In 2016, the Vanderbilt Heart and Vascular Institute (VHVI) saw continued growth of its innovative clinical and research programs.

This issue of Vanderbilt Heart highlights several of these initiatives. On page 4, Dr. Joshua Beckman describes the new Section of Vascular Medicine. In collaboration with vascular surgeons and imaging experts, this group provides comprehensive management of a broad range of vascular disorders within one program. Also new in 2016, the Vanderbilt Marfan Syndrome and Aortic Disorders Center was created to serve the complex needs of patients with rare and common aortic disorders.

A similar surgical-medical collaboration has fueled the dramatic success of the cardiac transplantation and ventricular assist programs at VHVI. In calendar year 2016, Vanderbilt was the 2nd busiest heart transplantation program in the country, performing 77 adult heart transplants. On page 2, Dr. Ashish Shah describes some of the innovative approaches employed by the group to promote outstanding patient outcomes.

For many patients with complex cardiac disease, arrhythmias remain a vexing problem. On page 8, Dr. Arvindh Kanagasundram reviews the broad range of techniques for ablation of ventricular tachycardias at VHVI and Dr. Chris Ellis describes novel approaches to reducing stroke risk in atrial fibrillation via left atrial appendage closure.

VHVI also continues to expand the transcatheter options for complex valvular heart disease. Drs. Joseph Fredi, Robert Piana and Mark Robbins present several cases on page 12 that illustrate how transcatheter aortic valve replacement and transcatheter mitral valve repair can transform the care of highly complicated patients with aortic and mitral valve disease.

VHVI continues to experience robust growth of its innovative research programs. NIH funding to cardiology increased by a remarkable 150 percent in 2016. Vanderbilt cardiologists played key roles in numerous national research initiatives, including a $71 million five-year grant to serve as the Data and Research Support Center for the NIH Precision Medicine Initiative Cohort program.
It has been 50 years since the first human heart transplant and the first mechanical device was implanted as a bridge to heart transplant. Since that time we have seen these remarkable achievements of the 20th century become integrated into 21st century management of the advanced heart failure patient. As Vanderbilt’s program has grown to become one of the largest heart transplant and mechanical support programs in the United States, we are exploring what’s next.

In 2016, Vanderbilt performed a record 77 adult heart transplants, built upon on a multidisciplinary approach to care involving heart failure cardiologists, cardiac surgeons, critical care specialists, advanced practice nurses, and dedicated cardiac operating room teams. This level of commitment appears to be a critical determinant of patient outcomes. This infrastructure is not possible in all programs and raises the important question of whether there should be fewer transplant programs around the country. A new collaborative study led by Vanderbilt cardiac surgeon Dr. Ashish Shah utilized national data and statistical modeling to examine this issue. As detailed in the American Journal of Transplantation, redirecting cardiac transplantation procedures from small volume programs to larger centers would potentially save lives.

Vanderbilt has worked to broaden the eligibility criteria for heart transplantation. In 2016, the Vanderbilt advanced heart failure team performed a successful heart-kidney transplant in a 70-year-old man with a left ventricular assist device (LVAD) on chronic peritoneal dialysis. Ten years ago, transplanting such a patient would...
have been unthinkable. Today, clinical teams around the world are faced with an aging heart failure population that expects better quality of life. As older patients become eligible for advanced therapies, it is clear that they also require tailored approaches to rehabilitation, monitoring, and pharmacotherapy.

LVADs are increasingly used as therapy for advanced heart failure. Advances in surgical techniques and improved perioperative management strategies have facilitated expanded utilization of LVADs. Significant challenges to the growth in LVAD utilization persist, however. Device-related complications, such as early and late right ventricular (RV) failure, continue to influence outcomes. Gastrointestinal bleeding and stroke also continue to pose significant risks. The Vanderbilt Mechanical Support team utilizes a variety of strategies to address these challenges, and has robust basic and clinical research programs in these areas. Concomitant procedures such as tricuspid valve repair at the time of implant and percutaneous right ventricular support are frequently performed in patients at risk of right heart failure, and LVAD devices themselves have become more reliable. Led by Dr. Mary Keebler, Vanderbilt participates in the Heartmate 3 clinical trial, evaluating whether changes in LVAD design will impact these complications. Future research will examine the long-term outcomes and cost effectiveness of broader application of newer mechanical support devices.

In 2016, Vanderbilt performed a record 77 adult heart transplants.

**Adult and Pediatric Heart Transplantation**

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**3-year Survival (Adult and Pediatric)**

**Adult Survival**

- Adult Graft: 86.75%
- Adult Patient: 87.8%

**Pediatric Survival**

- Pediatric Graft: 95%
- Pediatric Patient: 95%

Single organ transplants performed between 7/1/12 and 12/31/15.
The Vascular Programs in the Vanderbilt Heart and Vascular Institute (VHVI) have taken several great leaps forward in the last year in terms of personnel, clinical initiatives, and research. VHVI has recruited two nationally known vascular surgeons, Drs. R. James Valentine, recently the Chief of Vascular Surgery at the University of Texas, Southwestern, and John Curci, from Washington University at St. Louis, bringing the surgical division to its current strength of four members. In addition, Dr. Joshua Beckman began the section Section of Vascular Medicine last year, and recruited Dr. Esther Kim from the Cleveland Clinic to join the section. The addition of two nationally prominent Vascular Medicine faculty has advanced the collaborative model of care at Vanderbilt, facilitating expert, team-based care for vascular disease of the highest levels of acuity and complexity. Rounding out the recent arrivals, Drs. Ashish Shah and Clayton Kaiser of Cardiac Surgery provide advanced expertise in the surgical management of aortic disease.

As VHVI has accumulated additional expertise, we are now offering more comprehensive care. Recently, the Vanderbilt Marfan Syndrome and Aortic Disorders Center has been developed to create a focus of expertise drawing from Vascular Surgery and Medicine, Cardiac Surgery, and our Adult Congenital Heart Disease programs to provide comprehensive care for patients with aortic disease. This center promises to organize diagnostic evaluation, medical therapy, endovascular interventions, and surgery under one roof to provide a one-stop shopping experience for patients. The recent additions to the program have also fostered efforts to
create similar programs for patients with peripheral artery disease and venous thromboembolism. VHVI has developed and acquired a level of expertise in vascular disease unparalleled in our region and recognized nationally for its quality.

One mechanism by which we stay in the vanguard is through investigation. The team is participating in several of the most important clinical trials in vascular disease. The Carotid Revascularization and Medical Management for Asymptomatic Carotid Stenosis Trial (CREST-2) is a national, multicenter clinical trial studying the role of both carotid surgery and carotid stenting compared with medical therapy in patients with asymptomatic internal carotid artery stenosis. Led by Dr. Louis Garrard, the Vascular Surgery team at Vanderbilt is an important enrolling site.

The Best Endovascular vs. Best Surgical Therapy in Patients With Critical Limb Ischemia (BEST-CLI) clinical trial is studying the role of endovascular and surgical therapy in patients with severe peripheral artery disease. Dr. Beckman of Vascular Medicine recently obtained National Institutes of Health (NIH) funding to study the mechanisms behind both surgical graft and endovascular stent failure. This grant is the sole ancillary study funded by the NIH and will provide information important to the interpretation of this national clinical trial.

The recent arrival of Dr. Kim has catalyzed VHVI’s program in arteriopathies. In addition to the creation of the Fibromuscular Dysplasia (FMD) and Spontaneous Coronary Artery Dissection comprehensive clinic, VHVI will become an important enrolling center for the Fibromuscular Dysplasia Society of America Patient Registry. This registry is responsible for the most important advances in our understanding of FMD in the last half century. VHVI is now home to a nationally recognized expert in FMD and provides the principal locus of expertise in the mid-South. As FMD is likely present in 4 – 6 % of the population, better recognition of this disease will enable earlier discovery, surer diagnosis, and the development of improved therapies for patients and families with this disorder.

Other investigative efforts include the studies of aortic endografts in aortic dissection, penetrating atherosclerotic ulcer, and thoracoabdominal aneurysm and dissection, with Dr. Thomas Naslund of Vascular Surgery as the local lead for each. In addition, Dr. John Curci, is a Principal Investigator of the NIH Non-Invasive Treatment of Abdominal Aortic Aneurysm Clinical Trial (N-TA^3CT ).

Finally, VHVI has begun collaborative efforts within the Medical Center at large to provide comprehensive care for patients with venous thromboembolism (VTE). The Vascular Medicine Team is working with colleagues in Benign Hematology, Interventional Cardiology, and the Emergency Department to create a systems approach to VTE.
**FIBROMUSCULAR DYSPLASIA**

Andrea was getting frustrated with her blood pressure. She had high blood pressure for the last 10 years and it was always easily controlled with one medication. However, over the last year she began getting headaches and her co-workers reported that she occasionally looked flushed. One day, she had the sudden onset of severe right-sided neck pain and a terrible headache, went to the emergency department, and was found to have very high blood pressure and a carotid artery dissection (a tear of the vessel’s inner lining). She was admitted to the hospital for blood pressure control and observation. Two additional medications were needed to control her blood pressure.

After discharge, she was referred to the Vanderbilt Vascular Medicine program for evaluation and met with Dr. Esther Kim. Kim reviewed Andrea’s medical history and performed a physical examination. In addition, Kim elicited a symptom that had eluded her previous physicians: ringing in the ear. Dr. Kim realized that Andrea likely had fibromuscular dysplasia, an inherited condition that can narrow the renal arteries and increase blood pressure. Kim ordered a CT scan that revealed the renal artery stenosis.

Kim worked with Vanderbilt interventional cardiologist Dr. Mark Robbins, who performed an angiogram, found the narrowed artery to the kidney, and repaired it with balloon angioplasty. Andrea’s blood pressure improved immediately, and she was discharged after the procedure taking only her original medication. VHVI brings together experts in vascular disease to provide comprehensive and complete care.

**MARFAN SYNDROME**

Susan was expecting the news. Her aorta was enlarged. In fact, it had been enlarging slowly but surely over the past few years. Susan was only 36 and young to have a dilated aorta, but Marfan Syndrome ran in her family. Her uncle died suddenly, her cousin had surgical repair of the aorta at age 33, and her father had aorta and heart valve surgery as well. Not everyone in the family had Marfan, but Susan underwent testing and was found to be affected.

Susan was referred to the Vanderbilt Marfan Syndrome and Aortic Disease Center and met with Dr. Clayton Kaiser of cardiothoracic surgery. Kaiser found that her aortic valve was regurgitant and consulted Dr. Joshua Beckman of cardiovascular medicine to help gauge the severity. Beckman obtained an echocardiogram and recommended a simultaneous repair of both her aortic valve and ascending aorta.

Kaiser performed a Bentall procedure, replacing both the valve and the ascending aorta. Susan did very well, left the hospital in 5 days, and was able to return to work in 4 weeks. The Vanderbilt Marfan Syndrome and Aortic Disease Center brings together specialists in Cardiovascular Medicine, Cardiothoracic Surgery, and Vascular Surgery to harness the necessary expertise to provide the highest level of care in a collaborative, team-based approach.
PERIPHERAL ARTERY DISEASE

James is a 78-year-old who has been managing his diabetes for several decades, trying to follow his doctor’s advice. He is careful with his diet and tries to get some exercise most days of the week, but it has become harder to do so recently because his right leg aches when he takes a walk around the neighborhood.

When James met with Vanderbilt vascular specialist, Dr. Joshua A. Beckman, he reported his progressively worse leg discomfort with walking. A physical exam revealed reduced peripheral pulses on the right. A CT scan created a road map of blockages in the blood vessel supplying the leg, accounting for the symptoms. Beckman then worked with Vanderbilt vascular surgeon Dr. Thomas Naslund, who implanted a stent to re-open the major areas of blockage found in the leg.

The procedure went well and James was able to go back to walking for exercise as his primary care physician recommended. In fact, he felt far more confident going to the store, parking far away from his destination, and just doing what he wanted to do.

Vanderbilt medical and surgical vascular specialists collaborate to bring the most advanced diagnostic and therapeutic modalities to our patients. This team-based approach to peripheral artery disease is central to the mission at Vanderbilt.

The addition of two nationally prominent Vascular Medicine faculty facilitates expert, team-based care for vascular disease of the highest levels of acuity and complexity.
At 80 years old, Katie has been managed for mild coronary artery disease, pulmonary hypertension, diastolic heart failure, chronic kidney disease, and prior stroke. She developed new-onset atrial fibrillation (AF) in early 2016 and anticoagulation with warfarin was initiated as she was deemed high risk for recurrent stroke (CHA2DS2-VASc score of 8). This was complicated by severe epistaxis requiring hospitalization and surgical treatment. After multidisciplinary consideration of the optimal approach to stroke prevention, she underwent closure of the left atrial appendage (LAA) using a WATCHMAN™ (Boston Scientific, Inc.) device. Anticoagulation was able to be stopped 6 weeks later. Her risk of recurrent stroke is now reduced to the same level as would be expected on chronic anticoagulation, but without the attendant bleeding complications.

Traditionally, oral anticoagulation has been the mainstay of stroke prevention in AF patients at risk for LAA thrombus. However, maintaining anticoagulation in the therapeutic range is challenging in practice and bleeding can complicate this strategy. Based on the results of the PROTECT-AF, PREVAIL, CAP, and CAP-2 studies, the FDA approved the WATCHMAN™ device in 2015. The approved indication is to reduce the risk of thromboembolism in patients with non-valvular AF who are at increased stroke risk and who are able to take warfarin, but who also have an appropriate rationale to seek a non-pharmacologic alternative to warfarin. From the femoral vein a transseptal puncture is performed and the device is deployed into the LAA, effectively plugging

Left to right: Arvindh N. Kanagasundram, M.D.; Christopher R. Ellis, M.D., FACC, Director, Electrophysiology Laboratory; M. Benjamin Shoemaker, M.D., M.S.C.I.
the LAA from within. At 4 years of follow-up, patients who received the WATCHMAN™ had fewer hemorrhagic strokes and lower overall mortality than patients randomized to warfarin therapy. After 45 days, patients who have successful WATCHMAN™ LAA closure are able to permanently discontinue anticoagulation (closure defined by <5mm peri-device ostial leak by TEE). Subsequent analysis has shown the WATCHMAN™ to be cost effective, and the continued improvement in implant technique has lowered adverse event rates below 1-2 %, with >98 % implant success.

Under the guidance of Dr. Christopher R. Ellis and Dr. Robert N. Piana, the Vanderbilt Heart and Vascular Institute LAA closure program was launched in 2013. Over 90 patients have already had a successful WATCHMAN™ implant, and all of them have been able to stop taking long-term anti-coagulation. Current candidates for a WATCHMAN™ LAA closure device include patients with non-valvular AF who have a
CHA2DS2-VASc score of 3 or higher and a suitable rationale to avoid the risks of long-term oral anti-coagulation.

Closure of the LAA is the focus of a vibrant clinical research program at Vanderbilt. Several studies are underway with the goal of supporting LAA closure as first-line therapy for stroke prevention in high-risk AF patients. The Amulet device (St. Jude Medical, Inc.) is an LAA closure device currently available in Europe, which will be compared head-to-head with the WATCHMAN™ device at Vanderbilt, starting in 2017. Patients with an absolute contraindication to oral anticoagulation may also be enrolled in the ASAP-TOO trial, randomizing patients to WATCHMAN™ followed by 6 months of aspirin plus clopidogrel versus medical therapy alone.

As opposed to the endovascular approach used to close the LAA with the WATCHMAN™ or Amulet device, the LARIAT device is a snare that is used to close the LAA from outside. The snare is delivered from a subxiphoid approach into the pericardial space and navigated to encircle the LAA, which is then sutured closed. The AMAZE trial is an ongoing Investigational Device Exemption study of the LARIAT system for LAA ligation as an adjunctive therapy to catheter ablation for persistent AF. The rationale for the study is based on evidence that a reduction in total AF burden by 25% may be seen following either catheter-based RF ablation with electrical isolation of the LAA, or by ligation of the LAA with LARIAT. Over 50 patients at Vanderbilt have had a successful LARIAT procedure, and Vanderbilt is now the second highest enroller in the AMAZE trial nationwide.
Catheter ablation of recurrent ventricular tachycardias (VTs) continues to be a rapidly evolving field and an important option in the management of patients with VT. Ablation can be used as sole therapy (often in patients without associated structural heart disease) or combined with an implantable cardioverter defibrillator (ICD) and pharmacologic therapy.

Significant advances in mapping and ablation techniques have resulted in high success rates in both idiopathic VT (>90% success rate) and scar-based VT (50-75% success rate). Several multi-electrode catheters are currently available to allow the collection of multiple points in space at one time. These allow for the creation of high-density maps with clean electrical signals that have improved both the accuracy and efficiency of ablation procedures. Intracardiac echocardiography now allows VT ablations to be performed with little-to-no fluoroscopy.

Combined endocardial and epicardial mapping is sometimes required in patients with non-ischemic cardiomyopathies. Percutaneous epicardial access can be obtained by a subxiphoid pericardial puncture or a minimally-invasive surgical approach can be utilized (in patients with prior cardiac surgery or pericardial adhesions). Cryothermal energy may have several potential advantages compared to radiofrequency energy (RF), including better stability and improved lesion formation. In hemodynamically unstable VTs, percutaneous left ventricular assist device placement can allow for end-organ perfusion while effectively mapping the VT. In cases of recalcitrant VTs that don’t respond to pharmacologic and catheter-based therapies, bilateral cardiac sympathetic denervation can be a safe and effective option.

The continued improvement in VT ablation techniques has contributed significantly to the understanding and success of catheter ablation. Novel Technologies and adjunctive therapies make this a field of exciting growth. The indications for VT ablation continue to expand, and ablation is increasingly recommended earlier in the course of the disease to prevent multiple ICD shocks and VT storm.
Continued Technical Innovation and a Patient-Centered, Multidisciplinary Approach

The multidisciplinary “heart team” approach is a central tenet of the Structural Heart Disease Program at Vanderbilt. Dedicated nurses and access coordinators ensure prompt access to the program, efficient testing, and exemplary communication with patients and families. Physicians from multiple disciplines come together to evaluate patients. Centralized testing facilitates this assessment and avoids redundant visits. Interventional Cardiology, Cardiac Surgery, Adult Congenital Heart Disease, imaging experts, and specialized nurses together formulate the optimal treatment strategy for each patient.

The Structural Heart Disease Program strives for continued innovation. Indications for TAVR have continued to evolve with the FDA recently approving this procedure for patients at intermediate risk for conventional surgery. There are two ongoing trials evaluating low-risk surgical patients, the PARTNER III trial (Edwards Lifesciences) and the CoreValve (Medtronic Inc.) Low-Risk Trial. Vanderbilt is currently enrolling patients in the CoreValve Low-Risk Study.

Through the Structural Heart Program, Vanderbilt offers a number of innovative approaches to clinical dilemmas. For instance, in select patients, TAVR technology may be employed for valve-in-valve procedures to address bioprosthetic mitral, aortic, and tricuspid stenosis. In patients whose leg arteries are too small to accommodate the standard arterial access for TAVR, we have adopted a novel “transcaval” approach in which a puncture is created between the inferior vena cava and the aorta to allow delivery of the TAVR system. Furthermore, transcatheter...
placement of valves in the inferior vena cava has now been utilized to treat tricuspid valve regurgitation.

We are committed to optimizing clinical outcomes in this dynamic field. Drs. Robert Piana and Mark Robbins, along with Sonia Scalf, RN, are participating in a multicenter prospective assessment of clinical outcomes in TAVR patients, focusing on biomarkers and objective measures of frailty.

As the field of structural heart interventions continues to expand, Vanderbilt is positioned at the leading edge of technical advances and robust clinical research. This commitment to continued technical innovation is balanced by an unwavering dedication to patient-centered care using a team-based approach.

**Structural heart procedures offered at Vanderbilt currently include:**

- Transcatheter Aortic Valve Replacement (TAVR)
- Transcatheter Mitral Valve Repair (MitraClip)
- Valvuloplasty: Aortic, Mitral, Pulmonary
- Closure of Atrial Septal Defects and Patent Foramen Ovales
- Alcohol Septal Ablation for Hypertrophic Obstructive Cardiomyopathy
- Paravalvular Leak Closure
- Pulmonary Vein Stenosis Stenting
- Adult Congenital Heart Disease Interventions (in collaboration with the Monroe Carell Jr. Children’s Hospital at Vanderbilt)

**Advances in Structural Heart Disease Management**

**Transcatheter Mitral Valve Intervention**

LL underwent mantle radiation for Hodgkin’s Lymphoma at age 22. Cardiac evaluation at age 58 for chest discomfort and dyspnea with exertion revealed severe multi-vessel coronary artery disease (CAD) and severe aortic valve (AV) stenosis, both of which were attributed to prior radiation therapy. He underwent successful 4-vessel coronary artery bypass grafting and mechanical AV replacement.

Ten years later, at age 68, he developed recurrent severe dyspnea and was hospitalized twice for treatment of congestive heart failure. Echocardiogram demonstrated preserved systolic function, a normally functioning prosthetic AV, and severe mitral regurgitation (MR). Transesophageal echo (TEE) showed a partially flail posterior leaflet and severe MR. All grafts were widely patent by coronary angiography and his ascending aorta was severely calcified. He was considered for MV replacement or repair, but his risk for open surgery was felt to be prohibitive.

At the Vanderbilt Heart and Vascular Institute, TEE images suggested that the primary problem was degenerative valve disease affecting primarily the P2 segment of the posterior MV leaflet. He was therefore considered for transcatheter mitral valve repair using the MitraClip (Abbott Vascular) system. This device is currently approved for treatment of degenerative MR with severity ≥3+ resulting in New York Heart Association functional class III or IV heart failure in patients who are at prohibitive risk for mitral valve surgery. In the hybrid catheterization lab-operating room, Dr. Joseph Fredi
(Interventional Cardiology) and Dr. Stephen Ball (Cardiac Surgery) together placed one MitraClip device to attach the P2 segment of his posterior MV leaflet to the A2 segment of the anterior leaflet. His MR was reduced from severe to mild. He was discharged the following day. At 4-week follow-up, LL was able to walk ½ mile without difficulty. Echocardiogram now demonstrated only mild MR.

Transcatheter Aortic-Valve Replacement (TAVR)

JF is a 49-year-old man with severe aortic and moderate mitral stenosis, both thought to be secondary to radiation therapy received in childhood for Hodgkin’s lymphoma. A variety of cardiologists and cardiac surgeons have deemed him to be at prohibitive risk or very high risk for conventional surgery due to his history of mediastinal radiation. JF was evaluated at Vanderbilt’s TAVR clinic by Dr. Stephen Ball (Cardiac Surgery) and Dr. Mark Robbins (Interventional Cardiology). They both felt that TAVR would be JF’s best treatment option for aortic stenosis. He underwent successful transfemoral TAVR using a SAPIEN valve and was discharged home in 48 hours with full resolution of symptoms. This case highlights the remarkable advancements in the treatment of aortic stenosis over the past decade. Prior to the advent of TAVR, patients like JF would have either undergone a very high-risk surgery or received no treatment for their aortic stenosis.

JF’s story did not end with one successful valve replacement, however. After two years of stability, he presented with recurrent congestive heart failure. Echocardiogram confirmed proper function of the SAPIEN aortic valve, but the mitral stenosis was now severe. He was at extreme risk for conventional mitral valve replacement, and extensive valvular calcification precluded balloon mitral valvuloplasty. With concentric heavy calcification of the mitral annulus, it was thought that a valve-in-native mitral valve technique might be an option. JF subsequently underwent successful transapical SAPIEN implant within his native mitral valve (Image) and is doing well to date.
Resources:

Vanderbilt Heart & Vascular Institute Clinics

130,000 Clinic Visits in 2016

Vanderbilt Heart & Vascular Institute Mobile App for Referring Providers
Saving you time. Improving communications.

- Direct contact to our specialists via phone or email
- 24/7 access for transfers and referrals
- Current on-call providers
- Directory of treatment programs
- Physician profiles
- Clinic addresses and directions

Search for “Vanderbilt Heart and Vascular Institute” in the Apple App Store for iOS devices or Google Play for Android devices.

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