Relationship of Single Ventricle Filling and Preload to Total Cavopulmonary Connection Hemodynamics

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Background. **Single ventricle lesions are associated with gradual attrition after surgical palliation with the total cavopulmonary connection (TCPC). Ventricular dysfunction is frequently noted, particularly impaired diastolic performance. This study seeks to relate TCPC hemodynamic energy losses to single ventricle volumes and filling characteristics.**

Methods. **Cardiac magnetic resonance (CMR) data were retrospectively analyzed for 30 single ventricle patients at an average age of 12.7 ± 4.8 years. Cine ventricular short-axis scans were semiautomatically segmented for all cardiac phases. Ventricular volumes, ejection fraction, peak filling rate, peak ejection rate, and time to peak filling were calculated. Corresponding patient-specific TCPC geometry was acquired from a stack of transverse CMR images; relevant flow rates were segmented from through-plane phase contrast CMR data at TCPC inlets and outlets. The TCPC indexed power loss was calculated from computational fluid dynamics simulations using a validated custom solver. Time-averaged flow conditions and rigid vessel walls were assumed in all cases. Pearson correlations were used to detect relationships between variables, with p less than 0.05 considered significant.**

Results. **Ventricular end-diastolic ($R = -0.48$) and stroke volumes ($R = -0.37$) had significant negative correlations with the natural logarithm of a flow-independent measure of power loss. This power loss measure also had a significant positive relationship to time to peak filling rate (normalized to cycle time; $R = 0.67$).**

Conclusions. **Flow-independent TCPC power loss is inversely related with ventricular end-diastolic and stroke volumes. Elevated power losses may contribute to impaired diastolic filling and limited preload reserve in single ventricle patients.**

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In the present era, operative mortality of the Fontan procedure for single ventricle heart defects is low, but shortened life expectancy is a significant problem [1]. The contributions of ventricular dysfunction to these outcomes is well understood. Decreased systolic performance in the forms of reduced cardiac index [2] and ejection fraction [3] have been widely reported. More recently, appreciation for the incidence and importance of impaired diastolic performance has also grown. Anderson and colleagues [4] reported abnormal diastolic function in 72% of a 500-patient cohort, and Cheung and associates [5] found reduced ventricular relaxation times by echocardiography that are suggestive of reduced compliance.

Although fundamental deficiencies in myocardial structure may be central to this impaired diastolic performance, the effect of altered vascular function may also play a role. Limited preload reserve and reduced ventricular filling with increasing heart rate [6] are prime examples of such interactions. In this setting, the potential contributions of the total cavopulmonary connection (TCPC), the surgical palliation for single ventricle defects, are not well understood. The hemodynamics of this connection have been the focus of a large volume of research [7–11], with the general hypothesis that inefficient and suboptimal flow patterns would have negative implications for broader cardiovascular health and function. Although insightful, these studies have mostly been performed in isolation (ie, focused only on the TCPC) and not inclusive of broader physiologic endpoints against which TCPC hemodynamics could be compared to further advance understanding. For example, no study to date has evaluated the associations between TCPC hemodynamics and single ventricle function based on patient data.

In this study, we analyzed concurrent data for ventricular function and patient-specific TCPC power loss, one important component of the hemodynamic profile, using image-based computational fluid dynamics

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(CFD) simulations [9, 12] for a group of single ventricle patients after the Fontan procedure. We hypothesize that elevated TCPC power losses are associated with impaired ventricular filling and volumes.

Patients and Methods

Patient Selection

Forty-four consecutive single ventricle patients from the National Institutes of Health–supported Georgia Tech–Children's Hospital of Philadelphia Fontan Cardiac Magnetic Resonance database were selected for analysis on the basis of the retrospective availability of (1) a ventricular short-axis cine image stack spanning the entire ventricular volume; (2) a transverse stack of steady-state free precession images through the thorax; and (3) cross-sectional through-plane phase contrast magnetic resonance acquisitions at all TCPC inlets and outlets. The data from the short-axis cine images were used to quantify ventricular function, data from the transverse stack were used to create a patient-specific TCPC model, and flow data from the phase contrast images are the needed inputs for computational fluid dynamics simulations to assess local TCPC hemodynamics. All images were acquired on a 1.5-T Siemens Magnetom Avanto (Siemens Healthcare, Erlangen, Germany). The imaging details are provided in Table 1. The Institutional Review Boards at the Children's Hospital of Philadelphia and Georgia Tech approved the study, and informed consent was obtained for each patient.

Ventricular Segmentation

Semiautomatic segmentation of the ventricular cavity was performed at Georgia Tech using an in-house algorithm implemented in Matlab (The Mathworks, Natick, MA) and based on active contours. An endocardial contour was initialized on the first phase (end diastole) for a given slice and propagated through the rest of the cine set. Manual corrections were made as necessary to ensure a visually appropriate segmentation. Papillary muscles were included in the blood pool. Once the stack was entirely segmented, the ventricular volume of each cardiac phase was calculated by summing the products of the cross-sectional areas and slice thicknesses. These measurements were used to derive ventricular volumes, ejection fraction, and cardiac output. Additionally, a smooth ventricular volume versus time curve was generated using a Fourier curve fitting analysis with the use of three harmonics [13]; the first derivative of this curve was then computed to derive the maximum time rates of volume change (ie, peak ejection rate and peak filling rate [6]), and time to peak filling rate (from end systole). The peak filling and ejection rates are presented normalized by end-diastolic volume [s^{-1}]. Time to peak filling rate was normalized to cardiac cycle time and reported as a "time ratio" [14].

To verify the precision of the segmented volumes, interobserver and intraobserver variability was assessed on a select number of patient data sets. For interobserver variability, another expert user separately segmented the end-diastolic and end-systolic phases for 8 patients. For intraobserver variability, segmentations for 5 patients were repeated by the same user 7 to 8 months after the initial analysis.

TCPC Hemodynamic Assessment

Computational fluid dynamics models are the current standard for quantifying TCPC flow associated energetics [9, 14, 15] because of their excellent spatial resolution and their ability to robustly handle patient-specific connections. In this study, hemodynamics through the TCPC were assessed using a validated [12, 16] in-house computational fluid solver based on the hybrid Cartesian immersed boundary method [17]. The transverse abdominal image stack and through-plane phase contrast magnetic resonance imaging data were used to provide the anatomic [18] and patient-specific flow [19] boundary conditions, respectively, needed to perform the computational simulations (Fig 1). Because the primary CFD endpoint was a representative, time-averaged measure of power loss, the patient-specific simulations assumed time-averaged boundary conditions based on the phase contrast CMR data measured for each vessel and for each patient. Recent studies have demonstrated that this approach yields power loss estimates with acceptable limits of agreement compared to simulations with time-varying boundary conditions [20]. The inlets were artificially extended by 1 cm, and a flat velocity profile was

Table 1. Cardiac Magnetic Resonance Imaging Detail for Ventricular Function, Total Cavopulmonary Connection Anatomy, and Velocity Acquisitions

CMR Details	Ventricular Short-Axis Cine Stack	Transverse Thoracic Stack	Through-Plane Phase Contrast
Slices	7.9 ± 1.0	45.6 ± 6.6	1
Slice thickness, mm	8.3 ± 1.3	4.2 ± 0.7	5.6 ± 0.7
No. phases per cardiac cycle	25.6 ± 4.4	1	25.8 ± 4.2
Temporal resolution, ms	34 ± 5	NA	33 ± 6
In-plane spatial resolution, mm	1.35 ± 0.37	1.16 ± 0.22	1.16 ± 0.25

Values are mean ± SD.

CMR = cardiac magnetic resonance; NA = not applicable.