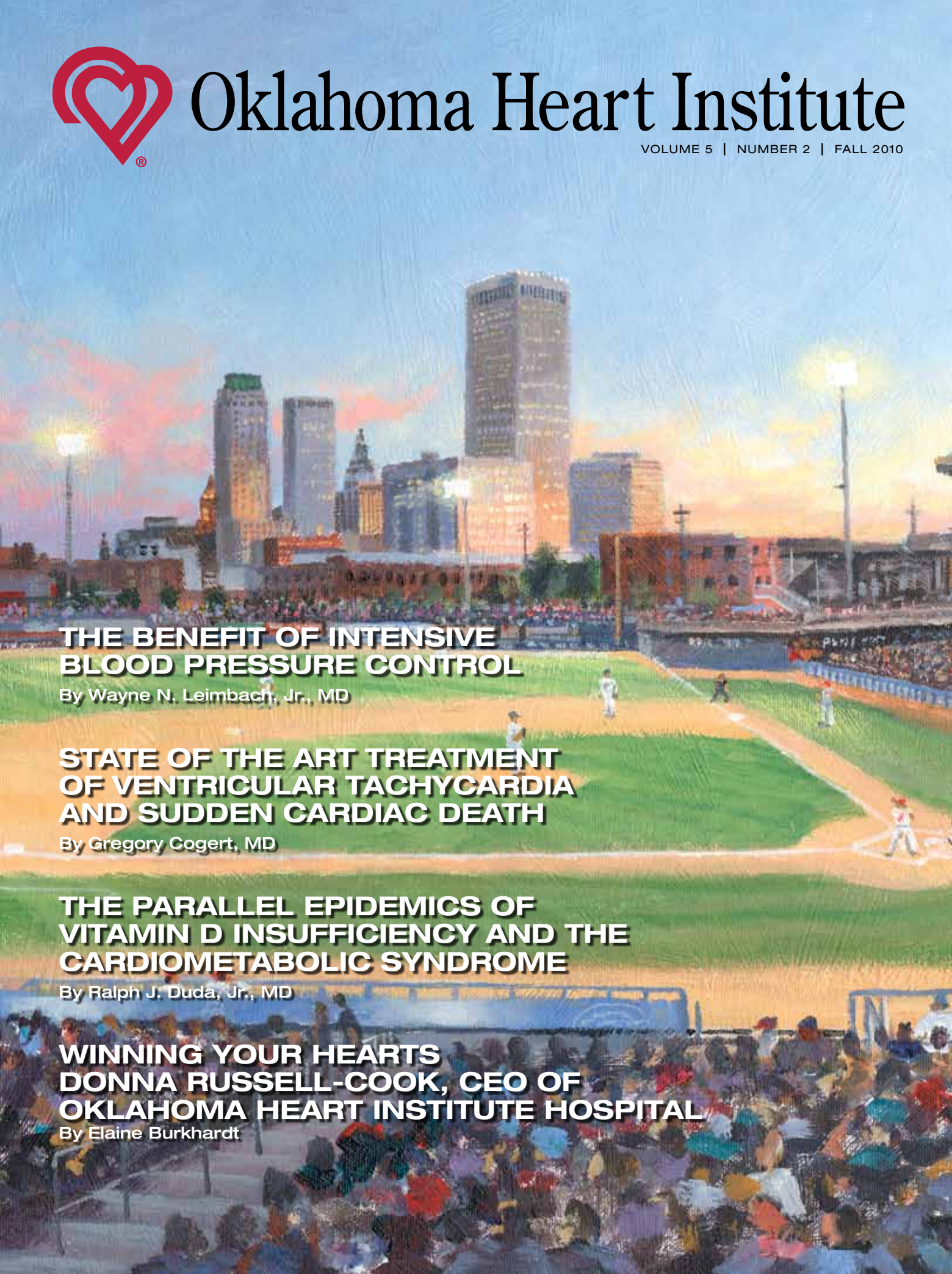
Oklahoma Heart Institute

VOLUME 5 | NUMBER 2 | FALL 2010



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WINNING YOUR HEARTS DONNA RUSSELL-COOK, CEO OF OKLAHOMA HEART INSTITUTE HOSPITAL

By Elaine Burkhardt

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The Oklahoma Heart Institute Magazine is mailed directly to referring physicians and other referring health care professionals in the Tulsa area and is also available in our patient waiting rooms.

features

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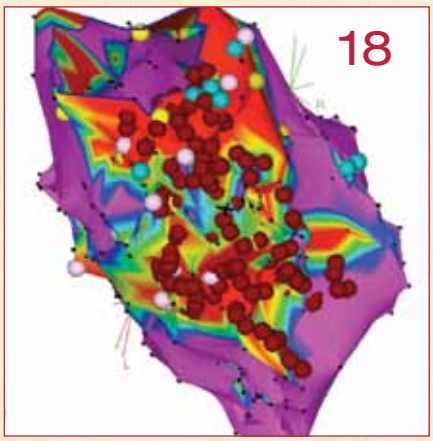

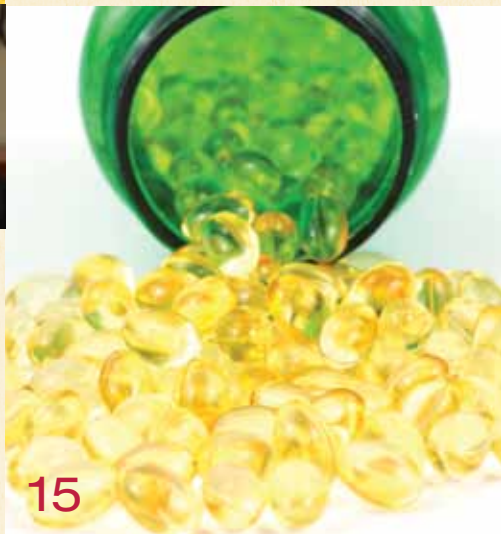

ON THE COVER

"Take Me Out to the Ballgame"
by Tulsa artist Christopher Westfall
Acrylic 15"x 30"

to our readers

The current issue of the Oklahoma Heart Institute Magazine focuses on a variety of topics related to new concepts in the fields of cardiology and endocrinology.

Dr. Gregory Cogert, an electrophysiologist at Oklahoma Heart Institute with an expertise in treating ventricular tachy-dysrhythmias, discusses the exciting re-emergence of ventricular tachycardia ablation which significantly improves the quality of life for patients with recurrent ventricular tachycardia. With the change in the ablation strategy from ablating the actual ectopic foci to the current approach of isolating the electrically unstable areas from the rest of the myocardium, success rates have dramatically increased and procedure times have dramatically decreased. Catheter ablation of ventricular tachycardia has now become a safe and very effective option for eliminating ventricular tachycardia in symptomatic patients.

Dr. Ralph Duda, Jr., in the Division of Endocrinology at Oklahoma Heart Institute, highlights the increasing importance of identifying Vitamin D deficiency in patients with resistant hypertension and with multiple cardiovascular risks and its possible association with the cardiometabolic syndrome. In addition, once identified, it is relatively easily treated.

Also provided in this issue is a discussion regarding the controversy of how aggressively we should treat blood pressures in patients with diabetes mellitus. In addition, several of the late-breaking clinical trials that were presented at the Oklahoma Heart Research and Education Foundation Spring Symposium are presented. These trials highlight clinical results that either support or refute several current clinical practice guidelines.

Finally, Elaine Burkhardt interviews Donna Russell-Cook, the new CEO of the Oklahoma Heart Institute. She explores the reasons behind the rapid growth in the Oklahoma Heart Institute Hospital and the future plans for the Institute.

We hope you enjoy these articles and welcome any comments or suggestions regarding the content.

Sincerely,

Wayne N. Leimbach, Jr., MD
Publisher, Oklahoma Heart Institute Magazine

The Benefit of Intensive Blood Pressure Control: The Controversy Continues

By Wayne N. Leimbach, Jr., MD, FACC, FSCAI, FCCP, FAHA

Current guidelines recommend treating patients with antihypertensive therapy when their blood pressure is 140/90 or greater. For patients with diabetes mellitus and with known coronary artery disease, it is now recommended that treatment goals should be lower and treatment should start for blood pressure of 130/80 or higher (Figure 1). Analysis of the data from many large clinical trials has suggested that even more aggressive blood pressure lowering is beneficial. Two large randomized clinical trials were presented at the American College of Cardiology meetings in March of 2010 that questioned whether more aggressive blood pressure goals will further reduce cardiovascular disease events compared to the standard blood pressure goal of achieving systolic blood pressures of less than 140mmHg.

The ACCORD Blood Pressure Trial looked at the effects of intensive blood pressure therapy on cardiovascular events in type II diabetes mellitus and was originally designed to test three medical strategies to reduce cardiovascular disease events in diabetic patients. The ACCORD Trial tested intensive glycemic control versus standard glycemic control, intensive blood pressure control versus standard blood pressure control, and finally intensive lipid control versus standard lipid control. The intensive glycemic control versus standard glycemic control arm of the trial was stopped prematurely due to the fact that the intensive glycemic control had an increase in adverse cardiovascular events.

Over 4,733 patients were evaluated in the intensive versus standard therapy arms of the blood pressure portion of the trial. Blood pressure targets were successfully achieved in both arms of the study. After the first year, the standard therapy group achieved an average systolic blood pressure of 133.5mmHg. The intensive blood pressure control group achieved an average systolic blood pressure of 119.3mmHg. This trial focused on patients who had type II diabetes mellitus and who were felt to be at high risk for cardiovascular disease events. However, when analyzing the primary outcome of the study which included total mortality, cardiovascular deaths, non-fatal MI, non-fatal stroke, and total stroke, the intensive therapy group demonstrated a 1.87% per year event rate compared to the standard treatment group of 2.09% per year, which was not statistically significant. The P-value was 0.20.

In evaluating secondary outcomes of the trial, total mortality was not significantly different between the two groups. The intensive therapy group had a 1.28% per year event rate as compared to a 1.19% per year event rate in the standard therapy group. The P-value for this was 0.55. There was, however, a significant reduction in non-fatal strokes and total strokes in the intensive treatment group as compared to the standard treatment group. The intensive group experienced a 0.30% per year non-fatal stroke rate as compared to a 0.47% per year non-fatal stroke rate in the standard group. This had a P-value of 0.03. In looking at total stroke rates, the intensive group experienced a 0.32% per year total stroke rate ver-

Table 1
How Low Should Blood Pressure Be Lowered?

JNC 7[1]: Blood Pressure Goals	
Condition	**BP Target**
Uncomplicated HTN	<140/90 mm Hg
HTN + Diabetes	<130/80 mm Hg
HTN + Chronic Renal Disease	<130/80 mm Hg

AHA[2]: Blood Pressure Goals	
Condition	**BP Target**
Uncomplicated HTN	<140/90 mm Hg
HTN + High Risk of CAD*	<130/80 mm Hg
HTN + Angina	<130/80 mm Hg

*High risk for CAD is defined as patients with: diabetes mellitus, chronic kidney disease, known CAD or CAD equivalent, or 10-year Framingham risk score ≥10%.

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winning your hearts

Donna Russell-Cook

CEO of Oklahoma Heart Institute Hospital

By Elaine Burkhardt

Sit down to chat with Donna Russell-Cook, the new CEO of Oklahoma Heart Institute Hospital, and the first thing you'll notice is her contagious energy. The second is her aquamarine eyes. The third, she knows her stuff.

Russell-Cook is one of only a few women CEOs of a Heart Hospital in the United States. She's come to Tulsa from Bangor, Maine, where she most recently served three years as Heart Center Administrator at Eastern Maine Medical Center. And for more than 20 years, she has worked in professional health care: at Sisters of Charity of Leavenworth Health System in Lenexa, Kan.; St. Vincent Healthcare in Billings, Mont.; and Arnett Clinic, Lafayette Heart Institute, in Lafayette, Ind.

Her current mission? To lead the strategic initiatives for OHI Hospital, the state's largest hospital dedicated exclusively to the treatment of cardiovascular disease. That requires leadership, vision and the ability to listen to others, be a team player and stay focused, yet flexible. Those qualities are no stranger to Russell-Cook, who grew up in a Naval family that traveled across the United States and in Asia, requiring an uncanny ability to remain adaptable and forward thinking in the face of constant challenges, dynamic change and diversity.

After graduation from Parklane Academy in McComb, Miss., she earned her Bachelor's degree from the University of Nebraska in Lincoln, and her Master's from the University of Wisconsin in La-Crosse. She also attended the Healthcare Advisory Board, Harvard Business School Affiliated Leadership Fellowship Academy. Russell-Cook is a Fellow in the American College of Healthcare Executives and a member of the American College of Cardiovascular Administrators.

In Tulsa, Russell-Cook lives in south Tulsa with her husband and their two children. A horse lover for many years, Russell-Cook works with the Tulsa Community Foundation toward placement and ongoing care of the displaced Tulsa Police Department Mounted Patrol Unit horses. She is also actively involved in the American Heart Association's "Go Red for Women" campaign and is a member of the Circle of Red.

Oklahoma Heart Institute Hospital has been open now for over a year. It's been called Tulsa's newest crown jewel of cardiovascular care. Why is it considered such a distinctive hospital?

Russell-Cook: It's a brand new $69 million dollar facility that's very high tech inside and out. It's the state's largest, most comprehensive hospital dedicated strictly to the cardiovascular and metabolic needs of its patients. That in itself makes it unique to Tulsa.

Until now, there's been no other facility like it here. People had to travel away from home to receive this kind of treatment before we opened in March 2009.

Over the past year, OHI Hospital has experienced overwhelming success. Tell us about it.

Russell-Cook: We have seen double-digit growth in all of our cardiac procedural areas: heart surgery, angioplasties, electrophysiology, and in the heart failure clinic. We are actually running extended hours in our procedural areas to handle the needs of our community. Our entire OHI staff is the best, and we thank them for their dedication and hard work.

Continued on page 8

"We have seen double-digit growth in all of our cardiac procedural areas: ... Volume is off the charts and the demand has exceeded all expectations."

Continued from page 7

Demand is surging, everything is running full throttle. Have you proven there was a need in Tulsa for a heart hospital of this caliber?

Russell-Cook: Oh yes, definitely. We are seeing patients from all over the state and the region.

In just over a year, you have attracted many patients who used to go elsewhere to be hospitalized for cardiovascular conditions. Why are they making the switch to OHI Hospital?

Russell-Cook: People who have gone elsewhere are making the switch for the advanced care we offer. The reputation of our physicians, staff and facility has spread quickly, so patients increasingly are seeking care at OHI Hospital, as well as their second opinions.

We're finding they are often told they'll have to leave home and go out of town or even out of state. When they come to Oklahoma Heart Institute Hospital for a second opinion, we often determine that we can do the procedure here. Those patients are then admitted, have the procedures and often go home the next day.

For example, a Ventricular-Tachycardia ablation is one of those procedures — we have that specialty and no one else in the state has the skill set we have to do them. Last week we did a V-Tach ablation procedure. It requires the highly skilled, high level of competency that our physicians bring to the OHI Hospital. This example is indicative of the skills and the training that all of the cardiologists, endocrinologists and surgeons have here.

How do you stay in touch with patients and their families?

Russell-Cook: Our patient relationship is of utmost importance. We provide numerous monthly community education clinics and screenings. The OHI website is another resource we provide to keep the public updated on new technology, procedures, physicians and the like. It's easy to access and provides everything they need to know about our services. They can even make appointments online.

Specifically, what innovations has OHI Hospital brought to Tulsans?

Russell-Cook: We have some impressive firsts.

For example, our bypass surgery program has the best in state mortality rate. And, our heart attack door to balloon time is better than the national average of 90 minutes or less.

We also offer brand new procedures that patients statewide can only access at Oklahoma Heart Institute Hospital. For example, in our cath lab we were the first institution in Oklahoma to use the Impella device, a left ventricular assist device for patients who are in significant trouble until we can treat the underlying problem. Our invasive cardiologists also were the first to perform PFOs, non-surgical closure of holes in the heart in adults.

Our electrophysiology team treats abnormal heart rhythms with ablation, pacemakers and defibrillators, and our EP physicians have become known for ablating difficult ventricular and atrial dysrhythmias that could not be done elsewhere in Northeastern Oklahoma.

And for patients with heart failure, we're the only facility in Tulsa and one of two in Oklahoma offering inpatient aquapheresis and the only facility in the state offering outpatient aquapheresis, a unique approach to fluid removal for heart failure patients. It's a very effective outpatient treatment that significantly reduces the need for re-hospitalization of heart failure patients.

OHI Hospital also has the largest Division of Endocrinology in the state. Metabolic disorders are a primary risk factor for cardiovascular disease, so treatment and control can reduce the incidence of heart disease. This helps us treat a significant population of patients.

Tell us about the physical nature of the hospital.

Russell-Cook: We have the capacity of 104 beds in all private rooms. The privacy is a big plus for patients often dealing with very complex health problems. Once inside the facility, you'll notice the open, natural feeling. The concept is using the natural elements, such as natural light through lots of windows and natural colors, to aid in the healing process. Research shows patients who have access to these natural, quiet environments heal more quickly. Also, a family member can room in. Since we provide care for patients throughout the region, and a number of people come from out of town, they appreciate that a family member can stay right here with them.

Can you give us an idea of the wide scope of services offered by the hospital?

Russell-Cook: OHI Hospital provides a full range of cardiovascular services including a comprehensive Cardiovascular Diagnostic Center, Cardiovascular Interventional and Electrophysiology Laboratories, Pre- and Post-Cardiac Cath Lab Procedure Beds, a Cardiovascular Intensive Care Unit, Cardiac Telemetry Beds, a Heart Failure CARE Center, a Cardiovascular Research program and an Education Center.

We also offer seven Centers of Excellence, which are highly specialized programs dedicated to the treatment of cardiovascular conditions, ranging from diabetes and hypertension to more complex conditions such as heart fail-

ure and atrial fibrillation.

Let's talk about your physicians and how they make OHI Hospital different than other area hospitals.

Russell-Cook: A hospital of this kind attracts the most educated and specialized cardiologists, endocrinologists and surgeons in the field. No matter what kind of cardiovascular problem a patient has, the OHI hospital has the expertise to treat it. This is a dedicated place for a very large population. By locating the OHI Hospital with the tertiary hospital, patients are assured that, no matter how complicated their health problems become, they can be successfully treated here.

All of our physicians are very committed — to the program, to their patients and to this community. Since they are recognized internationally and not just locally, they are also engaged in ongoing research to prevent and treat cardiovascular disease. OHI has an excellent, highly skilled team of MDs and staff ready to provide the highest quality of care to our patients.

How important is the hospital staff to its success?

Russell-Cook Invaluable. Many of our staff have partnered over many years with our physicians to provide the best quality of care and service.

Because of them, our patient satisfaction is very high. Our physicians and staff together provide a very cohesive, experienced team.

You were recently recognized with an award from Blue Cross Blue Shield. What exactly was it?

Russell-Cook: Oklahoma Heart Institute Hospital was invited to apply for a Blue Distinction Center of Cardiac Care® designation by Blue Cross Blue Shield. Based on our scores, we received the first and one of only 2 designations in the whole state of Oklahoma. What it recognizes is high quality of care and value. It is an award of high distinction.

Oklahoma Heart Institute is a regional cardiology program that reaches throughout Northeastern Oklahoma. How have referring physicians from those outlying communities contributed to the OHI Hospital growth?

Russell-Cook: Our referral providers know that we will treat their patients courteously and provide the best results in a timely manner. They are an important part of our relationship with their patients.

Our physicians have a strong relationship with referring providers and work with them as a team to provide patients a continuum of cardiovascular care, from diagnostics and treatment all the way through to rehab. With 12 weekly outreach clinic locations, we routinely admit many patients from outlying areas who need more extensive treatment or a tertiary care facility.

What are some of the primary strengths of the hospital, and how does it differentiate itself from other hospital-based cardiology programs?

Russell-Cook: I think the specialty training of our physicians is distinctive in that it creates the team approach to handling what can be complex cases. In every area of cardiology and endocrinology, we have a specialist with extra years of dedicated training.

In the area of cardiac and vascular imaging, Oklahoma Heart Institute has the most sophisticated program in the state, from nationally certified nuclear, echo and CT facilities to an internationally recognized cardiac MRI program.

Also, we never turn away a heart attack patient. That's why we're here and we find a way to accommodate all heart patients.

Research is also an important part of our program. OHI has participated in landmark trials for the past 20 years, and many of these have greatly improved the quality of care available to patients. It gives them access to cutting-edge therapies that would otherwise take 5-10 years to become available in standard medical practices. Along with our physicians, five dedicated research nurses make ours a very active clinical research program.

Most importantly for our patients, we consistently provide great, quality results. That translates into superior patient care. And that's just what our patients want; it's the reason they trust their hearts to us.

What does the future hold for the Oklahoma Heart Institute Hospital?

Russell-Cook: Cardiology is a dynamic field that experiences periods of explosive, rapid growth. Our ongoing challenge is to be poised and ready to implement new technologies and procedures as they become available for patient care. Our physicians have the ability to optimize technology, and we will continue to stay at the forefront. We'll also continue recruiting and retaining physicians with the finest educations, training and credentials in their fields.

By servicing such a large and growing population, our challenge is continuing to meet the ongoing needs of the communities we serve. Prevention programs and screenings will be emphasized to help reduce the incidence of cardiovascular disease in Oklahomans. We will continue to work with outlying regional communities, providing care and prevention close to home and easy access to higher levels of care when needed. We'll grow the program, continue providing the highest quality patient care and elevate our international recognition as leaders in the field of cardiovascular diseases.

Elaine Burkhardt is a writer, editor and producer with Newsgroup Communications, a marketing firm in Tulsa, Okla.

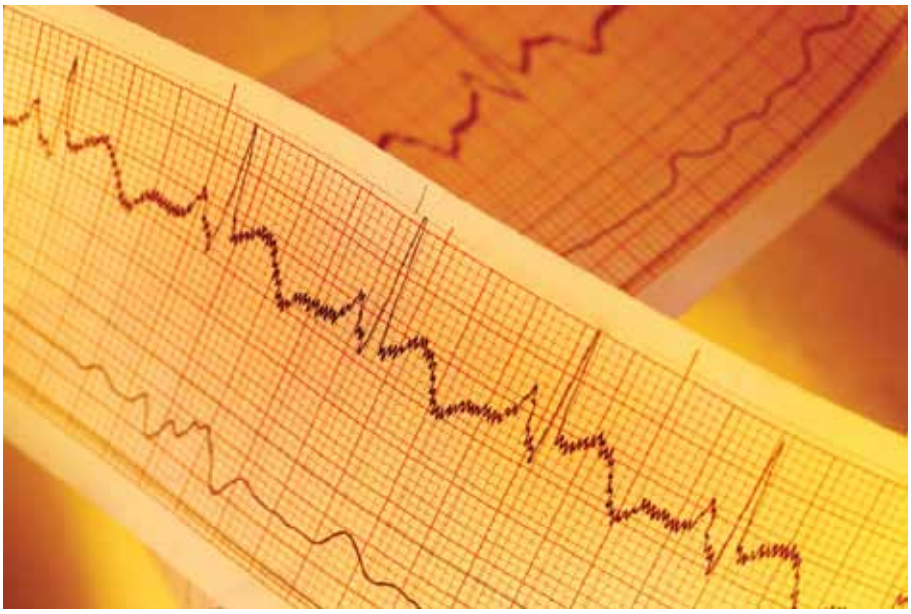
Continued from page 5

sus a 0.53% per year in the standard group. This had a P-value of 0.01, which was highly statistically significant.

There were no significant differences in non-fatal myocardial infarction or fatal myocardial infarctions between the two groups. The conclusions of the ACCORD Blood Pressure Trial investigators was that there was no conclusive evidence that the intensive blood pressure control strategy reduced the composite of major cardiovascular events in diabetic patients. However, there was a significant reduction in non-fatal and fatal strokes. This raises the issue that perhaps blood pressure control is more important in diabetics to reduce cerebral vascular events than cardiac events. The results of this trial were published in the New England Journal of Medicine online on 03/14/10.

A second study also questioned whether aggressive blood pressure goals should be followed in patients with diabetes mellitus. This study looked at patients with diabetes and coronary artery disease who had been randomized in the INVEST Trial (International Verapamil SR-Trandolapril Study). In the INVEST Trial, there were 5,077 patients who had diabetes mellitus as well as known coronary artery disease. The objective of the retrospective review was to determine the effect of increasing amounts of systolic blood pressure reduction on the adverse cardiovascular outcomes in a cohort of patients with the combination of diabetes mellitus and known coronary artery disease. The hypothesis was that diabetic patients who achieved systolic blood pressures less than 130mmHg (in accordance with current guidelines) would have reduced cardiovascular outcomes compared with diabetic patients who achieved systolic blood pressures of greater than 130 but less than 140mmHg. Patients were stratified as to whether or not they achieved tight control with systolic blood pressures less than 130mmHg, usual control with blood pressures between 130 and 140mmHg, and uncontrolled, those patients who did not get their systolic blood pressures less than 140mmHg. When evaluating patients for the primary outcome, which included fatal and non-fatal myocardial infarctions and strokes, it was found that patients who did not achieve blood pressure control (systolic blood pressure of less than 140mmHg) had significantly higher event rates as compared to patients who had been treated and had achieved either usual control or tight control.

However, when comparing patients with usual control (systolic blood pressures between 130 and 140mmHg) and tight control (systolic blood pressure less than 130mmHg), there was no significant difference between the groups at three years or five years in the combined primary outcome. When evaluating all-cause mortality, once again patients who did not achieve blood pressure control had a higher mortality rate than either of the treated groups. What was surprising was the tight control group had an increase in all-cause mortality as compared to the usual control group. The increase in all-cause mortality for the intensive control group was statistically significant with a P-value of 0.036. It should also be noted when the U.S. cohort was followed out to 12 years, the increased mortality in the tight control group persisted as compared to the usual blood pressure control group.



Perhaps blood pressure control is more important in diabetics to reduce cerebral vascular events than cardiac events.

The authors' conclusions were that as expected, diabetic patients with systolic blood pressures that were not controlled (blood pressures greater than or equal to 140mmHg) had the worst outcomes. However, tight control (systolic blood pressures < 130mmHg) was not associated with improved cardiovascular outcomes compared with usual control (blood pressures greater than or equal to 130 and less than 140mmHg). Systolic blood pressures of less than 115mmHg were associated with the highest risk for mortality. This finding poses the issue of the J-curve effect. where there may be increased CV events when the blood pressure is aggressively lowered in patients with coronary artery disease.

Based on these two studies, the authors have questioned whether we need to re-evaluate how aggressively we should be lowering blood pressures in diabetic patients, especially if they also have known coronary artery disease. Further studies will now be required in order to clarify this issue.

It is important to remember, however, that significant benefit was clearly demonstrated for those patients who achieved blood pressures goals of systolic blood pressures less than 140mmHg. Therefore, aggressive efforts should be made to get hypertensive patients to blood pressures at least less than 140mmHg systolic.

Wayne N. Leimbach, Jr. is an Oklahoma Heart interventional cardiologist specializing in cardiac catheterization, coronary angioplasty, percutaneous closure of PFOs & ASDs and related interventional procedures such as stents, atherectomy, laser, intravascular ultrasound imaging and direct PTCA for acute myocardial infarction.

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- Center for the Treatment of Venous Disease

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THE DOCTORS OF OKLAHOMA HEART INSTITUTE

Wayne N. Leimbach, Jr., MD, FACC, FSCAI, FCCP, FAHA

Dr. Leimbach is a specialist in interventional cardiology, including cardiac catheterization, coronary angioplasty, percutaneous closure of PFOs & ASDs and related interventional procedures such as stents, atherectomy, laser, intravascular ultrasound imaging and direct PTCA for acute myocardial infarction. He is Chief of Cardiology at Oklahoma Heart Institute Hospital, where he is also Director of the Cardiac and Interventional Laboratories. Dr. Leimbach is Co-Founder of the Lipid and Wellness Clinic at Oklahoma Heart Institute. He is Director of the James D. Harvey Center for Cardiovascular Research at Hillcrest Medical Center, as well as Director of the Oklahoma Heart Research and Education Foundation. He also serves as Clinical Associate Professor of Medicine at the University of Oklahoma College of Medicine – Tulsa. Dr. Leimbach completed a Clinical Cardiology Fellowship and a Research Fellowship at the University of Iowa Hospitals and Clinics. He also completed his Internal Medicine Internship and Residency programs at Iowa, where he was selected Chief Resident in Medicine. He received his medical degree from Northwestern University in Chicago and his Bachelor of Science degree from the University of Michigan.

Board certified in Internal Medicine, Cardiovascular Disease and Interventional Cardiology

Robert C. Sonnenschein, MD, FACC, ASE, RVT

Dr. Sonnenschein specializes in echocardiography and noninvasive peripheral vascular imaging. He is past Director of Peripheral Vascular Ultrasound Imaging at Hillcrest Medical Center and Oklahoma Heart Institute and serves as Clinical Associate Professor of Medicine at the University of Oklahoma College of Medicine – Tulsa. He completed his Cardiology Fellowship at the State University of New York Upstate Medical Center in Syracuse, where he also completed his Internal Medicine Internship and Residency programs. Dr. Sonnenschein received his medical degree from Rush Medical College in Chicago and his Bachelor of Arts degree from the University of Pennsylvania.

Board certified in Internal Medicine, Cardiovascular Disease, and Adult Echocardiography Registered Vascular Technologist

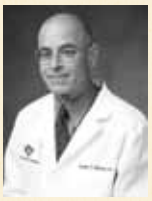
Robert E. Lynch, MD, FACC

Dr. Lynch is a specialist trained in noninvasive and invasive cardiology with a special interest in the prevention of cardiovascular disease. He is former Chief of Cardiology at Hillcrest

Medical Center, where he also has served as Chief of Medicine and President of the medical staff. Dr. Lynch is former Co-Director of the Lipid and Wellness Clinic at Oklahoma Heart Institute and Director of the Executive Health Program. Dr. Lynch is also a Clinical Assistant Professor at the University of Oklahoma College of Medicine – Tulsa. He completed his Cardiology Fellowship, as well as his Internal Medicine Internship and Residency, at the University of Oklahoma Health Sciences Center. Dr. Lynch received his medical degree from the University of Oklahoma School of Medicine and his Bachelor of Science degree from the University of Tulsa. Before establishing his practice in Tulsa, he served as Chief of Medicine at the U.S. Army Hospital, Bangkok, Thailand.

Board certified in Internal Medicine and Cardiovascular Disease

James J. Nemec, MD, FACC



Dr. Nemec is a specialist in echocardiography, stress echocardiography and nuclear cardiology. He serves as Director of Nuclear Cardiology for Oklahoma Heart Institute. Dr. Nemec has served as Assistant Professor of Internal Medicine, Division of Cardiology, at Creighton University and as Assistant Professor, Department of Radiology, also at Creighton University. He completed his Clinical Cardiology Fellowship at the Cleveland Clinic Foundation and his Internal Medicine Internship and Residency at Creighton University. Dr. Nemec also completed a year of training in pathology at the University of Missouri, Columbia, MO. He received his medical degree from Creighton University, where he also received his Bachelor of Arts degree.

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Dr. Johnsen is an interventional cardiologist with expertise in cardiac catheterization, angioplasty and related interventional procedures, such as stents and atherectomy. He is Director of Cardiac Rehabilitation at Hillcrest Medical Center and Director of the Hillcrest Exercise and Lifestyle Programs. He completed his Clinical Cardiology Fellowship at the University of Oklahoma – Oklahoma City, where he then finished an extra year of dedicated training in interventional cardiology. He completed his Internal Medicine Internship and Residency training at the University of Oklahoma – Oklahoma City, where he also received his medical degree. Dr. Johnsen received his Bachelor of Science degree from Oklahoma State University.

Board certified in Internal Medicine, Cardiovascular Disease and Interventional Cardiology

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Dr. Kaneshige is a noninvasive cardiologist with expertise in adult echocardiography, stress echocardiography and transesophageal echocardiography. He is past Chief of Cardiology at Hillcrest Medical Center. Dr. Kaneshige is also the Director of the Adolescent and Adult Congenital Heart Clinic at Oklahoma Heart Institute and Director of the Congestive Heart Failure C.A.R.E. Center at Oklahoma Heart Institute Hospital. Dr. Kaneshige completed his Internal Medicine Internship and Residency at Creighton University School of Medicine, where he also received his medical degree. He received a Bachelor of Science in chemistry at Creighton University. Dr. Kaneshige completed his Clinical Cardiology fellowship at Creighton, where he also served as Chief Cardiology Fellow for two years. He completed an additional Cardiac Ultrasound Fellowship at the Mayo Clinic in Rochester. Dr. Kaneshige served as Assistant Professor of Medicine at Creighton University School of Medicine, where he was Director of the Noninvasive Cardiovascular Imaging and Hemodynamic Laboratory.

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Edward T. Martin, MS, MD, FACC, FACP, FAHA

Dr. Martin is a noninvasive cardiologist with specialty expertise in non-invasive imaging. He is Director of Cardiovascular Magnetic Resonance Imaging at Oklahoma Heart Institute and Hillcrest Medical Center. In addition, he is a Clinical Associate Professor of Medicine at the University of Oklahoma College of Medicine – Tulsa. Dr. Martin has specialty training in Nuclear Medicine, as well as additional training dedicated to Cardiovascular Magnetic Resonance Imaging. He completed his Cardiology Fellowship at the University of Alabama. Dr. Martin's Internal Medicine Internship and Residency training were performed at Temple University Hospital in Philadelphia. He received his medical degree from the Medical College of Ohio. Dr. Martin completed his Master of Science degree in mechanical engineering at the University of Cincinnati and his Bachelor of Science degree in physics at Xavier University. Dr. Martin is a founding member of the Society of Cardiovascular Magnetic Resonance and is an editorial board member of the Journal of Cardiovascular Magnetic Resonance.

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Dr. Des Prez is a noninvasive cardiologist with specialty expertise in echocardiography, nuclear cardiology and cardiac computed tomography. He is Director of Cardiac Computed Tomography at Oklahoma Heart Institute Hospital, at Hillcrest Medical Center and Bailey Medical Center. Dr. Des Prez received his medical degree and Bachelor of Arts degree from Vanderbilt University. He completed his Residency in Internal Medicine and Pediatrics at University Hospital of Cleveland. Dr. Des Prez practiced for six years as an internist with the Indian Health Services in Gallup, NM. He returned to Vanderbilt University as a member of the Internal Medicine Faculty, at which time he also completed his cardiology training.

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Dr. Smith is a noninvasive cardiologist with specialty expertise in transthoracic echocardiography, transesophageal echocardiography, intraoperative echocardiography, stress and pharmacological echocardiography and contrast echocardiography. Dr. Smith is Director of the Echocardiography and TEE Departments at Oklahoma Heart Institute Hospital. She completed an Advanced Cardiac Imaging Fellowship at the Cleveland Clinic Foundation and her Cardiology Fellowship at the University of New Mexico Health Sciences Center, Albuquerque, NM. Dr. Smith's Internal Medicine Internship and Residency training were performed at the University of Arizona Health Sciences Center in Tucson. She received her medical degree from the Medical College of Ohio. Dr. Smith completed her Bachelor of Science degree at Cleveland State University.

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Tobie L. Bresloff, MD

Dr. Bresloff is a specialist in Endocrinology, Metabolism and Hypertension, with expertise in diabetes, lipids, hypertension and thyroid diseases. She also serves as Assistant Professor in Clinical Medicine at the University of Oklahoma College of Medicine -Tulsa and Chief Quality Officer at Hillcrest Medical Center. She completed an NIH Fellowship in Endocrinology and Metabolism at Vanderbilt University in Nashville, TN. Dr. Bresloff's Internal Medicine Internship and Residency were completed at Sinai Hospital of Detroit, Detroit, MI. She received her medical degree from Wayne State University School of Medicine in Detroit and her Master of Science and Bachelor of Science degrees at the University of Michigan, Ann Arbor, MI.

David A. Sandler, MD, FACC, FHRS

Dr. Sandler is a cardiologist with subspecialty expertise in electrophysiology, complex ablation, and atrial fibrillation management. Dr. Sandler is Director of Electrophysiology at Oklahoma Heart Institute Hospital. He completed his Cardiac Electrophysiology Fellowship and his Cardiovascular Medicine Fellowship at New York University Medical Center, New York, NY. Dr. Sandler performed his Internal Medicine Internship and Residency at Mount Sinai Medical Center, New York, NY. He earned his medical degree from Georgetown University School of Medicine in Washington, DC. Dr. Sandler received his Bachelor of Arts degree at the University of Pennsylvania in Philadelphia.

Board certified in Internal Medicine, Cardiovascular Disease and Cardiac Electrophysiology

Raj H. Chandwaney, MD, FACC, FSCAI

Dr. Chandwaney is an interventional cardiologist with expertise in cardiac catheterization, coronary angioplasty and related interventional procedures such as coronary stents, atherectomy, intravascular ultrasound and peripheral vascular interventional procedures. Dr. Chandwaney is Director of the Chest Pain Center and Cardiology Telemetry Unit at Oklahoma Heart Institute Hospital. He completed his Clinical Cardiology Fellowship at Northwestern University Medical School in Chicago, IL., where he also completed an Interventional Cardiology Fellowship. Dr. Chandwaney's Internal Medicine Internship and Residency were performed at Baylor College of Medicine in Houston, TX. He received his medical degree from the University of Illinois at Chicago. Dr. Chandwaney completed his Master of Science degree at the University of Illinois at Urbana-Champaign, where he also received his Bachelor of Science degree.

Board certified in Internal Medicine, Cardiovascular Disease, Interventional Cardiology and Endovascular Medicine

D. Erik Aspenson, MD, FACE, FACP

Dr. Aspenson is a subspecialist in Endocrinology, Metabolism and Hypertension at Oklahoma Heart Institute, with expertise in diabetes, lipids, hypertension and thyroid diseases. He completed a fellowship in Endocrinology at Wilford Hall Medical Center, Lackland AFB, Texas. Dr. Aspenson's Internal Medicine Internship and Residency were completed at David Grant Medical Center, Travis AFB, California where he served as Chief Resident. He received his medical degree from the University of Oklahoma and his Bachelor of Science degree at Oklahoma State University.

Board certified in Internal Medicine, Endocrinology and Metabolic Diseases

Frank J. Gaffney, MD, FACC

Dr. Gaffney is an invasive and non-invasive cardiologist with subspecialty expertise in transesophageal echocardiography, nuclear cardiology, and coronary angiography. He completed his Cardiovascular Medicine Fellowship at Scott & White Memorial Hospital in Temple, Texas. Dr. Gaffney completed his Internal Medicine Internship and Residency at Brooke Army Medical Center in San Antonio. He then remained on staff at Scott & White Memorial Hospital for several years, before entering his Fellowship in Cardiovascular Medicine. Dr. Gaffney earned his medical degree from New York Medical College, Valhalla, New York, and he received his Bachelor of Arts degree at Hofstra University in Hempstead, New York.

Board certified in Internal Medicine, Cardiovascular Disease and Nuclear Cardiology

Eric G. Auerbach, MD, FACC

Dr. Auerbach is a general cardiologist who is particularly interested in preventative cardiology and cardiovascular risk reduction. He completed his cardiology fellowship at the University of Miami/Jackson Memorial Hospital in Miami, FL, following which he obtained additional subspecialty training in cardiovascular MRI, nuclear cardiology, and cardiac CT imaging. His areas of expertise also include echocardiograpgy, transesophageal echocardiograpgy, stress testing, and management of lipid disorders. Dr. Auerbach's Internal Medicine Internship and Residency were performed at the University of Miami/Jackson Memorial Hospital. He earned his medical degree at the University of Miami, Miami, FL, and his Bachelor of Arts degree at Princeton University, Princeton, NJ.

Board certified in Internal Medicine, Cardiovascular Disease, and Nuclear Cardiology

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Dr. Flesner is a subspecialist in Endocrinology, Metabolism and Hypertension at Oklahoma Heart Institute, with expertise in diabetes, lipids, hypertension and thyroid diseases. Prior to joining Oklahoma Heart, she was at St. John Medical Center in Tulsa. She completed her fellowship in Endocrinology at the University of Texas at Galveston. Her Internal Medicine Internship and Residency were completed at the University of Texas in Houston, where she also received her medical degree. She earned her Bachelor of Science degree at Texas A&M University in College Station, TX.

Board certified in Internal Medicine, Endocrinology, Diabetes and Metabolic Diseases

Robert L. Smith, Jr., MSc, MD, FACC, FSCAI

Dr. Smith specializes in interventional cardiology including cardiac catheterization, coronary angioplasty, and related interventional procedures such as coronary stents, atherectomy, intravascular ultrasound, and peripheral vascular interventional procedures. He completed an Interventional Cardiology Fellowship at the University of Florida College of Medicine in Jacksonville, FL. Dr. Smith performed his Clinical Cardiology Fellowship at Vanderbilt University School of Medicine in Nashville, TN and Tulane University School of Medicine in New Orleans. He received his medical degree from the University of Oklahoma College of Medicine in Oklahoma City and then completed his Internal Medicine Internship and Residency at Emory University School of Medicine in Atlanta, GA. Dr. Smith received his Bachelor of Arts, Bachelor of Science and Master of Science degrees at the University of Oklahoma in Norman, OK.

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Dr. Cameron is a specialist in cardiac electrophysiology, including catheter ablation of arrhythmia, atrial fibrillation management, pacemakers, implantable defibrillators, and cardiac resynchronization devices. He completed his Cardiac Electrophysiology Fellowship and his Cardiovascular Disease Fellowship at Baylor University Medical Center in Dallas, TX. Dr. Cameron's Internship and Internal Medicine Residency were performed at Baylor College of Medicine in Houston. He earned his medical degree from the University of Kansas School of Medicine in Kansas City, KS. Dr. Cameron received his Bachelor of Science degree at Pittsburg State University in Pittsburg, KS.

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Eugene J. Ichinose, MD, FACC

Dr. Ichinose specializes in interventional cardiology including cardiac catheterization, coronary angioplasty and related interventional procedures such as coronary stents, atherectomy, intravascular ultrasound and peripheral vascular interventional procedures. He completed his Interventional and Clinical Cardiology Fellowships and his Internal Medicine Residency at the University of Massachusetts Memorial Health Care Center in Worcester, MA. Dr. Ichinose received his medical degree from Louisiana State University in New Orleans. He earned his Bachelor of Science degree from Texas Christian University in Fort Worth, TX.

Board certified in Internal Medicine, Cardiovascular Disease, Interventional Cardiology and Nuclear Cardiology

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Dr. Bruns is a specialist in Endocrinology, Diabetes and Metabolism at Oklahoma Heart Institute, with expertise in diabetes, thyroid disease (including thyroid cancer) and polycystic ovary syndrome. She completed her Internal Medicine Internship and Residency and Endocrinology Fellowship at the University of Wisconsin Hospital and Clinics in Madison, WI. Dr. Bruns earned her medical degree from Saint Louis University School of Medicine in St. Louis, MO and her Bachelor of Arts and Bachelor of Science degrees in biology from Truman State University in Kirksville, MO. Prior to joining Oklahoma Heart Institute, Dr. Bruns worked as a clinical endocrinologist at the Dean Clinic in Madison, Wisconsin.

Board certified in Internal Medicine, Endocrinology and Metabolic Diseases

Gregory A. Cogert, MD, FACC

Dr. Cogert is a cardiologist who specializes in electrophysiology, including catheter ablation of arrhythmia, as well as the implantation and management of cardiac pacemakers, defibrillators, and cardiac resynchronization devices. He completed his Cardiac Electrophysiology Fellowship at Mayo Clinic in Rochester, MN and his Cardiovascular Fellowship at Cedars-Sinai Medical Center in Los Angeles, CA. Dr. Cogert's Internal Medicine Internship and Residency were completed at UCLA Medical Center in Los Angeles. He earned his medical degree from the University of California in Irvine and received his Bachelor of Science degree in microbiology and molecular genetics from the University of California in Los Angeles.

Board certified in Internal Medicine, Cardiovascular Disease, Echocardiography, Nuclear Medicine and Cardiac Electrophysiology.

John S. Tulloch, MD, FACC

Dr. Tulloch is a noninvasive cardiologist with expertise in adult echocardiography, peripheral vascular imaging, nuclear cardiology, cardiac computed tomography and MRI. He completed his Cardiovascular Fellowship at the University of Kansas Medical Center in Kansas City, KS. Dr. Tulloch's Internal Medicine Internship and Residency also were completed at the University of Kansas Medical Center. He earned his medical degree from Ross University School of Medicine in New Brunswick, NJ and received his Bachelor of Science degree in biology from Avila University in Kansas City, MO.

Board certified in Internal Medicine, Cardiovascular Computed Tomography, and Nuclear Cardiology

Anthony W. Haney, MD

Dr. Haney is a noninvasive cardiologist with expertise in nuclear cardiology, echocardiography, peripheral vascular imaging and MRI. He also performs diagnostic cardiac catheterization. He completed his Cardiovascular Fellowship at the Medical College of Virginia in Richmond. Dr. Haney's Internal Medicine Internship and Residency were completed at the Mayo Clinic in Scottsdale, AZ. He earned is medical degree from the University of Oklahoma School of Medicine.

Board certified in Internal Medicine, Cardiovascular Disease and Nuclear Cardiology

Ralph J. Duda, Jr., MD

Dr. Duda is a specialist in Endocrinology, Diabetes and Metabolism at Oklahoma Heart Institute, with expertise in diabetes, lipids, hypertension and thyroid diseases. He completed his Fellowship in Endocrinology and Metabolism at the Mayo Graduate School of Medicine, where he also completed his Residency in Internal Medicine. Dr. Duda received his medical degree from Northwestern University School of Medicine in Chicago, IL. He earned his Bachelor of Science degree from Benedictine University in Lisle, IL.

Board certified in Internal Medicine, Endocrinology, Diabetes and Metabolism, Clinical Lipidology, Clinical Hypertension, Clinical Bone Densitometry and Thyroid Ultrasonography

The Parallel Epidemics of Vitamin D Insufficiency and The Cardiometabolic Syndrome – Coincidence or Causal?

By Ralph J. Duda, Jr., MD

The Cardiometabolic Syndrome (CMS) reflects a constellation of metabolic abnormalities giving rise to enhanced atherogenesis and subsequent rise in myocardial infarction and stroke. Common characteristics of CMS, as defined by organized agencies (WHO, NCEP-ATP III) include dyslipidemia (hypertriglyceridemia, hypo-HDL-emia), hypertension, visceral-centered obesity, and dysglycemia. While the genetic and environmental connections to this syndrome have been well studied and cannot be refuted, it is intriguing that the discovery of an alarming prevalence of vitamin D insufficiency has followed on the heels of the epidemic climb of CMS. Could it not be conceivable that the changing nature of the modern day diet coupled with reduced outdoor recreation has allowed for the emergence of a basic nutritional deficiency state giving rise to factors that accelerate atherosclerosis?

CMS is a major public health problem. The NHANES database, obtained between 1988 and 1994, confirmed that the age-adjusted prevalence of CMS was 24% of the U.S. population, and increased from 7% in 20-year-olds to 45% in subjects greater than 60 years of age. Latest NHANES data also cites that prevalences in both men and women are continuing to increase.

Recent surveys indicate that between 40 to 45% of elderly Americans and greater than 50% of American postmenopausal women have vitamin D insufficiency/deficiency. Prevalence rates also increase with age. This is thought to be due to reduced skin 7-dehydrocholesterol, a precursor of vitamin D_3, from reduced sun exposure (specifically, UV-B radiation) from residencies in northern latitudes, prolonged winter seasons, and use of SPF lotions, as well as reduced nutritional sources of vitamin D_2 and D_3 (Figure 1). Most humans synthesize sufficient vitamin D without dietary supplementation. However, pigmented skin requires additional sun exposure to activate vitamin D precursors.

While 1, 25-OH-D is the major active form of the vitamin and the final product following renal hydroxylation of 25-OH-D, it is the 25-OH-D levels that are the best indicators for sufficiency since it serves as the body's siphon for the vitamin in the circulation and has the longest half-life. Cardiomyocytes also express 1-alpha hydroxyglase and activate 25-OH-D locally, but this conversion depends on cytokine activation and nascent serum 25-OH-D levels. In addition, myocardial dysfunction has been associated with vitamin D deficiency in vitamin D receptor knockout models. Vitamin D deficiency is defined as a level of 25-OH-D less than 20 ng/mL, and insufficiency is recognized when levels fall below 30 ng/dL. Redefining daily vitamin D intake is currently being addressed (Table 1 and Table 2). Debatable issues include how normals should be defined in a specific population/location/season and whether raising 25-OH-D contributes to clinical benefit. There are not, as yet,

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Figure 1
Synthesis and Effects of Vitamin D

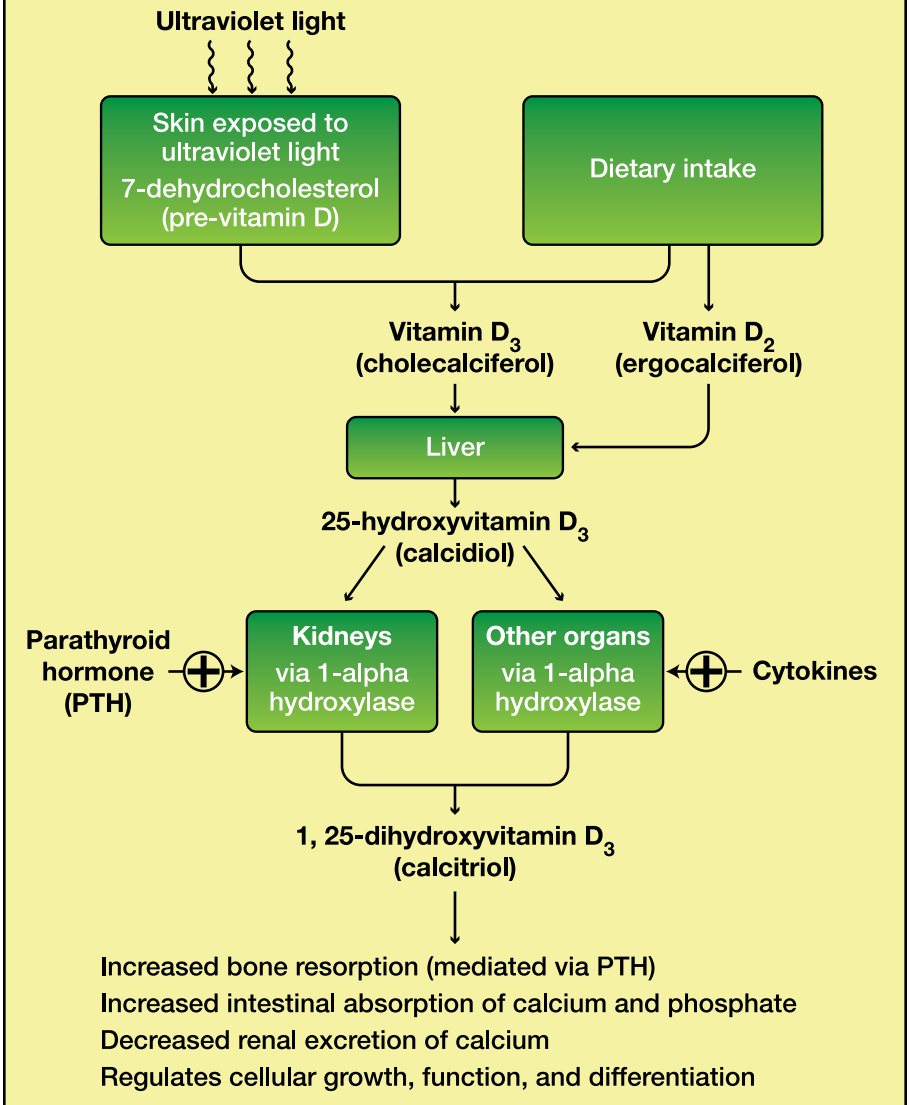

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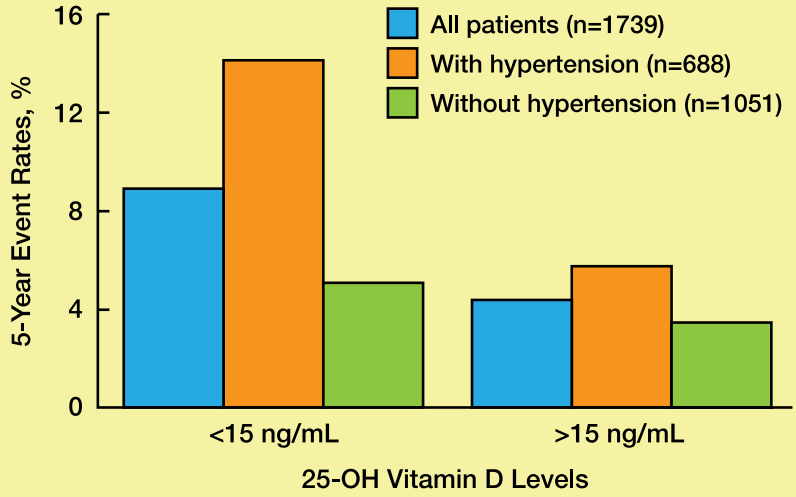
Figure 2

Five-year cardiovascular event rates (%) according to varying levels of 25-hydroxyvitamin D in the Framingham Offspring Study. Rates were adjusted for age and sex and grouped according to the presence or absence of hypertension. Modified with permission from Wang et al.



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definable biomarkers in the cardiovascular and immune systems reflecting vitamin D adequacy.

The role of vitamin D in calcium metabolism is well known. Recent data also supports integral roles of vitamin D in immune and neuromuscular functions. The association of vitamin D deficiency with diabetes, hypertension, and CMS has been less well appreciated until recently. In the Framingham Offspring Study, patients followed for a median of 5.4 years had a higher relative risk of a cardiovascular event if they had low vitamin D levels. The risk of an event increased by 2.13 in patients with hypertension and 25-OH-D levels less than 15 ng/mL. The risk is comparable to that defined by the Framingham-derived risk ratio, if the patient had CMS, hypertension, dyslipidemia, hyperfibrinogenemia, or homocysteinemia (Figure 2)[2].

Data from the Health Professionals Followup Study and the Nurses Health Study derived from 117,730 patients with a median followup of 4 years found an inverse correlation of vitamin D levels and blood pressure. When comparing patients whose 25-OH-D fell less than 15 ng/mL against those patients whose levels were greater than 30 ng/mL, the relative risk of hypertension was an astronomic 3.18 with a marked sex difference (6.13 in men and 2.67 in women). Further, low 25-OH-D levels are correlated with high prevelances of both heart failure and ASHD[3].

Putting bench research into play, vitamin D receptor knockout mice have plasma renin and angiotensin II levels 2.5 times higher than wild-type mice and secondarily developed hypertension and cardiomyopathy. Vitamin D has since been found to directly suppress renin by reducing renin mRNA transcription[4]. Experiments using transgenic mice also brought to light a 30% suppression of renin when vitamin D receptor-positive renin-producing cells were manipulated with vitamin D (Figure 3). Thus the interrelationship between vitamin D and renin expression is strong. In addition, there is further evidence in animals that vitamin D directly inhibits vascular smooth muscle cell proliferation by altering epidermal growth factor receptor response, and that vitamin D improves endothelial function by reducing endothelial-derived contractile factors in the aorta. Vitamin D receptors are ubiquitous in the human body and are especially present in vascular smooth muscle, myocytes, juxtaglomerular renal cells, and leukocytes, where input into cardiovascular integrity can have paracrine importance. In humans, raising 25-OH-D from an average of 6 mg/dL to 28 mg/dL caused a 4 mmHg reduction in pulse pressure in patients greater than 50 years of age (NHANES-III), suggesting a direct blood pressure response through mechanisms affecting arterial stiffness and compliance. Krause, et al, found that UV-B given 3 times weekly raised 25-OH-D by 162% and decreased mean blood pressure by an average of 6/6 mmHg by 24-hour ambulatory blood pressure monitoring studies[5]. Finally, Pfeifer, et al., did comparison trials with 145 elderly women greater than 70 years of age given 8 weeks of the calcium supplement without vitamin D versus calcium supplements with 800 IU of vitamin D. Women given calcium alone experienced a 5.7/6.9 mmHg drop, while women given the additional vitamin D dropped 13.1/7.2 mmHg from baseline, and a rise from 25.6 nM/mM to 64.8 nM/mM of 25-OH-D[6].

A cross-sectional study by Maki, et al., was reported recently to assess the relationship between 25-OH-D and selected markers of CMS in adult men and women[7]. In 257 subjects, anthropometric measurements and blood pressure were measured, dietary intake was assessed, and fasting blood for vitamin D levels were assayed. Dietary and supplemental vitamin D intake were associated directly with 25-OH-D tertiles. The mean serum HDL increased in a graded fashion ($P < 0.001$) from the lowest (48.4 +/- 1.8 mg/dL) to the highest (62.3 +/- 2.1 mg/dL) 25-OH-D tertile, and the relationship between 25-OH-D and HDL-C remained significant ($P<0.001$) after adjustment for established determinants of HDL-C with each 10 ng/mL increase in 25-OH-D associated with 4.2 mg/dL rise in HDL-C. Serum triglycerides ($P < 0.008$), waist circumference ($P < 0.001$), and body mass index ($P < 0.001$) showed graded inverse relationship with 25-OH-D tertiles, and the prevalence of CMS decreased significantly from the lowest to the highest 25-OH-D tertile (31%, 14%, and 10% respectively with P value for trending equal to 0.001).

Table 1

Recommended Daily Vitamin D Intake for Men and Women

Age (Years)[a]	Adequate Intake (IU)[b]	Tolerable Upper Intake (IU)[c]
14-18	200	2,000
19-50	200	2,000
50-70	400	2,000
>70	600	2,000

[a] Recommendations are the same for pregnant or lactating women.

[b] "Adequate intake" refers to the recommended daily intake of vitamin D to maintain bone and calcium in healthy individuals and assumes that vitamin D is not synthesized by exposure to ultraviolet light. A recommended daily allowance has not been established due to insufficient evidence.

[c] "Tolerable upper intake" refers to the maximum daily intake associated with the fewest adverse effects.

Institute of Medicine, Food and Nutrition Board. Dietary Reference Intakes: Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. Washington, D.C.: National Academy Press, 1997.

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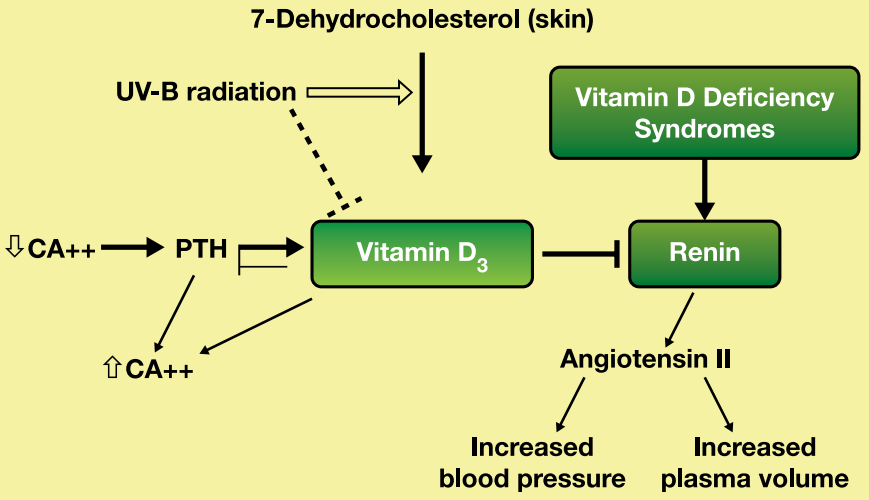
Since much has been written regarding the heterogeneity and differential functionality of HDL-C itself, despite its sound assayable reproducibility and relative refractoriness to treatment, Kaylaushaite, et al., recently reported in 78 Chicagoland women, a strong correlation between 25-OH-D and HDL-C particle size, inferring at least theoretically, an atheroprotective conferral with vitamin D-promoting formation of large HDL particles independent of race, season, and total HDL-C in a multivariable adjusted regression model. Each 5 mcg/L higher 25-OH-D predicted a 0.57 mM/L higher amount of large HDL-subclass. The association of large HDL-subclass with 25-hydroxy D can be the link to understanding the cardioprotective effects of vitamin D.

Not only is it known that macrophage function is regulated by vitamin D, but vitamin D may be found to be key in the atherogenic process by its effect on up-regulating the efficiency of reverse cholesterol transport due to its selective effects on HDL subclass and functionality, an association that is independent of total body fat mass and subcutaneous abdominal fat mass (but partially confounded by visceral fat mass by measurement of fat by DEXA). If increasing 25-OH-D is found to promote large HDL particle formation by interventional studies, and thus stimulate reverse cholesterol transport with proven endpoint reduction, it would begin to serve Koch's postulates and provide an attractive target for single and inexpensive interventional therapy for reducing cardiovascular events, and render further understanding about the temporal relationships involved in the evolution of CMS and type 2 diabetes mellitus in the last 30 years.

In practice, Vitamin D behaves more like a hormone than a vitamin, and its myriad effects on cellular function and differentiation, inflammation, and other hormones may help prevent hypertension, protect the kidneys by suppressing RAAS, reduce CHF, prevent secondary hyperparathyroidism and its effects on vascular stiffness, reduce insulin resistance, suppress vascular inflammation through cytokine intermediaries, and facilitate reverse cholesterol transport. Future elucidation of vitamin D's exact roles on these horizons remains anticipatingly encouraging and intriguing.

Figure 3

Schema for the relations among vitamin D, vitamin D deficiency, the renin-angiotension-aldosterone system, and hypertension.



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[1]*Tishkoff DX, et al, VDR Knockout Cardiomyocyte Contractility. Endocrinology 2008; 149:558-564.*

[2]*Kim DH, et al, Prevalence of Hypovitaminosis D in CVD (N Hanes, '01 – '04), American Journal of Cardiology 2008; 102:1540–1544.*

[3]*Wang TJ, et al, Vitamin D Deficiency and Risk of CVD, Circulation 2008; 117:503–511.*

[4]*Li YC, et al, 1, 25 Dihydroxyvitamin D_3 is a Negative Endocrine Regulator of RAAS and Blood Pressure, Journal of Investigation 2002; 110: 229-238.*

[5]*Krause R, et al, Ultraviolet B and Blood Pressure, Lancet 1998; 352:709-710.*

[6]*Pfeifer M, et al, Effects of Vitamin D_3 and Calcium Supplementation on Blood Pressure and PTH in Elderly Women, Journal of Clinical Endocrinology & Metabolism 2001; 86:1633-1637.*

[7]*Maki K, et all, Serum 25-OH-D is Independently Associated with HDL and CMS in Men and Women, Journal of Clinical Lipidology, 2009; 3, #4: 289-295.*

Table 2

Common Causes of Vitamin D Deficiency

Cause	Reason
Age	Reduction in precursor of vitamin D (7-dehydrocholesterol) in skin; particularly in individuals >70 y
Chronic liver disease	Impaired hydroxylation of 25-hydroxyvitamin D
Chronic renal disease	Impaired hydroxylation of 1,25-dihydroxy-vitamin D
Malabsorption	Reduced bioavailabilty of vitamin D
Obesity	Increased confiscation of vitamin D in body fat cells
Reduction in UV light	UV-B radiation is required for conversion of 7-dehydrocholesterol to vitamin D_3 in skin; associated with the northern latitudes and winter season
Skin pigments (melanin)	Melanin absorbs UV-B radiation (important in dark-skinned ethnicities)
Sunscreens (sun protection)	Absorbs UV-B radiation factor 30 or higher

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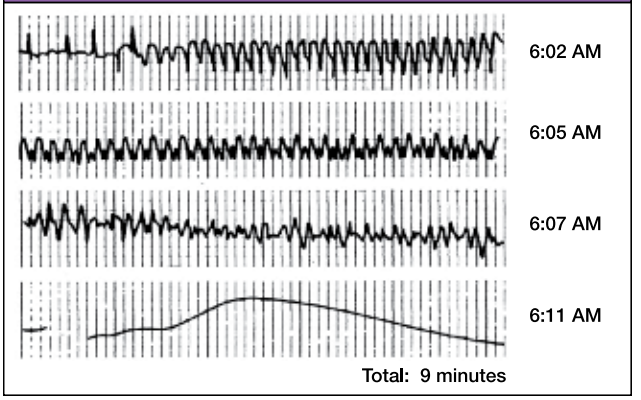
State of the Art Treatment of Ventricular Tachycardia and Sudden Cardiac Death

By Gregory Cogert, MD, FACC

Sudden cardiac death is the leading cause of death in the United States. It accounts for more deaths than stroke, lung cancer, and breast cancer combined. Sudden cardiac death is the direct result of ventricular tachycardia (VT). Figure 1 depicts the typical progression from normal electrical conduction in the heart to VT and cardiac arrest within nine minutes. Symptoms of VT that may be a harbinger of sudden death include palpitations, light-headed or dizzy spells, loss of consciousness, or seizures. In most cases, these symptoms warrant an evaluation of heart function. If the heart is found to be damaged or VT is seen on a heart monitor, treatment is required.

Figure 1
Onset of Ventricular Tachycardia with Rapid Progression to Sudden Cardiac Death



The cornerstone of treatment of VT is to electrically shock the heart and reset its electrical activity. Traditionally this treatment has been provided by emergency medical providers using an external defibrillator applied to the chest of the VT victim. Unfortunately, in the majority of sudden death cases, the rapid progression of VT does not allow time for emergency medical services to practically provide this therapy. Over the past thirty years, the implantable cardioverter defibrillator (ICD) has revolutionized the treatment of VT and sudden death. Currently, implanted models are capable of diagnosing and treating VT in less than 30 seconds.

Although ICDs are highly effective at acutely treating VT and saving lives, they do not address the underlying pathology responsible for this arrhythmia and thus do not prevent VT. Additionally, the ICD delivered electrical shocks often required to treat VT are painful. ICDs have proven in multiple clinical research trials to prolong the quantity of life in patients with VT, but have not been successful improving their quality of life. Conversely, research suggests that receiving ICD therapies results in a depressed quality of life and psychological stress. For this reason, patients who receive appropriate ICD therapy often require an additional treatment modality.

Medical therapy in the form of antiarrhythmic medication has proven of limited benefit for VT. Efficacy is incomplete and these medications may result in a paradoxical increase in VT. Additionally, medication interactions and extensive side effects preclude their use in certain patients. Alternatively, catheter ablation of VT is rapidly becoming a suitable and often superior therapy to reduce ICD shocks.

Catheter ablation of VT is a procedure performed at specialized centers across the country by an electrophysiologist. The goal of catheter ablation is to uncover the cause of VT in a patient's heart and eliminate its capacity for the rhythm. Over 95% of patients who develop VT have suffered some previous damage to the heart. Most commonly this is in the form of a heart attack. During a myocardial infarction, an obstructed coronary artery deprives blood from

Figure 2
Substrate Guided Ablation of Unstable Ventricular Tachycardia.

Left: Ventricular tachycaradia exiting inferior wall myocardial infaction scar.

Right: Electroanatomic substrate map of the left ventricle: normal tissue (purple), damaged tissue (red), ablation (maroon dots) of abnormally conducting channels within damaged tissue successfully eliminate ventricular tachycardia.

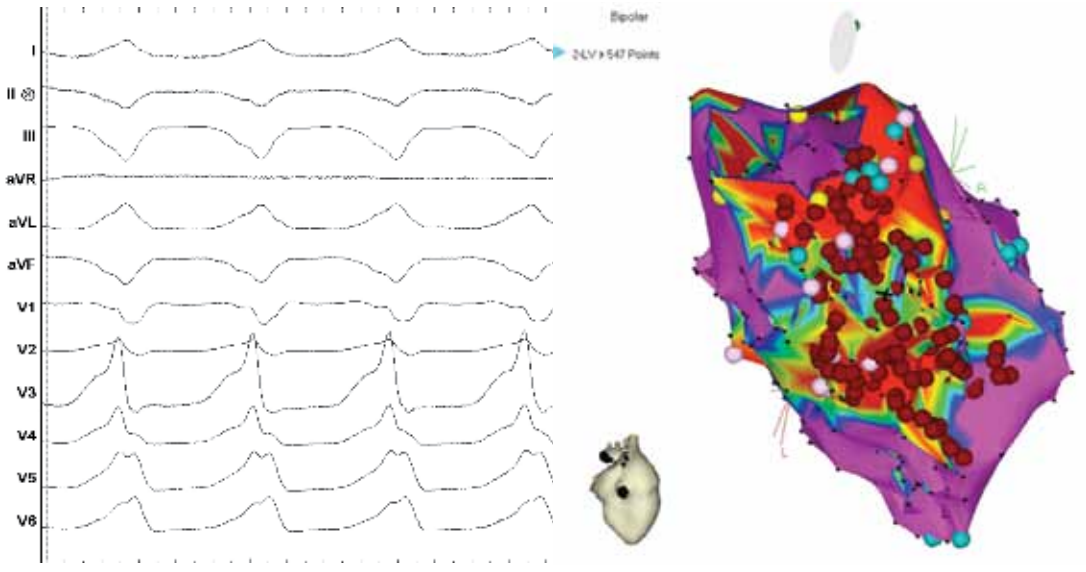
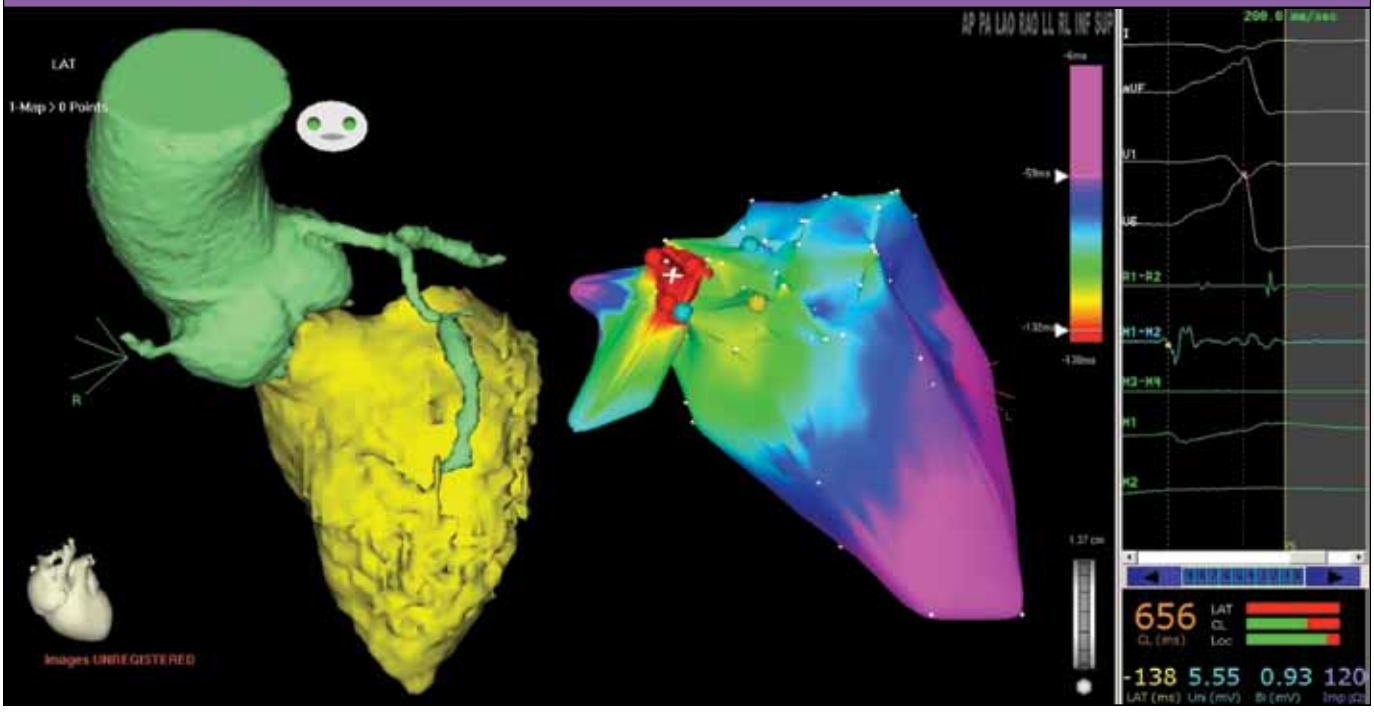


Figure 3

3-Dimensional image integration of CT scan (left), electroanatomic data (middle), and local electrogram (right) to localize focal ventricular tachycardia to the left coronary cusp of the aorta. On the electroanatomic map, the earliest activation is in red progressing to late activation in purple. Successful ablation locations (maroon dots) are shown.



a portion of the heart resulting in cell death and ultimately scar formation. These scars disrupt the normal flow of electricity through the heart muscle. Within these scars are channels of surviving heart tissue that permit the abnormal flow of electricity. In most cases, VT results from electrical conduction through these abnormal channels setting up a short circuit of continuous electrical activation in the heart. The electricity travels along these channels within the scarred heart tissue prior to exiting to activate the heart in an abnormal and inefficient manner. After activating the heart, the electricity travels back into these abnormal scar channels only to exit again prior to the requisite relaxation time needed for the heart to adequately pump blood. The heart is thus continuously electrically activated without supplying the organs of the body with blood. Without treatment or a fortuitous spontaneous termination of VT, loss of consciousness will ensue in seconds followed shortly thereafter by death.

The VT ablation procedure is performed in the electrophysiology procedure room under sedation or general anesthesia. X-ray fluoroscopy, intracardiac ultrasound, and 3-dimensional electroanatomic mapping are integrated to define VT circuits in the heart. Once identified, abnormal tissues in the heart are targeted for radiofrequency ablation to eliminate VT. The procedures generally last from 3-6 hours, depending on the number of abnormal electrical circuits identified and ease of eliminating them. Figure 2 shows an example of substrate-guided ablation of unstable VT. This patient had a previous myocardial infarction involving the inferior wall of the left ventricle. The 12-lead ECG (left) confirms the induced tachycardia is identical to the VT afflicting this individual. The voltage map of the left ventricle (right) shows normal tissue in purple and scar tissue in red. Ablation (red areas) was performed along the abnormal conducting channels within the scar to eliminate VT. After ablation, no further VT could be induced. This patient, once plagued with multiple ICD shocks, has returned to a high quality of life with no recurrent VT.

Less commonly, VT can arise from a focal location rather than abnormally conducting scar channels. Figure 3 is from a patient with VT arising from a focal source of abnormal tissue. In this case, 3-dimentional image integration of a computed tomography (CT) scan, electroanatomic activation map, and local electrical data were used to localize the source of VT to the left coronary cusp of the aorta. On the electroanatomic activation map, the site of earliest activation is red and progresses to late activation in purple. Successful ablation locations (red dots) are shown.

Catheter ablation of VT is a well-tolerated procedure in the majority of cases, despite the critically ill nature of these patients. In the recently published Euro-VT study[i], there was a 1.5% risk of major complication. Success rates are variable depending on the severity of underlying heart disease. Success rates exceed 90% when minimal heart disease is present, but decline to 50-75% at 6-12 months in patients with extensive previous heart damage. The majority of patients with recurrent VT will experience >75% reduction in VT burden translating to less ICD therapies and an improved quality of life[ii].

In summary, sudden cardiac death is the most common cause of death in this country and is the result of ventricular arrhythmia. ICDs are highly effective in saving lives in patients at risk for sudden death. ICDs do not treat the cause of VT or improve the quality of life in these patients. Medications are often not effective or tolerated in treating VT. Catheter ablation of VT is offered at highly specialized centers such as the Oklahoma Heart Institute Hospital. Ablation is a safe and effective option to eliminate or significantly reduce VT in the majority of patients and should be considered early in the course of this disorder.

Gregory A. Cogert is a cardiologist at Oklahoma Heart Institute who specializes in electrophysiology, including catheter ablation of arrhythmia, as well as the implantation and management of cardiac pacemakers, defibrillators, and cardiac resynchronization devices.

[i] Tanner H, Hindricks G, Volkmer M, et. al., Catheter Ablation of Recurrently Scar-Related Ventricular Tachycardia Using Electroanatomical Mapping and Irrigated Ablation Technology: Results of the Prospective Multicenter Euro-VT-Study, J Cardiovasc Electrophysiol 2010, 21:47-53.

[ii] Tung R, Boyle N, Shivkumar K, Catheter Ablation of Ventricular Tachycardia, Circ 2010, in press.

LATE-BREAKING CLINICAL TRIALS:

Highights from the Oklahoma Heart Research and Education Foundation Symposium — Spring 2010

By Wayne N. Leimbach, Jr., MD, FACC, FSCAI, FCCP, FAHA

Each year at the Oklahoma Heart Research and Education Foundation Spring Symposium, highlights from recently released late-breaking clinical trials are presented. These randomized double blind clinical trials may have an impact on how physicians treat their patients. Highlights from some of these trials will be discussed.

Clopidogrel and Proton Pump Inhibitors:

Over the past two years a significant controversy has developed as to whether proton pump inhibitors can be used safely with the anti-platelet agent clopidogrel. Two very large randomized clinical trials look at this issue.

Each year in the United States, over 900,000 patients receive intracoronary stents for the treatment of coronary artery disease. Dual anti-platelet therapy using aspirin and a thiopyridine such as clopidogrel are essential therapies to prevent stent thrombosis. Proton pump inhibitors are often administered with dual anti-platelet therapy for gastric protection to prevent significant GI bleeding. Ex vivo studies have shown diminished platelet inhibition in response to clopidogrel in the presence of a proton pump inhibitor such as omeprazole. Such recent studies have raised concerns that proton pump inhibitors may attenuate the clinical benefits of clopidogrel and place patients at increased risk of sub-acute stent thrombosis. In fact, the FDA issued a black box warning for clopidogrel. As of 5-29-09, "the product information for all clopidogrel containing medicines shall be amended to discourage concomitant use of proton pump inhibitors unless absolutely necessary". To examine the association between proton pump inhibitor use and the risk of cardiovascular events for patients on either clopidogrel or prasugrel (Effient), the data from the TRITON-TIMI 38 Trial was analyzed to see whether or not the concomitant use of a proton pump inhibitor placed patients at increased risk of cardiovascular events. The TRITON-TIMI 38 Trial evaluated 13,608 patients undergoing percutaneous coronary interventional procedures for either acute coronary syndromes or planned elective interventions. All patients were treated with aspirin and then randomized in a double blind fashion to receive either prasugrel or clopidogrel. The primary end point of the study was cardiovascular death, MI, or stroke, and the patients were followed for a medium duration of therapy of 14.5 months. Proton pump inhibitor use was at the discretion of the treating physician and was captured on the case report forms at each patient visit. 4,529 patients (33% of the study population) received proton pump inhibitors. The proton pump inhibitors used included pantoprazole (Protonix) in 40% of patients, omeprazole (Prilosec) in 37%, esomeprazole (Nexium) in 14%, lansoprazole (Prevacid) in 9.7%, and rabeprazole (AcipHex) in 1.5%. When the primary end point of CV, death, MI, or stroke was analyzed, it was found that there was no difference in end points between those patients who were on dual anti-platelet therapy with a proton pump inhibitor versus those who were not on a proton pump inhibitor (Figure 1). Specifically, in regards to the use of clopidogrel with a proton pump inhibitor, there were absolutely no significant differences in outcomes whether the patients were on a proton pump inhibitor or not on a proton pump inhibitor. In conclusion, in the TRITON-TIMI 38 Trial, proton pump inhibitor use was not associated with an increased risk of cardiovascular events for patients on either clopidogrel or prasugrel. These findings did not support the need to avoid concomitant use of proton pump inhibitors in patients treated with thiopyridines along with aspirin for the prevention of stent thrombosis (this trial was published in the Lancet online September 1, 2009).

A second large trial addressing the issue as to whether it is safe to use proton pump inhibitors in patients on aspirin and clopidogrel for the prevention of sub-acute stent thrombosis was the COGENT Trial. This trial specifically looked at whether the proton pump inhibitor omeprazole would significantly inhibit the anti-platelet effects of clopidogrel in patients who receive an intracoronary stent. The rationale for this trial was that clopidogrel is a pro-drug and requires conversion by the liver to form its active metabolite. The conversion by the liver uses the CYP2C19 enzymatic pathway. Omeprazole is a strong inhibitor of the CYP2C19 pathway. In the OCALA Study published in the Journal of American College of Cardiology in 2008, in vitro trial data suggested that there was a decrease in platelet inhibition when omeprazole was used with clopidogrel.

The COGENT Trial was designed to determine if there was any cardiovascular interaction between clopidogrel and the proton pump inhibitor omeprazole, and to also determine whether proton pump inhibitor versus placebo use significantly reduced GI events in patients on dual anti-platelet therapy, since this was the major rationale for using the proton pump inhibitors. The COGENT Trial was a multi-center international randomized double blind, double dummy, placebo controlled parallel group efficacy and safety study. It randomized patients to receive clopidogrel 75mg a day plus omeprazole 20mg a day versus clopidogrel 75mg a day with placebo. The GI end point consisted of significant GI bleeding, which included upper GI bleeding with a decrease in hemoglobin of greater than 2 grams/dl, symptomatic gastric duodenal ulcer confirmed by endoscopy or radiography, or pain of presumed GI origin with underlying multiple gross ulcerative disease lesions confirmed by endoscopy obstruction or perforation. The cardiovascular end point was the composite of cardiovascular death, non-fatal MI, need to have bypass graft surgery or percutaneous coronary interventional procedure or ischemic stroke. Over 3,500 patients were randomized in this trial to receive clopidogrel with a proton pump inhibitor or placebo. Follow up evaluation at one year showed there was no significant difference in the composite primary outcome (Figure 2). In addition, there were no significant differences in myocardial infarctions or in the need for revascularization in those patients treated with a proton pump inhibitor versus placebo. Sub-group analysis failed to identify any group that was at increased risk for cardiovascular events by being on a proton pump inhibitor versus placebo.

The study did, however, demonstrate that there was significantly greater risk of serious GI bleeding in those patients treated with placebo instead of the proton pump inhibitor (Figure 3). There was a 45% reduction in serious GI bleeding with the use of the proton pump inhibitor and the P-value was highly significant at 0.007.

The COGENT Trial was the first randomized trial that assessed the use of clopidogrel and proton pump inhibitors and clinical events. The data provided strong reassurance that there are no clinically relevant adverse cardiovascular interactions between clopidogrel and proton pump inhibitors. The results call into question the exact relationship between Ex vivo platelet studies and clinical outcomes, especially with respect to assessing drug interactions.

Both the TRITON-TIMI 38 Trial and the COGENT Trial do not support a prohibition of the use of proton pump inhibitors with dual anti-platelet therapy using clopidogrel in patients receiving coronary stents. However, there still remains a black box warning for clopidogrel in regards to this issue. Therefore, physicians will need to assess the risk of bleeding in patients receiving dual anti-platelet therapy with aspirin and clopidogrel, and if the patient is felt to be at increased risk of bleeding, then it may still be worthwhile to use a proton pump inhibitor. Proton pump inhibitors such as esomeprazole (Nexium) and pantoprazole (Protonix) may be preferable to other proton pump inhibitors since they seem to have less of an effect on the CYP2C19 enzymatic pathway used to convert clopidogrel to its active metabolite. In addition, patients who present with an acute coronary syndrome can receive prasugrel (Effient), which is not dependent upon the CYP2C19 pathway for an active metabolite. Additional clinical trials will be necessary to fully understand and to guide treatment algorithms for patients who are receiving dual anti-platelet therapy and who need proton pump inhibitors to prevent serious bleeding problems.

Figure 1
Primary Endpoint Stratified By Use of a PPI
PPI Use at Randomization (n=4529)

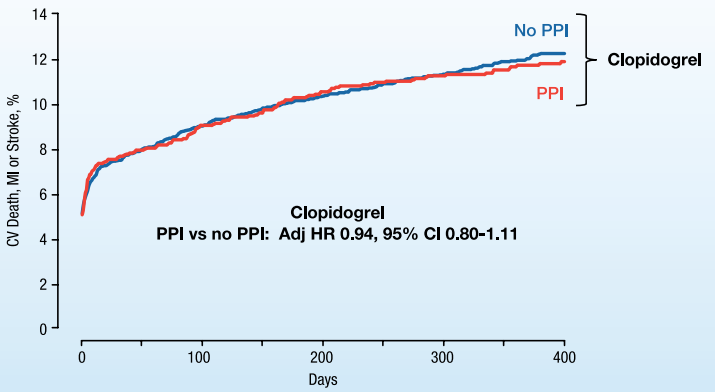
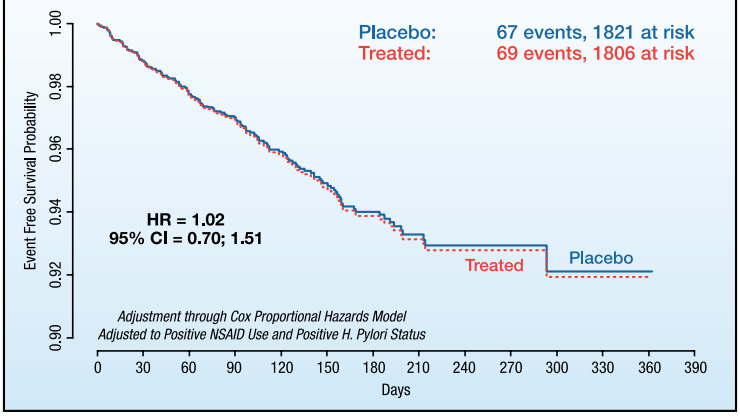


Figure 2
Survival Curves for PPI Treated vs Placebo
Composite Cardiovascular Events



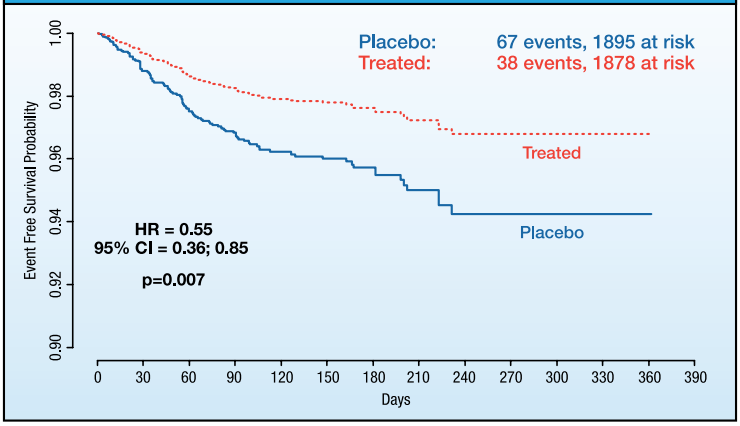
Studies Assessing Optimal Treatment Strategies:

The results of the NAVIGATOR Trial were presented at the American College of Cardiology meetings in March of 2010. The primary objective of the NAVIGATOR Trial was to evaluate whether patients with impaired glucose tolerance but not overt diabetes mellitus would benefit from treatment with valsartan (angiotensin receptor blocker that increases patients' sensitivity to insulin) and nateglinide, a diabetic medication to prevent postprandial excessive rises in blood sugars. The rationale for the NAVIGATOR Trial was that current medical practice waits for patients to become overtly diabetic and then attempts to treat the diabetes aggressively enough to prevent its complications of stroke, heart attacks, renal failure, blindness, and neuropathy. The concept behind the NAVIGATOR Trial was that it would be better to treat patients with impaired glucose tolerance before they became overtly diabetic. Therefore, they would be less likely to develop the vascular complications associated with dia-

betes mellitus. After six years of follow-up, the NAVIGATOR Trial failed to show any decrease in the primary outcome for either valsartan or nateglinide or the combination of the two.

Another trial presented at the American College of Cardiology meetings in March of 2010 was the DOSE Trial. This trial looked at 308 patients with acutely decompensated heart failure and asked the question, what is the optimal diuretic therapy for treating these patients? Is it better to treat patients with IV bolus furosemide versus an IV continuous infusion of furosemide? Background for the study was that IV loop diuretics are the most commonly prescribed therapy for acute decompensated heart failure. Few prospective studies exist to guide practice as to the optimal way to administer the IV loop diuretics. Patients were randomized to receive either IV boluses of furosemide q.12 hours or to receive an IV continuous infusion of furosemide. A second randomization involved differences in dosing strategies. Patients were randomized to receive low intensification diuretics, which consisted of one time the oral dose they had been taking prior to admission. The other dosing strategy was high intensification dosing which consisted of 2.5 times the oral dose they had been taking before admission. The study found that the primary end point of death, rehospitalization, or emergency department visits was not significantly different between the continuous infusion versus q.12 hour bolus dosing strategies. In addition, there was not a significant difference between the high dose versus low dose strategy, although there was a trend favoring the high dose strategy. In evaluating secondary end points, there was no statistically significant difference in global symptom relief or change in renal function at 72 hours for either the q.12 hour bolus group or the continuous infusion group. In addition, there was no significant difference in the global symptom relief scores for the low intensification versus high intensification dosing groups. There was no evidence of benefit for continuous infusion compared to q.12 hour bolus infusion on either of the secondary end points that were analyzed. There was a trend towards greater improvement in weight loss, net volume loss, and proportion free from signs of congestion in the high intensification group (2.5 times the oral dose) as compared to the low dose group. Therefore, it appears that physicians should be able to use whichever dosing strategy they feel most comfortable with. This study does not show a definite benefit of one dosing strategy over the other strategy.

Figure 3
Survival Curves for PPI Treated vs Placebo Composite GI Events



Another trial presented at the American College of Cardiology meetings this past year was the RACE Trial. It looked at rate control efficacy in permanent atrial fibrillation. It was a randomization comparing lenient rate control versus strict rate control and looked at the effects on morbidity and mortality. The hypothesis for the RACE-II Trial was that lenient rate control is not inferior to strict rate control in patients with permanent atrial fibrillation in terms of cardiovascular morbidity and mortality. Lenient rate control consisted of patients who had permanent atrial fibrillations with heart rates greater than 80 beats per minute. They were allowed to continue with elevated heart rates as long as their heart rate was less than 100 beats per minute. The strict rate control group received medications to keep their heart rate less than 80 beats per minute and to keep their heart rate less than 110 beats per minute when they exercised at 25% of their maximum duration exercise time.

Over 300 patients were randomized to each of the two arms of the trial and followed for 36 months. The primary outcome of the trial was found to be not statistically different between the two groups. The three-year incidence of adverse cardiovascular events occurred in 12.9% in the lenient treated group as compared to the 14.9% in the strict group. These results were not statistically significant between the two groups.

The conclusions demonstrate that lenient rate control is not inferior to strict rate control. In addition, lenient rate control is found to be more convenient since fewer outpatient visits, fewer examinations, and lower doses of medications were needed.

In February of 2010 the results of the CREST Trial were presented. This trial was the randomized carotid revascularization endarterectomy versus stenting trial. The CREST Trial evaluated whether carotid stenting is an effective alternative to carotid endarterectomy. The trial was a prospective, randomized, controlled trial with blinded end point adjudication. 2,502 patients at 117 medical centers were randomized. The primary end points included stroke, myocardial infarction, and death during a 30-day periprocedural period or ipsilateral stroke over the follow up period of 2.5 years. In evaluating the primary end point no significant difference was found between carotid artery stenting versus carotid endarteretomy. The trial found that carotid artery stenting had a 7.2% event rate versus a 6.8% event rate for carotid endarterectomy. The incidence of any stroke was higher in the stenting group as compared to the carotid endarterectomy group. For the stenting group, there was a 4.1% stroke rate as compared to a 2.3% for the carotid endarterectomy group. However, there were no significant differences in major strokes between the two groups. In addition, there was a significantly higher increased risk of myocardial infarction in the carotid endarterectomy group versus the stenting group. 2.3% of the patients had a myocardial infarction in the carotid endarterectomy group versus 1.1% in the stent group. Looking at the composite of death, any stroke, or any myocardial infarction, the event rate between the two groups was not statistically significant. Looking at cranial nerve palsy, there was a 0.3% event rate in the stent group as compared to a 4.8% event rate in the carotid endarterectomy group and this was statistically significant. The overall conclusions of the CREST Trial were that in healthcare settings with experienced staff, the periprocedural and long-term outcomes are comparable between carotid artery stenting and carotid endarterectomy. The CREST Trial represented the second randomized trial between carotid stenting and carotid endarterectomy that showed similar results between the two. This data is now being reviewed by the Food and Drug Administration and CMS to determine whether the restrictions on carotid artery stenting will be removed. Their decision will determine whether patients and physicians will be given the option to decide whether to proceed with carotid endarterectomy or carotid stenting for the treatment of significant carotid artery stenoses.

Wayne N. Leimbach, Jr. is an Oklahoma Heart interventional cardiologist specializing in cardiac catheterization, coronary angioplasty, percutaneous closure of PFOs & ASDs and related interventional procedures such as stents, atherectomy, laser, intravascular ultrasound imaging and direct PTCA for acute myocardial infarction.

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