Guidelines for the Outpatient Management of Complex Congenital Heart Disease

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ABSTRACT

An increasingly complex group of children is now being followed as outpatients after surgery for congenital heart disease. A variety of complications and physiologic perturbations, both expected and unexpected, may present during follow-up, and should be anticipated by the practitioner and discussed with the patient and family. The purpose of this position article is to provide a framework for outpatient follow-up of complex congenital heart disease, based on a review of current literature and the experience of the authors.

Key Words. Heart Defects, Congenital, Transposition of the Great Arteries, Tetralogy of Fallot, Fontan, Arrhythmia, Exercise

Introduction

The surgical successes of the past 2 decades have resulted in a growing outpatient population with complex congenital heart disease (CHD). An increasing number of follow-up studies have led to an improved understanding of the hemodynamic and electrophysiologic sequelae following neonatal and infant surgery. Although inpatient perioperative management and clinical practice guidelines are frequently utilized to minimize variance in care[1,2] and to provide a structure for outcome studies, this model has not been typically adopted in the outpatient setting.

"Consensus" can be defined as an opinion or position reached by a group as a whole; within our division of pediatric cardiology there are certainly varying opinions regarding types and frequency of outpatient testing. It must be emphasized that these guidelines are not meant to substitute for variation in individual practices based on clinical needs, nor should they be applied to all patients with a given condition. The purpose of this document is to provide a framework for outpatient follow-up in a broad sense, to describe the practices of the cardiologists at our institution, and to engender discussion on these issues from other groups and professional societies. We also feel that these guidelines provide for some consistency in parental expectations during follow-up, and provide a series of tests that will be helpful to the young adult with CHD (and their practitioners) as they transition into the world of adult medicine.

Methods

This review is based on a recent review of the literature and the clinical experience of members of The Cardiac Center at The Children's Hospital of Philadelphia. A series of "consensus meetings" was held involving the authors and other members of our clinical practice, with a review of relevant literature, description of the expected and unex-

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pected course following surgery, and the description of each practitioner's personal practice for follow-up testing. We decided to assess 3 common lesions: tetralogy of Fallot, transposition of the great arteries (TGA), and various forms of single ventricle; together these lesions comprise perhaps one-third of the surgical procedures performed in neonates and young infants at our institution. We felt that various epochs during follow-up could be marked by important transitions: prior to entry into elementary education, prior to entering middle school, and during puberty when children enter high school and prepare to transition to self-care.

Issues Related to All Survivors of Complex CHD Surgery

Endocarditis Prevention

Infective endocarditis is a serious and potentially life-threatening complication in the patient with congenital or acquired heart disease. Given the successful management of complex heart disease over the past 2 decades, the number of patients at risk continues to rise steadily. Studies show a variable prevalence of approximately 0.5–1.0 case per 1000 pediatric hospital admissions.[3] Endocarditis may be community-acquired or nosocomial.[4] The latter is most commonly seen in premature infants, patients with indwelling catheters, intravenous drug abusers, and other immunocompromised hosts, with potentially more virulent infectious agents, such as *Staphylococcus aureus*, Gram-negative bacteria, and fungal infections. Community-acquired infective endocarditis is generally caused by bacteria native to the upper respiratory and upper gastrointestinal tract, such as alpha-hemolytic streptococci, *S. aureus*, and enterococci. In otherwise well patients, dental manipulations or poor dental hygiene have been targeted as the most likely sources of transient bacteremia. Various studies have supported or refuted that claim.[5,6]

Bacterial endocarditis requires a protracted course of antibiotic therapy (monotherapy or a combination of antibiotics for synergy). Treatment strategies are determined by the causative agent and degree of cardiac dysfunction. Cardiac valves may suffer severe damage, and intramyocardial abscesses may occur. Surgery is often necessary to repair or replace infected cardiac valves. Because the consequences of bacterial endocarditis may be severe, preventative recommendations have been promoted.[7]

Rhythm Disturbances

With few exceptions, patients who undergo cardiac surgery risk the development of early and late postoperative arrhythmias and conduction abnormalities including supraventricular tachycardia, atrial flutter or fibrillation, ectopic atrial tachycardia, sick sinus syndrome, ventricular tachycardia, atrioventricular block, and sudden death. Electrophysiologic abnormalities may precede the operative repair, and postoperative arrhythmias may reflect these pre-existing problems. These abnormalities may result from long-standing pressure overload and ventricular fibrosis that may be seen in patients with tetralogy of Fallot, or from volume overload as seen in lesions with left-to-right shunting, such as single ventricle. Some residual hemodynamic problems that may affect postoperative events are unavoidable, such as elevation of atrial pressure after the Fontan procedure or residual pulmonary insufficiency after tetralogy of Fallot repair. Others may be avoidable, but occur commonly, including residual septal defects or right ventricular outflow obstruction. Other functional hemodynamic problems that greatly influence postoperative events include the presence or development of pulmonary vascular disease or ventricular dysfunction. Factors that affect myocardial preservation such as long-standing myocardial hypertrophy, cardiopulmonary bypass time, myocardial ischemic duration, and techniques of cardioplegia also influence postoperative events. In the postoperative arrhythmia patient, sudden death may occur in association with any of the previously mentioned arrhythmias, but is often associated with distinct arrhythmias in the presence of specific heart defects and their repairs. Specific recommendations for diagnostic testing are listed in the lesion-specific sections below.

Sudden Death and Exercise Limitations

As survival of children with CHD improves, so does the need for a rational approach to assess physical and athletic limitations in this growing population of adolescents and young adults. Despite the greatly increased numbers of children with surgically repaired or palliated heart disease, they constitute a very small portion of the sudden deaths during competitive athletic activity. These children have often been identified since birth and are usually excluded from competitive activity that is likely to put them at risk for sudden death. Rather, previously undiagnosed CHD is the major cause of sudden death. These diagnoses include

hypertrophic cardiomyopathy, anomalies of the coronary arteries, aortic valve disease, and Marfan syndrome,[8] and recommendations for preparticipation screening and competitive restrictions for this latter group of children have been published.[9,10]

Making recommendations for exercise participation and competitive athletic limitations in children and adolescents with other types of CHD is frequently difficult. The most recent Bethesda Conference addresses competitive sports participation for these groups, but as the authors state in their preamble, ". . . absolute or hard data are incomplete." Therefore, while published guidelines such as the Bethesda Conference are useful for this population,[11] *we believe that individual assessment of the child's cardiopulmonary function during exercise combined with the routine resting cardiovascular evaluations is essential to tailor appropriate activity level recommendations for these children and adolescents.* This assessment may require noninvasive testing such as echocardiography, magnetic resonance imaging (MRI), electrocardiographic evaluation, and exercise testing; less commonly invasive testing such as cardiac catheterization is necessary to make recommendations.

Patients with repaired shunt defects such as an atrial or ventricular septal defect usually need no restrictions.[11] Recommendations from the Bethesda Conference for isolated outflow obstructive lesions are based on the degree of obstruction, symptoms, and ventricular function.[11] Complex defects are often much more problematic. Although some patients with defects such as TGA repaired by the arterial switch operation may have normal exercise capacity, most have slightly decreased aerobic capacity.[12] In addition, recent data suggest abnormalities of coronary vascular reserve and a surprisingly high prevalence of intracoronary lesions.[13,14] As such, patients should be fully evaluated prior to allowing them to participate in vigorous competitive athletics.[11] Finally, many children with single ventricle palliated by the Fontan procedure may have good or even normal exercise capacity.[15] Individual variations in these populations are great, especially in the younger populations, and recommendations for sports participation must be made on an individual basis.

School Performance and Academic Difficulties

Advances in prenatal detection, perioperative management, and cardiothoracic surgical techniques have contributed to a significant increase in the number of children with complex CHD entering preschool and beyond. As initial survival has increased, and indeed is now expected for most forms of CHD, greater attention has been directed toward understanding the long-term neurodevelopmental and functional outcomes of this growing patient population. Studies have shown that children with complex CHD requiring surgery in early infancy have an increased incidence of fine and gross motor delays, academic and behavioral difficulties, and inattention/hyperactivity; they are also more likely to have executive planning deficits, delays in expressive language, and lower than expected scores on standardized intelligence quotient (IQ) tests.[16–41] During follow-up visits, pediatric cardiologists should inquire about school performance, behavior, and other developmental issues, and partner with the child's primary care provider and necessary consultants and therapists to formulate a plan for evaluation and management of possible behavior and academic difficulties. Parents should be made aware of the potential for academic and behavioral difficulties early in the follow-up process.

Insurance, Medication Burden, and Family Stress

Although not frequently discussed in the course of a routine outpatient office visit, financial considerations and family stress play a major role in the long-term well-being for patients with CHD. In the United States, children and young adults are frequently covered as dependents of parents with private health insurance. Coverage may last until age 19, 21, or 25 years, depending on marital status and educational status (i.e., coverage may remain in place if the patient remains in ongoing study). In addition, in the United States if a parent of a child with CHD changes employment to which health insurance is tied, The Consolidate Omnibus Budget Reconciliation Act requires employers to continue healthcare coverage for up to 18 months. Children without private insurance may qualify for Medicaid or crippled children's services. As patients with CHD age, the difficulties with obtaining health insurance coverage has been well documented.[42–44] As CHD may be considered a "pre-existing condition," adults with CHD face the loss of or lack of health insurance, and many are counseled to obtain employment with large groups to obtain health insurance coverage; unfortunately this is not a guarantee of adequate or affordable healthcare coverage. Life insurance,

loans, and mortgages may also be difficult to obtain as an adult with CHD, as qualifications vary among banks and insurance companies. Medication burden will vary depending on the severity of the CHD and compliance can be particularly challenging in the adolescent. In general, we try to use medications with the lowest daily dosing regiment to encourage compliance. Finally, family stress may be considerably influenced by the presence of CHD, with higher rates of divorce and other markers of family dysfunction.[45] Caregivers are encouraged to set aside some time during each visit to question financial and mental health issues for the patient and family.

Documentation and Communicating with the Pediatrician

The general medical needs of the child with congenital or acquired heart disease are for the most part the same as other children. The severity of cardiac involvement, however, leads to certain needs that are different from other children, and can be a source of anxiety for the parent and primary physician. It is not uncommon for parents to contact the pediatric cardiologist directly, or at the request of their primary physician, with problems that directly or indirectly relate to the cardiovascular system.[46] Conversely, the primary care physician is the "eyes and ears" of the specialist in the community.

Each outpatient interaction should have several goals. Foremost is a thorough assessment of the cardiovascular system, and appropriate evaluation and treatment of any cardiovascular concerns. The second goal is to educate the family, at each encounter, on any aspect of the health of their child (cardiac or global health issues). This may require the input of other support personnel, such as nurses, nutritionists, and social workers. Stress levels are high in many families of children with cardiac disease, and they need support, both from cardiac specialists and from their primary care physicians.[47] The third goal is for the pediatric cardiologist to communicate in a clear and concise manner with the primary physicians, so that they will be up to date on the current issues. Feedback from the cardiovascular specialist (either in the form of a written communication and/or in the form of telephone call) provides the primary doctor with the knowledge to better understand the child's condition, and subsequently, be a more capable and active part of the child's overall healthcare.

Appropriate documentation is a critical part of the medical record in all cases, but pediatric cardiology, in particular, has important needs. Serial comparison of pertinent physical findings (e.g., intensity of murmurs, pulses, etc.) vital signs and ancillary testing is necessary from visit to visit. Because multiple physicians may be involved in the care of these patients, written documentation is critical when the patient is evaluated by those not directly familiar with their case. In an effort to be consistent, the use of an outpatient template for each visit (new or follow-up) is now commonplace. One option is an outpatient template that is filled out in part by the parent, and in part by the physician. Vital signs, height, and weight are recorded and graphed by the medical assistant. In general, the template includes sections for history of present illness, review of systems, past medical and surgical history, family history, social history, medications, allergies, immunization status, and an area regarding menses, birth control, and substance use (cigarettes, alcohol, etc.). A large section is dedicated to the physical examination, with concentration on pertinent features of the cardiac component. There are sections for ancillary testing results, physician impression and recommendations, need for endocarditis prophylaxis or activity restrictions, as well as plans for future follow-up. Each outpatient visit is further documented by a transcribed letter to the primary physician. Increasingly, the dictated letter is stored in an electronic database, which allows ready access to patient information without retrieving charts. This is especially valuable in the emergency department setting. Finally, the combined data documented from the outpatient template and dictated letter are the basis for physician billing.

A critical role of the primary healthcare provider is making sure that the overall medical needs of the patient are met. Immunizations (both for general pediatric needs and unique to the cardiac population) as well as access to neurodevelopmental evaluation (see above) and dental care are extremely important; indeed, some studies show that cardiac patients seek dental care less often than other children.[48]

Communication with the Cardiac Surgeon

Although cardiac repairs have become increasingly successful for complex forms of CHD over the past 2 decades, it is clear that most patients continue to have ongoing issues that will require additional surgical input. Some surgical reintervention

is planned and expected, such as staged reconstruction leading up to the Fontan operation. Others may be unplanned, such as reintervention for supravalvar pulmonary stenosis after an arterial switch. It is often advisable, when a catheter-based intervention is planned following prior surgery, that there be direct communication with the primary surgeon to ensure that placement of stents or devices will not complicate later surgical procedures. For example, stents implanted in pulmonary arteries or conduits may occasionally impede additional surgical intervention such as conduit replacement. In addition, sometimes coordinated timing with simultaneous or sequential cardiac catheter intervention and surgery may be the best option.

Surgical reconstructions for CHD may be associated with the usual complications of any surgical intervention, such as wound infection. Superficial wound infections are usually managed successfully with oral antibiotics. However, patients who develop signs of deep sternotomy wound infection should have blood cultures obtained and be given intravenous antibiotics; if there is any concern about sternal instability or an increase in drainage, then communication with the primary surgeon is recommended. Documentation of postoperative wound infections is important for continuous quality improvement; these data are usually prospectively collected by the primary surgical team, and as such, it is often best to have the patient return to the surgical center for wound management. Early drainage of mediastinal wounds and primary reclosure can result in good healing with less morbidity and also make additional surgical procedures through the same sternotomy less troublesome.

Finally, it is valuable for the primary surgeon to receive progress reports from the primary cardiologist regarding follow-up visits, especially if any issues have been identified with the surgical repair, or if additional surgical procedures are contemplated. Surgical input into the timing and type of additional interventions is useful, and often reassures the parents that the surgeons remain involved in the child's overall management.

The Transition to Self-care and Adult Medicine

There are now as many adults with CHD as there are children and adolescents. It is timely that we prepare for the transition to adult care for these patients and meet their healthcare needs effectively once they transfer to adult practices. Adolescents with CHD need to be trained to take responsibility for their own health and lives through "the transition process." In the ideal world, this takes place over several visits and several years with their pediatric caregivers, often with substantial nursing input. The main elements are education, motivation, and direction. The *education aspect* helps the patient to know what his/her diagnoses are and what treatments have been delivered, what ongoing health issues there are, how these should affect life planning and activities, and what symptoms should be watched for in particular. The *motivation piece* makes it clear to the patient that they are expected to live to adult life and should prepare for it. Often an optimistic picture can be created for the young person, and at least some good possibilities can always be stated. The *direction component* helps them understand what educational and career planning goals they might consider, what lifestyle restrictions (if any) may need to be planned, and what care they will need to receive to protect their own health interests. This transition process should be offered to all young adolescents with congenital heart defects. It is as important that someone with an excellent outlook knows to expect a normal life as it is that someone with more serious problems knows how best to protect their health and life interests. When patients appear in adult practices without this preparation, the adult caregivers should complete the process as completely as they can.

All of this stands in contrast to the *transfer* of the care of these patients to adult practices. When the time for transfer is to occur, relevant documents including operative notes should be made available from the pediatric files to the adult practice cardiologist, the family physician, and the patient. The adult practitioner should be comfortable caring for the patient, or should seek out an expert opinion in the region when the problems are complex and/or uncommon.[49,50]

Lesion- and Repair-specific Issues in Survivors of Complex CHD Surgery

Transposition of the Great Arteries Repaired by the Mustard or Senning Procedures

Most current adults with TGA have had an atrial switch (either Mustard or Senning) procedure. By virtue of this repair, the morphological right ventricle supports the systemic circulation. Most of these patients are in New York Heart Association classes I and II as adults. A minority, perhaps up to 15%, will develop overt heart failure in late

follow-up. More than mild systemic tricuspid regurgitation may be present in 10–40%, both exacerbating and reflecting right ventricular dysfunction. Atrial flutter occurs in 20% of patients by age 20, and evidence of sinus node dysfunction is seen in about 50% in the adult age group. Shortened life expectancy takes the form of 70–80% survival at 20- to 30-year follow-up. Patients with complex TGA (most commonly with associated ventricular septal defect repairs) do worse than patients with less complicated forms of TGA (with intact ventricular septum). Patients should generally be seen annually. Regular echocardiography in skilled hands can qualitatively assess systemic right ventricular function, the degree of systemic tricuspid regurgitation, the presence or absence of subpulmonary left ventricular outflow tract obstruction, as well as baffle leaks or obstruction. Because the assessment of right ventricular function is often key to the assessment of these patients, and because echocardiography may not accurately assess right ventricular systolic function or acoustic access may be limited, periodic MRI examinations may be of great value. If the patient has a pacemaker or other contraindication to MRI, computerized tomographic angiography may also be very helpful in assessing the systemic right ventricle. A summary of current findings and recommended follow-up are found in Tables 1 and 2.[51–60]

Table 1. Postoperative Sequelae After the Mustard and Senning Operations

Postoperative Sequelae	Incidence (%)
Right ventricular failure	15
Moderate–severe tricuspid regurgitation	20
Bradyarrhythmias requiring pacing	20
Tachyarrhythmias requiring treatment	15
Subpulmonary obstruction	10
Pulmonary hypertension	10
Sudden death	1 (per year)

Table 2. Recommendations for Routine Follow-up After the Mustard and Senning Operations for Transposition of the Great Arteries

Yearly to every 3 years
Electrocardiogram
Transthoracic echocardiogram
Cardiac MRI
24-hour ambulatory electrocardiogram
Exercise testing
Additional testing as indicated
Cardiac catheterization
Lung ventilation and perfusion scanning
Stress echocardiography

Transposition of the Great Arteries Repaired by Arterial Switch

In the 30 years since the introduction of the arterial switch operation by Jatene and colleagues in 1975, arterial level repair has replaced atrial level repair as the surgical procedure of choice for both simple and complex forms of TGA. Although frequently referred to as "anatomic" correction, in reality, there are important differences in the postoperative patient compared with the structurally normal heart. The anatomic pulmonary valve must serve in the systemic circulation lifelong, and there are accumulating data on progressive neoaortic valve dysfunction and root dilation during the second and third decades of follow-up. In addition, as opposed to the normal heart, following the Lecompte maneuver both pulmonary arteries are anterior to the ascending aorta; posterior tension can cause further distortion of the neoaortic root and/or cause supravalvar pulmonary stenosis. In patients without significant comorbidities or major coexisting cardiac defects (e.g., dextrocardia, aortic arch obstruction), surgical mortality can be expected to be <5%. The most commonly described postoperative sequelae are listed in Table 3, with follow-up guidelines in Table 4.[13,14,61–76]

Tetralogy of Fallot

Remarkably, anatomic repair of tetralogy of Fallot now enters its sixth decade. Changes in practice such as younger age at repair, modifications of surgical technique, and improved myocardial protection have made the treatment of this lesion today something quite different from it was decades ago. This evolution must be kept in mind when considering guidelines for follow-up: the concerns arising in the care of a 40-year-old

Table 3. Postoperative Sequelae Following the Arterial Switch Operation

Postoperative Sequelae	Incidence
Supravalvar pulmonary stenosis*	~10%
Supravalvar aortic stenosis*	<5%
Neoaortic root dilation	Essentially 100%†
Neoaortic regurgitation	~50%†
Significant arrhythmia	Rare
Asymptomatic coronary occlusion	2–3%
Pulmonary hypertension	Rare
Hypertrophied bronchial collaterals*	<5%
Abnormal coronary flow reserve[14]	Unknown
Sudden death	Rare

*Requiring intervention.
†Increases with increasing duration of follow-up.

Table 4. Recommendations for Routine Follow-up After the Arterial Switch Operation

Yearly or alternating years
- Electrocardiogram
- Echocardiography
  - Assessment of supravalvar anastomoses, ventricular size and function, segmental wall motion, serial measurements of neoaortic root, valvular regurgitation

Age 4–6 years (pre-elementary school)
- Testing as above
- Screening for academic and behavioral difficulties*

Age 10–12 years (pre-middle school)
- Testing as above
- Exercise testing

Age 14–16 years (pre-high school; during transition to ACHD program)
- Testing as above
- Resting and peak exercise myocardial perfusion combined with routine exercise study
- MRI if echocardiography windows inadequate or if right ventricular function needs evaluation
- 24-hour ambulatory electrocardiogram

At transfer to ACHD
- Electrocardiogram
- Echocardiography
- Summary of operative course, outpatient testing

In symptomatic patients, or for those with concerning noninvasive studies
- Cardiac catheterization with angiography†

*If history suggests neurodevelopmental problems, referral for complete developmental evaluation may be indicated.
†Should also be considered prior to "highly competitive" sports participation.
ACHD indicates adult with congenital heart disease.

Table 5. Postoperative Sequelae Following Repair of Tetralogy of Fallot

Postoperative Sequelae	Incidence (%)
Left pulmonary artery stenosis/hypoplasia	10–20*
Significant exercise intolerance	5–10†
Symptomatic heart failure from severe pulmonary regurgitation	5–10†
Ventricular tachycardia (requiring treatment)	5–10†
Pulmonary valve replacement	5–10†
Sudden death	2–8

*More frequent following earlier age at repair.
†Increases with increasing duration of follow-up.

Table 6. Recommendations for Routine Follow-up After Repair of Tetralogy of Fallot

Age 1 year—complete evaluation of repair
- Electrocardiogram
- Echocardiography
  - Assessment of residual right ventricular outflow tract obstruction and branch pulmonary arteries, ventricular or atrial septal defect, atrioventricular valve regurgitation, aortic root dilation or regurgitation, ventricular size and function
- If left pulmonary artery not visualized or stenosis/hypoplasia suspected, MRI and/or lung perfusion scan
- Pulse oximetry
- 24-hour ambulatory electrocardiogram (Holter)

Yearly
- Electrocardiogram
- Echocardiography

Age 4–6 years (pre-elementary school)
- Testing as above at 1 year
- Screening for academic and behavioral difficulties*

Age 10–12 years (pre-middle school)
- Testing as at 1 year
- Exercise testing
- Cardiac MRI
  - Quantitative evaluation of cardiac output, regurgitant fraction, branch pulmonary arteries

Age 14–16 years (pre-high school, at transition to ACHD program)
- Testing as at 1 year
- Exercise testing

At transfer to ACHD
- Electrocardiogram
- Echocardiogram
- Holter monitor
- Summary of operative course, outpatient testing

*If history suggests neurodevelopmental problems, or chromosomal abnormality, referral for complete developmental evaluation may be indicated.

patient who underwent a palliative shunt as an infant followed by complete repair many years later are likely to be very different from those in a child who underwent a primary reparative procedure as a young infant. Long-term studies (over 30 years) of patients undergoing repair at a mean of 10–12 years of age have suggested a persistent ongoing risk of dying that is relatively linear after the early postoperative phase. By far the most common mode of death is sudden. Although the long-term course is unknown for individuals treated in recent years by primary repair at increasingly younger ages, it is encouraging that a recent long-term follow-up study of patients who underwent repair as infants demonstrates a low risk of dying between 1 and 25 years after repair.[77]

In recent series, early postoperative mortality after repair of uncomplicated tetralogy of Fallot is 7–10% in newborns and 5% or less in infants. Early reintervention (3 years) occurs in 15–20% of patients after neonatal and 5–10% after infant surgery. The most common indications for reintervention are right ventricular outflow or branch (more commonly left) pulmonary artery obstruction. Beyond adolescence, exercise performance, arrhythmia, ventricular function, and sudden death become the paramount concerns. Pulmonary insufficiency is a major cause of ventricular dysfunction, exercise limitation, and probably an important risk for arrhythmia and sudden death. The most commonly described postoperative sequelae are listed in Table 5,[60,77–95] with follow-up guidelines in Table 6.

Single Ventricle

Patients with a functional single ventricle undergoing staged reconstruction ultimately resulting in a Fontan circulation are perhaps the most hetero-

geneous group followed by pediatric cardiologists, and present unique challenges during follow-up. Follow-up issues during early infancy and childhood are quite different from the long-term challenges for the adolescent and young adult with a Fontan, and the frequent modifications of technique and timing of surgery over the past 2 decades make applicability of long-term outcome studies to younger patients with more current techniques a bit difficult. Nonetheless, the following represents our current approach to the infant, child, and adolescent with a Fontan circulation, based on recent published data and the experience of our institution with over 2000 patients with a single ventricle.

Although some patients with various forms of single ventricle may not require newborn palliation, most require intervention in the newborn period if there is either unrestricted or ductal-dependent pulmonary blood flow, or if there is ductal-dependent systemic blood flow. Options include systemic to pulmonary artery shunts, pulmonary artery banding, aortic to pulmonary artery anastomosis (Damus–Kaye–Stansel, DKS), Norwood stage I reconstruction, or arch repair (usually with concomitant pulmonary artery banding). The general principles involved in newborn palliation include providing unobstructed systemic blood flow, unobstructed pulmonary and systemic venous return, limited pulmonary blood flow at normal pulmonary artery pressure, and adequate intra-atrial mixing. Frequent surveillance in infancy and early childhood is important to minimize the eventual risk factors for an eventual Fontan operation, including pulmonary artery distortion, pulmonary artery hypertension, ventricular dysfunction, ventricular hypertrophy, and loss of sinus rhythm. Important follow-up issues are summarized in Table 7.

Table 7. Postoperative Sequelae Following Staged Reconstruction and the Fontan Operation

Postoperative Sequelae	Incidence
Newborn and infant	
Interstage mortality*	5–20%
Shunt thrombosis/narrowing†	5–10%
Arch obstruction†	5–10%
Restrictive atrial septum*	2–5%
Significant atrioventricular valve regurgitation	10–20%
Following superior cavopulmonary connection	
Progressive hypoxemia/pulmonary AVM‡	5–10%
Subaortic obstruction	<5%
Following Fontan	
Sinus node dysfunction	~50%
Sinus node dysfunction§¶	~10–15%
Chronotropic impairment	>75%
SVT/atrial flutter or fibrillation¶	~10–20 %
Decreased exercise capacity	Essentially 100%
Protein-losing enteropathy clinical¶	3–5%
Protein-losing enteropathy subclinical	Unknown
Thrombus¶	5–10%
Stroke¶	5–10%
Plastic bronchitis	Rare
ADHD/learning disabilities	Up to 50%

*Following stage I Norwood.
†Requiring intervention.
‡Especially in heterotaxy syndrome.
§Requiring pacemaker.
¶Incidence increases with increasing duration of follow-up.
AVM indicates arteriovenous malformations; SVT, supraventricular tachycardia; ADHD, attention deficit hyperactivity disorder.

Interstage Issues Before Cavopulmonary Anastomosis

Outpatient Follow-up. Newborns with single ventricle require particularly frequent outpatient follow-up prior to their cavopulmonary anastomosis. Usual newborn issues such as gastroesophageal reflux, viral infections, and weight gain must be followed carefully, as well as trends in transcutaneous oxygen saturation. Home nursing and monitoring may reduce the incidence of interstage mortality.[96]

Shunt-related Issues. Insufficient pulmonary blood flow can be related to thrombus formation in the shunt, distortion of the shunt or pulmonary arteries, compromise to shunt flow from the innominate artery or right ventricle, or simply "outgrowing" the shunt. Early hypoxemia can often be managed by transcatheter interventions including stent placement. Although not studied as of yet in randomized clinical trials, the use of antiplatelet therapy or anticoagulants (aspirin [5 mg/kg/day] or subcutaneous low-molecular-weight heparin) is widely used by many practitioners to decrease the risk of thrombus formation.

Restriction at the Atrial Septum. Patients with left or right atrioventricular valve atresia or severe hypoplasia must be monitored for the development of a restrictive atrial septum. Early restriction can be addressed by transcatheter approach, occasionally requiring stent placement to maximize the likelihood of long-term patency. Later restriction can be addressed with a surgical septectomy at the time of the cavopulmonary anastomosis.

Arch Obstruction. Patients with single ventricle physiology and obstruction to systemic flow most commonly require arch reconstruction as a part of their first-stage palliative surgery. In our experience, development of arch obstruction at the distal end of the arch reconstruction occurs in 9% of

patients with hypoplastic left heart syndrome.[97] Arch obstruction can result in pulmonary overcirculation, as the shunt is proximal to the obstruction, as well as diminished ventricular function. In the face of diminished ventricular function or lowered cardiac output, the measured gradient may not reflect the severity of anatomic obstruction, and even a mild arch gradient may require balloon angioplasty. *A high suspicion for arch obstruction should be present for the young infant with unexplained ventricular dysfunction and/or systemic atrioventricular valve regurgitation.*

Subaortic Obstruction. Subaortic obstruction may develop in patients in whom the single ventricle gives rise to the aorta through a restrictive ventricular septal defect or bulboventricular foramen. This obstruction is often relieved with an anastomosis between the pulmonary artery and aorta (DKS). The timing of the DKS can be either with the initial palliative surgery or with the cavopulmonary anastomosis. Caution must be taken not to damage the pulmonary valve prior to the DKS (e.g., with a proximally placed pulmonary artery band or during cardiac catheterization).

Pulmonary Overcirculation. While patients with insufficiently limited pulmonary blood flow may have medically controlled heart failure and acceptable growth initially, they must be monitored carefully for the development of both elevated pulmonary vascular resistance (PVR) and ventricular dysfunction (with or without atrioventricular valve regurgitation) from a volume overload state. Patients with low-pressure gradients between their single ventricle and pulmonary arteries should undergo heart catheterization in early infancy to directly measure pulmonary artery pressure and PVR. Patients with elevated PVR should be considered for a pulmonary artery band, shunt revision, or early cavopulmonary anastomosis, based on age and catheterization findings.

Issues Prior to Fontan (Total Cavopulmonary Connection)

The superior cavopulmonary connection (SCPC) first reported by Glenn nearly 50 years ago is now nearly universally utilized prior to the Fontan procedure. Advantages of an early SCPC include reduction of volume load to the single ventricle, amelioration of symptoms of congestive heart failure, an increased amount of effective pulmonary (rather than admixed) blood flow, and the ability to surgically manage other anatomic defects (e.g., pulmonary artery distortion) during the procedure. Early volume unloading has been shown to provide beneficial effects of the long term as well, with improved exercise performance.[15] In the asymptomatic patient, most centers now recommend the SCPC to take place electively between 4 and 6 months of age. The timing of the procedure may be earlier if there is unacceptable hypoxemia, ventricular dysfunction, atrioventricular valve regurgitation, or if there is an alternative indication for surgery (e.g., severe pulmonary artery hypoplasia). Although there may be situations when a preoperative catheterization can be avoided,[98] at our center we currently perform cardiac catheterization prior to surgery to assess the anatomy and physiology in most cases.

The SCPC can be performed with either a bidirectional Glenn or "hemiFontan" technique; perhaps 10–15% of children with a single ventricle also have a left-sided superior vena cava that is typically also anastomosed to the ipsilateral pulmonary artery. It is beyond the scope of this review to describe the advantages of one technique over the other; however, the physiology is essentially identical and follow-up issues are similar. Important issues include screening for congestive heart failure and ventricular dysfunction, atrioventricular or semilunar valve regurgitation, or progressive hypoxemia. Pulse oximetry, weight checks, developmental assessment, and rhythm screening are routinely used; upper and lower extremity blood pressure measurements are also important to the evaluation in those children who have undergone aortic arch reconstruction. In general, patients with single ventricle physiology have improved weight gain following the SCPC than before because of the ventricular volume unloading. Increasing cyanosis may result from decompressing veins or the development of pulmonary arteriovenous malformations, and may warrant early cardiac catheterization.

The primary form of diagnostic assessment prior to the Fontan procedure is transthoracic echocardiography. Important issues to delineate prior to Fontan completion include assessment of ventricular performance and atrioventricular valve regurgitation. Both systolic and diastolic function can be assessed noninvasively by a variety of techniques including ejection fraction, myocardial performance index, tissue Doppler imaging, and color M-mode propagation; however, subjective assessment remains the primary tool used by most pediatric cardiologists. Distal arch obstruction can be assessed by echocardiography although accurate measures of distal arch pressure gradients remain

challenging because flow acceleration in the distal aorta is a normal finding in patients who have had arch reconstruction.[99] Pulmonary artery anatomy can occasionally be difficult to image, and additional imaging techniques may be necessary, such as MRI. Patients with single left ventricle with transposed great arteries need to be monitored closely for the development of subaortic obstruction following the volume unloading of the SCPC.[100]

Most institutions perform a cardiac catheterization in anticipation of the completion of the Fontan procedure.[101] Cardiac catheterization provides some data that echocardiography cannot, including ventricular end-diastolic pressure and PVR. In addition, angiography allows for better definition of the distal pulmonary vasculature as well as assessment for pulmonary arteriovenous fistula or other collateral vessels. However, patients considered low risk for the Fontan operation by clinical evaluation and echocardiography (pulse oximetry > 75%, hemoglobin ≤ 18 gm/dL, well-visualized and nonstenotic pulmonary arteries, no significant atrioventricular valve regurgitation, adequate ventricular function, no arch obstruction, no restriction at atrial septum) may not require cardiac catheterization prior to surgery.[102] *If cardiac catheterization is performed, we believe that coil embolization of hemodynamically insignificant aortopulmonary collaterals should not be performed, as placement of coils renders the patient unsuitable for future MRI examination in many cases.* In addition, while large collateral vessels with a significant volume burden should be considered for coil embolization,[103] there are few data to support the routine coil embolization for small collaterals in the absence of a significant volume load on the single ventricle.

The timing of the Fontan procedure remains quite variable among institutions. Some institutions perform the Fontan completion as early as 1 year of age while others wait until 4 years of age or longer. The primary reason to perform the Fontan operation early is to reduce the duration of hypoxemia and subnormal pulmonary blood flow, while waiting longer results in lower inferior vena caval pressures during early childhood, and if an extracardiac conduit will be used, allows for a larger conduit to be placed at the time of the Fontan operation. For poorly understood reasons, pulmonary arteries that are not exposed to hepatic venous blood may develop arteriovenous fistulae,[104] which may regress following the Fontan procedure.[105] A recent study shows that performance of the Fontan operation during respiratory viral season is associated with higher morbidity and mortality,[106] and in our institution most Fontan procedures are scheduled electively between April and October. Further studies in other geographic areas should be conducted to support this practice.

Outpatient Issues After the Fontan Procedure

All modifications of the Fontan operation consist of incorporation of the inferior vena caval return into the pulmonary circulation. Considered the last (planned) phase of staged reconstruction for single ventricle, the Fontan operation comes at a considerable cost resulting in persistent physiologic aberration. Factors such as relatively low cardiac output,[107,108] elevated central venous pressure with abnormal venous patterns of flow,[109] and vascular endothelial dysfunction[110,111] all contribute to a suboptimal physiologic state, with ongoing hazard for late problems. Long-term chronic morbidity and a lingering risk of mortality persist indefinitely after surgery. In a recent review, actuarial survival of Fontan operation for double-inlet left ventricle type of single ventricle at 5, 10, 15, and 20 years was 91%, 80%, 73%, and 69%, respectively.[112] The Fontan operation is therefore considered a long-term "palliation" and not a curative treatment for patients with single ventricle type of heart disease. Patients who have undergone various modifications of the Fontan operation require careful and regular surveillance for a series of potential complications.

Structural/Myocardial Issues. Concerns after the Fontan operation include observation for adequate growth and development of the pulmonary arteries and continued patency of the systemic venous pathway in conjunction with somatic growth. A variety of possible Fontan pathways are possible (lateral tunnel, extracardiac conduit, native tissue, with or without fenestration). The long-term status and possible late problems as growth takes place are unknown, therefore requiring diligent surveillance on the part of the practitioner. Placement of a fenestration at the time of Fontan operation is currently our practice at The Children's Hospital of Philadelphia.[113] In our experience, the majority of ~4 mm fenestrations placed at the time of surgery close spontaneously within 1 year, with very few cases of patients manifesting important cyanosis requiring active closure with device deployment.[114] Separate from generic matters related to the Fontan circulation,

specific concerns related to the individual type of single ventricle may require attention as patients are followed forward in time. For example, those with hypoplastic left heart syndrome require observation for right ventricular dysfunction, tricuspid regurgitation, neoaortic root dilation and insufficiency, and aortic arch narrowing, while those with ventricular inversion ("L-looping") require long-term monitoring for heart block and subaortic stenosis.[115–118]

Stroke/Thrombosis. Patients after Fontan operation are at increased risk for thromboembolic events, with a prevalence of 3–19%.[119,120] Coagulation abnormalities have been identified both after[121,122] and before Fontan operation,[123,124] suggesting that patients with single ventricle at all points in time may have an inherent thrombophilic tendency. The low cardiac output, low-flow state of the Fontan operation may further exacerbate the risk of thrombus formation. Finally, conditions such as arrhythmia and protein-losing enteropathy add further incremental risk to thrombus formation.[125] Although there are currently no published prospective/randomized studies demonstrating the benefits of anticoagulation, we have generally recommended the use of low-dose aspirin (3–5 mg/kg/day) in *all* patients after Fontan operation, with consideration given to addition of warfarin or enoxoparin (Lovenox) in high-risk patients with: (1) history of thromboembolic event; (2) uncontrolled atrial arrhythmia; (3) protein-losing enteropathy; (4) severe ventricular dysfunction; or (5) branch pulmonary artery distortion with or without stent placement.

Protein-losing Enteropathy and Plastic Bronchitis. An enigmatic and poorly understood problem seen after Fontan operation is protein-losing enteropathy.[126] The disease results in hypoalbuminemia and concomitant ascites and peripheral edema. The magnitude of abnormal enteric protein loss can be substantial leading to loss of elements critical to immune function, clotting processes, and metabolic functions. Gastrointestinal symptoms of diarrhea and steatorrhea can be significant or oftentimes surprisingly subtle. Abnormal protein extravasation can also take place into the bronchial airways leading to cast formation and expectoration (chyloptysis), a disease known as plastic bronchitis.[127] The pathophysiology of these diseases is poorly understood and no treatment strategy has been found to be universally effective.[128] Frequency of bowel movements and presence or absence of inexplicable swelling should be asked at outpatient visits after Fontan operation, with affirmative answers prompting examination of serum total protein and albumin levels. If low, then 24-hour fecal alpha-1-antitrypsin clearance, or more simply spot fecal alpha-1-antitrypsin concentration, should be performed to quantify the degree of enteric protein loss.[129]

Exercise Limitations. Exercise capacity is limited after Fontan operation.[108] Chronotropic impairment is a key factor as is a limitation to stroke volume at peak exercise, likely related to impaired ventricular filling.[130] The presence of a Fontan circulation, per se, is not a contraindication to exercise, with recent data suggesting improved overall capacity and quality of life in patients with single ventricle who undergo a program of cardiac exercise rehabilitation.[131] In general, patients are encouraged to participate in sports activities in conjunction with their interests and abilities, but should be allowed to rest when desired. Regular interval exercise testing can provide objective data for each individual patient, and can be used to craft-specific regimens to target areas for improvement.

Arrhythmias. The postoperative arrhythmias seen in patients with functional single ventricle are similar to those seen after the intra-atrial repair of TGA because of the extensive intra-atrial surgery, and include sinus node dysfunction, ectopic atrial rhythms, atrial flutter, and ventricular tachycardia.[60,132,133] Atrial dilatation, injury to the sinus node, and intra-atrial scarring provide the substrate for the development of atrial arrhythmias. The type of Fontan procedure has been associated with the type of long-term arrhythmias, with a higher incidence of atrial arrhythmias associated with atriopulmonary connections when compared with total cavopulmonary connections.[134] In our experience, up to 50% may develop sinus node dysfunction, but thus far, <10% of patients have required pacemaker therapy.[135]

Suggested follow-up studies during and after staged reconstruction for single ventricle are found in Table 8.

Summary

The surgical successes of recent decades have resulted in an increasingly complex group of patients followed as outpatients, many of whom are now entering adolescence and young adulthood. These guidelines are based on a review of

Table 8. Recommendations for Routine Follow-up During and Following Staged Reconstruction and the Fontan Operation

Weekly or biweekly during infancy
Weight, pulse oximetry
Upper and lower extremity blood pressure measurements (if arch reconstruction required)
1–2 months
Electrocardiogram
Echocardiography
Pulse oximetry
3–5 months—preoperative evaluation
Electrocardiogram
Echocardiography
Pulse oximetry
±Holter monitor
Cardiac catheterization (in most cases)
Each 3–6 months prior to Fontan
Electrocardiogram
Echocardiography
Pulse oximetry
Pre-Fontan
Electrocardiogram
Echocardiography
Pulse oximetry
±Holter monitor
Complete blood count
±Cardiac MRI
±Cardiac catheterization
Age 4–6 years (pre-elementary school)
Electrocardiogram
Echocardiogram
Holter monitor*
Pulse oximetry
±Cardiac MRI
Screening for academic and behavioral difficulties†
Age 10–12 years (pre-middle school)
Testing as at 4–6 years
Exercise testing
Cardiac MRI
Complete blood count, coagulation studies, renal and liver function, total protein, albumin
Age 14–16 years (pre-high school, at transition to ACHD program)
Testing as at 10–12 years
±Cardiac catheterization
±Cardiac MRI
At transfer to ACHD
Electrocardiogram
Echocardiogram
Holter monitor
Summary of operative course, outpatient testing

*More frequent if concerning clinical symptoms or prior arrhythmia. †If history suggests neurodevelopmental problems, or chromosomal abnormality, referral for complete developmental evaluation may be indicated.

the published literature and the opinions and experience of the authors. All follow-up testing should be individualized and based on clinical conditions and available testing modalities. Not all centers will have ready availability of MRI, for example, and newer diagnostic modalities (e.g., ultrafast computerized tomographic imaging) may replace currently utilized testing strategies. Of course, the frequency of testing and types of tests utilized must be based on individual circumstances, and more invasive testing such as cardiac catheterization should be utilized if there are concerning historical, physical, or noninvasive findings.

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