Commentary: Fontan assist device support: Road map to "stage 4" palliation

Christopher R. Broda, MD,[a] and Iki Adachi, MD[b]

From the [a]Department of Pediatrics, Pediatric and Adult Congenital Cardiology, and [b]Department of Surgery, Congenital Heart Surgery, Texas Children's Hospital/Baylor College of Medicine, Houston, Tex.

Disclosures: Dr Adachi serves as a consultant and proctor for Berlin Heart Inc, Medtronic Inc, Jarvik Inc, BiVACOR, and Sony-Olympus Medical Solutions Inc. Dr Broda has nothing to disclose with regard to commercial support.

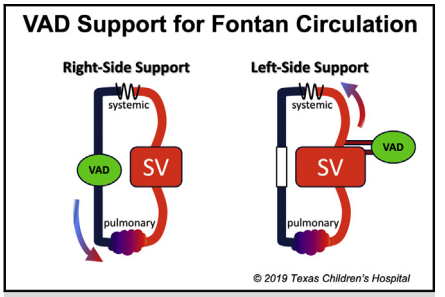
Received for publication June 17, 2019; revisions received June 17, 2019; accepted for publication June 18, 2019; available ahead of print Sept 4, 2019.

*Address for reprints: Iki Adachi, MD, Congenital Heart Surgery, Texas Children's Hospital, 6651 Main St, Legacy Tower, 19th Floor, Houston, TX 77030 (E-mail: ixadachi@texaschildrens.org).

J Thorac Cardiovasc Surg 2019;158:1422-3

0022-5223/$36.00

https://doi.org/10.1016/j.jtcvs.2019.06.101



Ventricular assist device support for failing Fontan circulation: right-sided versus left-sided.

Central Message

There is currently an unmet need for mechanical circulatory support devices specifically focusing on the right-sided hemodynamics to treat failing Fontan physiology.

See Article page 1413.

The "un-natural" history of the Fontan circulation portends a rather grim long-term outlook for patients with single ventricle congenital heart disease. Decades of experience with the Fontan circulation have shown the advantages of the total cavopulmonary connection that minimizes power loss to improve subpulmonary flow efficiency; yet, the altered hemodynamics impart a chronic attrition to the organ systems of the body leading to a range of complications and limited life expectancy for this patient cohort.[1] Recently, mechanical circulatory support (MCS) has emerged as a viable therapeutic option in patients with Fontan circulation, with excellent outcomes and approximately 95% survival at 6 months of support.[2] It must be emphasized, however, that this success is mostly in patients who have systolic ventricular dysfunction as the primary etiology of Fontan failure. More directly, the successful use of MCS in the Fontan population was a result of proper selection of a phenotype that was compatible with clinically available MCS devices. The other end of the spectrum within the Fontan failure is characterized by restriction in the subpulmonary circulation. From a viewpoint of MCS, this phenotype is more challenging. Several groups endeavor to create an MCS approach to assist the subpulmonary circulation in patients undergoing the Fontan, with the intent to reverse the "Fontan paradox."[3,4]

To this end, Trusty and colleagues[5] present an impressive work demonstrating the potential for subpulmonary support using commercially available, extracorporeal centrifugal continuous-flow devices. The group tested the PediMag and CentriMag (Abbott Inc, Plymouth, Minn) for a subpulmonary circulatory support scenario in a mock circulation loop representative of single ventricle heart disease with a failing Fontan circulation. Their main findings demonstrate the PediMag device was able to significantly reduce inferior vena cava pressure and increase cardiac output, but resulted in increased superior vena cava pressure and required a Fontan pathway restriction. In contrast, the CentriMag device was able to reduce inferior vena cava pressure, avoid superior vena cava pressure increase, and increase cardiac output without the requirement of Fontan pathway restriction. This study is unique in a sense that it involves commercially available devices and requires minimal surgical modifications to the Fontan pathway, making the suggested approach practical, if the study findings hold true in the clinical arena. Because of the nature of the in vitro experiments, however, clinical validity of the findings from the simple mock circulation loop is uncertain. The mock loop is unable to mimic physiologic adaptation including single ventricle mechanics, such as the effects of ventilation and the Frank-Starling mechanism of a single ventricle. Therefore, an important next step will be to move from benchtop experimentation to in vivo evaluation in an animal model of Fontan circulation before clinical implementation. The known difficulties in replicating the Fontan failure in animals may forestall such a transition.[6]

A potential issue with the approach used by Trusty and colleagues[5] is related to the fact that the subpulmonary support device forces blood to the pulmonary vasculature that has been chronically "deconditioned" with nonpulsatile circulation.[7] One must presume abnormalities in the pulmonary vascular bed if subpulmonary circulation is failing in the setting of normal systemic ventricular function. Attempt at forcing blood flow into the abnormal

pulmonary vascular bed could possibly cause damage to the naïve micro-vasculature that has seen only reduced, attenuated blood flow for nearly the entire life. In the past, an enthusiasm existed in the use of the right ventricular assist device to treat right heart failure in patients with primary pulmonary hypertension. However, eagerness for such MCS use waned and has been abandoned because of concern for lung injury and high mortality.[8,9] Diastolic dysfunction of a single ventricle, often seen with failing Fontan circulation,[10,11] may increase the vulnerability of tenuous lungs, because the stiff ventricle may not tolerate a sudden increase in preload imposed by subpulmonary support devices.

Finally, the fact that the study by Trusty and colleagues[5] focused only on an acute hemodynamic effect should be seen as its most fundamental limitation. Most of the issues surrounding Fontan failure result from chronic, long-standing processes. To reverse the "Fontan paradox," the need for prolonged support (ie, not months rather years) would be necessary. It is unlikely that the configuration suggested by the Atlanta group is capable of providing such a durable support. The lack of durability likely stems from the fact that the proposed support is equipped with the extracorporeal centrifugal pumps that are designed for acute support. To substantially address the fundamental issues underlying Fontan failure, durable subpulmonary support may require a completely different approach such as the one currently under development by the Indiana group.[12]

Nonetheless, the report from Trusty and colleagues[5] is a valuable addition to the field. It also highlights the unmet need for devices designed for subpulmonary support to fully cover the entire spectrum of Fontan failure. We envision the accumulation of efforts by the investigators in the field will eventually lead to sublimation of MCS intervention for failing Fontan, which may be termed "stage 4" palliation.

References

1. Rychik J. The relentless effects of the Fontan paradox. *Semin Thorac Cardiovasc Surg Pediatr Card Surg Annu*. 2016;19:37-43.
2. Peng DM, Koehl DA, Cantor RS, McMillan KN, Barnes AP, McConnell PI, et al. Outcomes of children with congenital heart disease implanted with ventricular assist devices: an analysis of the pediatric interagency registry for mechanical circulatory support (Pedimacs). *J Heart Lung Transplant*. 2019;38:420-30.
3. Broda CR, Taylor DA, Adachi I. Progress in experimental and clinical subpulmonary assistance for Fontan circulation. *J Thorac Cardiovasc Surg*. 2018;156:1949-56.
4. Rodefeld MD, Boyd JH, Myers CD, LaLone BJ, Bezruczko AJ, Potter AW, et al. Cavopulmonary assist: circulatory support for the univentricular Fontan circulation. *Ann Thorac Surg*. 2003;76:1911-6.
5. Trusty PM, Tree M, Maher K, Slesnick TC, Kanter KR, Yoganathan AP, et al. An in vitro analysis of the PediMag and CentriMag for right-sided failing Fontan support. *J Thorac Cardiovasc Surg*. 2019;158:1413-21.
6. Van Puyvelde J, Rega F, Minami T, Claus P, Cools B, Gewillig M, Meyns B, et al. Creation of the Fontan circulation in sheep: a survival model. *Interact Cardiovasc Thorac Surg*. 2019;29:15-21.
7. Adachi I, Ueno T, Hori Y, Sawa Y. Alterations in the medial layer of the main pulmonary artery in a patient with longstanding Fontan circulation. *Interact Cardiovasc Thorac Surg*. 2010;11:682-3.
8. Gregoric ID, Chandra D, Myers TJ, Scheinin SA, Loyalka P, Kar B. Extracorporeal membrane oxygenation as a bridge to emergency heart-lung transplantation in a patient with idiopathic pulmonary arterial hypertension. *J Heart Lung Transplant*. 2008;27:466-8.
9. Bernhardt AM, De By TM, Reichenspurner H, Deuse T. Isolated permanent right ventricular assist device implantation with the HeartWare continuous-flow ventricular assist device: first results from the European Registry for patients with mechanical circulatory support. *Eur J Cardiothorac Surg*. 2015;48:158-62.
10. Hebson CL, McCabe NM, Elder RW, Mahle WT, McConnell M, Kogon BE, et al. Hemodynamic phenotype of the failing Fontan in an adult population. *Am J Cardiol*. 2013;112:1943-7.
11. Egbe AC, Connolly HM, Miranda WR, Ammash NM, Hagler DJ, Veldtman GR, et al. Hemodynamics of Fontan failure: the role of pulmonary vascular disease. *Circ Heart Fail*. 2017;10(12).
12. Rodefeld MD, Marsden A, Figliola R, Jonasd T, Neary M, Guruprasad GA. Cavopulmonary assist: long-term reversal of the Fontan paradox. *J Thorac Cardiovasc Surg*. September 29, 2019 [Epub ahead of print].