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REVIEW ARTICLE

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Frontiers in Fontan failure: Innovation and improving outcomes: A conference summary

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Abstract

The initial "Frontiers in Fontan Failure" conference in 2015 in Atlanta, Georgia, provided an opportunity for experts in the field of pediatric cardiology and adult congenital heart disease to focus on the etiology, physiology, and potential interventions for patients with "Failing Fontan" physiology. Four types of "Fontan Failure" were described and then published by Dr Book et al. The acknowledgment that even Dr Fontan himself realized that the Fontan procedure "imposed a gradually declining functional capacity and premature late death after an initial period of often excellent palliation." The purpose of the second "Frontiers in Fontan Failure" was to further the discussion regarding new data and technologies as well as novel interventions. The 2017 "Frontiers in Fontan Failure: Innovation and Improving Outcomes" was sponsored by Children's Healthcare of Atlanta, Sibley Heart Center Cardiology, and Emory University School of Medicine. Future directions in the management of Fontan failure include further investigations into the risk of sudden cardiac death and how to properly prevent it, achievable interventions in modifying the Fontan physiology to treat or prevent late complications, and improved and refined algorithms in Fontan surveillance. Finally, further research into the interventional treatment of lymphatic-related complications hold the promise of marked improvement in the quality of life of advanced Fontan failure patients and as such should be encouraged and contributed to.

KEYWORDS

failure, Fontan, innovation, outcomes

1 | INTRODUCTION (FRED RODRIGUEZ III, MD)

The initial "Frontiers in Fontan Failure" conference in 2015 in Atlanta, GA, provided an opportunity for experts in the field of pediatric cardiology and adult congenital heart disease (CHD) to focus on the etiology, physiology, and potential interventions for patients with "Failing Fontan" physiology. Four types of "Fontan Failure" were described and then published by Dr Book et al.[1] The acknowledgment that even Dr Fontan himself realized that the Fontan procedure "imposed a gradually declining functional capacity and premature late death after an initial period of often excellent palliation."[2] The purpose of the second "Frontiers in Fontan Failure" was to further the discussion regarding new data and technologies as well as novel interventions. The 2017 "Frontiers in Fontan Failure: Innovation and Improving Outcomes" was sponsored by Children's Healthcare of Atlanta, Sibley Heart Center Cardiology, and Emory University School of Medicine.

2 | SUMMARY OF FRONTIERS IN FONTAN FAILURE: 2015 (CAMDEN HEBSON, MD)

The Frontiers in Fontan Failure meeting of 2015 was recapped.[3] Dr Brian Kogon spoke on Fontan design and its evolution over time. Similar clinical outcomes are present, although arrhythmia burden is greater in the atriopulmonary Fontan. Dr Robert Elder discussed the long-term outcomes of Fontan palliation, with emphasis on the importance of Fontan-associated liver disease. The VAST (Varices, Ascites, Splenomegaly, Thrombocytopenia) score is a key predictor of Fontan outcomes. Dr Maan Jokhadar described Fontan pathophysiology as multi-organ system with unique consequences. Abnormal pulmonary arterial histology and diastolic dysfunction of the systemic ventricle were emphasized. Dr Anne Marie Valente discussed the medical management of Fontan patients. The lack of evidence behind the use of diuretics, ACE inhibitors, pulmonary vasodilators, and beta-blockers in the Fontan population was outlined. The use of antiplatelet and/or anticoagulation therapies and importance of nonpharmacologic therapies, namely compression stockings and resistance training, was highlighted. Dr Michael Lloyd outlined the benefits of a lower heart rate in Fontan physiology, given the known impairments in systemic ventricular preload reserve without a subpulmonary ventricle. The often limited benefits of pacing, as well as the remaining indications for pacing in these patients, were detailed. Drs Veldtman, Romero, and Ford discussed Fontan-related liver disease—screening strategies, reliance on the VAST score for prognostication, and various treatments. Dr Preeti Reshamwala discussed liver transplantation, with emphasis on the combined heart/liver transplantation and the appropriateness of single organ transplant. Drs Kanter and Kogon presented current surgical strategies in Fontan patients, including efforts at minimizing energy loss in the Fontan circuit using the "Y-graft" technique with prior MRI modeling. Alternative surgical approaches emphasized the prospects of reverting the failing Fontan to balanced physiology, Glenn, or Kawashima shunt physiology. Dr Anne Marie Valente discussed the challenges of transition to adult congenital care and strategies to address this. Dr Rebecca Levit presented the future prospects of stem cell therapy in single ventricle patients and Dr Adrienne Kovacs discussed the importance of quality of life and patient-centered goals, as well as addressing end of life care properly. Finally, Dr Kevin Maher discussed future directions and the prospects for the use of nanotechnology in single ventricle patients.

3 | ACTIVE RESEARCH IN FONTAN FAILURE (ANITHA JOHN, MD, PHD)

The population of adult patients with CHD is increasing, with a rising prevalence of patients with complex CHD.[4] It is estimated that there are 20 000 patients with single ventricle CHD in the United States, accounting for around 1.5% of the adult congenital heart disease (ACHD) population. Their rate of hospitalization has increased, and not surprisingly, their associated comorbidities have led to increased length of stay and in-hospital mortality.[5] Despite this shift in demographics, the majority of research in single ventricle CHD has focused on improving neonatal and childhood survival rates. There are limited studies, unfortunately, focusing on survival, long-term outcomes, risk stratification, comorbidities, and optimal treatment strategies in adults with single ventricle CHD. This is a challenging aspect for medical providers, patients, and their families as there is very little data guiding medical decision making and long-term prognosis. This clearly highlights the need for further research in the field to improve long-term outcomes.

Several factors contribute this paucity of data:

- Heterogeneity of CHD:
  - Single ventricle CHD represents a number of heterogeneous anatomical substrates, with relatively small patient numbers at each medical center. Within each anatomical subtype, there are questions related to prognosis and best treatment practices and existing national inpatient datasets do not provide the information needed for these types of studies.
- Lack of longitudinal registries for CHD:
  - Currently, population estimates in the Unites States are based on survival rates for children with CHD and birth rates, with some extrapolation of survival rates of ACHD patients from other countries.[4,6,7] There are some natural history studies on unrepaired lesions; however, few have been performed with current medical and interventional therapies. The lack of data on prognosis is often a struggle for patients as they are contemplating life decisions such as marriage, career, and children and are unable to factor lifespan or long-term quality of life in their decision making.
- Variable treatment strategies in CHD over time:
  - The Fontan operation was first described by Fontan and Baudet in 1971.[8] Since then, advances have been made in

surgical techniques and Fontan "subtypes" and catheter-based therapies. Given that treatment strategies have changed, outcomes and survival depend on the era when the patient was born.

- High rates of loss of follow-up:
  - In a study of over 900 ACHD patients, 42% reported a >3-year gap in care with the mean age at loss to follow-up being 19.9 years.[9] This loss of follow-up also presents a challenge to understanding the long-term outcomes and natural history of CHD as the patients in research cohorts represent only a subset of the true patient population. Improved transition practices in childhood and adolescence are needed to address this issue and educate patients about the need for continuing subspecialty care.

In addition, variability in practice patterns and paucity of funding are additional barriers to conducting multicenter research in the single ventricle CHD population. Multicenter research networks attempt to overcome some of these challenges by bringing together a diverse panel of investigators to design comprehensive research questions.

Recognizing the rapidly growing ACHD population and the lack of quality outcomes data, the National Heart, Lung, and Blood Institute (NHLBI) convened an ACHD working group in 2004. A three-part research strategy was outlined and included goals of: Development of a multicenter research network; working toward a national ACHD patient registry; and better definition of high-impact research areas.[10] In response to these goals, the Alliance for Adult Research in Congenital Cardiology (AARCC, Inc.) was formed in 2006 and is currently comprised of over 40 physician scientists from 30 institutions. To better define high-impact research ideas, the NHLBI and the Adult Congenital Heart Association (ACHA), the leading ACHD patient advocacy organization, convened a multidisciplinary working group in 2014 to develop a list of high-impact research questions which was recently published.[11] This follows a report from AARCC, Inc. in 2013, where a list of the top 10 research priority questions were generated by patient input through the ACHA and ACHD providers worldwide.[12] The high-priority research topics included heart failure and transplantation, sudden cardiac death in CHD, vascular disease, pregnancy outcomes, neurocognitive deficits in ACHD, and long-term outcomes and multisystem complications in single ventricle disease.

AARCC has created a framework for multicenter collaborative research, and the group has conducted numerous multicenter research studies. Based on previously determined high-impact areas of research in ACHD, the group created focus subgroups with separate subgroup for single ventricle/Fontan patients. Specific priority areas for Fontan-related research were: optimal medical therapy, multi-organ system involvement, arrhythmia control and management, pregnancy outcomes, and surgical strategies/advanced mechanical support/transplant among others. The group has a number of projects related to Fontan physiology as noted below:

1. Fontan Associated Liver Disease (FALD). A multicenter cross-sectional study was performed examining laboratory assessment, radiological assessment, and liver biopsy in adult patients with Fontan physiology. Data from a total of 241 patients from six centers was collected. All patients with liver biopsies and radiological imaging had abnormal findings.[13] In addition, abnormal biomarkers of hepatic fibrosis and specimen-proven hepatic fibrosis are common in adults with Fontan circulation. However, FibroSure and HA do not accurately predict the degree of histologic hepatic fibrosis.[14] Currently, the group is working with other pediatric centers to develop a histological scoring system for hepatic disease in Fontan patients.
2. FOSTER (Fontan Outcomes Study to Improve Transplant Experience and Results) study. Better understanding of transplantation outcomes in addition to determining optimal listing criteria is needed in this patient population. An ongoing study involving 13 centers is in progress to determine risk factors and mortality rate in Fontan patients who have undergone cardiac transplantation, are currently undergoing listed for transplantation, and those who have been declined for cardiac transplantation listing. The goal will be to determine clinical outcomes in these patients and to determine if listing criteria are appropriate for this unique population.
3. Arrhythmia outcomes and anticoagulation management. There is a high atrial arrhythmia prevalence in CHD patients and thrombosis risks are often difficult to delineate based on standard risk stratification scores. The TACTIC (The Anticoagulation Therapy in Congenital Heart Disease) study included 482 CHD patients from 12 centers across North America.[15] The goal was to quantify the incidence of thromboembolic events in patients with CHD and atrial arrhythmias, assess the rate of bleeding complications associated with antiplatelet and anticoagulation therapy, and identify factors associated with thromboembolic and hemorrhagic events. Not surprisingly, atrial arrhythmias in CHD were associated with a modest rate of thromboembolic events, which was predicted by disease complexity but not $CHADS_2$/CHA_2DS_2-VASc scores. An ongoing study is currently in progress that will examine outcomes after first arrhythmia occurrence specifically in Fontan patients.
4. Skeletal muscle and inspiratory muscle training in the Fontan population. Through a collaborative effort between AARCC and the ACHA, a proposal for a web-based platform for a skeletal muscle and inspiratory muscle training program was developed and recently presented for consideration to the Pediatric Heart Network (PHN). The protocol is in ongoing development but is an example of how multicenter research groups can harness the experience and expertise of multiple investigators and centers. In addition, the ACHA played a key role in study design through housing the web-based platform and study advertising.

Participation in AARCC, Inc. has also led to multiple successful collaborations including with the ACHA. Patient participation and involvement in research design and execution is essential for successful multicenter prospective studies. ACHA has partnered closely with AARCC and there have been several successful grant funded projects.

Additional cross-collaborations include AARCC participation in the Patient Centered Outcomes Research (PCOR-net) ACHD research interest group, the American College of Cardiology, and the Congenital Heart Public Health Consortium. Multicenter networks such as AARCC also serve as a platform for grant preparation and generation both through the ability to generate large numbers of patients in addition to providing subspecialty expertise, key stakeholder input, and patient feedback. Working together as part of a multicenter network addresses many of the challenges in conducting research in CHD and is vital to advancing new discoveries for the single ventricle/Fontan patient population.

4 | SSI AND SINGLE VENTRICLE PATIENTS (ESTELLA MOORE, LCSW)

Failing Fontan patients suffer from various obstacles, including lack of income, insurance benefits, and quality of life. Therefore, it is only a matter of time before they require Social Security disability benefits. However, securing these benefits is an ordeal, even via expedited processing programs. Physicians are advised to encourage patients to prepare for the inevitable by securing insurance, opt for careers with large employers for group insurance coverage. This route will allow the patient to enroll in private short- and long-term disability plans, providing them a bit of a safety net while waiting on Social Security disability benefits. Resources such as the ACHA website will give patients a firm grasp on the process at hand pertaining to disability. From a physician's perspective, it is important to document the onset of decline and detailed description of the patient's functional capacity over time.

5 | ANTICOAGULATION AND THE FONTAN PATIENT (MAAN JOKHADAR, MD)

Fontan patients are at higher risk of thromboembolic events and this risk is increased in the presence of atrial arrhythmia and/or atriopulmonary Fontan.[16] Primary prevention in these patients is a controversial topic. Based mostly on expert opinion, current practice guidelines from the American College of Cardiology (ACC) and American Heart Association (AHA) recommend warfarin with a goal INR of 2–3 in most Fontan patients with an atrial shunt, atrial thrombus, atrial arrhythmias, or a thromboembolic event.[7] The Heart Rhythm Society (HRS) expert consensus statement recommends anticoagulation in Fontan patients with atrial arrhythmias. Warfarin is the preferred agent and the HRS recommends against using direct oral anticoagulants (DOACs) due to a paucity of safety data.[17] Data comparing warfarin and aspirin in Fontan patients are limited with one multicenter, randomized clinical trial comparing warfarin and aspirin for primary thromboprophylaxis in children that showed similar outcomes. However, only 45% of INR readings were within therapeutic range.[18] Anticoagulation with warfarin can be performed safely, while achieving a high time within therapeutic range (TTR), using a pharmacist-managed anticoagulation clinic and this has been shown to reduce thromboembolic and bleeding complications, albeit in retrospective analysis and in adherent patients.[19]

As previously mentioned, safety and efficacy data are limited to case reports for the use of DOACs in Fontan patients.[20-22] It should be mentioned that the coagulation cascade is deranged in Fontan patients, which may help explain increased risk of both thromboembolic events and bleeding.[23,24]

Thromboembolic prophylaxis strategy must to be individualized to each patient with many factors to be considered that include age, arrhythmia, Fontan type (atriopulmonary vs total cavopulmonary connection), cyanosis, protein-losing enteropathy, thromboembolic events, bleeding history, thrombocytopenia, cirrhosis, varices, hemoptysis, and patient adherence.

To summarize, aspirin is the mainstay of therapy for many patients and there should be a low threshold to start warfarin anticoagulation under the supervision of a pharmacist-managed anticoagulation clinic to help achieve a high TTR. Clinical trials are needed to determine safety and efficacy of DOACs in Fontan patients. There is probably no role for clopidogrel and other antiplatelet agents based on current data. Poorly controlled warfarin is not safe, particularly in these patients due deranged coagulation.

6 | EXERCISE TESTING AND SINGLE VENTRICLE PATIENTS (CAMDEN HEBSON, MD)

The importance of exercise has been extensively demonstrated in the general adult population. It reduces all-cause and cardiac mortality.[25] A majority of Fontan patients do not achieve recommended physical activity levels. Heart-focused anxiety and physician/parent restrictions contribute to this.[26,27] Reports of exercise training, mostly aerobic, in patients with Fontan circulation show no significant adverse events during exercise.[28] Known benefits of exercise in these patients include improved exercise capacity, physical activity level, quality of life, and muscle strength.[29-38] Standardized methods to quantify exercise capacity are valuable in the care of Fontan patients. Cardiopulmonary exercise testing provides such information including peak oxygen consumption (VO_2), heart rate reserve, and VE/VCO_2 slope, a marker of respiratory efficiency. The latter can be elevated principally due to cyanosis, however. Literature on the topic was reviewed, including reports that a peak VO_2 < 16.6 mL/kg/min and a peak heart rate <122 bpm have been predictive of mortality, whereas VO_2 at anaerobic threshold <10 mL/kg/min and VE/VCO_2 slope >35 have been associated with hospitalization, protein-losing enteropathy, and heart failure in younger patients.[39] Exercise testing is recommended as part of a prepregnancy assessment in both the AHA/ACC and European guidelines for ACHD.[7,40] Finally, the impact of lower extremity resistance training on the improvement of Fontan physiology was reviewed.[38]

7 | LIVER DISEASE IN FONTAN PATIENTS: HOW DO YOU MONITOR? (RYAN FORD, MD)

One component of Fontan failure, long term, is the development of liver disease. Progressive fibrosis in the setting of chronic passive congestion and high central venous pressure (CVP) can eventually lead to true clinical cirrhosis and changes in physiology. To add to the concern is the observed risk of hepatocellular carcinoma (HCC) in this population. Predicting which patient is more advanced or more likely to develop HCC is the true conundrum at this point in time. Patients with FALD do not seem to follow the same rules as adult patients with other types of chronic liver disease, such as viral hepatitis or nonalcoholic steatohepatitis (NASH).[41] They do not exhibit hepatic inflammation and thus their liver enzymes are most often normal. Encephalopathy and variceal bleeding are rare. INR is difficult to interpret as many patients are also on warfarin. Renal function is often normal or altered by diuretics. The MELD score is not very helpful in predicting those who may be nearing the edge of the cliff either. Transjugular pressure measurements are inaccurate and liver biopsies can be misleading (sampling error due to the patchy/zonal nature of fibrosis). Thick bands of collagen in this population may not have the same implication as an adult with 40 years of hepatitis C and hepatocellular injury.[42] Some collagen deposition may even be reversible. Perhaps the future will include antifibrotic therapies.

The liver is very resilient and even has regenerative ability, so the vast majority of adult Fontan patients have compensated hepatic congestion. When physiology changes, such as a drop in systemic vascular resistance (SVR) that is not explained by the heart or the development of hepatorenal syndrome, one should be more concerned about the development of true liver decompensation. Patients with decompensated liver disease should certainly be considered for a combined heart-liver transplant if this is an option. Otherwise, we are limited in our medical options to relieve the high CVP and hepatic congestion.[43] If there is a reversible cardiac problem, such as a stenosis that can be opened up, this can improve some liver complications such as ascites. Magnetic resonance elastography (MRE) or Fibroscans are newer modalities that measure liver stiffness and may assist in quantifying the degree of hepatic congestion in the future.[44-47]

What to do with patients who develop hepatocellular carcinoma is another dilemma.[48-50] Ideally, a liver transplant is the first approach to adult patients with cirrhosis who develop HCC.[14,51,52] In the Fontan population, a liver transplant alone is not an option, and a combined transplant has its own risks to consider.[53-57] Furthermore, not every center in the US performs heart-liver transplants, especially in this situation. For now, interventional radiology-directed therapy when an HCC develops seems quite reasonable. We also need to figure out the best frequency and image modality to use in order to screen for HCC.[58] At Emory, we currently recommend annual screening with either ultrasound or MRI, understanding that MRI is a higher resolution scan that has its own pros and cons.[59] If someone has concerning lesions or a suboptimal ultrasound, MRI scan should be ordered (as long as the patient does not have a pacemaker or an automated implantable cardiac defibrillator (AICD) that would prohibit such a scan). We have a long way to go in understanding Fontan failure and how to prevent or treat FALD. At the very least, we have learned that these patients definitely should be screened for HCC, possibly starting at 5-10 years post-Fontan.

8 | PREGNANCY AND FONTAN PATIENTS (GRUSCHEN VELDTMAN, MBCHB, FRCP)

Pregnancy can present significant cardiovascular challenges to women with complex CHD. Indeed pregnancy remains the leading cause of maternal mortality in the United States. In prepregnant Fontan patients, there is decreased cardiac output at rest and during exertion, and they have both a thrombotic and a hemorrhagic tendency. Pregnancy physiology, therefore, presents a considerable challenge. However, beyond the cardiovascular sequelae of pregnancy in Fontan patients such as heart failure affecting approximately 4%, and worsening arrhythmias in around 8%,[60,61] there are other concerns to keep in mind such as a high postpartum hemorrhage rate (up to 50%) as well as a high prevalence of recurrent (more than 3) miscarriages affecting up to 52%.[62,63] Infants born to mothers with a Fontan circulation are very often born prematurely and have intrauterine growth restriction.[63,64] These observations have prompted use of the term “an adverse uterine environment.” These and other concerns make pregnancy in Fontan women an extremely challenging to manage.[64,65] Hemorrhage and heart failure frequently complicate the pregnancy course. Appropriate strategies to achieve the best results include timely and informed antenatal counseling, antepartum monitoring and planning by an experienced multidisciplinary team, and meticulous peripartum monitoring.

9 | THE LYMPHATIC SYSTEM IN THE FAILING FONTAN PATIENT (YOAV DORI, MD, PHD)

One of the main causes of failure of the Fontan circulation is abnormal lymphatic flow (type IV Fontan failure).[1] To date, this aspect of Fontan failure has not obtained the attention it deserves. However, mounting evidence regarding its diagnosis, impact on outcomes, and results of new therapies has led to more structured approaches to dealing with the lymphatic system. Several recent developments including dynamic contrast MR lymphangiography (DCMRL) and T2-weighted MR lymphatic mapping have demonstrated the etiology and led to new treatment options for patients with chylothorax, plastic bronchitis, and protein-losing enteropathy (PLE).[66-68] T2-weighted magnetic resonance imaging is also proving to be a reliable tool for proper assessment of the lymphatic system prior to the Fontan operation.[69] A brand new classification of the lymphatic system based on T2 imaging prior to Fontan completion carries the prospect of predicting future

outcomes of Fontan physiology. Finally, evidence of lymphostasis leading to tissue edema and a cascade of events that result in tissue inflammation and fibrosis might prove to shed light on the end organ abnormalities seen in all patients with Fontan physiology. New lymphatic-based diagnosis tools and treatments provide the promise of meaningful impact to patients' outcomes with the expectation that longitudinal implementation of these measures will lead to improvements in patients' quality of life, and reduction in morbidity and mortality.

10 | USE OF SOCIAL MEDIA IN CLINICAL RESEARCH (MICHELLE GURVITZ, MD)

We should recognize the role social media plays in our daily life and the lives of our patients as well as the potential as a research and educational tool.[70] As an integrative component of both social and professional endeavors, it is very tempting to harness social media for the benefit of clinical research. Thanks to its connectivity, even a small subset of the general population such as ACHD (1%) can be actively recruited and involved in investigative efforts aimed at improving outcomes in patient care.[71] Previous attempts in this way have demonstrated that social media can constitutes a user-friendly, inexpensive, and efficient means to achieve the above-mentioned goals in recruitment and it can be beneficial for public health messaging and certain types of studies.[72] However, at this time, the control of this instrument remains limited as there is no practical way to control it, and as such ascertain the veracity of the subjects' information or the validity of the content being shared.

11 | SURGICAL INTERVENTIONS FOR FAILING FONTAN PATIENTS (BRIAN KOGON, MD)

The ultimate goal of single ventricle palliation is to have patients survive and achieve active normal life expectancies. We are not likely going to achieve that with the current Fontan operation. Surgical options that may improve outcomes in single ventricle patients can be grouped into three categories: (1) options that maintain Fontan anatomy and physiology, (2) options that convert the Fontan to biventricular anatomy and physiology, and (3) options that convert the Fontan to more primitive forms of palliation.

11.1 | Options that maintain Fontan anatomy and physiology

Intra-extracardiac Fontan: The proposed benefit of the intracardiac Fontan is that it combines all of the best traits of the intracardiac and extracardiac Fontans—the fenestration is easy to make, access to the common atrium is easy through the intraatrial conduit segment, and arrhythmogenic atrial suture lines near the sino-atrial (SA) node, SA node artery or crista terminalis are minimized.[73] While it may have its advantages, it is not likely going to change the long-term outcome of Fontan anatomy and physiology.

Bifurcated Y-graft Fontan: While computational fluid dynamic modeling shows that the bifurcated Y-graft Fontan may be superior to the t-connection and offset-connection with respect to efficiency, superior and inferior vena cava pressure, and pulmonary blood flow distribution, it is unclear whether this translates into a clinical benefit.[74] Again, while it may have its advantages, it is not likely going to change the long-term outcome of Fontan anatomy and physiology.

Destination mechanical ventricular support: Numerous and various ventricular assist devices have been used to support the systemic ventricle in the failing Fontan. While mechanical systemic ventricular support may be lifesaving in some instances, it continues to subject the patient to Fontan physiology. This is not a reasonable strategy for destination therapy, and the only option for these patients is short-term support and bridge to transplant.

11.2 | Options that convert the Fontan to biventricular anatomy and physiology

Heart transplant: Heart transplant is becoming increasingly frequent in the adult congenital population, in particular in the failing Fontan population, and patients can have excellent outcomes. Unfortunately, for numerous reasons, Fontan patients are oftentimes not great transplant candidates. In addition, heart transplant replaces Fontan anatomy and physiology with transplant pathology. Many of our patients are still quite young, and transplant after Fontan may still not achieve our goal of a normal lifespan. Overall, it will help a minority of these patients, but not the masses.

Destination mechanical Fontan support: For destination mechanical support to be successful, the assist device must be placed in the Fontan circuit, creating a biventricular Fontan. The single ventricle pumps to the body, the mechanical assist device pumps to the lungs, and there is restoration of normal vena cavae pressures. The unique characteristics of the Fontan circulation make this challenging.[75] These devices are currently being designed and trialed, but are not yet in clinical use.

11.3 | Options that convert the Fontan to more primitive forms of palliation

11.3.1 | Balanced physiology

There are reports of single ventricle patients surviving into adulthood unoperated.[76] Most often, these patients have a diagnosis of double-inlet left ventricle with transposed great vessels and pulmonary stenosis, a physiology that allows survival into adulthood with good quality of life. Unfortunately, Fontan takedown to balanced physiology raises numerous questions: will the single ventricle tolerate the volume load, what will be the new source of pulmonary blood flow, and what size shunt will maintain adequate saturations and not create heart failure? Such an operation has not been previously attempted.

11.3.2 | Glenn physiology

There are numerous reports suggesting that Glenn physiology, with or without augmented pulmonary blood flow, may be a reasonable final palliative strategy.[77-80] At Emory University, Fontan takedown to Glenn anatomy with augmented pulmonary blood flow has been performed. Both patients had atriopulmonary Fontan connections and intractable arrhythmias. Social issues that precluded future transplant led us to consider this option over standard conversion. Unfortunately, this strategy also raises numerous questions: Will the single ventricle tolerate the volume load, is an additional source of pulmonary blood flow needed, and if so, where is it placed and how big does it need to be to maintain adequate saturations and not create heart failure?

11.3.3 | Kawashima physiology

There are numerous reports suggesting that Kawashima anatomy can serve as a final palliative strategy for single ventricle heart disease.[43,81] At Emory University, Fontan takedown to Kawashima anatomy and physiology (Fontan with hepatic vein exclusion) has also been performed. Both patients had atriopulmonary Fontan connections and intractable arrhythmias. Social issues that precluded future transplant led us to consider this option over standard conversion. The extracardiac conduit was connected to the infrahepatic inferior vena cava and pulmonary arteries. In follow-up, patients were asymptomatic with a normal daily routine, had oxygen saturations 80%-85%, and had normal hepatic venous Doppler signals.[43] Takedown of a failing Fontan to Kawashima physiology may be a promising alternative. It does not change the volume load of the single ventricle, the resultant hemodynamics and saturations are adequate, and the liver and intestines, which are often major drivers of Fontan circulatory failure, are excluded from the Fontan pathway.

12 | MAINTAINING MENTAL HEALTH WHEN DEALING WITH DIFFICULT DISEASES: LESSONS FOR PATIENTS AND PROVIDERS (ADRIENNE KOVACS, PHD AND MEGHAN ROSWICK)

Coping with chronic illnesses, like complex CHD, can present challenges for patients (and their loved ones) and providers. From a patient's perspective, it is important to balance realism and optimism. Ideally, the illness would be integrated within one's identity although not be the defining feature. Many adults living with Fontan physiology are successful in their personal lives as well as education and employment pursuits.[82] However, even the most resilient patient is not immune to psychological distress.[83] Many adults will also describe an emotional impact that may at times include low mood, anxiety, and recalled traumatic experience. Hospitalizations and surgeries often present specific challenges for patients and families. However, much can be achieved through open dialog between patients and providers. Engaging a patient as an active member in their health care can be a powerful first step. This ideally begins during the process of transitioning patients from pediatric to adult care.[84] A proactive approach to important life issues such as education, employment, and family planning can set the stage for a successful care plan.

Given their primary aim of providing excellence in clinical care to patients with complex CHD, health care providers also face challenges in the context of a busy health care environment that often includes commitments in research and/or education. Therefore, it is important that providers also attend to their own physical, social, and emotional well-being. Maintaining a healthy work/personal life balance can often be a struggle. Providers are encouraged to engage in important self-care behaviors, including physical activity and sleep; one is better able to take care of others when one also takes care of oneself. Providers are also encouraged to support one another (and work with leadership) to establish systematic approaches to ensure adequate time away from work demands (eg, vacation time).

13 | FONTAN FAILURE, CLINICAL MANAGEMENT OF A COMPLICATED PATIENT (CASE PRESENTATIONS FROM THE BOSTON, COLUMBUS, AND EMORY GROUPS)

The case presentations focused on challenging aspects of the management of Fontan patients. The case from the Boston group displayed the impact of arrhythmias of the well-being of Fontan patients and most importantly the previously underappreciated role of endocardial fibroelastosis in hypoplastic left heart patients and its potentiation of the risk of sudden cardiac death. Outlooks into the best way to screen, monitor, and treat such issues were then discussed. The case from the Columbus group showcased the challenge multi-organ poses to the management of Fontan patients. It highlighted the interrelation between the heart, liver, and the kidneys with the continuous challenge of balancing the dysfunctional circulation, and recognition of referral for transplant is necessary. They also discussed the potential of using continuous home hemodynamic monitoring devices in Fontan patients. Finally, the Emory group presented a case of hepatocellular carcinoma in a clinically stable Fontan patient without overt Fontan failure. This case highlighted the ubiquitous nature of hepatic fibrosis in adult Fontan patients with the associated risk of HCC. Implementation of HCC screening protocols in this population can detect these cancers at an early and potentially treatable stage. The indications for heart-liver transplant in Fontan patients with HCC were also discussed.

14 | FUTURE DIRECTIONS (MICHAEL MCCONNELL, MD)

Future directions in the management of Fontan failure include further investigations into the risk of sudden cardiac death and how to properly prevent it, achievable interventions in modifying the Fontan physiology to treat or prevent late complications, and improved and refined algorithms in Fontan surveillance. Finally, further research into the interventional treatment of lymphatic-related complications hold the promise of marked improvement in the quality of life of advanced Fontan failure patients and as such should be encouraged and contributed to.

CONFLICT OF INTEREST

The authors have no conflicts of interest or industry relationships to disclose.

DISCLOSURES

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AUTHOR CONTRIBUTIONS

All listed authors were speakers at the conference. Author Ephrem wrote the article in its entirety and authors Ephrem, Hebson, Rodriguez, and McConnell were primary authors in terms of Concept/Design. All authors provided critical revision of the article.

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