Oklahoma Heart Institute

VOLUME 6 | NUMBER 1 | SUMMER 2011

Dabigatran Etexilate: A New Oral Anticoagulant For Non-valvular Atrial Fibrillation

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

The Destiny Trial: A New Destination for Coronary Drug Eluting Stents-Below the Knee Intervention

By Raj H. Chandwaney, MD, FACC, FSCAI, FSVM

Nephrogenic Systemic Fibrosis

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

Understanding Heart Disease

An Interview with Edward T. Martin, MD, FACC, FACP, FAHA
By Elaine Burkhardt

Guidelines Update for Management of Atrial Fibrillation

By Craig S. Cameron, MD, FACC

Heart problems? Think Oklahoma Heart Institute first. Our special training and team approach tackles even the most difficult problems. Great Results. So you can live well. Isn't that what you want?

Live Well.

Oklahoma Heart Institute

918.592.0999 | **www.oklahomaheart.com** | 1120 S. UTICA AVE. Oklahoma Heart Institute (The Heart Hospital) | 1265 S. UTICA (Utica Physicians Office) | 9228 S. MINGO (SouthPointe Physicians Office)

Oklahoma Heart Institute

Oklahoma Heart Institute Hospital
1120 Utica Avenue
Tulsa, OK 74104
P) 918.574.9000

Oklahoma Heart Institute
at Utica Physicians Offices
1265 S. Utica Avenue, Suite 300
Tulsa, OK 74104
P) 918.592.0999 • F) 918.595.0208

Oklahoma Heart Institute
at Southpointe Physicians Offices
9228 S. Mingo Road, Suite 200
Tulsa, OK 74133
P) 918.592.0999 • F) 918.878.2408

The Doctors of Oklahoma Heart Institute

Wayne N. Leimbach, Jr., MD
Robert C. Sonnenschein, MD
Robert E. Lynch, MD
James J. Nemec, MD
Gregory D. Johnsen, MD
Alan M. Kaneshige, MD
Edward T. Martin, MD
Roger D. Des Prez, MD
Christian S. Hanson, DO
David A. Sandler, MD
Raj H. Chandwaney, MD
D. Erik Aspenson, MD
Frank J. Gaffney, MD
Eric G. Auerbach, MD
Kelly R. Flesner, MD
Robert L. Smith, Jr., MD
Craig S. Cameron, MD
Eugene J. Ichinose, MD
Cristin M. Bruns, MD
Gregory A. Cogert, MD
John S. Tulloch, MD
Anthony W. Haney, MD
Ralph J. Duda, Jr., MD
Douglas A. Davies, MD

Published by Oklahoma Heart Institute
Edited by Newsgroup Communications, Tulsa, OK
Designed by Langdon Publishing
For advertising information contact:
Elaine Burkhardt at 918.749.2506
newsgroupcom@sbcglobal.net
visit our website at www.oklahomaheart.com
Edition 19

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

VOLUME 6 | NUMBER 1 | SUMMER 2011

ON THE COVER

"Autumn Grounds of Philbrook,"
Acrylic on Canvas, 11" x 14"
Jimmy Leach, artist

Stilwell artist Jimmy Leach's paintings focus on the Impressionistic and Expressionistic landscape. His work, described as "a tapestry of individual bits of color," is inspired by local gardens and lawns, such as his own and his late grandmother's, and the wild beauty of his surroundings. Leach's paintings are in many private and public collections throughout the USA and four foreign countries and have also been featured in "200 Great Painting Ideas for Artists" by Carole Katchen, and Southern Accents Magazine, March 1998. He was the featured artist at the 2011 Oklahoma Heart Research & Education Foundation's 22nd Annual Symposium.

to our readers

The field of cardiology continues to rapidly expand and change. New medications, new therapies and new treatment guidelines continue to develop. In addition to the newer therapies, new problems are also being found.

Raj Chandwaney, MD discusses the Destiny trial, which highlights the value of drug-eluting stents for the treatment of below-the-knee, severe peripheral vascular disease.

Craig Cameron, MD outlines the new guidelines regarding the management of atrial fibrillation.

Wayne N. Leimbach, Jr., MD summarizes the information concerning dabigatran etexilate, a new oral anticoagulant available for non-valvular atrial fibrillation.

Finally, Edward T. Martin, MD describes nephrogenic systemic fibrosis, a newly recognized and rare but potentially serious side effect from the imaging agents used with MRA scanning. Also included in this issue is an interview with Dr. Martin by writer Elaine Burkhardt regarding heart disease.

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

Wayne Leimbach

Sincerely,
Wayne N. Leimbach, Jr., MD
Editor, Oklahoma Heart Institute Magazine

Dabigatran Etexilate:

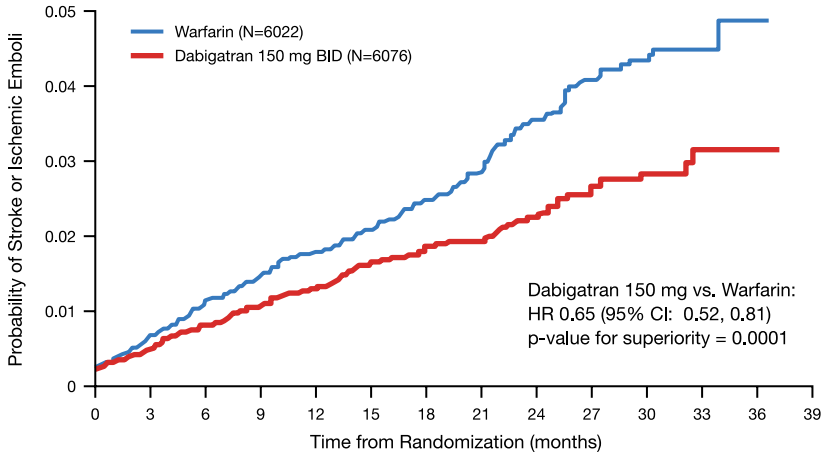
A New Oral Anticoagulant For Non-valvular Atrial Fibrillation

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

Patients with atrial fibrillation have nearly a 5-fold increased risk of stroke as compared to the patients without atrial fibrillation.

Figure 1

Dabigatran 150 mg BID Significantly Reduced the Risk of Stroke and Systemic Emboli vs. Warfarin (RE-LY Trial)



For over 50 years, oral vitamin K antagonists, Coumadin and warfarin, have been the standard therapy for chronic oral anticoagulation for non-valvular atrial fibrillation. However, physicians are well aware of the limitations of vitamin K antagonist. The delayed onset and offset of action has caused prolonged hospitalizations. In addition, there is significant inter-individual variability in dose response, and the narrow therapeutic window makes it difficult to keep patients in the therapeutic range. Therefore, patients require frequent monitoring of their international normalized ratio (INR). Despite careful dose adjustments and the use of "Coumadin Clinics," patients still frequently fall outside the target therapeutic range, which increases the risk of either thromboembolism or bleeding. Patients also quickly learn of the limitations of vitamin K antagonists. Many find it difficult to adapt to the frequent blood sampling necessary to measure their INRs. Because of its limitations, a significant portion of patients with atrial fibrillation who are at risk of stroke are not treated with a vitamin K antagonist. They are, instead, treated with less potent and less effective anticoagulants, such as aspirin and clopidogrel.

Dabigatran etexilate (Pradaxa) is a new oral thrombin inhibitor that is the first oral anticoagulant available for the treatment of non-valvular atrial fibrillation in over 50 years. Dabigatran etexilate is a low molecular weight pro-drug that exhibits no pharmacological activity in itself. After oral administration, dabigatran is absorbed into the bloodstream where it is converted to its active metabolites. It is activated by ubiquitous esterases in the gut and plasma, and it is metabolized in the liver where a small portion (<20%) is conjugated with gluconic acid and excreted via the biliary system.

Dabigatran has the ability to inhibit both circulating and fibrin-bound thrombin. By inhibiting thrombin, dabigatran prevents conversion of fibrinogen into fibrin, which prevents the positive feedback amplification of the coagulation cascade. In addition, it prevents the crosslink of fibrin monomers, platelet activation, and inhibition of fibrinolysis.

It is estimated the prevalence of atrial fibrillation in the United States is somewhere between 2.5 and 3 million people. As the population ages, this prevalence is expected to almost double by 2050.

Dabigatran etexilate has been approved for the treatment of non-valvular atrial fibrillation. It is estimated the prevalence of atrial fibrillation in the United States is somewhere between 2.5 and 3 million people. As the population ages, this prevalence is expected to almost double by 2050. Patients with atrial fibrillation have nearly a 5-fold increased risk of stroke as compared to the patients without atrial fibrillation. The risk of stroke is true for patients with sustained atrial fibrillation, as well as for patients with paroxysmal atrial fibrillation. The annualized ischemic stroke rate for patients with paroxysmal atrial fibrillation or sustained atrial fibrillation is about 3.2-3.3%.

Analysis of 6 large trials has demonstrated that vitamin K antagonists such as warfarin effectively reduce the risk of stroke as compared to placebo in patients with non-valvular atrial fibrillation. Effective anticoagulation with warfarin reduces the relative risk of stroke by 64% (reference Annals of Internal Medicine 2007: Volume 146, 857-867). In addition, studies have shown that when patients fall out of the therapeutic range in regards to their INRs, their risk of stroke significantly increases.

The value of dabigatran in preventing stroke and systemic emboli was demonstrated in the RE-LY trial. This was an open label non-inferiority intention to treat trial. The trial was very large, and randomized 18,113 patients to receive either warfarin, or dabigatran 110 mg twice a day or dabigatran 150 mg twice a day. More than 6,000 patients were in each arm of the trial. At least 50% of the patients in the trial were vitamin K antagonist naive. The primary outcome of the trial was incidence of stroke (ischemic and hemorrhagic) and systemic emboli in patients with non-valvular atrial fibrillation. In addition, there was a primary safety outcome, which looked at the incidence of major bleeding. To be eligible for inclusion in the trial, the patients had to have non-valvular persistent or paroxysmal or permanent atrial fibrillation. One or more additional risk factors had to be present. These included previous stroke or transient ischemic attack or systemic embolism, left ventricular ejection fraction less than 40%, symptomatic heart failure with New York Heart Association Class II or more, age greater than or equal to 75, or age greater than or equal to 65 years, if they also had one of the following: diabetes mellitus, coronary artery disease or hypertension. In addition, the patients were allowed to be on concomitant medications such as aspirin less than 100 mg per day, clopidogrel, proton pump inhibitors, antihypertensives and antiarrhythmics including amiodarone and verapamil. The patients were excluded if they had renal impairment with creatinine clearance less than 30 mL per minute.

The mean age of the patients was 71.5 years. More than 40% of the patients were greater than or equal to 75 years in age. Almost 80% of patients were hypertensive, and about half of the patients were vitamin K antagonist naive at entry into the study.

The primary endpoint of the study was the risk of stroke and systemic emboli. The study demonstrated a relative risk reduction of 35% for dabigatran 150 mg twice a day versus warfarin. Dabigatran was found to be superior in preventing stroke and systemic emboli as compared to warfarin with a p-value of 0.0001 (Figure 1).

Not only did the risk of all strokes decrease, but also the risk of hemorrhagic stroke decreased by 74%.

The benefit was seen in all the sub-groups that were analyzed. In addition, bleeding was less with dabigatran. The risk of total bleeds was 16.6% for dabigatran and 18.4% for warfarin. Major bleeds and life-threatening bleeds were less with diabiatran. There was a slight increase in GI bleeds with dabigatran (Figure 2).

Potential drug interactions with dabigatran are relatively infrequent. P-gp inducer (i.e., rifampin) reduces exposure to dabigatran and should generally be avoided. Other P-gp inhibitors do not require dosing adjustments for dabigatran. These medications include verapamil, amiodarone, clonidine, clarithromycin and ketoconazole. Dabigatran is not a substrate, inhibitor or inducer of the CYP450 enzymes.

Figure 2

Summary of Clinical Outcomes in the RE-LY Trial: Dabigatran 150 mg BID vs. Warfarin

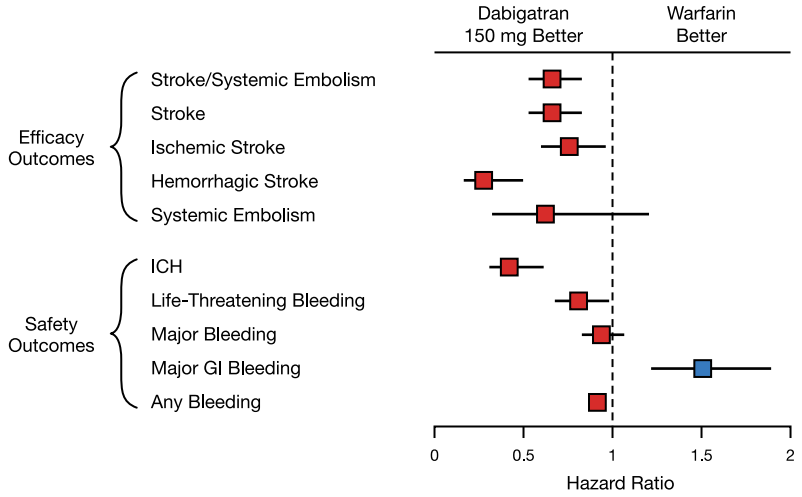


Figure 3

Renal Function Should Be Considered When Selecting the Dose of Dabigatran

Creatinine Clearance	Recommended Dose of Dabigatran
>30 mL/min	150 mg twice daily
15-30 mL/min	75 mg twice daily
<15 mL/min or on dialysis	Dosing recommendations cannot be provided

Figure 4

Conversion from Dabigatran to Warfarin

Creatinine Clearance	Recommended Starting Time of Warfarin
>50 mL/min	3 days before discontinuing Dabigatran
31-50 mL/min	2 days before discontinuing Dabigatran
15-30 mL/min	1 day before discontinuing Dabigatran
<15 mL/min	No recommendations can be made

Because dabigatran can contribute to an elevated INR, the INR will better reflect warfarin's effect after dabigatran has been stopped for at least two days.

In the RE-LY trial, the rate of discontinuation of dabigatran was higher than with warfarin during the first 3 months of the trial. The rates of adverse reaction leading to treatment discontinuation is 21% for dabigatran 150 mg twice daily and 16% for warfarin. The most frequent adverse events leading to discontinuation of dabigatran were bleeding and gastrointestinal events such as dyspepsia, nausea or upper abdominal discomfort, and diarrhea.

FORMULATION: Dabigatran etexilate is a capsule, which contains multiple pellets including dabigatran and tartaric acid. Tartaric acid is necessary for dabigatran etexilate to be absorbed efficiently from the gastrointestinal tract. Dabigatran etexilate capsules must be taken as the entire capsule. The capsule cannot be opened and the contents cannot be mixed with food.

PHARMACOKINETICS: After oral administration, dabigatran etexilate is rapidly absorbed from the gut. Plasma concentrations and anticoagulant effects are dose dependent. Peak plasma concentrations are usually seen within 1-1/2 to 2 hours after oral administration. The steady state half life of the dabigatran is about 12-14 hours. The half life is increased to greater than 24 hours in patients with a creatinine clearance of less than 30 mL per minute.

Dabigatran etexilate is primarily eliminated from the body by renal excretion. Consequently, reduced kidney function can result in elevated dabigatran plasma concentrations and prolong drug half life.

Dabigatran prolongs the activated partial thromboplastin time (aPTT), which targets the intrinsic pathway of anticoagulation. The aPTT will indicate whether the patient is anticoagulated with dabigatran. However, the aPTTcannot be used to reliably measure degrees of anticoagulation. The ecarin clotting time does accurately reflect the level of anticoagulation. Dabigatran has relatively little effect on the prothrombin time and INR, which targets the extrinsic coagulation pathway. Therefore, the PT and INR are not useful for determining the degree of anticoagulation achieved in patients taking dabigatran.

Renal function should be considered when selecting the dose of dabigatran. For patients with a creatinine clearance of greater than 30 mL per minute, dabigatran 150 mg twice daily is the recommended dose. For patients with a creatinine clearance of 15-30 mL per minute, dabigatran 75 mg twice daily is the recommended dose. For patients with a creatinine clearance of less than 15 mL per minute or patients on dialysis, dabigatran should not be used. It should be noted that dabigatran is removed by dialysis (Figure 3).

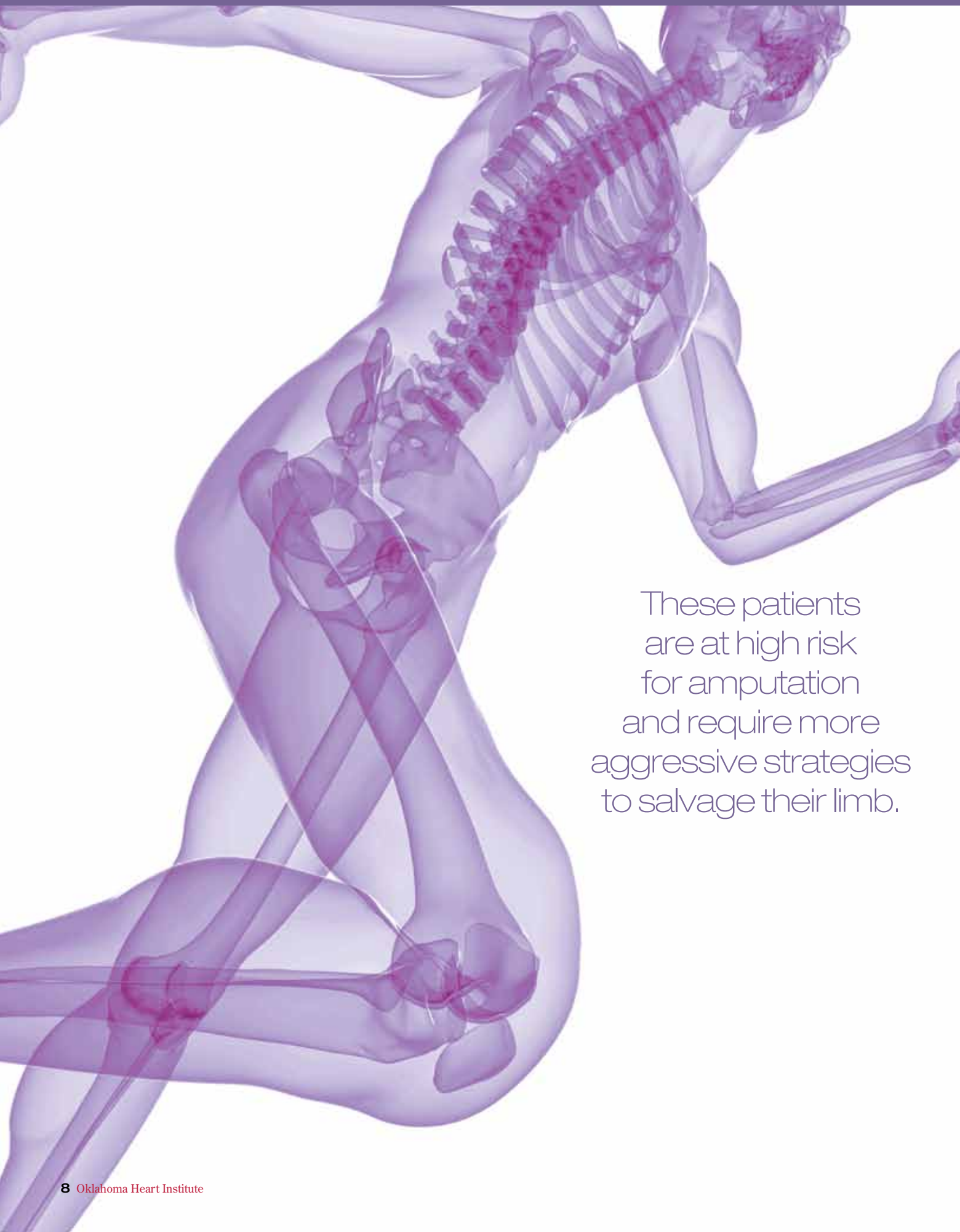
When converting from warfarin to dabigatran, the warfarin should be discontinued. Dabigatran should be started when the INR is less than 2. When considering conversion from dabigatran to warfarin, see Figure 4. When converting from parental anticoagulation with dabigatran, stop the heparin and start dabigatran at the time of discontinuation of heparin. When using enoxaparin, start dabigatran 0-2 hours before the next dose of enoxaparin. When converting from dabigatran to parental anticoagulation, if the creatinine clearance is greater than 30 mL per minute, start the parenteral anticoagulation 12 hours after the last dose of dabigatran. If the creatinine clearance is less than 30 mL per minute, start the parental anticoagulation 24 hours after last dose of dabigatran.

Dabigatran can be used before and after surgery. If possible, discontinue dabigatran 1-2 days before invasive surgical procedures and 3-5 days for high risk bleeding surgical procedures. This is if patients' creatinine clearance is greater than 50 mL per minute. Consider longer times for patients undergoing major surgery who also have renal insufficiency.

In summary, dabigatran 150 mg twice daily was found to be superior to warfarin for the prevention of stroke and systemic emboli. Not only was dabigatran superior to warfarin for the prevention of stroke and systemic emboli, but it also was found to produce less bleeding. Intracranial hemorrhages were markedly reduced by the use of dabigatran as compared to warfarin. Life-threatening bleeds were significantly reduced. There was a slight increase in major GI bleeding with dabigatran as compared to warfarin.

Currently, dabigatran etexilate is only approved in the United States for the treatment of non-valvular atrial fibrillation. Patients with non-valvular atrial fibrillation also tend to prefer dabigatran etexilate because they do not have to undergo repeated blood testing to assess their levels of anticoagulation. Studies are ongoing for the use of dabigatran in venothromboembolic diseases; however, this indication has not been approved in the United States.

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.



These patients are at high risk for amputation and require more aggressive strategies to salvage their limb.

The Destiny Trial

A New Destination for Coronary Drug Eluting Stents-Below the Knee Intervention

By Raj H. Chandwaney, MD, FACC, FSCAI, FSVM

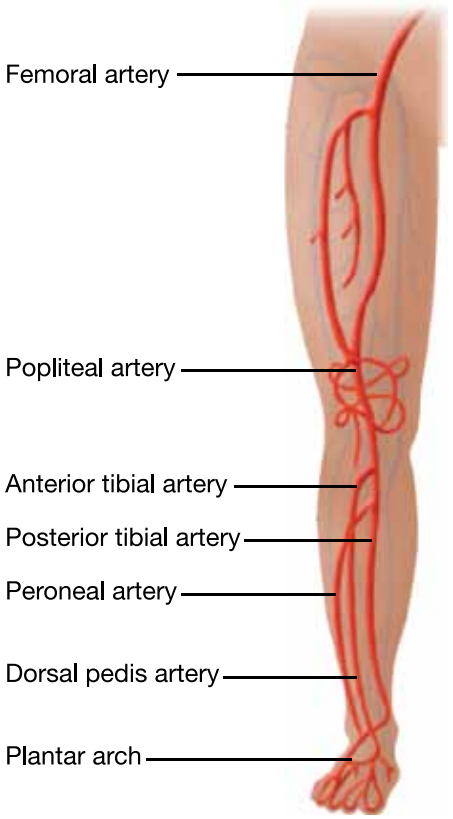
Below the knee intervention refers to the use of endovascular techniques such as balloon angioplasty, cutting/scoring balloon angioplasty, stenting, directional atherectomy, rotational atherectomy, or laser atherectomy to treat blockages in the infrapopliteal arteries. These infrapopliteal arteries are the arteries below the popliteal artery and include the anterior tibial artery, the tibioperoneal trunk, the posterior tibial artery, and the peroneal artery (see figure 1).

Below the knee endovascular intervention has proven to be the achilles' heel for endovascular PAD (peripheral artery disease) specialists. Despite efforts to approach this challenging vascular bed with a wide variety of endovascular techniques such as balloon angioplasty, scoring/cutting balloon angioplasty, bare metal stents, directional atherectomy, rotational atherectomy, and laser atherectomy, researchers have not been able to demonstrate durable angiographic proven vessel patency.

Consequentially, well-trained endovascular PAD specialists usually limit below the knee endovascular intervention to patients who are suffering with critical limb ischemia or non-healing foot ulcerations. These patients are at high risk for amputation and require more aggressive strategies to salvage their limb. The working concept is that blood flow will be restored to the affected extremity for a relatively short period of time (perhaps a month or two). This time period may be sufficient enough to allow enough wound healing to prevent an amputation. Although it is unlikely that the vessel treated will remain patent for the long term, the patient is likely to avoid amputation as long as they do not reinjure their foot and develop a new ulceration. Most research published on the various endovascular techniques used to approach the infrapopliteal arteries define limb salvage rates rather than angiographic patency rates as the primary endpoint studied. Limb salvage rates are reported to be as high as 70-80% in some studies using the techniques described above. Angiographic vessel patency rates are usually not reported in these studies but are expected to be dismally lower.

Figure 1

Lower Extremity Arterial Anatomy



The results of the DESTINY trial were recently presented at the LINC 2011 meeting (Leipzig Interventional Course) in Leipzig, Germany. These results are likely to change the way endovascular specialists approach the infrapopliteal arteries. The DESTINY trial is a 140-patient, investigator-sponsored, randomized, controlled, multicenter trial. DESTINY compared the Abbott Vascular everolimus coronary drug-eluting stent to the Abbott Vascular coronary bare-metal stent in patients with critical limb ischemia of the lower leg. Patients with lesion lengths < 40 mm were included in this trial. The 12-month results from DESTINY demonstrated that everolimus drug eluting stents had significantly better patency compared to the bare-metal stents at 12 months (85.2% vs. 54.4%, respectively; p = 0.0001). This difference was especially pronounced between six and 12 months, where the difference in patency rate significantly diverged, as the rate for the bare metal stent fell to nearly 50% while the rate for everolimus drug eluting stent remained above 85%. These results demonstrate that there is a significant benefit from an everolimus eluting stent versus a bare-metal stent in below the knee intervention. Furthermore, the 85% angiographic patency rate demonstrated at 12-month follow-up is an astonishing finding best described as a game changer for below the knee intervention.

In the European Union the CE Mark designation for a medical device is comparable to a medical device receiving FDA approval in the United States. As a result of the DESTINY trial 12-month findings, the Abbott everolimus drug eluting stent has received the CE Mark for treatment of critical limb ischemia or *claudication* due to blockages in the infrapopliteal arteries. It is noteworthy that regulators in the European Union are so impressed by the 85% angiographic patency rates documented at 12 months in the DESTINY trial that they propose below the knee intervention could be offered with everolimus drug eluting stents to patients with claudication alone (without a need for limb salvage) in addition to those patients with critical limb ischemia.

As a result of the recently presented DESTINY trial 12-month findings, the endovascular PAD specialists at the Oklahoma Heart Institute have already advanced their practice.

Figure 2

Baseline Angiogram Demonstrating Critical Stenosis in the Right Tibio-Peroneal Trunk Below the Knee

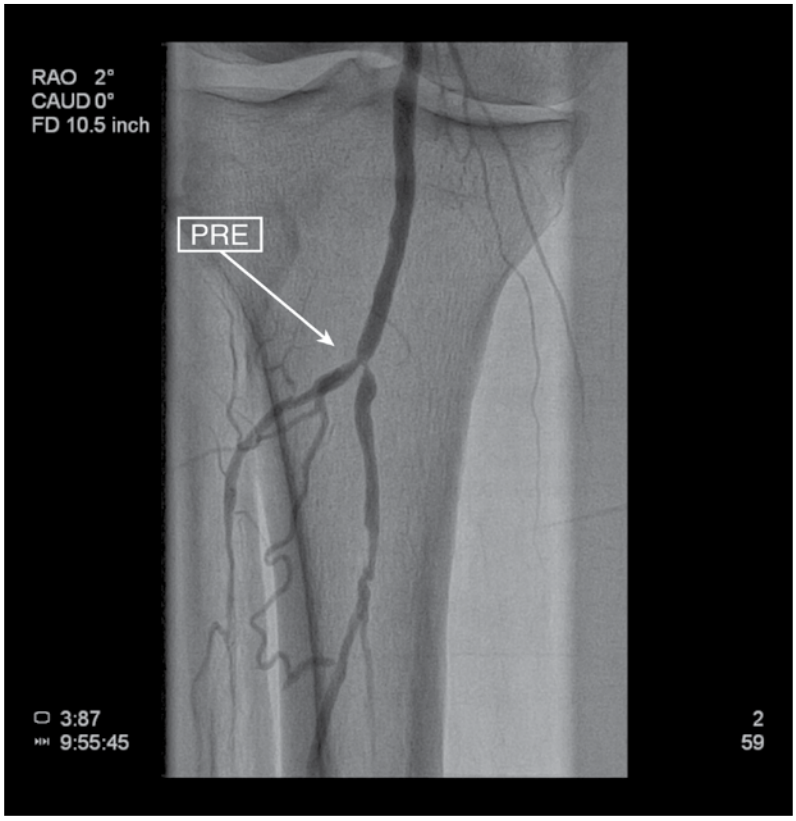
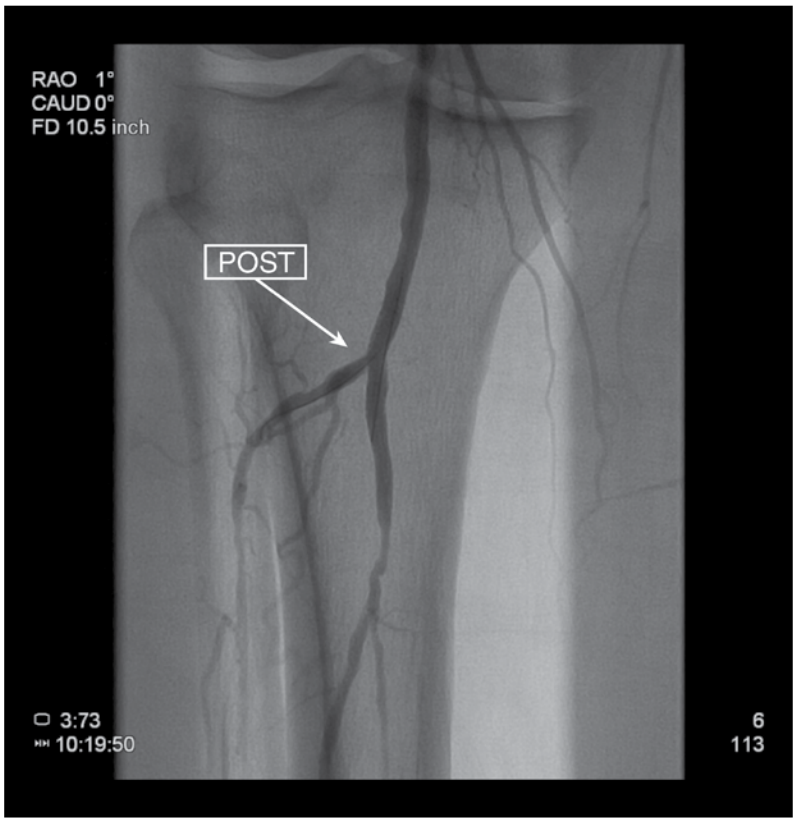


Figure 3

Final Angiogram Performed After Deploying a Coronary Drug Eluting Stent in the Right Tibio-Peroneal Trunk Below the Knee



Fortunately, once a medical device is approved by the FDA in the United States for a specific indication, physicians are able to utilize those devices for other off-label medically appropriate indications. Figure 2 demonstrates baseline angiogram in a patient who presented for a second opinion to the endovascular PAD specialists at the Oklahoma Heart Institute with critical limb ischemia. Physicians at another local hospital had advised the patient to continue medical therapy. Figure 2 shows a severe stenosis in the right tibio-peroneal trunk below the knee. Note that the right anterior tibial and posterior tibial arteries are chronically occluded. To facilitate wound healing, well-trained endovascular PAD specialists are advised to strive for single vessel unobstructed runoff to the foot as a minimum in patients with critical limb ischemia. This patient was treated with an everolimus coronary drug eluting stent in the right tibio-peroneal trunk. An excellent angiographic result was achieved (see figure 3).

In conclusion, the infrapopliteal arteries have proven to be an extremely challenging area for endovascular PAD specialists to achieve long-term durable results. Thus far, poor long-term patency rates have limited the role of below the knee intervention to critical limb ischemia patients with non-healing ulcerations who require aggressive treatments to salvage their limbs. The recently presented results of the DESTINY trial suggest that application of coronary drug eluting stent technology in below the knee intervention can dramatically improve long-term patency rates. Broadening the use of coronary drug eluting stent technology below the knee may expand the indications for infrapopliteal intervention to include patients with severe claudication. The endovascular PAD specialists at Oklahoma Heart Institute will continue to closely follow this exciting area of research so we may offer our patients the most progressive treatment options available.

Raj H. 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. In addition to receiving board certifications in Internal Medicine, Cardiovascular Disease, and Interventional Cardiology by the American Board of Internal Medicine, Dr. Chandwaney has also received board certification in Endovascular Medicine from the American Board of Vascular Medicine

Oklahoma Heart Institute

Services of Oklahoma Heart Institute

Interventional Cardiology

- Cardiac Catheterization
- Coronary Angioplasty
- Multivessel Angioplasty and Stenting
- Atherectomy
- Rotablator Atherectomy
- Thrombolytic Therapy
- Coronary Stents
- Carotid Stenting
- Fractional Flow Reserve
- Intravascular Ultrasound
- Myocardial Biopsy
- Pericardiocentesis
- Peripheral Angioplasty
- Peripheral Stents
- Percutaneuos ASD Closures
- Percutaneous PFO Closures
- Impella Circulatory Support
- Therapeutic Hypothermia for Cardiac Arrest Patients
- Venous Ablation

Noninvasive Cardiology

- CT Angiography
- CT Heart Scan
- Cardiac and Vascular Screening Services
- Nuclear Cardiology
- Echo and Doppler Studies
- Nuclear and Echocardiographic Exercise and Pharmacological Stress Testing
- Retinal Imaging
- Thyroid Ultrasound
- Transesophageal Echocardiography, Arterial Venous Peripheral Vascualr Imaging and Doppler Studies
- Peripheral Arterial Doppler and Duplex Imaging
- Cardiovascular Magnetic Resonance Imaging
- External Counterpulsation (ECP) Therapy
- Transcranial Doppler
- Aquapheresis Therapy

Electrophysiology

- Electrophysiology Studies
- Ablation Therapy
- Pacemaker Implantation
- Pacemaker and Lead Extraction
- Pacemaker Programming
- Pacemaker Monitoring and Clinic
- Implantable Cardioverter Defibrillator (ICD) Replacement
- ICD and Hardware Removal
- ICD Programming
- ICD Monitoring and Clinic
- Holter Monitoring and Interpretation
- 30 Day Cardiac Event Monitors
- Implantation and Interpretation of Long-Term Heart Monitors
- Signal Averaged EKGs and Interpretation
- Head Up Tilt Testing and Interpretation
- Direct Current Cardioversion
- Antiarrhythmic Drug Loading and Monitoring

Metabolic Disorders

- Diabetes
- Thyroid
- Hypertension
- Other Endocrine Problems

Specialty Clinics

- Advanced Center for Atrial Fibrillation
- Dysrhythmia and Pacer Clinic
- Hypertension Clinic
- Adolescent and Adult Congential Heart Clinic
- Lipid and Wellness Clinic
- Heart Failure Clinic
- Same Day Appointment Clinic
- Pre-Operative Clinic
- Center for the Treatment of Venous Disease
- Sleep Care

Oklahoma Heart Institute Hospital

1120 Utica Avenue
Tulsa, OK 74104
P) 918.574.9000
www.oklahomaheart.com

Oklahoma Heart Institute at Utica Physicians Offices

1265 S. Utica Avenue
Tulsa, OK 74104
P) 918.592.0999 • F) 918.595.0208

Oklahoma Heart Institute at Southpointe Physicians Offices

9228 S. Mingo Road
Tulsa, OK 74133
P) 918.592.0999 • F) 918.878.2408

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.

Board certified in Internal Medicine, Cardiovascular Disease and Nuclear Cardiology

Gregory D. Johnsen, MD, FACC, FSCAI

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

Alan M. Kaneshige, MD, FACC, FASE

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.

Board certified in Internal Medicine, Cardiovascular Disease, Adult and Transesophogeal Echocardiography

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.

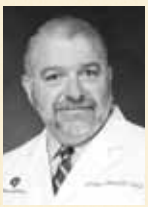
Board certified in Internal Medicine and Cardiovascular Disease

Roger D. Des Prez, MD, FACC

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.

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

Christian S. Hanson, DO, FACE



Dr. Hanson is a specialist in Endocrinology, Metabolism and Hypertension at Oklahoma Heart Institute with expertise in diabetes, lipids and hypertension. He also serves as Clinical Associate Professor of Medicine in the College of Osteopathic Medicine – Oklahoma State University. He completed a Fellowship in Endocrinology, Metabolism and Hypertension at the University of Oklahoma in Oklahoma City. Dr. Hanson's Internal Medicine Residency and Rotating Internship were completed at Tulsa Regional Medical Center. He received his medical degree from Oklahoma State University and his Bachelor of Science degree from Northeastern Oklahoma State University in Tahlequah.

Board certified in Internal Medicine, Endocrinology and Metabolic Diseases

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 interventional and noninvasive 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

Kelly R. Flesner, MD

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.

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

Craig S. Cameron, MD, FACC

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.

Board certified in Internal Medicine, Cardiovascular Disease and Cardiac Electrophysiology

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

Cristin M. Bruns, MD

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. Dr. Tulloch is Director of the Cardiac and Vascular Ultrasound Department of Hillcrest Medical Center's Cardiovascular Diagnostics. 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

Douglas A. Davies, MD, FACC

Dr/ Davies is a hospital-based cardiologist who provides continuity of care for patients admitted to Oklahoma Heart Institute – Hospital. He completed a Clinical Cardiology Fellowship and additional training in nuclear cardiology at the Medical College of Virginia, where he also completed his Internal Medicine and Residency programs. Dr. Davies received his medical degree from Johns Hopkins University School of Medicine in Baltimore.

Board Certified in Internal Medicine, Cardiovascular Disease, Nuclear Cardiology and Cardiovascular Computed Tomography Angiography

Nephrogenic Systemic Fibrosis

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

Background

Gadolinium chelates, the contrast agents used in magnetic resonance imaging (MRI), were first instituted in clinical practice in 1988. Since their inception, they have revolutionized MRI by improving diagnostic confidence, visualization and characterization of pathology. One of the most important diagnostic areas improved by gadolinium chelates has been the area of MR angiography. This improvement in vessel imaging has shifted a large number of diagnostic studies from the invasive lab to noninvasive imaging, thus improving patient safety, convenience and leading to potential cost savings to the healthcare system in general. Additionally, the clinical safety profile led many physicians to believe that giving gadolinium to patients was almost like giving water. Anaphylactic reactions were extremely rare, and unlike iodinated contrast, gadolinium contrast was thought to be safe in renal impaired patients. MR physicians would double and triple dose patients with impunity, seeking additional improvement in image quality. Gadolinium was also used with success as a contrast agent in the invasive lab when renal impairment was present. Only within the last 5 years has there been a "chink in the armor" of the gadolinium safety profile, with the emergence of nephrogenic systemic fibrosis (NSF).

Nephrogenic systemic fibrosis was first identified as a disease entity in the United States in 1997. At that time 15 hemodialysis patients were noted to have skin hardening, thickening, and hyperpigmentation with subcutaneous nodules on the extremities (1). This disease state was initially termed nephrogenic fibrosing dermopathy because it was thought to only affect the skin and subcutaneous tissue of renally-impaired patients. But later the disease process was renamed NSF to better reflect the systemic nature of the disease found in subsequent patients.

An association between NSF and prior gadolinium exposure in patients with end-stage renal disease was first demonstrated in 2006, and impaired renal function appears to be the necessary condition for the development of NSF (2, 3). Since the early 1980s, greater than 200 million patients have received gadolinium, and no cases of NSF have occurred in patients with normal renal function. This association led to warnings by the U.S. Food and Drug Administration (USFDA) and the European Agency for the Evaluation of Medicinal Products regarding the use of gadolinium containing contrast agents in patients suffering from renal failure (4, 5). as well as new black box warnings on all gadolinium contrast agents.

Figure 1

Typical Cutaneous Lesions on a Leg of a 78-Year-Old Male Patient with NSF. (8)

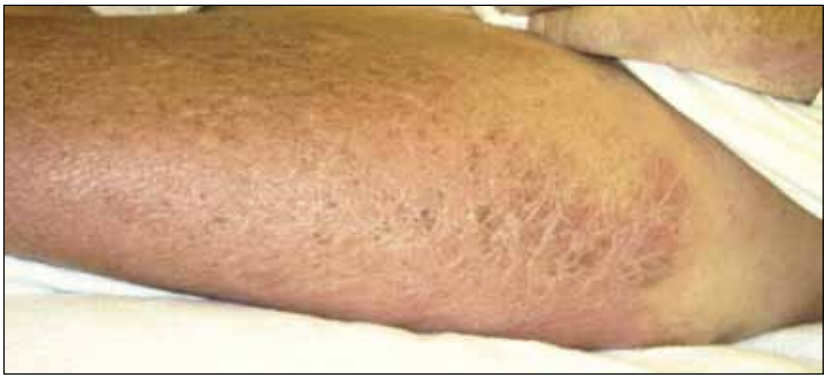


Figure 2

Swelling of the Arm Extending From the Wrist to the Center of the Upper Arm in the Same 78-Year-Old Male Patient With NSF. (8)

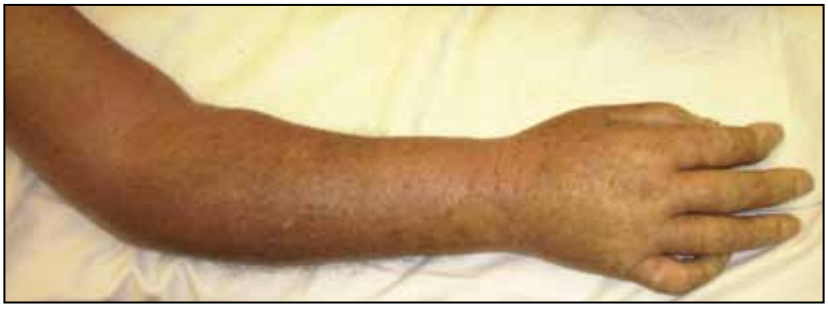


Table 1

Chronic Kidney Disease (CKD)

CKD 1	GFR >90 ml/min/1.73m^2
CKD 2	GFR >60-90 ml/min/1.73m^2
CKD 3	GFR >30-60 ml/min/1.73m^2
CKD 4	GFR 15-30 ml/min/1.73m^2
CKD 5	GFR <15 ml/min/1.73m^2 and/or peritoneal or hemodialysis

Epidemiology and Risk Factors

As of December 2009, the USFDA has documented 612 cases of nephrogenic systemic fibrosis. In Europe, there have been 80 cases in Europe as of May 2008. NSF occurs equally in both sexes and tends to affect the middle-aged most often. The oldest patient was 87 years old. However there have also been 9 reported cases in schoolchildren and teenagers (age 8-19 years), but none in infants.

All NSF patients have been reported to have renal dysfunction. The renal dysfunction has ranged from acute kidney injury to chronic kidney disease and end-stage renal disease on dialysis. There are 5 stages of chronic kidney disease (Table 1), and to date there have been no reported cases of NSF with a GFR of greater than 30 ml/min/1.73m^2. The greatest risk appears to be for patients on dialysis or with acute renal failure. With normal renal function, the majority of the gadolinium agents are removed by the kidney with a half life of 2 hours. In impaired renal function, this is considerably longer, thus allowing gadolinium a longer time to be exposed to tissues. Despite the association between gadolinium and kidney disease, it is

not clear why all patients with advanced renal failure do not develop NSF after exposure to gadolinium.

There have been a variety of clinical conditions, disease states and drugs reported to be associated with NSF without any direct evidence of causality (Table 2). Older age (greater than 60) and angiotensin-converting enzyme inhibitors appear to be protective. However none of these findings have been reproduced to date.

For patients with stage 5 chronic kidney disease or in those on dialysis at the time of gadolinium administration, it appears that prompt hemodialysis (within 24 hours) reduces NSF risk, (6) perhaps by as much as 20-fold. One hemodialysis session removes about 80% of the gadolinium, while a second session removes approximately 95%. Despite the literature saying that one has 24 hours to begin hemodialysis, many nephrologists and MRI safety experts believe that it should be instituted as soon as possible after the MRI gadolinium study and usually within 2 hours (7). Because peritoneal dialysis has been reported to clear gadolinium poorly, use of gadolinium in this population is contraindicated. Prompt hemodialysis may also help reduce the NSF risk in acute renal failure patients who have received gadolinium as well (8).

Table 2
NSF Risk Factors and Mechanisms

- Acute or chronic renal failure (GFR <30 ml/min/1.73 m^2)
- Protracted retention (extended half life) of gadolinium in renal insufficiency provides the condition for enhanced tissue exposure
- Hepatorenal syndrome or in the perioperative liver transplantation patient
- Epoetin (proinflammatory)
- IV iron
- Sevelamer (Renagel)
- Inflammatory burden (recent surgery, acute thrombosis, infection, sepsis etc.)
- Age <60
- Acidosis
- Idiopathic pulmonary fibrosis
- Systemic lupus erythematosus
- Hyperparathyroidism
- Hyperphosphatemia and hypercalcemia
- Hypercoagulable state
- After surgery

Table 3
Gadolinium Chelates for Use in Magnetic Resonance Imaging

Generic Name	Brand Name	Chemical Structure	Charge	Elimination
Gadodiamide	Omniscan	Linear	Nonionic	Renal
Gadoversetamide	OptiMARK	Linear	Nonionic	Renal
Gadopentetic acid	Magnevist	Linear	Ionic	Renal
Gadobenic acid	MultiHance	Linear	Ionic	97% renal, 3% bile
Gadoxetic acid	Primovist	Linear	Ionic	50% renal, 50% bile
Gadofosveset	Vasovist	Linear	Ionic	91% renal, 9% bile
Gadoteridol	ProHance	Cyclic	Nonionic	Renal
Gadobutrol	Gadovist	Cyclic	Nonionic	Renal
Gadoterat	Dotarem	Cyclic	Ionic	Renal

From Kribben A, Witzke O, Hillen U, Barkhausen J, Daul AE, and Erbel R.
Nephrogenic Systemic Fibrosis: Pathogenesis, Diagnosis, and Therapy. J. Am. Coll. Cardiol. 2009; 53; 1621-1628.

Table 4
The FDA Black Box Warning for Gadolinium Chelates

- Gadolinium-based contrast agents increase the risk of nephrogenic systemic fibrosis (NSF) in patients with:
  - Acute or chronic severe renal insufficiency (GFR <30 mL/min/1.73m^2), or
  - Acute renal insufficiency of any severity due to the hepato-renal syndrome or in the perioperative liver transplantation period.
- In these patients, avoid using gadolinium-based contrast agents unless the diagnostic information is essential and not otherwise available.

Where gadolinium itself is concerned, higher single doses (greater than 0.1mMol/kg) as well as higher cumulative doses appear to put one at risk for NSF. In one study, 0 out of 74,124 unscreened patients developed NSF when they received the standard 0.1mMol/kg gadolinium dose (6). Nonionic linear gadolinium agents may also have a higher incidence of NSF because they have the lowest stability. The macrocyclic agents are most stable and thought to be less prone to NSF development (9) (Table 3). In addition, the recently FDA-approved intravascular agent, gadofosveset (ablavar), also offers some theoretical advantages for avoiding NSF. This agent has increased intravascular retention time leading to reduced extravasation and thus less exposure to the tissues, as well as a higher relaxivity which translates into less contrast volume given to each patient. Finally, it has a biliary excretion pathway as well as a renal excretion pathway. However despite the potential theoretical advantages of some agents over others, the FDA black box warning applies to all gadolinium agents (Table 4).

Clinical Presentation

The cutaneous lesions of NSF appear to predominate. The lesions are typically symmetrical and usually extend from the feet to mid thigh and from the hands to the middle upper arms (Figures 1 and 2). In general, the trunk is less commonly affected and the face is usually spared. The primary lesions consist of firm skin-colored to erythematous papules or nodules that coalesce into reddish-brown indurated plaques (10). The skin usually becomes thickened and shiny and can possess a peau d'orange aspect. The lesions can extend beyond the joints leading to restriction of movement.

Extracutaneous or systemic involvement is subject to some debate. Most of the cases were published before 2006 and therefore before gadolinium was associated with NSF. Some systemic involvement also was based on functional testing and not always proven by histology. Finally, some of the neuropathic and myopathic changes reported were nonspecific and occurred in patients with sequelae of end stage renal disease or other co-morbid conditions. Given these caveats, NSF may be seen to affect the skeletal muscles, gastrointestinal tract (esophagus and stomach), cardiac muscle (fibrosis), central nervous system (fibrosis of serous membranes and meninges) and eyes (scleral plaques).

Diagnosis

The diagnosis of NSF is predominantly a clinical diagnosis. Because it is rare, it is not usually suspected and is usually misdiagnosed as cellulitis. There is no laboratory biomarker for NSF. The most significant laboratory finding is impaired renal function. NSF should be suspected in any patient with the history of renal dysfunction who has received gadolinium contrast and who develops scleroderma-like cutaneous lesions on the distal extremities.

The differential diagnosis includes other fibrosing skin disorders (Table 5). It should be noted that an important diagnostic feature of NSF is that it spares the face.

The diagnosis of NSF can be confirmed by a deep incisional skin biopsy. The histopathological findings depend on the point of time in the disease process. Mature lesions show proliferation of spindle cells, thick collagen bundles with surrounding clefts and some mucin and elastic fibers. The immunohistochemical identification of CD34-positive spindle cells, procollagen-I producing cells with a stellate appearance, CD68-positive multinuclear macrophages, and factor XIIIa-positive cells all support the diagnosis of NSF.

Treatment

Currently there is no effective treatment for NSF. Therapeutic strategies have been directed at improving renal function, hindering the progression of fibrosis and physical therapy with pain control to improve joint contractures.

The literature describes multiple different treatment methods for NSF. These include ultraviolet light, plasmapheresis, extracorporeal photopheresis, compression stockings in combination with steroids and methotrexate, sodium thiosulfate and imatinib. However all of these therapies lack controlled trials.

It has been shown that improvement of kidney function has terminated the progression of NSF and occasionally allowed the disease to resolve. The best current option for treatment of patients with end stage renal disease and NSF is kidney transplantation. However, in some cases even kidney transplant did not result in improvement.

Prevention

Since no effective treatment exists, prevention of NSF is most important. The current OHI policy for the prevention of NSF begins with obtaining a creatinine and estimated glomerular filtration rate (eGFR) for all patients at risk for reduced renal function. These patients would include age greater than or equal to 65, diabetics, anyone with a history of renal disease or renal transplantation, or anyone with a history of liver transplantation or hepato-renal syndrome.

Table 5
Clinical Differential Diagnosis for NSF

- Scleromyxedema
- Eosinophilia-myalgia syndrome
- Eosinophilic fasciitis (Shulman syndrome)
- Systemic sclerosis/morphea
- Sclerodermoid graft-versus-host disease
- Porphyria cutanea tarda
- Fibroblastic rheumatism
- Scleredema
- Toxic oil syndrome
- Vinyl chloride exposure
- B2-microglobuline amyloidosis
- Amyloidosis
- Dermatofibrosarcoma protuberans
- Carcinoid syndrome
- Calciphylaxis
- Dystrophic calcification

From Mayr M, Burkhalter F, and Bongartz G. Nephrogenic Systemic Fibrosis: Clinical Spectrum of Disease. J Magn Reson Imaging 2009; 30:1289-1297.

For patients with stage 4 or 5 chronic kidney disease (CKD) (eGFR < 30mL/min/1.73 m^2): 1. the cardiologist determines if gadolinium use is essential for the diagnosis and that alternative tests are not adequate or available. 2. The patient is informed of all potential risks and patient consent for gadolinium is obtained. 3. The dose of gadolinium will not exceed a single dose or 0.1 mmol/kg. 4. Nonionic linear gadolinium agents will not be used. 5. If the patient has stage 5 CKD or is on hemodialysis then hemodialysis, is to be scheduled the same day as soon as possible after the MRI. The patient must also have a second dialysis session one day following. So, hemodialysis is required on 2 successive days. If the patient is on peritoneal dialysis the use of gadolinium is strongly discouraged.

Conclusions

Despite the recent concerns regarding NSF, it remains a rare disease that occurs predominately in patients with severe acute or chronic renal impairment who receive gadolinium. It presents initially as a skin disease. Its diagnosis can be confirmed with a skin biopsy, and currently there is no established effective therapy. If patients require a gadolinium MRI the risk of NSF can be greatly reduced using certain prevention strategies.

Edward T. Martin is a noninvasive cardiologist with subspecialty expertise in non-invasive imaging. He is a founding member of the Society of Cardiovascular Magnetic Resonance and is an editorial board member of the Journal of Cardiovascular Magnetic Resonance.

References

1. *Cowper SE, Robin HS, Steinberg SM, Su LD, Gupta S, Leboit PE. Scleromyxoedema-like cutaneous diseases in renal-dialysis patients. Lancet 2000; 356:1000-1001.*
2. *Grobner T. Gadolinium — a specific trigger for the development of nephrogenic fibrosing dermopathy and nephrogenic systemic fibrosis? Nephrol Dial Transplant 2006; 21:1104–8.*
3. *Marckmann P, Skov L, Rossen K, et al. Case-control study of gadodiamide-related nephrogenic systemic fibrosis. Nephrol Dial Transplant 2007; 22:3174–8.*
4. *Food and Drug Administration Public Alert. Information for health care professionals: gadolinium-based contrast agents for magnetic resonance imaging (marketed as magnevist, Multihance, Omniscan, OptiMARK, ProHance). Available at: http://www.fda.gov/cder/drug/InfoSheets/HCP/gcca_200705.htm. Accessed May 5th, 2011.*
5. *European Agency for the Evaluation of Medicinal Products (EMEA). Public assessment report: increased risk of nephrogenic fibrosing dermopathy/nephrogenic systemic fibrosis and gadolinium-containing MRI contrast agents. Available at: http://www.ismrm.org/special/EMEA3.pdf. Accessed May 5th, 2011.*
6. *Prince MR, Zhang H, Morris M, et al. Incidence of nephrogenic systemic fibrosis at two large medical centers. Radiology 2008; 248:807–16.*
7. *Kanal E, Barkovich AJ, Bell C, et al. ACR Guidance Document for Safe MR Practices: 2007. AJR Am J Roentgenol 2007; 188:1447–74.*
8. *Prince MR, Zhang HL, Roditi GH, Leiner T, and Kucharczyk W. Risk Factors for NSF: A literature review. J Magn Reson Imaging 2009; 30:1298-1308.*
9. *Kribben A, Witzke O, Hillen U, Barkhausen J, Daul AE, and Erbel R. Nephrogenic Systemic Fibrosis: Pathogenesis, Diagnosis, and Therapy. J. Am. Coll. Cardiol. 2009; 53; 1621-1628.*
10. *Mayr M, Burkhalter F, and Bongartz G. Nephrogenic systemic fibrosis: clinical spectrum of disease. J Magn Reson Imaging 2009; 30:1289-1297.*

Understanding Heart Disease

By Elaine Burkhardt

An Interview with Edward T. Martin, 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.

He is a founding member of the Society of Cardiovascular Magnetic Resonance and is an editorial board member of the Journal of Cardiovascular Magnetic Resonance.

Where does Oklahoma, or Tulsa to be more specific, rank in terms of heart disease-related deaths?

Dr. Martin: Heart disease is the leading killer of both men and women in the state of Oklahoma. The last detailed United States state rankings were from 2009 and showed that Oklahoma was 48 out of 50 states in cardiovascular deaths. The third worst.

From a statewide standpoint, the last compiled statistics for Oklahoma were from 2004-2006. In those rankings, Tulsa County ranked 28 out of Oklahoma's 77 counties for heart-related deaths. Oklahoma City was slightly better and ranked 25th. From an overall state perspective, heart-related deaths generally occurred more in the southeastern counties of Oklahoma and were lowest in the northwest counties.

What are the warning signs?

Dr. Martin: The most classic symptom for a heart attack is discomfort in the center of the chest that lasts more than a few minutes, or that goes away and comes back. It can feel like uncomfortable pressure, squeezing, fullness or pain. However other symptoms can include pain or discomfort in one or both arms, the back, neck, jaw or stomach. Other symptoms that may or may not occur include breaking out in a cold sweat, nausea or lightheadedness.

As with men, a woman's most common heart attack symptom is chest pain or discomfort. But women are somewhat more likely than men to experience some of the other common symptoms, particularly shortness of breath, nausea/vomiting, and back or jaw pain.

What is a person's risk of having a heart attack or suffering from a heart-related condition?

Dr. Martin: The controllable risk factors that increase the risk of developing a heart attack or stroke are smoking, high blood pressure, high cholesterol, diabetes, overweight and obesity and physical inactivity. Additional risk factors include male gender and family history of heart disease.

Multiple risk calculators exist to help the individual person calculate his or her own risk of having a heart attack or dying from coronary heart disease over the next 10 years. One of the better ones can be found at the American Heart Association (AHA) website at http://www.heart.org/HEARTORG/Conditions/HeartAttack/HeartAttackToolsResources/Heart-Attack-Risk-Assessment_UCM_303944_Article.jsp. But. in general, the greater the number of risk factors you have, the greater the risk; especially if the risk factors are not well controlled.

What screenings are important to help someone learn their risks and what can the doctors at Oklahoma Heart Institute do to help people manage those risks?

Everyone should know their risk factors, including your cholesterol, blood pressure, blood sugar and hs-CRP blood test for inflammation. At OHI, we offer inexpensive screening tests to evaluate carotid arteries, cardiac function, peripheral artery disease and your risk for abdominal aneurysm. We also offer a cardiac calcium score to measure arterial plaque buildup, which can cause blockages and heart attacks. All of the tests are painless and literally can save your life and prevent heart attack and strokes.

What local resources are available to help people facing heart disease?

Dr. Martin: Because of the internet, these days it is not as important as it used to be to have local resources available. A wealth of information can be garnered online. Multiple resources are available at the American Heart Association website at http://www.heart.org/HEARTORG/. There you'll find information on diet, exercise, weight loss, nutrition, research, smoking cessation and much more.

However local resources do exist. In Oklahoma, the following resources are available:

The Oklahoma State Department of Health's Heart Disease and Stroke Prevention Program has resources available at http://www.ok.gov/health/Disease,_Prevention,_Preparedness/Chronic_Disease_Service/Heart_Disease_and_Stroke_Prevention_Program/index.html.

Smoking cessation help from the Oklahoma Tobacco Settlement Endowment Trust is available at 1(800) quit-now and at http://www.ok.gov/tset/Programs/Helpline.html. Additional smoking cessation help

and resources can be found under the Oklahoma State Plan for Tobacco Use Prevention and Cessation at http://www.ok.gov/health/Disease,_Prevention,_Preparedness/Tobacco_Use_Prevention_Service/.

Tips on weight control, nutrition and physical activity can be found at Get Fit Eat Smart Oklahoma at http://www.ok.gov/strongandhealthy/%3Ci%3EGet_Fit_Eat_Smart%3C_i%3E_State_Plan/index.html.

Finally, local hospital websites can be loaded with useful information on preserving heart health. Take a look at www.oklahomaheart.com

How can we all reduce our risks? Are there nutrition and exercise tips?

Dr. Martin: Certain lifestyle modifications can help you reduce your risk of developing coronary heart disease. Most are simple to start but require dedication to implement completely.

- Exercise. The AHA recommends 30 minutes of moderate exercise a day at least five days per week. Or 15 minutes per day of vigorous activity. A simple positive change you can make to effectively improve your heart health is to start walking. A walking program is flexible and boasts high success rates because people can stick with it.

- Reduce the amount of "bad fats" or saturated fats and *trans*-fatty acids in your diet. These fats are bad and raise the bad or LDL cholesterol levels in the blood. They are commonly found in animal meats and dairy products and in many baked goods, fried foods and snack foods.

- Eat more fish. At least two times per week. They provide omega 3 fatty acids, which may help prevent heart disease and heart arrhythmias. Omega-3 fatty acids are one of the "better fats". These are the monounsaturated and polyunsaturated fats. You should try to replace the bad fats with the better fats. These fats are commonly contained in canola oil, olive oil, peanut oil, sunflower oil, avocados, many nuts and seeds and oily fish (salmon, tuna, mackerel, herring and trout).

- A heart healthy diet should include a variety of fruits, vegetables, grains, legumes, fat-free or low-fat dairy products, fish, poultry and lean meats.

- Reduce your salt intake. High-sodium diets are linked to an increase in blood pressure and a higher risk for heart disease and stroke. Americans on average consume 3,436 mg of sodium daily. Many experts now believe that lowering daily consumption to no more than 1,500 mg of sodium daily would be an effective way to prevent or lower high blood pressure.

- If you are overweight, lose weight. Losing as few as 10 pounds can lower your heart disease risk. Last year 32% of Oklahoma adults were classified as obese. That is having a Body Mass Index (BMI) of 30 or higher. BMI is a numerical value of your weight in relation to your height. BMIs are good indicators of healthy or unhealthy weights for adult men and women, regardless of body frame size. A BMI of less than 25 indicates a healthy weight. A BMI of less than 18.5 is considered underweight. A BMI between 25 and 29.9 is considered overweight. BMI calculators can be found at multiple websites. However The National Heart Lung and Blood Institute has many resources in addition to a BMI calculator at http://www.nhlbisupport.com/bmi/.

- If you smoke, stop. Smokers are 4 times more likely to develop coronary heart disease. One in four Oklahoma adults, or 650,000 people, currently smoke. Smoking cessation is the most important lifestyle modification that one can make to reduce the risk of heart disease and stroke. If you can only make one change, this should be it.

If a person does have heart disease, what treatment options are available?

Dr. Martin: The treatment options will vary depending on the nature and severity of the coronary heart disease. The options will range from medical therapy to possibly angioplasty or heart stent to coronary artery bypass surgery. Once you have been affected with coronary heart disease. it is important to try and prevent it from getting worse to improve overall quality of life and extend survival. This is called secondary prevention. The goals for secondary prevention are:

- Complete smoking cessation.
- Blood pressure under 140/90 mmHg and under 130/80 mmHg in people with diabetes or chronic kidney disease.
- Exercise 30 to 60 minutes of moderate-intensity aerobic activity, such as brisk walking, on most but preferably all days of the week, supplemented by an increase in daily lifestyle activities (e.g., walking breaks at work, gardening, household work). High risk patients (e.g., recent acute coronary syndrome or revascularization, heart failure) benefit from medically supervised cardiac rehabilitation programs.
- Weight management with a Body Mass Index (BMI) between 18.5–24.9 kg/m^2 and waist circumference less than 40 inches in men and less than 35 inches in women.
- Start dietary therapy. Reduce intake of saturated fat (to less than 7 percent of calories) *trans*-fatty acids, and cholesterol (to less than 200 mg dietary cholesterol per day). Add plant stanol/sterols (2 grams/day) and viscous fiber (more than 10 grams/day) to further lower LDL cholesterol blood levels. Increased intake of omega-3 fatty acids in the form of fish or in capsule form (1 gram/day) for risk reduction. For treating elevated triglycerides, higher doses are usually necessary for risk reduction.
- In diabetics HbA1c less than 7 percent.
- Aspirin therapy 75-162 mg/day in all patients unless contraindicated.
- Reduce LDL cholesterol levels to less than 100 mg/dL and ideally less than 70 mg/dL.

These are the essential secondary prevention guidelines. Consult with your physician or cardiologist to individualize additional medical therapy and lifestyle changes.

Oklahoma Heart Institute Sleep Care
of Hillcrest Medical Center

Oklahoma Heart Institute now offers comprehensive sleep care at our new diagnostic facility located in Columbia Plaza:

2651 E. 21st Street, Suite 400
Tulsa, OK 74114
Phone: 918.747.5337 (918.74 SLEEP)
Toll Free: 855.437.5337 (855.43 SLEEP)
Fax: 918.728.3307

The facility features 6 beds, and operates most nights per week.

What to expect during a sleep study:

- A warm welcome by highly qualified technicians
- An informal orientation during which the sleep study process will be explained, and you will have an opportunity to ask questions
- A comfortable, stylish and luxurious bedroom featuring:
  - Queen sized, luxury bed with pillows
  - 300+ thread count sheets
- A continental breakfast in the morning

OklahomaHeart.com

Guidelines Update for Management of Atrial Fibrillation

By Craig S. Cameron, MD, FACC

Recently, focused updates to the guidelines for management of atrial fibrillation (AF) were published.[1,2] This article summarizes the major updated guideline recommendations regarding dronedarone, catheter ablation, and dabigatran.

Classification of recommendations:

- Class I – Benefit >>> Risk. The procedure/treatment should be performed or administered.
- Class IIa – Benefit >> Risk. It is reasonable to perform procedure/administer treatment.
- Class IIb – Benefit ≥ Risk. Procedure/treatment may be considered.
- Class III – No benefit or possibly causes harm.

Dronedarone

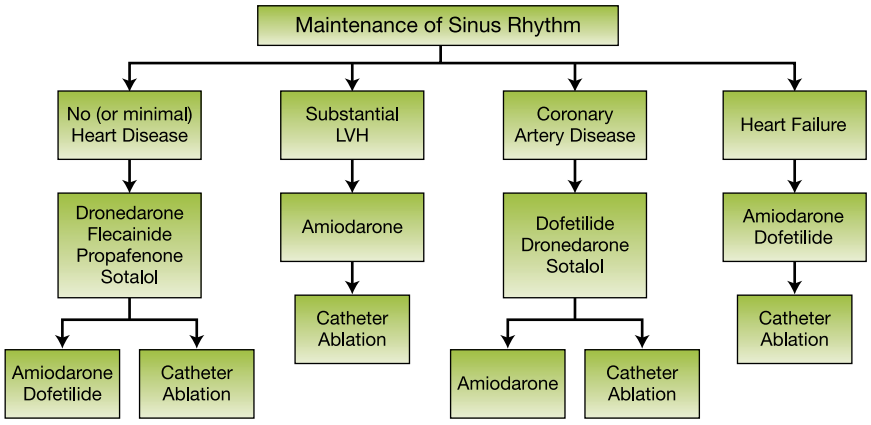
Dronedarone is a chemical derivative of amiodarone with multiple electrophysiologic effects including sympatholytic actions and blockade of calcium, sodium, and potassium channels. Because dronedarone lacks an iodine moiety, it does not cause end-organ (e.g., thyroid, liver, and lung) toxicity like amiodarone. In the ATHENA trial[3], dronedarone reduced the combined endpoint of cardiovascular hospitalizations and death by reducing cardiovascular mortality and hospitalizations secondary to AF. All-cause mortality was not reduced. Patients with recently decompensated (within 4 weeks) or NYHA Class IV heart failure were excluded from ATHENA. There was, however, no evidence for adverse events in the subgroup of patients with LV ejection fraction <35% or a history of congestive heart failure. In the ANDROMEDA trial[4], dronedarone increased mortality when used in patients with depressed LV function and recently decompensated heart failure. This higher mortality occurred after a median follow-up of only 2 months and was associated with greater progression of heart failure. On the basis of this trial data, use of dronedarone is reasonable to decrease cardiovascular hospitalization in patients with paroxysmal or persistent AF (Class IIa Recommendation). Dronedarone should not be used in patients with class IV or recently decompensated (within 4 weeks) heart failure, especially if the LV ejection fraction is ≤ 35% (Class III Recommendation). Therapies for maintenance of sinus rhythm in patients with AF, including dronedarone, are summarized in Figures 1 and 2.

Catheter Ablation for AF

Trials and meta-analyses of catheter ablation for AF now include data from over 6900 patients. Optimal patients for catheter ablation are those with symptomatic, paroxysmal AF who have failed treatment with at least one antiarrhythmic drug, have a structurally normal heart, and lack comorbidities such as obesity, sleep apnea, and lung disease (Figure 3). Following ablation, the majority of such patients remain free of recurrent AF at 1 year or more. When compared to trials of antiarrhythmic drug therapy, studies of AF catheter ablation report higher efficacy rates with lower adverse event rates.[5] Taking into consideration rapidly accumulating trial data, growing clinical experience, and the superior efficacy of catheter ablation, the 2011 focused guideline update makes several important changes to recommendations regarding catheter ablation of AF. First, catheter ablation for AF now receives a Class I recommendation as a "rea-

Continued on p. 22.

Figure 1



Adapted from 2011 ACCF/AHA/HRS Focused Update on the Management of Patients With Atrial Fibrillation (Updating the 2006 Guideline) Heart Rhythm Vol 8, No 1, January 2011

Figure 2

Anti-Arrhythmic Drugs

Generic Name	Trade Name
Amiodarone	Cordarone, Pacerone
Dofetilide	Tikosyn
Dronedarone	Multaq
Flecainide	Tambocor
Propafenone	Rhythmol
Sotalol	Betapace

Continued from p. 21.

sonable alternative" to pharmacological therapy to prevent AF recurrence in symptomatic patients with little or no left atrial enlargement. Catheter ablation also receives a Class I recommendation to treat symptomatic paroxysmal AF that has failed antiarrhythmic drug therapy in the setting of normal or mildly reduced LV function, normal or mildly dilated atria, and no severe pulmonary disease. Class II recommendations for catheter ablation of AF now include the treatment of symptomatic persistent AF (Class IIa) and treatment of symptomatic paroxysmal AF in patients with significant LV dysfunction or significant left atrial dilation (Class IIb).

Dabigatran

The RE-LY trial[6] was a large, open-label, randomized trial comparing two doses of dabigatran etexilate (110 mg and 150 mg twice daily) to adjusted-dose warfarin (goal INR 2-3) in 18,113 patients with nonvalvular AF and one or more risk factors for stroke. The primary outcome was systemic embolism or all-cause stroke (hemorrhagic or ischemic). As compared to warfarin, dabigatran 150 mg twice daily reduced the rate of the primary endpoint by 35% ($p<0.001$ for superiority) without an increase in major bleeding. (See Dr. Wayne Leimbach's article on dabigatran ~ pages 5-7). With regards to safety, both doses of dabigatran demonstrated a reduction in life-threatening bleeding (intracranial and total bleeding). Dyspepsia was the only adverse event that was significantly more frequent in the dabigatran groups. Rates of drug discontinuation were also slightly higher with dabigatran.

On October 19, 2010, the FDA approved dabigatran etexilate for the prevention of systemic embolism and stroke in patients with nonvalvular AF, with 150 mg twice-daily dosing for patients with a creatinine clearance above 30 ml/min and 75 mg twice-daily dosing for patients with a creatinine clearance of 15-30 ml/min.

The updated guidelines recommend (Class I) that dabigatran is useful as an alternative to warfarin for prevention of thromboembolic complications in patients with AF and risk factors for stroke or systemic embolism who do not have severe renal failure (creatinine clearance < 15 ml/min), impaired clotting function, hemodynamically significant valve disease, or a prosthetic heart valve.

When compared to trials of antiarrhythmic drug therapy, studies of AF catheter ablation report higher efficacy rates with lower adverse event rates.

Craig S. Cameron is a specialist in cardiac electrophysiology, including catheter ablation of arrhythmia, atrial fibrillation management, pacemakers, implantable defibrillators, and cardiac resynchronization devices.

References

1. *Heart Rhythm 2011; 8(1):157.*
2. *JACC 2011; 57(11): 1530.*
3. *NEJM 2009; 360(7):668.*
4. *NEJM 2008; 358:2678.*
5. *Circ Arrhythmia Electrophysiol. 2009;2:349-361.*
6. *NEJM 2009; 361(12):1139*

Figure 3

Patient Selection for AF Ablation

Variable	More Optimal Patient	Less Optimal Patient
Symptoms	Highly symptomatic	Minimally symptomatic
Failed anti-arrhythmics	≥1	0
AF type	Paroxysmal	Longstanding persistent
Age	Younger (<70)	Older (>70)
LA size	Smaller (<5 cm)	Larger (>5 cm)
Ejection fraction	Normal	Reduced
Congestive heart failure	No	Yes
Other cardiac disease	No	Yes
Pulmonary disease	No	Yes
Sleep apnea	No	Yes
Obesity	No	Yes
Prior stroke/TIA	No	Yes

HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation Heart Rhythm Vol 4, No 6, June 2007

all heart.

close to home.

Now you don't have to leave home to get the most advanced heart care in the region. Oklahoma Heart Institute's 25 specialists provide top-notch care where you need it most. We see patients in our Oklahoma Heart Institute Hospital, two Tulsa offices, full time offices in Cushing and Owasso, and we also travel weekly to Bartlesville, Bristow, Claremore, Fairfax, Pryor, Vinita, Henryetta, Cleveland, Tahlequah, and Pawnee.

We'll take care of your heart in any of our convenient locations. It's all part of our commitment to expanding your access to our nationally recognized cardiovascular care.

Trust your heart to Oklahoma Heart Institute. Wherever you go, we are there.

918.592.0999
OklahomaHeart.com

Oklahoma Heart Institute
A Nationally Recognized Cardiovascular Institute

Heart Hospital
1120 S. Utica Ave.

Utica Physicians Office
1265 S. Utica Ave.

SouthPointe Physicians Office
9228 S. Mingo Rd.

OKLAHOMA HEART INSTITUTE
1265 S. Utica Avenue
Suite 300
Tulsa, OK 74104

IT'S A NEW DAY

In Cardiology. At Oklahoma Heart Institute.

It's a new day in cardiology because of what the doctors at Oklahoma Heart Institute are bringing you. We treat every kind of heart problem - even the most difficult ones. Day and night, our special training and team approach gives people like you great results. So you can live well. Isn't that what you want?

Oklahoma Heart Institute

918.592.0999 | **www.oklahomaheart.com** | 1120 S. UTICA AVE. Oklahoma Heart Institute (THE HEART HOSPITAL) | 1265 S. UTICA (UTICA PHYSICIANS OFFICE) | 9228 S. MINGO (SOUTHPOINTE PHYSICIANS OFFICE)