HeartWATCH

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Texas Heart® Institute

at St. Luke's Episcopal Hospital

Mesenchymal Stem Cells Improve Healing After an Acute Myocardial Infarction

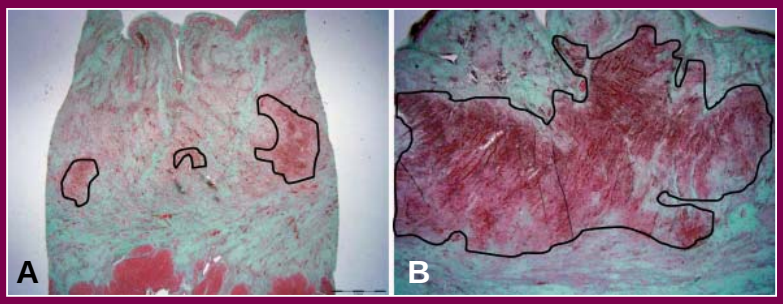
Abstract: Mesenchymal stem cells delivered 7 days after acute myocardial infarction in dogs positively affect the healing process, probably via a paracrine mechanism.

After an acute myocardial infarction (AMI), the heart undergoes a reparative process. Increased amounts of collagen are deposited in the infarct area to replace necrotic myocytes, and the wound matures into a scar. The extracellular matrix (ECM) is a key player in this healing process. Comprising an organized network that connects cellular components, the ECM not only provides structural support but also modulates cell behavior by activating signaling pathways during infarct healing. Changes in the balance of ECM synthesis and degradation may disrupt the collagen network in the heart and define the type and extent of myocardial remodeling after an AMI.

Adverse left ventricular remodeling that progresses to dysfunction is a significant complication after an AMI. Cell therapy is a newer approach for avoiding adverse remodeling and for regenerating or repairing the damaged myocardium. Multiple cell types and delivery methods have been studied. Both intracoronary and transendocardial cell delivery have shown promise. Furthermore, bone marrow–derived mononuclear cells appear to positively affect the postinfarction remodeling process. One specific small subset of bone marrow cells—mesenchymal stem cells (MSCs)—has shown a high degree of plasticity and may be especially suited for cell therapy.

Deborah Vela, MD, Senior Research Scientist, and other researchers in the Department of Cardiovascular Pathology at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at SLEH) have studied the role of MSCs in the healing process after AMI (*J Histochem Cytochem* 2009;57:167-76). These researchers treated dogs with allogeneic (obtained from a donor source) MSCs, via either intracoronary or transendocardial injection, 7 days after creation of an AMI; the histologic characteristics of the infarct were studied 14 days later (21 days after the AMI).

The investigators found that MSC treatment improved the healing process (*see Figure*). "Although infarct sizes were similar in cell-treated versus control dogs, cell-treated dogs showed less unresolved infarct and had smaller areas of necrotic myocytes that were surrounded by collagen deposits. Intracoronary delivery may be advantageous in this regard, because it allows cells to reach the center of the infarct more easily," says Dr. Vela.



Trichrome stain showing the center of an infarct in a dog that underwent intracoronary delivery of mesenchymal stem cells (A) compared with the infarct in a control dog (B). Note the large confluent area of unresolved necrotic myocardium (outlined in black) in the control dog, compared with the multiple small foci in the cell-treated dog. From *J Histochem Cytochem* 2009;57:167-76, with permission.

In examining the effect of MSCs on ECM composition, the investigators found that deposits of collagen, as well as laminin (a component of the basement membrane) and other extracellular matrix components, were greater in cell-treated dogs than in control dogs. Unresolved infarct was seen only in the middle of the infarct in dogs given MSCs, whereas necrotic myocardium extended almost to the edge of the infarct in control dogs.

"The greater collagen content associated with MSC treatment is important, because it suggests that cell therapy may provide the scar with sufficient mechanical characteristics to reduce negative remodeling and possibly even prevent wall rupture in large infarcts," explains L. Maximilian Buja, MD, Chief of Cardiovascular Pathology Research at THI at SLEH.

Another issue examined in the THI study was the fate of cells after their delivery to the heart. The mechanism by which cell therapy benefits heart patients is not known, but some research suggests that transplanted cells may differentiate into vascular endothelial cells or cardiomyocytes. Using special staining techniques, the THI researchers showed that most of the transplanted MSCs did not proliferate in situ. Furthermore, the investigators found no evidence that the MSCs differentiated into native cardiac cells.

"Our results support a paracrine mechanism for MSC treatment. MSCs may provide benefits by altering the microenvironment of the infarct and enhancing angiogenesis and wound repair, rather than by differentiating into vascular cells," says Dr. Vela. "Indeed, MSCs seem to help fortify the nascent scar by accelerating wound healing and altering the ECM components to prevent negative ventricular remodeling. We don't know, however, whether these benefits are maintained long-term." ●

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Delayed-Enhancement Magnetic Resonance Imaging Can Predict Survival in Cardiac Patients

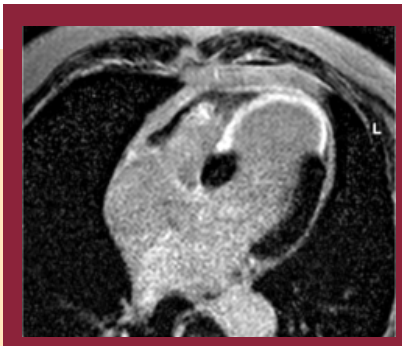
Abstract: Delayed-enhancement magnetic resonance imaging can accurately identify irreversible myocardial injury, the degree of which appears to strongly predict all-cause mortality in cardiac patients.

In patients with coronary artery disease (CAD), the left ventricular ejection fraction (LVEF) is a powerful independent predictor of survival. Cardiovascular magnetic resonance imaging (CVMRI) has emerged as the gold standard in assessing ventricular morphology and function because of its high contrast and signal-to-noise ratio, high spatial resolution, and relatively high temporal resolution.

Delayed-enhancement MRI (DE-MRI) is a CVMRI technique that can accurately discriminate between subendocardial and transmural fibrosis, thereby accurately predicting functional recovery after revascularization. Investigators have reported in small studies that DE-MRI is also capable of providing independent prognostic information about survival in patients with and without ischemia. For these reasons, researchers in the CVMRI Department at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at SLEH) examined the prognostic value of DE-MRI in patients referred there for CVMRI (*Circulation* 2009;120:2069-76).

"Although an accurate estimate of LVEF alone is clinically useful, noninvasive DE-MRI can also show us the extent of myocardial fibrosis, with a spatial resolution previously unavailable in clinical practice," says Benjamin Cheong, MD, Director of Clinical CVMRI at THI at SLEH. "We wanted to know whether the presence of delayed enhancement, when combined with the ejection fraction, could provide additional discriminatory information about patient prognosis and survival."

Dr. Cheong and his colleagues reviewed the medical records and CVMRI findings of 857 consecutive patients who had complete cine and DE-MRI evaluation, regardless of their CAD status. Patients with a diagnosis of hypertrophic cardiomyopathy, myocarditis, sarcoidosis, or any type of infiltrative cardiomyopathy were excluded from the study. The primary end point was combined all-cause mortality or cardiac transplantation. Mortality data were confirmed through the Social Security Death Index, and transplantation data were obtained through a medical records review.



Delayed-enhancement magnetic resonance imaging (4-chamber orientation) showing hyperenhancement and thinning at the apex throughout most of the inferoseptum and at the distal lateral wall of the left ventricle. Such hyperenhancement is indicative of chronic, transmural myocardial infarction.

In all cases, standard cine images were obtained. Fifteen minutes after gadolinium administration, inversion-recovery–prepared, T1-weighted, gradient-echo sequences were performed to obtain DE-MRI images. The imaging sequences were optimized by Raja Muthupillai, PhD, a scientist in the Department of Diagnostic and Interventional Radiology at SLEH. After the imaging data were acquired, an experienced observer qualitatively evaluated the presence and extent of myocardial scarring (*see Figure*).

The median follow-up period was 4.4 years. Of the 857 patients (567 men; age, 59.1±13.6 years), 252 (29%) reached the end point of death (n=230) or transplantation (n=22). Traditional risk factors, such as congestive heart failure, an LVEF of <30%, and increased age, were all significantly associated with a reduced likelihood of transplant-free survival ($P<0.0001$ for each), as was the extent of myocardial scarring (hazard ratio [HR], 1.26; 95% confidence interval [CI], 1.02 to 1.55; $P=0.033$). In patients with or without CAD, myocardial scarring was also an independent predictor of mortality (HR, 1.33; 95% CI, 1.05 to 1.68; $P=0.018$) or transplantation (HR, 5.65; 95% CI, 1.74 to 18.3; $P=0.004$). Cox regression analysis showed poorer outcomes in patients who had any sign of DE combined with an LVEF of <50%.

"Our most important finding was that even in the presence of traditional cardiovascular prognosticators, DE was a strong, independent predictor of our end point of all-cause death or transplantation," says Dr. Cheong. "Our results also emphasize that further independent prognostic information can be obtained by combining LVEF and DE. In patients with a low LVEF (<30%), who already had an increased mortality risk, survival was worse when DE was present. Also, as the extent of DE increased, so did the risk of death or transplantation."

"Our findings suggest that DE-MRI could be another important tool—in addition to the traditional prognosticators—for risk stratification in these patients. Further prospective studies will be needed to confirm our findings," adds Dr. Cheong. ●

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Contents

Researchers Characterize an Atherogenic Pathway for a Negatively Charged Low-Density Lipoprotein

Abstract: Low-density lipoprotein L5 targets endothelial cell apoptosis via the LOX-1 receptor-mediated pathway.

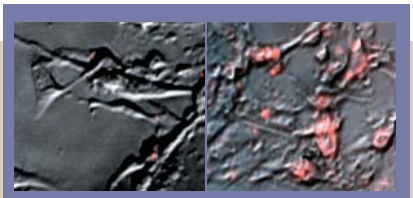
The development of atherosclerosis is enhanced by elevated plasma levels of low-density lipoprotein (LDL). Although LDL is generally referred to as "bad cholesterol," not all subtypes of LDL particles are atherogenic. Much of what is known about the effects of harmful LDL comes from studies of laboratory-derived, oxidized LDL. However, a naturally occurring LDL species with a propensity for oxidative modification has never been isolated from human plasma.

Chu-Huang (Mendel) Chen, MD, PhD—the new Director of Vascular and Medicinal Research at the Wafic Said Molecular Cardiology Research Laboratories at the Texas Heart Institute at St. Luke's Episcopal Hospital—and his colleagues have used a novel approach to pursue the identity of the "culprit" LDL responsible for the atherogenic properties of LDL. They obtained LDL from patients with hypercholesterolemia and separated it into 5 subfractions (L1-L5) that had increasingly negative charge. The most negatively charged subfraction, L5, exhibited atherogenic properties similar to those of oxidized LDL (*Circulation* 2003;107:2102-8).

L5 accounts for up to 5% of the total LDL in hypercholesterolemic plasma (but not normolipidemic plasma) and is also found in patients who have other risk factors for cardiovascular disease, including type 2 diabetes and chronic smoking. Dr. Chen and his group recently showed that L5 promotes endothelial cell apoptosis—an important step in the initiation of atherogenesis. They also characterized the mechanistic pathway for this process (*Circ Res* 2009;104:629-7).

"Apoptosis contributes to the development of atherosclerotic plaque, in both the initial and the progressive stages," states Dr. Chen. "Our work brings to light a pathophysiologic picture of how atherosclerotic lesions may form."

Dr. Chen and his colleagues identified the endothelial cell receptor responsible for the uptake of L5 from the bloodstream and the transduction of its pro-apoptotic signals. The lectin-like oxidized LDL receptor (LOX-1), highly expressed in human atherosclerotic arteries, is a scavenger receptor that binds and internalizes modified lipoproteins, including laboratory-derived oxidized LDL. To determine whether LOX-1 mediates the uptake of pathologically derived L5 into endothelial cells, Dr. Chen's group fluorescently labeled L5 with a tracking dye and inhibited LOX-1 by blocking it with antibody or by knocking it down with siRNA. Indeed, the cellular uptake of fluorescently labeled L5 was blocked when LOX-1 was inhibited, suggesting that LOX-1 mediates the internalization of L5 in endothelial cells. Furthermore, L5-induced apoptosis was no longer observed in cells when LOX-1 was compromised.



Fluorescence microscopy showing the uptake of L5 into bovine aortic endothelial cells that were transfected with LOX-1 siRNA (left) or non-targeting siRNA (right). Cells no longer internalize fluorescently labeled L5 when the LOX-1 receptor is knocked down.

To further determine the mechanisms by which L5 promotes endothelial cell apoptosis, the researchers examined how L5 affects the expression of proteins that regulate apoptosis. Using biochemical assays, they found that L5 reduced the expression of fibroblast growth factor-2, which in turn inhibited other proteins that promote endothelial cell growth and survival. Moreover, treating endothelial cells with L5 selectively downregulated the expression of prosurvival proteins Bcl-2, Bcl-xL, and endothelial nitric oxide synthase, while concomitantly upregulating pro-apoptotic factors Bax, Bad, and tumor necrosis factor-α. All of these signal-transduction events were abolished when the LOX-1 receptor was blocked or knocked down, confirming that apoptotic signaling by L5 requires LOX-1.

These results provide a clearer understanding of how atherogenesis may occur in patients with hypercholesterolemia or other cardiovascular risk factors associated with L5.

"The more we understand the pathways that contribute to atherosclerosis, the more opportunities arise for exciting new therapeutic targets," says Dr. Chen. "We believe that L5 may prove to be an important cause-effect biomarker for determining atherogenicity." ●

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Residents Perform Safe Aortic Valve Replacement in Octogenarians

Senile calcific aortic stenosis is the main indication for aortic valve replacement (AVR). Because the elderly population in the United States is increasing, it is important that future cardiac surgeons be well trained in this procedure. For this reason, several members of the Division of Cardiovascular Surgery at the Texas Heart Institute at St. Luke's Episcopal Hospital participated in a study that examined the safety and efficacy of AVR as performed on 23 men (mean age, 83 years) by supervised residents at Houston's Michael E. DeBakey Veterans Affairs Medical Center. There was no operative mortality, and—despite the high prevalence of preoperative comorbidities in this group—there were relatively few serious adverse postoperative events. Additionally, after an average of 3.9 years of follow-up, 14 (61%) of the patients were still alive. According to Faisal Bakaeen, MD, senior author of the study report (*J Surg Res* 2009:156;139-44), "These results suggest that properly supervised residents can perform AVR safely, even in elderly patients."

Nationwide Database Review Shows That CABG and OPCAB Yield Equivalent Early Outcomes

Abstract: Coronary artery bypass grafting (CABG) and off-pump coronary artery bypass grafting (OPCAB) both yield similar early outcomes, but OPCAB increases hospital stays and costs.

Of the more than 13 million Americans who have multivessel coronary artery disease, many will undergo coronary artery bypass grafting (CABG) with the aid of cardiopulmonary bypass (CPB). Although CABG with CPB is still one of the most commonly performed cardiac procedures, the physiologic derangements associated with CPB have led surgeons to develop off-pump coronary artery bypass (OPCAB)—a revascularization technique that does not require CPB.

With numerous studies touting the benefits of both procedures, the question remains: is one approach better than the other? In hopes of finding the answer, researchers at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at SLEH) participated in a retrospective study to compare CABG and OPCAB outcomes in 63,047 patients, using the 2004 Nationwide Inpatient Sample (NIS), a large database of hospital inpatient stays (*Ann Thorac Surg* 2009;87:1820-7). The researchers included Joseph S. Coselli, MD, Chief of Adult Cardiac Surgery at THI at SLEH and Professor and Cullen Foundation Endowed Chair in the Division of Cardiothoracic Surgery at Baylor College of Medicine; Danny Chu, MD, Assistant Professor of Surgery at Baylor College of Medicine, Associate Chief of Cardiothoracic Surgery at the Michael E. DeBakey Veterans Affairs Medical Center, and a cardiovascular surgical staff member at THI at SLEH; and their colleagues.

"We wanted to provide insight into the real-world outcomes of CABG and OPCAB," says Dr. Chu. "The NIS database was perfect for this purpose because it is nonvoluntary, so institutional and surgeon biases are eliminated. Also, the enormity of its sample size allows adequate statistical power for detecting low-frequency outcome measures, such as deaths."

The NIS was used to identify 63,047 discharge records of patients who underwent CABG (n=48,658) or OPCAB (n=14,389). Records were then analyzed for certain preoperative variables, including the Deyo comorbidity index, which is a weighted index with a 0-to-3 scale (3 indicating greatest comorbidity) to compare preoperative morbidity in the 2 groups. The primary end point was in-hospital mortality, and the secondary end points were postoperative stroke, length of hospital stay, rates of routine discharge, and overall hospitalization costs. Multivariable logistic regression was used to identify independent predictors of outcomes.

The in-hospital mortality rate was similar for CABG and OPCAB (3.0% vs 3.2%), as were the incidence of postoperative stroke (1.8% vs 1.7%) and the rate of routine discharge (51.2% vs 53.7%). The similarities ended, however, with regard to the length of hospital stay and the overall costs of hospitalization. Multivariable logistic regression analysis showed that OPCAB independently predicted 0.6 more days of hospital stay ($P<0.0001$) and $1497 more expense in overall hospitalization costs ($P<0.01$) per patient.

"We found it interesting that OPCAB did not improve early outcomes, and it independently predicted longer hospital stays and increased costs," says Dr. Coselli. "We attribute this finding, in part, to surgical and support team inexperience, necessitating emergency conversion to CABG because of technical problems during OPCAB."

Drs. Chu and Coselli admit that referring cardiologists and even patients themselves sometimes insist on OPCAB and that the decision to proceed with it can be influenced by political and economic pressures. In other words, patient outcomes are affected by biased patient selection, which also may be why OPCAB is associated with increased hospital stays and costs.

"The cost increase associated with OPCAB may seem small on its own, but cumulatively, it means that $1.4 million is saved for every 1000 patients who undergo CABG instead of OPCAB," says Dr. Chu.

"We hope the finding that OPCAB and CABG have equivalent early—and perhaps long-term—outcomes will lead to greater acceptance of conventional CABG by patients and their referring cardiologists," says Dr. Coselli. "The know-how and technical skill to perform OPCAB need to be in every cardiac surgeon's repertoire; however, OPCAB should be used as an alternative to conventional CABG with CPB, rather than as a replacement for it." ●

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THI at SLEH Receives Grants for Cutting-Edge Research

THI at SLEH has recently received approximately $14 million in grant support to fund cutting-edge research projects: $8.2 million from federal agencies, $4 million from State of Texas agencies, and $1.8 million from foundations and corporations. The largest grant, $4.1 million from the National Institutes of Health (NIH), will be used to clarify the physiologic effects of pulseless blood flow. Led by O.H. Frazier, MD, investigators will use this knowledge in the development of a continuous-flow total artificial heart. Also awarded to Dr. Frazier's research group was an NIH grant to develop a miniature heart assist device for use in neonates and pediatric patients. Another large award, $2.5 million from the State of Texas, will be used for stem cell research under the direction of James T. Willerson, MD, and project leaders Emerson Perin, MD, PhD, Richard Dixon, PhD, Robert Schwartz, PhD, and Edward Yeh, MD. THI also received NIH stimulus funds appropriated under the American Recovery and Reinvestment Act of 2009. A Challenge Grant, which was awarded to THI (Dr. Perin) and includes collaboration with Rice University, will focus on refining cell-tracking nanotube technology that could make MRI up to 40 times more sensitive for guiding and tracking stem cells. Another Challenge Grant, awarded jointly to Dr. Dixon and his collaborators at the University of Houston, will focus on developing and testing a cell-based approach for treating pulmonary arterial hypertension (PAH) by genetically engineering cells that stably overexpress prostacyclin, which is deficient in PAH patients. A stimulus grant for 2-year support of a new investigator, 1 of only 33 such grants nationwide (2 in Texas), was awarded to THI on behalf of Drs. Willerson and Schwartz, who will serve as the mentoring team leaders for promising young scientist Jun Wang, MD, PhD. Read more about these research efforts in an upcoming issue of *Heart Watch*.

Nationwide Study Examines Genetically Triggered Thoracic Aortic Aneurysms

Abstract: The GenTAC study has begun to reveal details about the treatment histories of patients with thoracic aortic aneurysms suspected to be of genetic origin.

The National Registry

of Genetically Triggered Thoracic Aortic Aneurysms and Cardiovascular Conditions (GenTAC) is a longitudinal, multicenter study of the causes and natural history of genetically triggered thoracic aortic aneurysms and dissections (TAADs). Sponsored by the National Heart, Lung, and Blood Institute, the National Institute of Arthritis and Musculoskeletal and Skin Diseases, the National Marfan Foundation, and the Ehlers-Danlos National Foundation, GenTAC collects clinical data and banked blood and tissue samples from patients who have been diagnosed with genetic conditions associated with TAADs. These include patients who have heritable conditions or syndromes known to be associated with TAAD formation (eg, Marfan syndrome, Ehlers-Danlos syndrome), familial TAADs, or certain congenital heart defects (eg, bicuspid aortic valve). The target sample size is 2800.

Data and tissue samples are collected at 5 clinical centers in the United States. Jointly, the Texas Heart Institute (THI) at St. Luke's Episcopal Hospital (SLEH), the University of Texas at Houston, and Baylor College of Medicine (BCM) constitute 1 of these collection centers; the Houston center is led by Dianna M. Milewicz, MD, PhD, who is the Director of the Division of Medical Genetics at the University of Texas Medical School at Houston. (For more information on GenTAC, see *Heart Watch*, Summer 2008, p. 5, at http://www.texasheart.org/Education/Pubs/upload/HeartWatch_2008_sum.pdf).

Recently, the GenTAC investigators—including Scott A. LeMaire, MD, a cardiovascular surgeon at THI at SLEH and an Associate Professor and Director of Research in the Division of Cardiothoracic Surgery at BCM—performed a preliminary analysis of data from the first 606 GenTAC patients for whom complete data had been obtained. The main purpose of this analysis was to examine what types of cardiovascular conditions were most common among GenTAC participants and what sort of operations the participants had undergone before they enrolled in the study.

THE MOST COMMON PRIMARY DIAGNOSES AND CARDIOVASCULAR SURGICAL HISTORIES OF PATIENTS WITH GENETIC CONDITIONS ASSOCIATED WITH THORACIC AORTIC ANEURYSMS OR DISSECTIONS (TAADs)

Primary Diagnosis	Patients (no.)	Previous Surgery	Mean Age at 1st Operation (y)	Most Common Indications for Surgery
Marfan syndrome	217	117 (54%)	34.3	1. Aortic aneurysm 2. Aortic valve dysfunction 3. Aortic dissection
Bicuspid aortic valve (no family history)	153	100 (65%)	44.4	1. Aortic valve dysfunction 2. Aortic aneurysm 3. Aortic dissection
TAADs before age 50 (no history of heritable conditions or syndromes)	74	43 (58%)	34.4	1. Aortic aneurysm 2. Aortic valve dysfunction 3. Aortic dissection
Familial TAADs	65	35 (54%)	51.6	1. Aortic aneurysm 2. Aortic valve dysfunction* 2. Aortic dissection*

**Aortic valve dysfunction and aortic dissection were about equally common in this group.*

"Because our ultimate goal is to find the optimal treatment for patients with different types of genetically induced TAADs," Dr. LeMaire says, "we first need to examine the differences in how these patients present with their disease, such as the age at which operations are first necessary and the primary indications for operation."

The results of the analysis, which were published in the *Annals of Thoracic Surgery* (2009:88;781-8), showed that 509 (84%) of the patients had 1 of 4 conditions: (1) Marfan syndrome, (2) bicuspid aortic valve (but no family history of it), (3) TAADs that occurred before age 50 (but no history of heritable conditions or syndromes), and (4) familial TAAD. Additionally, 341 (57%) of the patients had undergone some type of cardiovascular surgery before enrollment (*see Table*). In all patients who had undergone repair procedures for previous aneurysms or dissections, the proximal aorta was the most common location for repair.

The groups also differed in the average age at which the patients underwent their first cardiovascular operation. Among the 4 largest groups of patients, the average age was highest in patients who had familial TAAD and lowest in patients with Marfan syndrome or with TAADs that occurred before age 50 without a history of heritable conditions or syndromes.

"These results, although preliminary, give us some clues about where and when to look for cardiovascular disease in patients with different types of genetically related TAAD disorders," says Dr. LeMaire. "As our sample size grows, and as we accumulate long-term data about the patients, we expect to expand the scope of our research to include outcomes and plasma-biomarker studies. We also expect to search for single-nucleotide polymorphisms associated with TAADs." ●

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MRI Is Effective for Assessing Myocardial Perfusion After Transmyocardial Laser Revascularization

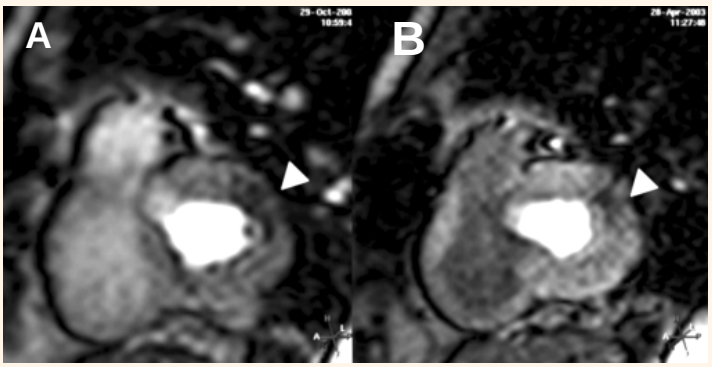
Abstract: Magnetic resonance imaging can be used to accurately assess subendocardial perfusion in patients who undergo transmyocardial laser revascularization for refractory angina.

Transmyocardial laser revascularization (TMLR) is a procedure whereby a specialized carbon dioxide (CO_2) laser is used to create transmural channels approximately 1 mm in diameter through the left ventricular myocardium. The procedure has been shown to relieve angina refractory to medical therapy in patients who are not candidates for conventional surgical or percutaneous revascularization.

In 1999, the Transmyocardial Carbon Dioxide Laser Revascularization Study Group conducted a multicenter, randomized, controlled trial to determine the effect of TMLR on symptoms and cardiac perfusion in patients with end-stage coronary artery disease (CAD) (*N Engl J Med* 1999;341:1021-8). O. H. Frazier, MD, Director of Cardiovascular Surgical Research and Chief of Cardiopulmonary Transplantation at the Texas Heart Institute at St. Luke's Episcopal Hospital (THI at SLEH), was a member of the group. Results of this study showed improved overall myocardial perfusion after TMLR; however, subendocardial perfusion could not easily be assessed directly.

"It is generally believed that improved subendocardial perfusion after TMLR is a result of the direct communication between the laser channels and the ventricular cavity," says Benjamin Cheong, MD, Director of Clinical Cardiovascular Magnetic Resonance Imaging at THI at SLEH. "Because MRI is an established and validated tool for correlating myocardial perfusion with functional improvement, we felt that it also would be useful for analyzing the effectiveness of TMLR. Although positron emission tomography and single-photon emission computed tomography are widely used in clinical practice for assessing perfusion, MRI provides better spatial resolution for evaluating subendocardial perfusion than do those modalities."

Thus, Dr. Frazier and his team studied 3 TMLR patients (aged 51, 53, and 70 years) who had severe, diffuse CAD not amenable to conventional surgical revascularization and Canadian Cardiovascular Society (CCS) class 3-4 angina refractory to maximal medical therapy (*Heart Surg Forum* 2009;12:E199-201). Stress and resting myocardial perfusion studies (with intravenous adenosine and gadolinium) were performed before and after TMLR to assess left ventricular perfusion and wall-motion changes in the laser-treated areas. Three short-axis slices (representing the base, middle, and distal regions of the left ventricle, covering 16 segments of the 17-segment model) were obtained during the stress and resting perfusion sequences. Postoperative MRIs were performed within 6 months after TMLR and again at 12 months. Quality of life was assessed with the Seattle Angina Questionnaire.



Adenosine stress perfusion before (left, October 2002) and after (right, April 2003) TMLR. Perfusion defect is seen in the basal anterolateral wall; however, the extent is less after TMLR.

Perfusion data were interpreted visually. For a segment to be considered ischemic, there had to be reversible hypoperfusion present between the adenosine and rest-perfusion sequences, with viable myocardium documented by the delayed-enhancement images. In the setting of critical ischemia, hypoperfusion would be visible in both the stress and rest images of viable myocardium and would be accompanied by regional wall-motion abnormalities.

In all 3 patients, postoperative adenosine stress myocardial perfusion imaging with MRI revealed an improvement in overall perfusion and a reduction in hypoperfused subendocardial areas when compared to preoperative images. In 2 of the patients, angina improved from CCS class 3 to class 1; in the third patient, it improved from CCS class 4 to class 1. Of note, the improvement in CCS class was consistent with the improvement in perfusion.

"The results of this limited study suggest that adenosine stress myocardial perfusion imaging with MRI may be a valuable tool after TMLR because of the direct visual assessment and analysis of subendocardial and overall perfusion that it provides," says Dr. Frazier. "Our ability to assess perfusion in this manner may be useful not only for determining the effect of TMLR on subendocardial perfusion in the postoperative setting, but also for correlating further follow-up studies, particularly if a patient's symptoms recur." ●

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Cover: Statue donated by the Bob and Warner Roberts family for the Celebration of Hearts display in the Wallace D. Wilson Museum of the Texas Heart Institute at St. Luke's Episcopal Hospital—The Denton A. Cooley Building. Warner Roberts was the driving force behind the entire Celebration of Hearts collection.

Calendar of Events

Texas Heart Institute Continuing Medical Education Symposia

Eleventh Symposium on Cardiac Arrhythmias
The Houstonian
February 20, 2010 • Houston, Texas
Program Director: Ali Massumi, MD

Twenty-fifth Cardiovascular Magnetic Resonance Imaging Practicum
St. Luke's Episcopal Hospital
February 22–25, 2010 • Houston, Texas
Program Directors: Ben Cheong, MD, and Raja Muthupillai, PhD
For further information, please contact Teresa Rose at trose@sleh.com or 832.355.4201.

Future Direction of Stem Cells in Cardiovascular Disease Satellite Symposium at American College of Cardiology Scientific Sessions
The Westin Peachtree Plaza
March 13, 2010 • Atlanta, Georgia
Program Director: James T. Willerson, MD

For information about Texas Heart Institute CME activities, please e-mail cme@heart.thi.tmc.edu or call 832.355.2157. To view or complete selected CME presentations (certificates are available online), please visit www.texasheart.org/cme. New courses are added regularly.

Selected Upcoming Local, National, and International Meetings

Society of Thoracic Surgeons 46th Annual Meeting
January 25–27, 2010 • Ft. Lauderdale, Florida

American College of Cardiology 59th Annual Scientific Sessions
March 14–16, 2010 • Atlanta, Georgia

International Society for Heart and Lung Transplantation 30th Annual Meeting and Scientific Sessions
April 21–24, 2010 • Chicago, Illinois

American Association for Thoracic Surgery 89th Annual Meeting
May 9–13, 2010 • Toronto, Ontario, Canada

Heart Rhythm Society 31st Annual Scientific Sessions
May 12–15, 2010 • Denver, Colorado

The Texas Heart Institute website (www.texasheart.org) recieved a 2009 eHealthcare Leadership Award, a silver award in the category of Best Health/Healthcare Content in the division of Hospital Subsite/Center of Excellence.

For 19 consecutive years, the Texas Heart Institute at St. Luke's Episcopal Hospital has been ranked among the top 10 heart centers in the United States by *U.S. News & World Report*'s annual guide to "America's Best Hospitals."