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Pro-inflammatory diseases, such as rheumatoid arthritis, Crohn’s disease and psoriasis, are associated with an increased risk of cardiovascular disease.

“These are all high inflammatory states that are associated with an increased risk of myocardial infarction and stroke,” says George Farah, MD, a cardiologist at University Hospitals Harrington Heart & Vascular Institute. “We know in preclinical and clinical studies that inflammation drives the initiation, progression and complications of atherosclerosis. However, we do not currently have targeted anti-inflammatory therapies for atherosclerosis – only the pleiotropic, nonlipid effects of statins.”

To provide more integrated, holistic care for these patients, Dr. Farah and colleagues within the UH Harrington Heart & Vascular Institute are piloting a new program for patients with chronic inflammatory diseases who are over age 45. The initial target is patients with pro-inflammatory conditions, including systemic lupus erythematosus, ankylosing spondylitis, rheumatoid arthritis, Crohn’s disease, ulcerative colitis and psoriasis. The rationale for this program is that inflammation is a marker of increased risk as defined by the JUPITER study, in which patients with normal LDL, but elevated high sensitivity CRP were found to have decreased risk of future cardiovascular death, myocardial infarction and stroke when treated with rosuvastatin compared to placebo. Established risk scores (i.e., Reynolds or ASCVD) and coronary artery calcium scoring are used to stratify patients and initiate preventive strategies based on very low risk (CAC score=0), low risk (CAC score 1 – 99), intermediate risk (CAC score 100 – 399) and high risk (CAC score >400).

“One of the questions is whether anti-inflammatory treatments will reduce the risk of cardiovascular disease in people with inflammatory conditions,” adds UH cardiologist Chris Longenecker, MD. “There may be anti-inflammatory drugs that will reduce risk.”

Dr. Longenecker is employing a similar approach for another group of patients at cardiovascular risk from inflammation – patients with HIV. He runs a twice-monthly cardiometabolic risk clinic, housed where they receive their primary HIV care.

“These patients have a very strong sense of community within their ‘medical home’ and don’t necessarily feel as comfortable traveling outside of their clinic to other providers,” he says. “There’s a comfort level there. Whenever you talk about trying to prevent cardiovascular disease, a lot of it is behavioral change, so you really need to have good relationships.”

Dr. Longenecker typically sees these patients every three to six months. About half have risk factors for cardiovascular disease that he manages with them, but they have no established heart disease. For his patients with established cardiovascular disease, Dr. Longenecker manages the sometimes-tricky interactions between statins and antiretroviral therapy.

“Traditionally, many cardiologists and primary care providers have been worried about the interactions between statins and antiretroviral drugs, so they’ve stayed with the statins that don’t have as many interactions, such as pravastatin,” he says. “That, I think, has set us back because it’s not a very strong statin. Atorvastatin and rosuvastatin are stronger and can be safely prescribed to patients with HIV who are taking antiretroviral drugs.”

Both Dr. Farah and Dr. Longenecker believe the multidisciplinary approach to inflammation will lead to better cardiovascular outcomes for patients, both now and in the future.

“Patients with chronic inflammatory disorders are at increased risk of cardiovascular disease and should be treated aggressively for risk factors,” Dr. Farah says. “However, chronic inflammation contributes to cardiovascular risk in everybody. Two studies testing new anti-inflammatory approaches using methotrexate or blocking IL-1 are in the follow-up phase and will report soon whether targeting inflammation can reduce cardiovascular events, even in the general population.”

For more information or to refer a patient, call 216-844-3800 or 1-866-UH4-CARE (1-866-844-2273).

The commitment to exceptional patient care begins with revolutionary discovery. University Hospitals Case Medical Center is the primary affiliate of Case Western Reserve University School of Medicine, a national leader in medical research and education and consistently ranked among the top research medical schools in the country by U.S. News & World Report. Through their faculty appointments at Case Western Reserve University School of Medicine, physicians at UH Case Medical Center are advancing medical care through innovative research and discovery that bring the latest treatment options to patients.
Approximately 10 percent of patients with hypertension have resistant hypertension, defined as a blood pressure that remains above goal in spite of the concurrent use of three antihypertensive agents of different classes, including a diuretic at an appropriate dose. Patients with resistant hypertension have high rates of cardiovascular complications. In my experience, many patients are misclassified as having resistant hypertension. It is important to titrate antihypertensive medications to maximally tolerated recommended dosages and to strongly consider the addition of spironolactone, which is particularly effective in helping patients achieve blood pressure treatment goals.

Jackson, many cardiologists are confused with the new guidelines on the management of adult hypertension, which contained significant changes from previous recommendations.

DR. WRIGHT: I would start with a thiazide diuretic like chlorthalidone. For a second agent, I would recommend a drug that has been shown to reduce cardiovascular events, such as a calcium channel blocker, ACE inhibitor or ARB.

DR. SIMON: Many of us do not completely understand the rationale for the guideline change. In fact, our uncertainty in the new hypertension treatment guidelines carries over to our confusion in the new hyperlipidemia treatment recommendations, which eliminated hard LDL targets in primary (less than 100 mg/dL) and secondary (less than 70 mg/dL) prevention. What antihypertensive medication do you recommend as first agent? What is your second medication of choice, recognizing that most patients require at least two antihypertensive medications for adequate control?

DR. WRIGHT: I would start with a thiazide diuretic like chlorthalidone. For a second agent, I would recommend a drug that has been shown to reduce cardiovascular events, such as a calcium channel blocker, ACE inhibitor or ARB.

DR. SIMON: What do you recommend for patients with resistant hypertension?

DR. WRIGHT: Approximately 10 percent of patients with hypertension have resistant hypertension, defined as a blood pressure that remains above goal in spite of the concurrent use of three antihypertensive agents of different classes, including a diuretic at an appropriate dose. Patients with resistant hypertension have high rates of cardiovascular complications. In my experience, many patients are misclassified as having resistant hypertension. It is important to titrate antihypertensive medications to maximally tolerated recommended dosages and to strongly consider the addition of spironolactone, which is particularly effective in helping patients achieve blood pressure treatment goals.

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JACKSON WRIGHT JR., MD, PHD: Yes, Dan. The JNC-8 (Joint National Committee) relaxed the blood pressure targets in two key groups, the elderly and those younger than 60 with diabetes or kidney disease. For patients age 60 and older, the JNC-8 guidelines recommend treating patients to a target of 150/90 mm Hg rather than 140/90 mm Hg. In patients with diabetes or kidney disease, JNC-8 guidelines recommend treating to 140/90 mm Hg rather than lower blood pressure targets (i.e., 135/85 mm Hg).

DR. WRIGHT: The results of SPRINT are very exciting. This study shows that intensive blood pressure management can prevent the cardiovascular complications of hypertension and save lives. As the NHLBI reported, treating high-risk hypertensive adults age 50 and older reduced cardiovascular events by 30 percent and reduced all-cause mortality by nearly 25 percent when compared with patients treated to a systolic target of 140 mm Hg. SPRINT was designed as a target-based study, which gave physicians flexibility in selecting antihypertensive medications to achieve the assigned blood pressure target. Hypertensive patients with a 10-year Framingham General cardiovascular risk ≥15%, age >75 years of age or pre-existing kidney disease were randomized to intensive blood pressure control (less than 120 mm Hg) or standard blood pressure control (less than 140 mm Hg). In the intensive-therapy arm, patients were treated with a combination of thiazide diuretics, calcium channel blockers and ACE inhibitors. You can read more about the SPRINT results in The New England Journal of Medicine.

DR. SIMON: The NHLBI just issued a press release regarding SPRINT (Systolic Blood Pressure Intervention Trial). You are one of the principal investigators of SPRINT. Fill us in on this landmark announcement.

DR. WRIGHT: The results of SPRINT are very exciting. This study shows that intensive blood pressure management can prevent the cardiovascular complications of hypertension and save lives. As the NHLBI reported, treating high-risk hypertensive adults age 50 and older reduced cardiovascular events by 30 percent and reduced all-cause mortality by nearly 25 percent when compared with patients treated to a systolic target of 140 mm Hg. SPRINT was designed as a target-based study, which gave physicians flexibility in selecting antihypertensive medications to achieve the assigned blood pressure target. Hypertensive patients with a 10-year Framingham General cardiovascular risk ≥15%, age >75 years of age or pre-existing kidney disease were randomized to intensive blood pressure control (less than 120 mm Hg) or standard blood pressure control (less than 140 mm Hg). In the intensive-therapy arm, patients were treated with a combination of thiazide diuretics, calcium channel blockers and ACE inhibitors. You can read more about the SPRINT results in The New England Journal of Medicine.

DR. SIMON: Congratulations to you, Jackson, and the SPRINT investigators. We look forward to inviting you back to discuss how the results of SPRINT will change clinical practice. I suspect guideline writers will be huddling closely in the coming months.

*All National Institutes of Health funding for basic and clinical research is awarded to the School of Medicine at Case Western Reserve University.
Despite the plethora of cardiac devices available today, sometimes there is no perfect solution for a particular patient. In that situation, out-of-the-box thinking is in order.

Left ventricular assist devices (LVADs) are a case in point. Although designed for the unique shape, anatomy and flow dynamics of the left ventricle, in experienced hands, they can be modified and implanted in both left and right ventricles. To date, cardiac surgeons have performed modern continuous flow biventricular assist device (BVAD) procedures just a few dozen times in the U.S. and fewer than 100 times worldwide.

“This can be a solution for patients who have run out of options and need right side support,” says Benjamin Medalion, MD, a cardiac surgeon and Director of the Mechanical Circulatory Support program at UH Harrington Heart & Vascular Institute. “We don’t have very good right heart support currently. Hopefully, with time, we’ll have more dedicated devices for the right side.”

LVADS: Pushing the Envelope, Looking to the Future

UH cardiac surgeons and heart failure specialists use LVADs in novel ways, aim to test smaller, minimally invasive devices in development

Dr. Medalion and Guilherme Oliveira, MD, Director of the Advanced Heart Failure & Transplant Center at UH Harrington Heart & Vascular Institute, recently performed the first durable BVAD procedure in Ohio, using two HeartWare devices. These LVADs are approved by the U.S. Food and Drug Administration (FDA) as a bridge to transplantation. Their patient was a 58-year-old man with fulminant heart failure. He had lost 85 percent of his heart’s function due to viral myocarditis, leaving him with a left ventricle ejection fraction (LVEF) of less than 10 percent and failed right ventricle.

The complex, seven-hour surgery required decisions first about where to place the device and then how best to modify its flow rate for the unique, right ventricular environment.

Fortunately, the patient has done well. He continues to regain strength while awaiting transplantation.

“The infection caused a shock state, and he was debilitated for a long period of time,” Dr. Medalion says. “We hope he can rebuild himself a bit before we bring him back for another major surgery, to give him the best chance possible.”

LVAD for SCAD

UH cardiac surgeon Basar Sareyyupoglu, MD, a new member of the UH Harrington Heart & Vascular Institute, also recently had an unusual LVAD case. His patient was a young, postpartum woman who developed a spontaneous coronary artery dissection (SCAD) – a condition occurring more commonly among younger women and among postpartum women in particular.
Eight weeks after the birth of her child, she experienced chest pain. Physicians at an outside hospital identified it as a heart attack caused by SCAD. The patient had a CABG procedure there, but her condition continued to worsen and she was transferred to UH. After several weeks of acute cardiogenic shock supported by venoarterial extracorporeal membrane oxygen, temporary LVAD support and dialysis, Dr. Sareyyupoglu and his team implanted her with a HeartMate 2 LVAD and Centrimag RVAD. Her RVAD device was placed in a percutaneous fashion and was taken out without entering her chest again. She recovered her renal function and successfully discharged home.

Like the biventricular patient, she continues to do well.

“She now has the LVAD as a destination device,” Dr. Sareyyupoglu says. “It will last for many years safely, but she’s a young patient and should be considered to have a heart transplant down the road.”

**New LVADs in the Pipeline**

Despite their recent successes with existing LVAD technology, the team at UH is looking to next-generation devices to create even better outcomes for their patients.

“In the next two or three years, we’ll be seeing more and more of two new devices: the HeartMate 3 and the HeartWare micro-ventricular assist device (MVAD),” says Soon Park, MD, Chief of the Division of Cardiac Surgery and Co-Chair of the Clinical Executive Committee at UH Harrington Heart & Vascular Institute.

HeartMate 3, manufactured by St. Jude Medical, received CE Mark approval in Europe in October 2015. The HeartWare MVAD, manufactured by HeartWare International, Inc. is still in clinical trials there.

“The MVAD CE Mark trial is hopefully going to include some centers in the United States, of which we hope to be part,” Dr. Park says. “We’d love to be able to offer that option to our patients.”

The HeartMate 3 matches the current HeartWare device in its small size. It also uses magnetic levitation, allowing the device’s rotor to be suspended by magnetic forces. This design aims to reduce trauma to blood passing through the pump, reduce friction and “wear-and-tear” on the rotor and improve outcomes for patients. The HeartWare MVAD is an even smaller device – half the size of its current HVAD. A further distinction is that it can be implanted via a less invasive thoracotomy approach.

But more importantly, Dr. Oliveira says, both the HeartMate 3 and HeartWare MVAD provide pulsatility. Early-concept LVADs used pulsatile motion, but that feature was abandoned in later models because the amount of mechanical stress the device had to endure was unsupportable over time. Now, however, the problems of continuous flow LVADs have become apparent.

“A lot of the side effects of these devices, such as bleeding and thrombosis, are caused by the lack of pulsatility in flow,” Dr. Oliveira says. “Because of that, both companies have implemented the ability to provide pulsatility to their devices.”

For Dr. Oliveira, the next frontier is an LVAD that can be charged transcutaneously without causing skin damage.

“The real breakthrough is going to come when we’re able to charge these devices without an exterior drive line connected to an exterior battery source,” he says. “There are some prototypes being tested, but they are still in the early stages of development. Stay tuned.”

For more information or to refer a patient, call 216-844-3800 or 1-866-UH4-CARE (1-866-844-2273).
Increased understanding of the specific genetic mutations responsible for hypertrophic cardiomyopathy (HCM) has led to increased requests for evaluation among those at risk.

“Most of the people with a diagnosis or suspicion of HCM are seen because they have a family history of the condition,” says Guilherme Oliveira, MD, Director of the Advanced Heart Failure & Transplant Center at University Hospitals Harrington Heart & Vascular Institute. “However, with HCM, there’s often a dissociation between genotype and phenotype. There are patients who have the same genotype but have different manifestations of the disease. Disease may not manifest at all, or it may manifest in a completely different way.”

For patients with a positive genetic test, the next step is noninvasive evaluation with an echocardiogram to determine whether there is a phenotype of hypertrophy. Supplemental cardiac MRI with gadolinium is also particularly useful, Dr. Oliveira says.

“Even if the echo does not show hypertrophy, there is value in proceeding with a cardiac MRI to evaluate the amount of fibrosis in the myocardium,” he says.

For patients without a positive genetic test and unexplained hypertrophy, the diagnostic focus shifts to ruling out other possibilities. Endomyocardial biopsy is useful, for example, to rule out amyloid or storage diseases.

“Without a positive family history of HCM, it’s particularly important to look for amyloidosis and to identify the specific type,” Dr. Oliveira says. “Storage diseases, such as glycosgen storage disease and lysosomal storage diseases, the most common which is Fabry’s disease, can also masquerade as HCM.”

Managing Hypertrophic Cardiomyopathy

Success requires interplay of genetics, cardiology, electrophysiology and cardiac surgery.
As complex as the diagnosis may be, medical treatment for HCM is equally fraught with challenges.

“In terms of medical therapy for this disease, it really has been very disappointing,” Dr. Oliveira says. “We use beta blockers, calcium channel blockers, some ACE inhibitors, and that’s about it.

What is being increasingly realized, however, is that atrial fibrillation (AF) is very common in patients with HCM, occurring in about 30 percent, and that it significantly exacerbates their symptoms.

“These patients have very poor tolerance to AF,” Dr. Oliveira says. “When they go into AF, they become very symptomatic and go into heart failure. In these patients, it’s very important to try to maintain sinus rhythm. AF ablation is particularly attractive in this group of patients.”

Treatment for HCM also sometimes includes an implantable defibrillator, due to the high risk of sudden cardiac death associated with the condition. However, this risk is not uniform throughout the HCM patient population.

“Patients with known disease are evaluated to see whether they fall into a high-risk category,” says Judith Mackall, MD, Director of the Center for Cardiovascular Genetics at UH Harrington Heart & Vascular Institute. “We consider imaging, exercise stress test, monitoring results, personal history of syncope and family history of sudden cardiac death. We put all of the clinical factors together with the structural factors, such as wall thickness and obstruction, to see whether they’re at high risk of sudden death. Those that are at high risk are offered an implantable defibrillator.”

For many patients with HCM, however, the best solution is often a surgical one.

“The most efficacious and long-lasting therapy we have is septal myectomy,” says Soon Park, MD, Director of Cardiac Surgery at UH Harrington Heart & Vascular Institute. “What we call extended septal myectomy is really ideal. We do more than take out the thickened septum that is obstructing bloodflow out of the heart. We excavate further to create more space. It mostly involves the septum, but may involve papillary attachment. In doing that, you create a larger opening. With the resulting decrease in velocity of bloodflow, the mitral valve does not get pulled in. When this surgery is thorough and effective, mitral valve regurgitation either goes away entirely or is very mild.”

“It’s imperative to do a thorough job of removing all the obstructive muscles and creating an opening deep into the left ventricle, excavating obstructive muscles that do not need to be there,” Dr. Park adds. “Symptoms sometimes recur after surgery, but the most common reason for repeat surgery is that the extensive excavation has not been done.”

Dr. Park gained extensive experience with septal myectomy during his time at Mayo Clinic. In the two years since his arrival at UH, he has completed about 15 procedures. Dr. Park is also a national leader in performing concomitant septal myectomy in patients undergoing aortic valve replacement.

“Patients with severe aortic stenosis are often found to have asymmetric septal hypertrophy,” Dr. Park says. “Echo often misses it. In fact, in about one-third of patients, the septal thickening is only diagnosed introperatively via visual and digital inspection.”

For more information or to refer a patient, call 216-844-3800 or 1-866-UH4-CARE (1-866-844-2273).
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