Celebrating 100 Years of Cardiology at Mayo Clinic

Colleagues,

The introduction of electrocardiography in 1914 marked the beginning of the modern era of cardiology at Mayo Clinic. The machine was ordered in 1912, but due to the time it took to manufacture, assemble, and ship, it did not arrive for 2 years. Later, Fredrick A. Willius, MD, who had recently completed the Mayo Clinic graduate training program, was hired as the first physician with a special interest in cardiovascular disease. Dr Willius established the electrocardiography laboratory in 1917, and in 1922 was asked to chair a new section of cardiology at Mayo Clinic.

In the intervening 100 years, amazing developments in the understanding and treatment of heart disease in all of its manifestations have occurred. We are proud of the many contributions by Mayo Clinic cardiology and cardiovascular surgery staff to the field of cardiovascular diseases. In the upcoming year, we will share some of the highlights of the past 100 years. We remain committed to our mission of excellence by providing unsurpassed care to every patient through integrated practice, education, and research.

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The apical variant of hypertrophic cardiomyopathy (HCM) accounts for approximately 25% of the total HCM population in Asians and less than 10% in non-Asians. It is an autosomal dominant genetic disease with variable phenotypic penetrance. Studies in Asian populations suggest that it has a more benign prognosis than other types of HCM. Data in non-Asian populations is limited, but small studies suggest that the prognostic implications of apical HCM may be more severe in this group than in affected Asian individuals.

A review of the comprehensive Mayo Clinic HCM and echocardiographic databases was conducted by Kyle W. Klarich, MD, cardiologist and director of the Cardiovascular Graduate Training Program at Mayo Clinic in Rochester, and published in 2013 in the American Journal of Cardiology. She and her colleagues retrospectively identified 2662 individuals with HCM evaluated at Mayo Clinic between June 1976 and September 2006. Of these individuals, 193 patients (7.3%) without confounding factors were classified as apical HCM, and follow-up was obtained in 187 of them (114 men, mean age 62 ± 19 years; 73 women, mean age 66 ± 16 years). Mean duration of follow-up was 94 ± 76 months.

There were 55 deaths; 21 had noncardiac causes, 27 were from unknown causes, and 7 were of cardiac etiology. While Kaplan–Meier analysis demonstrated that the observed overall survival of this group of North American patients was significantly worse than expected, this finding was entirely due to excess mortality in women (Figure). Survival in men with apical HCM was almost identical to age-matched controls. Multivariate predictors of increased mortality included female sex, age at first visit, chronic atrial fibrillation, and history of stroke.

Figure. Kaplan-Meier survival curves.
A. 10- and 20-year survival in all patients.
B. Survival in men with apical HCM was equivalent to age- and sex-matched controls.
C. Survival in women with apical HCM was significantly worse than age- and sex-matched controls.

(Reproduced with permission from American Journal of Cardiology 2013;111:1784-1791.)
"The increased mortality observed in women with apical HCM is likely due to older age at first visit and the presence of chronic atrial fibrillation. The mortality rate approaches what has been reported for other HCM phenotypes," says Dr Klarich. "However, as with other cardiovascular diseases, we do not yet understand the role of hormonal and other sex-specific factors that may affect phenotypic onset, expression, and progression of this disease."

Genetic testing for and analysis of sarcomeric mutations characteristic in HCM were not routinely performed in these patients, so mutational correlation could not be performed. While cardiac MRI is currently the preferred imaging modality for assessing both apical wall thickness and the presence of an apical pouch (although echocardiographic detection of apical pouch can be improved by contrast imaging) in these patients, this technology was introduced after the time frame included in this study and therefore not included in this analysis.

"Unfortunately, to date, genetic mutations in isolation are not reliable prognostic predictors," says Dr Klarich. "As our understanding of the role of environmental and other genetic factors on mutational gene expression expands, we hope to better predict and improve outcomes for this group of patients."

This study suggests that apical HCM has different prognostic implications for affected women than affected men. The finding that the excess mortality in women is responsible for decreased survival in North Americans with apical HCM will help to focus future investigations.

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**IN THE NEWS**

**Mayo Clinic Study Suggests ICDs and Pacemakers Not Affected By Hybrid Cars**

Electromagnetic interference (EMI) in the environment can have deleterious effects on implantable cardioverter-defibrillator (ICD) and pacemaker function. Little is known about the effect on device function by EMI generated by hybrid cars, although a study reported by cardiologists from Mayo Clinic in Arizona and presented at the 2013 Scientific Sessions of the American College of Cardiology has shed some light on the topic.

The authors enrolled 30 patients with ICDs from 3 major United States device manufacturers, and EMI was measured from 6 locations (the driver seat, front passenger seat, right and left back seats, and outside at the back and front of the car) in a 2012 Toyota Prius hybrid.

Each position was evaluated at variable speeds of acceleration and deceleration; 7,800 data points were acquired per patient during continuous monitoring. The levels of EMI generated at all speeds and locations within the car were below the recommended threshold, and there were no episodes of oversensing or programming changes after exposure.

This is the first study to address this issue using an in vivo model, and the results suggest that hybrid cars do not generate clinically relevant amounts of EMI. Further studies are necessary to evaluate the interaction between ICDs and other models of hybrid cars or exclusively electric cars.

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**Mayo Clinic Children’s Center is First Accredited Pediatric Heart Failure Institute in Midwest and Fourth in Nation**

On October 1, 2013, the Healthcare Accreditation Colloquium announced that Mayo Clinic Children’s Center had become the first accredited Pediatric Heart Failure Institute in the Midwest and only the fourth in the nation. This accreditation was given based on a rigorous process focused on quality improvement in the diagnosis and treatment of pediatric heart failure within the hospital, community, clinician, and science domains.

The process was led by Jonathan N. Johnson, MD, pediatric cardiologist at Mayo Clinic in Rochester, and Ms. Sonja H. Dahl, RNP, CNP. With the backing of the Healthcare Accreditation Colloquium and its member hospitals, Mayo Clinic Children’s Center will seek to continually improve outcomes for this challenging group of patients and promote the Mayo Clinic legacy of “The needs of the patient come first.”

To learn more about Mayo Clinic Children’s Center, visit http://www.mayoclinic.org/pediatrics.

To learn more about Accredited Pediatric Heart Failure Institutes, visit http://colloquiumhealth.com/who-we-are/?post=1275.
Role of Cardiac MRI in the Assessment of Cardiac Amyloidosis

Amyloidosis is caused by extracellular deposition of autologous protein that is laid in a conformation described as beta-pleated sheets and known as amyloid fibrils. Cardiac amyloidosis is a clinical condition in which the cardiac structures are infiltrated by beta-amyloid protein, leading to a constellation of findings on history, physical examination, and cardiac imaging. The protein that is deposited has varied subtypes, with each having its own natural history. Amyloid deposition typically occurs in a uniform pattern, but certain variants may show a more patchy involvement. These proteins are deposited in the interstitial space and on biopsy, which remains the current gold standard of diagnosis, amyloid fibrils bind Congo red stain, yielding apple-green bifringence under cross-polarized light microscopy.

Noninvasive imaging features of cardiac amyloidosis are generally sufficient to detect or at least suspect the diagnosis, and cardiac MRI has an emerging role in diagnostic evaluation. It is important, however, to note that the diagnosis is based upon the integration of several clinical features and basic testing, including laboratory testing and electrocardiogram, that leads to the clinical suspicion of the disease.

Cardiac imaging is typically performed in patients with known systemic amyloidosis presenting with cardiac symptoms or signs. Echocardiography is usually the first cardiac imaging test performed, typically because it is more widely available, portable, and affordable; has robust and well-established techniques to measure diastolic function, which is the most important physiologic abnormality in cardiac amyloidosis; and has developed newer applications such as strain imaging.

Cardiac MRI is, however, emerging as a first-line modality or at least a complementary imaging modality in patients with suspected cardiac amyloidosis, specifically with regard to its superior ability to characterize the myocardial tissue on postcontrast myocardial delayed enhancement sequences. A comprehensive assessment of cardiac amyloidosis using cardiac MRI requires tailored, flexible imaging protocols to complement other clinical information. Cardiac MRI has shown considerable promise in the diagnostic evaluation of cardiac amyloidosis.

Cardiac morphologic features are evaluated using steady-state free precession sequences. This particular sequence allows visualization of both cardiac structure and function. Images of the heart are taken throughout the cardiac cycle, affording the ability to determine cardiac volumes and ejection fraction. Similarly, the myocardial thickness
can be assessed, including both ventricular and atrial wall and interatrial septal thickness. These findings in the setting of low-voltage electrocardiogram should raise the suspicion of the diagnosis. The ability to image the heart in any plane is one of the major advantages over traditional echocardiographic assessment, which may be limited by the available acoustic windows.

The steady-state free precession sequence is also useful in the identification of pericardial and pleural effusions, which may be accompanying findings. Impaired diastolic function may also be apparent and, similar to the Doppler echocardiographic assessment of diastolic function, mitral inflow measurements can be obtained using cine phase-contrast pulse sequences.

One of the utilities of cardiac MRI that makes it an attractive imaging modality in patients with cardiac amyloidosis is its ability to characterize abnormalities in the tissue structure. In order to achieve this goal, though, intravenous administration of gadolinium contrast is necessary. This becomes an important consideration when selecting a patient for cardiac MRI. The major factor precluding the use of intravenous gadolinium contrast is the presence of significant renal dysfunction; at Mayo Clinic, we use a cutoff for glomerular filtration rate of 30 mL/min/BSA, and those above this threshold are considered candidates for contrast administration. This becomes a particularly important consideration in patients with amyloidosis, as these patients may commonly be afflicted by significant renal dysfunction.

After administration of contrast medium, there are often striking abnormalities of myocardial tissue characteristics that are seen on myocardial delayed enhancement pulse sequences. Patients with cardiac amyloidosis typically demonstrate diffuse and irregular hyperenhancement of the myocardium. The hyperenhancement pattern may be circumferential and subendocardial in distribution but is quite variable. Right ventricular involvement may also be apparent on these sequences. The delayed enhancement sequence can also be useful in the identification of intracardiac thrombus, particularly intra-atrial thrombi, which may also be a feature in patients with the disease who may be presenting with stroke-like symptoms.

One of the important distinctions that needs to be made is between cardiac amyloidosis and other nonischemic cardiomyopathies, most notably hypertrophic cardiomyopathy, that can have potentially similar imaging findings. Abnormalities in myocardial nulling are a common feature in amyloidosis and can be useful in such a distinction. The term "myocardial nulling" refers to an inversion recovery pulse sequence that is used to null the signal from a desired tissue to accentuate surrounding pathology. A common use of this technique is to null the signal from normal myocardium during delayed-enhanced imaging. The nulled normal myocardium will be dark in contrast to the enhanced abnormal myocardium. For example, in the setting of a myocardial infarction, the infarcted myocardial will appear "bright" next to the normally "dark" nulled noninfarcted myocardium (Figures 1 and 2).

The inversion recovery pulses have a special parameter known as the inversion time. In order to null normal myocardium, the MRI technician must find the appropriate inversion time at which the normal myocardium is dark. This time does vary slightly from person to person and as such is a parameter that is determined at the time of the scan. A cine multi-inversion time inversion recovery sequence, in which each image is acquired with a slightly longer inversion time, is often used to select the optimal inversion time for the delayed enhancement acquisition. As the inversion time increases, the blood and myocardium pass through a null point at which signal is minimized.

Generally, the blood pool contains a higher concentration of gadolinium and passes through the null point before the myocardium. In cardiac amyloidosis, however, this normal blood-pool-to-myocardium relationship is reversed and as such, the myocardium reaches the null point before the blood pool. The actual timing of the null point in the blood pool and myocardium can be graphed using on-board software contained on the imaging platform that is used in a particular institution.

The evaluation of cardiac amyloidosis is clearly multifaceted and is directed initially by patient characteristics, laboratory studies, and electrocardiographic studies. Noninvasive imaging techniques, particularly cardiac MRI, are having a more central role in the evaluation of patients with cardiac amyloidosis and, when integrated with other clinical features, may lead to an efficient and cost-effective clinical evaluation.

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**RECOGNITION**

Hal Dietz, MD (right), was the 2013 Robert L. Frye, MD, Lecturer. (Dr Frye is at left.) Dr Dietz is the Victor A. McKusick Professor of Medicine and Genetics at Johns Hopkins University and an investigator at Howard Hughes Medical Institute. He also is director of the William S. Smilow Center for Marfan Syndrome Research, part of the McKusick-Nathans Institute of Genetic Medicine at Johns Hopkins, as well as a professor of pediatrics, medicine, and molecular biology and genetics at Johns Hopkins University School of Medicine.

The Department of Medicine at Mayo Clinic in Rochester has announced recipients of the 2013 Faculty Recognition Awards. Jae K. Oh, MD (left), received the Outstanding Mentor Award, and David A. Foley, MD (right), received the Division of Cardiovascular Diseases Laureate Award. Both are members of the Division of Cardiovascular Diseases.
Robotic Mitral Valve Repair is a Cost-Effective Treatment Compared With Standard Approach

The rapidly changing health care economic environment necessitates the pursuit of innovation in order to improve patient outcomes in a cost-effective manner. Technical advances must add value to clinical and financial outcomes.

The approach to treating mitral valve regurgitation is but one example of changing practice guided by technological innovation. Many valves can be repaired rather than replaced, negating the need for long-term anticoagulation, and less-invasive robotic procedures can frequently be employed earlier in the clinical course, resulting in fewer atrial arrhythmias and preserved left ventricular function.

In a study published in 2013 in Mayo Clinic Proceedings, Rakesh M. Suri, MD, DPhil, cardiothoracic surgeon at Mayo Clinic in Rochester, demonstrated the affordability of robotic mitral valve repair compared with traditional sternotomy.

Dr Suri and colleagues reviewed a total of 747 consecutive patients at Mayo Clinic in Rochester who underwent mitral valve repair either via traditional sternotomy or minimally invasive robotic repair between July 1, 2007, and January 31, 2011. Patients were excluded from review if they required concomitant cardiac surgery, such as coronary artery bypass grafting or repair of congenital cardiac defects; had prior thoracotomy or sternotomy; or had rheumatic valvular disease, active endocarditis, or peripheral vascular disease. Of the 482 remaining patients, 282 had open mitral repair, while 200 underwent robotic repair. One hundred eighty-five pairs were identified for comparative baseline characteristics, and propensity matching was performed on the basis of preoperative variables.

Direct costs were calculated by using standardized values for services and procedures obtained from the Olmsted County Healthcare Expenditure and Utilization Database, which has been used for cost studies since 1995. Provider and institutional costs were determined by applying appropriate Medicare fees. Costs were standardized over the time period studied. The results were then aggregated into categories to enable comparison between the 2 approaches.

Additionally, Mayo Clinic in Rochester implemented a surgical process improvement project in July 2009 specifically designed to reduce the cost of cardiac surgical care without negatively impacting quality of care. Components of that redesign process included:

- Staggered start times
- On-time operating room start times
- Integrated staff
- Standardized postoperative care algorithms

Robotic and open operative groups were evaluated before and after implementation of the process improvement project.

Early complications were infrequent in both the open and robotic repair groups, with the exception of the need for blood transfusion and early atrial fibrillation; both were statistically less frequent in the robotic repair group. Hospital length of stay initially was shorter in the robotic group (3.5 vs 5.3 days; P < .001).

Costs in both groups fell after implementation of the surgical process improvement project, but costs declined more dramatically in the robotic group. Overall costs of those undergoing robotic mitral repair were slightly less but statistically indistinguishable in comparison to the open group also exposed to the improvement project (Table).

There are 3 important findings in this study, according to Dr Suri:

- Systems innovation can lead to cost savings, even in a large diverse cardiac valve surgery program
- Technical innovation can be optimized to be cost neutral
- Patients treated under this combined model benefit from accelerated recovery and shorter hospital stays

The current health care environment mandates that new medical treatments demonstrate added value either by reducing cost or improving outcomes. This study demonstrates that improvements in both are facilitated by concurrent deployment of both technical and systems innovations in a large and diverse academic heart valve practice.

<table>
<thead>
<tr>
<th>Group</th>
<th>Median Cost ($)</th>
<th>Median LOS (Days)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Open</td>
<td>Robotic</td>
</tr>
<tr>
<td>Before Redesign</td>
<td>32,650</td>
<td>34,920</td>
</tr>
<tr>
<td>After Redesign</td>
<td>31,310</td>
<td>30,606</td>
</tr>
<tr>
<td>All</td>
<td>31,838</td>
<td>32,144</td>
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Table. Summary of total hospital costs and length of stay (LOS) of patients treated with open sternotomy or robotic mitral repair, before and after implementation of surgical process improvement project.
Robotic heart valve repair is also associated with a shorter recovery time after hospital dismissal due to lack of sternotomy. "Patients have less pain, shorter recovery times, and are usually able to return to work and other activities sooner than individuals who have open repair," says Dr Suri. "While these factors were not addressed in this review, they are important considerations for patients, their families, and the American economy. We are currently studying these very important outcomes and will hopefully have more to share on this topic in the very near future."

David R. Holmes Jr., MD

Dr Holmes is the former director of the Cardiac Catheterization Laboratory at Mayo Clinic in Rochester and past president of the American College of Cardiology. He spoke recently at the dedication of the Cardiac Catheterization Laboratory in honor of the late Earl H. Wood, MD, PhD.

Earl H. Wood, MD, PhD (1913-2009), was born in Mankato, Minnesota. He received both his medical degree and doctorate in physiology from the University of Minnesota, joining the Mayo Clinic staff in 1942. His 40-year career was marked by intellectual curiosity and a collaborative spirit. Calvin Coolidge, the 30th president of the United States, wrote, "Nothing in the world can take the place of persistence ... persistence and determination are omnipotent." This characteristic, added to talent and genius and combined in the single individual of Earl H. Wood, formed a giant on whose shoulders all of us stand in order to see the future and move toward it.

Dr Wood initially led the Mayo Clinic team charged with studying the effects of gravitational forces on World War II pilots in planes flying higher and faster than before. He built a human centrifuge in which he could replicate various gravitational forces and measure the effects on human physiology. He was both a leader and a participant, having actually sat in the business end of his self-designed centrifuge to personally experience 8-G acceleration levels during which time consciousness fades to nonexistence; an example of "leading from the front."

His work resulted in the invention of anti-gravitational suits ("G-suits") and physical maneuvers to counteract the effects of gravitational forces. The design of the modern space-suit used by astronauts today is based on Dr Wood’s G-suit.

His discoveries and inventions made it possible to perform real-time assessment of cardiovascular physiology. Modern versions of those inventions, such as the strain gauge manometer to directly measure arterial pressure and the ear oximeter to measure oxygen saturation of blood, are still in use today. He pioneered the use of indocyanine dye to measure cardiac output—a technique that is independent of variations in hemoglobin concentration—and identified dye curves characteristic of specific cardiac abnormalities.

A cherished letter mailed December 31, 1992, from the Holiday Inn, Room 6-172, Yorkdale, Toronto, Canada, begins, "Dear Dave: Thanks for your nice note [regarding] my current research activities: the information herein is a current status report." He and his beloved wife, Ada, were living in Canada in the Holiday Inn for 11 months as he worked on a Canadian Defence grant on gravitational forces and new designs of fighter planes. That note, written at the age of 80 years, was a continuation of the work started at Mayo Clinic in 1942 and that resulted in a President’s Certificate of Merit by President Harry Truman in 1947. Dr Wood concluded that letter by saying, "My career and fulfillment have been based on making seemingly impossible dreams for the betterment of biomedicine come true."

As a problem solver, he defined eclecticism—bringing together scientists and physicians from every specialty and every corner of the world to bring into sharp focus the issues at hand. The people he brought together, those he taught, those he worked with, and those he learned with and shared experiences with included pioneers, many of whom have gone on to make continued seminal advances worldwide as part of his legacy.

Yet he was a real person, a man devoted to his family, and not a theoretical construct. Each year beginning in 1942, he, family, and friends came together in the fall of the year for family traditions revolving around a deer hunt. After each hunt, statistics of the adventure were circulated. A little-known story relates that when he retired from Mayo Clinic, he and family and close friends sailed from Hawaii to Seattle. Family and friends were an essential core of his life.

Dr Wood once told his son, "Complicated things are just a series of very simple things put together." From the days of his 1942 thesis, "The Distribution of Electrolytes and Water Between Cardiac Muscle and Blood Serum with Special Reference to the Effects of Digitalis," through his multiple scientific accolades, his presidential citation, to the naming of the Earl Wood Strasse on the grounds of a superb bioscience company in Germany, the qualities of persistence, talent, and genius allowed Earl H. Wood—the man and the legend—to live his life and his career of making impossible dreams come true.
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Echo Revolution: Adult Echocardiography for Physicians and Sonographers
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Cardiac Rhythm Device Summit: Implantation, Management, and Follow-up
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Jul 20-24, 2014
Vail, CO

Success with Heart Failure: Strategies for the Evaluation and Treatment of Heart Failure in Clinical Practice
Aug 11-13, 2014
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19th Annual Mayo Cardiovascular Review Course for Cardiology Boards and Recertification with Pre-Course Echo Focus Session
Aug 15-20, 2014
Rochester, MN

Pediatric Cardiology 2014 Review Course
Aug 17-22, 2014
Dana Point, CA

Mayo Clinic Satellite Educational Symposia at ACC 2014
Mar 29-31, 2014, Washington, DC
Symposia to be announced

Mayo Clinic Satellite Educational Symposia at ASE 2014
Jun 21-24, 2014, Portland, OR
Symposia to be announced

Mayo Clinic Satellite Educational Symposia at AHA 2014
Nov 15-19, 2014, Chicago, IL
Symposia to be announced

CARDIOVASCULAR SELF-STUDY
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