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Review

Challenges, opportunities and solutions in hypoplastic left heart syndrome: Surveillance strategies for the patient with HLHS and a Fontan circulation☆

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ABSTRACT

Children with single ventricle heart disease undergo a series of palliative surgeries that culminates in the Fontan operation. Directing systemic venous blood into the pulmonary arteries in the absence of a sub-pulmonary ventricle results in a significant increase in central venous pressure. Related to this aspect of Fontan physiology, a myriad of disease-specific comorbidities have been identified. As the type and severity of end-organ damage has been catalogued, multidisciplinary clinics and surveillance testing algorithms have been developed. To better understand current challenges and opportunities to surveillance testing after Fontan operation, individuals and programs providing care for patients with Fontan physiology were surveyed. From this data, quality metrics and hypotheses can be generated, so that the next iteration of learning networks and research protocols can be informed by both historical practice and nascent outcomes data.

1. Introduction

Children with single ventricle heart disease may undergo palliative procedures during infancy to achieve a viable circulation, with a goal of establishing unobstructed blood flow to the systemic arterial bed and pressure-limited flow to the pulmonary vasculature. Regardless of their anatomy and initial management, the current goal is for all children with single ventricle heart disease to ultimately undergo a Fontan operation [1]. After the Fontan procedure, or total cavopulmonary anastomosis, caval flow is directed into the pulmonary arteries, without the benefit of a sub-pulmonary ventricle [2]. The benefits of this approach are near-normal saturations, separation of the systemic and pulmonary circulations and improvement in functional capacity. With iterative successes in management strategy, there are now a significant number of patients surviving their palliative surgeries and moving toward young adulthood.

With the improved survival and increased attention toward surveillance of children and adolescents with Fontan physiology came the realization that there are profound and unintended consequences of this surgical strategy.

2. Late consequences of Fontan physiology on end-organ function

To illustrate the need for a comprehensive, multidisciplinary approach to the care of patients with Fontan physiology, a brief summary of the most important and pervasive comorbidities will be discussed. Most importantly, Fontan physiology results in a significantly elevated central venous pressure, mimicking the clinical syndrome of right-sided heart failure [3]. The consequences of this physiologic derangement are pervasive and insidious end-organ damage, for which there are few, if any, well validated surveillance tools.

From a cardiac standpoint, the consequences of staged surgical palliation include a significant volume load in the newborn period, following a systemic-to-pulmonary-arterial shunt; this results in a dilated and hypertrophied ventricle. The superior cavopulmonary anastomosis (SCPA or Glenn shunt) and total cavopulmonary anastomosis (Fontan operation) volume unload the ventricle but create a mismatch between the decreased preload and the poorly compliant ventricle. There is also evidence of increased cardiac fibrosis after single ventricle palliation [4,5]. In this setting, there is evidence of both decreased global ventricular function [6] and mechanical dyssynchrony [7]. Heart rhythm problems are common after Fontan, both tachyarrhythmias as well as sinus node dysfunction [8,9].

The liver is subject to the elevated central venous pressures after Fontan, creating significant hepatic congestion, but also suffers from relatively poor perfusion in the setting of decreased cardiac output and alterations in mesenteric arterial flow properties [10,11]. This results in a gradual but progressive hepatic fibrosis, which is universally present, but with considerable variability in severity between individuals [12]. In more rare cases, advanced cirrhosis and hepatocellular carcinoma have been diagnosed [13].

There are significant risks for abnormal neurodevelopment during the course of single ventricle palliation, and beyond [14,15]. Common developmental abnormalities after Fontan operation in pre-school aged

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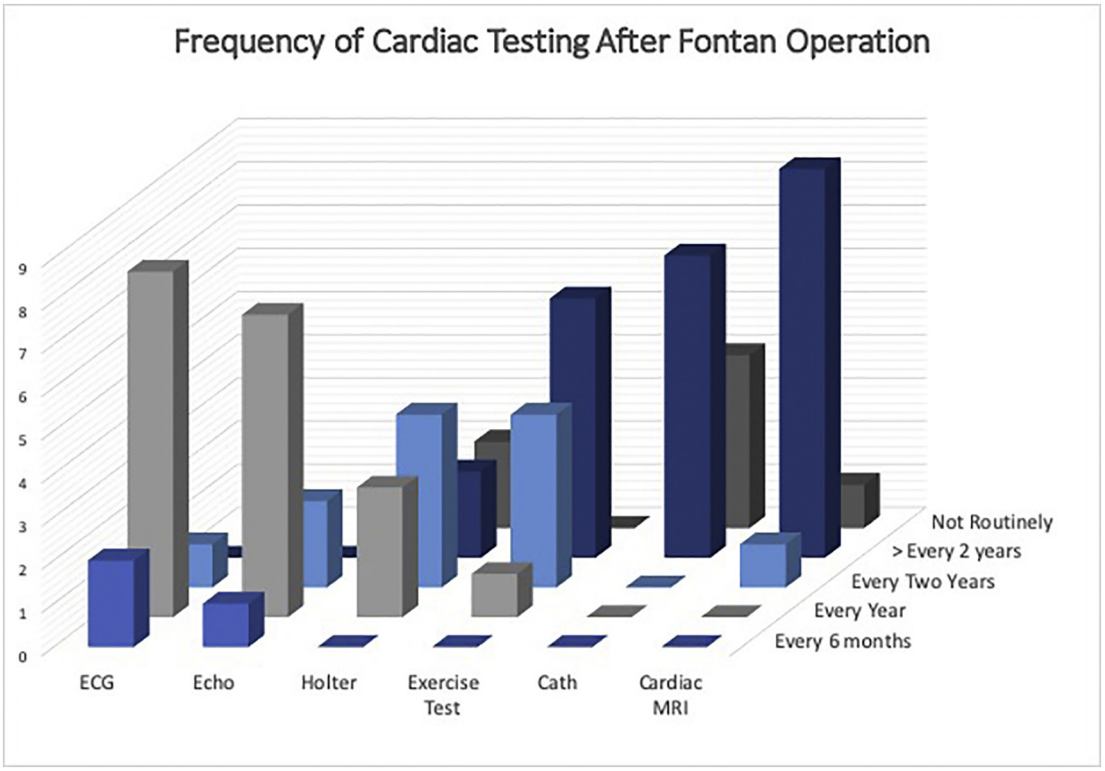

Fig. 1. Frequency of cardiac surveillance testing after Fontan operation.
Legend: As shown, there was considerable variability in the type and frequency of surveillance testing for cardiac pathology after Fontan operation.

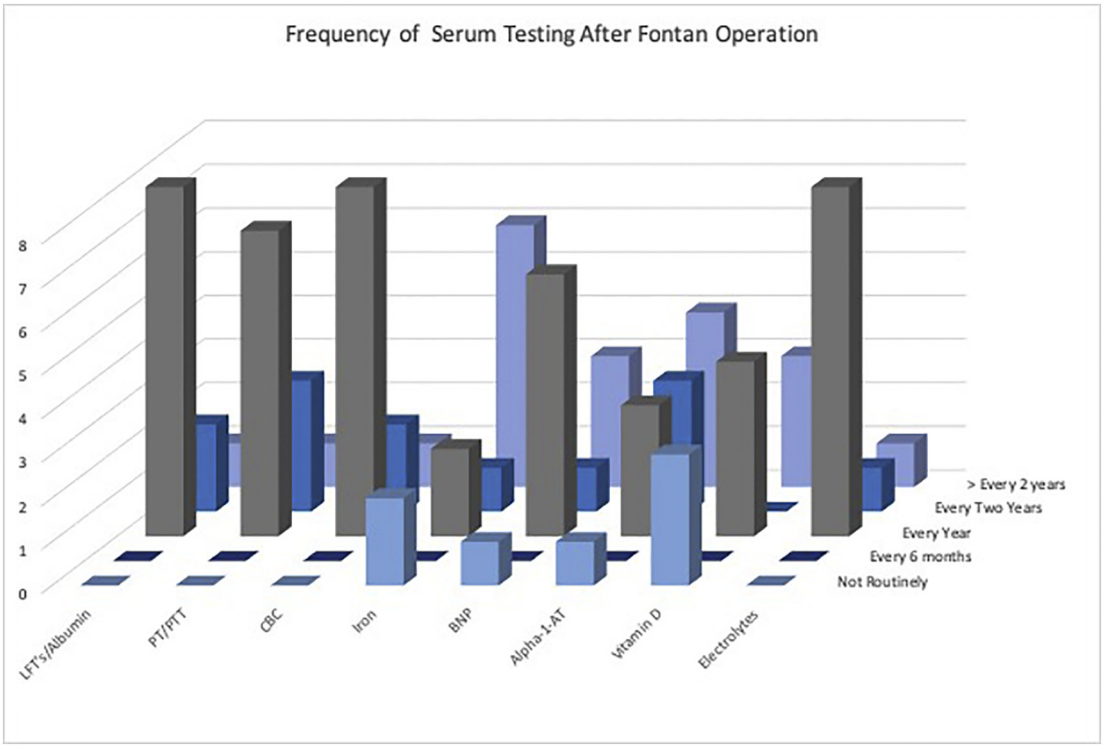

Fig. 2. Frequency of serum testing after Fontan operation.
Legend: Commensurate with the practice variability noted in cardiac testing, there were a broad range of approaches to how and when to check serum studies after Fontan operation.

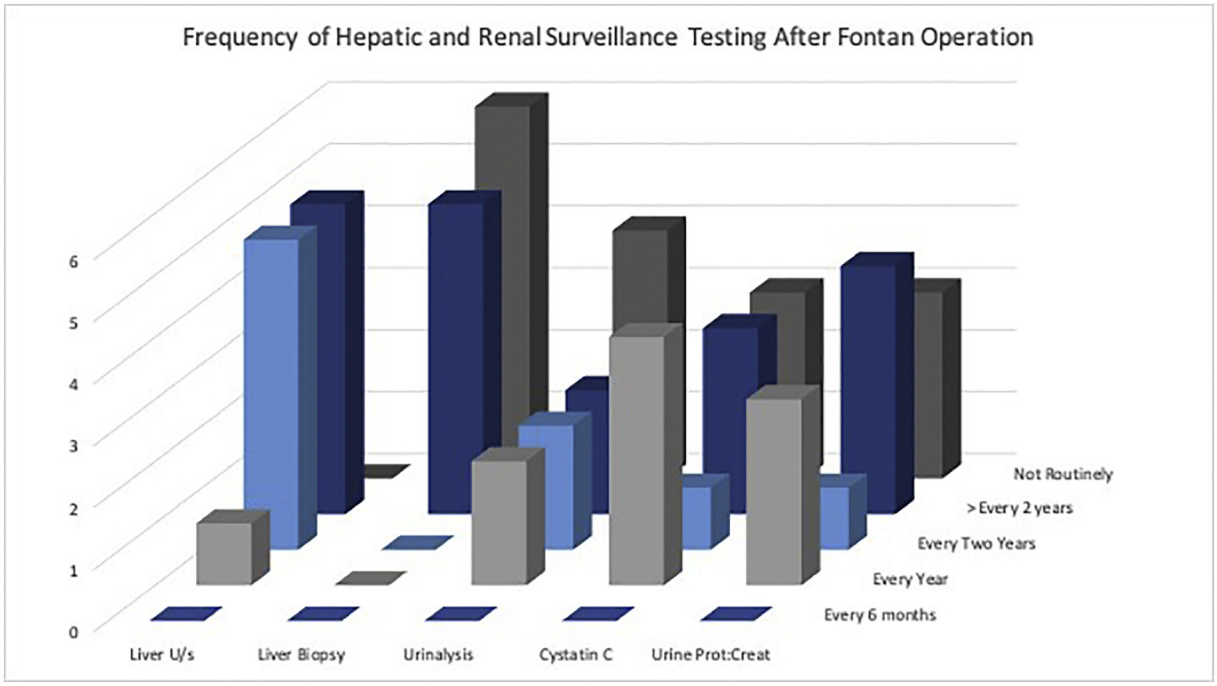

Fig. 3. Frequency of hepatic and renal surveillance testing after Fontan operation.
Legend: Testing for non-cardiac end-organ damage was similarly very different between institutions surveyed, with considerable variation in testing frequency.

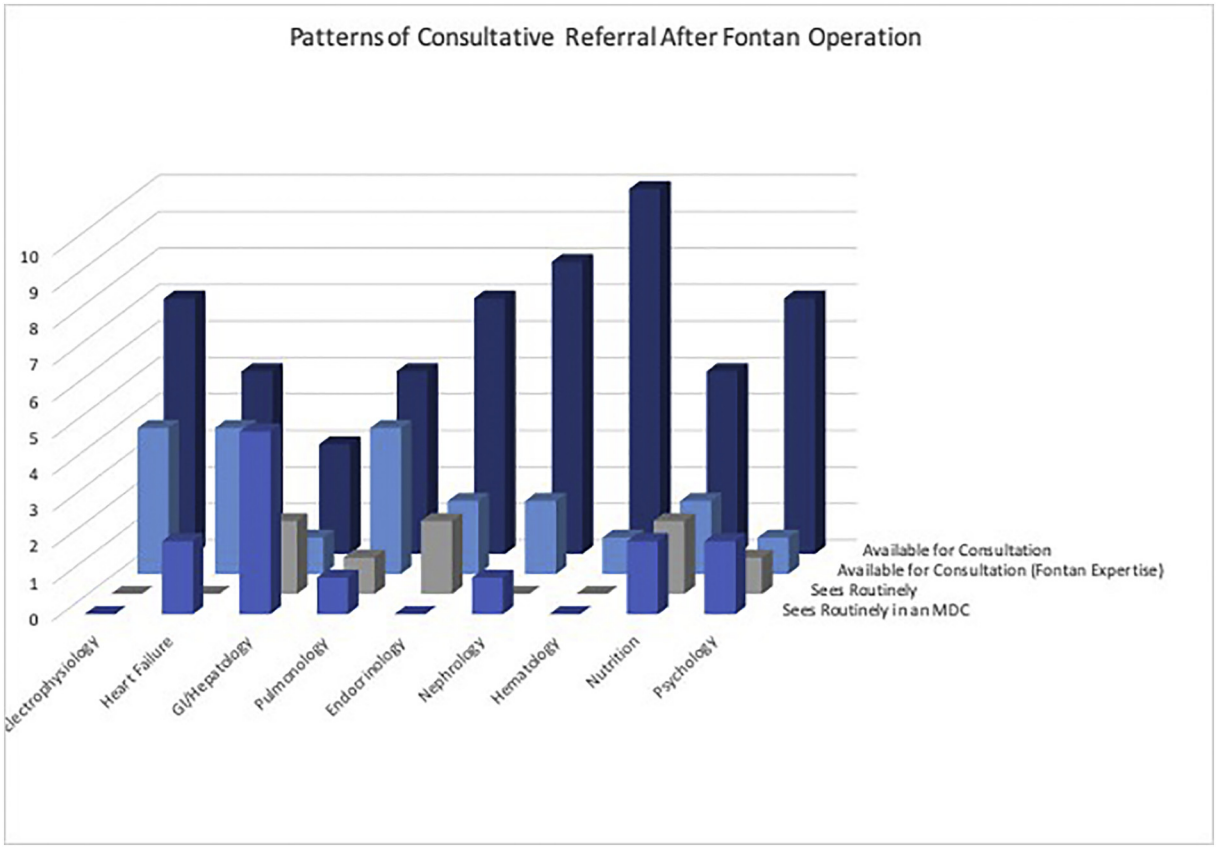

Fig. 4. Pattern of consultative referral after Fontan operation.
Legend: Centers surveyed nearly all reported having sub-specialty consultants available on an as needed basis, but incorporation of these subspecialists into a Fontan clinic was more rare.

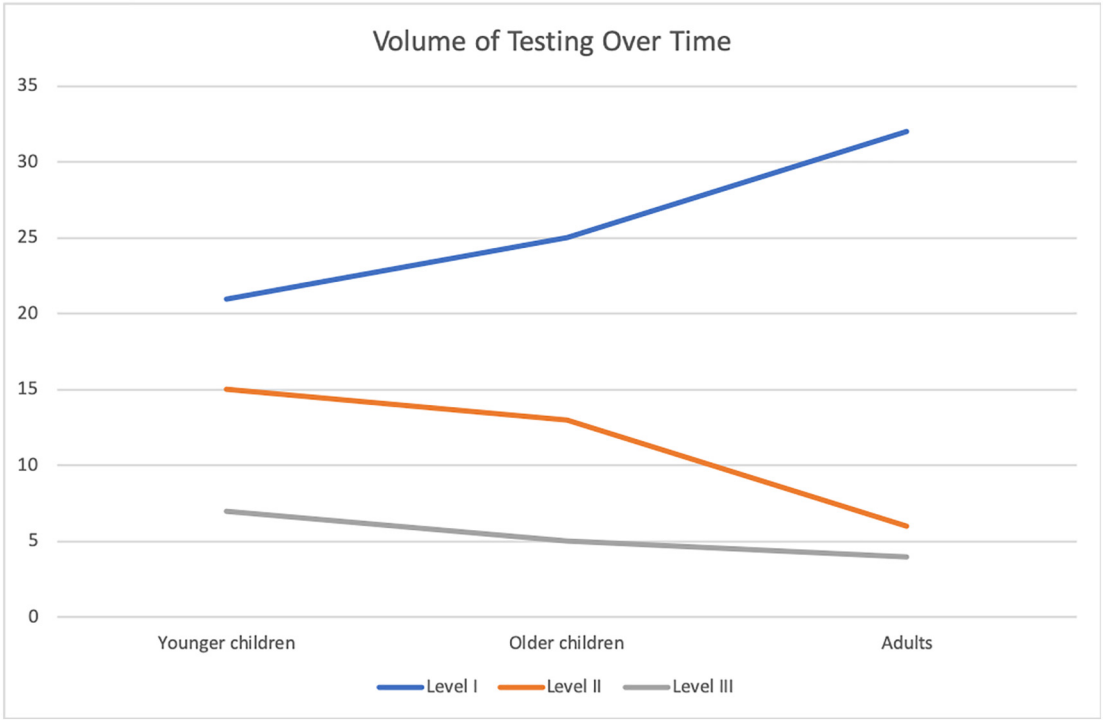

Fig. 5. Volume of recommended testing over time by age after Fontan operation.
Legend: Broadly speaking there was an increasing trend toward more aggressive surveillance testing with increasing patient age. Respondents were more likely to recommend a higher number of tests for older patients with Fontan physiology.

children include abnormalities in processing speed, inattention, and impulsivity [16]. Abnormalities in somatic growth and pubertal delay are also common [17].

Many other organ systems are affected by similar processes. Both restrictive and obstructive lung disease have been demonstrated in a group of children undergoing screening for pulmonary processes [18]. There are also abnormalities in bone density [19] and calcium & vitamin D metabolism. Patients with Fontan physiology are at risk for chronic kidney disease, both related to serial episodes of acute kidney injury as well as chronic nephrotoxin exposure [20,21]. The incidence of patient and family anxiety, depression and post-traumatic stress is increased [22,23].

3. Review of current practices

To better understand the current approach to the care of children and adolescents with Fontan physiology, a survey of programs with dedicated, multi-specialty clinics for the care of patients with Fontan physiology was conducted in 2016 [24]. The majority of these programs are located in academic, university-affiliated children's hospitals. Among the 11 respondents, there was considerable variability in the total number of cardiac surgeries performed per year, as well as Fontan operations in particular. The majority of programs cared for a population of between 150 and 300 patients with Fontan physiology, with a range varying between < 50 patients in total to > 300. Of note, a majority of programs operated as “second opinion” clinics, with the primary cardiologist directing management and seeing the patients annually in most cases. The multidisciplinary teams include physicians, but all programs also included nurses and at least one advanced practice provider.

The survey also included questions about routine surveillance testing after Fontan operation. In short, there was significant practice variability in all domains. From a cardiac standpoint, programs were asked about the frequency of routine electrocardiogram, chest x-ray, echocardiogram, Holter monitor, cardiopulmonary exercise test, cardiac catheterization, and cardiac MRI testing. Responses ranged significantly from very intermittent to common use for most tests (Fig. 1). Similarly, respondents were asked about routinely ordered bloodwork, as well as hepatic and renal testing (Figs. 2 & 3, respectively).

Patterns of consultative referral were also investigated, with a focus on the availability of local expertise in several important areas. More specifically, respondents were asked to rate the availability of subspecialty clinics such as pulmonary medicine and endocrinology as not available, available for consultation (with or without special expertise in Fontan physiology), routine incorporation in the care plans or incorporation into a Fontan-specific multidisciplinary clinic (Fig. 4). Consistent with other areas in the survey, responses varied widely. In addition, around half of the surveyed programs routinely involved a neuropsychologist or other developmental specialist.

Respondents were also asked about the routine use of medications in this setting, including digoxin, angiotensin converting enzyme inhibitors (ACEi), beta blockers, and phosphodiesterase-5 inhibitors (PDE5i). A large majority of participants recommended routine use of either on as-needed bases, or there was no discernable practice pattern. A majority of participating centers recommended aspirin as empiric thromboprophylaxis, and reserved anticoagulation for more high-risk cases.

4. State of the art – level of evidence recommendations

In a follow-up study, a group of physicians involved in a number of Fontan centered initiatives and publications that self-identified as having a specific interest in this population were asked to evaluate current evidence for many of the available tests that could be included in a routine surveillance program. In the absence of any evidence, they were asked to provide an expert opinion as to what class the test in question should be placed in with the following options provided:

- Class I = Highly or very likely of clinical value. I would like for this

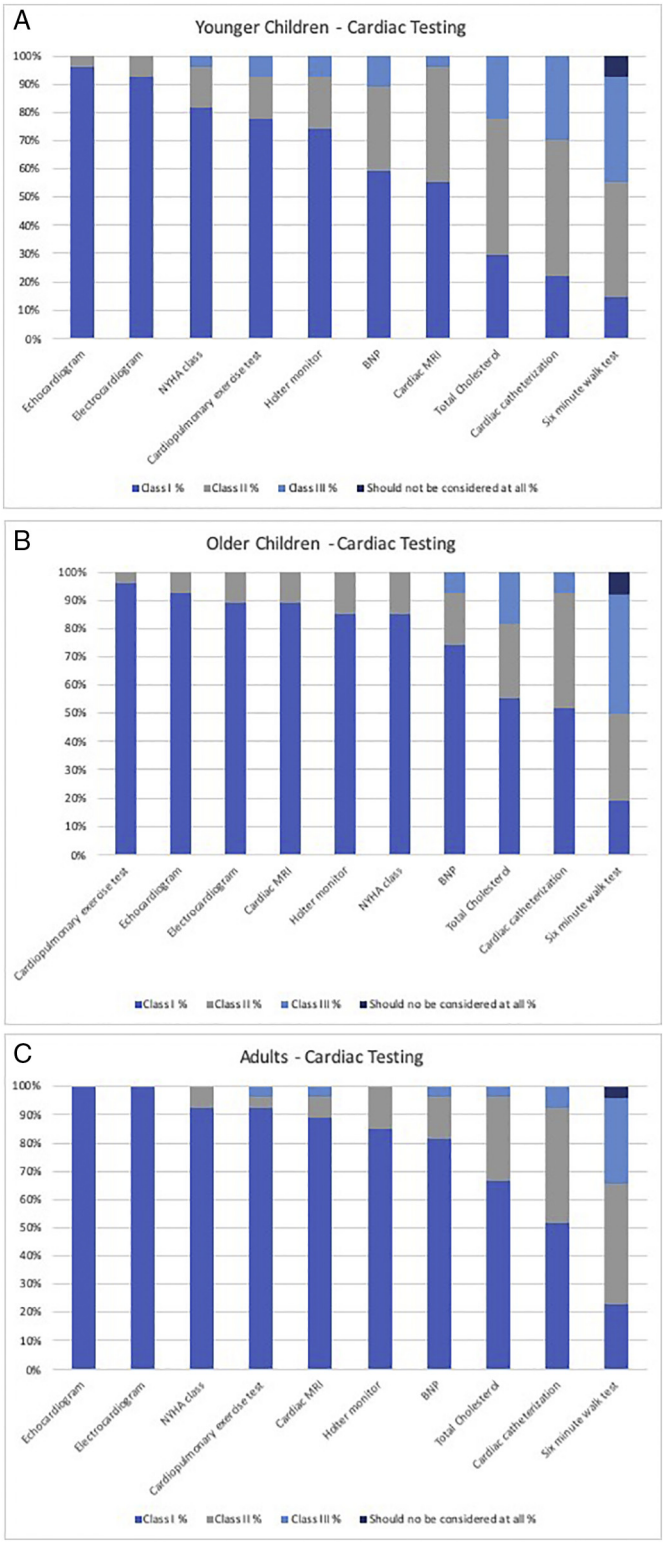

Fig. 6A-C. Level of evidence recommendations for cardiac testing in younger children, older children and adults.
Legend: The trend toward more liberal testing is notable in this panel of figures, where the dark blue bars represent recommendations for more frequent testing, shown to be increasing progressively from younger children (A), to older children (B) and adults (C).

test to be assessed in all patients with a Fontan circulation and I would favor this to become part of accepted standard clinical practice.

- Class II = Likely of clinical value. I believe this test to be justified for patients with a Fontan circulation. I believe this test is a reasonable approach and has merit, however, it may not need to be performed in all patients.
- Class III = Possibly of clinical value. Although it may be of clinical value in select cases, this test may benefit from further investigation in its utility.
- The test should not be considered at all.

The respondents were asked to render an opinion for three age groups of patients with Fontan physiology, younger children (< 12 years), older children (12–18 years) and adults (> 18 years).

In the younger children, there was a trend toward less frequent testing, with a larger proportion of tests being classified as Level 3 (primarily investigational). In the older children, there was a small increase in the number of tests classified as Level 1, and hence routinely recommended (Fig. 5). In adulthood, the respondents classified significantly more tests as Level 1, indicating some consensus around the idea that more rigorous surveillance is needed in the second and third decade of live. More specifically, the trend toward more aggressive testing can be appreciated by comparing survey results of cardiac testing between younger children (Fig. 6A), older children (6B) and adults (6C). Similar patterns were present in screening recommendations for non-cardiac end-organ damage.

5. The multidisciplinary approach

As these multidisciplinary programs emerge and evolve, clear advantages to this approach have also become apparent. First, consultants with local expertise in the care of children with Fontan physiology have distinct advantages over a rotating group of organ-specific experts that might be called on to help troubleshoot comorbidities such as plastic bronchitis, for example. With incidence rates of 4–16% [25], a pediatric pulmonologist may seldomly encounter a patient with Fontan-associated plastic bronchitis, even in a larger center, if the consultative work is divided between a large pool of providers. Familiarity with contemporary diagnostic and therapeutic approaches would be difficult to maintain, unless the clinical experience was concentrated into one provider's clinic.

In addition to consistent referral patterns, integration into a multidisciplinary clinic provides the opportunity for frequent and robust interaction between multispecialty teams. This affords the group an opportunity to build common experience, develop practice patterns that ideally evolve into care guidelines, develop quality improvement metrics and research hypotheses. Our group recently published our experience with designing and creating a multidisciplinary clinic for children with Fontan physiology, including the results of our screening protocol and treatments that were instituted [26].

On a larger scale, these Fontan-specific clinics have begun the process of forming a learning network, where data can be aggregated and analyzed to define new quality metrics, design new care paradigms based on a larger, combined experience, and drive improvement in outcomes.

6. Conclusion

With the improved survival of patients with single ventricle heart disease comes an understanding that multiple organ systems are adversely affected in ways that we are just beginning to describe. The care of patients with Fontan physiology must now account for the myriad non-cardiac comorbidities that continue to reveal themselves. With this added complexity and the challenge of delivering multidisciplinary care, a great opportunity can be found. Through organization and both intra- and extra-mural collaboration, the opportunity to make substantive improvements in the quality of care for this population must be seized.

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