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The Medical Director of Intermountain Medical Center's Structural Heart Disease Program discusses the significance of mitral regurgitation, advances in imaging, and the latest PFO trials that aim to determine the best devices and patient populations for closure.

How has the CLOSURE I trial affected the patent foramen ovale (PFO) space, and where do we go from here?

CLOSURE I has not yet been published. We need a peer-reviewed publication before we make too many conclusions from this study. However, CLOSURE I was designed early in the PFO closure experience and suffered from our collective lack of knowledge regarding which patients are most likely to benefit from PFO closure. CLOSURE I cast a wide enrollment net of poorly defined cryptogenic stroke or transient ischemic attack with any degree of right-to-left shunting while excluding those with DVT and hypercoagulable disorders who may be most likely to benefit.

Many patients with trivial right-to-left shunts were enrolled, and most of the recurrent events were not PFO mediated. The RESPECT trial, sponsored by AGA Medical Corporation (Plymouth, MN), and the REDUCE trial from Gore & Associates (Flagstaff, AZ) have made modest incremental steps to more narrowly define higher-risk populations. However, they are handicapped by competing with off-label closure devices that are indicated for atrial septal defect in the highest-risk patients. The recurrent event rate in CLOSURE I was reassuringly low and should facilitate randomization of patients who are most likely to benefit from PFO closure. If we are unable to commit our patients to randomization, insurance companies may make this decision for us. Ultimately, our patients would benefit from a study that randomizes large-shunt stroke patients with high-risk features such as DVT who have been rigorously screened to exclude alternate stroke etiologies. Given the repeated failures in the PFO space, industry and government should consider funding a multidevice study of this nature.



Where do we stand in regard to PFO closure to treat migraine?

An enormous unmet clinical demand persists to help those who suffer from migraine. The retrospective and ongoing observational data on PFO closure for migraine are compelling. The PREMIUM trial from AGA Medical Corporation holds promise. However, there is little evidence to suggest that the targeted episodic and refractory population of PREMIUM is the most likely to respond to PFO closure. We need prospective registry data in various populations to better predict which patients may respond to PFO closure. The PRIMA trial from AGA Medical Corporation and the RESPONDER registry from Coherex Medical, Inc. (Salt Lake City, UT) are being conducted in Europe and may help steer us toward the correct patients.

What impact do you think the PFO Research Foundation has had to date? Are there any upcoming educational programs for physicians?

The PFO Research Foundation has brought together leaders from multiple disciplines including neurology, cardiology, patient advocacy, industry, and federal agencies in a forum that emphasizes patients first and foremost. The foundation reminds all of us working in this emotionally charged field that there are patients with PFOs, strokes, and migraines who deserve and demand the best care possible. Whether physicians or representatives of industry or government, we all have a duty to push forward and conduct science that will provide guidance for these patients. The 2011 PFO Research Foundation Summit is scheduled as a part of the PICS & AICS meeting in Boston on July 26.

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How can institutions improve their delivery of care for patients with PFO?

Closing a hole in the heart is easy. Selecting patients who are likely to benefit from PFO closure is difficult. Patients who are suffering from stroke and migraine warrant care and counseling beyond having a device placed in their hearts. An efficient PFO care center demands multidisciplinary cooperation between neurology and cardiology departments. The multidisciplinary team should develop institutional guidelines for PFO closure, patient information forms, and consent forms and provide cooperative patient consultation. Cardiologists are vascular disease experts but may benefit from a core curriculum in stroke and migraine, which would allow us to better evaluate, diagnose, and manage patients presenting with symptoms that may or may not be related to PFOs. Industry's ability to facilitate this education in an era of off-label PFO closure is limited. Although the PFO Research Foundation may be the best example of multidisciplinary education in the PFO space to date, many institutions could organize events of this nature.

Can you tell us about your institution's participation in the PROTECT AF trial?

At Intermountain Medical Center (Murray, UT), we have enrolled 95 patients in trials sponsored by Atritech, Inc. (Plymouth, MN) (PROTECT AF, CAP, and PREVAIL) beginning nearly 6 years ago. Left atrial appendage (LAA) closure has become an alternative to warfarin for patients with atrial fibrillation, particularly in those with modest bleeding risks. We see patients who have had devices implanted confronting the ailments of an elderly population, including falls, fractures, acute coronary syndromes, and malignancies. Their complications are minimized and care simplified by the avoidance of anticoagulation. We are looking forward to initiating a program of pericardial LAA closure using the SentreHeart system (SentreHeart, Inc., Palo Alto, CA). This system will allow us to address a population that is contraindicated for warfarin, among whom there is a tremendous unmet clinical need.

What areas of structural heart disease warrant the greatest need for awareness?

Mitral regurgitation is undertreated. Many patients with severe degenerative mitral regurgitation would benefit from earlier repair prior to the onset of left ventricle dysfunction and atrial fibrillation. The role of surgery for functional mitral regurgitation remains in doubt. This large functional mitral regurgitation popu-

lation stands to derive tremendous benefit from percutaneous therapies. As valvular heart disease has traditionally received its most definitive treatment from surgeons, cardiologists' understanding of mitral regurgitation may be superficial. Among the benefits of the evolving structural heart disease procedures is the collaboration and education that occurs between interventionists, surgeons, and imaging specialists, which enhance patient care.

Are there any new imaging technologies that you believe will improve minimally invasive therapies?

Real-time, three-dimensional color Doppler is ready for prime time and has already allowed us to better understand mitral valve anatomy and jet origins. It is helpful in evaluating paravalvular leaks and guiding their transcatheter closure. Reconstruction with three-dimensional computed tomographic angiography is underutilized and facilitates better quantification of the vascular system, which is essential for transcatheter aortic valve implantation. Computed tomography can also predict angiographic projection angles perpendicular to the aortic valve plane and help guide transcatheter aortic valve implantation procedures. The concept of translating tomographic slices to three-dimensional images has been around for a while in search of an application. SentreHeart, Inc. is using this technology to determine anatomic suitability for pericardial approaches to LAA closure. Whether it is with echo or computed tomography, acquiring and processing these various images is labor intensive and cannot be simply approached in the traditional cookie-cutter fashion. Intermountain Medical Center has benefited from the partnering of radiologists and cardiologists in our structural heart endeavors, with a great commitment of time and energy.

What made you want to get involved in the device development aspect of interventional cardiology?

Creativity in any form is alluring. The potential of creating devices that advance medical care is compelling. I am working with an incredibly talented and committed team at Coherex Medical, Inc. that is driven by the promise of affecting patients' lives and advancing medical science. This is not work but rather a completely captivating indulgence. ■

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