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Original Article

Primary care cardiology for patients with hypoplastic left heart syndrome

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Abstract Primary care cardiology is also known as ambulatory cardiology and outpatient cardiology. Primary care cardiology for the longitudinal management of patients with hypoplastic left heart syndrome is both poorly described and has limited evidence to justify its basis. This article briefly discusses the various complications that these patients can develop, reviews the medical literature, and describes a framework for the care of these complex patients from infancy to transition to care by specialists in adults with congenital cardiac disease.

Keywords: Ambulatory cardiology; outpatient cardiology; single ventricle; functionally univentricular heart; Norwood; Glenn; Fontan

It is a dirty little secret about Fellowship training in Paediatric Cardiology in the United States of America that, although trainees typically feel quite comfortable caring for newborns with hypoplastic left heart syndrome in the hospital, the management of these patients outside of the hospital is rather an opaque and poorly understood process. In fact, primary care cardiology, better termed ambulatory cardiology or outpatient cardiology, has very little in the way of guidelines for care of either simple or complex patients. In the case of patients with hypoplastic left heart syndrome, variability of practice is no less as compared with that of other lesions. In fact, it is likely even more of a unique and challenging cardiac lesion for caregivers as compared with other congenital cardiac defects. General paediatricians and family practitioners, knowing the easily fragile and lethal history of hypoplastic left heart syndrome, typically feel uncomfortable managing the primary care of these patients, especially early on in their operative series. In reality, the likelihood of their ability to master the complex physiology and complications associated with these patients during the interstage periods is limited, and thus their hesitance is appropriate. Meanwhile, paediatric cardiologists are often hypervigilant, with both the frequency of their visits and their testing. To be fair, a young patient with hypoplastic left heart syndrome is at risk for a number of potentially lethal complications that can often be subtle to the untrained provider until it is too late. The staged repair for hypoplastic left heart syndrome has existed for approximately the last 25 to 30 years, but has only been able to be implemented "routinely", more recently with diminishing mortality and morbidity. Patients with this lesion are especially at risk in the interstage period between the first and second stages. This increased risk is due to multiple factors. Cardiac factors that can be additive, or even multiplicative, to the risk for these young children include:

- residual arch obstruction,
- subaortic obstruction,
- poor right ventricular function (that is, poor systemic ventricular function),
- restriction of the interatrial communication,
- residual moderate or severe regurgitation of the atrioventricular valve,
- compromise to the coronary arteries,
- obstruction of the systemic to pulmonary shunt,
- pulmonary overcirculation, and
- other complicating cardiac malformations.

Recently, a number of extracardiac factors have also been recognised as raising risk and are being

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associated with poor outcomes. These include developmental delay, feeding abnormalities, and genetic syndromes. Prolonged hospitalisation and other complications, such as necrotising enterocolitis, cerebrovascular accidents, renal disease, prematurity, and the need for extracorporeal membrane oxygenation, also add to the morbidity of these patients and raise their risk for early death. As these patients survive into later adolescence and adulthood, further risks await because of the combination of multiple surgeries, residual scar tissue and suture lines, the utilisation of the right ventricle as a systemic ventricle, which was never architecturally or geometrically intended to be used as such, and residual complex structural defects. Well-documented complications of this unnatural physiology include:

- systemic ventricular failure,
- electrical disturbances, including sinus node dysfunction and intra-atrial re-entry tachycardia,
- formation of intra-pulmonary arteriovenous malformations and aortopulmonary collateral vessels,
- thromboembolism,
- exercise intolerance,
- development of pulmonary hypertension,
- protein-losing enteropathy, and
- cirrhosis, or other liver failure.

Our colleagues who are specialists in caring for adults with congenital cardiac disease are now seeing patients who require not only cardiac transplantation, but also combined transplantation of both heart and liver.

With the various short- and long-term developments in these patients, as well as the lack of an understanding of the very long-term outcomes and complications, surveillance of these patients becomes the hallmark of care. In fact, surveillance ends up being what distinguishes paediatric and congenital cardiologists from adult cardiologists, who typically see their patients only after they present themselves after a complication or after a specific concern has arisen. Unfortunately, at this time, evidence-based guidelines do not exist to determine

- how frequently a patient with hypoplastic left heart syndrome should be seen in the outpatient clinic,
- which tests should be performed, and
- when they should be performed.

One of the first attempts at comprehensive guidelines for ambulatory cardiology for the follow-up of patients with congenital cardiac defects was published in 2006 by the Children's Hospital of Philadelphia.[1] This publication was a consensus-based document that looked at various defects and the frequency of both their follow-up and surveillance studies. Specifically for patients with functionally univentricular hearts, including those with hypoplastic left heart syndrome, it was recommended that patients be seen less frequently as they age, but with more surveillance testing (Table 1).

Table 1. Guidelines for Follow-Up of Patients with Functionally Univentricular Hearts

- Infancy
  - Weekly/biweekly: weight, arterial saturation, upper and lower extremity arterial pressure
  - 1–2 months: electrocardiogram, echocardiogram, arterial saturation
  - 3–5 months: electrocardiogram, echocardiogram, arterial saturation, catheterisation, ±Holter monitor
- Interstage
  - Every 3–6 months electrocardiogram, echocardiogram, arterial saturation
- Pre Fontan
  - Electrocardiogram, echocardiogram, arterial saturation, complete blood count, ±Holter monitor, ±magnetic resonance imaging study of the heart, ±catheterisation
- Post Fontan
  - 4–6 years: electrocardiogram, echocardiogram, Holter monitor, arterial saturation, screen for academic/behavioural problems, ±magnetic resonance imaging study of the heart, discussion of transition to a physician who specializes in caring for adults with congenital cardiac disease
  - 10–12 years: as above, exercise stress test, magnetic resonance imaging study of the heart, complete blood count, coagulation studies, renal and liver function tests, total protein and albumin, discussion of transition to a physician who specializes in caring for adults with congenital cardiac disease
  - 14–16 years: as 10–12 years, ±catheterisation, ±magnetic resonance imaging study of the heart, discussion of transition to a physician who specializes in caring for adults with congenital cardiac disease
  - Transfer to a physician who specializes in caring for adults with congenital cardiac disease: electrocardiogram, echocardiogram, Holter, summary of operative course, and outpatient testing

Adapted from Wernovsky et al[1]

Monitoring between stages

Three years before the publication of this consensus-based document by the team from the Children's Hospital of Philadelphia,[1] Ghanayem et al at the Children's Hospital of Wisconsin published a landmark paper[2] that attempted not only to determine guidelines for follow-up of a subset of these patients, but also did so with an evidence-based approach. Patients with hypoplastic left heart syndrome who were discharged from the hospital after their first stage of surgical intervention were sent home with a pulse oximeter, an infant scale, a

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log to record daily saturations and weight, and instructions to contact the clinic if

- the saturations of oxygen in room air were less than 70%,
- the patient experienced weight loss of at least 30 grams in 24 hours, or
- the patient failed to gain 20 grams in 3 days.

This level of monitoring was to be continued until the time of the second operative stage. These simple interventions markedly improved interstage survival of these patients, with 36 consecutive patients surviving this interstage period and demonstrating the specific parameters that required surveillance and the frequency of their surveillance.[3] Since that time, numerous programmes have anecdotally increased their surveillance in one way or another, such as

- mimicking the protocol developed by the team from Wisconsin, or
- sending nurse practitioners to the house, or
- increasing clinic visits to every 1 to 2 weeks.

In an effort to establish these criteria on a larger scale, the Joint Council on Congenital Heart Disease has launched a new study, the National Paediatric Cardiology Quality Improvement Collaborative.[4] This protocol attempts to limit variation in practice at multiple steps along the timeline of care of the patient, starting from when the patient is in the post-operative phase still in the hospital. During that time, training and preparation of the planned caregiver at home after discharge from the hospital is provided for:

- administration of any medications,
- the plan for feeding,
- assessment of the cardiac status of the infant, and
- specific guidelines for surveillance in the home.

In the phase of transition to the home, the hospital staff ensures that

- the medications are available,
- the appointment for follow-up is scheduled and confirmed, and
- any other necessary resources for the patient and family are available.

While at home, the family performs daily measurements of:

- oxygen saturations,
- weight, and
- intake of calories.

They also review any parameters that may be outside of the normal range, which could put the patient in a "Red Flag" situation requiring further action. Finally, clinic visits are standardised as well. The clinic is to have in place a system for generating a rapid medical response to the data from surveillance that is out of range or to a "Red Flag" event. Documentation is strictly maintained, ensuring continued observation of several variables:

- parameters of growth,
- intake of calories,
- immunisations, and
- communication with the provider of primary care.

The clinic is to provide a written set of expectations for the care of the child, nutritional guidelines, and list of medications. This study organised by the Joint Council on Congenital Heart Disease involves multiple centres and will evaluate many aspects of care for these patients that will hopefully lend insight into not only management and prevention of complications in these patients, but also into that of patients with other types of congenital defects.

The visit to the office

Overall, the repertoire of the routine follow-up of patients with hypoplastic left heart syndrome is similar to that of the ambulatory care of most patients, although extra care is given to certain aspects of the history and physical examination germane to this class of complex cardiac defects.

History

The history is often typical for the clinic, including enquiry into the activity level of the child and the ability to keep up with their peers in exercise. In addition, the typical questions for infants apply, such as assessment of their ability to feed and whether there is dyspnoea or diaphoresis associated with feeds. Caloric intake should be estimated, and querying for worsening cyanosis or syncope should be completed. In older children, more questions about the tolerance of exercise will be germane, including queries about pain in the chest, palpitations, and dizziness with activity.

Physical examination

Often, an initial evaluation of the vital signs of the patient can give a rapid snapshot into the clinical state of the patient, even before the provider enters the room. Reviewing the rate of the heart for evidence of bradycardia or tachycardia, as well as the rate of respirations for increased rate of breathing, can give immediate clues to wellness, or its lack. Recording the weight of the patient and the percentile of this weight is probably a sensitive indicator of the cardiac status in these patients, as there is often poor gain in stature as compared with

weight. Finally, the amount of oxygen saturated in the blood and the arterial pressures in the right arm and a leg can suggest worsening cardiac shunting or obstruction to output from the heart, respectively.

The examination begins with a detailed assessment of the physical findings present or absent on evaluation. Although these points of examination are listed from approximately head to toe, consideration should be given to ensuring that the evaluation of a paediatric patient, especially in very small, apprehensive patients, moves from "least invasive" to "most invasive". This strategy means that auscultation of the heart and lungs, which requires that the patient be calm and quiet, be performed as early as possible, before the child potentially becoming more agitated and less cooperative with the examiner.

The physical examination in a patient with hypoplastic left heart syndrome requires classical observation and examination skills. A visual assessment of cyanosis and for evidence of dysmorphic features can be rapidly achieved in these patients. Evaluation of the chest includes auscultation of the lungs, noting respiratory effort, and appraisal of the status of the scar from the sternotomy. Evaluation of the heart involves inspection, palpation, and auscultation. Typical findings in the precordium include a tap over the right ventricle, as well as the presence of a thrill associated with the Sano shunt or other valve or conduit with significant stenosis. The routine sounds of the heart can include either normal, or single, first heart sounds, and a single second heart sound. Gallops and/or clicks may be heard if there is evidence of ventricular dysfunction, or a bileaflet valve in the neo-aortic position. Non-specific murmurs and specific murmurs of a shunt or regurgitation of an atrioventricular valve are important to identify. The murmurs associated with the various shunts are either continuous, as in a Blalock–Taussig shunt, or ejection, as in the Sano shunt. The murmur of the residual coarctation of the aorta may also be found. Stenosis of a branch pulmonary artery and aortopulmonary collaterals can also create murmurs, although these are often much quieter and may not be as easy to hear.

Examination of the rest of the body gives both clues to cardiac sufficiency or insufficiency and information regarding any other systems that may influence the heart. During examination of the abdomen, palpation of the liver and spleen can demonstrate both size and abdominal sidedness – (situs), the importance of the latter needed for patients with heterotaxy syndrome. If required, visual review of the gastrostomy tube ensures that the site is clean without evidence of erosions. The presence of ascites is rare in children, and typically indicates disease of the liver or kidneys; however, patients with functionally univentricular hearts are at risk of development of ascites in association with protein-losing enteropathy. Finally, ensuring that there is no cyanosis, clubbing, or oedema of the extremities, as well as checking for evidence of lag between the pulse in the right radial artery and a femoral artery completes the examination.

Diagnostic testing

As suggested earlier, the timing of ancillary testing is a subject for debate. However, certain indications for testing seem constant. Electrocardiography can assess function of the sinus node, demonstrate the electrical rhythm, and usually reveals right axis deviation and right ventricular hypertrophy. A reasonable frequency of testing with electrocardiography could be monthly during the first interstage period followed by semi-annually thereafter. Echocardiography assesses a multitude of cardiac findings, both anatomic and functional. Echocardiography is likely best performed monthly during the first interstage period as well, and then limited to semi-annually after the second surgical stage. Ambulatory 24 hours, or Holter, monitoring demonstrates sinus node function and performs surveillance for occult arrhythmias. Holter monitoring should probably be performed at least once per decade, although the frequency for these studies may increase, as clinically indicated. Exercise stress testing also demonstrates sinus node function, although under periods of maximal physical stress. It can also induce exercise-associated arrhythmias and unmask abnormal responses of systemic arterial pressure and residual gradients across the aortic arch. Exercise stress testing should likely be performed at least once per decade, although the first study would need to be performed at a time when the patient is physically able to cooperate, and is mentally willing to do so as well. Exercise stress testing may be more likely to be successful after the age of 6 to 7 years. Several tests of the blood should probably be reviewed annually starting at the age of 10 years:

- complete blood count,
- studies of coagulation,
- studies of renal function,
- enzymes associated with hepatic function, and
- total protein and albumin.

Neurodevelopmental evaluation

As the medical literature regarding long-term neurodevelopmental complications seen in patients with complex congenital cardiac disease grows, the Children's Hospital of Philadelphia has initiated a

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Neuro-Cardiac Care Program. This multi-disciplinary programme combines surveillance, evaluation, baseline collection of data, preventive care, and parent education into a consultant clinic. Patients are typically referred for evaluation at the age of 4 months, and are assessed by specialists in Physical Therapy, Occupational Therapy, Speech Therapy, Social Work, Neurology, Developmental Paediatrics, and Nutrition, as well as receiving an auditory brainstem response. Owing to the fact that initial evaluations are completed and these patients are discussed among the various providers, plans for further testing, imaging studies, or referral for early interventional services are made in a pre-emptive manner, so as not to wait for the child to be diagnosed with various delays or difficulties at school until it is much later in the clinical course. Follow-up evaluations occur at age 8, 12, 18, 24, 36, and 48 months, with the continuation of subsequent studies pending initial outcomes.

Counselling

Standard counselling is required for these patients as well. This counselling includes assuring prophylaxis of infective endocarditis, which is a lifelong necessity in the face of persistently exposed prosthetic materials and persistent right-to-left shunting. These patients should routinely avoid prolonged exposure to altitudes greater than 7500 feet (2286 metres) above sea level, because of the risk of increasing pulmonary vascular resistance. They should have filters placed on all intravenous catheters, at minimum until all potential right-to-left shunting is resolved. Appropriate routine vaccination and special immunisations, such as influenza vaccine and anti-respiratory syncytial virus monoclonal antibody, can be life-saving. Finally, discussion of transition to a physician who specializes in caring for adults with congenital cardiac disease should be performed early and continued through to the time of transfer of the patient. This discussion includes ensuring that first the parent, and, eventually the patient, understand the disorders of anatomy that the patient has, and that the surgical intervention on the heart only improved, but did not fully repair, its physiology. This situation means that the child who becomes an adult with congenital cardiac disease will need lifelong and specialised care.

Summary

Are there much data to support these recommendations? Unfortunately, there are only limited data to demonstrate whether we are performing our evaluations appropriately. We may be over-testing or under-testing, depending on the circumstances.

We are at a new juncture in congenital cardiology. Previously, surgeons and cardiologists intervened upon patients, or groups of patients, with lots of creativity but little institutional oversight. Reporting of results came through case reports, case series, or single institutional retrospective reviews. However, in the environment of practice today, the ability to collaborate across institutions has grown, as has external regulation. We are now at the point in medicine where evaluation of our methods can, and should, be done. The borrowing of strategies of improvement of quality from business has spread to medical research. The concept of benchmarking of practices at baseline, intervening upon them, assessment of the results of that intervention, then implementation of the improved-upon practices, followed by repeating that cycle, can lead to overall progress usually realised by groups such as the Children's Oncology Group.[5] The Children's Hospital at Boston, Massachusetts, has developed their "Standardized Clinical Assessment and Management Plan", which creates a framework for internal institutional improvement.[6] The Joint Council on Congenital Heart Disease Quality Improvement Collaborative established a similar structure for patients specifically with hypoplastic left heart syndrome.[4] The Paediatric Heart Network[7], sponsored by the National Heart, Lung, and Blood Institute, a part of the National Institutes of Health of the United States of America, collects normative cross-sectional data for patients with the physiology of the functionally univentricular heart, which can be subsequently acted upon.

In the future, as numerous medical centres and hospitals transition to electronic health records, new opportunities arise to collect data and improve the care of these patients. Wider acceptance and utilisation of the International Paediatric and Congenital Cardiac Code,[8] as well as eventual standards for data created by the American College of Cardiology and American Heart Association for the electronic health record for paediatric and congenital cardiology, will better standardise the ability to use the electronic health record for gathering of information. The next wave of collection of information will be framed by concepts of governance of data. Commitment to this model includes development of stringent criteria for the collection of data, ensuring validity of the data, and guaranteeing auditing and oversight of that data on a routine basis. Finally, the last area for growth in this paradigm, which has already started, involves the more extensive collaboration in the collection of data, such that retrospective studies of limited numbers of patients at single centres will morph into large, multi-centric prospective studies of large numbers of patients, powered to quickly change and improve the methods of caring for all of our patients, including those with hypoplastic left heart syndrome.

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