Dear Colleague:

It is a pleasure to bring to your attention a new endeavor in cardiovascular medicine at The University of Toledo. With the publication of the first issue of The Heart of the Matter, a quarterly communication designed to highlight the newest developments in cardiovascular care, we hope to provide you with a convenient and informative update on the challenges and controversies in managing patients with cardiovascular disease. We hope that you will find this communication practical, helpful and timely. The content will address broad topics within cardiology, vascular surgery and cardiac surgery as well as provide you with appropriate references for more in-depth information. In addition, we would like to share with you the various research endeavors at the University that may be of value for your patients.

Please feel free to contact us should you wish to discuss any information that is presented in the current or future issues. We look forward to working collaboratively with you to successfully address the clinical and economic challenges facing both physicians and patients as we strive to provide our patients in northwest Ohio and southeast Michigan the best cardiovascular care.

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Heart failure is a huge problem. Congestive heart failure (CHF) remains the number one expense for Medicare ($39 billion annually) and there are nearly 6 million people in the United States with heart failure. Some 500,000 new cases are diagnosed every year, with more than 300,000 dying each year from the condition. Its course is unpredictable, especially as a patient nears the end stages, i.e., NYHA class III or IV. Frequently, advanced CHF not only significantly limits life expectancy — with a typical prognosis of six to 12 months — but it robs patients of their quality of life, often leaving them too short of breath or too tired to go out, travel or even dress themselves, with hospital stays becoming more frequent. While medical treatment has certainly advanced, disease progression is inevitable, albeit unpredictable. Frequently, advanced CHF becomes a progressive downhill spiral, an existence punctuated with frequent readmission rates of 25 percent within a month of an index hospitalization. While heart transplant remains the gold standard treatment, only 2,500 donor hearts are available each year. A combination of advances in engineering and medicine with a significant influx of venture capital has led to increasingly sophisticated mechanical circulatory support platforms — or Left Ventricular Assist Devices (LVADs) — that are capable of fully supporting the function of the left side of the heart. The idea is not new, but it has taken decades to produce pumps that can offer nearly the same quality of life and survival as heart transplantation.

The HeartMate II LVAD is currently the only such pump that is FDA approved for patients with end-stage heart failure whether or not they qualify for transplant. The operation is both less lengthy and much less invasive than previous generation devices, recovery times are faster, two-year survival now rivals transplantation at up to 75 percent. Compared to a two-year survival of only 8 percent with optimal medical management available only a decade ago, the current survival rate represents a dramatic improvement. Most importantly, patients stay out of the hospital, return to their primary doctors and communities, and to their lives, friends, families and even their pets (our last patient was eager to walk his Rottweiler again, which he did six weeks after his implant). As the experience with this technology grows, the outcomes are improving, and patients have been maintained on these devices for as long as seven years.

UT is pleased to offer this technology to the Toledo community and surrounding area. Our LVAD program operates as a partnership with both the University of Michigan and The Ohio State University to offer heart transplantation for those who may qualify. This program and its partnerships uniquely position UT to offer a comprehensive heart-failure treatment program in collaboration with all cardiovascular specialists within the community. To ensure success, an integrated team approach to the management of these complex patients, encompassing input from all providers, is absolutely necessary.

If you would like to speak with one of our physicians about our program or refer a patient, please call 419.383.5150 or 419.383.3963 and we will be happy to work with you.
Peripheral vascular disease (PVD) is a common problem that increases in the aging population. The term peripheral vascular disease includes several categories such as peripheral arterial disease (PAD), cerebrovascular disease, aortic aneurysms and a wide range of venous disease such as varicose veins, deep venous thrombosis and pulmonary embolism.

PAD alone affects more than 8 million Americans with significant morbidity and mortality. It is more prevalent in older age groups and is estimated to affect 10 percent to 12 percent of Americans older than 65 years of age. In spite of its prevalence, only 25 percent of people affected by PAD are undergoing treatment, partly because only 10 percent of individuals with PAD are symptomatic. Another manifestation of PVD is stroke, which, according to the 2010 statistics, affects more than 70,000 people each year, causing more than 140,000 deaths. The risk of stroke doubles each year after age 55 and doubles in smokers compared to nonsmokers.

Venous disease is another vascular problem with an estimated total cost of $3.2 billion to $13.5 billion per year. In a screening study, 6 percent of subjects had venous obstruction in one or more segments, while 40 percent had one or more segments of venous reflux in the lower extremities. Varicose veins were present in 32 percent, edema without skin changes in 11 percent, skin changes attributable to venous disease in 8 percent, and healed or active venous stasis ulcers in 1.3 percent.

Knowing the breadth and depth of vascular disease in the community, the vascular surgery group at The University of Toledo developed a one-stop center for the management of all aspects of vascular disease starting from non-invasive evaluation of all vascular disorders to medical therapy to the most complex open procedures, including all minimally invasive procedures with the most modern technological advances available, supplemented by a comprehensive wound and hyperbaric oxygen therapy center to treat all ulcers in the body.

UT surgeons were some of the first in the area to utilize carotid artery stenting, a less invasive approach to vascular care. We were instrumental in implementing endoluminal stent grafting as a way to treat aortic aneurysms, a technique that has proven to be a life-saving technology. We treat peripheral artery disease (PAD), with state-of-the-art techniques while participating in multiple research trials bringing otherwise unavailable technology to our community. Our approach to PAD, treating both the underlying condition and any resulting wounds, truly saves limbs and lives.

The University of Toledo’s commitment to ongoing research includes constant evaluation of less invasive vascular treatments compared to surgery, to determine the most effective and efficient measures to facilitate excellent patient outcomes. Most importantly, our integrated approach to care creates an unmatched patient-centered experience.

The UT Medical Center is a premier provider of inpatient and outpatient care to treat the whole range of vascular conditions with all treatment options available to our patients. Having mastered the entire range of treatment options, treatment offered is tailored to the needs of each patient for diseases such as:

- Peripheral arterial disease (PAD)
- Carotid artery disease
- Thoracic diseases/aortic diseases
- Atherosclerosis in aortic and its branches
- Mesenteric ischemia and renal artery disease
- Iliac disease
- Arterial blockages to arms
- Acute venous thrombosis, pulmonary embolism and chronic venous insufficiency
- Varicose veins

Our treatment specialties include:

- Open and minimally invasive aneurysm repair, both in the abdominal and thoracic
- Carotid artery stents and carotid endarterectomy
- Peripheral arterial disease (PAD), including drug therapy, balloon angioplasty, surgical revascularization and arterial stenting
- Thrombolytic therapy and other treatments to dissolve and suction deep vein thrombosis (DVT)
- Endolaser ablation and microphlebectomy for varicose veins
- Sclerotherapy for spider veins

Diagnostic services are performed at the Non-invasive Vascular Laboratory. We are nationally certified to perform carotid duplex ultrasound imaging; arteriovenous (AV) fistula, bypass grafts; and upper- and lower-venous studies; and arterial pressure studies.

We utilize our lab to screen the members of the community to identify vascular disease and prevent its complications.

The state-of-the-art Wound Care & Hyperbaric Center allows us to customize patient therapies to provide the best possible outcomes for our patients using regular treatment measures and utilizing oxygen therapy in our multi-patient oxygen chamber.

Our surgeons see patients in satellite offices in Monroe, Michi, as well as Fulton County, Bellevue and Bowling Green, Ohio.

Jihad T. Abbas, MD
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For more information on our vascular program, or to schedule an appointment, call 419.383.3588, 419.383.3576 or email vascularsurgery@utoledo.edu.
One of the main challenges clinicians face while treating patients with chronic heart failure is maintaining an optimal long-term medical regimen. Since patients are subject to unpredictable factors, changes to medical therapy are constantly needed to adapt to different situations. Progression of the underlying disease, changes in diet, exercise pattern, emotional stress, compliance to therapy as well as infectious illnesses are only some of these factors. Medication adjustments are continuously warranted to avoid overt decompensation and need for hospitalization. Beyond frequent clinic visits and standard assessments, several biomarkers have been proposed as tools for clinicians to help risk-stratify heart failure patients, tailor therapy and reduce the need for inpatient management. The extensive list includes natriuretic peptides, cardiac troponins, blood urea nitrogen, ST2 and microRNAs. The concept of biomarker-guided therapy revolves around titrating medical therapy to target reduction in the levels of a certain biomarker.

Of the many biomarkers in heart failure, natriuretic peptides, in particular brain natriuretic peptide (BNP) and N-Terminal-pro-BNP (NT-proBNP), have gained a lot of attention during the past decade. Several studies addressed their utility in the diagnosis, prognosis and management of patients with varying degrees of heart failure. Current ACC/AHA Guidelines encourage the use of BNP and NT-proBNP to help in the evaluation of patients in whom the diagnosis of heart failure is uncertain [1]. BNP and NT-proBNP are synthesized and released into the bloodstream in response to the stretching of the cardiac myocyte. These biomarkers attenuate the effects of the renin-angiotensin system, promote natriuresis and vasodilatation.

Several randomized clinical trials were conducted to test the benefit of using a biomarker-guided strategy in the management of heart failure. The findings were somewhat inconsistent; however, those trials differed in their design, enrollment criteria and the target levels of natriuretic peptides. The main characteristics and results of these trials are shown in Table 1. Of note, none of the trials showed a mortality benefit with either strategy, except for the subgroup of patients who were ≤75 years of age in the BATTLESCARRED trial [2], where a biomarker strategy showed a mortality benefit with either strategy, except for the subgroup of patients who were ≤75 years of age in the BATTLESCARRED trial [2].

The two largest studies were TIME-CHF [4] and NorthStar [10], which enrolled 499 and 1,125 patients, respectively. In TIME-CHF, patients with an NYHA class of at least II and NT-proBNP levels more than twice the upper limit of normal (ULN) were randomly assigned to either a biomarker-guided (targeting levels less than twice the ULN) or a clinically guided (to maintain NYHA class of ≤ II) approach to tailoring of therapy. About 75 percent of patients included in this trial were in NYHA class III or IV. There was no difference in the primary outcome of survival free of all-cause hospitalization, and no difference in the measures of quality of life. However, survival free of heart failure hospitalization was improved in the biomarker arm (72 percent vs. 62 percent, p=0.01). This finding is in accordance with other smaller scale trials that enrolled patients with advanced heart failure symptoms, including NYHA class IV.

Alternatively, less symptomatic patients do not seem to be better served by a biomarker-guided approach. The NorthStar trial, a multicenter Danish study, was recently presented at the 2011 American College of Cardiology Annual Scientific Meeting. This is the largest randomized controlled trial to address the issue of biomarker use in heart failure management. Importantly, patients enrolled were clinically stable (NYHA class II) and received optimal medical therapy with ACE-Inhibitors, beta-blockers, aldosterone antagonists and device therapy (cardiac resynchronization and defibrillation device). They were then randomly assigned to follow up with general practitioners or at heart failure centers with the goal of preventing a more than 30 percent increase in NT-proBNP levels from baseline. Patients were also stratified based on NT-proBNP levels, with a cutoff of 1000 pg/ml. The main result of the trial was that biomarker-guided follow up in specialized heart failure clinics did not improve the main outcome of time to death or heart failure hospitalization. Elevated levels of NT-proBNP did identify a higher risk group of patients; however, there was no difference in the outcome between treatment groups. This is partly explained by adequacy of therapy at the start of the trial, but is also a testimony to the good follow up care and of the heart failure patients by general practitioners in this particular study.

It is also noteworthy that these trials mostly included patients with left ventricular systolic dysfunction. Patients with heart failure and preserved ejection fraction (HFpEF) present yet another distinct challenge for the clinician. Two of the trials, PRIMA and BATTLESCARRED, did include patients with HFpEF; neither patient subgroups appeared to benefit from a biomarker-guided approach.

An important lesson can be drawn from the aforementioned trials in treating the increasingly complex heart failure patient. Specifically, the impact of a biomarker-guided strategy depends on the clinical characteristics and symptomatology of the patients with heart failure. Patients who are clinically stable and are maintained on an optimized medical regimen probably do not derive a great benefit from follow-up at specialized heart failure centers, or through a biomarker-guided approach; this is true provided they receive adequate clinical care by the general practitioner or internist. However, high-risk patients with advanced NYHA symptom class are likely to have improved outcome and reduced need for hospitalization for decompensated heart failure when carefully treated with a biomarker-guided strategy. Once stabilized through an optimal medical regimen, these patients can be safely released to non-specialized centers of care.

The Advanced Congestive Heart Failure (CHF) Team at The University of Toledo, composed of fellowship-trained cardiologists and cardiac surgeons in CHF, provides an integrated convenient one-stop resource for patients with end-stage heart failure. It would be our privilege to work collaboratively with referring physicians to assist with the management of these complex patients. By offering the full spectrum of state-of-the-art technologies and techniques, the ability to enroll in various CHF trials and continuous communication and feedback to our referring physicians, we hope to meaningfully impact CHF in northwest Ohio and southeast Michigan.

Please feel free to contact us at 419.383.3963.

For references, please visit utmc.utoledo.edu/clinics/hvc.

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* Improved survival in patients ≤ 75 years with biomarker-guided strategy

Table 1. Summary of the clinical trials examining the role of biomarker-guided therapy in chronic heart failure.
In autumn of 1995, a virus attacked the heart of James (Jim) Howell of Toledo. By December, he was diagnosed with congestive heart failure that resulted in cardiomyopathy. Extensive complications led his physician to refer him to UT Medical Center, where he was placed on a heart transplant list. A medication prescribed the following year showed promise, seemingly improving his condition until he experienced a serious setback in September 2011. Despite hospitalization at UTMC, Howell’s condition steadily declined; his kidneys and liver began to fail. Dr. Samer J. Khouri, associate professor of cardiovascular medicine, who cared for Jim for years, as well as others in the Advanced Congestive Heart Failure Team, were rapidly running out of options.

During this time, Dr. Mark Bonnell, assistant professor of vascular surgery, joined the cardiothoracic surgery team to lead the Left Ventricular Assistance Device (LVAD) program under the leadership of Dr. Thomas Schwann, professor of cardiothoracic surgery. Howell’s case was referred to Dr. Bonnell by the congestive heart failure team. Dr. Bonnell spoke to Howell about the benefits of the implant as well as the risks.

“Naturally I was nervous and anxious,” Howell said. “When it came down to it, I didn’t have a choice: either [opt for the implant or] try to exist on medications where I probably wouldn’t have lasted long, since my ejection fraction was only 5 percent because [my heart] wasn’t pumping blood to the organs.”

After several series of tests and many prayers by Howell’s family and his friends at St. Andrew’s Episcopal Church, he became the first candidate for the LVAD at UTMC. Just two weeks after Dr. Bonnell’s arrival, he gave Howell his life back. “He’s a brilliant doctor but he’s a good human being. You can tell [Dr. Bonnell] truly cares about his patients,” Howell said.

The procedure was conducted Nov. 3 and Howell was home by Nov. 18. It has only been two months since the LVAD was implanted, and the patient is doing things he hasn’t done in 16 years. Something as simple as climbing stairs once made him short of breath, lightheaded and on the verge of fainting. He now does it with ease. In fact, Howell has been able to walk up multiple flights of stairs without complication.

“I was astounded with the strength I have. It’s going to take me awhile to get where I want to go, but from September to now, it’s amazing,” Howell said.

Howell is looking forward to returning to something he once loved: golf. Due to his condition, that activity seemed to be something he’d never experience again. Now he can join his friends in the senior league with the help of the LVAD team at UTMC.

“I’ve been in a number of hospitals in my life. It was not just the surgeons, but the whole experience,” Howell said. “From the doctors to the transport staff, the experience just couldn’t have been better than what I received at UTMC. I am just astonished at the care I received.”

Jim Howell, at home pictured with his Rottweiler, Lacey.