patients at low surgical risk.** The multicenter PARTNER 3 trial is evaluating whether TAVR is noninferior to surgical AVR in patients at low surgical risk in addition to its established indications for aortic stenosis in patients at intermediate or high surgical risk. Enrollment is completed, and initial safety data are expected at the American College of Cardiology meeting in March 2019, says Cleveland Clinic's Section Head of Interventional Cardiology, Samir Kapadia, MD, who is on the PARTNER 3 steering committee. A key question will be valve durability in this large low-risk population, with follow-up continuing for approximately 10 years, notes Dr. Svensson, who is on the PARTNER 3 executive committee.

› **Bicuspid aortic valve stenosis.** Patients with bicuspid aortic valves were excluded from the pivotal early TAVR trials, but off-label use of TAVR for bicuspid valve stenosis has mounted. Now this use is being studied in a registry within the larger PARTNER 3 trial noted above. "Patients with bicuspid valves are a sizable and generally younger population," says Dr. Svensson, "so long-term valve durability is of particular interest."

› **Valve-in-valve TAVR.** Dr. Kapadia predicts valve-in-valve TAVR will increasingly eclipse redo AVR surgery for patients with a failed surgical bioprosthesis. "An analysis of the TVT Registry™ we recently published (*J Am Coll Cardiol.* 2018;72:370-382) showed that the outcomes of valve-in-valve TAVR are as good as, or better than, those with native valve TAVR," he says. Valve manufacturers are now designing

new surgical valves to be more amenable to potential future valve-in-valve TAVR procedures, he notes. This development may nudge patients toward undergoing initial bioprosthetic valve placement at a younger age if eventual redo surgery can likely be avoided in the event of valve deterioration.

2 **Continuing valve refinements.** TAVR valves will continue to be refined for better performance and tailoring to specific anatomies. Our experts identified several notable TAVR devices that are in late-stage investigation or likely to be available soon:

› The Lotus™ valve is designed to be mechanically expandable to reduce the risk of paravalvular leak, notes Dr. Kapadia, who served on the steering committee of the pivotal REPRISE III trial of the device. FDA approval is expected in the first quarter of 2019.

› The self-expanding CENTERA valve has a larger orifice for the same diameter of valve, promising improved hemodynamics, says Dr. Kapadia. Cleveland Clinic is participating in the soon-to-begin EXCEED randomized trial comparing the CENTERA valve with the established Sapien 3 valve.

› Additionally, next-generation versions of current TAVR valves from Medtronic and Edwards have been developed to enable better coronary access and more reliable deployment.

3 **Accessory TAVR treatments.** Therapies and developments to watch in this area include:

› **Anticoagulation.** Early termination of the GALILEO trial in October dealt a blow to the notion that an anticoagulation strategy following TAVR may reduce thromboembolic and bleeding complications compared with standard antiplatelet therapy. The phase 3 study, in which Cleveland Clinic participated, was stopped when a preliminary analysis showed excess thromboembolic events, all-cause mortality and bleeding with a rivaroxaban-based anticoagulation strategy relative to a dual antiplatelet strategy. Further insight into a potential protective role for anticoagulation following TAVR is expected from the phase 3 ATLANTIS trial comparing an apixaban-based antithrombotic strategy against standard of care.

› **Embolic protection.** Use of the Sentinel® device for embolic protection in patients undergoing TAVR got a significant boost with the recent CMS decision green-lighting its reimbursement for Medicare beneficiaries. That's likely to expand use of the device, says Cleveland Clinic cardiac surgeon Stephanie Mick, MD. "We're one of the few U.S. centers that uses the embolic protection device in all TAVR patients," she says. "This is likely to change, especially as more randomized trials assessing clinical outcomes with Sentinel are completed." Dr. Kapadia, who served as lead investigator of the pivotal SENTINEL trial, says such studies will launch soon.

› **Strategies to promote valve durability.** Various analyses are underway to examine registry data and longitudinal follow-up from pivotal TAVR trials to identify determinants of valve deterioration and how to avoid them. "We're looking at the type of valve, how we deploy it, how we expand it, how high or low we place it, the impact of various anatomies and other variables to see how we might better promote valve durability," explains Dr. Kapadia. One promising approach is a Cleveland Clinic-developed dry storage technology to better preserve bioprosthetic leaflets. That technology is used in the recently approved Inspiris Resilia™ valve for surgical AVR and is now being introduced to TAVR bioprostheses.

Mitral valve: Four fronts of activity

1 **Percutaneous approaches to degenerative disease.** Degenerative mitral regurgitation (MR) is not a huge area of opportunity for transcatheter approaches since it's already treated successfully with mitral valve repair surgery. Moreover, leading centers like Cleveland Clinic increasingly offer minimally invasive robot-assisted surgical repair. Still, a percutaneous approach holds appeal for some elderly patients and for individuals who want even less-invasive options than robotic repair.

That appeal has fueled development of two off-pump, transapical, echo-guided options for minimally invasive mitral valve repair through use of artificial chords. The two systems, known as NeoChord DS1000 and Harpoon, are intermediate steps toward percutaneous repair in that they involve a mini-thoracotomy, but both offer the potential for faster recovery than surgery. Both systems will be assessed in clinical trials that compare them to surgery, with Cleveland Clinic's Cardiothoracic Surgery Chair A. Marc Gillinov, MD, involved in the Harpoon trial.

Continued next page ›

2 Percutaneous repair of functional MR. The big news in this space is the multicenter COAPT trial of the commercially available MitraClip® device. As reported in September, the study found that transcatheter mitral valve repair with MitraClip significantly reduced all-cause mortality and hospitalization compared with medical therapy in symptomatic patients with heart failure and secondary MR.

"COAPT has changed the paradigm," says Dr. Kapadia, one of COAPT's lead investigators and a member of its steering committee. "It's the first large trial to show that treating functional MR not only makes patients feel better and prevents further worsening of the regurgitation, but also prevents death. This has fueled enthusiasm for treating functional MR with percutaneous repair, whether by targeting the annulus or by targeting the leaflets." A variety of investigational transcatheter approaches are being studied, including:

› Reduction of mitral annulus dilation with the Carillon® Mitral Contour System® in patients with functional MR associated with heart failure. This approach places a device in the coronary sinus via transjugular access. Three Cleveland Clinic staff — Drs. Kapadia and Gillinov, plus Randall Starling, MD — are co-principal investigators of the international CARILLON trial of the device, which is being coordinated by the Cleveland Clinic Coordinating Center for Clinical Research (C5Research).

› Annular reduction with the Cardioband™ Mitral Reconstruction System in patients with functional MR and heart failure. This approach places an adjustable sutureless band in the posterior annulus via the femoral artery. Cleveland Clinic is participating in the ACTIVE multicenter trial of the system.

› Annular reshaping with the Millipede IRIS System. A feasibility study is testing transatrial placement of this annuloplasty ring in patients with functional MR deemed appropriate for mitral valve surgery.

› Edge-to-edge repair with the PASCAL Mitral Repair System. This approach, similar to the MitraClip procedure, is performed transseptally and allows for independent leaflet clasping in patients with complex mitral valve anatomy. It's being evaluated in the ongoing CLASP investigation.

"The COAPT findings and all these similar investigational efforts are highly welcome, since functional MR is the area of mitral valve disease where treatment options have been most limited, including from a surgical perspective," says Dr. Mick.

3 Percutaneous mitral valve replacement. Transcatheter valve replacement is also an option for mitral valve disease, but it's more challenging than with aortic valve disease, as the native mitral valve cannot simply be pushed aside without risking left ventricular outflow tract obstruction. Anchoring of the valve in the correct position and delivery of devices also raise significant challenges. For these reasons, establishing safety and reproducibility will take longer for transcatheter replacement than for transcatheter repair in the mitral valve setting.

Still, several replacement technologies are in development for patients with degenerative or functional MR. These include the Cleveland Clinic-developed Navi™ mitral valved stent, which is not yet implanted entirely percutaneously but is expected to ultimately be. Two options are delivered transapically: the Intrepid™ device, being studied in the multicenter APOLLO trial, and the Tendyne Mitral Valve Replacement System, being studied in the international SUMMIT trial, in which Cleveland Clinic is participating. Two additional options are delivered transseptally: the CardiAQ™ system and the Caisson system, both of which are in feasibility studies involving or led by Cleveland Clinic.

"Key questions in the coming years include which patients are candidates for transcatheter mitral valve replacement and which for transcatheter mitral valve repair," says Dr. Kapadia. "That's a central issue to keep an eye on."

4 Transcatheter valve-in-valve mitral valve replacement. Cleveland Clinic and a few other centers are successfully inserting replacement valve prostheses via catheter in patients with degeneration of a prior mitral valve prosthesis or ring. "We're now doing valve-in-valve mitral valve replacements fairly regularly, with the patient under conscious sedation," explains Dr. Kapadia. He expects the practice to become more widespread — and with good reason. "Mitral valve reoperations are quite difficult and arduous for patients," he says. "So this is an important advance."

Tricuspid procedures: Quest to percutaneously eliminate TR

In the tricuspid valve arena, the central question for the next few years is whether any single device can combine two key criteria: (1) fully percutaneous implantation and (2) complete elimination of tricuspid regurgitation (TR).

The current crop of devices and procedures succeed on one but not both fronts. Transcatheter tricuspid valve repair approaches — which involve either annular repair, clip-based leaflet repair, the Kay annuloplasty technique to improve coaptation, or placement of a spacer device — have shown success in improving patients' quality of life and significantly reducing TR but not eliminating it.

Meanwhile, the leading transcatheter tricuspid valve replacement approach — implantation of the GATE™ tricuspid valved stent — has successfully reduced TR to nonexistent or trivial levels in most of the 26 high-risk patients treated with it to date. Four of those patients — including the first in the world — were treated at Cleveland Clinic by a team led by cardiac surgeon Jose Navia, MD, and Dr. Kapadia. The catch is that current delivery of the GATE valved stent is not completely percutaneous for a large number of patients, as it requires a transatrial approach and mini-thoracotomy in most patients. Notably, the first totally percutaneous tricuspid valve replacement in humans was performed by the same investigators at Cleveland Clinic.

"We're working to reduce the size of the GATE delivery system so it can be fully percutaneous," says Dr. Navia, who holds several patents related to the device. Meanwhile, feasibility studies of this replacement system are likely to start in the U.S. and Europe in 2019.

TPVR: Look for progress in treating dilated native RVOTs

Transcatheter pulmonary valve replacement (TPVR) was among the earliest percutaneous valve procedures, and it's been established as a safe alternative to surgery in selected patients with congenital pulmonary valve and right ventricular outflow tract (RVOT) abnormalities.

In the setting of the native RVOT, such as in patients with tetralogy of Fallot after transannular patch repair, the dynamic RVOT — with its dilated, compliant and muscular nature — adds complexity to the TPVR procedure. Despite this, the established Melody and Sapien valves can be safely used in native RVOTs up to 29 mm in size. "The problem is that many native RVOTs become considerably dilated beyond that dimension," says Cleveland Clinic interventional cardiologist and adult congenital heart disease (CHD) specialist Joanna Ghobrial, MD.

Dr. Ghobrial notes that the newer valve systems currently in clinical trials — such as the Harmony™ valve, the Venus P-Valve and the Altera RVOT reducer — can accommodate dilated native RVOTs, which should substantially expand the realm of TPVR in CHD patients. "As these systems become commercially available, a much larger group of patients with CHD will benefit from the reduced invasiveness of transcatheter techniques for pulmonary valve replacement," she says. "The result should be decreased morbidity and improved outcomes." ■

Contact Dr. Svensson at 216.444.6962, Dr. Kapadia at 216.444.6735, Dr. Mick at 216.444.2288, Dr. Navia at 216.444.5104 and Dr. Ghobrial at 216.444.5923.

› Heart Failure and LVADs: Eight Trends to Watch

1 Tech advances will make LVADs equal to, and eventually better than, heart transplant

A magnetically suspended pump made Abbott's HeartMate 3™ left ventricular assist device (LVAD) a recent game changer. Improved blood flow through the pump virtually eliminated clot formation and significantly reduced strokes. The result is an LVAD with two-year survival rates approaching those of transplantation, according to the pivotal MOMENTUM 3 trial.

This is only the beginning of changes in LVAD design, says Jerry Estep, MD, Cleveland Clinic's Section Head of Heart Failure and Transplantation, who co-chaired the trial's flow optimization subcommittee. These changes will include a pump that automatically regulates its speed to enhance functional capacity and quality of life, a key factor in hemodynamics that defines congestive heart failure.

He also expects LVADs to become fully implantable, lowering the risk of infection from holes in the skin.

This possibility is nearing reality, notes Edward Soltesz, MD, MPH, Surgical Director of Cleveland Clinic's Kaufman Center for Heart Failure and Recovery. "We're looking at a transcutaneous energy transmission system, or TETS, that would allow an LVAD or other device to be charged through the skin," he says.

Both specialists also foresee increased miniaturization and greater hemocompatibility to further reduce gastrointestinal bleeding, infection and stroke risks.

2 Better-informed patients and patient selection will improve outcomes

New benchmarks for LVAD appropriateness are needed, and the recent landmark ROADMAP trial has been a step forward, says Dr. Estep, who served as ROADMAP's national principal investigator. "This trial provided an objective measurement of the risk/benefit ratio that's helping us determine who should receive an LVAD," he says. "It showed that ideal patients are less sick than what traditional criteria had called for."

Patient and caregiver understanding of LVAD benefits and risks is key, Dr. Estep adds. He served as a senior

investigator in the VAD Decision Aid (VADDA) trial, which showed that this tool helps patients and their significant others be better informed in LVAD decision-making. The decision aid is available at *lvaddecision-aid.com* and is routinely offered at Cleveland Clinic in addition to standard-of-care education.

3 Changes in patient management will curb LVAD-associated morbidity

As one of few centers with a comprehensive, multi-disciplinary program of research and clinical care in heart failure, Cleveland Clinic has been involved in all major LVAD trials and developed a large database for outcome analyses designed to establish best practices. Current efforts aim to streamline care processes to speed recovery and reduce pain and its sequelae.

Minimally invasive LVAD implantation is one option being studied, though the jury's still out on whether the pain reduction is significant enough to justify the more complex surgical approach. Separately, a protocol to reduce opiate dependency in LVAD patients has proved successful and is ready for widespread adoption. The program coaches patients preoperatively on postoperative pain and how it will be managed. Today, few Cleveland Clinic patients with LVADs are discharged on opiates.

4 Mechanical devices may serve as permanent support in biventricular dysfunction

If one LVAD is good, can two be better? For patients with biventricular dysfunction, the answer appears to be yes. Cleveland Clinic is developing a protocol for implanting two permanent VADs in these patients — one to support the left ventricle and another for the right ventricle.

In the future, such patients may opt for the Cleveland Clinic continuous-flow total artificial heart (CFTAH), which is under development in adult and pediatric sizes. Its unique design has a circulating flow pump that rotates between right and left ventricles as it auto-regulates and balances blood flow. The device is expected to enter human trials in the next few years.

5 Durable temporary mechanical support devices will be worn at home

Dr. Soltesz foresees development of durable versions of percutaneous devices like the Impella® pump that can be inserted in the axillary or femoral artery for temporary circulatory support. These new pumps will be durable enough to last several months and can be worn at home while patients await transplant.

6 Use of mechanical support devices for temporary support after open-heart surgery

When a heart struggles to recover after open-heart surgery, temporary use of a mechanical support device like the Impella can ease recovery. "We've found that supporting a poorly functioning heart for two or three days makes a significant difference," says Dr. Soltesz. "If the heart doesn't recover, we move toward LVAD implantation."

7 Emergence of effective treatments for cardiac amyloidosis

Tafamidis is the first drug to show benefit in patients with transthyretin (TTR) amyloid cardiomyopathy. In the recent phase 3 ATTR-ACT study, tafamidis significantly reduced all-cause mortality and cardiovascular-related hospitalizations relative to placebo over 30 months. Cleveland Clinic's Amyloidosis Center is engaged in additional investigator-initiated and multi-center trials related to the diagnosis and treatment of TTR and AL amyloidosis, both of which are associated with progressive heart failure and have traditionally been resistant to therapy.

8 Using distance health to lower readmissions

Remote hemodynamic monitoring with the CardioMEMS™ device reduces hospital readmissions while improving quality of life. The wireless pulmonary artery pressure sensor allows providers to monitor and guide treatment for patients who are at home. Based on positive initial experience, Cleveland Clinic is participating in the multicenter GUIDE-HF trial to evaluate the effectiveness of CardioMEMS in a broader spectrum of patients. "We plan to implement use of this device at the system level to curb heart failure morbidity in patients with both reduced and preserved ejection fraction," explains Dr. Estep.

Conducting one-week post-discharge visits online via virtual visits, rather than in person, also may reduce poor outcomes in heart failure patients following hospital discharge. Cleveland Clinic is leading a study to evaluate whether virtual visits improve adherence to appointments and improve outcomes. Trial completion is expected in 2019. ■

Contact Dr. Estep at 216.444.7646 and Dr. Soltesz at 216.444.5680.

› Endovascular Therapy for Aortic and Peripheral Vascular Disease: Four Trends to Watch

1 Stent-graft innovations will continue to push the envelope for aortic repair

Endovascular aneurysm repair has already changed the way aortic aneurysms and dissections are managed, involving less blood loss, shorter operative times and hospital stays, and lower morbidity and mortality. But in cases involving inadequate landing zones, curves or complex vasculature, open repair is usually preferred — if the patient can tolerate it.

"Durability of a graft must always be balanced by considerations of patient tolerability of the procedure," says Eric Roselli, MD, The Stephens Family Endowed Chair in Cardiothoracic Surgery and Surgical Director of Cleveland Clinic's Aorta Center. "But expanding indications for endovascular procedures are changing the equation, increasingly giving high-risk patients a chance to receive lifesaving therapy."

Innovations in stent-graft designs and techniques — including fenestrations, new branch configurations and parallel placements — are opening up endovascular repair of the ascending aorta, aortic arch and thoracoabdominal aorta, as well as reshaping repair for other complex situations.

Cleveland Clinic is helping advance aortic stent-graft technology on multiple fronts, notably with the MATADORS (Multidisciplinary Study of Ascending Tissue Characteristics and Hemodynamics for the Development of Novel Aortic Stentgrafts) partnership, detailed at *consultqd.clevelandclinic.org/matadors*. The project — a collaboration among Cleveland Clinic experts, biomedical engineers from device manufacturers, and the FDA — is characterizing the pathogenesis of aortic dissection and aneurysms and defining the boundary conditions for new endovascular device development and testing to treat the ascending aorta.

Cleveland Clinic is also involved in multiple feasibility and pivotal trials testing new stent-graft designs for aortic repair. These include studies of a new disease-specific stent graft from Gore for treating ascending dissections (ARISE trial); the Medtronic Valiant® Mona LSA and Gore TBE device trials of single-branched arch stent grafts; a study of the Terumo Aortic double-branched arch device; a trial of Bolton Medical's Relay®Pro low-profile thoracic stent graft for thoracic aortic dissection; and an investigation of a thoracoabdominal branch endoprosthesis (TAMBE) device from Gore.

"As techniques continue to advance, expect to see equal or better outcomes relative to open repair, as well as increasing use for average-risk patients," Dr. Roselli notes.

2 Drug-eluting stents and balloons will improve outcomes in lower extremity artery disease

New polymer-based technologies are allowing development of better platforms and coating matrices for drug-eluting stents and balloons, addressing the most frequent cause of failure of any endovascular intervention: restenosis. The cancer drug paclitaxel is increasingly being incorporated into such devices to inhibit cell proliferation and migration after a vessel is opened.

"Drug-eluting stents, long used in cardiac surgery, are being adapted to peripheral artery disease, and multiple trials have already demonstrated good clinical outcomes," says Sean Lyden, MD, Chairman of Vascular Surgery. "We expect this area to rapidly expand with more device options and more indications."

Dr. Lyden is the Cleveland Clinic site lead for the new international clinical trial called SAVAL comparing a drug-eluting stent system with percutaneous transluminal angioplasty for infrapopliteal artery lesions in patients with critical limb ischemia. "We are also very excited with the data from the recently completed IMPERIAL trial," he says, noting that the study tested two different paclitaxel-eluting self-expanding stent systems for the superficial femoral and proximal popliteal arteries.

3 Percutaneous long-segment femoral-popliteal bypass is becoming a reality

Advanced endovascular techniques are making this conventionally open surgery fully percutaneous. After the successful DETOUR I study that used the femoral vein as a conduit for modular stent bypass grafting, Dr. Lyden will be leading the Cleveland Clinic site in the pivotal DETOUR II trial.

He notes that the earlier study showed excellent outcomes for patients with severely calcified or long-segment (lesions > 25 cm) disease. "This procedure gives us a new way to treat patients with very difficult lesions," he adds.

4 We'll be seeing more hybrid repairs — and collaboration

Some patients have aortic disease involving multiple segments, requiring different interventions. Dr. Roselli says that in such situations, hybrid approaches — combining conventional open surgery and endovascular techniques — will be increasingly used as surgeons become more comfortable with the new strategies. Integrating different procedures in a single operation avoids the additional risk and pain of a multiple-stage operation.

He cites the frozen elephant trunk procedure and novel devices to perform it as examples of innovative solutions for high-risk patients with extensive aortic disease. Such devices that will begin U.S. trials soon include the Terumo Thoraflex™ device (for which study enrollment is complete), the CryoLife EVITA stent graft and the next-generation PHASTER (Proximal Hybrid Aortic Stent graft for Thoracic Extended Repair) device. (Dr. Roselli is the inventor of the PHASTER device.)

Dr. Lyden adds that with the increasing complexity of endovascular procedures, we should also see a trend toward better collaboration between cardiac and vascular surgeons. He notes that it's common for Cleveland Clinic surgeons of both types to consult — and scrub in — together for a single patient.

"Rather than turf-claiming, it's important to look at the patient and the disease first and foremost," he says. "A multidisciplinary approach will usually deliver the best outcome." ■

Contact Dr. Roselli at 216.444.0995 and Dr. Lyden at 216.444.3581.

How Cleveland Clinic Helps Affiliated Providers Improve Efficiency and Reduce Costs

Success lies in a systematic, data-driven, communication-oriented approach.

The pressures in healthcare today are nearly universal: Accommodate higher volumes. Improve quality and outcomes. Optimize patient experience. And do all of this while keeping costs to a minimum without compromising patient care.

Helping other hospitals and health systems balance these seemingly competing challenges is a primary goal of Cleveland Clinic's Miller Family Heart & Vascular Institute Affiliate Program. This is the objective of the program's Continuous Improvement Service (i.e., CI team), which provides advisory services to healthcare organizations across the U.S. Some of these organizations partner with Cleveland Clinic as affiliates for cardiovascular care. The Affiliate Program team also does assessments of specific clinical or operational challenges in affiliates' cardiovascular programs.

Cath Lab Process Revamp Brings Big-Time Efficiency Gains

In 2014, Cleveland Clinic adopted process improvements to curb inefficiencies in its cardiac cath lab. A new study reports the results, which include:

17 minutes	4.1 minutes	7.7% → 77.3%	5 hours/day
Improvement in procedure start times	Reduction in mean time between cases	Before/after shift in the share of days at full cath lab utilization	Across the cath lab, these efficiencies added 5 hours of procedure time a day

Source: Reed GW, Hantz S, Cunningham R, et al. *JACC Cardiovasc Interv.* 2018;11:329-338.

The value of continuous improvement

The Affiliate Program recognizes that healthcare value is driven through four key areas: quality and reporting, clinical care delivery, cost containment and programmatic growth. The program's CI team focuses on cost containment and programmatic growth in recognition that both can stem from efficiency improvement. Specifically, more-efficient operations tend to save costs in equipment, staff time, etc., while potentially freeing up facilities and staff to care for more patients and grow program volumes.

The CI team's approach is modeled on insights gained through experience with projects completed in Cleveland Clinic's internationally recognized cardiovascular program. An example of such a project is a catheterization lab process improvement initiative whose results are shown in the graphic at the top of this page.

CI Assessment Process at a Glance

The CI assessment focuses on identifying opportunities for efficiency improvement, cost reduction and program growth throughout the affiliate hospital's cardiovascular service line. The CI team completes this assessment by following the systematic, data-driven process illustrated in the graphic at the bottom of the page.

As a part of the data analysis phase, the CI team completes a thorough operational analysis. Among the metrics analyzed for cath/electrophysiology labs and operating rooms (ORs) are:

- Lab/room utilization
- Turnaround time
- First-case start times
- Staffing utilization relative to actual caseload
- Overtime and weekend cases

These metrics are benchmarked to Cleveland Clinic metrics, just as national registries (e.g., Society of Thoracic Surgeons databases) serve as benchmarks for quality metrics and best-practice implementation efforts.

This approach to data submission and analysis yields many benefits, including:

- Allowing the partner organization to see more clearly how its operations are running
- Identifying what does and doesn't work, often in terms of specific areas
- Keeping the organization focused on goals
- Supporting communication of results across the organization
- Engaging the front-line team in improving daily operations

Industry-proven CI methodologies, such as Lean and Six Sigma, are used throughout the process. The CI team works closely with Cleveland Clinic Heart & Vascular Institute physicians and clinical consultants for each area/subspecialty to provide well-rounded recommendations that include both clinical and operational perspectives.

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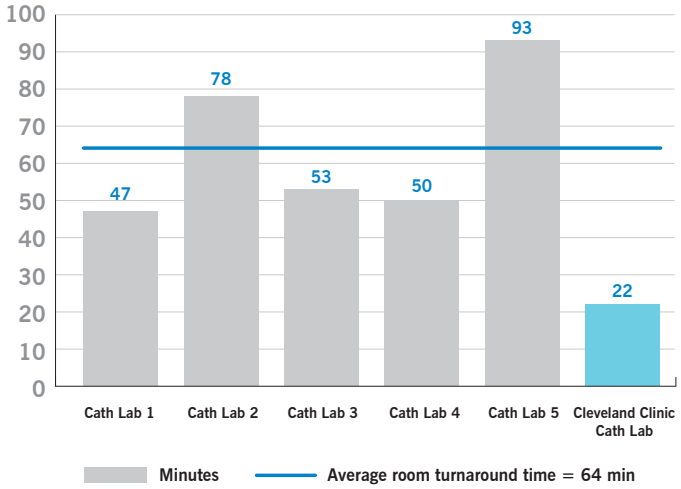
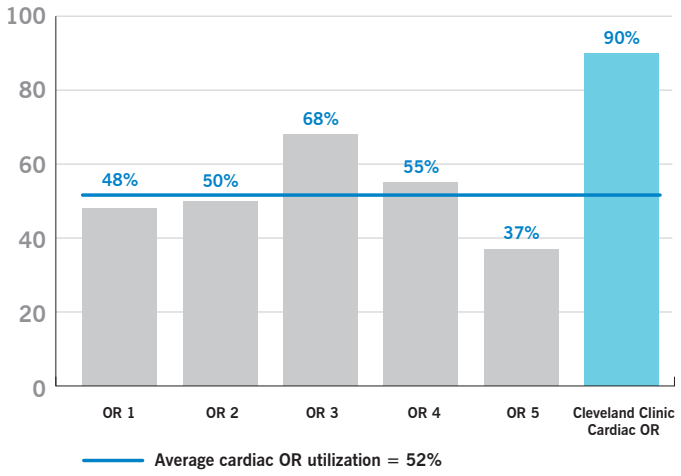
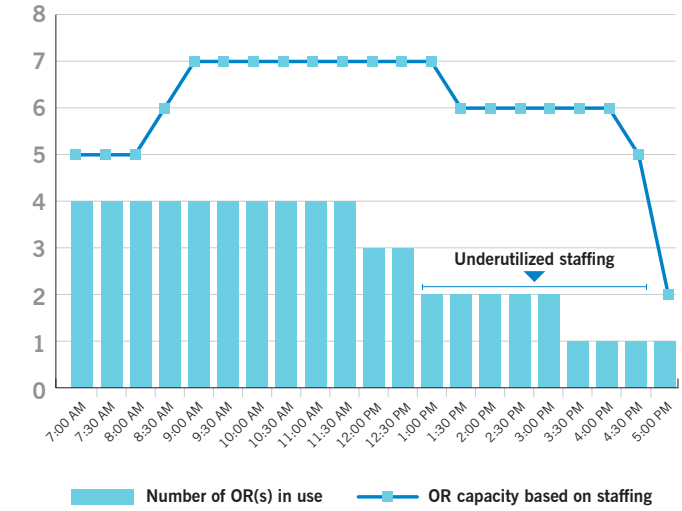
Sample Cath Lab Room Turnaround Time



Sample OR Utilization by Room (7 a.m. to 5:30 p.m.)



Sample OR Nursing Staff Utilization



Examples of identified opportunities and projects

Based on the list of recommendations, the CI team works with the affiliate hospital's administrative, physician and clinical teams to prioritize areas of focus. They then determine a project implementation plan for these areas using the Plan-Do-Check-Act approach to drive improvements and sustain gains.

This type of CI assessment was completed at more than 20 hospitals across the country, during which the team identified multiple opportunities for efficiency improvement and cost reduction. Examples include:

- **Improving cath lab room turnaround time.** The top graph in the left column shows cath lab room turnaround times relative to Cleveland Clinic's benchmark time, revealing significant opportunity for improvement. In cases like this, the CI team and clinical consultants work closely with the affiliate hospital and share Cleveland Clinic lessons learned to help reduce turnaround time.
- **Improving room utilization.** The middle graph on the left shows operating room (OR) utilization from an affiliate hospital along with the Cleveland Clinic benchmark rate. These utilization rates would prompt recommendations to consolidate volume into fewer ORs and coordinate physicians' operating schedules accordingly, to enhance both OR and staff efficiency.
- **Reducing labor cost and improving staff utilization.** The bottom graph on the left shows nursing staff levels relative to the number of ORs running by time of day. The results shown would prompt a recommendation to review staffing levels in detail (by day, by OR, etc.) and adjust staff start times to align with case start times.

Detailed insights yield actionable plans for improvement

The thorough and systematic process outlined above provides insight into affiliate hospitals' operations down to a highly detailed level. It also facilitates communication of key operational issues and opportunities to their clinical teams and administrative leadership while aligning CI efforts with strategic enterprise initiatives. Identifying specific areas to focus on enables feasible plans to be put in place for steady progress toward program goals.

These services from the CI team are included in the scope of offerings from Cleveland Clinic's Heart & Vascular Institute Affiliate Program and are central to efforts to drive down cost while improving quality, patient flow and overall service line excellence. ■

For more information, contact Murali Dodla (dodlam@ccf.org) or Christina Seekely (seekelc@ccf.org).

ECMO as a Bridge to Lung Transplantation: A Case Study

BY KENNETH MCCURRY, MD

In a recent report of our experience, bridging to transplant with ECMO was successful in 87% of patients, with 80% patient survival at three years.

Presentation

A 55-year-old man had elective aortic valve replacement at an outside hospital for aortic stenosis. He was discharged after one week without complications, but it was noted that weaning him from ventilatory support took longer than usual.

Two weeks after discharge, his home nurse noted that his blood oxygen level was very low. The nurse sent him to the emergency department, and he was rehospitalized with acute respiratory distress syndrome. When ventilatory support proved inadequate, he was placed on venovenous extracorporeal membrane oxygenation (ECMO) with double-site cannulation and then sedated and chemically paralyzed.

Over the next six weeks, he developed multiple complications, including renal failure. The medical team grew concerned that he could not be weaned off ECMO. They reached out to Cleveland Clinic for consideration for lung transplantation and transfer to Cleveland Clinic.

Bridging to transplant

The patient arrived at Cleveland Clinic by Life Flight helicopter on venovenous ECMO under sedation and chemical paralysis. Having been bedbound for two months, he was so weak that he could not lift his arms or legs. He was also emaciated, weighing 120 pounds (down from 170 before hospitalization).

Lung evaluation revealed extensive fibrosis. It was deemed likely that he had previously unrecognized lung disease and that he could not survive without lung transplantation. Normally, someone in this extremely debilitated state would not be considered a candidate for transplant. But because he was young and had strong social support, it was decided that efforts would be made to improve his status so he could be considered for transplant.

Our clinical team took the following steps:

- *Stopped paralysis and weaned (and ultimately stopped) sedation.* This was done to allow the patient to engage in physical therapy and interact with healthcare staff and family.

Continued next page ›

- *Replaced the dual-site ECMO cannulation with a dual-lumen single-cannula system.* Removing the cannula from the groin and having a single site in the internal jugular vein enabled him to get out of bed, work with physical therapy to ambulate, and perform spontaneous breathing trials to strengthen the respiratory muscles. (The subclavian vein can be used as an alternative site and is now our preferred site, for reasons of patient comfort and care.)
- *Instituted progressive, aggressive physical therapy.* He underwent daily physical therapy, which advanced to standing squats with assisted weight-bearing, all while he was still on ECMO.
- *Addressed kidney function.* Support of his cardiorespiratory status ultimately allowed the kidneys to recover function.
- *Increased nutrition.* He was provided nutritional support via enteral feeding to replenish protein stores and improve strength.

Under this program, the patient regained cognitive function, gained weight and became more physically fit. Setbacks did occur during hospitalization — including additional complications of kidney failure and sepsis — but two months after arrival at Cleveland Clinic, he was well enough to be listed for transplant.

Transplantation and follow-up

Six days after listing, he underwent double-lung transplantation. At that point, he had been sustained on ECMO for 125 days. After the surgery, he remained in the hospital for another two months as he regained strength and pulmonary function. He developed recurrent acute kidney injury following transplantation and ultimately required dialysis. He was discharged home doing well.

It is now four years since his transplant, and his annual checkups have been unremarkable. While he remains on dialysis, he is being evaluated for a renal transplant and has good functional capacity with excellent lung function. He recently sent a picture of himself and his wife on vacation, enjoying themselves at the beach.

Case highlights and lessons

As outlined below, this case underscores important shifts in our thinking around lung transplantation, as well as keys to success.

ECMO can be a tool for bridging to transplant. With proper patient selection, awake ambulatory ECMO can lead to successful lung transplantation outcomes. Age 65 is generally our cutoff for this approach, with older patients considered if they are robust and have few medical issues. Patients with fibrotic lung disease should especially be considered for ECMO bridging, as they tend to do poorly with mechanical ventilation.

Acute respiratory failure and prolonged ECMO don't rule out transplant. Lung transplantation is most commonly done in the setting of chronic lung disease, but for selected patients, it can be considered for acute decompensation (in the setting of chronic disease or not), even after prolonged ECMO.

We recently reported in *Annals of Thoracic Surgery* (2018;106:192-198) Cleveland Clinic's experience with 30 patients who underwent ECMO as a bridge to lung transplantation from 2012 to 2015. Bridging to transplant with ECMO was successful in 87 percent of patients, and among those patients, survival rates were 92 percent at 30 days and 80 percent at three years (91 percent among patients who underwent primary transplants).

Dedication across a multidisciplinary team is essential. This patient arrived in very poor shape and required exceptional efforts from surgeons, ICU intensivists, physical and respiratory therapists, pulmonologists, social workers and nurses to improve his physical and mental status to prepare him for transplant listing. We routinely conduct multidisciplinary rounds on ECMO patients to drive home this "recovery culture" to the entire team.

Transplant is becoming possible for more patients. With a dedicated heart/lung failure ICU, Cleveland Clinic has had the highest-volume lung transplant center in the United States cumulatively over the past nine years, and we accept many patients who have been rejected elsewhere. Additionally, the emergence of normothermic ex vivo lung perfusion technology is making more lungs available for transplant, which coincides with our ability to prepare sicker patients for listing and successful outcomes. ■

Dr. McCurry is Surgical Director of Lung Transplantation and Director of the Respiratory ECMO Program at Cleveland Clinic. Contact him at 216.445.9303.

Tall Rounds® Goes Large:

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It's hard to find a clinician who doesn't lament the "silo-ization" of medicine, but what can actually be done about it?

For cardiothoracic surgeon Eric E. Roselli, MD, a good place to start is to "de-silo" continuing education. That's exactly what Dr. Roselli did when he established Cleveland Clinic Miller Family Heart & Vascular Institute's Tall Rounds® continuing education series a few years ago. The initiative has been such a hit within Cleveland Clinic that it's now also being made available to healthcare providers beyond Cleveland Clinic at *clevelandclinic.org/tallrounds*.

What makes Tall Rounds different

Tall Rounds are one-hour teaching sessions, but rather than focusing on a clinical topic from one or two subspecialty perspectives, these sessions take a much more multifaceted, interdisciplinary approach.

The format is simple: A fellow presents a real-world patient case and relevant imaging, and four to seven experts from various medical and surgical cardiovascular subspecialties (and often other disciplines, such as genetic medicine or infectious disease) speak to the topic from their particular angles of expertise for five to 10 minutes each. The cases are generally complex, so much attention is paid to considerations in the decision-making process. The final 15 minutes are devoted to a discussion with the audience in attendance at Cleveland Clinic, which can number close to 200.

The design gives each Tall Rounds a dynamic pace that keeps learners engaged. "Each subspecialty section is just long enough to provide a focused, relevant perspective," explains Dr. Roselli, The Stephens Family Endowed Chair in Cardiothoracic Surgery and Surgical Director of Cleveland Clinic's Aorta Center. "The whole always ends up being greater than the sum of its parts, especially with the lively back-and-forth during the discussion. Because so many subspecialty perspectives intersect, everyone comes away having learned something valuable."

Now freely available to all

The response to Tall Rounds among Cleveland Clinic cardiovascular caregivers — physicians, surgeons, trainees, nurse practitioners, physician assistants, nurses, technicians and others — has been so favorable that Cleveland Clinic has now made a full slate of archived Tall Rounds videos available online to external healthcare providers.

Four to seven subspecialists speak to a case from their angles of expertise for five to 10 minutes each. "Each section is just long enough to provide a relevant perspective. The whole always ends up being greater than the sum of its parts."

– Eric Roselli, MD

Each hourlong session can be viewed in full or by chapters. Speakers can be contacted by email for follow-up discussion. Access is free but requires one-time online registration at *clevelandclinic.org/tallrounds*. CME credit is not currently offered.

"The range of issues involved in patient management today can be mind-boggling," says Dr. Roselli. "Delivering the best care takes a team with access to all options and tools. Promoting understanding of what everyone on the team can offer improves collaboration and patient care. That's the philosophy behind Tall Rounds. The goal is to bring together clinicians from a diversity of disciplines to teach each other and stimulate learning. We invite providers everywhere to join us." ■

Register for free at clevelandclinic.org/tallrounds.

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Live CME Events from Cleveland Clinic

3RD ANNUAL

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events.medtelligence.net/ccfval19.html

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Information/registration: ccfcme.org/echo

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Fri., March 15, 2019, 7-9:15 p.m.
(complimentary dinner symposium)

Westin New Orleans Canal Place | New Orleans, Louisiana

An independent certified session at the American College of Cardiology Scientific Session (ACC.19)

Information/registration:
ccfcme.org/cvprevention

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

For a deeper dive into continuing education, see page 19.

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