The diagnosis and prognostic assessment of patients with suspected or known cardiac disease has become increasingly dependent upon the use of noninvasive cardiac imaging technologies. Two of these are well established, echocardiography and nuclear cardiology, and two are relatively recent, cardiac CT and cardiac magnetic resonance (CMR). Cardiac CT provides high-resolution images of the coronary arteries without invasive cardiac catheterization, and allows accurate assessment of coronary disease severity by visualizing and quantifying the magnitude of atherosclerosis and characterizing coronary plaque morphology. This technology improves physicians’ ability to detect coronary disease at earlier stages and improve estimates of patient risk, thereby allowing physicians to target those who most need aggressive medical intervention and follow-up.

**Cardiac patient database**

For the past three decades, a team of cardiac imaging specialists at Cedars-Sinai has studied the process of diagnostic testing of cardiac patients. Key to their efforts is the development of a large patient registry – now more than 30,000 patients strong – that includes approximately 400 distinct variables per patient. Information from the database has helped researchers determine how cardiac imaging tests can benefit patients, as well as guide the most effective test choice for a patient in a particular clinical setting. To date, research has focused on:

- Understanding pre- and post-test likelihood of coronary artery disease and pre- and post-test risk of a cardiac event
- Learning how to look at the true information content of testing
- Defining how to deal with equivocal test responses
- Defining test efficacy according to each separate goal of testing

Continued on page 2 (see “Imaging”)
Applying debiasing methods to assess test efficacy
Delineating the various factors that are relevant to detection of disease in asymptomatic patients, as well as to diagnostic and prognostic assessment of symptomatic patients

Database research findings
Over the years, the research associated with the Cedars-Sinai patient database (IRB #1752) has been a dominant source defining the prognostic information from nuclear cardiology studies, including:

Myocardial perfusion imaging is a strong predictor of patient outcome, providing incremental information over that obtained from risk factors, clinical assessment and standard stress testing. A normal myocardial perfusion SPECT (MPS) study defines patients at low risk for subsequent cardiac events. Risk increases exponentially with worsening perfusion abnormality. Patients presenting with shortness of breath and ischemia are at very high risk.

The amount of ischemia documented by MPS is predictive of whether or not a patient might benefit from revascularization. Revascularization compared with medical therapy has greater survival benefit in patients with moderate to large amounts of inducible ischemia. For patients with 10 percent or more ischemia, revascularization appears to reduce subsequent mortality. Patients with low ejection fractions are at high risk, and those who have greater than 10 percent ischemia have the greatest benefit from revascularization. In patients with normal ejection fractions and those with no or lesser degrees of ischemia, medical management rather than revascularization is often more effective.

An abnormal MPS and the extent and severity of the perfusion defects is predictive of risk throughout the spectrum of cardiac patients, from patients who have had no history of coronary artery disease (CAD), all the way through patients who have a history of CAD, such as myocardial infarction, bypass surgery or angioplasty.

Automated computer quantification of test results
The other major focus of the cardiac imaging research team at Cedars-Sinai has been the development of automated computer-based methods for assessing MPS images (IRB #1752). Various myocardial perfusion defect parameters – such as extent, severity, and location of ischemia – can now be assessed automatically by comparing the patient’s perfusion findings to normal limits derived from the patient database. Furthermore, accurate measurements of ventricular function, such as left ventricular ejection fraction and volumes, can be computed automatically.

These quantification methods have been shown to detect CAD as well as – or better than – the expert physician, thereby improving the accuracy of test reporting over that based on visual analysis alone.

Linking patient information across the Heart Institute
Cedars-Sinai researchers have extended the same concepts of database formation into the field of cardiac CT (IRB #3354) and cardiac MRI (IRB #4317). A database of 20,000 patients undergoing cardiac CT has been collected and studied at Cedars-Sinai for the past ten years, thanks to support from The Eisner Foundation. Through the EISNER study, the research team is studying whether CT coronary calcium measurements, which are a manifestation of the extent of coronary atherosclerosis, result in improved patient outcomes by allowing patients without known CAD to be appropriately treated with preventive therapies. It is the goal of the Cedars-Sinai Heart Institute to incorporate the use of databases throughout its imaging areas so that a comprehensive cardiac imaging database will be available across clinical settings.

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More than 40,000 children a year are born with heart defects in the United States. Severe defects are usually diagnosed and surgically corrected during infancy or childhood. Advances in minimally invasive techniques to reduce surgical trauma for congenital heart repairs continue to evolve at a rapid rate, in part due to findings that scarring from open sternum surgeries performed on infants have been associated with postoperative deformities, including scoliosis, pectus carinatum, shoulder girdle abnormalities, and breast deformities in females.

**The trend toward minimally invasive techniques**

The concept of chest wall protection has been increasingly accepted as an important standard for congenital heart surgeons. The advantages of this approach include less trauma; partial or complete preservation of sternum continuity and integrity; and elimination of postoperative deformities. Many extracardiac and intracardiac repairs are now being performed thoracoscopically with excellent results. In fact, progress with thorascopes and miniaturized tools for infant heart repairs are being replicated on adult patients with increased frequency.

**Seeking an alternative to open heart surgery**

A 67-year-old woman who had borne two children and maintained a highly active lifestyle, including participation in golf and tennis, presented with a previously undetected sinus venosus atrial septal defect (ASD) that was not amenable to repair with a transcatheter procedure. Initially diagnosed at a medical center in her home state, she was offered standard direct-closure surgical repair using a full median sternotomy incision. The patient then flew to Cedars-Sinai Medical Center and requested an alternative approach to open heart surgery. After being evaluated for endoscopic surgical repair, she was found to be a suitable candidate for the procedure.

**The procedure**

Endoscopic closure of an ASD typically results in less blood loss and scarring, lowered infection risks, and faster resumption of normal activities. In the case of this patient, the procedure was simple and the results were excellent:

- A submammary incision, approximately two inches in length, was made on the patient’s right side. In addition, a one-inch incision was made in the groin region for insertion of cardiopulmonary bypass machine tubes.
- The pericardium was opened and the cardiopulmonary bypass machine was put into operation.
- The patient’s body was cooled, her heart was stopped, and her aorta clamped off through a small chest incision.
- With the venous return diverted to the heart-lung machine, the right atrium was opened and a portion of the pericardium was used to close the abnormal interatrial communication and correct pulmonary venous drainage.
- A pericardium baffle was constructed to redirect blood flow from the right superior and middle pulmonary veins into the left atrium.
- The heart was closed and aortic clamp removed.

The patient’s body functions rapidly returned to normal, allowing the bypass machine to be removed and the small incision closed. The patient was taken off the ventilator in the operating room and sent to recovery. She was discharged 48 hours later and, within a few weeks, was back to her very active schedule.

**The future is now**

Minimally invasive techniques for congenital heart repairs are creating new therapeutic options. In addition to thoracoscopic repairs, intracardiac procedures can be performed through smaller incisions. Full sternotomy is giving way to a variety of sternal-sparing incisions for open-heart repairs; operative strategies to avoid or minimize the effects of cardiopulmonary bypass have emerged; and hybrid procedures that utilize a combination of transcatheter and minimally invasive techniques have come to the fore.

**Case Study: Adult Thoracoscopic Repair of a Congenital Heart Defect**

**Gregory P. Fontana, MD**

RA = right atrium, LA = left atrium, LV = left ventricle, SVC = superior vena cava, ASD = atrial septal defect. **Left:** CINE MRI image showing superior venous atrial septal defect (ASD). **Right:** MR angiogram showing pulmonary venous anomaly.

Dr. Fontana is Vice Chairman of Surgery for Pediatric Surgical Services and a attending adult and pediatric cardiac surgeon at the Cedars-Sinai Heart Institute.
The National Heart, Lung and Blood Institute-sponsored Women’s Ischemia Syndrome Evaluation (WISE) study, which began in 1996 and is ongoing, includes more than 1,200 women (IRB #Pro00014906). The goal of the study is to evaluate innovative diagnostic methods that will improve the reliability of cardiovascular testing in the evaluation of ischemic heart disease (IHD) in women. Other objectives include developing safe, accurate and cost-effective approaches for evaluating women with suspected ischemic heart disease, and determining whether evidence of myocardial ischemia occurs in the absence of obstructive coronary disease. Findings from the study have significantly added to the current management approach to heart disease in women.

Ischemic heart disease in women

Despite a dramatic decline in mortality over the past three decades, IHD is the leading cause of death and disability in the United States and is the dominant contributor to the nation’s morbidity and healthcare expenditures.

Importantly, recent advances in the field of cardiovascular medicine have not led to significant declines in case fatality rates for women when compared to the dramatic declines realized for men. For the sizeable proportion of women presenting for coronary artery disease (CAD) evaluation, traditional disease management approaches that focus on detection of a critical stenosis often fail to identify those women critically at-risk. In fact, for women presenting for evaluation of suspected ischemic symptoms, a diagnosis of normal coronary arteries is five times more common in females than males. Yet more than a quarter of a million women die each year in the United States from IHD and its related conditions, and current projections indicate that this number will continue to rise as the population ages.

Focus on microvascular angina

Microvascular angina (MVA), a symptom of IHD, is an etiologic mechanism in women with cardiac symptoms and abnormal vascular dysfunction without obstructive CAD. It should also be noted that not all patients with MVA show detectable ischemia, and the vascular dysfunction may occur in the microvascular bed, macrovascular bed, or both. The dysfunction results in subjectively manifested chest pain or objectively evidenced abnormal ischemic responses to stress with resultant hemodynamic changes, metabolic abnormalities, electrocardiogram change, myocardial perfusion, or regional wall motion abnormalities.

The WISE study is providing important data for an improved understanding of coronary vascular dysfunction and the resultant myocardial ischemia that define MVA. As a result, many researchers now believe that women with MVA do not have a benign prognosis and may be better classified at intermediate risk. Data summaries from the WISE study that relate to MVA include prognosis factors, diagnosis modalities and treatment options.

Prognosis factors

Prognosis of MVA is determined by its components, including chest pain, endothelial dysfunction as defined by reduced coronary blood flow to acetylcholine, and myocardial ischemia. In a large cohort of women with chest pain and no obstructive CAD by angiography, persistent chest pain occurred in 45 percent of the women and yet was associated with more than twice the cardiovascular events, including myocardial infarctions, strokes, congestive heart failure and cardiovascular death, compared with those without chest pain.

Follow-up with patients with mild coronary atherosclerosis associated with microvascular endothelial dysfunction revealed that cardiac events occurred only in those with a severe degree of endothelial dysfunction, while no adverse events were detected in individuals with normal or mild dysfunction.

Diagnosis modalities

The absence of a reference standard for a diagnostic tool for MVA is a major challenge for its management. The complex and speculative nature of its pathogenesis adds to that challenge. Assisted by co-investigator Louise E. J. Thomson, MBChB, the WISE study seeks to evaluate current approaches for diagnosis, which include:

- **Stress echocardiography and myocardial perfusion SPECT imaging**, however limited for diagnosing, are recommended for risk assessment. Particular attention is paid to the stress ECG, which is often abnormal.
- **Invasive coronary reactivity testing and intravascular ultrasound** can be used for patients with persistent chest symptoms; evidence of ischemia; evidence of myocardial injury, including abnormal troponin levels and/or ECG change; and no obstructive CAD.
- **Cardiac MRI** is a promising noninvasive diagnostic and prognostic technique that is being tested, as it is the only modality which can detect subendocardial ischemia and/or infarct that is most common in MVA.

Treatment options

No consensus has been reached regarding treatment of MVA, although treatment may include risk-factor management and symptomatic anti-anginal and anti-ischemic management. The paucity of diagnostic and treatment guidelines is further intensified by a lack of public awareness about the disease on the part of patients and clinicians alike. Creating a model of risk assessment in women with MVA – which does not currently exist – is essential to developing and optimizing a management strategy. The high prevalence of this condition, lack of consensus regarding treatment and adverse prognosis make MVA a research priority.