

# NewYork-Presbyterian Advances

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NewYork-Presbyterian  
Cardiology and Heart Surgery  
ranks #4 in the nation.

## Research Highlights: Targeting Challenges in Cardiovascular Disease

Each and every day, NewYork-Presbyterian researchers and clinician-scientists are advancing knowledge in virtually every medical specialty. At Weill Cornell Medicine and Columbia University Vagelos College of Physicians and Surgeons, faculty are targeting some of today's most formidable health challenges, pushing scientific discoveries forward and applying research breakthroughs to improving the lives of patients everywhere. In this issue of *Advances*, we share several recent investigations in cardiovascular care.

### New Hope for Patients with Underdiagnosed Form of Heart Failure

Patients with transthyretin amyloid cardiomyopathy (ATTR-CM), a life-threatening and progressive form of heart failure, are finding treatment with the drug tafamidis. Researchers at Columbia University Vagelos College of Physicians and Surgeons conducted a Phase 3 clinical trial showing that tafamidis significantly reduces deaths and hospitalizations. Their findings were published in the September 2018 issue of *The New England Journal of Medicine* by the trial's co-chair **Mathew S. Maurer, MD**, a cardiologist and heart failure specialist at NewYork-Presbyterian/Columbia, and colleagues.

If tafamidis receives FDA approval for transthyretin amyloid cardiomyopathy, it would be the first medical therapy for this life-threatening disease, which may be more common than doctors realize. Compared to a placebo, the drug reduced deaths by 30 percent, reduced cardiovascular-related hospitalizations by 32 percent, and slowed the decline in quality of life among the 441 patients enrolled in the two-and-a-half-year study.

Once diagnosed, patients with ATTR-CM only live on average three to five more years. "ATTR-CM is considered to be a rare disease, but it is underdiagnosed," says Dr. Maurer. "Until recently, cardiologists rarely tested for ATTR-CM, because diagnosis required a heart muscle biopsy and there has been no treatment for the disease. But now that we can detect the disease with noninvasive imaging, we're finding more cases."

ATTR-CM occurs when the protein transthyretin becomes unstable and clumps together forming sticky amyloid in heart muscle. The disease is most common in men over the age of 60 and is caused by heritable genetic mutations or age-related changes in the regulation of transthyretin.

"Until recently, cardiologists rarely tested for ATTR-CM because diagnosis required a heart muscle biopsy and there has been no treatment for the disease. But now that we can detect the disease with noninvasive imaging, we're finding more cases."

— Dr. Mathew S. Maurer

Tafamidis acts by stabilizing transthyretin, preventing its dissociation and ability to form amyloid. "Based on this study, tafamidis may offer the first treatment for patients with this type of heart disease," says Dr. Maurer. "Right now, the best we can do is manage the symptoms of ATTR-CM." The study also found that tafamidis slowed decline in heart function and quality of life without causing more adverse effects.

The FDA will consider whether to approve tafamidis for the treatment of transthyretin amyloid cardiomyopathy. Patients can receive

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## New Hope for Patients with Underdiagnosed Form of Heart Failure (continued from page 1)

tafamidis at certain sites through an early access program established by Pfizer. NewYork-Presbyterian/Columbia University Irving Medical Center is the program's first site and is now accepting and enrolling patients.

"Tafamidis prevents progression of the disease, and like other preventive drugs, it should be given as early as possible," says Dr. Maurer. "We'll need to diagnose people with ATTR-CM earlier in order for this drug to have the biggest benefit. Currently, patients are diagnosed with advanced disease, and we need to change that."

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## Valve Replacement Volume Leads to Successful Outcomes

Weill Cornell Medicine researchers have shown that hospitals that routinely perform a heart valve replacement procedure that requires open heart surgery are more likely to adopt a newer, less invasive technique. When hospitals have a high caseload of patients undergoing both approaches, they are likely to achieve the best patient outcomes for those who undergo the newer procedure. The results of the Weill Cornell investigation appeared in the October 31, 2018 issue of *JAMA Cardiology*.

"You can imagine that hospitals known for valve care are more likely to attract valve patients and adopt transcatheter aortic valve replacement – TAVR – more quickly," says senior author **Art Sedrakyan, MD, PhD**, Professor of Healthcare Policy and Research at Weill Cornell Medicine. "And it's likely that the more experience the hospitals have in performing valve surgery, the better patient outcomes are."

In the study, the researchers sought to examine the relationship between the number of times hospitals perform the established procedure – surgical aortic valve replacement (SAVR) – and patient outcomes from the less invasive TAVR. First approved in 2011 for high risk patients who were considered inoperable, TAVR has gained popularity in recent years.

The Centers for Medicare and Medicaid Services recently set criteria to promote high quality implementation of TAVR, including the requirement that hospitals perform at least 50 SAVR procedures a year prior to beginning TAVR procedures. Due to scrutiny over the requirements, a Medicare Evidence Development and Coverage Advisory Committee panel took place in July to discuss the issue. While some attendees argued for lowering the requirements, as they are difficult to reach in less populated areas, others posited that hospitals with high SAVR numbers would have lower complication rates for TAVR.



Dr. Art Sedrakyan

To discern that relationship, the Weill Cornell Medicine team, led by Dr. Sedrakyan, analyzed more than 60,000 TAVR procedures performed at hospitals between 2011 and 2015. They ultimately found that high volumes of both procedures were associated with the best outcomes for TAVR. "It's important that we evaluate TAVR and SAVR in a conjoined way. That's what makes this study novel – previous studies have not assessed the effect of SAVR volume," says first author **Jialin Mao, MD, MS**, an instructor in Healthcare Policy and Research at Weill Cornell Medicine.

When researchers looked at patient mortality rates 30 days and then one year after undergoing TAVR, they found that patients treated at hospitals with high SAVR volume and high TAVR volume had the lowest mortality. "Patients need to know that getting care at institutions with the highest volume of aortic valve interventional care is most beneficial to them," says Dr. Sedrakyan.

The findings suggest that federal requirements determining hospital eligibility for Medicare and Medicaid reimbursement for TAVR procedures are appropriate and could even be more restrictive. "Current restrictions need to be maintained and made even stronger," says Dr. Sedrakyan. "We don't believe the time is right for widespread access to these technologies at the expense of patient safety."

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Mao J, Redberg RF, Carroll JD, Marinac-Dabic D, Laschinger J, Thourani V, Mack M, Sedrakyan A. Association between hospital surgical aortic valve replacement volume and transcatheter aortic valve replacement outcomes. *JAMA Cardiology*. 2018 Nov 1;3(11):1070-78.

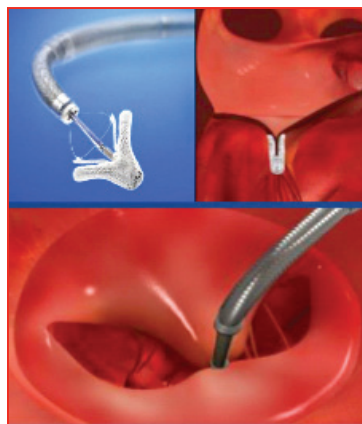
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## MitraClip Improves Outcomes for Mitral Regurgitation

A multicenter clinical trial has found that minimally invasive transcatheter mitral valve repair significantly reduced hospitalizations and mortality for heart failure patients with moderate-to-severe or severe functional mitral regurgitation. Findings from the Cardiovascular Outcomes Assessment of the MitraClip Percutaneous Therapy for Heart Failure Patients with Functional Mitral Regurgitation (COAPT), published in the September 28, 2018 online issue of *The New England Journal of Medicine*, has shown that the procedure improved two-year survival for heart failure patients with moderate-to-severe functional mitral regurgitation.

“Although some drugs can help alleviate symptoms of functional mitral regurgitation due to heart failure, those therapies are of limited benefit,” says **Gregg W. Stone, MD**, Co-Principal Investigator of the trial and Director of Cardiovascular Research and Education at the Center for Interventional Vascular Therapy at NewYork-Presbyterian/Columbia, and Professor of Medicine at Columbia University Vagelos College of Physicians and Surgeons. “To be able to reduce hospitalizations and improve



By approximating the anterior and posterior mitral leaflets and forming a double-orifice valve, the MitraClip device reduces mitral regurgitation.

survival is a breakthrough for patients who previously had few treatment options.”

Functional mitral regurgitation (MR), also known as secondary MR, the focus of this study, occurs when the left ventricle enlarges after heart damage from any cause, such as a heart attack. Primary MR can be treated effectively

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## PFO Closure Recommended for Select Stroke Patients

Young people with a history of strokes caused by blood clots should be evaluated for a patent foramen ovale (PFO) closure, according to **Hooman Kamel, MD**, a neurologist with expertise in stroke at NewYork-Presbyterian/Weill Cornell. In an editorial published in *JAMA Neurology* in February 2018, Dr. Kamel argues that data from recent clinical trials confirms that PFO closure

“Presence of a PFO alone is not enough reason to close. We work together with our colleagues in neurology to evaluate every patient.”

— Dr. Harsimran S. Singh

should be considered in certain stroke patients. “Clinicians can now make recommendations with much more certainty about the risks and benefits, and eligible patients have an additional proven treatment option for preventing stroke,” says Dr. Kamel.

PFO, which happens in about 25 percent of the population, is a risk factor for ischemic stroke. Whether or not surgical closure of a PFO prevents stroke has long been a matter of debate among physicians.

According to Dr. Kamel, recent research shows that PFO closure should be considered only in patients under 60 who have had an ischemic stroke that has no other apparent cause. PFO closure should not be offered to patients with other types of stroke or to those with transient ischemic attack. It is also important to note, says Dr. Kamel, that PFO should not automatically be considered the cause of an ischemic stroke. “Before agreeing to PFO closure, patients should ask whether their profile fits the profile of patients

in the clinical trials,” he says. “If it does not, there is no knowing whether PFO closure will lead to more benefit than harm.”

At Weill Cornell Medicine and NewYork-Presbyterian, the decision to close a PFO is made in consultation with a multidisciplinary team of neurologists and interventional cardiologists. “A good relationship between the two services is crucial,” says **Harsimran S. Singh, MD**, an interventional cardiologist at NewYork-Presbyterian/Weill Cornell and the David S. Blumenthal Assistant Professor of Medicine at Weill Cornell Medicine, who performs the PFO closure procedure. “Presence of a PFO alone is not enough reason to close. We work together with our colleagues in neurology to evaluate every patient.”

Even when indicated, PFO closure does not provide lifelong protection against stroke, because patients can develop other risk factors as they age. “When a decision is made to perform PFO closure, our interventional cardiologists have the experience and skill to perform these procedures safely, and our stroke neurologists then provide expert follow-up care,” adds Dr. Kamel. “Patients should receive lifelong monitoring and intensive management of common stroke risk factors.”

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## MitraClip Improves Outcomes for Mitral Regurgitation (continued from page 3)

with surgical valve replacement or repair. However, there is little evidence that surgical procedures improve outcomes for patients with secondary mitral regurgitation, who tend to have a worse prognosis and are thus typically managed medically with drugs such as beta blockers or with pacemakers to regulate heart rhythm. Nearly one in 10 adults age 75 or older in the U.S., or four million Americans, suffer from primary MR. The prevalence for secondary MR is uncertain as it is frequently undiagnosed, but is believed to be substantially higher than that of primary MR.

The COAPT trial enrolled 614 heart failure patients with moderate-to-severe or severe secondary MR at 78 sites in the U.S. and Canada who remained symptomatic despite treatment with recommended medical therapies. Participants were randomized to treatment with MitraClip® – a minimally invasive treatment that fastens the mitral valve leaflets together – and medical therapy or medical therapy alone. The researchers then compared the number of heart failure-related hospitalizations and deaths over 24 months in both groups.

Patients who had the minimally invasive procedure had 47 percent fewer heart failure-related hospitalizations and 38 percent fewer deaths than those who were managed medically. “The improvement in symptoms and reduction in need for hospitalization due to heart failure was almost

immediate after the MitraClip,” says Dr. Stone. “In contrast, the improvement in survival emerged about a year after the procedure, a delayed response consistent with the long-term benefits of reducing volume overload on the heart.”

The procedure was also associated with significant improvements in quality of life and functional capacity. The treatment was determined to be safe, with low 30-day rates of death or stroke, and the reduction in MR was durable through the two-year follow-up of the study.

“Patients with heart failure and severe secondary or functional MR who remain symptomatic despite all the best medical therapies now have substantially more hope because we can improve their quality of life and survival by reducing their MR with a safe, low-risk procedure,” says Dr. Stone.

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