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CardiovascularUpdate

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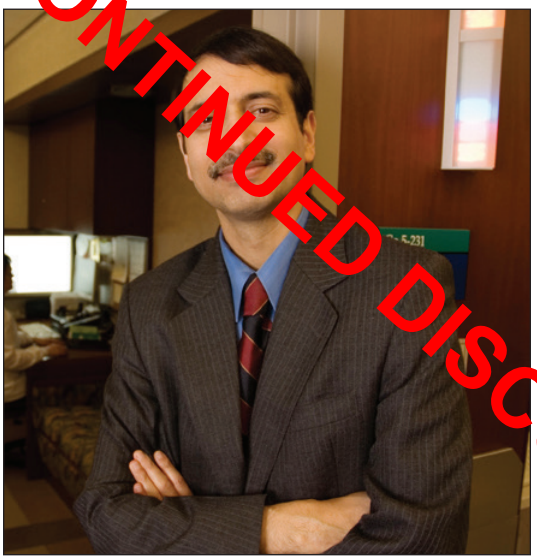
INSIDE THIS ISSUE

PCSK9 Inhibition: A Game Changer in Cholesterol Management



Iftikhar J. Kullo, MD

Statins are among the most widely prescribed drugs in the world, having been shown to markedly reduce adverse atherosclerotic cardiovascular (ASCVD) events in the primary and secondary prevention settings. Muscle and liver adverse effects, increased risk of diabetes, and the potential for drug interactions are limitations of this class of drugs. Furthermore, patients on statins may be at substantial residual risk, highlighting the need for an alternative class of potent lipid-lowering agents. A cross-sectional analysis of a National Health and Nutrition Examination Survey (NHANES) dataset revealed low-density lipoprotein cholesterol (LDL-C) levels higher than 70 mg/dL in about 75% of patients at high ASCVD risk. The addition of ezetimibe and niacin may provide a moderate additional decrease in LDL-C; however, this may not be sufficient in patients with very high baseline LDL-C levels.

Proprotein convertase subtilisin/kexin type 9 serine protease (PCSK9) plays an important role in cholesterol metabolism by regulating LDL receptor degradation (Figure 1A). Shortly after its discovery in 2001, the gene encoding PCSK9 was implicated in familial hypercholesterolemia (FH). Gain and loss-of-function variations in *PCSK9* resulted in high and low levels of LDL-C, respectively. Genetically determined decreases in LDL-C levels—28% in African Americans and 15% in white subjects—were associated with a substantial reduction in the coronary heart disease risk as compared with LDL-C levels in noncarriers—88% and 47%, respectively. These findings triggered a race to develop PCSK9 inhibitors to reduce LDL-C for prevention of ASCVD-related adverse events.

Binding of circulating PCSK9 by parenteral monoclonal antibodies results in augmented recirculation of LDL receptor to the hepatocyte surface and accelerated clearance of circulating LDL-C (Figure 1B). First tested in animals in 2009, anti-PCSK9 antibodies have shown a significant lipid-lowering effect comparable to that of lipoprotein apheresis, ie, a 55% to 75% decrease from baseline regardless of whether patients are on statins or ezetimibe. More than 70% of high-risk patients are able to achieve an LDL-C level less than 70 mg/dL. In placebo-controlled trials of patients on a maximally tolerated statin dose, LDL-C reduction was twice that achieved with ezetimibe, and the lipid-lowering effect was not affected by age, sex, intensity of statin regimen, ASCVD risk, or presence of diabetes.

Data demonstrating the safety and efficacy of PCSK9 inhibitors led to the recent US Food and Drug Administration approval of 2 human monoclonal antibodies: 1) alirocumab (Praluent; Sanofi-Aventis and Regeneron Pharmaceuticals Inc), 75-150 mg every 2 weeks; and (2) evolocumab

(Repatha; Amgen Inc), 140 mg every 2 weeks or 420 mg monthly. The drugs are approved for the following indications: (1) patients with heterozygous FH, and (2) individuals with ASCVD, who require additional LDL-C lowering. Evolocumab, 420 mg once monthly, is additionally approved for homozygous FH based on results of the TESLA trial, in which LDL-C levels were reduced by 18% to 44% with monthly injections during a 3-month period in 50 homozygous FH patients showing at least 2% of functioning LDL receptors.

In the longer-term and extension trials, the lipid-lowering effects were enduring and consistent with those attained at 3 and 6 months. Additionally, a significant reduction in apolipoprotein-B, non–high-density lipoprotein cholesterol (non–HDL-C), and lipoprotein(a) (about 25%-30% decrease) as well as modest favorable effect on HDL-C and triglyceride levels has been observed with anti-PCSK9 drugs. The mechanisms by which PCSK9 inhibitors decrease levels of lipoprotein(a) are unknown at present.

Two simultaneously published studies—the ODYSSEY long-term study carried out in 2,341 patients at high risk for ASCVD events on maximally tolerated statin dose and the OSLER study in 4,465 patients, including those at high ASCVD risk—showed comparable decreases of 60% in LDL-C level from the mean of 120 mg/dL for both evolocumab and alirocumab. This effect was associated with a halving of the rate of composite ASCVD end points in a post hoc analysis.

Placebo- as well as ezetimibe-controlled trials in statin-intolerant patients showed no excess in adverse events such as insulin resistance, glucose intolerance, or myopathy. Common adverse effects (seen in ≥5% of treated patients) included upper respiratory tract infections, nasopharyngitis, influenza, and injection site reactions. For evolocumab, back pain was additionally described. Reassuringly, anti–drug antibody development has not yet been reported. The frequencies of serious treatment-related adverse events are not different from placebo, although potential for neurocognitive effects is unclear.

"PCSK9 inhibitors fill an obvious therapeutic niche in selective high-risk patients, eg, FH or statin-intolerant patients, who are not able to achieve the desired LDL-C level with conventional treatments," according to Iftikhar J. Kullo, MD, cardiologist at Mayo Clinic in Rochester. However, objective criteria to determine who should get these drugs are yet to be established. Another important consideration is cost, which is comparable to lipoprotein apheresis and antisense oligonucleotide technologies but far greater than statin therapy. Results of large outcome studies of PCSK9 inhibition are eagerly awaited by the medical community and patients.

A summary of ongoing trials is available at the *Cardiovascular Update* website: http://www.mayoclinic.org/medical-professionals/publications/cardiovascular-update.

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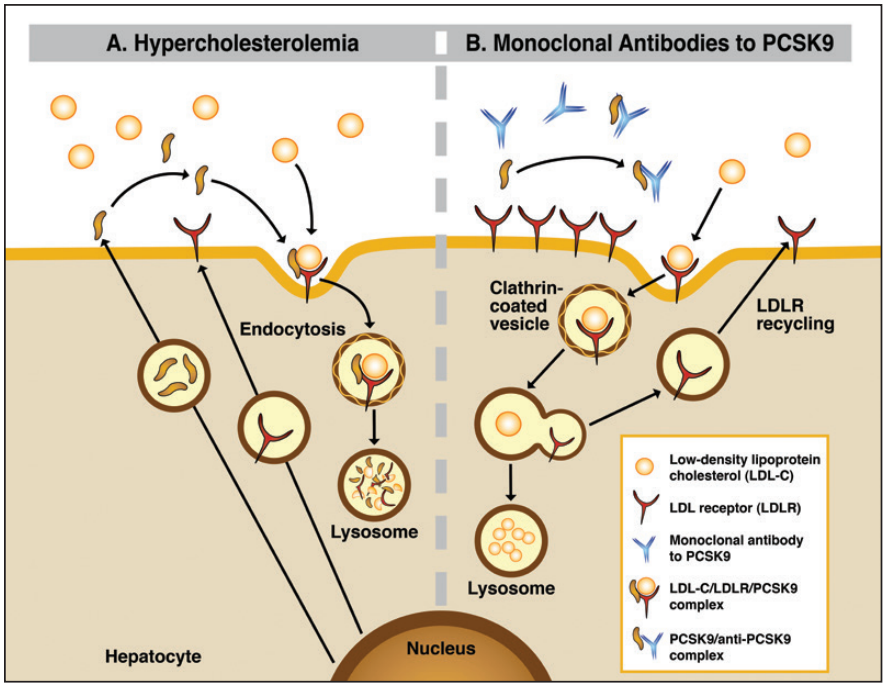

Figure 1. A. *PCSK9 is synthesized in the liver and regulates LDLR expression at the posttranscriptional level. After secretion, PCSK9 specifically binds to the extracellular domain of the LDLR, a transmembrane protein, triggering LDLR uptake by the hepatocyte. A complex comprising PCSK9, LDLR, and LDL-C is internalized via clathrin-dependent endocytosis, followed by degradation in the lysosome. The resulting reduction in LDLR lowers the number of LDLRs expressed on the hepatocyte surface, thereby increasing circulating LDL-C levels (hypercholesterolemia).* **B.** *Human monoclonal antibodies against PCSK9 prevent binding of PCSK9 to LDLR. Clathrin-dependent LDLR endocytosis accompanied by the dissociation of LDLR and LDL complex leads to recycling of the LDLR back to the hepatocyte surface. The number of LDLRs degraded in the lysosome is reduced and the number expressed on hepatocyte surface is increased. Thus, targeted inhibition of PCSK9 promotes LDLR recycling and reduces plasma LDL-C levels.*

Philip L. Wackel, MD

Ventricular arrhythmia is a rare occurrence in the pediatric population and is often an unexpected finding in patients with otherwise normal hearts. However, when a child does present with ventricular arrhythmia, specific causes warrant consideration and guide the subsequent work-up and treatment strategy. Patients with known heart disease (for example, congenital heart disease, cardiomyopathy, or channelopathies) may be at risk for ventricular arrhythmia and require a different approach compared with patients who have normal hearts. Ventricular arrhythmia in a normal heart can range from infrequent ectopy to incessant ventricular tachycardia (VT).

Premature Ventricular Complexes

Premature ventricular complexes (PVCs) are a common finding in pediatric patients of all ages and may be seen on a Holter monitor in about 40% of otherwise healthy children. When PVCs are rare, isolated, and monomorphic, they usually do not require extensive evaluation in an otherwise healthy child and have an excellent prognosis. Spontaneous resolution over time is quite possible and is more likely the younger the patient is at the time of presentation. However, when the PVC burden is more frequent or more complex (ie, multiform PVCs, couplets, or nonsustained VT), it necessitates further work-up and possibly longitudinal follow-up.

The initial work-up for PVCs should include electrocardiography, echocardiography, Holter monitoring, and thorough history taking and physical examination (Figure 1) to assess for underlying heart disease such as myocarditis, cardiomyopathy, and channelopathy. With frequent ectopy (generally defined as ≥10% of beats in a 24-hour period), there is a risk of developing ventricular dysfunction even in a normal heart. The exact PVC burden at which ventricular dysfunction may occur is unclear, but in most studies, 20% to 30% ectopy is needed to increase the risk of ventricular dysfunction.

"Treatment of PVCs in the setting of a normal heart is rarely required," according to Philip L. Wackel, MD, a pediatric cardiologist at Mayo Clinic in Rochester, Minnesota. "Declining ventricular function or symptomatic complaints of palpations that are clearly attributable to the PVCs are 2 situations in which treatment may be warranted." The usual first-line treatment is medical therapy, and often a β-blocker is used; however, calcium channel blockers could also be considered as first-line agents in patients older than 1 year. If these medications fail or have adverse effects, a number of second-line antiarrhythmics could be initiated or catheter ablation could be attempted. Catheter ablation is generally highly successful in eliminating a single PVC focus. However, the risks of the procedure must be weighed carefully against the indication and the chance for spontaneous resolution with time.

Accelerated Ventricular Rhythm

It is important to differentiate accelerated ventricular rhythm (AVR) from VT in pediatric patients because the prognosis differs. The exact rate at

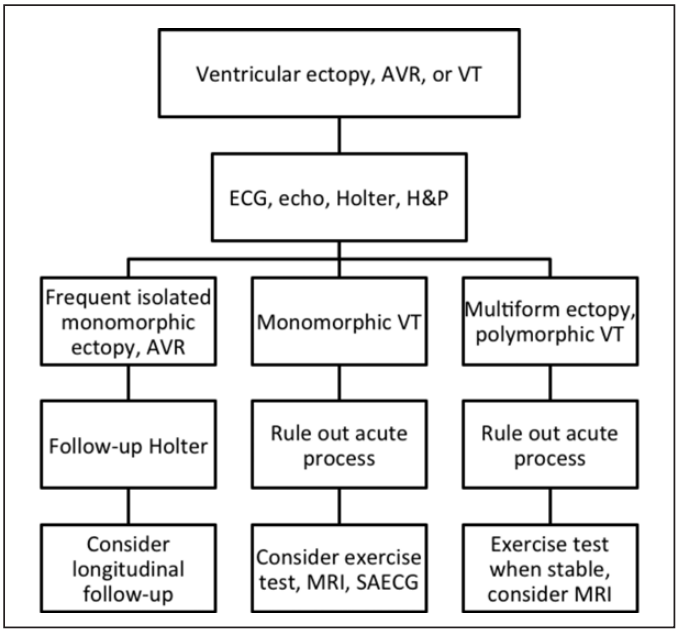

Figure 1. *Pediatric ventricular arrhythmia evaluation. AVR, accelerated ventricular rhythm; ECG, electrocardiogram; echo, echocardiogram; H&P, history and physical examination; MRI, magnetic resonance imaging; SAECG, signal averaged electrocardiogram; VT, ventricular tachycardia.*

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which this distinction is made varies with age and is based on the rate of the ventricular arrhythmia compared with sinus rhythm. AVR is generally defined as rates up to 15% to 20% faster than the expected sinus rate or greater than 120 beats per minute in an older teenager at rest. AVR is typically benign, rarely requires treatment, and carries the same excellent prognosis as PVCs. AVR can occur at any age and may present as early as the first hours of life."In the absence of heart disease or metabolic or electrolyte abnormalities, AVR in the neonate is usually also benign but does require longitudinal follow-up until the arrhythmia resolves to ensure ventricular function remains normal," says Dr Wackel. Neonatal AVR usually resolves within the first year of life. AVR presenting in older children can be followed as isolated PVCs are, as discussed previously with longitudinal follow-up, to assess the burden of ectopy and for the potential development of ventricular dysfunction if the ectopy is frequent.

Monomorphic Ventricular Tachycardia

There are several distinct clinical scenarios in which monomorphic ventricular tachycardia can be seen in a child with a normal heart, and these carry a much different prognosis than VT in an abnormal heart. Therefore, establishing that a heart is normal is vital before entertaining one of the common causes of normal heart VT in a child. The initial evaluation should thus be aimed at confirming that a heart is indeed normal and that there are no acute causes of VT. The appearance of some types of benign VT can overlap with that of arrhythmogenic right ventricular cardiomyopathy, myocarditis, cardiomyopathy, or channelopathies. Therefore, ruling out underlying heart disease in the face of VT may also require additional testing with an exercise stress test, cardiac MRI, and/or signal averaged electrocardiogram. Once a heart is determined to be completely normal, the causes of VT are generally benign.

The most common cause of childhood VT in a normal heart is right ventricular outflow tract (RVOT) tachycardia. This accounts for 60% to 80% of all childhood VT in a normal heart. Typically childhood VT is caused by a single focus in the RVOT and results in a single QRS morphology with an inferior axis and left bundle branch block morphology. Less commonly, the focus can originate from areas outside but near the RVOT such as from above the pulmonary valve, from near the bundle of His, and from the left ventricular outflow tract or aortic cusps. Careful evaluation of the QRS morphology can often help more specifically localize the focus. The mean age of presentation is 8 years, and childhood VT may be discovered incidentally. Many patients with RVOT tachycardia will be asymptomatic, but symptoms of palpations or near syncope are also commonly seen. However, true syncope is uncommon and warrants further investigation for an alternative diagnosis. Additional work-up beyond the basic testing may include an exercise stress test because typically RVOT tachycardia suppresses with exercise, although there is a variant that actually increases with exercise. Despite the response to exercise, RVOT tachycardia should remain monomorphic, and polymorphic ectopy seen with exercise strongly suggests an alternative diagnosis. The prognosis of RVOT tachycardia is usually benign, and many patients eventually have spontaneous resolution or a declining ectopy burden over time in those that persist. Similar to the management of PVCs and AVR, treatment is recommended only if symptoms are bothersome or if ventricular dysfunction occurs. If treatment is indicated, as in PVCs, usually β-blockers and/or calcium channel blockers are used as first-line treatment, with second-line antiarrhythmics and ablation as alternatives.

Another common cause of monomorphic VT is posterior fascicular VT (also referred to as verapamil-sensitive VT or Belhassen VT). This VT accounts for 10% to 15% of childhood VT in a normal heart. This tachycardia is due to a reentrant circuit typically involving the left posterior fascicle, but can actually involve any portion of the fascicle. Typically, this circuit results in a QRS morphology that is relatively narrow compared with other types of VT, and it usually has a superior axis with right bundle branch morphology (Figure 2). This type of VT commonly occurs as sustained episodes of monomorphic VT and may be brought out with exercise. It is generally well tolerated at slower rates less than 200 beats per minute. As the name implies, it is highly responsive to intravenous verapamil in the acute setting and may be treated with oral verapamil moving forward to attempt to prevent future recurrence. However, 20% of patients experience breakthrough episodes of VT despite treatment with oral verapamil. In such cases, alternative antiarrhythmics or an ablation may be considered.

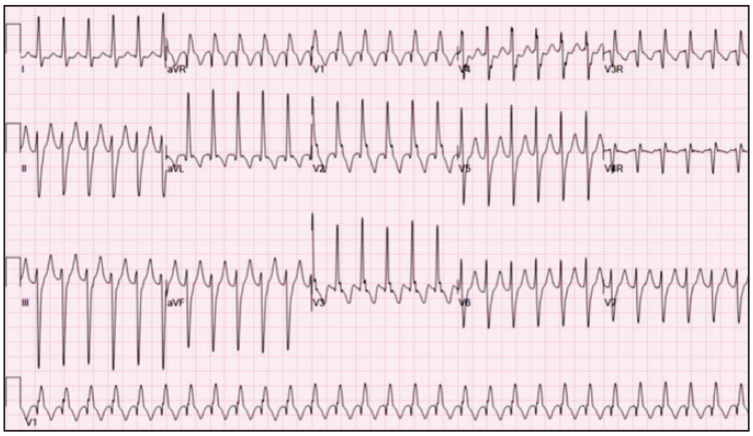

Figure 2. *Electrocardiogram of posterior fascicular ventricular tachycardia.*

Ablation can be safely accomplished in pediatric patients who weigh more than 15 kg, but varying degrees of success have been reported. In the largest study of fascicular VT ablation in pediatric patients, the initial success rate was 72%, with a recurrence rate of 18%. Therefore, a common approach to treatment of fascicular VT has been to treat a patient medically until the child is larger, at which time ablation can be attempted.

A rare form of incessant VT seen in the newborn period is usually monomorphic and arises most commonly from the left ventricle. Monomorphic VT of the newborn has been associated with ventricular tumors. Commonly it is an isolated hamartoma (Purkinje cell tumor) although in 50% of cases no etiology is identified. Neonatal myocarditis should also be ruled out. The VT rate may be very fast and is often higher than 200 beats per minute. The QRS duration in neonatal VT can be relatively narrow and may be as short as 60 milliseconds, which can sometimes make differentiating incessant VT from supraventricular tachycardia difficult. Careful comparison of the QRS in tachycardia to the QRS in sinus rhythm can help make this distinction. Incessant VT of the newborn may be associated with tachycardia-induced cardiomyopathy, especially in patients in whom more than 80% of the day is spent in VT.

Antiarrhythmic medication is almost always required to achieve a level of control to avoid tachycardia-induced cardiomyopathy and maintain adequate perfusion. Most infants with incessant VT have spontaneous resolution in 1 to 2 years at which point they can be weaned from antiarrhythmics. However, mortality in this disorder may be as high as 15% related to tachycardia-induced cardiomyopathy.

Polymorphic Ventricular Tachycardia

Polymorphic VT defined as beat-to-beat variations in the QRS morphology and/or QRS axis during VT is rare in childhood and generally carries a worse prognosis than monomorphic VT. It is even more uncommon to have polymorphic VT in children with no underlying heart disease as it is almost always associated with an underlying cardiac abnormality. Therefore, the presence of multiform ventricular ectopy or polymorphic VT in a child warrants a thorough investigation into underlying structural heart disease, cardiomyopathy, myocarditis, and channelopathies. In addition, metabolic or electrolyte abnormalities and toxicity from the mother's use of medications or recreational drugs should be investigated. "Even if no etiology is identified, these patients warrant longitudinal follow-up and, depending on their degree of ectopy and symptoms, may require antiarrhythmics or even implantation of an internal cardioverter-defibrillator, depending on the severity of the presentation," says Dr Wackel.

RECOGNITION

Jeffrey P. Jacobs, MD, from All Children's Hospital and Florida Hospital for Children, was the visiting professor for the 2015 David J. Driscoll Pediatric Cardiology Lectureship. Dr Jacobs (left) is pictured with Dr Driscoll (right).

Bryan C. Cannon, MD, a pediatric cardiologist at Mayo Clinic in Rochester, Minnesota, has been elected vice-president of finance for the Pediatric and Congenital Electrophysiology Society (PACES). PACES is an international group of physicians and allied professionals dedicated to improving the care of children and young adults with cardiac rhythm disturbances.

Nandan Anavekar, MD, a consultant in the Division of Cardiovascular Diseases at Mayo Clinic in Rochester, Minnesota, is a recipient of a 2015 Innovation Award, conferred by the Department of Internal Medicine. Dr Anavekar's project, "iTunes University Cardiology Curriculum Delivery System," used mobile technology interfaces to deliver cardiology curricula via interactive modalities. The awards are given to support excellence and innovation in clinical practice.

Rick A. Nishimura, MD, and Samuel J. Asirvatham, MD, have been selected as the 2015 Teachers of the Year by the Mayo Fellows in the Department of Internal Medicine, Division of Cardiovascular Diseases. The awards, presented at the Annual Award Celebration held April 16, 2015, recognize superior compassion and commitment to education, mentoring, and patient care.

Muhammad Yasir Qureshi, MBBS

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Advancing Single Ventricle Imaging for Application of Regenerative Techniques in Congenital Heart Disease

With advancements in cardiac surgical techniques, an increasing number of patients with a single ventricle are surviving to adulthood. Ventricular dysfunction is one of the frequent consequences of palliative surgical procedures as these individuals age, and assessment of ventricular dysfunction in these complex patients is challenging. "Functionally, single ventricles have unique anatomy and physiologic stresses that cannot be compared to any biventricular circulation owing to a combination of increased volume and pressure load," says Muhammad Yasir Qureshi, MBBS, a pediatric cardiologist at Mayo Clinic in Rochester, Minnesota. "In addition, many of these patients undergo several staged surgical procedures that may further injure the myocardium. Therefore, it is not surprising that ultimately myocardial dysfunction develops in many of these patients."

Categorizing the single ventricle as a morphologically left or right structure is an inadequate classification because of variations between disease entities. For example, in both tricuspid atresia and double inlet left ventricle, the single ventricle is a morphologic left ventricle; however, these ventricles are very different anatomically. Double inlet left ventricle is characterized by 2 inlets and excessive papillary muscle and chordal tissue, whereas these are not seen in tricuspid atresia. Additionally, there are individual variations in both anatomy and physiology.

The unique features of a single ventricle make assessment of ventricular function a challenge. Currently, the predominant imaging modality in clinical practice is echocardiography supplemented by magnetic resonance imaging (MRI). In general, the goals of imaging in patients with a single ventricle are to assess patency of pulmonary or systemic pathways, valve competency, and ventricular function. Each imaging modality has its own pros and cons in achieving these goals.

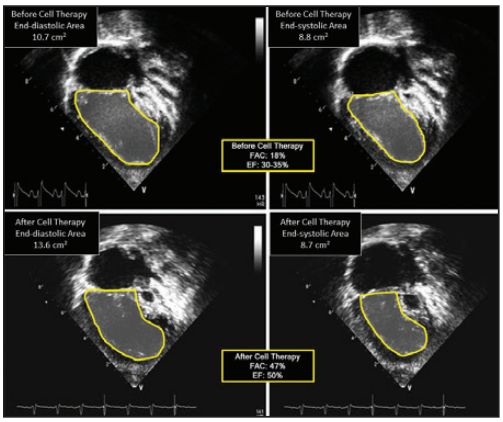

Figure 1. *Apical echocardiographic views performed before (top panels) and 3 months after (bottom panels) intramyocardial injection of umbilical cord blood–derived stem cells. Images show improvement in right ventricular function, with an increase in the ejection fraction from 30%-35% to 50%. FAC, fractional area change; EF, estimated ejection fraction.*

Echocardiography

Echocardiography is readily available and usually does not require sedation, even in pediatric patients. However, it is limited by availability of acoustic windows. The echocardiographic quantification of ventricular function can be challenging, and there are no guidelines or recommendations for quantifying function in a single ventricle by echocardiography. The most commonly used method of assessing function in these patients is a visual estimate or qualitative assessment of ejection fraction. Multiple views of a single ventricle are obtained in both short axis and long axis to estimate ejection fraction. The accuracy and precision of this method improve with experience but remain suboptimal in day-to-day assessment of individual patients. Better quantification tools are needed for more objective evaluations. Because of the unique anatomy of single ventricles, the echocardiographic parameters that use geometric assumptions in quantification of ventricular function (such as biplane method to measure ejection fraction) cannot be used.

Fractional area change (Figure 1) has been shown to have good correlation with pressure-volume loop–derived indices of ventricular function. The fractional area change can be measured in both morphologic left and right single ventricles. The biggest limitation of fractional area change is the interobserver variability. Myocardial performance index can be calculated by spectral Doppler imaging, as well as by tissue Doppler. Significantly higher values in single ventricles versus normal controls have been seen in various studies, which point toward reduced ventricular function even in patients generally considered to have normal function. Studies in tissue Doppler imaging have shown reduced peak systolic, peak early diastolic, and peak late diastolic annular velocities in all patients with a single ventricle. However, these measures do not correlate well with MRI-derived ejection fraction. Deformation imaging offers an alternative strategy for assessment of function in a single ventricle. Universally, all patients with a single ventricle show reduced longitudinal strain and strain rate. For example, at birth, longitudinal strain in neonates with hypoplastic left heart syndrome (HLHS) is more negative than that in normal neonates, which means the ventricular function is better in HLHS at birth. But after the first surgery, the longitudinal strain becomes less negative, suggesting reduced systolic function. It improves somewhat after the second and third stages of palliative repairs, but never becomes normal. The circumferential strain also remains abnormal in these patients. Three-dimensional echocardiography is an additional modality that can help in assessing ventricular function in patients with a single ventricle. This method may offer less inter- and intraobserver variability, but its utility is limited by the need for breath holds, which cannot be performed in small children without general anesthesia.

Magnetic Resonance Imaging

Cardiac MRI can be extremely useful in evaluating ventricular function, vascular anatomy, and flow quantification. Ventricular function is assessed by volumetric methods in MRI. A stack of cine images is obtained in axial or short-axis planes, and the endocardial borders are traced in end systole and end diastole to generate end-diastolic and end-systolic volumes. This allows calculation of stroke volume and ejection fraction. This technique is considered to be the best method and standard reference for assessing ventricular function; however, it is influenced by the operator variability. Vascular anatomy can be seen very well by cardiac MRI, with or without contrast (Figure 2). Flow quantification is one of the major strengths of cardiac MRI. An imaging plane can be set up across any blood vessel in the body, and the blood volume going across that plane can be calculated. This method allows calculation of stroke volume, cardiac output, pulmonary flow, differential flow to branch pulmonary arteries, and also flows in superior and inferior venae cavae. This can also be a useful tool in quantifying valve regurgitation. The limitations of cardiac MRI include limited availability, susceptibility artifacts from metallic hardware, need for anesthesia in pediatric patients, and operator variability.

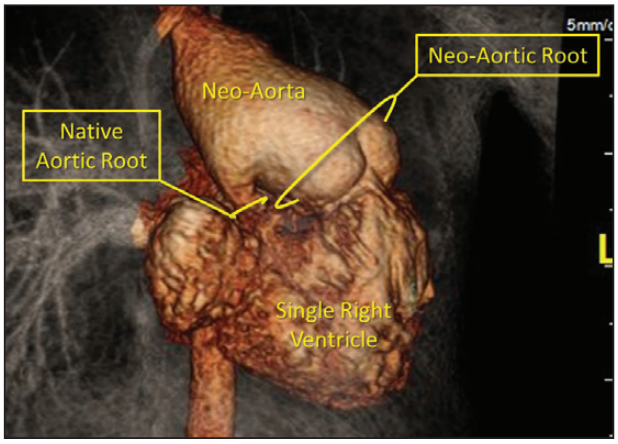

Figure 2. *Magnetic resonance angiogram in a patient with hypoplastic left heart syndrome who has undergone Norwood, Glenn, and Fontan procedures. This 3-dimensional reconstructed image shows severe dilation of neoaortic (native pulmonary) root and single right ventricle. Norwood anastomosis between native aortic and neoaortic roots to create neoaorta can be appreciated.*

Current Research Studies for Imaging of a Single Ventricle

The Todd and Karen Wanek Family Program for Hypoplastic Left Heart Syndrome is dedicated to advancements in diagnostic and therapeutic sciences to help patients with HLHS as well as those with other congenital heart diseases, especially single ventricle physiology. Under the umbrella of this program, specialists at Mayo Clinic in Rochester are trying to develop better imaging strategies that can be used to quantify and predict ventricular dysfunction in these patients earlier in the disease course. In an ongoing prospective study at Mayo Clinic, participating patients with HLHS have transthoracic echocardiography and cardiac MRI. "Preliminary data suggest that echocardiographically derived fractional area change and longitudinal strain are the best parameters to assess function in these patients with a single ventricle, as these 2 parameters correlate very well with MRI-derived ejection fraction," says Dr Qureshi. Newer imaging parameters to better quantify and predict ventricular function are also being developed. A prospective observational study of patients with HLHS following stage II surgical palliation is also under way. The goal of this study is to document the natural history of postsurgical HLHS patients who have undergone standard of care procedures with protocol-specific follow-up over a course of 6 months.

Clinical Trials of Cell-Based Therapies in Single Ventricle Disorders

The goal of ongoing research is to develop regenerative strategies to strengthen the myocardium of the single ventricle after the initial palliative surgical procedures. As part of the Todd and Karen Wanek Family Program for Hypoplastic Left Heart Syndrome, physicians and scientists at Mayo Clinic are running clinical trials of cell-based therapies in patients with a single ventricle. (A summary of ongoing trials is available at the *Cardiovascular Update* website: http://www.mayoclinic.org/medical-professionals/publications/cardiovascular-update.) The advancements in imaging strategies are much needed for better patient selection and recognition of the early changes in ventricular function with these therapies. Current phase 1 clinical trials are focusing on evaluating the safety and feasibility of using mononuclear cells derived from autologous umbilical cord blood or bone marrow. After baseline imaging and clinical evaluations of the enrolled patients, the cells are delivered to the myocardium either by direct intramyocardial injection at the time of planned surgery (Figure 3) or by coronary artery catheterization. The patients are then followed clinically with repetitive cardiac imaging for 6 months.

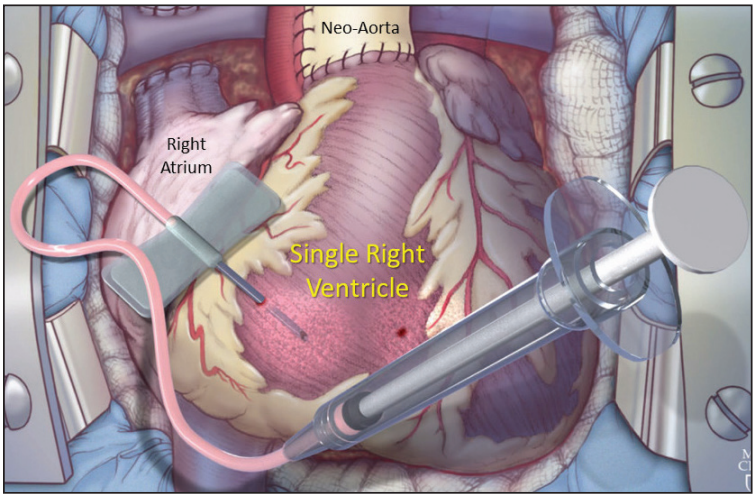

Figure 3. *In an ongoing clinical trial, autologous mononuclear cells derived from umbilical cord blood are injected in the right ventricular myocardium at the time of stage II surgical palliation in patients with hypoplastic left heart syndrome.*

The initial case report (Burkhart et al. J Thorac Cardiovasc Surg. 2015;149:e35-7) highlights the promise of cell-based therapies in patients with a single ventricle. This report described a patient with HLHS and reduced ventricular function (fractional area change, 18%; estimated ejection fraction, 30%-35%) who had remarkable improvement of ventricular function (fractional area change, 47%; estimated ejection fraction, 50%) 3 months after cell therapy.

All of these efforts are with the goal of preventing heart failure in patients with a single ventricle.

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Feb 7-12, 2016, Kauai, HI

Cardiovascular Conference at Snowbird
Feb 12-15, 2016, Snowbird, UT

21st Annual Cardiology at Cancun: Topics in Clinical Cardiology
Feb 22-26, 2016, Cancun, Mexico

23rd Annual Echocardiographic Workshop on 2-D and Doppler Echocardiography at Vail
Mar 7-10, 2016, Vail, CO

Echo Revolution: Adult Echocardiography for Physicians and Sonographers
Mar 11-13, 2016, Boston, MA

Heart Failure Management for Nurse Practitioners, Physician Assistants, and Primary Care Providers
Mar 18-20, 2016, Lake Buena Vista, FL

Case Studies From the Heart of Manhattan: A Mayo Clinic Cardiovascular Update
Apr 7-9, 2016, New York, NY

Echo Fiesta: An In-Depth Review of Adult Echocardiography for Sonographers and Physicians
Apr 7-10, 2016, San Antonio, TX

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